MICROSPHERE-BASED DRUG DELIVERY SYSTEM: RATIONALIZED DESIGN AND OPTIMIZATION USING SPRAY DRYING METHOD – A REVIEW

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Abstract

Microsphere-based drug delivery systems have gained significant attention in pharmaceutical research due to their ability to provide controlled and sustained drug release, enhance bioavailability, and improve patient compliance. Among various fabrication techniques, spray drying has emerged as a highly efficient and scalable method for microsphere production, offering precise control over particle size, morphology, and drug encapsulation efficiency. This review provides a comprehensive overview of microsphere formulation principles, focusing on the rationalized design and optimization strategies using the spray drying method. Key factors influencing microsphere characteristics, including polymer selection, solvent systems, process parameters, and drug-polymer interactions, are discussed. Additionally, the advantages and limitations of spray-dried microspheres in drug delivery applications are highlighted. Future perspectives on technological advancements and regulatory considerations for translating these formulations into clinical practice are also explored. This review aims to guide researchers in optimizing microsphere-based drug delivery systems for improved therapeutic outcomes.

Keywords: Microsphere, Spray drying method, sustained release.

1. Introduction

1.1 Oral drug delivery

The oral route has the highest amount of patient compliance, making it the most recommended way to administer drugs. Drug delivery via mouth accounts for more than half of the global medicine delivery market. Therefore, creating new, oral drugs and technologies is the cornerstone of pharmaceutical research. Medication with limited aqueous solubility, permeability, and/or metabolic stability can be challenging to take orally, but drugs with high solubility and gastrointestinal permeability can be administered orally with remarkable success. Furthermore, many biotechnological treatments, like peptides and drugs based on nucleic acids, are insoluble in liquid form. This article will provide a summary of how nanotechnology might be used to enhance oral medicine delivery and promptly address some of the problems related to it.[1]

1.1.1 Challenges in oral drug delivery

Poor water solubility and intrinsic dissolution rate—the mass of the drug dissolved per time unit and area—are the two primary problems influencing the oral administration of many modern drugs. Additionally, around 40% of the unique chemical entities generated by drug discovery screens display limited water solubility [2]. These drugs are usually categorised as Class II or IV by the Biopharmaceutical Classification System (BCS) [3]. When administered orally, they often result in a lack of dosage proportionality, substantial variations in intra- and inter-subject pharmacokinetics, irregular absorption, and restricted bioavailability. Poor gut permeability is another significant factor that significantly affects the oral bioavailability of many medications. BCS Class III medications are those with low membrane quality but good solubility. For instance, in order to achieve therapeutic concentrations, large dosages of antiviral medications, such as acyclovir, are typically needed. The gastrointestinal tract (GIT) contains several chemical and enzymatic barriers that affect drug distribution via mouth [4]. The pH of the GIT varies according to its location. For example, the intestines have a pH between 6.8 and 7.4, while the stomach has an acidic pH. Arte mether, erythromycin, candesartan, and cilexetil are among the drugs whose chemical breakdown at acidic pH levels significantly affects their oral bioavailability. Furthermore, a variety of drugs, such as anti-

hyperlipidemic drugs (simvastatin, ezetimibe) and cephalosporin antibiotics (cefpodoxime proxetil), are broken down by a number of gastrointestinal tract enzymes (lipases, esterases). The oral bioavailability of drugs including ACE inhibitors, b-blockers, calcium channel blockers, and ACE inhibitors, as well as ACE inhibitors and anti-diabetic pharmaceuticals like repaglinide, is notably low because of a high degree of first pass (hepatic) metabolism. Finally, drug efflux transporters such as P-glycoprotein carry out the efflux of some drugs, such as digoxin, paclitaxel, and doxorubicin, from the site of absorption, resulting in poor oral bioavailability.

1.1.2 Strategies to Improve Oral Drug Delivery

To create oral formulations for drugs with limited water solubility, it is essential to understand obstacles. The solubility of hydrophobic medications is a major factor in their low oral bioavailability. Other characteristics linked to decreased bioavailability of hydrophobic medications include food influence, gastrointestinal discomfort, delayed onset of action, lack of dosage proportionality, and significant intra- and inter-subject variability. Consequently, many methods are employed to improve a drug's water solubility. It is necessary to carefully consider formulation aspects such as salt selection, particle size reduction, and surfactant selection in order to produce poorly soluble drug formulations. Historically, a combination of surfactants has been used to improve the absorption of oral medications. Interfacial tension is decreased by the hydrophilic and lipophilic groups in the hydrophilic head and hydrophobic tail of surfactants, which help localise the drug molecules at the interface [5]. Surfactants boost the bioavailability of pharmaceuticals by a variety of mechanisms, including as momentarily opening tight intracellular junctions to improve the permeability and solubility of drugs. The use of surfactants must be carefully examined because higher concentrations may provide a safety risk. Other techniques, such as micro/nanonization, can also greatly improve the bioavailability of drugs. Pharmaceutical particles are greatly reduced in size by these techniques, which increases their surface area and, eventually, their rate of dissolution.

Liposomes have gained a lot of attention as a drug carrier that can improve therapeutic activity, decrease side effects, and boost drug stability since they protect molecules from deterioration or modification. Because of its versatility, security, and patient compliance, the oral route is recommended over alternative liposome administration techniques. However, decreased liposome integrity at the absorption site and physicochemical instability, which includes hydrolysis, drug separation from liposomes, sedimentation, and aggregation, limited the use of liposomes for oral drug administration.

1.2 Microspheres

Small, spherical particles that range in size from 10 to 1,000 millimetres are what define microspheres [6]. By improving the absorption of conventional medications and reducing side effects, microspheres dramatically increase patient compliance. The controlled release of the medication is the primary advantage of using microspheres as a drug delivery technique. By reducing the frequency of doses and preserving a steady medicine plasma concentration, microsphere improves patient compliance. Microspheres made of polymers are frequently employed as controlled-release dosage forms.

1.2.1 Polymeric microspheres are mainly two types

- **Biodegradable polymeric microsphere**

The majority of biodegradable polymeric microspheres are composed of natural polymers, such as starch. Natural polymers are bio-sticky and decompose rapidly. These polymers increase the residence time when they come into contact with the mucous membrane because of their high degree of swelling in aqueous solutions. As a result, a gel is created that readily adheres to the mucous membrane. The rate and magnitude of drug release from the microsphere are largely determined by the concentration of the polymer.

- **Synthetic polymeric microsphere**

These microspheres, which serve as bulking agents, embolic particles, drug delivery vehicles, and fillers, are made of synthetic polymers. These microspheres' primary drawback is their rapid migration away from the injection site, which can cause organ damage and embolism [7]. We have selected the ionotropic gelation procedure for microsphere preparation out of several methods that can be used to produce polymeric microspheres, including the single emulsion/double emulsion technique, spray drying technique, emulsion solvent evaporation technique, phase separation coacervation technique, and ionotropic technique.
The type of polymer, the type of medication, and the length of treatment all influence the technique selection [8]. The following are the most crucial physical and chemical parameters that can be managed during the production of microspheres:

- The particle size requirement
- Molecular weight of polymer
- Polymer to drug ratio

- No stability problem
- Final product should be non-toxic.
- Total mass of drug and polymer
- Reproducibility
- Controlled particle size and dispersability in aqueous vehicles for injection
- Release of active reagent with a good control over a wide time scale

1.2.2 Techniques for microsphere preparation

- Single emulsion techniques
- Double emulsion techniques
- Polymerization
  - ➢ Normal polymerization
    - ✓ Bulk
    - ✓ Suspension
    - ✓ Emulsion
  - ➢ b. Inter-facial polymerization
- Phase separation coacervation technique
- Spray drying
- Solvent extraction
- Solution-enhancement dispersion method
- Wax coating Hot-melt method

1.2.2.1 Single emulsion technique

This method is used to prepare a variety of proteins and carbs. It involves dispersing the natural polymers in an oil phase, or non-aqueous medium, after they have been dissolved in an aqueous medium. That is the initial phase in Cross-linking is done in the next phase using two techniques. [9]

- Cross linking by heat: by adding the dispersion into heated oil, but it is unsuitable for the Thermolabile drugs.
- Chemical cross linking agents

The use of agents such as formaldehyde, glutaraldehyde, and di acid chloride, among others, has the drawback of exposing the active component to excessive amounts of chemicals if it is introduced during production and subsequently centrifuged, washed, and separated. When chitosan solution (in acetic acid) is added to liquid paraffin that contains a surfactant, a w/o emulsion is formed. Glutaraldehyde 25% solution is used as a cross-linking agent to create metformin hydrochloride microspheres.

1.2.2.2 Double emulsion technique

In order to prepare W/O/W, the primary w/o emulsion is poured into an aqueous solution of poly vinyl alcohol, resulting in the production of numerous emulsions. For 30 minutes, this w/o/w emulsion was continuously stirred. Over the course of 30 minutes, gradually add water to the emulsion. Gather microcapsules by filtration and vacuum-dry them [10]. It works best with water-soluble medications, proteins, peptides, and vaccinations. Both synthetic and natural polymers can be used using this technique. A lipophilic organic continuous phase disperses the aqueous protein solution. The active ingredients may be present in this protein solution. Disperse in oil/organic phase homogenization/vigorous, that is, form a first emulsion and then add it to an aqueous solution of PVA (Poly Vinyl Alcohol), forming multiple emulsions. This is done by adding to a large aqueous phase denaturation/hardening after the microspheres have been separated, washed, dried, and collected. It was done using the o/w/o multiple emulsion method.

1.2.2.3 Polymerization techniques

Mainly two techniques are using for the preparation of microsphere are classified as:

(a) Normal polymerization

An initiator or catalyst, a monomer, or a combination of many monomers are typically heated to start the polymerization process in bulk polymerization. The resulting polymer can be shaped into microspheres. Adding the drug during the polymerization process is one way to accomplish drug loading. Although it is a pure polymer production method, the thermolabile active components are impacted by the difficulty of dissipating the heat of reaction. Lower

temperatures are used for suspension polymerization, also known as pearl polymerization, which involves heating the monomer combination containing the active medication to create droplets that disperse in a continuous aqueous phase. The size of the microsphere produced using suspension techniques is smaller than 100 µm. Because an initiator is present in the aqueous phase, emulsion polymerisation differs from suspension. It is also conducted at a lower temperature than suspension, which often uses water for the external phase in the last two methods, allowing heat to disperse readily. These methods can produce higher polymers more quickly, but they can also cause the polymer to associate with unreacted monomers and other additives. [11]

(b) Interfacial polymerization

In order to create a polymer film that effectively envelops the dispersed phase, different monomers react at the interface between the two immiscible liquid phases. This method uses two reactive monomers: one dissolves in a continuous phase, while the other disperses in an aqueous continuous phase, which emulsifies the second monomer. The solubility of the produced polymer in the emulsion droplet results in two circumstances. If the polymer is soluble in a droplet, the carrier will form a monolithic form. If the polymer is insoluble in a droplet, a capsule-like structure is produced.

1.2.2.4 Spray drying and spray congealing

The idea behind the spray drying method Spray drying and spray congealing are two procedures that rely on whether the solvent is removed or the solution is cooled. In spray drying, the fundamental mechanism is evaporation; in spray congealing, it is a phase inversion from a liquid to a solid. With the exception of energy flow1, both processes are comparable. The most used industrial method for drying and particle creation is spray drying. As a result, spray drying is the best method when the final product needs to meet exacting quality requirements for bulk density, particle shape, residual moisture content, and particle size distribution. The idea 7-9 Spray drying has three processes.

a.) Atomization: of a liquid feed change into fine droplets.

b.) Mixing: it involves the passing of hot gas stream through spray droplets which result in evaporation of liquids and leaving behind dried particles.

c.) Dry: Dried powder is separated from the gas stream and collected.

This method involves first dissolving the polymer in an appropriate volatile organic solvent, like acetone, dichloromethane, etc. Following high-speed homogenization, the solid medication is subsequently distributed throughout the polymer solution. Following the atomization of this dispersion in a stream of hot air, tiny droplets or a fine mist are created, from which the solvent immediately evaporates to form the microspheres. The range of sizes is 1–100 µm. The cyclone separator uses hot air to separate the microparticles, and vacuum drying eliminates any remaining solvent. The process's operational viability is one of its advantages. This method works well for encapsulating several types of penicillin's. Spray congealing is used to encapsulate thiamine mononitrate10 and sulpha ethylthiadizole in a combination of stearic acid and palmitic acid mono- and diglycerides. However, extremely quick solvent evaporation results in the creation of porous microparticles. Either rotary (wheel) or nozzle atomisers are used to create the sprays. Under regulated temperature and airflow conditions, moisture evaporation from the droplets and the creation of dry particles take place. Temperature (in drying and collection chambers), nozzle size, spraying rate, and polymer drug solution input rate all affect the size of the microsphere. The use of plasticiser improves the product's quality; the flow rate should be maintained at about 6 millilitres per minute.

The spray drying method can also be used to prepare chitosan microspheres. Cimetidine and famotidine were trapped in microspheres made by spray drying multiple emulsions (o/w/o or w/o/w) in 1999 by He et al., who also used formaldehyde as a crosslinking agent. They discovered that, in contrast to those made using the traditional spray drying or o/w emulsion methods, the release of the medications from microspheres made using this innovative technique was noticeably maintained. In 1994, Giunchedi et al. prepared PCL microspheres of ketoprofen via spray drying.2 (c2) He made use of the drug's organic solution along with two polymers, PCL and cellulose acetate butyrate, which were created in a 1:1 mixture of dichloromethane and chloroform. The prepared solution was sprayed through a nozzle in a spray-drier under different experimental conditions. Solid microspheres were collected into final bottom vessel spray-drier.

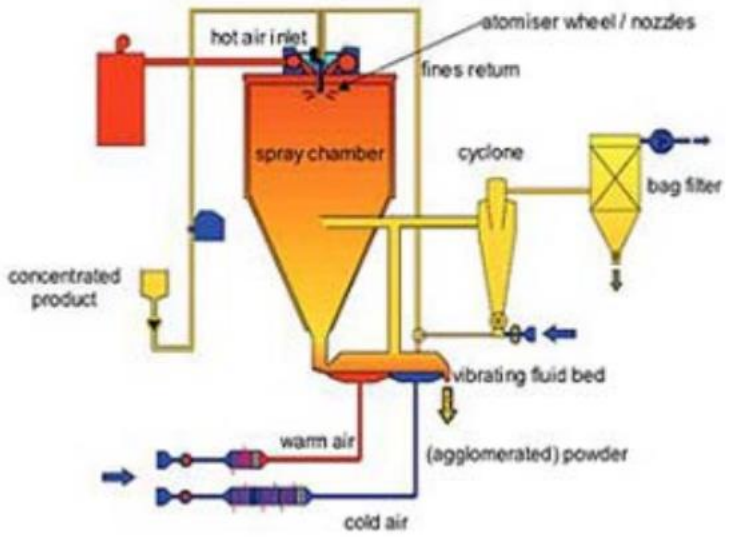

Figure 1: Spray drying method for preparation of microspheres.

1.2.2.4.1 Advantages and disadvantages

Both oral dosage forms and pulmonary drug delivery benefit greatly from spray drying, which is a remarkably versatile process that yields a wide variety of products. Many businesses utilise this approach for drying operations since it is very reproducible and adaptable. Almost any capacity that is needed can be simply incorporated into it. Both heat-sensitive and heat-resistant items can use it. The quality of the powder doesn't change when drying. The bulk density of the product is decreased by particles that are homogeneous in size and often hollow. However, there are certain shortcomings in technology; the equipment is costly and quite large. Because so much heated air flows through the chamber without coming into contact with any particles, the overall thermal efficiency is low [12].

1.2.2.5 Wax Coating and Hot Melt

In order to create the microspheres, the polymer is dispersed in an appropriate dispersion media and then gradually cooled. This method makes it simple to create microspheres out of polymers with low melting points [13]. Wax is mostly used for particle coating and coring. This disperses the medication in the melted wax to encapsulate it. High-speed mixing is used to distribute the wax suspension into a cold solution, such as liquid paraffin. For an hour, agitate the mixture. The exterior phase was then decanted, and the solvent's suspended microspheres gathered. Additionally, let it air dry. Compared to other methods, it is less

expensive and releases the medicine faster. The most common coating ingredients are beeswax and carnauba wax, which can be combined in any way.

1.2.2.6 Solvent evaporation method5

For both aqueous (o/w) and non-aqueous (w/o) emulsion generation between a polymer solution and an immiscible continuous phase. Bogataj et al. (2000) used the evaporation method to create microspheres using liquid paraffin and acetone as solvents. The chitosan solution was mixed with the medication solution (in acetone), and the mixture was emulsified in liquid paraffin while being agitated. The microsphere suspension underwent filtering, washing, and drying. Additionally, magnesium stearate was used as an agglomeration-preventing agent [14]. The average particle size dropped as the amount of magnesium stearate used to prepare the microspheres increased, according to the data. Hyaluronic acid and gelatin microcapsules made by complicated coacervation were compared with mucoadhesive microspheres of hyaluronic acid, chitosan glutamate, and a mixture of the two made by solvent evaporation by Lim et al. (2000).

1.2.2.7 Phase separation coacervation technique

A micromolecular solution is simply separated into two immiscible liquid phases. The polymer is dissolved in a solution during this process. This procedure is intended to construct reservoir-type systems, such as encapsulating water-soluble medications like proteins, peptides, etc. In order to influence the creation of a polymer-rich phase known as coacervates, the coacervation principle involves lowering the solubility of the polymer in the organic phase. By dispersing drug particles in a polymer solution and adding an incompatible polymer to the mixture, this approach causes the first polymer to phase separate and absorb the drug particles. This method can also be used to make matrix-type preparations for hydrophilic drugs, such as steroids, where the addition of a non-solvent causes the polymer to solidify. This technique has been used to create polylactic acid (PLA) microspheres utilising butadiene as an incompatible polymer.

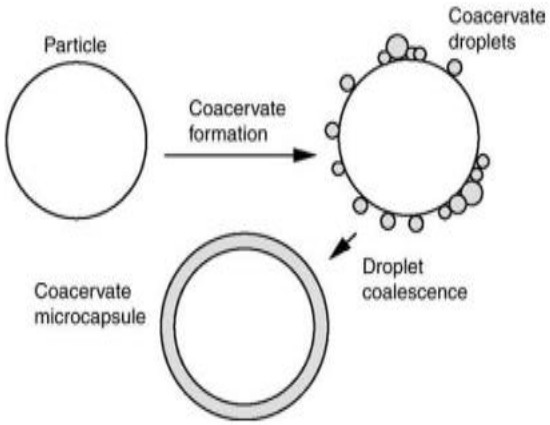

Figure 2: Schematic diagram of the formation of a coacervate around a core material

However, organic solvents and glutaraldehyde, which are naturally poisonous, are not appropriate for this procedure. Berthold et al. (1996a) used sodium sulphate as a precipitant to create chitosan microspheres loaded with prednisolone sodium phosphate. When sodium sulphate was added to a chitosan solution in acetic acid, the chitosan's solubility was reduced, and the resulting weakly soluble derivative precipitated. [15]

1.2.2.8 Solvent extraction

By extracting the organic solvent, the organic phase is eliminated throughout the microparticle production process. Isopropanol is an organic solvent that is miscible in water. The organic phase is extracted using water. This technique can reduce the microsphere's hardening time. Directly adding the medication or protein to an organic polymer solution is one such variation. The temperature of the water, the emulsion volume to water ratio, and the polymer's solubility profile all affect how quickly the solvent is removed using the extraction procedure.

1.2.2.9 Emulsification method

They can also generate several emulsions. For instance, a water-in-oil emulsion can be created by dispersing a heated aqueous drug solution in molten wax, and then emulsifying it in a heated external aqueous phase to create a water-in-oil-in-water emulsion. The microcapsules are gathered after cooling the system [16]. Drug loss to the external phase can be avoided by using a nonaqueous phase for very aqueously soluble medications. When the primary emulsion is in the external aqueous phase, there is also the option of quickly lowering the temperature [17].

1.2.3 Pharmaceutical application of microspheres [18]

1.2.3.1 Microspheres in vaccine delivery

Protection from the microbe or its harmful byproduct is a requirement for a vaccination. The perfect vaccination should meet the following criteria: affordability, ease of use, safety, and effectiveness [19]. Using the solvent evaporation approach, Limin et al. created polymicroparticles in 2000 as an insulin medication carrier. Safety and minimising negative reactions are complicated topics. The way of application has a direct impact on the safety level of antibody response production [20]. The drawback of traditional vaccines may be addressed by biodegradable delivery methods for parenterally administered vaccines. Parenteral (subcutaneous, intramuscular, or intradermal) carriers are of interest because they provide certain benefits, such as:

1. Improved antigenicity by adjuvant action

2. Modulation of antigen release

3. Stabilization of antigen.

In 2000, Lamprecht et al. used the double emulsion approach to create bovine serum albumin (BSA) nanoparticles. They discovered that while particle size had no discernible effect, BSA encapsulation efficiency dropped as the protein concentration in the inner aqueous phase increased. When compared to PCL NP37, the release rate of PLGA NP is higher [19].

1.2.3.2 Monoclonal antibodies mediated Microspheres targeting

Many antibiotic medications are administered as microspheres to increase their effectiveness and compatibility with other salts. For example, griseofulvine, sulfadiazine, sulfathiazole, tetracycline, ampicillin, and amoxicillin. Immunomicrospheres are monoclonal antibodies that target microspheres [20]. Selective targeting to particular areas is accomplished with this targeting technique [21]. The molecules known as monoclonal antibodies are incredibly selective. Monoclonal antibodies' (Mabs') high specificity can be used to direct microspheres containing bioactive compounds to specified locations. Covalent coupling allows mabs to be directly bonded to the microspheres [22]. The antibodies can be attached to the free aldehyde,

amino, or hydroxyl groups on the microspheres' surface. Any of the following techniques can be used to attach the Mabs to microspheres:

1. Nonspecific adsorption
2. Specific adsorption
3. Direct coupling
4. Coupling via reagents

Shan et al. (1999) Ready To treat Helicobacter pylori infection, chitosan microspheres loaded with amoxycillin and metronidazole for stomach-specific delivery were made by crosslinking in addition to precipitating with sodium tripolyphosphate. Because of the great porosity of the drug-loaded microspheres, in vitro experiments in simulated stomach juice shown that the entire amount of drug was released in two hours [23]. In contrast, metronidazole remained stable for 24 hours, whereas amoxicillin degraded 40% in 10 hours in simulated stomach juice. This study demonstrated the effectiveness of chitosan microspheres containing porous metronidazole in the elimination of the aforementioned infection [24]. Methylpyrrolidinone chitosan, a novel chitosan derivative, was utilised to create ampicillin microparticles using the spray-drying approach. In 1998, Giunchedi et al. used The microparticles were characterised using scanning electron microscopy, particle size analysis, differential scanning calorimetry, and in vitro drug release investigations. Microbiological assays were also conducted using several bacterial strains. The assay's findings demonstrated that ampicillin microspheres might sustain the medication's antibacterial properties [23].

1.2.3.3 Imaging

The imaging of certain areas is significantly influenced by the particle size. The intravenous particles will become caught in the lung's capillary bed if they are administered outside of the portal vein [24]. Labelled human serum albumin microspheres are used to take advantage of this phenomena in order to perform scintiographic imaging of lung tumour masses. Amiji and Hejazi (2003) Ionic crosslinking and precipitation were used to prepare the microsphere. investigated the tetracycline-loaded chitosan microspheres' stomach residence time [25]. Both the nonacid-suppressed and acids-suppressed gerbils chitosan microsphere suspensions were administered orally. A gamma counter was used to monitor the radiation in the tissues and fluids after animals were slaughtered at various intervals [26].

1.2.3.4 Topical porous microspheres

The porous microspheres known as microsponges are made up of several interconnected spaces with particle sizes ranging from 5 to 300 µm [27]. These porous microspheres with active ingredients can be added to formulations like creams, lotions, and powders. These microsponges are used as topical carriers because they have the ability to entrap a wide variety of active ingredients, including emollients, fragrances, essential oils, and more. Microsponges are made of non-collapsible structures with porous surfaces that allow for the regulated release of active substances [28].

1.2.3.5 Nasal Drug Delivery [29]

For the local and systemic distribution of a variety of medicinal compounds, intranasal (IN) administration offers numerous theoretical and practical benefits. IN administration can be self-administered, is needle-free, non-invasive, and basically painless. It also doesn't require sterile preparation [30]. Due to the existence of numerous microvilli, a porous endothelium membrane, and a highly vascularised epithelium, the nasal mucosa has a vast surface area and a quick beginning of therapeutic effect. It explains different drug administration systems, tools, formulations, and techniques for the nose or nasal cavity [31]. Intranasal medications may be intended for systemic or local treatment, depending on the therapeutic goal. for the management and avoidance of nasal symptoms, such as local inflammation, allergies, congestion, and rhinitis, among others. By spray-drying dispersions, emulsions, and suspensions with varying polymeric compositions and solvents, Martinac and El (2004) created Loratadine-loaded microspheres [32]. Additionally, he created a bioadhesive microsphere to administer the lipophilic medication loratadine via nasal drug delivery [33]. Combining bioadhesive qualities with microspheres is crucial for nasal drug delivery because of the following benefits: improved drug absorption and bioavailability, closer contact with the mucus layer, and a decrease in the frequency of drug administration because of the decreased mucociliary clearance of the drug delivery system adhering to the nasal mucosa [34].

1.2.3.6 Oral drug delivery [35]

Shefi Angel Timmy et al. are working on oral insulin delivery by creating cyclodextrin-containing microspheres that form an inclusion complex with the medication molecule. Insulin is used orally to treat diabetes mellitus [36]. The primary issue with insulin was that the GI tract's enzymes caused the medicine to degrade. Enteric and aliginate polymers, which

shield insulin from acidic environments. Chitosan alginate membranes were employed by Polk et al. to achieve delayed protein release [37].

1.2.3.7 Targeting drug delivery [38]

Because microspheres have a longer residence period at the application site, they help medications work more effectively. For systemic or local effects, microspheres have been created for the oral, buccal, ophthalmic, rectal, nasal, and vaginal routes [39]. The development and sophisticated medicinal uses of bioadhesive microspheres are discussed in this article. There are several medications that have good targeting effects and are administered via various routes [40].

1.2.3.8 Pharmaceutical applications [41]

Aspirin, theophylline and its derivatives, vitamins, pancrelipase, antihypertensives, potassium chloride, progesterone, and combinations of contraceptive hormones are among the many pharmacological microencapsulated products that are currently available on the market [42]. The purpose of microencapsulated KCL (Micro-K, R.H. Robins, and Richmond, VA) is to avoid the gastrointestinal problems that potassium chloride might cause [43]. Because to the microcapsules' dispersibility and the ions' regulated release, there is less chance of localised high salt concentrations, which could cause ulcers, bleeding, or perforation. Additionally, microspheres have shown promise as products for injection or inhalation [44]. The quantity of commercially available items does not accurately represent the benefits that can be obtained from this technology or the amount of study that has been done in this field [45]. The amount of medicinal microencapsulated products has been mostly determined by economic factors. The majority of encapsulation procedures are costly and necessitate a large equipment capital expenditure [46]. Spray drying and pan or spray coating are an exception, as the company may already have the required equipment. The majority of microencapsulation techniques are patent protected, which adds to the cost [47].

2. Conclusion

Microsphere-based drug delivery systems offer a versatile and effective approach to enhancing drug stability, bioavailability, and controlled release profiles. Among various fabrication techniques, spray drying has emerged as a highly efficient and scalable method for microsphere production, providing precise control over particle size, morphology, and drug encapsulation efficiency. The success of microsphere formulations depends on multiple

factors, including polymer selection, solvent systems, process parameters, and drug-polymer interactions, all of which must be carefully optimized to achieve the desired therapeutic outcomes.

Despite the numerous advantages of spray-dried microspheres, challenges such as maintaining drug stability, preventing burst release, and ensuring uniform drug distribution must be addressed. Advances in polymer engineering, process optimization, and characterization techniques will play a crucial role in overcoming these limitations. Furthermore, regulatory considerations and large-scale manufacturing strategies need to be explored to facilitate the translation of microsphere-based drug delivery systems into commercial pharmaceutical applications.

Future research should focus on integrating novel biomaterials, advanced spray drying technologies, and personalized medicine approaches to further improve the effectiveness and applicability of microsphere drug delivery systems. With continued innovation, spray-dried microspheres hold great promise in revolutionizing drug formulation strategies and improving patient outcomes across various therapeutic areas.

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