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Microspheres – A Novel Drug Delivery System: An Overview

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ABSTRACT

Because of their small size and high carrying capacity, microspheres are a significant feature of the new drug delivery system. Furthermore, Bioadhesive properties such as mucoadhesion can be combined with microspheres to create mucoadhesive microspheres due to their lengthy residence period.Bioadhesion is when two materials, at least one of which is biological,are together by interfacial forces for an extended length of time. Microspheres are a carrier-linked drug delivery system with a drug core and an outside polymer layer as a coating material, with particle sizes ranging from 1 to 1000µm in diameter.Due to the high surface-to-volume ratio, much more intimate contact with the mucus layer, controlled and sustained drug release from the dosage form. Furthermore, precise targeting of drugs to the absorption site, mucoadhesive microspheres have advantages efficient absorption and improved bioavailability of drugs.The purpose of this study is to give an overview of many features of mucoadhesive microspheres, including their preparation methods, method of evaluation, and application in drug delivery.

Keyword: Mucoadhesion, Mucoadhesive Microsphere, Controlled Release.

I. INTRODUCTION

An ideal drug delivery system should have two primary characteristics: one, it should be a single dosage for the whole treatment period, and two, it should transport the active medication directly to the site of action. Mucoadhesive drug delivery systems help improve and enhance medication bioavailability because they provide a regulated drug release over time and may also be used to localized the drug to a specific location in the body. [1-3]

Microspheres are homogeneous, monolithic particles ranging from 1 to 1000 micrometers and are commonly employed as medication carriers for controlled release. In biological applications, these systems are critical. Microspheres can be made for various purposes, including core material protection, stomach irritation reduction, liquid-to-pseudo-solid conversion, cell microencapsulation, and the development of pulsatile drug delivery systems.The therapy is generally improved by administering the medication in microspheres, which allows the active ingredient to be localized at the site of action and prolongs the drug's release. [4, 5]

1.1Advantagesof the microsphere[6-7]

1. Maintain a consistent and long-lasting therapeutic impact.
2. Improves patient compliance by reducing the frequency of daily administration.
3. Increase medication absorption, therefore increasing drug bioavailability and
4. Microsphere shape allows for controlled variations in drug release and breakdown.
5. It aids in the taste and arrangement of things**.**

1.2 Limitation of microsphere [8]

1. The difference in release rate between doses may be determined.
2. The pace of release can be affected by several factors, including the velocity of transit,
passage of food through the stomach, and so on.
3. Any deterioration in the dosage form's release pattern might result in toxicity.
4. These dose forms are not crushable or chewable.
5. The release form formulas may be altered.

Recent Advancement in microsphere with utilized drug

A large number of microspheres have been successfully produced with various drug candidates. The major goal of these microspheres' design and development is to enhance the bioavailability and solubility of active pharmaceutical ingredients (API). Therefore, the review concentrated on several recent advancements in microsphere technology, described in Table 1.

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Table 1. Microsphere formulation with utilized drug moieties.

Drug	Types of study	Particulars	Refs.
Stavudine	In-vitro studies	The results of the in-vitro dissolution experiments revealed an improved formulation with regulated drug release over 12 hours. In addition, zero-order kinetics were used to release the medication from the microspheres.	[9]
Simvastatin	In-vitro studies	The release of drugs from the microsphere was gradual and dependent on the coat composition. The FTIR tests show that the improved formulation has no drug-polymer interaction.	[10]
Valacyclovir	In-vitro studies	According to the analysis, the drug release mechanism from the formulations best fits Higuchi's drug diffusion mechanism model and follows Zero-order kinetics.	[11]
Metronidazole	In-vitro and In-vivo studies	Metronidazole mucoadhesive microspheres can aid in extending gastric retention time and maintain metronidazole release in the gastrointestinal system. The delivery method might be used to localized metronidazole release for the treatment of Helicobacter pylori-induced peptic ulcers.	[12]
Ciprofloxacin Hydrochloride	In-vitro studies	Because of the significant swelling and water absorption, the medication was released slowly from the produced Ciprofloxacin microsphere. In 10 hours, 99.68% of the medication was released. According to DSC investigations, the medication and the excipient have no interaction. According to stability testing, there is no change in the medication over three months.	[13]
Propranolol HCl	In-vitro studies	The developed formulation mucoadhesive microsphere is a superior option for Propranolol Hcl regulated distribution. In addition, there was no interaction between the medication and the excipients, according to FTIR tests.	[14]
Roxatidine Acetate HCl	In-vitro studies	In vitro results for Roxatidine mucoadhesive microspheres demonstrated excellent drug entrapment and percent yield. In a controlled in-vitro release trial, the improved formulation exhibited 99.4 percent after 12 hours, necessary for diseases like peptic ulcers. In addition, the lack of drug-polymer interaction was verified by FTIR and DSC analyses.	[15]
Repaglinide	In-vitro and in-vivo Studies	The current study discovered that the drug/polymer ratio had an impact on the microsphere's release. The mucoadhesive microsphere of repaglinide was found to have considerable blood-glucose-lowering efficacy in an in-vivo investigation. Because it is a cost-effective, safe, and bioavailable formulation, drug-loaded mucoadhesive microspheres are an ideal delivery method for repaglinide.	[16]
Pioglitazone	In-vitro studies	By extending drug retention in the stomach and	[17]

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HCl		improving drug bioavailability, the produced mucoadhesive microspheres appear to be a promising option for oral gastro retentive control release drug delivery system.	
Oseltamivir	In-vitro studies	In a kinetic model, the formulation was shown to be linear. After 12 hours, the optimized formulation showed 86.99 percent drug release. 76.4 percent drug entrapment efficiency, 73.8 percent yield, 80 percent mucoadhesive strength, and 75.3 percent swelling index.	[18]
Cimetidine	In-vitro studies	The improved formulation had a total drug release of 99.41%. Furthermore, it shows that a cimetidine mucoadhesive microsphere may release the medication for up to 12 hours.	[19]
Linagliptin	In-vitro studies	Studies using FTIR and DSC revealed that the medication excipients were compatible. In addition, radiographic pictures show that the microspheres were retained in the stomach for 7 hours, and the formulation was determined to be stable. This implies that linagliptin's stomach residence time has risen, allowing for improved absorption and bioavailability.	[20]
Clerodendrum phlomidis (CP)	In-vitro and in-vivo studies	In an in-vitro test, the microcapsules showed good mucoadhesive characteristics. The mucoadhesive microcapsule of CP extract showed substantial blood-glucose-lowering efficacy in an in-vivo investigation. After oral administration of CP extract, mucoadhesive microcapsules are ideal for a sustained effect.	[21]

Drug	**Type of Studies**	**Particulars**	**Refs.**
Acyclovir	In-vitro studies	The current study found that by forming acyclovir into a microsphere and encapsulating it in gum tragacanth, the retention period of acyclovir at its absorption location, the upper GIT, may be improved.	[22]
Olanzepine	In-vitro and in-vivo studies	In-vitro release and in-vivo tests revealed that the produced microsphere of olanzapine had good drug entrapment, present mucoadhesion, and good drug entrapment. In addition, advanced research, such as SEM morphology, yielded positive results.	[23]
Imatinib Mesylate	In-vitro Studies	According to the assessment and stability testing results, natural polymer formulations were superior to semi-synthetic polymer formulations for the oral administration of imatinib mesylate.	[24]

Recent patents on Microspheres.

Microspheres have been studied for their potential application in drug delivery systems during the last several decades. It has been discovered that microspheres can improve drug candidates' bioavailability and efficacy. As a result, the

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technology of microspheres has been the subject of several patents. The patents are included in Table 2 as a summary.

Table 2. Recent patent on, Microsphere

Patent/Application number	Publication Date and year	Patent Description	Ref.
TW201938204A	2019-11-01	The current invention pertains to a technique of preparing radiation microspheres for use in fixed-point internal radiation treatment.	[25]
CN107954429B	2020-01-01	This invention relates to the method and use of silicon dioxide hollow microspheres	[26]
CN108609649B	2020-06-09	The invention pertains to a technique for making hollow microspheres in the shape of sea urchins.	[27]
WO2020221052A1	2020-11-05	The innovation is about Alpha-Tocopherol microspheres and the method for making them.	[28]
CN111551713A	2020-08-18	The invention pertains to detecting COVID-19 viral antibodies and a preparation method and a kit including the microscope.	[29]
JP6792900B1	2020-12-02	Microspheres with evenly dispersed bioactive compounds that may withstand release preparations containing them.	[30]
CN108440712B	2021-01-01	The invention concerns hyper branching polymer composite microspheres having a core-shell structure and their manufacture and use.	[31]
JP2020079313A	2020-05-28	The current invention pertains to radiation-blocking embolic microspheres that may be imaged.	[32]
WO2021036491A1	2021-03-04	Microspheres screen, production-type efficient microsphere collection device, and application are among the inventions.	[33]
CN108246271B	2021-05-25	Method for making molecularly imprinted polymer microspheres that can detect 2, 4, 6-trinitrophenol.	[34]

Types of Microspheres

1. Bio-adhesive microspheres.

The attaching of a medication to a membrane via the adhesive properties of water-soluble polymers is referred to as adhesion. Bio adhesion is the attachment of a medication delivery device to a mucus membrane such as the buccal, ocular, rectal, or nasal mucosa. This type of microsphere has a longer residence time at the application site, which results in close contact with the absorption site and creates better therapeutic action. [35]

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2. Magnetic microspheres.

This delivery mechanism is critical because it allows the drug to be delivered to the illness location. Magnetic microspheres are free-flowing, spherically encapsulated particles with biodegradable and non-biodegradable components with sizes ranging from 130p to 135p suspended in an aqueous, organic, or inorganic vehicle. [36]

3. Floating microspheres.

Because the bulk density of floating microspheres is less than that of gastric fluid, they remain buoyant in the stomach without altering the gastric emptying rate. If the system is floating on stomach content, the drug is released slowly at the optimal rate, increasing gastric residence and plasma concentration variability. It also minimizes the likelihood of striking and dosage dumping. Another benefit is that it produces a longer-lasting therapeutic impact, reducing dose frequency. [37]

4. Radioactive microspheres.

The dimensions of the series range from 10 to 30 nm. When larger capillaries come across, they become trapped in the primary capillary bed. They inject into the significant tumor's arteries. These radioactive microspheres deliver a high radiation dosage to the action site while causing no harm to the surrounding tissues. This is a different drug delivery system in which radioactive substances' radioactive properties are avoided when released from microspheres instead of acting from a typical radioisotope distance. The different types of radioactive microspheres are emitters, emitters. [38]

5. Mucoadhesive microspheres.

Mucoadhesion is a hot topic in drug delivery system design. Mucoadhesive microspheres have a longer residence duration at the absorption site, allowing closer contact with the underlying surface, improving therapeutic drug effectiveness. As a result, the drug's absorption and bioavailability improve. Dosing is less frequent, and patent compliance is higher. [39]

- Advantages of mucoadhesive microspheres. [40]

➢ Controlled release over a more extended period.
➢ As a result of the reduced frequency, patient compliance improves.
➢ Because of the low density, the harmful effect is reduced.
➢ It is possible to target the tissue.
➢ The toxicity of other organs is much lower.

- Limitation of mucoadhesive microspheres. [41]

➢ From one dose to the next, the difference in release rate can be found.
➢ Several factors can affect the release rate, including transit time, food passing through the gut, etc.
➢ Any deterioration in the dosage form's release pattern could result in toxicity.
➢ These dose forms are not crushable or chewable.
➢ The formulation's release could be altered.

Mucoadhesion

Bio-adhesion is a process in which interfacial forces hold two chemicals together, at least one biological. The word "mucoadhesion" refers to the attachment of a polymer to the mucosal layer's surface. [42]

Mucous membrane

The moist surfaces lining the walls of numerous body cavities, such as the gastrointestinal (GI) and respiratory tracts, are mucus membranes. The goblet cell secretes mucus. Mucus can be found as a gel layer clinging to the mucosal surface, suspended mucus, or luminal soluble mucus. Many glycoproteins, water, lipids, and inorganic salts are the major components of all mucus gels. Mucus acts as a protective barrier as well as a lubricant. [43]

Mechanism of Mucoadhesion [44]

Mucoadhesion is defined as the attachment of medication to the mucosal layer with the help of an appropriate carrier. Mucoadhesion is a complicated phenomenon involving polymer chain wetting, adsorption, and interpenetration.

The mechanism of mucoadhesion is as follows:

✓ Mucoadhesive delivery system close to the mucosal membrane (Wetting or swelling, phenomenon).
✓ The mucoadhesive delivery system's penetration into the tissue or the mucus membrane's surface.

Theories of Mucoadhesion. [45]

The following are some of the hypotheses that are involved in mucoadhesion:

1. The electronic theory
2. The wetting theory
3. The adsorption theory
4. The diffusion theory
5. The mechanical theory

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6. The cohesive theory

1. The electronic theory
An electrical double layer is produced when an electron is transferred between the mucoadhesive and mucosal membranes.
2. The wetting theory
This hypothesis, which applies to liquids, states that the lower the liquid's contact angle with the substrate, the greater the affinity for adhesion.
3. The adsorption theory
According to this idea, intermolecular forces such as Vander Wall's forces and hydrogen bonding adsorb the mucoadhesive to the mucosal surface.
4. The diffusion theory
The formation of a networking structure between the mucoadhesive and mucosal surfaces is depicted in this hypothesis by the diffusion of polymers chains present on the mucoadhesive surface.
5. The mechanical theory
Explain how the liquid adhesives diffuse into the micro-cracks and imperfections on the mucoadhesive substrate, resulting in mucoadhesion, culminating in constructing an interlocking structure.
6. The cohesive theory
According to this idea, mucoadhesion is caused mainly through intermolecular interactions between like-molecules.

Factor affecting mucoadhesion [46]

The following parameters influence the mucoadhesion of the drug carrier system to the mucosal membrane.

- Polymer-based factor: Polymer molecular weight, concentration, stereochemistry, chain length, and hydration.
- Physical factor: pH at the polymer-substrate interface, polymer swelling, applied strength, and contact time are all factors that must be considered.
- Physiological factor: The rate of mucin turnover and the sick state.

Mucoadhesive microspheres are made from a variety of materials. [47]
Polymer is used to construct mucoadhesive microspheres. Natural or artificial origins are possible for mucoadhesive polymers. Mucoadhesive polymers that cling to the mucin-epithelial surface can be classified into three categories:

- Polymers become sticky when placed in water and acquire mucoadhesion as a result of the stickiness.
- Polymers that stick together due to a nonspecific, noncovalent electrostatic contact.
- The polymer binds to a receptor spot on the tile surface.

Classification of mucoadhesive polymers
Table 3 lists the several types of mucoadhesive polymers, both synthetic and natural.

Table3. A shortlist of mucoadhesive polymers [48]

Synthetic polymer	Natural Polymers
Hydroxypropylmethylcellulose	Chitosan
Poly hydroxyethyl methacrylate	Sodium alginate
Polyethylene Oxide	Pectin
Sodium carboxymethyl Cellulose	Locust bean gum
Hydroxypropyl cellulose	Guar gum
Hydroxyethylcellulose	Xanthan Gum
Ethyl Cellulose	Karaya Gum
Polyvinyl alcohol	Gelatin
Polyvinyl pyrrolidone	Tragacanth
Poly (acrylic acid) polymer (carbomer, polycarbophil)	Soluble starch

Characteristic of an ideal mucoadhesive polymer [49]
1. The polymer and its breakdown product must be non-toxic and non-absorbable by the gastrointestinal tract.
2. The mucus membrane should not be irritated by it.
3. It should stick to most types of tissue fast and have some site-specificity.
4. It should be simple to incorporate and release the medicine.
5. During storage or the shelf life of the dosage form, the polymer must not degrade.
6. The polymer's cost should not be prohibitively high for the created dosage form to be competitive.

Mucoadhesive microspheres: Method of Preparation

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The microencapsulation process can incorporate solids, liquids, or gases into one or more polymeric coatings. Particle size, route of administration, period of drug release, and these above characters connected to rpm, the technique of cross-linking, evaporation time, co-precipitation, and other factors all influence the diverse methods used to prepare various microspheres. The following are the many methods of preparation:

Phase separation method

Phase separation works by lowering polymer solubility in the organic phase, causing a polymer-rich phase called coacervates. The drug particles are spread in the polymer solution, and a mismatched polymer is introduced to the system, causing the first polymer to phase separate and swallow the drug particle. The solidification of the polymer occurs when a non-solvent is added. The pace at which the coacervates are generated impacts the dispersion of the polymer film, particle size, and agglomeration of the formed particles. Hence process variables are critical. Because the generated polymerize globules begin to cling together and form agglomerates as the microscope formation process begins, agglomeration must be avoided by stirring the suspension with a sufficient speed stirrer. Because there is no defined state of equilibrium attainment, the process factors are crucial because they govern the kinetics of the produced particles. [50]

Emulsion cross-linking method

The medication is dissolved in an aqueous gelatin solution heated for 1 hour at 40 degrees Celsius in this method. If there is no emulsion after 10 minutes of stirring at 1500rpm at 35°C, the solution is added dropwise to liquid paraffin. The prepared microspheres are washed three times with acetone and isopropyl alcohol, then dried in the air before being dispersed in 5 mL of aqueous glutaraldehyde saturated toluene solution at room temperature for three hours for cross-linking, and then treated with 100 mL of 10 mm glycine solution containing 0.1 percent w/v of tween 80 at 37°C for ten minutes to block unreacted. [51]

Solvent Evaporation

A liquid manufacturing vehicle is used to carry out this procedure. The coating on the microspheres is disseminated in a volatile solvent that is incompatible with the liquid production vehicle phase. In the coating polymer solution, a core material to be microencapsulated dissolves. The core material combination is distributed in the liquid manufacturing vehicle phase using agitation to obtain the proper microcapsule. When solvent for the polymer of the core material is disseminated in the polymer solution evaporates, the polymer shrinks around the core. Matrix-type microcapsules are created when two core materials are dissolved in a covering polymer solution. The core components can be water-soluble or non-water soluble. The creation of an emulsion between a polymer solution and an immiscible continuous phase, whether aqueous (o/w) or non-aqueous, results from solvent evaporation. [52].

Spray drying

Before spray drying, the polymer is first dissolved in a suitably volatile organic solvent such as dichloromethane, acetone, or another similar solvent. Under high-speed homogenization, the solid drug is disseminated in the polymer solution. A stream of hot air is used to atomize the dispersion. The atomization produces microscopic droplets or a fine mist, from which the solvent evaporates instantly, forming microspheres with sizes ranging from 1 to 100 micrometers. Microparticles act as a separator, while vacuum drying removes any remaining liquid. The ability to operate in an aseptic environment is one of the process's primary advantages. It is a quick technique that results in porous microparticles. [53]

Ionotropic gelatin

Microspheres are made using this method by dissolving a gel-type polymer, such as alginate, in an aqueous solution, suspending the active ingredient in the mixture, and extruding the solution through a needle to produce micro-droplets that fall into a hardening solution containing calcium chloride while being stirred at low speed. The hardening solution's divalent calcium ions crosslink the polymer, resulting in gelled microspheres. [54]

Evaluation parameters

1. Particle size

Microspheres' size, shape, and exterior structure can be determined using light microscopy or scanning electron microscopy (SEM).

2. Surface characterization of the mucoadhesive microsphere

SEM, STM, and electron microscopy data reveal microsphere surface shape and morphological changes caused by polymer breakdown. By incubating the microspheres in phosphate buffer saline at varying intervals, changes in the surface shape caused by polymer degradation can be investigated. Microspheres with a coarser surface promote adherence by allowing

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for more mechanical engagement, whereas microspheres with a smooth surface have poor mucoadhesive qualities. [55, 56]

3. Drug entrapment or capture efficiency.

The entrapment efficiency or percent entrapment can be measured by retaining the microspheres in the buffer solution and allowing lysing. The lysate is then filtered or centrifuged, and the active components are determined according to the monograph's specifications. The following equation is used to compute percent entrapment efficiency.

$$\text{Entrapment efficiency} = \frac{\%\text{drug loading}}{\%\text{ Theortical loading}} \times 100$$

Where,

$$\%\text{ Drug loading} = \frac{\text{weight of drug in microsphere}}{\text{weight of microsphere}}$$

4. Percentage Yield

A percentage yield is a tool that may be used to calculate the efficacy of any process. As a result, it aids in the selection of the best manufacturing method. [57]

$$\%\text{yield} = \frac{\text{Total weight of microparticle}}{\text{Total weight of polymer}} \times 100$$

5. Degree of swelling

It demonstrates the mucoadhesive microsphere's ability to enlarge at the absorbing surface by absorbing fluids present at the absorption site, which is a prerequisite for mucoadhesion to begin. [58]

The degree of swelling can be calculated by the change of polymer volume (Wg-Wi).

$$\text{Degree of swelling} = \frac{W_g - W_i}{W_g} \times 100$$

Where,

$W_{i=}$ Initial weight of microspheres

$W_{g=}$Final weight of the microsphere

6. Mucoadhesion test

In-vitro wash-off tests are used to assess the adhesive characteristics of microspheres. The thread connected a 1cm by 1cm piece of rat stomach mucosa to a glass slide (3 inches by 1 inch). The prepared slide was hung onto one of the groves of a USP pill disintegration test instrument, and microspheres were distributed onto the west-washed tissue samples. The tissue samples were moved up and down in a beaker containing simulated gastric fluid USP as part of the disintegration test device (pH 1.2). The amount of microspheres remaining to adhere to the tissue was counted after 30 minutes, 1 hour, and at hourly intervals up to 10 hours. [59]

7. Compatibility test

Differential scanning calorimetry (DSC)

It's a thermos analytical technique that measures the amount of heat required to raise the temperature of a sample and a reference as a function of temperature. The microspheres' DSC thermograms will be recorded using DSC. In pans, accurately weighed drug samples are taken. As a reference pan, an empty aluminum pan can be utilized. A nitrogen gas purge will be performed on the system. Heating will be provided at a predetermined rate. [46]

Fourier transfer infrared [FTIR] spectroscopy

By generating a pellet of materials with KBr, the IR spectra of a microsphere will be recorded using an FTIR spectrophotometer between the ranges. The resulting spectra will be compared to a standard reference, and any deviations from the standard will be noted. [46]

8. In-vitro release studies

Commonly, standard IP/BP/USP dissolution equipment is used to analyze in-vitro release profiles in dissolving media identical to the fluid present at the absorption site according to the monograph, employing a rotating basket or paddle-type dissolution apparatus. [60]

Application of mucoadhesive microsphere[61]

Microspheres are used in the following applications:

1. Dosage formulations with a controlled and long-term release.
2. Microspheres can be utilized to coat enteric coated dosage forms, allowing the medication to be absorbed more efficiently in the colon rather than the stomach.
3. Microspheres can help reduce volatility. Without significant evaporation, an encapsulated volatile material can be used for prolonged periods.
4. Microspheres have also been utilized to reduce the risk of dangerous or noxious substances being mishandled. For example, after microencapsulation, the toxicity caused by fumigants, herbicides, insecticides, and pesticides was reduced.
5. Microspheres can lower the hygroscopicity of various core materials.
6. To minimize stomach discomfort, many medications have been microencapsulated.
7. A method of preparing intrauterine contraceptive devices using microspheres has also been developed.
8. Chemotherapeutic agents are delivered to liver tumors via therapeutic magnetic microspheres. This

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technique can potentially be used to target drugs like proteins and peptides. In addition, mucoadhesive microspheres have a more extended residence period at the application site, resulting in closer contact with the absorption site and improved therapeutic activity.

The existing Problem of Microsphere preparation

Using the methods described above, microspheres usually have a wide range of particle sizes and a wide size distribution. The non-uniformity of these microspheres causes poor batch-to-batch reproducibility, necessitating screening during the preparation process. Furthermore, the size and distribution of microspheres are essential determinants in controlling the degradation and release profiles of encapsulated medicines and affecting the in-vivo fate of microspheres by influencing the cellular absorption process. As a result of the inhomogeneity of microsphere size, inconsistent drug release behavior may occur, resulting in inhomogeneous blood drug levels in patients and affecting the efficiency of the microsphere delivery system. Furthermore, the considerable energy consumption during the spray drying process might easily cause protein medicines to become inactive, lowering drug delivery efficiency. Coacervation is challenging to remove thoroughly due to the employment of a range of organic solvents. The coacervation-produced drug-loaded particles are easily agglomerated and difficult to scale up. As a result, a new preparation method capable of producing uniform-sized particles with minimal energy consumption and a high scare-up potential is being developed incredibly appealing. [62-66]

List of marketed microsphere drug products

A list of commercially available microsphere medication productsis shown in Table 4. [67]

Table 4 List of marketed microsphere drug product

S.no	Drug	Commercial Name	Company	Technology
1	Risperidone	RISPERDAL® CONSTA®	Janssen®/Alkermes, Inc	Double emulsion (oil in water)
2	Naltrexone	Vivitrol®	Alkermes	Double emulsion (oil in water)
3	Leuprolide	Lupron Depot® Enantone Depot®	Tap Takeda	Double emulsion (water in oil in water)
4	Octreotide	Sandostatin® LAR	Novartis	Phase separation
5	Somatropin	Nuptropin® Depot	Genentech/alkermes	Alkermes ProLease® Technology (Cryogenic spray-drying)
6	Triptorelin	Trelstar™ Depot Decapeptyl® SR	Pfizer Ferring	Phase separation
7	Buserelin	Supercur® MP	Sanofi-aventis	N/A
8	Lanreotide	Somatuline®LA	Ipsen-Beaufour	Phase separation
9	Bromocriptine	Parlodel LAR™	Novartis	Spray drying
10	Minocycline	Arestin®	Orapharma	N/A

Future challenges

Because of its wide range of applications in molecular biology, egg: the microsphere-based genotyping platform is used to detect six single nucleotide polymorphism, yttrium-90 microspheres are used to prevent tumor after liver transplantation, and it's the advanced way in delivering vaccines and proteins, the future challenges of microspheres look bright.

II. CONCLUSION

Medication absorption in the gastrointestinal tract is a very various process. However, keeping the dose form in the stomach for longer increases its time for the drug to be absorbed. The hollow microsphere appears to be a promising method for retaining gastric contents.Despite the numerous challenges that must be overcome to achieve prolonged gastric retention, a considerable number of businesses are working to

commercialize this approach.Furthermore, microspheres will play a central role in novel drug delivery in the future by combining various other strategies, particularly in diseased cell sorting, diagnostics, gene, and genetic materials, safe, targeted, and effective in vivo delivery, and supplements as miniature versions of diseased organs and tissues in the body.

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