



Microsphere : A Boon in Pharmaceuticals

Ravirajsinh Gohil^{1*}, Grishma P Dalal², Payal N Vaja²

1. Dr. Subhash Technical Campus, Junagadh, Gujarat, India.

2. Assistant. Professor, Department of Pharmacy, Dr. Subhash Technical Campus, Junagadh, Gujarat, India.

*Corresponding author's E-mail: ravirajsinh78@gmail.com

Received: 14-02-2021; Revised: 23-03-2021; Accepted: 02-04-2021; Published on: 20-04-2021.

ABSTRACT

The present review article introduce about various types of microspheres, different methods of preparation, its applications and also various parameters to evaluate their efficiency. Microspheres are various types like magnetic microspheres, floating microspheres, radioactive microspheres, bioadhesive microspheres, polymeric microspheres, biodegradable polymeric microspheres, synthetic polymeric microspheres and are prepared by methods like spray drying, solvent evaporation, single emulsion technique, double emulsion technique, phase separation coacervation technique, spray drying and spray congealing, solvent extraction. Microspheres have wide range of applications because of controlled and sustained release. Current aim of this review is to study various aspects of the microsphere drug delivery system Including method of formulation, evaluation parameter and characterization.

Keywords: Microspheres, Types of microspheres, Method of preparation, Application.

QUICK RESPONSE CODE →

DOI:

10.47583/ijpsrr.2021.v67i02.007



DOI link: <http://dx.doi.org/10.47583/ijpsrr.2021.v67i02.007>

INTRODUCTION

Microsphere is defined as the small spherical free flowing particles which is of size not more than 200 micrometer. It can be injects by 18 or 20 number needle. Generally, microsphere composed of protein or synthetic polymers. A microsphere-based drug delivery system can overcome the problems linked with conventional dosage form and improve the therapeutic action of drug given. Floating microspheres an example of gastro-retentive drug delivery systems based on non-effervescent approach. Magnetic microspheres Use for target to tumors. The clearance kinetics, tissue distribution, metabolism i.e., Kinetics and cellular interaction of the drug are strongly influenced by the behavior of the Carrier. The exploitation of these changes in pharmacodynamics behavior may lead to enhanced therapeutic efficiency.¹⁻²

Advantages of microsphere

1. Protect the drug from enzymatic and photolytic cleavage hence stable for long time.
2. Decrease dose and increase efficacy.
3. Drug release is constant hence prolonged therapeutic effect.

4. Increase solubility of the poorly soluble drug due to particle size reduction.
5. Provide constant drug concentration in blood there by less or no toxicity.
6. Provides prolonged therapeutic effect.
7. Improve the patient compliance by reducing the dosing frequency.
8. The spherical shape and smaller size makes them to be injected into the body.
9. The morphology of microspheres shows variability in controlled release of drug.
10. Conversion of oil and other liquids to solids for ease of handling.

Disadvantages of microsphere

1. The altered release from the formulations.
2. Thee release rate of the controlled release dosage form may vary from a variety of factors like GI content and the rate of transit though gut.
3. Differences in the release rate from one dose to another due to manufacturing faults.
4. Microsphere contains large amount of drug dose so if any change in physical integrity of microsphere that may shows potential toxicity.
5. Dose dumping: loss of physical integrity by various factors like manufacturing faults, crushing and co administering with other drugs.
6. Drug Release reproducibility is difficult.



Types of Microsphere

1. Bioadhesive microspheres
2. Magnetic microsphere
3. Floating microspheres
4. Mucoadhesive microspheres
5. Radioactive microspheres
6. Polymeric microspheres
 - A. Biodegradable polymeric microsphere
 - B. Synthetic polymeric microsphere

Bioadhesive microspheres

The word bioadhesive means any substance which binds to biological substance like mucosal membrane. When bioadhesive drug delivery device attached to a biological membrane it provides prolonged contact at site of administration. Due to the prolonged contact at the site of administration there will be greater absorption of particular drug and prolonged residence time thus it reduce the dosing frequency and improve the patient compliance. Microsphere, nanospheres, liposome, nanoparticle drug delivery system which modifies the absorption and release pattern of the drug. Microsphere is one of the most important part of these particulate drug delivery system.³

Magnetic microsphere

Magnetic microsphere is very much important which target the drugs to the particular disease site. In magnetic microsphere the large amount of release circulating drug can be replaced with small amount of magnetically target drug. After that microsphere is injected in the body. The high strength magnetic field is applied externally over the target organ to gather microsphere at the target site. Therapeutic magnetic microsphere delivers the chemotherapeutic agent to the liver tumor.⁴

Floating microspheres

The bulk density of floating microspheres is less than the gastric fluid so it floats over the gastric content in stomach without affecting gastric emptying rate. If the system is floating on gastric content it produce release of drug at desirable rate & increases stomach residence time. The drug ketoprofen is given in floating microsphere. Floating microspheres reduces the chances of dose dumping and provide prolonged therapeutic effect.⁵

Mucoadhesive Microspheres

Mucoadhesive microspheres are defined as the microsphere which are of size 1-1000 mm made up of mucoadhesive polymers. Mucoadhesive microspheres has following additional advantages like enhanced bioavailability & efficient absorption of drugs. Mucoadhesive microspheres can adhere to the any mucosal tissue membrane of eye, nasal cavity, GIT & thus

provides great possibilities of systemic & controlled released of drugs.⁶

Radioactive microspheres

Radioactive microsphere is of size 10-30 nm. Generally radioactive microspheres are differ from other drug delivery systems. The different types of radioactive microsphere are α Emitters, β emitters, γ emitters. There is no radioactivity released from microsphere. Radioactive microsphere are injected to the arteries that lead to tumor of interest. That produce high rate of radiation at the target site without damaging surrounding tissues.

Polymeric microspheres

Biodegradable Polymeric microsphere

Biodegradable polymeric microsphere are made up of biodegradable, biocompatible & bioadhesive polymer like starch. When this biodegradable polymer comes in contact with aqueous medium it swells & produce gel like structure. Due to this property biodegradable polymer prolongs the residence time. The release of drug from biodegradable polymeric microsphere is controlled by concentration of polymer & release pattern in a sustained manner.⁷

Synthetic polymeric microsphere

Synthetic polymeric microsphere are widely used in field of clinical application, moreover that also used as bulking agent, fillers, embolic particles, drug delivery vehicles. But here the main disadvantage is that when synthetic polymeric microsphere is injected to body that might tend to be migrate from the injection site to surrounding tissue organ that may lead to potential at risk and toxicity.⁸

Method of Preparation

The choice of method for the preparation of microsphere depends upon the nature of drugs and polymer used and it also depends on the duration of therapy. There are several important chemical factor that may be controlled in microsphere manufacture are

- Molecular weight of polymer
- Release of active reagent with a good control over a wide time-controlled particle Size and dispensability in aqueous vehicles for injection
- Reproducibility
- Total mass of drug and polymer
- Final product should be non-toxic.

Single emulsion technique

In single emulsion technique first the natural polymers are dissolved in aqueous media followed by dispersion of heated oil. i.e. non aqueous medium that lead to the formation of single emulsion. After that cross linking is carried out in two ways.



Cross linking by heat: by adding the dispersion into Heated oil, but it is unsuitable For the Thermolabile Drugs.

Chemical cross-linking agents : chemical cross-linking is carried out by chemical cross-linking agents like of glutaraldehyde, di acid chloride But here disadvantage of excessive exposure of active ingredient to chemicals if added during the preparation. After the crosslinking it is subjected to centrifugation, washing & separation. By using 25% glutaraldehyde solution as a crosslinking agent metformin hydrochloride microsphere were prepared.⁹⁻¹⁰

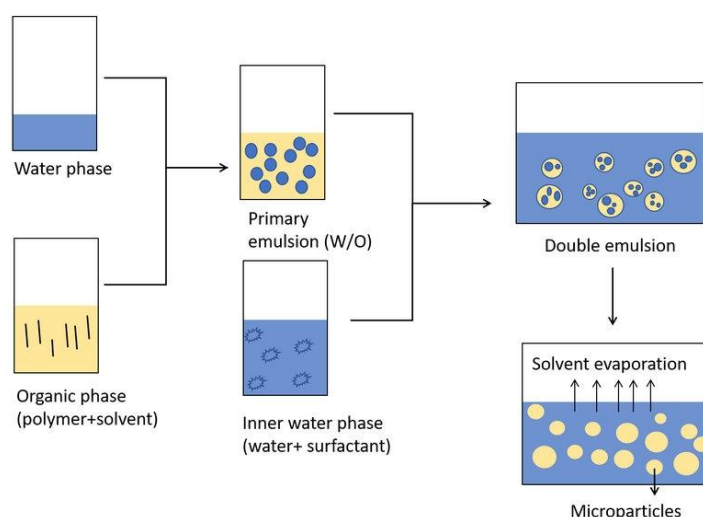


Figure 1: Double emulsion method

After the formation of single emulsion, it is subjected to homogenization before addition to aqueous solution of the polymer that results in the formation of a double emulsion. After that the emulsion undergoes to solvent removal either by solvent evaporation or by solvent extraction.

Ex: microspheres containing leutinizing hormone releasing hormone (LH- RH) Agonist, vaccines, proteins/peptides are successfully prepared by double emulsion method

Polymerization

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

- A. Normal polymerization
- B. Interfacial Polymerization

Normal Polymerization

In a process of bulk polymerization monomer mixture of monomer combined with initiator or catalyst usually heated to initiate polymerization. Generally, suspension polymerization is occurs at low temperature which is also known as polymerization in which heating the monomer mixture with active drug as droplets dispersion in continuous aqueous phase. Microspheres of size less than

Double emulsion technique

As the name suggests that there will be formation of double emulsion emulsions or the double emulsion of type w/o/w and is best suited to water Soluble drugs, peptides, proteins and the vaccines. In this method of microsphere preparation natural and semi synthetic polymer can be used. In single emulsion the continuous phase is generally made up of polymer solution which eventually encapsulates of the protein Contained in dispersed aqueous phase.¹¹

100 micrometer are obtained by suspension polymerization. Emulsion polymerization is also occurring at low temperature but it is differentiated from the suspension polymerization because the presence of initiator in aqueous phase.¹²

Interfacial Polymerization

It involves the reaction of various monomers at the interface between the two Immiscible liquid phases to form a film of polymer that essentially envelops the dispersed phase. In this technique two reacting monomers are employed; one is dissolve in continuous phase while other is disperse in continuous Phase (aqueous in Nature) throughout which the because of solubility of formed polymer in the emulsion droplet. That is formation is monolithic type of carrier.

Phase separation and Coacervation method

It is the simple separation of a micro molecular solution into two immiscible liquid Phase. This method is used to encapsulate water soluble drugs e.g. peptides, proteins. Method includes the dissolution of polymer in a suitable solvent followed by drug dispersion. Phase separation is then accomplished by changing the solution conditions by the salt addition, odd-solvent addition, addition of the incompatible polymer or change in PH.¹³

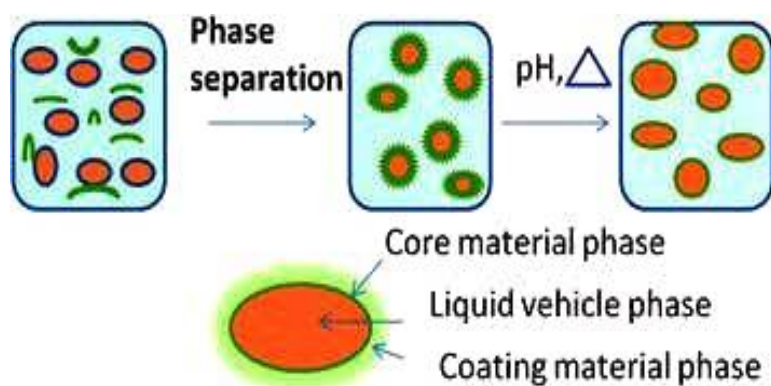


Figure 2: Phase separation and Coacervation

The principle of Coacervation is decreasing the Solubility of the polymer in organic phase to affect the formation of polymer rich phase called the coacervates. Here in this technique the polymeric solutions containing drug dispersion with incompatible polymer is added to the system which makes first polymer to Phase separate and engulf the drug particles. Generally, matrix type preparation are prepared by this method for hydrophilic drug e.g. steroids, addition of non-solvent Results in the solidification of polymer. Addition of sodium sulphate to the solution of chitosan in acetic acid resulted in decreased solubility of chitosan, leading to precipitation of chitosan as a poorly soluble derivative.

Spray drying

In spray drying method of microsphere preparation evaporation is the basic mechanism while spray congealing is the inversion from liquid to solid phase. Both processes are similar, except for energy flow spray drying is the most widely used Industrial process involving particle formation and drying. Here in spray drying first over polymer is preferred in volatile organic or volatile solvent like of chloroform and acetone and dichloro methane. After that the drug which is in solid form is dissolved in in polymer solution under high speed homogenization. This dispersion is then atomized in a stream of hot air, that results in the formation of small droplets. Solvents on the surface of small droplet is you are operated due to continuously flow of hot air leading to the formation of small microsphere. This technique is very useful to encapsulate various penicillins.¹⁴⁻¹⁶

There are three steps involved in spray drying

- i. Atomization
- ii. Mixing
- iii. Drying

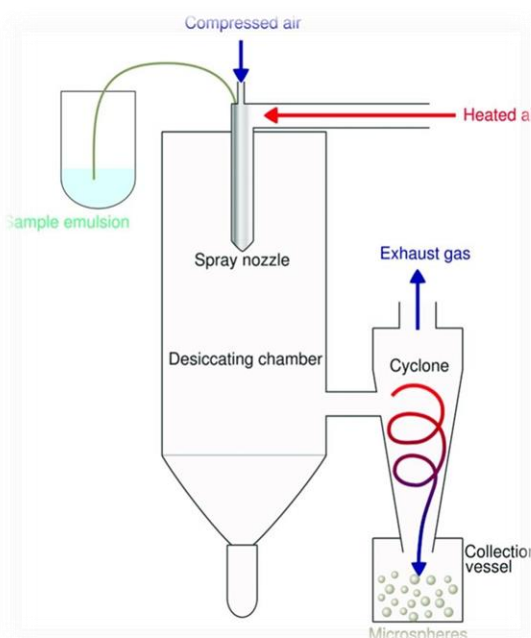


Figure 3: Spray drying

Spray drying technique is also useful for preparing chitosan microspheres In 1999 He et.al. Used formaldehyde as a crosslinking and also reported a novel method in which cimetidine and famotidine were entrapped in microspheres prepared by spray drying of multiple emulsion (o/w/o or w/o/w). They found that the Release of the drugs from microspheres this novel method was significantly sustained as compared to those prepared by conventional spray drying or o/w emulsion method. In a spray-drier under different experimental conditions. Solid microspheres were collected into final bottom vessel spray-drier.¹⁴⁻¹⁶

Solvent extraction

This method involves removal of organic phase by extraction of the organic solvent. The method involves water miscible organic solvents such as isopropanol. Organic phase is removed by extraction with water. This process reduces the time required for hardening of microsphere. Another variation of this process involve directly addition of drug to the polymer the rate of solvent removal by extraction method depends on the

temperature of water, ratio of emulsion volume to the water and the solubility profile of the polymer.¹⁷

Wax coating and hot melt method

Here in this technique first our polymer is dissolved in appropriate dispersion medium after that slowly cooled to form microsphere. The polymers which having low melting point fabricated into microspheres by this technique Easily. For coating and coring of particle wax is use mostly.

Emulsion Solvent evaporation

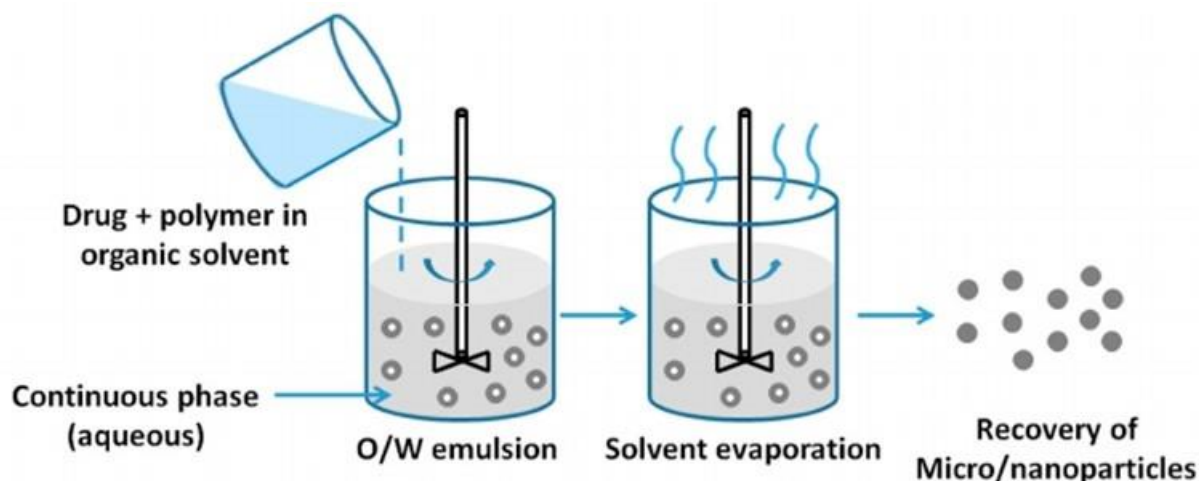


Figure 4: Emulsion solvent evaporation

This technique includes the drug is dissolved in polymer solution of chloroform and the resulting solution is added to aqueous phase containing 0.3 % sodium of PVP as Emulsifying Agent. The above mixture was agitated continuously then the drug and polymer was transformed into fine droplet which solidified into rigid microspheres by solvent evaporation and then collected by filtration and washed with demineralized water and desiccated at room temperature for 24 Hrs.¹⁹

Evaluation Parameters For Microspheres

1. Characterization
2. Particle size & shape
3. Isoelectric Point
4. Density determination
5. Angle of contact
6. Electron spectroscopy for chemical analysis
7. Alternated total reflectance fourier transform infrared spectroscopy
8. Drug release
 - A. In vitro method
 - a) Interface diffusion system
 - b) Modified Keshary Chien cell
9. Dissolution studies
 - a) vivo methods

Here the wax suspension is disturbed into cold solution with high-speed mixing. Agitate the mixture for one hour. Then decanted the external phase and suspended microspheres collect from solvent. And allows the microsphere to drying it in air. It is Inexpensive method as comparison to others and drug release is more Rapid. Mostly carnauba wax and beeswax can be used as the coating materials and these can be Mixed in order to get desired characteristics.¹⁸

b) In vitro In vivo correlation

Characterization

The characterization of microsphere is an important phenomenon that helps to design of appropriate carrier for the delivery of the drug or protein molecules. These microspheres have different microstructures. These microstructures determine the release and the stability of the carrier.²⁰

Particle size & shape

light microscopy and scanning electron microscopy widely used to visualise size and determine shape of microsphere. Both can be used to determine the shape and outer structure of microparticles. LM provides a control over Coating parameters in case of double walled microspheres. SEM produce higher resolution in contrast to the LM. Confocal fluorescence microscopy is used for the structure characterization of multiple walled microspheres. on another hand two non instrumental analytical technique laser light scattering & multisize couler counter used For the morphological characterization of microsphere.²¹

Isoelectric Point

The electrophoretic mobility of microsphere can be determined with the help of apparatus known as micro electrophoresis and on the basis of electrophoretic mobility isoelectric point can be determined. The electrophoretic mobility can be related to surface contained charge, ionisable behaviour or ion absorption

nature of the microspheres. The mean velocity at different pH values ranging from 3-10 is calculated by measuring the time of particle Movement over a distance of 1 mm.²²

Density determination

The density of the microspheres can be measured by using a multi volume pycnometer. Here first power sample of microsphere of which density to be determined is accurately weighed and placed into multivolume pycnometer. Helium is inserted at a constant pressure in the chamber and allowed to expand. This expansion results in a decrease in pressure within the chamber. Two consecutive readings of reduction in pressure at different initial pressure are noted. From the pressure reading density of the microsphere can be determined.²²

Angle of contact

The angle of contact can be measured at the solid/air/water interface. The advancing and receding angle of contact are measured by placing a droplet in a circular cell mounted above objective of inverted microscope. It is a very fast process generally contact angle is measured at 200°C within a minute of deposition of microsphere solid/air/water interface.

Spectroscopy for chemical analysis

Electron spectroscopy for chemical analysis (ESCA) used to determine surface chemistry of microsphere. ESCA can be used to determine of the atomic composition of the surface. The spectra obtained using ESCA can be used to determine the surficial degradation of the biodegradable microspheres.²³

Alternated total reflectance fourier transformed infrared spectroscopy

FT-IR provides information the degradation of the polymeric matrix of the carrier system. The surface of the microspheres is investigated measuring alternated total reflectance (ATR). The beam of IR radiation reflected many times from the sample to get IR spectra. The ATR FTIR gives idea about the surface composition of the microspheres.

Drug release

In vitro method

Drug release study is very important parameter which depends upon the release characteristic of the microsphere. For this purpose, a number of in vitro and in vivo techniques have been reported. In vitro drug release studies have been employed as a quality control procedure in pharmaceutical production, in product development etc. The dosage form in this method is made to adhere at the bottom of the beaker containing the medium and stirred uniformly using overhead stirrer.²³

Diffusion system

This method of microsphere preparation is discovered by Darden & Tomlinson. It consists of four compartments. The

compartment A represents the oral cavity, and initially contained an appropriate concentration of buffer. The compartment B represents the buccal membrane, contained 1-octanol, and compartment C represents body fluids, contained 0.2 M HCl. The compartment D represents protein binding which also contained 1-octanol. Before use, the aqueous phase & 1-octanol were saturated with each other. Samples were withdrawn and returned to compartment A with a syringe 1-octanol. Before use, the aqueous phase and 1-octanol were saturated with each other. After that samples were withdrawn and returned to compartment A with a syringe.²⁴

Modified Keshary Chien cell

A specialized apparatus was designed in the laboratory. It consists of a Keshary Chien cell which contains distilled water (50ml) at 37°C as dissolution medium. TMDDS (Trans Membrane Drug Delivery System) was placed in a glass tube fitted with a 10# Sieve at the bottom which reciprocated in the medium at 30 strokes per min.²⁵

Dissolution studies

Standards USP or BP dissolution apparatus have been used to study in vitro release profiles using both rotating elements, basket 28, 29 & paddle 25, 26, 27. The dissolution medium used for the study varied from 100-500 ml and speed of rotation from 50-100 rpm.²⁶

In vivo methods

The most commonly used methods include in vivo studies using animal models, buccal absorption tests, and perfusion chambers for studying drug permeability. Methods for studying the permeability of intact mucosa consist of techniques that show the biological response of the organism locally or systemically.

In vivo vitro correlation

Correlations between in vitro dissolution rates and the rate & extent of availability as determined by blood concentration & or urinary excretion of drug or metabolites are referred to as "in vitro-in vivo correlations". Such correlations allow one to develop product specifications with bioavailability

APPLICATIONS OF MICROSPHERE

Vaccine delivery

The vaccine is a form of protection against the microorganism or its toxic product. An ideal vaccine must satisfy the requirement of efficacy, safety and convenience in application and cost. Generally biodegradable delivery systems for vaccines that are given by parenteral route may overcome the shortcoming of the conventional vaccines or reduce the problems associated with the conventional vaccine. It acts as a carrier for vaccines delivery since they offer specific advantages including:

- Improved antigenicity by adjuvant action
- Modulation of antigen release



- Stabilization of antigen

Monoclonal antibodies mediated microsphere targeting

There are numbers of antibiotic drugs which are administrate in microsphere form, for better or Improve the efficiency as well as compatibility with other salt. Such as amoxicillin, Ampicillin, tetracycline, sulfadiazine, monoclonal antibodies Targeting microspheres are immunomicrospheres. This targeting Is a method used for selective targeting to the specific sites. Monoclonal antibodies are very Specific molecules. This very specificity of monoclonal antibodies (Mabs) can be utilized to target microspheres loaded drug molecules to selected sites. Monoclonal antibodies can be directly attached to the microspheres by means of covalent coupling. The various free aldehyde groups, amino groups or hydroxyl groups on the surface of the microspheres can be linked to the monoclonal antibodies.²⁷

Nasal drug delivery

In nasal drug delivery system bioadhesive microsphere are used which has great importance because of additional advantages: efficient absorption and enhanced bioavailability of the drug, a much more intimate contact. Due to prolonged contact with nasal mucosal membrane

there will be prolonged therapeutic effect so that the dosing frequency is reduced. IN delivery is needle-free, non-invasive, and essentially painless, does not require sterile preparation, and can be self-administered. For treatment and prevention of nasal symptoms E.g. Rhinitis, allergy, decongestion and local Inflammation etc.^{28,29}

Imaging

The particle size plays an critical role in determining the imaging of particular Sites. The particles which are injected Intravenously apart from the portal vein it will become entrapped in the capillary bed of the lungs. This phenomenon is exploited for the scintigraphic imaging of the tumor masses in lungs using labeled human Serum albumin microspheres.³⁰

Targeted drug delivery

Generally microsphere shows problem residence time at the contact side and therefore provides therapy effect for prolonged time. Microspheres have been Developed for oral, buccal, ocular, rectal, nasal and vaginal routes for either systemic or local effects. There are number of drugs which are given by different route of administration and having good targeting effect some of example are given In below table³¹

Table 1: Targeted drug delivery of drugs by different microspheres

Drug	Route of administration	Polymer used
Acyclovir	Ocular	Chitosan
Insulin	Nasal	Degradable strachmicrospheres and lysophosphatidylcholine
Furosemide	GI	polyglycerol esters of fatty acids
Insulin	Vaginal	Hyaluronic acid esterase

Topical drug delivery

Microsphere plays very important role in topical drug Delivery system. These microsphere having capacity to encapsulate wide range of active ingredients such as emollients, fragrances, essential oils etc.,are used as the topical carries system further, these porous microspheres with active ingredients can be Incorporated into formulations such as creams, lotions and powders.³²

Gastroretentive controlled release system

In which floating systems are low-density systems that have float over the gastric contents and remain in the stomach for a prolonged period than conventional dosage forms. Gastric emptying of dosage form is extremely variable process & ability to control the emptying time is valuable asset For dosage forms, there are several difficulties are faced in designing controlled released systems for better absorption and enhanced the bioavailability. The gastroretentive drug delivery system floats over the gastric content & release drug at slow rate & provide therapeutic effect for prolonged period.³³⁻³⁷

- Chitosan

- Polyacrylate
- Eudragit
- Polyvinyl acetate
- Carbopol
- Polyethylene oxide
- Polycarbonates

Biomedical applications

Microencapsulation has also been used medically for the encapsulation of live cells and vaccines. Biocompatibility can be improved by the encapsulation of artificial cells And biomolecules like peptides, proteins, and hormones, which can prevent unwanted immunological reactions that would lead to inactivation or rejection.³⁸

Pharmaceuticals application

A number of pharmaceutical microencapsulated products are currently on the market, Such as aspirin, theophylline and its derivatives, pancrelipase, vitamins,



Antihypertensives, potassium chloride, progesterone, and contraceptive hormone combinations.³⁹⁻⁴¹

Microencapsulated KCL is used to prevent gastrointestinal complications associated with potassium chloride. Most encapsulation processes are expensive and require significant capital investment for Equipment.⁴²⁻⁴⁵

Table 2: list of various marketed products containing microsphere

Drug	Commercial Name	Company
Risperidone	CONSTA®	Janseen
Naltrexone	VIVITROL®	Alkermes
Leuprolide	LUPRON DEPOT®	TAP
Octreotide	SANDOSTATIN®	Novartis
Somatropin	NUTROPIN®	Genentech
Triptorelin	TRELSTAR®	Pfizer
Buserelin	SUPRECLAR®	Sanofil-aventis
Lanreotide	SOMATULINE®	Ipsen- beafour
Bromocriptine	PARLODEL LAR®	Novartis
Monocycline	ARESTIN®	Orapharma

Acknowledgments: I am very thankful to my guide Ms. Grishma Dalal, the person who makes me to follow the right step during the review project. I expressed my deep sense of gratitude to Ms. Payal Vaja for her guidance, suggestion and expertise at every stage. Apart from that his valuable and expertise, suggestion during documentation of my report indeed help me a lot. I would heartily thankful to head of department Dr. C. J. Tank to give me an opportunity to work over this project and for their endless and great support.

CONCLUSION

Microspheres are better choice of drug delivery system than many other types of drug delivery system. In future by combining various other strategies, microspheres will find the central and significant place In novel drug delivery, microspheres offer several improvements over existing technologies. In recent years there have been increasing numbers of studies in which microspheres have been used in more diverse applications and it is evident that the Range of potential applications is enormous. In Microsphere is a short term but it is having wide applications in drug delivery systems to get desire biological activity. by combining various strategies, microspheres will find central place in novel drug delivery system mainly particularly in cell sorting, diagnostics and genetic engineering. From the study it is proved that microspheres act as a boon in pharmaceuticals.

REFERENCES

- Jain N K, Controlled and Novel drug delivery, 2004; 21: 236-237.
- Sinha V R, Bansal K, Kaushik R, Kumria R, Trehan A. Poly-Caprolactone microspheres and nanospheres, International Journal of Pharmaceutics 2004; 278: 1–23
- Patel J. Bioadhesion is a topic of current interest in the design of controlled or targeted Drug delivery system.
- Patel JK. [www.Pharmainfo.Net/Reviews/Bioadhesive microspheres- review](http://www.pharmainfo.net/reviews/bioadhesive-microspheres-review), 24th Nov 2010.
- Najmuddin M., Ahmed A., Shelar S, Patel V, Khan T. Floating Microspheres Of Ketoprofen: Formulation and Evaluation, International Journal Of Pharmacy and Pharmaceutical sciences. 2010; 2(2): 83-87.
- Chowdary KPR, Yarraguntla SR. Mucoadhesive microsphere for controlled drug Delivery. Biol. Pharm. Bull. 2004; 17: 17-24
- Saralidze K, Leo H., Koole, Menno L, Knetsch W. Polymeric Microspheres for Medical Applications, Materials. 2010; 3: 3357- 64.
- Trivedi P, Verma AML, Garud N. Preparation and Characterization of Acclufenac Microspheres, Asian Journal of pharmaceutics. 2008; 2(2): 110-15.
- Kreuter J, Nefzger M, Liehl E, Czokr. And Voges R. Polymer sci. and tech. J. Pharm. Sci. 1983; 72: 1146
- Jayaprakash S, Halith S M, Mohamed Firthouse P U, Kulaturanpillai K, Abhijith, Nagarajan M. Preparation and Evaluation of biodegradable microspheres of Methotrexate. Asian J Pharm, 2009; 3: 26-9.
- Sinha V R, Singla A K, Wadhawan S, Kaushik R, Kumria R, Bansal K, Dhawan S, Chitosan microspheres as a Potential carrier for drugs, International Journal of Pharmaceutics 2004; 274: 1–33.
- Jain N K, Controlled and Novel drug delivery, 2004; 21: 236-237.
- Remington, Oral Solid Dosage Forms, The Science and Practice of Pharmacy, 1995; 04: 16271628
- Gohel Mukesh C, Parikh R K, Stavan, A Spray drying a Review, pharmainfo, 2009; 7: 5.
- Parikh D, Spray drying as a granulation Technique; In: Handbook of Pharmaceutical Granulation Technology, Drugs and the Pharmaceutical Sciences. New York, Marcel Dekker 1997; 75-96.
- Swarbrick b j, Spray drying and Spray Congealing of Pharmaceuticals, In: Encyclopedia of Pharmaceutical Technology, Marcel Dekker. 1992; 207-221.
- Agusundaram M, MadhuSudanaChetty et al. Microsphere As A Novel Drug Delivery System A Review. International Journal of ChemTech Research. 2009; 1(3): 526-534.
- He P, Davis, S S, Illum, L, Chitosan microspheres prepared by spray drying. Int. J. Pharm, 1999a; 187: 53–65.
- Trivedi P, Verma AML, Garud N. Preparation and Characterization of Acclufenac Microspheres, Asian Journal of pharmaceutics. 2008; 2(2): 110-15.
- Alagusundaram M, Chetty MSC, Umashankari K, Badarinath AV, Lavanya C, Ramkanth S. Microspheres as a Novel Drug Delivery System- A Review. Int. J. of Chem. Tech Res. 2009; 1: 526-34.



21. Mathews BR. And Nixon JR. J. pharm. Pharmacol. 1974; 26: 283.
22. Orienti I, K Aiedeh E. Gianasi V Bertasi and V. Zecchi. Indomethacin loaded chitosan microspheres, correlation between the erosion process and release kinetics. J Microencapsul. 1996; 13: 463-472.
23. Jain NK. Advances in controlled & Novel drug delivery, 03 Edition, 71. CBS publication. Delhi, 2004.
24. Save T, Venkatachalam P. "Bioadhesive tablets of Nifedipine: Standardization of a novel Buccoadhesive erodible carrier". Drug Delivery. Ind. pharm. 1994; 20(19): 3005-14.
25. Lopez CR, Portero A, Vila-Jato JC, Alonso MJ. "Design and Evaluation of Chitosan/ Ethyl cellulose mucoadhesive bilayered devices for buccal drug Delivery." J. control. Rel. 1998; 55: 143-52.
26. Limin M, Yuzhin Z Q L, Zhongwel G, Study on preparation And pharmacodynamics of insulin-loaded polyester Microparticles. Yaoxue Xuebao 2000; 35: 850–853.
27. Shah S, Qaqish R, Patel V, Amiji M, Evaluation of the Factors influencing stomach-specific delivery of Antibacterial agents for Helicobacter pylori infection. J. Pharm. Pharmacol. 1999; 51: 667–672.
28. Giunchedi P, Genta I, Conti B, Muzzarelli R A, Conte U, Preparation and characterization of ampicillin loaded Methylpyrrolidinone chitosan and chitosan Microspheres. Biomaterials, 1998; 19: 157–161.
29. Funden berg H H, Stites D P, Caldwell J L, Wells J V ,In: Basic And clinical immunology, Lange Medical, Los Altosca, 1978; 2: 1346-1348.
30. Critchley H, Davis S S, Farraj N F, Illum L, Nasal absorption of desmopressin in rats and sheep effect of a bioadhesive Microsphere delivery system. J. Pharm. Pharmacol. 1994; 46: 651-656.
31. Lamprecht A, Ubrich N, Hombreiro Perez M, Lehr C, Hoffman M, Maincent P, Influences of process Parameters on nanoparticle preparation performed by a Double emulsion pressure homogenization technique. Int. J. Pharm. 2000; 196: 177–182.
32. Gental I, Conti B, Perugini P, Pavanetto F, Spadaro A, Puglisi G, Bioadhesive microspheres for ophthalmic Administration of Acyclovir. J. Pharm. Pharmacol. 1997; 49: 737-742.
33. Akiyama Y, Nagahara N, Novel formulation approaches to Oral mucoadhesive drug delivery system. In: Mathiowitz E, Chickering DE, Lehr CM. (Eds.), Bioadhesive Drug Delivery Systems-Fundamentals, Novel Approaches and Development 1998; 477–505
34. Geary S, Schlameus H W, Vancomycin and insulin used as Models for oral delivery of peptides. J. Control. Release 1993; 23: 65-74
35. Illum L, Farraj N F, Fisher A N, Gill J, Miglietta M, Benedetti L M, Hyaluronic acid ester microsphere as a nasal delivery System for insulin. J. Control. Release, 1994; 29: 133-141.
36. Punam.G, Floating Microspheres: A Review, Pharmainfo, 2008; 6: 5.
37. Patel J K, Amin A F, Patel M M Formulation optimization And evaluation of controlled release mucoadhesive Microspheres of glipizide for oral drug delivery using Factorial design. Drug Delivery Technology 2004; 4: 48-53
38. Geary S, Schlameus H W, Vancomycin and insulin used as Models for oral delivery of peptides. J. Control. Release, 1993; 23: 65-74
39. Chang, T M S. Artificial Liver and Artificial Cells, Plenum Press, New York, 1978; 34-35
40. Chang, T M S. Biomedical Applications of Microencapsulation, Lim, F., Ed, CRC Press, Boca Raton, FL, 1984; 85.
41. Donbrow, M Microcapsules and Nanoparticles in Medicine and Pharmacy, Donbrow, M, Ed, CRC Press London, 1991; 1–14.
42. Kissel, T , Demirdere, A Controlled Drug Delivery Mu ller , B W, Ed, Wissen-Schaftliche Verlagsge-Sellschaft mbH: Stuttgart, 1984; 103–131.
43. Gurney R , Peppas, N A Harrington, D D, Banks, G S, Dru Dev. Ind. Pharm. 1981; 7: 1–25.
44. MaggiMaggi G C, Di Roberto F M, Microencapsulation Nixon J R, Ed, Marcel Dekker, Inc, New York, 1976; 103–111.
45. Bodmeier R, Wang J, Bhagwatwar H J, Microencaps. J Pharm. sci 1992; 9: 99–107.
46. Koff US patent (March 21963) 3; 080; 292.
47. Seng C H, J Pharm Sci 1995; 74: 399-405.
48. Hirtz J. The git absorption of drugs in man: a review of Current concepts and methods of investigation. Br J Clin Pharmacol 1985; 19: 77-83.
49. Chickering D E, Jacob J S. Matho W E. Reactive Polymers 1995; 25: 189-206.

Source of Support: None declared.

Conflict of Interest: None declared.

For any question relates to this article, please reach us at: editor@globalresearchonline.net

New manuscripts for publication can be submitted at: submit@globalresearchonline.net and submit_ijpsrr@rediffmail.com

Corresponding Author Biography: Mr. Ravirajsinh Gohil



Mr. Ravirajsinh Gohil is currently a student in the Department of Pharmacy, Dr. Subhash Technical Campus, Junagadh. He has good knowledge for programs like Microsoft Word, Microsoft PowerPoint and Microsoft Excel. He has very good academic and extracurricular activities record.

