

Review Article

Microspheres: A Review

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Received 16 November 2018; received in revised form 27 December 2018; accepted 10 January 2019

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ABSTRACT

Microspheres are mostly the spherical in shape. They are consisting of 1-1000 μ m in size. Microspheres made up of natural as well as synthetic polymer. It contains proteins, carbohydrate as well as biodegradable polymer. Microspheres consist of micrometric matrix system. Before and after administration of the drug it provides protection for unstable drug. Microspheres involve various methods like single emulsion, double emulsion, spray drying solvent evaporation. Mucoadhesive, Floating, Radioactive, Magnetic, Polymeric are the different types of microspheres. Microspheres are prepared using a pharmaceutical industry. Microspheres having different microstructures determine the stability of carriers. Microsphere plays an important role in improving the bioavailability of the drug. It is having an ability to incorporate in concentration in drug. It controlled the particle size in aqueous vehicles for an injection. It gives rise to stability of preparation after synthesis. In this objective of article is review the evaluation of microspheres & research work carried out on these systems. This system reviews highlights method of preparation of microspheres, advantages, disadvantages, types, parameters and characterization method of microspheres.

KEYWORDS

Microspheres, method of preparation, application, advantages, disadvantages, types.

1. INTRODUCTION

Microspheres mostly improve the bioavailability of the conventional drug. Microspheres are also called as microparticles. Microspheres are improving quality and particle distribution. Microspheres mostly improve the availability of drug. Microbeads & beads are used alternatively for microspheres. Microspheres are classified into two types such as microcapsules & micromatrices. The spherical shell of microspheres is usually made up of polymer which are having a diameter a micrometer or nanometer range. Microspheres can be used for the controlled release of drugs, vaccines antibiotics & hormones.[1]

Microsphere may be defined as small spherical particles with diameter 1 μm to 1000 μm . Microspheres are free flowing powder consisting of proteins & synthetic polymers. Microspheres are made up of Polymeric waxy or other protective materials. Drug absorption & its side effects due to the irritating drug against the irritating drug against the gastrointestinal mucosa is improved because of small size of microspheres which get widely distributed through the gastrointestinal tract. [2]

Microsphere consists of core of material and polymer matrix. Some materials are coated that is the core of materials. Morphology of microspheres is observed by a scanning electron microscopy. It should provide opportunity for protection & masking. In case of microencapsulation is used to modify & retard drug release. Their small particle sizes are widely distributed throughout the gastrointestinal tract which improves drug absorption & reduces side effects due to localized build-up of irritating drug against the gastrointestinal mucosa. [3]

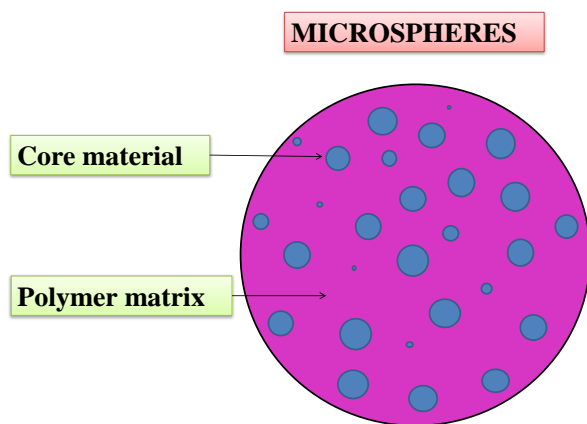


Fig.1. Microspheres

Microspheres may be coated with capture molecules. Capture molecules such as peptides oligonucleotides & antibodies etc. It is used in diagnostic & separation applications. Stability & development time will aid in determining the most fitting coating strategy for both short & long term objectives. Absorption, covalent coupling & affinity binding are the three basic strategies used in microspheres products. Microspheres widely used in quality, particle size distribution & uniformity particles.

2. Material used

Polymers are usually used in microspheres.

2.1 Synthetic Polymers-

- a) **Non-biodegradable polymers-** E.g. Poly methyl methacrylate, Epoxy polymers, Glycidyl methacrylate, Acrolein
- b) **Biodegradable polymers-** E.g. Lactides, Glycolides, Polyanhydrides etc.

2.2 *Natural Polymers-* It obtained from different sources like Proteins, Carbohydrates & chemically modified carbohydrates.

- a. **Proteins-** E.g. Albumin, Gelatin & collagen.
- b. **Carbohydrates-** E.g. Carrageenan, Starch, Chitosan.
- c. **Chemically modified carbohydrates-** E.g. Poly dextran, Poly starch.

3. *Method of Preparation*

For the preparation of microsphere some methods are used which as follows

- (1) Single emulsion method
- (2) Double emulsion method
- (3) Spray drying
- (4) Solvent evaporation
- (5) Ionic gelation method
- (6) Phase inversion method
- (7) Solvent removal
- (8) Polymerization

- 1. Normal polymerization
- 2. Interfacial polymerization

3.1 *Single emulsion method*

Single emulsion method is o/w type. Single emulsion method a long of time used in the preparation of a microsphere. In this method firstly select any aqueous solution of polymer. Stirring it continuously then add the dispersion in an organic phase like chloroform. Then heat it. After the heating there is a chemical crosslinking agent (formaldehyde, glutaraldehyde, di-acid chloride etc.) added. At that time there is a formation of microsphere in an organic phase. Then after the centrifugation, washing and separation there is a formation of microspheres. [4]

3.2 *Double emulsion method*

Double emulsion method is multiple emulsion as well as w/o/w type. In double emulsion method any aqueous solution of polymer or drug then there is dispersion in an organic phase take place. Then primary emulsion occurs. Then Homogenization before the addition of aqueous solution of a polyvinyl alcohol at that time first emulsion gets converted into a multiple emulsion. Solvent get evaporated. Then Addition of a large aqueous phase there is a microsphere in a solution. After the separation, washing & drying there is a formation of microsphere. [5]

3.3 **Spray drying**

Spray drying get occurs when an active material is dissolved or suspended in a melt or a polymer solution and becomes trapped in a dried particles. In this method polymer are dissolved in volatile organic solvent. Drug mostly in solid forms. Then polymer is dispersed in high speed of

homogenization. This is atomized using hot air oven. At that time formation of a small droplet or fine mist from which evaporates which leads to a formation of microspheres. All the microparticles are separated by a hot air by means of cyclone separator while a trace of the solvent is removed by vacuum drying. A lot of years spray drying technique used in microspheres. Mostly spray drying operation is economical. [6]

3.4 Solvent evaporation method

Solvent evaporation is a technique most widely used in a preparation of microspheres. In this method the solvent which is to be evaporated. Firstly there is a polymer which is to be dissolved in a volatile organic solvent with addition of drug particles. Then add the aqueous solution containing surfactant. Continuous stirring on it then agitation system is continued until the solvent particles into the aqueous phase which is to be removed by a solvent evaporation phase. At that time separate and dried the microspheres. [7]

3.5 Ionic gelation method

Ionic gelation method is most important method that is to be used in a preparation of microspheres. Sodium alginate or any other polymer is dissolved in distilled water. Stirring it continuously then viscous dispersion is formed. Then add any active pharmaceutical ingredient. Then take drop wise calcium chloride through syringe. Then added droplets are retained and curing reaction get take place. At that time microspheres are formed & collected by decantation. Product separated, washed & dried at 45 °C for 12 hours. [8]

3.6 Phase inversion method

Phase inversion method is used in the preparation of microspheres. It is a simple & fast method. In this method drug is mix in nonsolvent with unstirred bath. Then there is a microsphere in a solution. Then separate washed & dried.

3.7 Solvent removal

In this method, drug is dissolved or dispersed in a solution of polymer in a volatile mixture of solvents. Then this mixture is suspended in silicon containing span 85 or methylene chloride. After pouring stirred it continuously then the solvent is extracted into oil solution. The resulting microspheres dried in vacuum. [9]

3.8 Polymerization

a) Normal polymerization-

Normal polymerization carried out by different techniques such as emulsion, precipitation, bulk & suspension processes. Emulsion polymerization differ than suspension polymerization because as there is initiator in the aqueous phase, which later on diffuses to the micelles. Drug loading is also done by process of polymerization. Suspension polymerization also called as bead polymerization. In suspension polymerization is done by heating the monomer or mixture of monomers as droplet dispersion in a continuous aqueous phase. Bulk polymerization forms of pure polymers.

b) Interfacial polymerization-

Polymeric membrane are formed when two reactive monomers are dissolved in immiscible solvent, the monomers diffuse to the oil water interface where they react. Then drug is incorporated in polymerization of the medium. Then the suspension is purified to remove various

stabilizers & surfactants employed for polymerization by ultracentrifugation & suspending the particles in an isotonic surfactant-free medium. Interfacial polymerization involves reaction of various monomers at interface between the two immiscible liquid phases to form a film of polymer that essentially envelops the disperse phase.

4. *Criteria for the preparation of microspheres-*

- 1) In aqueous vehicles for injection, controlled the particle size & dispersability.
- 2) Release of active reagent with a good control over a wide time scale.
- 3) Susceptibility to chemical modification.
- 4) Ability to incorporate reasonably high concentrations of the drug.
- 5) Stability of preparation after synthesis with a chemically acceptable shelf life.

5. *Advantages of microspheres*

- 1) Reduce the dosing frequency.
- 2) Improve the patient compliance.
- 3) It provides prolong therapeutic effects.
- 4) It provides protection of drug against the environmental conditions, such as moisture, light etc.
- 5) Duration of action is more.
- 6) Improve the bioavailability of drug.
- 7) Improvement of flow of powder.
- 8) Reduce stability.
- 9) Protects the GIT from irritant effects of the drug. [10]

6. *Disadvantages of microspheres*

- 1) Reproducibility is less.
- 2) High cost.
- 3) Use to reduce the volatility of drugs.
- 4) Retrieval of drug is difficult in case of toxicity and poisoning.
- 5) Multiple formulation steps.
- 6) Proportionally higher need for excipients.
- 7) The modified release from the formulations.
- 8) The fate of polymer additives such as plasticizers, stabilizers, antioxidants & fillers. [11]

7. *Application of Microspheres-*

7.1 Medical application- Used for various viral diseases of the drug. Frequently used for clinical practices of drugs. Used for various diagnostic tests for infectious disease like bacterial, viral or fungal. Release of proteins peptides & hormones over the extended period of time. [12]

7.2 Taste masking- Improve fragrances. Improve flavor. e.g., fish, oils, alkaloids & salts.

7.3 Gene delivery- It includes viral vectors such as cationic liposomes, polycation complexes & also microencapsulated system. In gene delivery viral vectors are highly

efficient & have wide range of cell targets. When they are used in in-vivo they cause immune responses & oncogenic effects.

- 7.4 Vaccine delivery-** Topical delivery of vaccines offers needle based immunizations which including easy of administrations. For avoidance of hepatic first pass metabolisms of drugs. It gives protection against the microorganism or its toxic product. Several parenteral vaccines have been encapsulated in biodegradable polymeric microspheres. It improved the antigenicity by adjuvant action, Modulation of antigen release & stabilization of antigen e.g., diphtheria toxoids.
- 7.5 Ophthalmic drug delivery-** Polymer exhibits various biological behavior such as bioadhesion or permeability enhancing properties which make it a unique material for the drug delivery vehicles. e.g., alginate, gelatin
- 7.6 Drug targeting-** Drug targeting is a specific drug which is targeted to desired sites. Used for targeted drug for anticancer agent as a diagnostics purposes. The therapeutic efficacy of drug relies on its access & specific interaction with receptors. e.g., cornea.
- 7.7 Buccal drug delivery-** Polymers are mostly used in buccal drug delivery. It has bioadhesive or mucoadhesive properties & can act as an absorption enhancer. e.g., sodium alginate.
- 7.8 Enteric coating-** It provides protection against gastric environmental conditions. e.g., Aspirin, Erythromycin.
- 7.9 Cosmetics-** Opaque microspheres give color. e.g., Polyethylene.
- 7.10 Viscosity-** Thickening agent is added to paint to improve viscosity.
- 7.11 Imaging-** Radio labelled microspheres can be imaged by various cells, cell lines, tissue & organs. In imaging of particulate site important factor is particle size range of microspheres. The microspheres have been extensively studied & used for targeting purposes.
- 7.12 Monoclonal antibodies mediated microspheres targeting-** Immuno-microspheres are monoclonal antibodies targeting microspheres. It is important in selective targeting to specific sites. These are extremely specific molecules. This extreme specificity of monoclonal antibodies can be utilized to target microspheres loaded bioactive molecules to selected sites. The Mabs can be attached by microspheres by one of the following methods such as non-specific adsorption, specific adsorption, direct coupling & coupling via reagents etc.
- 7.13 Intratumoral & local drug delivery-** In case of intratumoral & local drug delivery strategies have gained momentum recently as a promising modality in cancer therapy. Polymer film containing paclitaxels were obtained by casting method with high loading efficiencies & chemical integrity of molecules was unaltered during preparation according to study. e.g., Gelatin, Chitosan.
- 7.14 Transdermal drug delivery system-** Provides safe, convenient & pain free self-administrations for the patients. Drug release from the devices is affected by membrane thickness & crosslinking of the film. e.g., Chitosan.
- 7.15 Nasal drug delivery-** Microspheres has been demonstrated to have good bioadhesive characteristics & swell easily when in contact with nasal mucosa increasing

bioavailability & residence times of the drug to the nasal route. Nasal absorption of insulin after administration into polymer powder were found to be the most effective formulation for nasal drug delivery of insulin in sheep compared to chitosan solution.e.g., Starch, Dextran.

7.16 Gastro-retentive drug delivery system- Gastro-retentive drug delivery system is a drug with specific site of absorption in stomach or upper part of intestines. Most of the mucoadhesive capsules are retained in stomach for more than four hours. e.g., Salbutamol, Atenolol. [13]

8. Types of Microspheres-

8.1 Mucoadhesive Microsphere-

They enhance intimate contact with a mucus layer & drug targeting absorption at a site of specific manner. Mucoadhesion means adhesion between two materials, at list one of which on mucosal surface. It gives good bioavailability. It involves various dosage forms like tablets, patches, films chewing gums, gels, spray or patches. In-vitro evaluation of methods includes measuring force of attachments, Viscometric methods, swelling index also In-vivo techniques including GI-transit using radio opaque tablets & Gamma Scintigraphy technique. Mostly the mucus layer transport micro particles into the body. Polymer& its degradation product should be nontoxic. [14]

8.2 Magnetic microspheres-

They are mostly used for targeting the drugs. Magnetic microspheres are important in pharmaceutical industry. It is composed of magnetic microspheres to ensure the magnetic response. In case of any part of body it is adoptable. They are biocompatible easy for surface of modifications. Magnetic carriers receive magnetic responses to the magnetic fields. From incorporated materials that are used for magnetic microspheres are dextran & chitosan etc. Magnetic microspheres are localize the drug to the disease site.

The different types of magnetic microspheres are

- a) **Therapeutic magnetic microspheres:** Used to deliver therapeutic agent to the liver system.
- b) **Diagnostic magnetic microspheres:** Used to imaging liver metastases & also distinguish bowel loops by other abdomen structures by forming nano size particles supra magnetic iron oxides. [15]

8.3 Floating microspheres-

It is also called as hollow microspheres. It is a spherical empty particle without core. Floating microspheres are free flowing of powder important in microsphere preparations. Floating microspheres are a gastro-retentive drug delivery system. In case of oral controlled drug delivery system their GIT time is important. Their outer polymer shell is prepared by spray drying technique. Floating drug delivery has a low density system. It gives rise to higher bioavailability & better patient compliance. This system mostly floating to the gastric content increases the gastric concentration within the flow of microorganisms. It reduces the dosing frequency for a long times. Moreover it also reduces the chances of Striking & dose dumping. It also produces

prolonged therapeutic effects & reduces dosing frequencies. Application of floating microspheres consists of NSAIDS & antibiotics. [16]

8.4 Radioactive microsphere-

Radio emobilisation microspheres size 10-30 nm range. Mostly radioactive microsphere targeted various tumor cells. Radioactive microspheres are useful in a treatment of cancer diseases. They get an injected into arteries provide its better therapeutics effects. They improve patient compliance which is good. Radioactive microspheres assess distribution of cardiac output in animals. Different kinds of radioactive microspheres are α emitters, β emitters, & γ emitters. [17]

8.5 Polymeric microspheres-

They are having an ability to precipitate out during the polymerizations. They are coated with recognition of molecules such as antigens, nucleic acid probes can be coated with hydrophobic dyes. Polymeric microspheres involves different polymers likes natural as well as synthetic polymer. Natural polymers like alginate, cyclodextrins, starch, cellulose etc. Synthetic polymers like polylactic acid, polyanhydrides, polyamides etc. biodegradable & non-biodegradable polymers swell in aqueous medium.

8.6 Bioadhesive microspheres-

The sticking of drug to the membrane by using sticking property of water soluble polymers is called as adhesion. Also the adhesion of drug delivery devices to the mucosal membrane such as buccal, ocular, rectal nasal etc can be termed as bioadhesion. It provides prolong residence time.

9. Recent advancement

9.1 Swine Flu Influenza DNA Vaccine Encapsulated In PLGA Microspheres

Swine flu influenza against DNA vaccine in polylactic co glycolic acid (PLGA) microspheres is prepares by emulsion evaporation method using PLGA as biodegradable matrix formic polymer. DNA vaccine can be used to achieve prolonged released of plasmid DNA.

9.2 Microspheres in Cancer Therapy

The latest trend in cancer therapy is cancer microsphere technology. Formulation of product with maximum therapeutic value & minimum therapeutic value helps in pharmacist. Cancer is a disease in which the abnormal cells are quite similar to the normal cells, with just minute genetic & functional change. There are various microspheres that have been formulated to exploit microspheres technology for targeted drug therapy in various cancers. [18]

9.3 Cosmetic Industry

Cosmetic compositions are disclosed for the treatment of hair or skin, characterized by a content of the new quaternary chitosan derivatives of the formula. Particularly to hair keratin & prove to have hair strengthening & hair conditioning characteristics. For example hair treatment compositions, Gel form.

10. Ideal characteristics of microspheres-

- Critical to the proper function of an assay is may be microsphere size.
- Increases the therapeutic efficacy.
- Susceptibility to chemical modification.
- Stability of preparation after synthesis with a clinically acceptable shelf life.
- Release of active reagent with a good controlled over a wide time scale.

- For use in a diagnostic & separation application, microspheres may be coated with capture molecules Such as antibodies, oligonucleotides & peptides etc.

11. Drug Loading & release kinetics-[19]

Active components are loaded by microspheres by two methods. First is during the preparation of microspheres & second is after the formation of microspheres by incubating them with drug or proteins. The active component can be loaded by Physical entrapment, chemical linkage & surface absorption.

Release of active constituent is most important factor in case of microspheres. The nature of polymer used in preparation as well as nature of active drug used in release profile for the microspheres. Structure morphology of the carrier is release of drug in case of biodegradable as well as non-biodegradable microspheres.

The drug could be released from by microspheres by three methods such as osmotically driven burst mechanism, Pore diffusion mechanism & by erosion or degradation of the polymer.

11.1 Osmotically driven burst mechanism- Water diffuse into the core through biodegradable & non-biodegradable coating. Burst mechanism controlled three factors such as particle size of the microspheres, particle size of the dispersed macromolecule or polymer ratio.

11.2 Pore diffusion mechanism- It penetrating water front continue to diffuse towards the core.

11.3 Erosion or degradation of the polymer- The erosion of polymer changes in the microstructure of carrier as water it leads to the plasticization of the matrix.

12. Evaluation of Microspheres

Drug Entrapments Efficiency-

In drug entrapment efficiency can be determined by allowing washed microspheres to lyse. The lysate is then Subjected to determination of active constitutes as per monograph requirements.

Drug entrapments efficiency can calculated following equation,

$$\% \text{ Entrapments} = \frac{\text{Actual content}}{\text{Theoretical content}} \times 100$$

12.2 Scanning electron microscopy-

In scanning electron microscopy photographs was obtained to identify & confirm spherical nature. Photographs were taken at an acceleration voltage of 20 KV & surface topography of the crystals. Morphology of dispersions was characterized by scanning electron microscopy.

12.3 Fourier transforms infrared spectroscopy-

In Fourier transform infrared spectroscopy, samples were dispersed in potassium bromide (KBr) powder & pellets were made by applying 5 ton pressure. FTIR spectra were obtained by powder diffuse reflectance on FTIR spectrophotometer. It determines the degradation of polymer matrix for carrier system.

12.4 Particle size analysis-

It is carried out by optical microscopy. The ocular micrometer was calibrated with stage micrometer. A 100 microspheres were evaluated & mean diameter was reported. So, the particle size analysis is most important in evaluation of microspheres. Calibrated ocular micrometer used

in microscopic method for determination of particle size of recrystallized samples & spray dried microspheres were determined. The microspheres were dispersed on a microscope slide. A microscopic field was scanned by video camera. The images of scanned field are analyzed by the software. [20]

12.5 Determination of drug content-

Microspheres (0.05gm) were triturated in 10ml of water. Occasional shaking for 8-12 min. & methanol added to produce 100ml of solution. After suitable dilution, take a reading of sample. Drug content was determined from the standard plot.

Microspheres in a particular quantity were dissolve in a solvent & at specified λ_{max} of drug. The drug content of microspheres is estimated.

12.6 Carr's index- [21]

Carr's index was determined from powder volumes at the initial stage & after 1250 tapping to constant volume.

Carr's index was calculated by following equations:

$$\text{Carr's index} = (\text{Tapped density} - \text{Bulk density}) \times 100 / \text{Tapped density}$$

Apparent particle densities of microspheres were measured using a Pycnometer.

12.7 Hausner's ratio-

Hausner's ratio was calculated by following equations:

$$\text{Hausner's ratio} = \text{Tapped density} / \text{Bulk density}$$

12.8 Percentage yield-

Percentage yield was calculated by following equation:

$$\text{Percentage yield} = \text{Weight of microspheres obtained after solvent evaporation} / \text{amount of drug \& polymer used} \times 100$$

12.9 Encapsulation efficiency-[22]

Drug loaded microspheres were powdered & suspended in 100 ml methanolic water solvent. Dispersion was kept for 20 min for continuous mixing with magnetic stirrer & filter using wattmann filter. Then drug content determined spectrophotometrically.

Encapsulation efficiency was calculated by following equation:

$$\text{Encapsulation efficiency} = \text{Practical drug content} / \text{Theoretical drug content} \times 10$$

12.10 Swelling index- [23]

The term swelling factor gives an idea about the mucilage content of drug, hence it is useful in the evaluation of crude drug containing mucilage. Swelling index was determined by measuring the extent of swelling microspheres in the given buffer. To ensure the complete equilibrium, exactly weighed amount of microspheres were allowed to swell in given buffer. The excess surface adhered liquid drops were removed by blotting & the swollen microspheres weighed by using microbalance. Then hydrogel microspheres then dried in oven at 60 °C for 5 hour until there was no change in dried mass of sample.

Swelling index was calculated by following formula,

$$\text{Swelling index} = (\text{mass of swollen microspheres} - \text{mass of dry microspheres} / \text{mass of dried microspheres}) \times 100.$$

12.11 In- vitro methods-

Release studies for different types of microspheres are carried out by using different suitable dissolution media mostly by rotating paddle apparatus. Invitro method is most important method of evaluation of microspheres. [24]

12.12 Differential scanning calorimeter-

DSC study was carried out to detect possible polymorphic transition during the crystallization process. DSC measurements were performed on differential scanning calorimeter with a thermal analyzer. [25]

12.13 Isoelectric point-

Isoelectric point can be determined by micro electrophoresis apparatus. It is used to measure the electrophoretic mobility of microspheres. The electrophoretic mobility can be related to surface contained charge or ion absorption nature of the microspheres.

12.14 Angle of contact-

Angle of contact determines the nature of microspheres in terms of hydrophobicity & hydrophilicity. The thermodynamic property is specific to solid & affected by presence of adsorbed component. At solid, air or water interface angle of contact measured.

12.15 Electron spectroscopy for chemical analysis-

The surface chemistry of the microspheres can be determined using electron spectroscopy for chemical analysis. It provides the determination of atomic composition of the surface. The spectra obtained using electron spectroscopy for chemical analysis can be used to determine the surface degradation of the biodegradable microspheres.

12.16 Density determination-

Using a multi volume pycnometer the density of microspheres can be measured. Firstly accurately weight sample in a cup is placed into a multi volume pycnometer. Helium is introduced at a constant pressure in the chamber & allowed to expand. This results in decrease in pressure in chamber. Two readings of reduction in pressure at initial pressure are noted. From two pressure readings volume & hence the density of microspheres can be determined.

12.17 In-vivo methods-

In-vivo study method used in animal model, buccal absorption tests.

Animal model- It is used mainly for the series of compounds, investigating the mechanisms & usefulness of permeation enhancers & evaluating a set of formulations. The procedure involves anesthetizing the animal followed by administration of dosage forms.

Buccal absorption test- It is a simple & reliable method. It measures the extent of drug loss of the human oral activity for single & multi component mixture of drugs. This test is important for drug structure, contact time, initial drug concentration & pH of the solution while the drug is hold in the oral cavity.

Table 1: Different types of microsphere and their polymer list

Types of microsphere	Polymer list
Mucoadhesive microsphere	Hydroxyl propyl cellulose, Pectin,
Magnetic microsphere	Polycaprolactone

Floating microsphere	Polystyrene
Radioactive microsphere	Ethyl cellulose, HPMC, Polylactic acid
Polymeric microsphere	Agarose, Polyvinyl alcohol
	Albumin, Dextran, Starch, Gelatin, Carrageenam

Table 2: Different parameters and characterization methods for microspheres

Parameters	Characterization methods
Molecular weight	Gel permeation chromatography, Differential refractometer detector
Particle size	Laser defractometry
Zeta potential	Electrophoresis
Solvent removal rate	Laser defractometry
Morphology	Optical & Scanning electron microscopy

2. CONCLUSION

From the present study it was concluded that microspheres are having different applications in drug delivery system. Microsphere improves bioavailability or stability to the specific drugs. They are having different polymers and properties involved in drug delivery system. Microspheres are having different method of preparation in drug delivery systems. Microspheres most important in targeted drug delivery, controlled as well as sustained drug delivery. Apart from that microspheres also allow drug targeting to various systems such as ocular, intranasal & IV route. Hence in the future microspheres, have a different role in advancement of medical field.

3. ACKNOWLEDGEMENT

I would like to thanks to Miss. M. T. Deshmukh madam for much helpful for their guidance. I express my humble thanks to DR. R. V. Shete sir, Prof. Solunke sir other faculty member of Rajgad Dnyanpeeth's college of pharmacy, Bhor, Pune for their valuable help for guidance.

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