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Microsphere A Novel Drug Delivery System – A Review

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ABSTRACT

The microspheres are also called as micro-particles. Microspheres are characteristically spherical & free flowing powders having particle size ranging from 1-1000μm consisting of proteins or synthetic polymers. Microsphere can be manufactured by various type of material such as glass, polymers, and ceramic microspheres Microspheres are used in drug delivery systems to overcome some of the problems of conventional therapy and enhance the therapeutic efficacy of a given drug they are designed. These delivery systems offer numerous advantages compared to conventional dosage forms, which include improved efficacy, reduced toxicity, improved patient compliance and convenience. At the target tissue the drug should deliver in an optimal amount in the right period of time with the minimum side effect & maximum therapeutic effect, to get the desired effect. The microspheres received much attention not only for the prolonged release or controlled drug delivery to improve bioavailability, stability and action at the specific site to predetermined rate but also for targeting of the anticancer drugs to the tumour. Microspheres are various types like Bioadhesive microspheres, Magnetic microspheres, Floating microspheres, radioactive microspheres, Polymeric microspheres, Biodegradable polymeric microspheres, Synthetic polymeric microspheres. The microsphere are spherical microparticles & are used where predictable & consistent particle surface area is important. The microspheres has the drug located centrally within the particle where it is encased within the unique polymeric membrane. This review focuses on types, materials used, drawbacks, advantage & disadvantage.

Keywords - Microsphere, Controlled Drug Delivery, polymethyl methacrylate (PMMA), Bioavailability & Biocompatibility.

I. INTRODUCTION

Microspheres may be defined as microspheres are the substances or compounds which having free flowing property (powders). Microspheres are consisting of proteins or synthetic polymers which are biodegradable in nature and ideally having a particle size from 1-1000μm. Microspheres are also called as

microparticals. Microsphere can be manufactured by various type of material such as glass, polymers, and ceramic microspheres. Micro sphere are two types microcapsules and micrometrics, which are described as, micro-capsules are those in which entrapped substance is distinctly surrounded by distinct capsule wall. And micrometrics in which entrapped substance is dispersed throughout the matrix (see figure 1). Microsphere plays an important role to improve bioavailability of conventional drugs and minimizing side effect [1, 2].

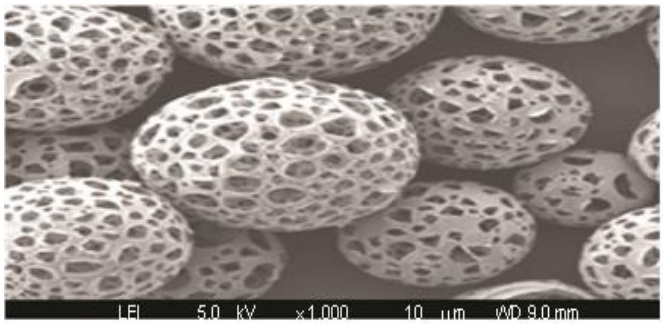


Figure 1 Porous microspheres.

Note: Springer, Colloid and Polymer Science, 291, 2013, [page 19], Double emulsion templated microspheres with flow-through pores at micrometer scale, Microsphere offers the Ball bearing effect due to their size & shape. [3,4] Microspheres vary in quality, sphericity, uniformity of particle and particle size distribution. The appropriate microsphere needs to be chosen for each unique application. To control the drug administration, various opportunities are there for the preparation of microspheres. It facilitates the accurate delivery of small amount of potent drugs and reduced drug concentration at the site other than the target site and protection of labile compound before and after the administration and prior to appearance at the site of action. By coupling the drug with carrier molecules we can change the behavior of drug in-vivo.[5-8]The behavior of carrier molecule can affect the clearance kinetics, tissue metabolism & cellular interaction of drug. The exploitation of these changes in Pharmacodynamics may lead to enhanced therapeutic effect 8. The goal of this controlled drug delivery system is to provide a therapeutic amount of drug at the required site promptly and after achieving therapeutic level, to maintain the desired drug concentration at the site of action [9].

CHARACTERISTICS OF MICROSPHERES:

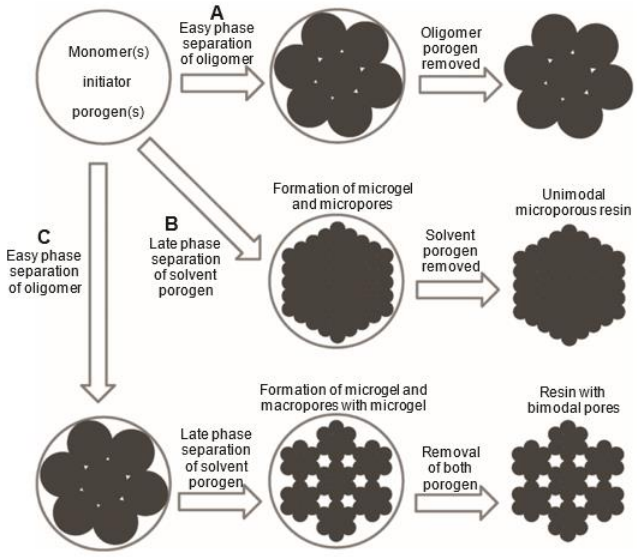
1.Microsphere size may be critical to the proper function of an assay, or it may be secondary to other characteristics. Considering traditional diagnostic methods, the test or assay format commonly dictates particle size, such as the use of very small spheres (~0.1- 0.4µm) to ensure satisfactory wicking in lateral flow tests, or the use of larger, cell-sized spheres (~4-10µm) for bead based flow cytometric assays.[10]

2.Common microsphere compositions include polystyrene (PS), poly(methyl methacrylate) (PMMA), and silica. These materials possess different physical and optical properties, which may present advantages or limitations for different applications. Polymer beads are generally hydrophobic, and as such, have high protein binding abilities. However, they often require the use of some surfactant (e.g. 0.01-0.1% Tween® 20 or SDS) in the storage buffer to ensure ease of handling. During synthesis, functional monomers may be co-polymerized with styrene or methyl methacrylate to develop beads with surface reactive groups. Functional groups may be used in covalent binding reactions, and also aid in stabilizing the suspension. Silica microspheres are inherently hydrophilic and negatively charged. Consequently, aqueous silica suspensions rarely require use of surfactants or other stabilizers. Carboxyl- and amine functionalized silica spheres are available for use in common covalent coating protocols, and plain silica microspheres may be modified using a variety of silanes to generate functional groups or alter surface properties.[10,11]

3. Microspheres may be coated with capture molecules, such as antibodies, oligonucleotides, peptides, etc. for use in diagnostic or separation

applications. Microsphere coatings are typically optimized to achieve desired specific activity, while minimizing nonspecific interactions. Consideration should also be given to the required stability, development time frame and budget, and the specific biomolecule to be coated. These factors will aid in determining the most fitting coating strategy for both short- and long-term objectives. Standard microsphere products support three basic coating strategies: adsorption, covalent coupling, and affinity binding.

4. Many applications in the life sciences demand added properties, such as fluorescence or a visible color, or iron oxide inclusions for magnetic separations. Polymer spheres (and polymer based magnetic spheres) are often internally dyed via organic solvent swelling, and many standard products are available. Dye concentrations can be adjusted to produce beads with different intensities to meet special needs, such as QuantumPlex™ for multiplexed flow cytometric assays, or our Dragon Green or Flash Red Intensity Standards, which support imaging applications and associated instrument QC. Many surface- or internally labelled fluorescent beads are also available as specialized flow cytometry standards [14]



General Properties of Microspheres

1. Biocompatibility with a controllable biodegradability
2. The ability to incorporate reasonably high concentrations of the drug.
3. Stability of the preparation after synthesis with a clinically acceptable shelf life.
4. Controlled particle size and dispersability in aqueous vehicles for injection.
5. Release of active reagent with a good control over a wide time scale
6. Susceptibility to chemical modification

Microspheres have four different types:

1. Bioadhesive microspheres
2. Magnetic microspheres
3. Floating microspheres
4. Radioactive microspheres
5. Polymeric microspheres

i) Biodegradable polymeric microspheres ii) Synthetic polymeric microspheres

1.Bioadhesive microspheres: Adhesion can be defined as sticking of drug to the membrane by using the sticking property of the water- soluble polymers. Bioadhesive microspheres that exhibit mucoadhesive property and permits the drug-coated on the surface of the polymer to stick to the targeted organ, resulting in prolonged delivery of the therapeutic agents to the diseased site. Adhesion of drug delivery device to the mucosal membrane such as buccal, ocular, rectal, nasal etc. can be termed as bio adhesion. These kinds of microspheres shows a prolonged action time at the site of application and causes intimate contact with the absorption site and produces better therapeutic action [15].

2. Magnetic microspheres: This kind of delivery system is very much important which localises the drug to the disease site. In this larger amount of freely circulating drug can be replaced by smaller amount of magnetically targeted drug. Magnetic carriers receive magnetic responses to a magnetic field from incorporated materials that are used for magnetic

microspheres are chitosan, dextran etc. The different types of a. Therapeutic magnetic microspheres used to deliver chemotherapeutic agent to liver tumour. Drugs like proteins and peptides can also be targeted through this system. b. Diagnostic microspheres, used for imaging liver metastases and also can be used to distinguish bowel loops from other abdominal structures by forming nano size particles supramagnetic iron oxides [16].

3. Floating microspheres: In floating types the bulk density is less than the gastric fluid and so remains buoyant in stomach without affecting gastric emptying rate. The drug is released slowly at the desired rate, and the system is found to be floating on gastric content and increases gastric residence and increases fluctuation in plasma concentration. Moreover, it also reduces chances of dose dumping. It produces prolonged therapeutic effect and therefore reduces dosing frequencies. Drug (ketoprofen) is given in the form of floating microspheres [17].

4. Radioactive microspheres: Radio embolization therapy microspheres sized 10-30nm are of larger than the diameter of the capillaries and gets tapped in first capillary bed when they come across. They are injected in the arteries that leads them to tumour of interest so all these conditions radioactive microspheres deliver high radiation dose to the targeted areas without damaging the normal surrounding tissues. It differs from drug delivery system, as radio activity is not released from microspheres but acts from within a radioisotope typical distance and the different kinds of radioactive microspheres are α emitters, β emitters, γ emitters [12,13].

5. Polymeric microspheres: The different types of polymeric microspheres can be classified as follows and they are biodegradable polymeric microspheres and Synthetic polymeric microspheres [13].

i) Biodegradable polymeric microspheres: Natural polymers such as starch are used with the concept that they are biodegradable, biocompatible, and also bio adhesive in nature. Biodegradable polymers prolongs the residence time when contact with mucous membrane due to its high degree of swelling property with aqueous medium, results gel formation. The rate and extent of drug release is controlled by concentration of polymer and the release pattern in a sustained manner. The main drawback is, in clinical use drug loading efficiency of biodegradable microspheres is complex and is difficult to control the drug release. However, they provide wide range of application in microspheres based treatment [14].

ii) Synthetic polymeric microspheres: Synthetic polymeric microspheres are widely used in clinical application, moreover that also used as bulking agent, fillers, embolic particles, drug delivery vehicles etc. and proved to be safe and biocompatible but the main disadvantage of these kind of microspheres, are tend to migrate away from injection site and lead to potential risk, embolism and further organ damage [15].

Advantage

1. They could be injected into the body due to the spherical shape and smaller size.
2. Microsphere morphology allows a controllable variability in degradation and drug release.
3. They facilitate accurate delivery of small quantities of potent drug and reduced concentration of drug at site other than the target organ or tissue.
4. The microspheres have the ability to bind & release the high concentration of the drug.
5. They provide protection for unstable drug before and after administration, prior to their availability at the site of action.
6. The microsphere morphology allows the controllable variability in the drug release & degradation.
7. They provide the ability to manipulate the in vivo action of the drug, pharmacokinetic profile, tissue distribution and cellular interaction of the drug. They enable controlled release of drug.

Examples: Narcotic, Antagonist, Steroid hormones

8. The microspheres avoid first pass metabolism
9. They have Improved protein & peptide drug delivery system.
10. Simple method of preparation. It enhance biological half-life

Disadvantage

1. High molecular weight compounds have limited & restricted loading & their release may be difficult
2. Formulation of complexes with blood compound
3. Difficult to maintain stability of dosage form.
4. Difficult to maintain in Process conditions like change in temperature, pH, solvent addition, and evaporation/agitation may influence the stability of core particles to be encapsulated.
5. The environmental impact of the degradation products of the polymer matrix produced in response to heat, hydrolysis, oxidation, solar radiation or biological agents
6. Require expert to manufacture
7. Relatively complex in operation.

Limitations

1. The modified release from the formulations.
2. The release rate of the controlled release dosage form may vary from a variety of factors like food and the rate of transit though gut.
3. Differences in the release rate from one dose to another.
4. Controlled release formulations generally contain a higher drug load and thus any loss of integrity of the release characteristics of the dosage form may lead to potential toxicity.
5. Dosage forms of this kind should not be crushed or chewed.

II. 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, particularly in diseased cell sorting, diagnostics, gene & genetic materials, safe, targeted, specific and effective in-vitro delivery and supplements as miniature version of diseased organ and tissues in the body. Microspheres are used in the life sciences industry primarily in tools and as consumables in drug discovery and development, clinical diagnostics and biomedical research.

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