Int. J. Drug Dev. & Res.
| October - December 2013 | Vol. 5 | Issue 4 | ISSN 0975-9344 |
www.ijddr.in

Study of incongruent upshot of Microsphere Technology & its Relevance

Om M Bagade*,

Dhanashri R Bhosale,

Dhanashri N Bhargude,

Dhanashree R Kad

Sejal K Kahane

Department of Pharmaceutics, Modern College of Pharmacy for Ladies, Moshi, Pune-412 105

Corresponding Authors:
Om M. Bagade (Asst. Prof)
ombagadescop@gmail.com
Department of Pharmaceutics
Modern College of Pharmacy For Ladies, Moshi, Pune-412 105

Abstract:

Microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers having a particle size ranging from 1-1000 µm. The range of Techniques for the preparation of microspheres offers a Variety of opportunities to control aspects of drug administration and enhance the therapeutic efficacy of a given drug. Microspheric drug delivery system has gained enormous attention due to its wide range of application as it covers targeting the drug to particular site to imaging and helping the diagnostic features.

It also has advantage over liposome as it is physicochemical more stable. Microsphere is a new design of controlled drug delivery system should primarily be aimed achieving more predictable & increased bioavailability of drug, Accurate delivery of small quantities of potent drugs, Protection of labile compounds before and after administration and prior Reduced drug concentrations at sites other than the target organ or tissue, Longer duration of action, etc.

It also has advantage over various other dosage forms like we know for lungs disease now a days aerolised drugs are used for local delivery of drugs but it has disadvantage of shorter duration of action so for sustained release and reducing side effects and hence to achieve better patient compliance microspheres can be used. Moreover the microspheres are of micron size so they can easily fit into various capillary beds which are also having micron size.

Keywords: Microsphere technology, Particle size, SEM, Drug Release kinetics, Absorption.

Review Paper

Introduction

Microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers, which are biodegradable in nature and ideally having a particle size less than 200micrometer.

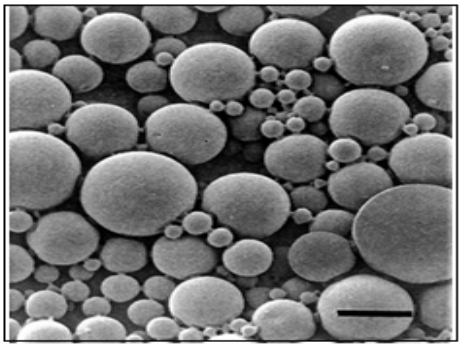


Figure 1: Microspheres

Classification of polymers

Microspheres used usually are polymers. They are classified into two types:

1. Synthetic Polymers
2. Natural polymers

Types of microspheres

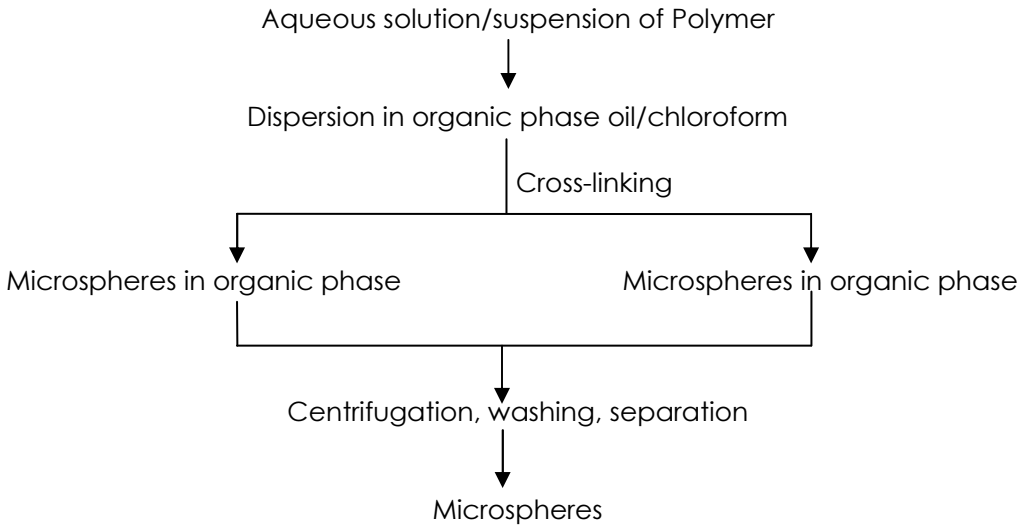
1) Bioadhesive microspheres
2) Magnetic microspheres
3) Floating microspheres
4) Radioactive microspheres
5) Polymeric microspheres
   a. Biodegradable polymeric microspheres
   b. Synthetic polymeric microspheres

GENERAL METHODS OF PREPARATION

1) Single emulsion technique
2) Double emulsion technique
3) Polymerization Techniques
4) Phase separation coacervation technique
5) Spray drying and Spray congealing
6) Solvent Extraction
7) Wax Coating and Hot Melt
8) Spray Coating and Pan Coating
9) Solvent evaporation
10) Freeze Drying
11) Emulsion/Aggregation Technology
12) Brace process

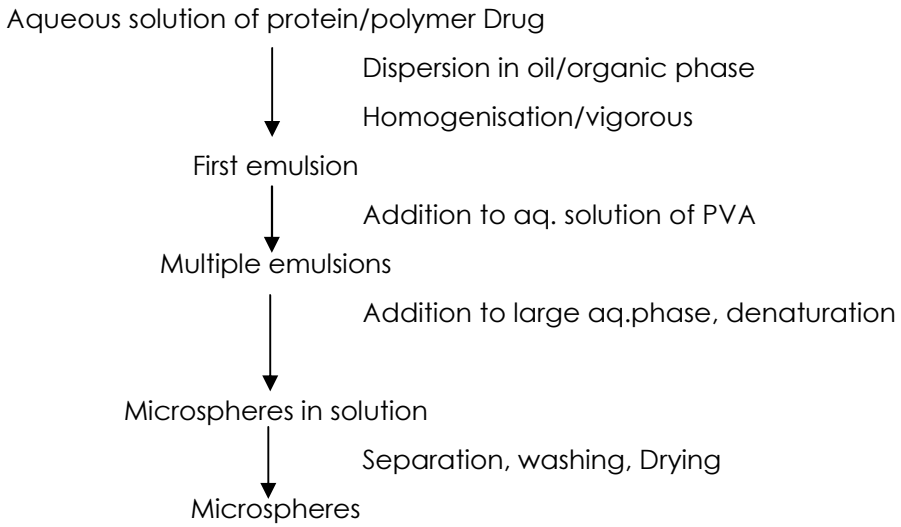
1. Single emulsion technique

The micro particulate carriers of natural polymers i.e. those of proteins and carbohydrates are prepared by single emulsion technique. [3, 4, 5]



2. Double emulsion technique

This method involves the formation of the multiple emulsions or double emulsion of type w/o/w .It is best suited to water soluble drugs, peptides, proteins and vaccines. This method can be used with both the natural as well as the synthetic polymers.[4,7,8]



3. Polymerization Techniques

The polymerisation techniques conventionally used for the preparation of the microspheres are mainly classified as:

i. Normal polymerisation
ii. Interfacial polymerisation

Normal polymerisation:

Normal polymerisation proceeds and is carried out using different techniques as bulk, suspension precipitation, emulsion and micelle polymerisation processes. [6, 9,10]

Bulk polymerisation

Monomer,Bioactive material,Initiator
↓ Polymerisation
Polymer block
↓ Mould/mechanical fragmentation
Microsphers

Suspension polymerisation

Monomer,Bioactive material,Initiator
↓ Dispensed in water and stabiliser
Droplets
↓ PolymerisationVigorous agitation
↓ Heat / irradiation
Separation and Drying
↓
Microspheres

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 of which is dissolved in the continuous phase while the other being dispersed in the continuous phase.

4. Phase separation coacervation technique

Phase separation method is mainly designed for preparing the reservoir type of the system. This method is used to encapsulate water soluble drugs e.g. peptides, proteins and some of preparations having matrix type particular, when the drug is hydrophobic in nature e.g. steroids.[7,8,9]

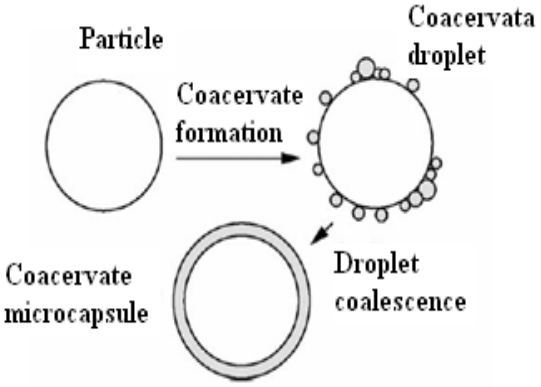


Figure 2: Phase Coacervation

The process is based on the principal of decreasing the solubility of the polymer in the organic phase to affect the formation of the polymer rich phase called the coacervates. The coacervation can be brought about by the addition of the third component to the system which results in the formation of the two phases, one rich in polymer, while other not, i.e. supernant, depleted of the polymer. There are

various methods which are effectively employed for coacervates phase separation. The methods are based on the salt addition, on-solvent addition, addition of the incompatible polymer or change in PH. [10, 11, 12]

5. Spray drying and Spray congealing

Spray drying and spray congealing methods are based on the drying of the mist of the polymer and the drug in the air . Depending upon the removal of the solvent or the cooling of the solution, the two processes are named spray drying and spray congealing respectively. Spray drying is a single-step, closed-system process applicable to a wide variety of materials, including heat-sensitive materials. This process is often used commercially, as a closed system; it is ideal for good manufacturing practice and the production of sterile materials.

The drug and the polymer coating materials are dissolved in a suitable solvent (aqueous or non-aqueous) or the drug may be present as a suspension in the polymer solution. Alternatively, it may be dissolved or suspended within an emulsion or coacervates system.[7, 5, 9]

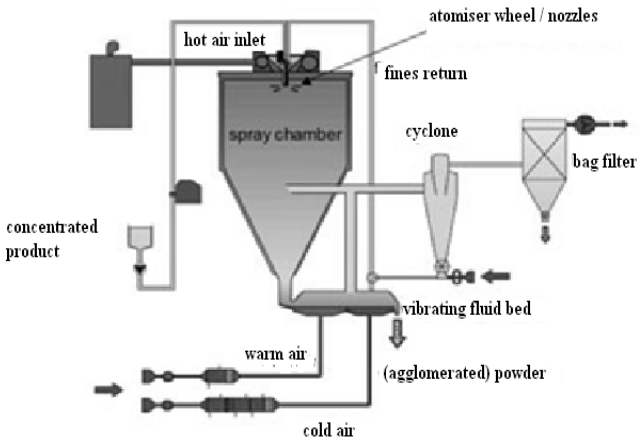


Figure 3: spray dryer

For example, biodegradable polylactide microcapsules can be prepared by dissolving the drug and polymer in methylene chloride. The microsphere size is controlled by the rate of spraying, the feed rate of the polymer drug solution, the nozzle size, the temperature in the drying and collecting chambers, and the size of these two chambers. The quality of spray-dried products is improved by the addition of plasticizers that promote polymer coalescence and film formation and enhance the formation of spherical and smooth surfaced microcapsules. [6,7,9]

6. Solvent Extraction

Solvent extraction method is used for the preparation of the microspheres, involves removal of the organic phase by extraction of the organic solvent. The method involves water miscible organic solvents such as isopropanol. This method is quite good as compared to the other to get the maximum efficiency regarding the good size of microspheres.

Organic phase is removed by extraction with water. This process decreases the hardening time for the microspheres. The process involves direct addition of the drug or protein to polymer organic solution. 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.[10]

Figure 4: Solvent-extraction equipment

7. Wax and Hot Melt (Emulsion techniques)

Wax may be used to coat the core particles, encapsulating drug by dissolution or dispersion in the molten wax. The waxy solution or suspension is dispersed by high speed mixing into a cold solution (such as cold liquid paraffin). The mixture is agitated for at least one hour. The external phase (liquid paraffin) is then decanted and the microcapsules are suspended in a non-miscible solvent, and allowed to air dry. Multiple emulsions may also be formed. For example, a heated aqueous drug solution can be dispersed in molten wax to form a water-in-oil emulsion, which is emulsified in a heated external aqueous phase to form a water-in-oil-in-water emulsion. The system is cooled and the microcapsules collected. For highly aqueous soluble drugs, a nonaqueous phase can be used to prevent loss of drug to the external phase. Another alternative is to rapidly reduce the temperature when the primary emulsion is placed in the external aqueous phase. Wax coated microcapsules, while inexpensive and often used, release drug more rapidly than polymeric microcapsules.

Carnauba wax and beeswax can be used as the coating materials and these can be mixed in order to achieve desired characteristics. Wax coated microcapsules have been successfully tableted. Small aerosol particles, 1–5 mm in diameter, have been condensation coated from a vapour of a fatty acid or paraffin wax. These particles have been shown to exhibit reduced dissolution rates in vitro, corresponding to reduced absorption rates following deposition in the lungs. Polyanhydrides have been chosen for the preparation of microspheres because of their degradation by surface erosion into apparently non-toxic small molecules. The mixture of polymer and active ingredient is suspended in a miscible solvent, heated 5°C above the melting point of the polymer and stirred continuously. The emulsion is stabilized by cooling below the melting point until the droplets solidify. [11]

8. Spray Coating and Pan Coating technique

Spray coating and pan coating employ heat-jacketed coating pans in which the solid drug core particles are rotated and into which the coating material is sprayed. The core particles are in the size range of micrometers up to a few millimetres. The coating material is usually sprayed at an angle from the side into the pan. The process is continued Spray until an even coating is completed. This is the process typically used to coat tablets and capsules. Coating a large number of small particles may provide a safer and more consistent release pattern than coated tablets. In addition, several batches of microspheres can be prepared with different coating thicknesses and mixed to achieve specific controlled release patterns.

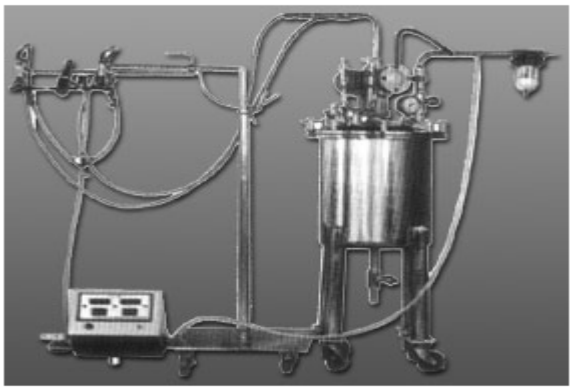


Figure 5: spray coating apparatus

The Wurster process, a variation of the basic pan coating method, is an adaptation of the fluid-bed granulator. The solid core particles are fluidized by air pressure and a spray of dissolved wall material is applied from the perforated bottom of the fluidization chamber parallel to the air stream and onto the solid core particles.

Alternatively, the coating solution can be sprayed from the top or the sides into an upstream of fluidized particles. This adaptation allows the coating of small particles. The fluidized-bed technique produces a more uniform coating thickness than the pan-coating techaniques. Problems can arise with inflammable organic solvents because of the high risk of explosion in the enclosed fluidizer chamber. Explosion proof units have been designed; now. Due to this aqueous coating solutions are being used more. [12,13]

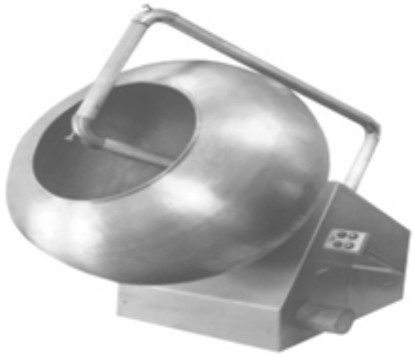


Figure 6: Pan coating apparatus

Examples of aqueous coating solutions include water soluble low molecular weight cellulose ethers, emulsion polymerization latexes of polymethacrylate, and dispersions of water-insoluble polymers such as ethylcellulose, these solvent-free coating solutions provide a range of different coatings such as fast disintegrating isolating layers, enteric and sustained-release coatings.

9. Solvent evaporation technique

This is one of the earliest methods of microsphere manufacture. The polymer and drug must be soluble in an organic solvent, frequently methylene chloride. The solution containing the polymer and the drug may be dispersed in an aqueous phase to form droplets. Continuous mixing and elevated temperatures may be employed to evaporate the more volatile organic solvent and leave the solid polymer–drug particles suspended in an aqueous medium. The particles are finally filtered from the suspension. Following figure shows polylactic acid particles prepared in this manner.

Figure 7: vacuum-flash-evaporator

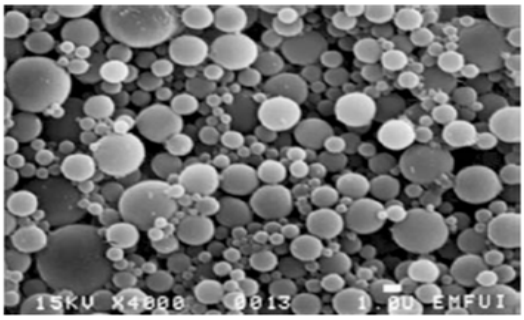


Figure 8: SEM of polylactic acid microsphere containing phenolphthalein prepared by the solvent evaporation method.

10. Freeze drying technique

This technique involves the freezing of the emulsion, the relative freezing points of the continuous and dispersed phases are important.

Figure 9: Freeze-Dryer

The continuous-phase solvent is usually organic and is removed by sublimation at low temperature and pressure. Finally, the dispersed phase solvent of the droplets is removed by sublimation, leaving polymer- drug particles.

11. Chemical and Thermal Cross-Linking technique

Microspheres made from natural polymers are prepared by a cross-linking process; polymers include gelatin, albumin, starch, and dextran. A water–oil emulsion is prepared, where the water phase is a solution of the polymer that contains the drug to be incorporated. The oil phase is a suitable vegetable oil or oil-organic solvent mixture containing an oil-soluble emulsifier. Once the desired water–oil emulsion is formed, the water soluble polymer is solidified by some kind of cross-linking process. This may involve thermal treatment or the addition of a chemical cross-linking agent such as glutaraldehyde to form a stable chemical cross-link as in albumin. If chemical or heat cross-linking is used, the amount of chemical and the period and intensity of heating are critical in determining the release rates and swelling properties of the microspheres. If glutaraldehyde is the crosslinking agent, residual amounts can have toxic effects. [12, 14]

12. The Brace-Process

A liquid is gently pumped through a vibrating nozzle system where upon exiting the fluid stream breaks up into uniform droplets. The surface tension of these droplets moulds them into perfect spheres in which gelation is induced during a short period of free fall. Solidification can be induced in a gaseous and/or liquid medium through cooling, drying, or chemical reaction. There are no constraints on the type of liquid—molten materials, solutions, dispersions, sols, or suspensions can be used to manufacture perfectly spherical Microspheres.

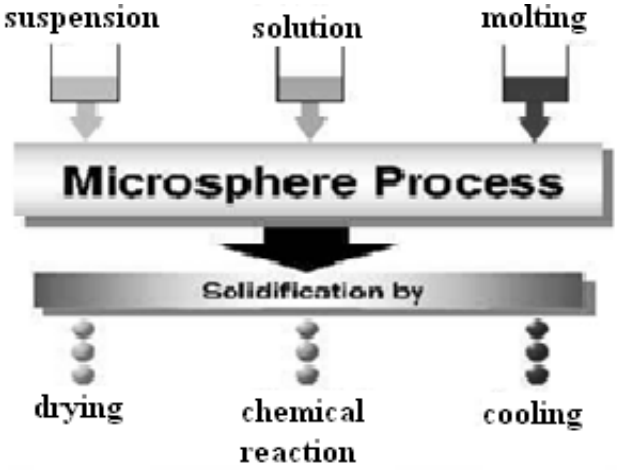


Figure 10: Brace process of microspheres preparation

13. Emulsion/Aggregation Technology

The Emulsion/Aggregation process begins with the preparation of nanometer sized polymer particles stabilized in water using various techniques. These particles are on the order of 10-300 nm in size. A variety of resin types are possible including styrene-based materials, acrylates, polyesters etc. The second step involves the growth of the nanometer-sized particles by mixing in deionized water in the presence of an aggregating agent.

It is at this stage that other ingredients can be incorporated into the particle by adding them as water based dispersions. All of the components are homogenized to ensure effective mixing and continuous mixing is utilized throughout the growth process. Once the desired particle size is reached, the growth process is terminated. Depending on the resin type utilized, the particles generated at this stage are either already spherical or require further treatment to coalesce into spheres. Once the microspheres are formed they can be isolated from the water and washed

to remove the various ions and surfactants used in the process.

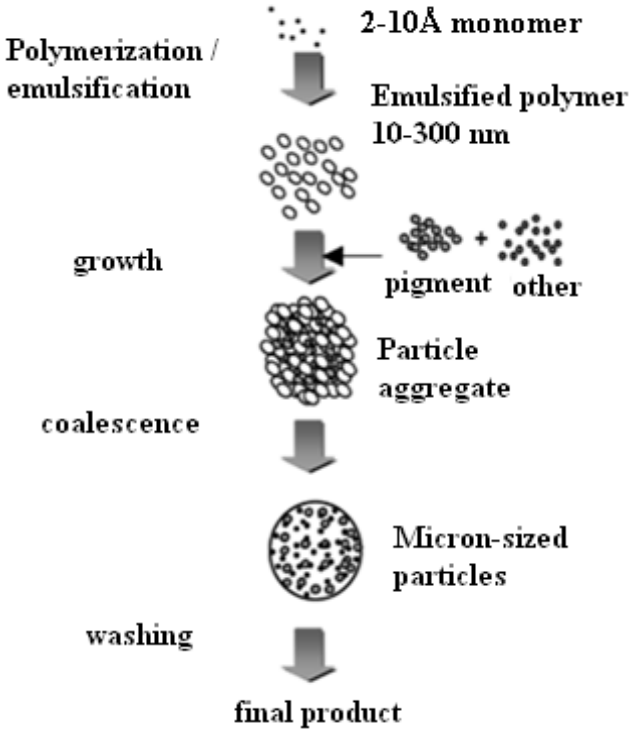


Figure 11: Microsphere preparation by the emulsion aggregation process

DRUG RELEASE KINETICS

Much theoretically possible mechanism may be considered for the release of drug from the microspheres;

i. Libration due to polymer erosion or degradation,
ii. Self diffusion through the pore,
iii. Release from the surface of polymer,
iv. Pulsed delivery initiated by the application of an oscillating or sonic field

In most of the cases, a combination of more than one mechanism for drug of release may operate so the distinct amongst the mechanism is not always trivial. The release profile from the microspheres depends on the nature of the polymer used in the preparation as well as on the nature of the active drug. In case of the biodegradable polymer, the release is controlled by both the erosion as well as diffusion process. The cleavage of the bond is facilitated by the presence of the enzyme (lysozymes) in the surrounding. The erosion of the polymer may be either surfacial or it may be bulk leading to the rapid release of the drug or active component.[7]

Reservoir type system:

Drug release from this type system with the rate controlling membrane proceeds by first penetration of water through the membrane followed by dissolution of the drug in the penetrating dissolution fluid. The dissolved drug after partitioning through the membrane diffuses across the stagnant diffusion layer. The release is essentially governed by the ficks first law of diffusion as

$J = -D (dc/dx)$

Matrix type system:

Release of the drug from the matrix type system is depend on the state of drug whether it is dissolved or dispersed in the polymer matrix. In case of the drug dissolved in the polymer matrix, amount of drug, and nature of polymer (whether hydrophilic or hydrophobic) affect the release profile.

TECHNOLOGY'S

A. Condutosphere Technology

I. Conductospheres are a range of light weight conductive fillers consisting of hollow glass microspheres coated with a thin layer of metal.
II. Conductospheres are a range of lightweight conductive fillers consisting of hollow glass microspheres coated with a thin layer of metal.

III. They can be incorporated into coatings, composites and adhesives to provide these materials with electrical conductivity and shield against electromagnetic interference (EMI).

IV. Due to their hollow core, Conductospheres have very low particle densities and so provide significant weight reductions over conventional solid metal fillers.

V. Conductospheres Silver products offer the highest conductivity and stability, and are available with a range of particle sizes and densities.[21]

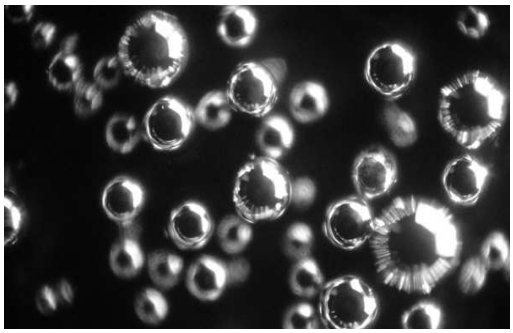


Figure 12: Conductospheres Nickel products are also available from Microsphere Technology

B. Ferrosphere Technology

Microsphere Technology ferrospheres offer a buoyant alternative to conventional magnetic microparticles used in diagnostics and other affinity-based purifications. The ferrosphere-N surface is functionalized with amine group to facilitate conjugation of ligands such as antibodies.

Material Description:

i. Shape: Hollow, thin walled spheres

ii. Composition: Superparamagnetic surface coating on soda-lime-borosilicate glass

iii. Surface functionality: Amine

iv. Coupling capacity: 2-4mg rabbit IgG/g

v. Appearance: Dry, brown powder

C. Micronax Microsphere Technology

i. Microsphere technology provides the highest degree of repositionability of any type of pressure sensitive adhesive (PSA) available. Micronax microsphere technology uses particles – or spheres – that are larger than particles found in conventional emulsion adhesive. The larger size of these still-microscopic spheres has a big impact on adhesive tack.

ii. Conversely, smaller particles used in conventional emulsion adhesives combine into a continuous film that typically does not enable clean removal of labels without damage to the labels or the surface to which they're applied.

iii. The development of micronax microsphere adhesives opens up new possibilities for adhesion to customers in a broad array of industries. They are ideal for use with everything from product decorations, wall graphics, temporary signage and repositionable notes to arts and crafts and advertising pieces.

iv. They also have been approved for FDA indirect food contact and, therefore, have applications in the food-packaging industry.

v. Application versatility grows with the ability of products coated with micronax microspheres to be screen-printed without adversely affecting adhesive performance micronax microsphere adhesives are one of the most exciting developments to emerge from our R&D lab, said Mike Witte, business manager, pressure sensitive adhesives at Franklin Adhesives & Polymers. We are thrilled to expand our PSA offerings to include unique micronax technology and to continue offering our expertise and service

to meet each customer's specific adhesive requirement. [22]

D. Photosphere Technology

i. Developed as a tool for the water treatment industry, Photospheres are titanium dioxide coated hollow microspheres. They are a low density composite material, buoyant in water and showing high Photocatalytic activity against organic pollutants. Unlike titanium dioxide nanoparticles, Photospheres can be easily filtered from treated water without blocking conventional filter materials.

ii. With a mean particle diameter of 45 microns, photospheres therefore represent the optimized handling and activity solution between the high surface areas offered by titanium dioxide nanoparticles, and the low surface areas of titanium dioxide coated panels and piping.

iii. Photospheres can be used in enclosed, artificially illuminated reactor formats using UV light sources. Their buoyancy also enables application in open water systems, such as tanks, ponds and lakes, where solar UV wavelengths stimulate the Photocatalytic activity.

iv. Photospheres have been shown to successfully degrade organic compounds, such as textile dyes and humic acids in aqueous solutions, and NOx gases in atmospheric tests. [23]

E. xMAP Technology

The xMAP technology uses 5.6 micron polystyrene microspheres which are internally dyed with red and infrared fluorophores. Using different amounts of the two dyes for different batches of microspheres, up to 100 different microsphere sets can be created. Each bead is unique with a spectral signature determined by a red and infrared dye mixture. The bead is filled with a specific known ratio of the two dyes. As each microsphere carries a unique signature, the xMAP detection system can identify to which set it belongs. Therefore, multiplexing up to 100 tests in a single reaction volume is possible. [22]

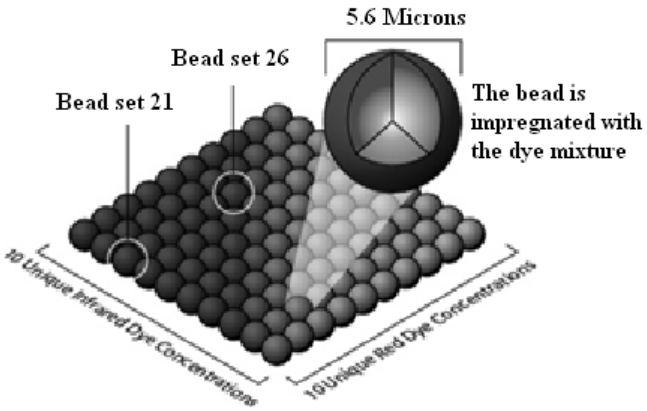


Figure 13: xMAP detection system

Fluidics: The reader detects individual beads by flow cytometry. The fluidics system of the reader aligns the beads into single file as they enter a stream of sheath fluid and then enter a flow cell. Once the beads are in single file within the flow cell, each bead is individually interrogated for bead color (analyte) and assay signal strength (PE fluorescence intensity)

Lasers: The reader uses a 532 nm green laser ("assay" laser) is used to excite the PE dye of the assay (streptavidin-PE). The 635 nm solid state laser (red "classify" laser) is used to excite the dyes inside the beads to determine their "color" or "region" and is also used for doublet discrimination by light.

Detectors: The reader has four detectors, one for each of the optical paths shown in the figure below. Detectors are used to measure the fluorescence of the assay, to make bead determination (1-100) and the last to discriminate between single and aggregate beads.

F. Suspension Array Technology

i. Suspension Array Technology (or SAT) is a high throughput, large-scale, and multiplexed screening platform used in molecular biology.

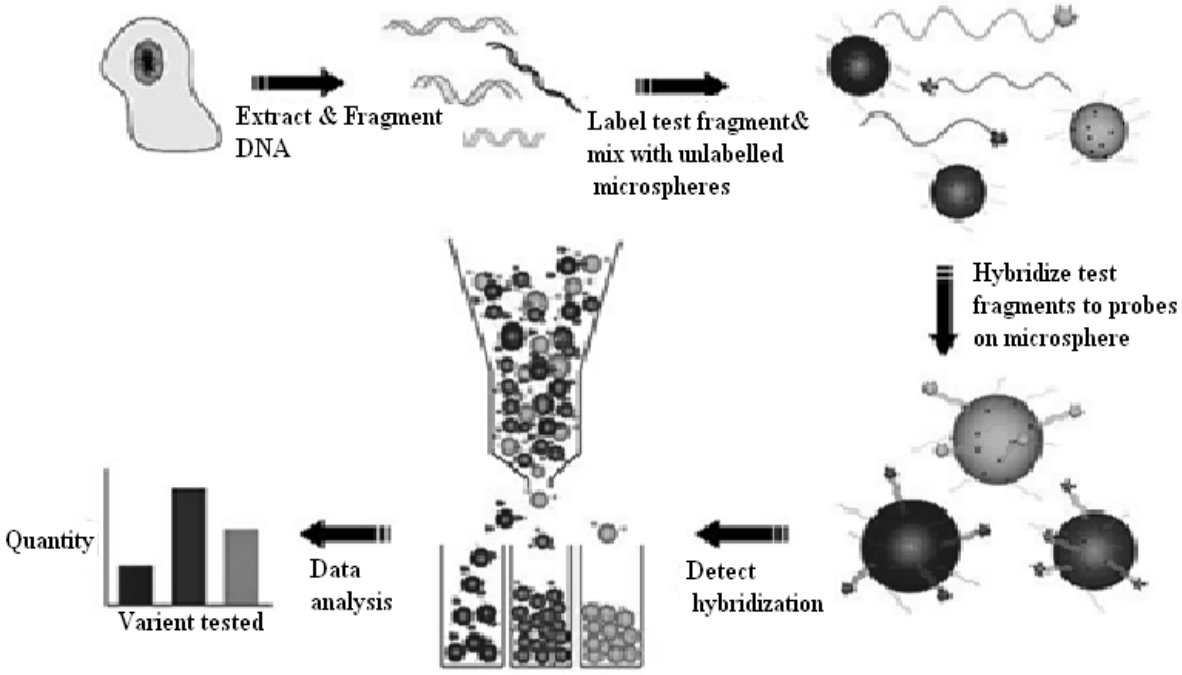


Figure 14: Overview of SAT using DNA hybridization

ii. SAT uses microsphere beads (5.6 um in diameter) to prepare arrays. SAT allows for the simultaneous testing of multiple gene variants through the use of these microsphere beads as each type of microsphere bead has a unique identification based on variations in optical properties, most common is fluorescent colour.

iii. DNA is extracted from cells used to create test fragments. These test fragments are added to a solution containing a variety of microsphere beads. Each type of microsphere bead contains a known DNA probe with a unique fluorescent identity.

iv. Test fragments and probes on the microsphere beads are allowed to hybridize to each other. Once hybridized, the microsphere beads are sorted, usually using flow cytometry. This allows for the detection of each of the gene variants from the original sample. The resulting data collected will indicate the relative abundance of each hybridized sample to the microsphere.

APPLICATIONS OF MICROSPHERES

1. Microspheres in vaccine delivery

The prerequisite of a vaccine is protection against the micro organism or its toxic product. An ideal vaccine must fulfill the requirement of efficacy, safety, convenience in application and cost. The aspect of safety and minimization of adverse reactions a complex issue. The aspect of safety and the degree of the production of antibody responses are closely related to mode of application. Biodegradable delivery systems for vaccines that are given by parenteral route

may overcome the shortcoming of the conventional vaccines. The interest inparenteral (subcutaneous, intramuscular, intradermal) carrier lies since they offer specific advantages including:

1. Improved antigen city by adjuvant action
2. Modulation of antigen release
3. Stabilization of antigen.

2. Targeting using micro particulate carriers

The concept of targeting, i.e. site specific drug delivery is a well established dogma, which is gaining full attention. The therapeutic efficacy of the drug relies on its access and specific interaction with its candidate receptors. The ability to leave the pool in reproducible, efficient and specific manner is enter to drug action mediated by use of a carrier system.[2,4]

3. Monoclonal antibodies mediated microspheres targeting

Monoclonal antibodies targeting microspheres are immune microspheres. This targeting is a method used to achieve selective targeting to the specific sites. Monoclonal antibodies are extremely specific molecules. This extreme specificity of monoclonal antibodies (Mabs) can be utilized to target microspheres loaded bioactive molecules to selected sites. Mabs can be directly attached to the microspheres by means of covalent coupling. The free aldehyde groups, amino groups or hydroxyl groups on the surface of the microspheres can be linked to the antibodies.

Chemoembolisation

Chemoembolisation is an endovascular therapy, which involves the selective arterial emobilisation of a tumour together with simultaneous or subsequent local delivery the chemotherapeutic agent. The theoretical advantage is that such emobilisation will not only provide vascular occlusion but will bring about sustained therapeutic levels of chemotherapeutics in the areas of the tumour.[6,8]

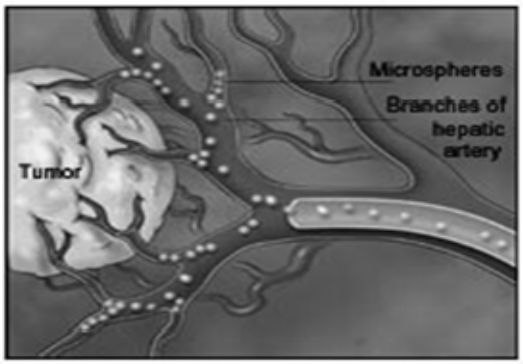


Figure 15: Microspheres injected during chemoembolization lock in chemotherapy

4. Imaging

The microspheres have been extensively studied and used for the targeting purposes. Various cells, cell lines, tissues and organs can be imaged using radio labelled microspheres. The particle size range of microspheres is an important factor in determining the imaging of particular sites. The particles injected intravenously apart from the portal vein will become entrapped in the capillary bed of the lungs. This phenomenon is exploited for the scintiographicimaging of the tumour masses in lungs using labelled human serum albumin microspheres.

5. Topical porous microspheres

Micro sponges are porous microspheres having myriad of interconnected voids of particle size range5-300 µm. These micro sponges having capacity to entrap 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. Micro sponges consist of no collapsible structures with porous surface through which active ingredients are released in a controlled manner.

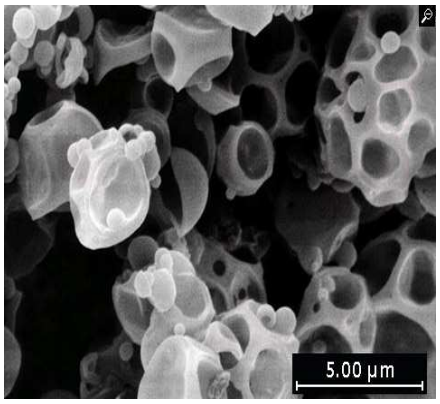


Figure 16: Micro sponges

6. Surface modified microspheres

Different approaches have been utilized to change the surface properties of carriers to protect them against phagocyte clearance and to alter their body distribution patterns. The adsorption of the poloxamer on the surface of the polystyrene, polyester or poly methyl methacrylate microspheres renders them more hydrophilic and hence decreases their MPS uptake. Protein microspheres covalently modified by PEG derivatives show decreased immunogenicity and clearance.

Such modifications are provided surface of microspheres in order to achieve the targeting to the discrete organs and to avoid rapid clearance from the body.

Conclusion

Microspheres offer several improvements over existing technologies. These have emerged as an exciting new platform for biologists to adopt these techniques in the investigation of biomolecules interactions and cellular processes. 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. The future certainly looks bright for these microspheres, particularly in the areas of genomics, proteomics and drug discovery etc. In addition, microspheres have been labeled with a variety of β & emitting radionuclide such as ^{131}I, ^{99m}Tc, ^{113m}In or ^{51}Cr. Such products have been used to scan the heart, brain, liver & gastro intestinal tracts and in a pulmonary perfusion and inhalation studies.

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 effective carriers for the novel drug delivery system

Reference

1) Nithya C., Mahato AK., Dr. Gupta R., International Journal of PharmTech Research, CODEN (USA): IJPRIF, Jan-Mar 2011, Vol.2, No.1, : 675-681.
2) Prasanth VV.et.al. (2011).Microspheres - An Overview, International Journal of research in pharmaceutical and biomedical sciences; 2 (2):332-337.
3) Vasir J. K.et.al. (2003). Bioadhesive microspheres as controlled drug delivery system, International journal of pharmaceutics; 255: 13-32.
4) Senthil A. (2011). Mucoadhesive microspheres, International journal of Research in Ayurveda and Pharmacy; 2(1):55-59.
5) Mumper RJ. and Jay M. (1992).Poly (L-lactic acid) microspheres containing neutron-

activatable Holmium-165: A study of the physical characteristics of microspheres before and after irradiation in a nuclear reactor:149-154.

6) Singh P., et.al. (2011).Biodegradable polymeric microspheres as drug carriers: A Review, Indian Journal of Novel Drug Delivery; 3(2): 70-82.
7) Vyas and Khar. (2001).Targeted and Controlled drug delivery, 1st edition, 417-454.
8) Chien YW., Concepts and System Design For The Rate Controlled Drug Delivery, Novel Drug Delivery System, 1992, 50, 2nd edition, Marcel Dekker New York,:8, 24
9) Wise DL., Microspheres Preparation by Solvent Evaporation Techniques, Handbook of Pharmaceutical Controlled Release Technology, 2000, Marcel Dekker, New York,:186.
10) Jain NK., Biodegradable Microparticals Of Peptide Drugs Using Polylactide Polymers, Advance In Controlled And Novel Drug Delivery, 2005, 1st edition, CBS Publishers and Distributors:12
11) Benita S., Microencapsulation Techniques for Parenteral Depot System And Their Application In The Pharmaceutical Industry, Microencapsulation Method And Industrial Application, 158, 2nd edition, Taylor And Francis:2,8.
12) Swarbrick J. and James CB., Microsphere Technology and Application, Encyclopaedia of Pharmaceutical Technology, 2002, 2, 2nd edition, Marcel Dekker, New York,:1783
13) Raghanaveen by preparation of Biodegradable Microspheres, pharmainfo.net, 2009:1, 2, 3.
14) Heller J., Microparticulate drug carrier, Inn: Robinson JR, Lee VHL editors. Controlled Drug Delivery: Fundamental and application. 29, 2nd edition, Marcel Dekker: New York 1987:555.
15) Jain D., et.al. (2005). Eudragit S100 Entrapped Insulin Microspheres for Oral Delivery, AAPS Pharm SciTech; 6 (1):101-107.
16) Chinna GB., et. al., (2010). Formulation and evaluation of Indomethacin microspheres using natural and synthetic polymers as controlled release dosage form, International Journal of Drug Discovery; 2(1):.8-16.
17) Wei-Qing Z., et.al. (2007). Synthesis of macroporous poly (styrene-divinyl benzene) microspheres by surfactant reverse micelles swelling method, Science direct. Polymer 48.
18) Jayan SC., et.al. (2009).Design and In-vitro evaluation of Gelatin microspheres of salbutamol sulphate, Hygeia; 1(1): 17-20.
19) Mahajan H., et.al. (2009).Spray dried mucoadhesive microspheres of ondansetron for nasal administration. International Journal of Pharmaceutical Sciences and Nanotechnology; 1(1): 268-274.
20) Semalty M., et.al. (2010).Preparation and characterization of gastroretentive floating microspheres of ofloxacin hydrochloride. International journal of pharmaceutical science and nanotechnology; 3(3):819-823.
21) Dunbar, Sherry A., "Applications of Luminex xMAP technology for rapid, high- throughput multiplexed nucleic acid detection". Clinica Chimica Acta 363;.71-82.
22) Nolan, John P., Sklar, Larry A. (2002). "Suspension array technology: evolution of the flat-array paradigm". TRENDS in Biotechnology 20 (1): 912.
23) Prasanth VV , Chakraborthy A., Mathew T., Mathapan R., International Journal of Research in Pharmaceutical and Biomedical Sciences;Vol-2 Apr-Jun 2011.
24) Microencapsulation, August 2005; 22(5): 521 bPaint and Coatings Industry Magazine, January 1st, 2010 : Opaque Polyethylene Microspheres for the coatings applications
25) Cosmetics and Toiletries, April 2010 Issue: Solid Polyethylene Microspheres for effects in color cosmetics.
26) Harikarnpakdee S. Lipipun V., Sutanthavibul N., Ritthidej G., Spray-dried Mucoadhesive Microspheres: Preparation and Transport Through Nasal Cell Monolayer. *AAPS Pharm*

SciTech. 2006; 7(1): Article 12. DOI: 10.1208/pt070112

27) Rajput MS., Agrawal P. Microspheres in Cancer Therapy. Indian Journal of Cancer. 2010; 47(4):458-468.

28) Prabhu P., Nayari M., Yadav B., β-cyclodextrin complexed insulin loaded alginate microspheres oral delivery system, Indian Journal of Pharmaceutical Education and Research, 41 Oct-Dec2007: 329

29) Srisagul S., Sriamornsak P., Preparation of Biodegradable Microspheres and Matrix Devices Containing Naltrexone, Europian Journal of Pharmaceutics and Biopharmaceutics, 69, 1,May 2008: 255.

30) Marks,. Kunath K, Dressman J., Albumin Microspheres as Carriers for the Antiarthritic Drug Celecoxib, Europian Journal of Pharmaceutics and Biopharmaceutic,68, 2, Feb 2008:330.

31) http://www.biospheremed.com/products/embosphere.cfm

32) Jain NK. (2001).Controlled and Novel drug delivery, 4 Edition, 236-237.

33) Patel Nirav R.et.al.(2011).Microspheres as a novel drug delievery,International journal of Pharmacy and Life science;.2:992-997.

34) Prasanth VV.et.al.(2011).Microspheres - An Overview, International Journal of research in pharmaceutical and biomedical sciences;2 (2):332-337.

35) Vasir JK.et.al.(2003).Bioadhesive microspheres as controlled drug delivery system, International journal of pharmaceutics;255:13-32.

36) Senthil A.(2011). Mucoadhesive microspheres, International journal of Research in Ayurveda and Pharmacy;2(1):55-59.

37) Chandrawanshi Pawan.et.al.(2009).Magnetic microsphere: as targeted drug delivery, Journal of Pharmacy Research;2(5):964-966.

38) Jain SK. et.al.(2005).Silicate based microscopheres of repaglinide for gastro-retentive floating drug delivery: Preparation and In-vitro characterization, Journal of Control Release ; 107:300-309.

39) Gholap SB.et.al.(2010). Hollow microsphere : A Review,International Journal of Pharmaceutical Sciences Review and Research;1(1):74-79.

40) Singh BN., Kim KH.(2000).Floating drug delivery systems an approach to oral controlled drug delivery via gastric retention , Journal of Control Release;63:235-259.

41) Mumper RJ and Jay M.(1992).Poly(L-lactic acid) microspheres containing neutron-activatable Holmium-165: A study of the physical characteristics of microspheres before and after irradiation in a nuclear reactor. Pharmaceut. Res;9: 149-154.

42) Surini S.et.al.(2009).Study of Mucoadhesive Microspheres Basedon Pregelatinsed Cassava Starch Succinate as a New Carrier for Drug Delivery, J.Med.Sci;9(6):249-256.

Article History:----------

Date of Submission: 22-06-2013

Date of Acceptance: 29-08-2013

Conflict of Interest: NIL

Source of Support: NONE