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A REVIEW ON MICROSPHERES IN DRUG DELIVERY AS CARRIER

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ABSTRACT

Microspheres are the central novel drug delivery systems consisting of protein or synthetic polymers of free flowing powder having a particle size ranging from 1 to 1000µm. Microspheres show increase in bioavailability with a reduction in dosing frequency, thereby achieving better patient compliance and reduction in toxicity. Compared to the conventional dosage forms this drug delivery can improve its therapeutic efficacy. The purpose of the review is to focus on various type of microspheres like bioadhesive microspheres, floating microspheres, magnetic microspheres, radioactive microspheres, polymeric microspheres and the methods of formulation such as solvent evaporation, spray drying, quasi-emulsion solvent diffusion method, single emulsion technique, double emulsion technique, phase separation, and its wide range of applications when compared to other novel drug delivery systems.

KEYWORDS: Microspheres, Novel Drug Delivery, Patient Compliance, Therapeutic Efficacy.

INTRODUCTION

Microspheres are defined as huge spheres or restorative agents disseminated throughout the medium either as a molecular distribution of particles (or) it can be defined as a structure made up of the continuous phase of one or more miscible polymers in which drug particles are detached at the macroscopic level. It has a particle size ranging from 1-1000nm. Presently oral dosage forms, such as enteric coated/double-layer tablets which release the drug for 12-24hrs still result in unsuccessful systemic delivery of the drug and possible gastrointestinal irritation. Microencapsulation for oral use has been employed to sustain the drug release, and to reduce or eliminate gastrointestinal tract irritation.[1] Microspheres can be formulated from

various natural and synthetic materials. Glass microspheres, Opaque microspheres, Ceramic microspheres, Fluorescent Microspheres are available commercially. Frozen and unfilled microspheres vary widely in density and, therefore, are used for different applications. Unfilled microspheres are typically used as additives to reduce the density of a material.[2] Solid microspheres have numerous applications depending on what material they are constructed of and what size they are. Some are mentioned below:

a) Glass microspheres: They are primarily weighed. Reduction can be done by filler and volumizer for retroreflector for better safety, an additive for cosmetic adhesives with limited applications in medical machinery.

b) Opaque microspheres: Opaque microspheres are greater opacifying agents and gives highest hiding power with just a single layer of microspheres as small as 40 microns in diameter. They can be formulated in any color conceivable and even a combination of two differently colored hemispheres. Opaque microspheres provide an attractive and functional solution to cosmetics, personal care, and skin care industries. The unique advantage of opaque microspheres in cosmetics is the highest hiding power achieved with one invisible and feather-light layer - revolutionizing make-up products.

c) Ceramic microspheres: They are used mainly as grinding media.

d) Fluorescent microspheres: Fluospheres and Trans fluospheres polystyrene fluorescent microspheres can be used for a wide range of applications as well as blood flow determination, tracing, calibration of imaging, in vivo imaging and flow cytometry instruments. Because of dyes included throughout the bead and not just on the surface, they are relatively immune to photobleaching and other ecological factors.[3]

The method of preparation of microspheres offers an assortment of opportunities to manage aspects of drug administration. This comes close to facilitates the precise delivery of a small quantity of the potent drugs, less drug concentration at the site other than the target site and the protection of the labile composite before and after the administration and prior to looking at the site of action. The performance of the drugs in vivo can be manipulated by coupling the drug to a transporter. The tissue distribution, clearance kinetics, metabolism and cellular interaction of the drug are powerfully influenced by the behavior of the carrier.[4]

Prerequisites for Ideal Microsphere Carriers

Some of the ideal characters are

- Release content should be controlled
- Duration of action will be extended
- Improve its therapeutic efficiency
- Reduce in toxicity
- Drug protection will be there
- Sterilizability is present
- Having the biocompatibility
- Having the relative stability
- It has bioresorbability
- Water solubility or dispersibility
- Targetability.[6]

Types of Microsphere

1. Bioadhesive microspheres

Adhesion can be termed as the accumulation of drug to the membrane by the help of sticking mentality of the water-soluble polymers. Mucosa membranes such as buccal, rectal, ocular, nasal etc are the sites of adhesion of drug delivery and it is termed as bioadhesion. This prolonged residence time can result in enhanced absorption and in combination with a controlled release of the drug also improves patient compliance by reducing the frequency of administration.[7]

2. Magnetic microspheres

This kind of delivery system is much more significant which localizes the drug to the disease site. In this bigger amount of freely circulating drug can be changed by the smaller amount of magnetically site targeted drug. Magnetic carriers receive magnetic responses to a magnetic field from incorporated materials that are used for magnetic microspheres are dextran, chitosan etc.[8]

3. Floating microspheres

In case of floating microspheres, The drug is released slowly at the preferred rate, fluctuation caused in plasma concentration due to increase in gastric residence by floating on gastric content. It also reduces the probability of striking and dose dumping.[9]

4. Polymeric microspheres

Polymeric microspheres can be classified as biodegradable polymeric microspheres and synthetic polymeric microspheres.

I. Biodegradable polymeric microspheres

Natural polymers such as starch are used as biodegradable, biocompatible, and they're also bioadhesive in nature. It will extend the residence time when contacted with mucous membrane due to its more swelling characters with an aqueous medium, and results in gel formation. The rate and degree of drug release are controlled by the concentration of polymer and the release pattern in a sustained mode. The main disadvantage is in clinical use. Drug loading competence of biodegradable microspheres is complex and is hard to manage the drug release.

II. Synthetic polymeric microspheres

The attention of synthetic polymeric microspheres are broadly used in the clinical application, and are also used as bulking agent, embolic particles, fillers, drug delivery vehicles etc and proved biocompatibility leads to safer than all these . But the main drawback of these kinds of microspheres tends to move around from the injection site and lead to danger, embolism and further injures the organ.[10]

Types of polymer

Microspheres used polymers are classified into

- Synthetic Polymers
- Natural polymers

➢ **Synthetic polymers are again categorised into two**

(A) Non-biodegradable polymers

Polymethyl methacrylate acrolein (PMMA), Epoxy polymers, Glycidyl methacrylate. Etc are the examples of Non-biodegradable polymers.

(B) Biodegradable polymers

Lactides and Glycolides and their copolymers, Polyanhydrides, Poly alkyl cyanoacrylates and Poly-ε-caprolactone (PCL) are examples of Biodegradable polymers.

- **Natural polymers**

They are found from different sources such as proteins, carbohydrates, and chemically customized carbohydrates. Albumin, Gelatin, and Collagen are the examples of Proteins and Carbohydrates examples like Agarose, Carrageenan, Chitosan, Starch and finally these are the examples of Chemically modified carbohydrates such as Poly dextran, Poly starch.[11]

5. Diagnostic microspheres

These are used for imaging the liver metastases and also can be used to distinguish bowel loops from abdominal structures by the arrangement of nano-size particles supramagnetic iron oxides.

6. Radioactive microspheres

Radioactive microspheres are helpful for lots of therapies, Once the encapsulated diagnostic radioisotopes have been exchanged for therapeutics from the β-emitter group. It is used for the treatment of rheumatoid arthritis, liver tumors, and cystic brain tumors. So their exploitation remains experimental because of slighter than predictable target uptake, unwanted toxicity and inadequate treatment effects that have resulted from radiochemical unsteadiness and suboptimal bio-distribution of theradiopharmaceuticals.[12]

7. Lipid microspheres

Targeting delivery of drugs to the diseased lesions is one of the most important aspects of Drug Delivery System (DDS). To convey a sufficient dose of drugs to the lesion, suitable carriers of drugs are needed. Lipid microspheres have been developed, mainly in Japan, as outstanding carriers of drugs. With advances in medicine and pharmaceutical science, many potent biologically active substances have been introduced into clinical practice. Prostaglandins, cytokines, and other biologically active polypeptides are the substances included. Hormones as potent biological substances are often produced locally when body wants them. Once they enter the systemic circulation, they are rapidly metabolized, to avoid side effects at distant sites. An example which is Prostaglandins. Pharmacological actions affect the whole body by which prostaglandins are administered systemically, and as a result, various side effects occurs. To transport huge number of drugs, suitable carriers are needed. Liposomes are wonderful drug carrier vehicles for DDS. Lipid microspheres, with an average diameter of 0.2 pm, and consisting of soybean oil and lecithin, however, are generally used in clinical medicine for parenteral nutrition. Lipid microspheres themselves are very constant and can be stored for up to 2yrs at room temperature. They have no particular side effects.[13]

8. Mucoadhesive microspheres

Mucoadhesive microspheres are of enormous pharmaceutical attention due to their adhesive nature to the mucous membrane of the eye, nasal cavity and urinary tract. These systems are well set for both systemic as well as localized. It will either consist of an entire mucoadhesive polymer or have an outer coating. Improved bioavailability is due to enhanced absorption of various drugs due to high contact of dosage with mucous membrane and specific drug targeting to the particular site is main use which makes them an effective drug delivery carrier for a variety of drugs.[14]

9. Ocular microspheres

Conventional drug delivery systems which include solutions, suspensions, ointments, gels, and inserts, suffer from the problems such as poor drainage of instilled solutions, tear turnover, poor corneal permeability, nasolacrimal drainage, systemic absorption, and blurred vision. Nanocarrier based approaches seem to be most attracting and are extensively investigated presently. It has been reported that particulate delivery system such as microspheres and nanoparticles; vesicular carriers like liposomes, niosomes, pharmacosomes, improves the pharmacokinetic and pharmacodynamic properties of various types of drug molecules. The maximum size limit for microparticles for ophthalmic administration is about 5-10 mm above which a scratching feeling in the eye can result upon ocular instillation. That is why microspheres and nanoparticles are promising drug carriers for ophthalmic application. Nanospheres made up of polylactic acid (PLA) coated with Poly Ethylene Glycol (PEG) shows better efficacy compared to a conventional dosage form of Acyclovir.[13]

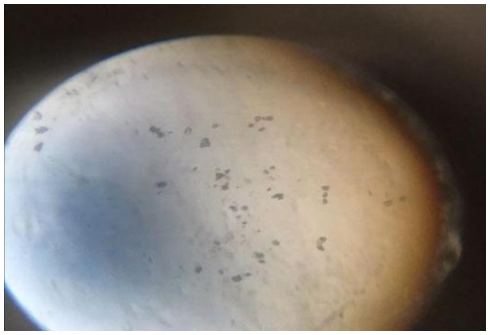
10. Starch microspheres

Starch is one of the plentiful biodegradable polymers that comes under carbohydrate class. It consists of the principle glucopyranose unit, which undergoes hydrolysis to yield D-glucose. It is a polysaccharide consist of a larger number of the free OH groups. By means of these free OH group a large number of the active anticancer agents and narcotic antagonists like cyclophosphamide, cisplatin, and doxorubicin.[15]

11. Structural microspheres

The silica composite microspheres are broadly used in many fields of colloid and material science since they exhibit particular properties that are significantly different from those of large sized material. According to the delivery of silica in the composite microspheres, there are scattered composite microspheres, core-shell composite microspheres, and hollow

microspheres, correspondingly. The composite microsphere with core-shell structure is attracting a great deal of interest because of the diverse applicability of this material.[13]



Photomicrograph of Microspheres

Advantages of Microspheres

- Microspheres have free flowing capacity.
- They are more accurate.
- More precise.
- High coating capability.
- High porosity.
- High density.[5]
- Protection of unstable, sensitive materials from their environments prior to use.
- By preventing degradative reactions and it leads to Self-life enhancement.
- Possibilities for handling Safe and convenient of toxic materials.
- Handling liquids as solids.
- To get better bioavailability.
- To increase the stability.
- Limiting fluctuations within a therapeutic range.
- Decreasing dosing frequency.
- Increasing patient compliance.[16]
- Odour and taste masking.
- Production of sustained-release, controlled-release, and targeted medications.
- For dispensing water-insoluble substance in aqueous media.[17]

Disadvantages

- In vivo- in vitro correlation is poor.
- Cost of the formulation is high.

- Drug recovery is difficult in case of toxicity and poisoning.[5]
- May not be not be compressed.
- The dissimilar release rate from one dose to another.[18]

Limitation

- Lower reproducibility.
- Release modification from the formulations may not be possible.
- Release rate differences between one dose to another.[19]
- The cost of the materials and indulgence of the controlled release formulation are significantly superior to the conventional dosage form.
- The effect of the polymer matrix and preservatives over the environment.
- Stability of the drug and polymer will be changed when the terms and conditions influence.[2]

Applications

1. Role of microspheres in vaccine delivery

The vaccine is a defense requirement against the micro-organism or its toxic product. An ideal vaccine must complete the prerequisite of safety, efficacy, expediency in function and cost. The characteristic of safety and minimization of an adverse reaction is a difficult issue. The part of safety and the amount of the production of the antibody are closely related to the mode of application. Ecological delivery systems for vaccines that are given by parenteral route may conquer the inadequately for the conventional vaccines. The interest in parenteral (subcutaneous, intramuscular, intradermal) carrier deceit since they offer specific compensation including.

- Antigenicity enhanced by adjuvant action.
- Antigen release modulation.
- Stabilization of antigen.[9]

2. Monoclonal antibodies mediated targeting microspheres

Immune microspheres targeting, is a method used to achieve discriminating targeting to the exact sites. Monoclonal antibodies are particularly specific molecules. This great specificity of monoclonal antibodies (Mabs) can be utilized to objective microspheres loaded molecules to chosen sites. Covalent coupling between Mabs and directly attached to the microspheres. Antibodies linked to the surface of the microspheres can be free aldehyde groups, amino

groups or hydroxyl groups. These are the following methods Mabs can be attached to microspheres.

1. Specific adsorption.
2. Nonspecific.
3. Direct coupling.
4. Coupling via reagents.

3. Imaging

The microspheres have been broadly studied and used for the targeting purposes. The image can be used in radiolabeled microspheres for the various cells, cell lines, tissues, and organs. The particle size range of microspheres is a significant factor informative the imaging of particular sites. The particles were injected intravenously apart from the portal vein will become entrapped in the capillary bed of the lungs. This phenomenon is broken for the scintigraphic imaging of the tumor masses in the lungs using labeled human serum albumin microspheres.[20]

4. Topical porous microspheres

Microsponges are absorbent microspheres having a countless of consistent voids of particle size range from 5-300 μm. These microsponges having the ability to entrap wide range of active ingredients such as fragrances, emollients, essential oils etc., are used as the topical carrier systems. Further, these porous microspheres with active ingredients can be incorporated into formulations such as lotions, creams, and powders. Active ingredients are released in a controlled manner when consisting of non-collapsible structures of porous surface microsponges.[21]

5. Surface modified microspheres

Different approaches have been utilized to alter the surface properties of carriers to defend them against phagocytic clearance and to modify their body delivery patterns. The adsorption of the poloxamer on the surface of the polystyrene, polyester or polymethyl methacrylate microspheres renders them more hydrophilic and hence decrease their MPS uptake. Protein microspheres covalently modified by PEG derivatives show decreased immunogenicity and clearance.

The most studied surface modifiers are

1. Antibodies and their fragments

2. Proteins
3. Mono- oligo, and polysaccharides
4. Chelating compounds like EDTA, DTPA or Desferrioxamine

6. Microspheres for DNA delivery

Microspheres have been recently used as a delivery vehicle for the transfer of plasmid DNA which leads to civilizing the transfer of their reliability in the bio-environment.

7. Microspheres for lymph targeting

The main objective of lymph targeting is to give effective anticancer chemotherapy to stop the metastasis of tumor cells by accumulating the drug in the regional lymph node. Poly alkyl cyanoacrylate microspheres bearing anticancer drugs for a tumor of the peritoneal cavity. Poly (lactide-co-glycolide) microspheres for the lymphatic of diagnostic agents are the examples.[22]

8. Chemoembolization

Endovascular therapy a kind of chemoembolization, which concerns the selective arterial embolization of a tumor together with coincident or consequent local delivery the chemotherapeutic agent. The theoretical wages is that such embolizations will not only supply vascular attack but will bring about sustained therapeutic levels of chemotherapeutics in the areas around a tumor. Chemoembolization is an extension of traditional percutaneous embolization techniques.[19]

Application of Microspheres in the Pharmaceutical Industry

1. Oral drug delivery.
2. Ophthalmic drug delivery.
3. Gene delivery.
4. Buccal drug delivery.
5. Intratumoral and local drug delivery.
6. Nasal drug delivery.
7. Gastrointestinal drug delivery.
8. Transdermal drug delivery.
9. Vaginal drug delivery.
10. Colonic drug delivery.
11. Targeting by using microparticulate carriers.[23]

Methods of Preparation

1. Spray Drying.
2. Solvent Evaporation.
3. Single emulsion technique.
4. Double emulsion technique.
5. Phase separation coacervation technique.
6. Spray drying and spray congealing.
7. Solvent extraction.
8. Quasi-emulsion solvent diffusion.

1. Spray drying

It is a most common technique to produce powders or granules from a mixture of drug and polymer solution or suspension. Mainly this method was based on drying of atomized droplets in a stream of hot air. In this method, the drug was dissolved in aqueous acetic acid solution along with polymer or dispersed in it and then add crosslinker. By using hot air the solution or dispersion was atomized. So it leads to the formation of small droplets from which solvent evaporates and the formation of free-flowing microparticles.[24]

2. Solvent evaporation

In this method, the drug and the polymer has been added into an organic solvent, in methylene chloride and solubilized properly. The current solution containing polymer and drug may be distributed in an aqueous phase to form droplets. Solid polymer-drug particles suspended in an aqueous medium due to continuous mixing and elevated temperatures may be employed to evaporate the more volatile organic solvents. Finally it is filtered from the suspension to get microparticles.[25]

3. Single emulsion technique

Proteins and carbohydrates are prepared by single emulsion technique. The natural polymers are dispersed in an aqueous medium followed by dispersion in oil as a non-aqueous medium. Cross-linking of the dispersed globules are carried out in the next step. The cross-linking can be reached either by means of chemical crosslinkers or by using heat. Formaldehyde, glutaraldehyde, acid chloride are some of the chemical cross-linkers. Heat denaturation is not appropriate for thermolabile substances. Chemical cross-linking suffers the drawback of excessive disclosure of active ingredients when added at the time of preparation and then subjected to centrifugation, washing, separation. The emulsion phases can greatly be

influenced by size, size distribution, surface morphology, drug release, loading, and bio performance of the final multi-particulate product due to nature of the surfactants used to stabilize.[16]

4. Double emulsion technique

This method is most suitable for water-soluble drugs, peptides, proteins, and the vaccines involves the formation of the multiple emulsions or the double emulsion of w/o/w type. Mainly both natural, as well as synthetic polymers, can be used. The aqueous active constituent's of a solution is discrete in a lipophilic organic continuous phase. The continuous phase usually consists of the polymer solution that ultimately encapsulates of the active constituents contained in a dispersed aqueous phase. The primary emulsion is then subjected to homogenization or the sonication before addition to the aqueous solution. This leads to the formation of a multiple emulsion.[26]

5. Phase separation co-acervation technique

This method is based on the principle of reducing the solubility of the polymer in the organic phase to disturb the formation of the polymer-rich phase called the coacervates. The drug particles are dispersed in a solution of the polymer which is incompatible, added to the system which makes the first polymer to phase distinct and immerse the drug particles. Solidification of the polymer happens with the addition of non-solvent. The variables are significant since the rate of achieving the coacervates determines the distribution of the polymer film, the particle size, and agglomeration of the formed particles. The accumulation must be avoided by stirring the suspension using a suitable stirrer at high speed, meanwhile the process of microspheres formation begins when the formed polymerize globules start to stick and form agglomerates. Hence the process variables are critical as they control the kinetics of the formed particles since there is no clear statement of balanced attainment.[16]

6. Spray drying and spray congealing

These methods are based on the principle of drying the mist of the polymer and drug in the air. Depending upon the elimination of the solvent or cooling of the solution, the two processes are called spray drying and spray congealing respectively. The polymer is first dissolved in a suitable volatile organic solvent such as dichloromethane and acetone, etc. Under high-speed homogenization, the drug in the solid form was dispersed in the polymer solution. Then it was atomized in a stream of hot air. The atomization leads to the development of fine mist or small droplets from which the solvent evaporates rapidly leading

the formation of the microspheres in a size range of 1-1000µm. With The help of hot air by means of cyclone separator are used to separate small particles and it leads to traces of solvent are removed by vacuum drying. The spray drying process is used to encapsulate numerous penicillins.[27]

7. Solvent extraction

In this method, preparation of microparticles, involves the removal of the organic phase by extraction of the organic solvent. Isopropanol can be used as water-miscible organic solvent and when extraction with water, Organic phase is removed. Hardening time of microsphere can be decreased by this method. One variation of the process involves the 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, the ratio of emulsion volume to the water and the solubility profile of the polymer.[28]

8. Quasi-emulsion solvent diffusion

A new novel quasi-emulsion solvent diffusion method to formulate sustained and controlled release microspheres. Microspheres can be manufactured by this method using distilled water and polyvinyl alcohol as an external phase, and drug, ethanol, and a polymer consisting of the internal phase. At first, the internal phase is prepared at 60 C and then added to the external phase at room temperature. After the emulsification process, the mixture is continuously stirred for 2 hours. Then the mixture can be filtered to separate the microspheres. The product is then washed and dried by vacuum oven at 40°C for a day.[29]

Factors Influencing Properties of Microspheres

1. Polymers commonly used to formulate microspheres.
2. Choice of solvent

- It should be able to dissolve the chosen polymer.
- Should be Poorly soluble in the continuous phase.
- High volatility and a low boiling point.
- Low toxicity.
- Alternative components (Dispersed phase).

(a) Co-solvent

The organic solvents miscible with water such as methanol and ethanol.

(b) Porosity generator

It will increase the degradation rate of the polymer and improves drug release rate.

Examples: Incorporating Sephadex (Cross-linked dextran gel) into insulin–PLA microspheres significantly increases microsphere porosity.

(3) Continuous phase

(a) Surfactant

- It reduces the surface tension of continuous phase.
- Avoids the coalescence and agglomeration of drops.
- Stabilizes the emulsion.

Widely used stabilizers include

i. Non-ionic: Methylcellulose, Tween, Span.

ii. Anionic: Sodium Dodecyl Sulphate (SDS), Sodium Lauryl Sulphate(SLS).

iii. Cationic: Acetyltrimethyl ammonium bromide.[30]

Characterization/ Evaluation of Microspheres

1. Particle size analyzer

Particle size characterization is an important category to ensure that the particle size of the formulation lies in the optimal range. Different variety of methods which employ physical principles for the identification of size include.

(A) Manual

a) Optical Microscopy

b) Electron Microscopy –

i. Transmission electron microscopy.

ii. Scanning electron microscopy

c) Sieving

d) Sedimentation (Andreason pipette method)

(B) Automated

a) Particle counters

(i) Optical particle counting

(ii) The counter principle

(iii) Permeability

(iv) Impaction & inertial techniques

b) Light Scattering

(i) Dynamic light scattering

(ii) Enhance laser diffraction

c) Flow cytometry

d) Field flow fractionation.[31]

2. Optical microscopy

This method is used to determine the particle size by using an optical microscope (Meizer OPTIK). The measurement is done under 450x (10x eyepiece and 45x objective) and 100 particles were calculated.

3. Scanning electron microscopy (SEM)

Surface morphology was determined by the method SEM. In this method, microcapsule were mounted directly on the SEM sample slub with the help of a double-sided sticking tape and coated with the gold film under reduced pressure.[32]

4. Swelling index

This technique was used for the identification of microspheres were performed with swelling index technique. Different solutions (each 100ml) were taken such as (distilled water, buffer solution of ph (1.2, 4.5, 7.4) were taken and microspheres (100mg) were placed in a wire basket and kept on the above solution and the swelling was done at 37ºc and changes in weight variation between initial weight of microspheres and weight due to swelling was measured by taking weight periodically and soaking with filter paper.[33]

5. Entrapment efficiency

Microspheres containing drug (5mg) are crushed and then dissolved in distilled water with the help of ultrasonic stirrer for 3 hrs, then filtered and assayed by UV-visible spectroscopy.

Entrapment efficiency = actual drug content/theoretical drug content.

6. X-ray diffraction

Change in crystallinity of the drug can be determined by this technique. Microparticles and its individual components were analyzed with the help of D & discover (Bruker, Germany). scanning range angle between 60ºc - 70 ºc. Scan speed - 4o/minscintillation detector primary silt=1mm Secondary silt=0.6 mm.

7. Thermal analysis

Thermal analysis of microcapsule and its component can be done by using-Differential scanning calorimetry (DSC), Thermogravimetric analysis (TGA), Differential thermometric analysis (DTA). Accurately the sample was weighed and heated in an alumina pan at a constant rate of 10oc/min under a nitrogen flow of 40 ml/min.

8. UV-FTIR (Fourier Transform Infrared Spectroscopy)

The drug-polymer interaction and also degradation of the drug while processing microencapsulation can be determined by FTIR.

9. Zeta potential

The polyelectrolyte shell was prepared by incorporating chitosan of different molecular weight into the W2 phase and the resulting particles1 were determined by zeta potential measurement.[32]

10. Dissolution apparatus

Dissolution apparatus like Standard USP or BP have been used to study *in-vitro* release profile susing rotating elements such as paddle, and basket type. Dissolution medium mainly varied from 100- 500ml and 50-100rpm as the speed of rotation.

11. Iso-electric point

The microelectrophoresis is an apparatus used to find out electrophoretic mobility of microspheres from which isoelectric point is determined. The electrophoretic mobility can be related to surface contained charge, ionizable behavior or ion absorption and nature of the microspheres.[34]

12. Angle of contact

The angle of contact is measured to determine the wetting property of a microparticulate carrier. It characterizes the nature of microspheres in terms of hydrophilicity or hydrophobicity. This thermodynamic property is specific to solid and is affected by the

presence of the adsorbed component. The angle of contact is measured at the solid/air/water interface. The advancing and receding angle of contact is measured by placing a droplet in a circular cell mounted above the objective of the inverted microscope. The contact angle is measured at 2000C within a minute of deposition of microspheres.[35]

13. Beaker method

The dosage form in this method is made to adhere at the bottom of a beaker containing the medium and stirred uniformly using overhead stirrer.[5] The volume of the medium used in the literature for the studies varies from 50-500 ml and the stirrer speed form 60-300 rpm.[36]

CONCLUSION

Microspheres are having wide applications in drug delivery system. Most important are the targeted drug delivery, controlled and sustained drug delivery. By combining various strategies, microspheres will find central place in novel drug delivery particularly in cell sorting, diagnosis and Genetic engineering.

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