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A BRIEF REVIEW ON MICROSPHARES

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ABSTRACT
Microspheres are the many molecular drug delivery systems which are consist from natural and synthetic material. Microsphere make drug bioavailable, stable and target the drug to specific site at predetermined rate and it is particularly used in novel drug delivery system. Microspheres are features free flowing powders having particle size ranging from 1-1000 µm consisting of proteins or synthetic polymers. The techniques for the preparation of microspheres provides various options to control as drug administration aspects and increased the therapeutic efficacy of a given the drug. The microspheres delivery system is very useful and it give many advantages compared to others dosage forms, which include efficacy of drugs, reduced the toxicity of drugs, improved patient compliance and convenience. Such as system often use macromolecules as carriers for the drugs. The many types of microspheres are available such as Bioadhesive, Magnetic, Floating, Radioactive, Polymeric microspheres, Biodegradable polymeric microspheres, Synthetic polymeric microspheres etc. The Solvent Evaporation, Spray Drying, Single and double emulsion technique, Phase separation coacervation technique, Spray drying and spray congealing, Solvent extraction, emulsion solvent diffusion etc. are the most important methods of preparation of microspheres. Microspheres have large area of applications because of controlled and sustained release.

KEYWORDS: Microspheres, Types, Preparation, Application.

INTRODUCTION[1-10]
Drug delivery system target drug to the specific body site which having large impact on the healthcare system. The ideal drug delivery system delivers the drug at rate decided by need of body throughout the period of treatment therefore carrier technology find out the intelligent approach for drug delivery by coupling the drug to carrier particles example, microspheres, nanoparticles, liposomes. Oral route of drug administration iseasyroute for taking medication. Microspheres are small spherical particles which diameter 1um to 1000um. Microsphere are the free fluent particles which are consisting of proteins or synthetic polymers this are biodegradable in nature. Microspheres are used in development of new drug delivery system for controlled release of drug.

There are two types of microspheres

1. Microcapsule-entrapped substance distinct surrounded by distinct capsule wall.
2. Micromeritics-entrapped substance is dispersed throughout the matrix.

IDEAL PROPERTIES[11]
1. The ability to incorporatedproper a high concentration of the drug.
1. **2.**The Stability of the preparation after synthesis with a clinically acceptable shelf life.
2. Controlled particle size and dispersible in aqueous vehicles for injection.
3. Release of the active reagent with a good control a wide time scale.
4. Biocompatibility with a controllable biodegradability.
5. Susceptibility to chemical modification.
6. Control of content release
7. Increase therapeutic efficiency
8. Reduction of toxicity
9. Sterilizability

ADVANTAGE[12]
1. Theyprovide protect before after administration for unstable drug.
2. They decrease concentration of drug and site other than the tissue or the target organ.
3. Decrease dose and toxicity.
4. Particle size reduction for enhance solubility of poorly soluble of the drugs.
5. Provide constant and prolonged therapeutic effect.
6. Provide constant drug concentration in blood there by increasing patent compliance.

7. Protect the drug from enzymatic and photolytic cleavage hence found to be best for drug delivery of protein.
8. Reduce the dosing frequency and thereby improve the patient compliance.
9. Better drug utilization will improve the bioavailability and reduce the incidence or intensity of adverseeffects.
10. Microsphere morphology allows a controllable variability in degradation and drug release.
11. Convert liquid to solid form & to mask the bitter taste.
12. Protects the GIT from irritant effects of the drug.
13. They Biodegradable microspheres have the advantage large polymer implants in that they do not required surgical procedures for the implantation and removal.
14. Controlled release drug delivery biodegradable microspheres are used to control drug release ratethereby decreasing toxic side effects, and elimination the inconvenience of repeated injections.

DISADVANTAGE[9,14,15]

1. In the formulations many varieties of factors like intrinsic and extrinsic factors, food and the rate of transit through gut.
2. One dose produces different type release rate.
3. Microspheres should not be crushed or chewed.
4. Drug loading for controlled release parental is less than 50%.
5. In the case of produce toxic effect/adverse effect remove the carrier completely from the body is very difficult.
6. In the case ofparental delivery of microsphere may interact with the blood component is difficulty.
7. This doses form is very expensive.
8. The fate of polymer additives.
9. Lessreproducibility.
10. The environment change may influence the stability of core particles to be encapsulated.
11. Environmental impact is very important for the doses form and it degradation products of the polymer matrix produced in response to heat, hydrolysis, oxidation, solar radiation or biological agents.

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

1. Bioadhesive microspheres[6,3,1]

The sticking of drug to membrane by using the sticking property can be define Adhesion of thewatermiscible polymers. This type of microspheres exhibits a prolong residence time atsite of application. drug delivery adhesion of the device to mucosal membrane such as the buccal, ocular, rectal, nasal etc.

2. Magnetic microspheres[2,6]

This type of delivery system is very much important for localizes the drug to the disease site. In which abundant amount of freely straggling drug can be replace by small amount of magnetically targeted drug. The Magnetic carriers received magnetic response to the magnetic field.

3. Floating microspheres[2,10]

In the floating microspherethe bulk density is less than the gastric fluid therefore it remains buoyant in stomach without affecting on gastric emptying rate. Drug is released slowly at the desired rate of the site. it also reduces chances of striking and dose dumping Produces.

4. Radioactive microspheres[6]

Radio embolization therapy microspheres having sized 10- 30 nm are of larger than capillaries. They are injected in to the arteries which lead to tumor of interest. These radioactive microspheres delivery high radiation dose to targeted area without harm the normal tissues. The Different type of the radioactive microspheres are α emitters, β emitters, γ emitters.

5. Polymeric microspheres

The different types of polymeric microspheres classified as -

1) Biodegradable polymeric microsphere[2,6]

The natural polymers are used to the starch concept that they are biodegradable, biocompatible, and bioadhesion in nature. Thispolymerprolonged residence time when touch the mucous membrane due to high degree of swelling property with aqueous medium, results get gel formation.

2) Synthetic polymeric microspheres[10,16,17,18]

The synthetic polymer microspheres are used to clinical application,and also used as bulking agent, fillers, embolic particles and drug delivery vehicles etc. synthetic polymer ismore safe and biocompatible but the some limitation of these kind of microspheres, are tend to migrate away from injection site and lead to potential risk, embolism further organ damage.

METHOD OFPREPRATION

1. Spray Drying
2. Solvent Evaporation
3. Single emulsion technique
4. Double emulsion technique
5. Phase separation coacervation technique
6. Solvent extraction
7. Quasi emulsion solvent diffusion

1. Spray drying[7]

In this technique, the firstly polymer is dissolved in avolatile organic solvent like dichloromethane, acetone, etc. The drug is solid form then disperse in the polymer

solution with a more high-speed homogenization. The dispersion is atomized in a stream of hot air. Atomizationdirection to made up of the small droplets or the fine mist from which the solvent evaporated immediately leading the creation of the microspheres in a size range 1-100µm. Micro-particles are distinct from the hot air with the help of cyclone separator until the trace of the solvent is removed by vacuum drying. Thesemajor advantages one of this process is feasibility of operation under aseptic conditions.

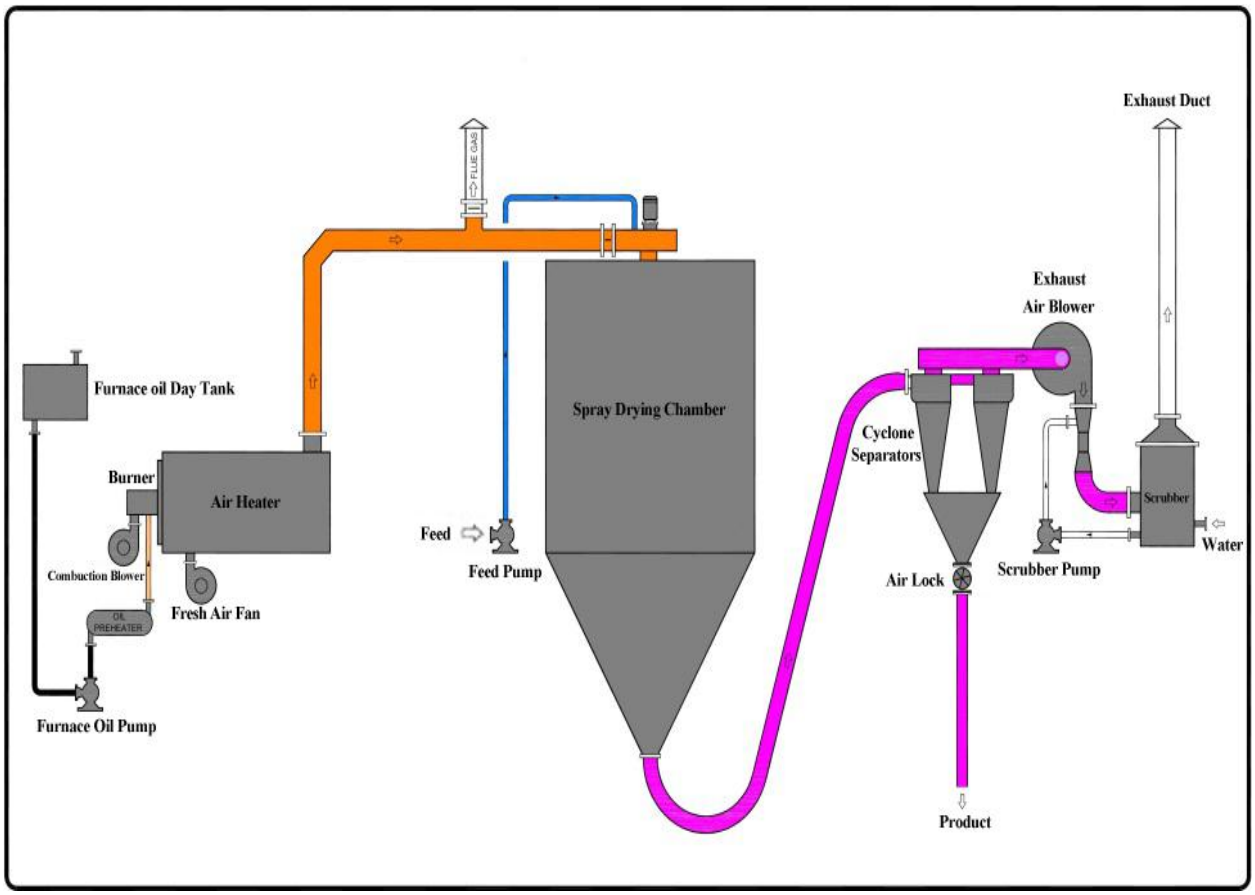

Fig – Spray Drying.

2. Solvent Evaporation[7,8]

The process is carried out in a liquid manufacturing vehicle phase. The microcapsule coating is dispersed in the volatile solvent which is immiscible with the liquid manufacturing vehicle phase. The basic material to be microencapsulated is dissolved or dispersible incoating polymer solution. by agitation the basic material mixture is dispersed in the liquid manufacturing vehicle phase to find the accurate size microcapsule. The mixture is then heated if the necessary to evaporate the solvent for the polymer of the core material is disperse in the polymer solution, polymer shrinks around the core. The basic material is dissolved in the coating polymer solution, matrix– type microcapsules are formed. The basic materials may be either water soluble or water in soluble materials. Involve the Solvent evaporation and formation of an emulsion between polymer solution and an immiscible continuous phase whether aqueous (o/w) or non-aqueous.

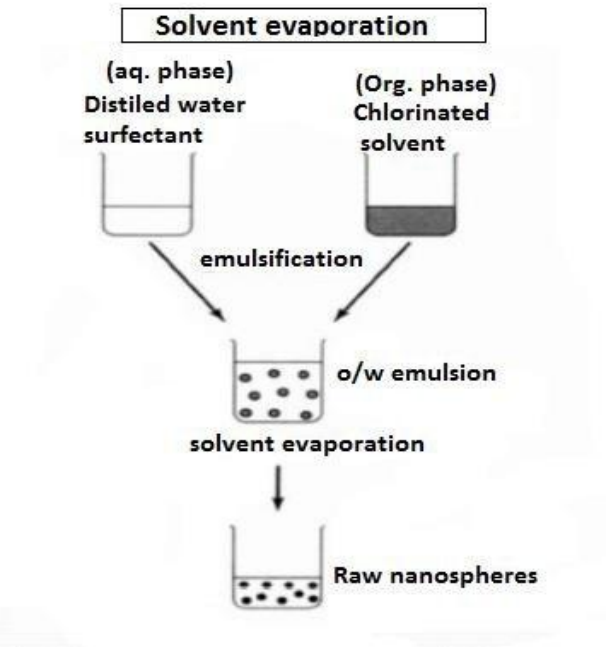

Fig – Solvent Evaporation.

3. Single emulsion technique[19]

The micro particulate carriers of natural polymers it is those of proteins and carbohydrates are prepared by single emulsion technique. The dissolved in nature polymers or dispersed in aqueous medium followed by dispersion in non-aqueous medium like oil. The cross linking can be obtained either by heat or by using chemical cross linkers. These cross-linking agents used are chemical glutaraldehyde, formaldehyde, acid chloride etc. Heat denatured is not suitable for thermolabile substances. Thechemical cross linking undergo the limitation of intense exposure of active ingredient to the chemicals added at the time of preparation and the subjected to centrifugation, washing, separation technique. The nature of the surfactants used the emulsion phase stabilized can be greater effect the size, size distribution, surface morphology, loading, drug release, and the bio performance of the final multi-particulate product.

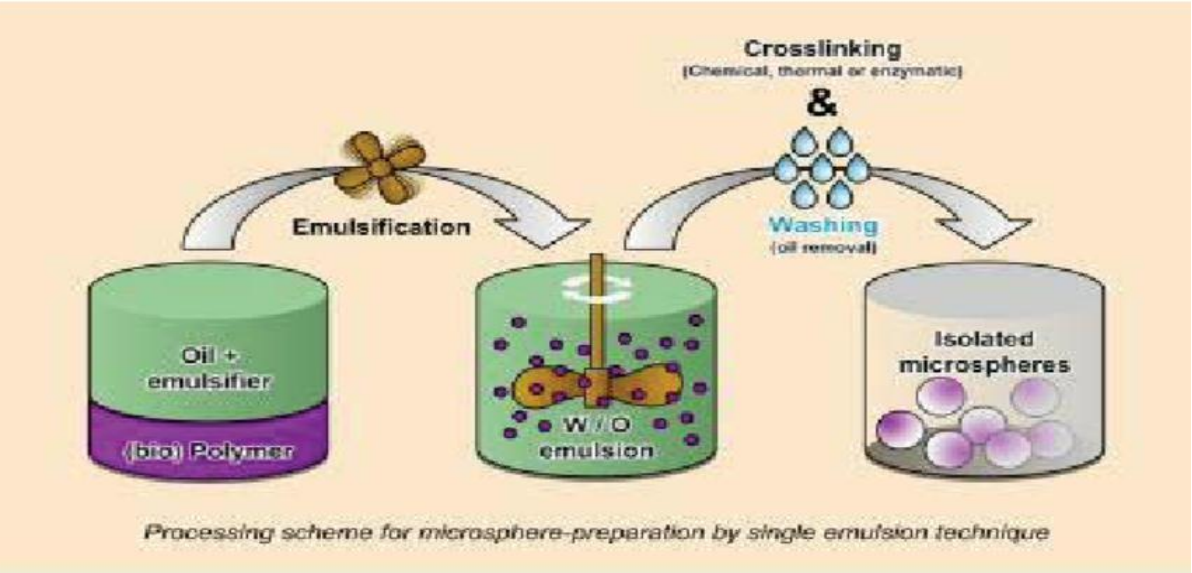

Fig – Single emulsion technique.

4. Double emulsion technique[19]

Double emulsion technique involved the formation of the multiple emulsions and double emulsion of type w/o/w and suitable for water soluble drugs, peptides, proteins and therefore the vaccines. This method areoften used with both the natural also as synthetic polymers. The aqueous protein solution is dispersed during a lipophilic organic continuous phase. This protein solution may contain the active constituents. The primary emulsion is subjected then to the homogenization or the sonication before addition to the solution of the poly vinyl alcohol (PVA). This leads to the formation of a double emulsion. A number of hydrophilic drugs like LH releasing hormone agonist, vaccines, proteins/peptides and traditional molecules are successfully incorporated into the microspheres using the tactic of double emulsion solvent evaporation/ extraction.

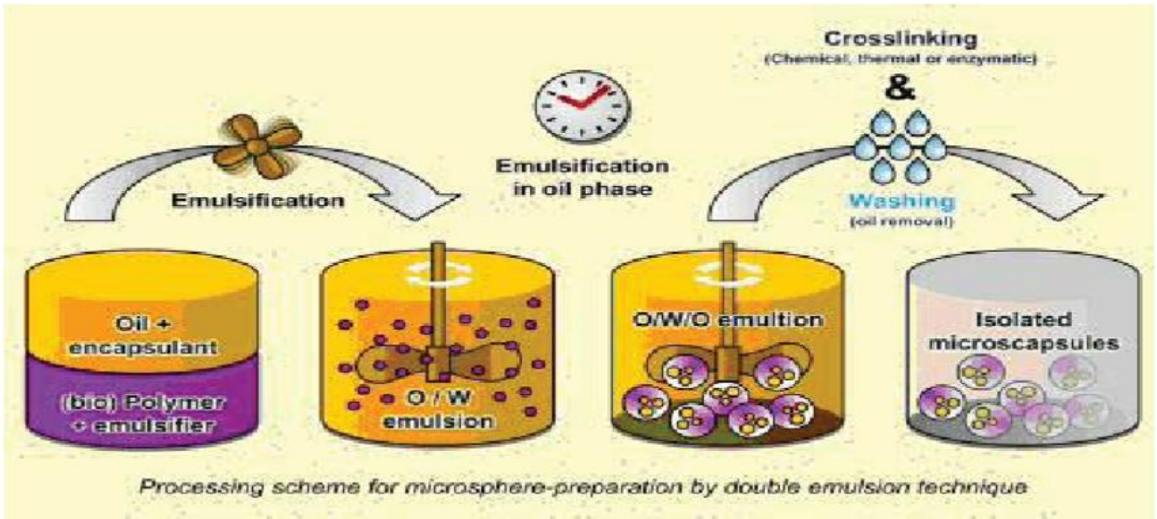

Fig – Double Emulsion Technique.

5. Phase separation coacervation technique[9,10]

This process is predicated on the principle of decreasing the solubility of the polymer in organic phase to affect the formation of polymer rich phase called the coacervates. In this method, the drug particles are dispersed during a solution of the polymer and an incompatible polymer is added to the system which makes first polymer to phase separate and engulf the drug particles. Addition of non-solvent leads to the solidification of polymer. The process variables are vital since the speed of achieving the coacervates determines the distribution of the polymer film, the particle size and agglomeration of the formed particles. The process variables are critical as they control the kinetic of the formed particles since there's no defined state of equilibrium attainment.

6. Solvent extraction[1]

Solvent evaporation method is used for the manufacturing of microparticles and involves removal of the organic phase by extraction of the non-aqueous solvent. This method involves the water miscible organic solvent which is isopropanol.

7. Quasi emulsion solvent diffusion[18,19]

Microspheres can be manufactured by the quasi-emulsion solvent diffusion method by using external phase which contains distilled water and polyvinyl alcohol. The internal phase consists of the drug, ethanol and polymers. Firstthe internal phase is manufactured at 60ºC and after then added to the external phase at room temperature. Then emulsification the mixture is continuously stirred for 2 hours. Then the mixture can be filtered for separate the microspheres.

APPLICATION OF MICROSPHERES IN PHARMACEUTICAL INDUSTRY[21,11]

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

EVALUATION OF MICROSPHERES[25,21,22,11,24]

1. Particle size and shape

The particle size and shapeisthat themost generally used procedures to see the microparticles are conventional light microscopy (LM) and scanning electron microscopy (SEM).

2. Electron spectroscopy for chemical analysis

The surface chemistry of the microspheres are often determined using the electron spectroscopy for chemical analysis (ESCA).

3. Density determination

The density of the microspheres measured by employing a multi volume pycnometer.

4. Isoelectric point

The isoelectric point is determined by the help of electrophoresis and it use to measure the electrophoretic mobility of microsphere.

5. Angle of contact

It in measured to the wetting property of a micro particulate carrier.

6. In vitro methods

Rotating paddle apparatus (USP / BP) is used for themeasure torelease studies of different type of microspheres are carried out by using different suitable dissolution media.

7. Drug entrapment efficiency

% Entrapment = Actual content/Theoretical content x 100.

CONCLUTION

It has been observed that microspheres are more sensible choice of drug delivery system than many other sorts of drug delivery system because thereto has the advantage of target specificity and better patient compliance. It is concluded from above that microsphere is that the promising candidate for sustained and as a targeted drug delivery in GIT, liver, colon, nasal, pulmonary system and ocular drug delivery etc. Its applications are enormous as they are not only used for delivering drugs but also for imaging tumor, detecting bio molecular interaction used as diagnostic agent and for treatment of cancer too, etc. many pharmaceutical companies are introducing their newer products to the market which can give good therapeutic response in comparison with conventional drug delivery. The development of upcoming drug delivery technologies are often applied for solving problems regarding pharmaceutical, biopharmaceutical and pharmacokinetic aspects thus, the delivery systems are growing and accepting worldwide for its better utilization.

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