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Review Article

A Technical Note: on Microspheres

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A B S T R A C T

Microspheres have become a center of research. Microspheres are an excellent way to deliver drugs to specific sites and control their effects. They are characterized by free-flowing spheres composed of biodegradable or non-biodegradable proteins or synthetic polymers, with an ideal particle size of 1-1000 microns. Microspheres encapsulate active pharmaceutical ingredients (APIs) in a polymer matrix that protects the API from environmental degradation. Pharmacokinetic limitations can be overcome by modifying the formulation to release the drug slowly during prolonged action. The purpose of this review is to list the different types of microspheres, their different preparations, limitations, advantages and disadvantages, characterization, applications, and recent developments in microspheres and various compatibility studies.

Keywords - Microspheres, drug delivery, target site, method of preparation, application

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INTRODUCTION:

As drug carriers, microspheres are one of the best ways to deliver and control the effect of the drug at specific sites. They are characterized as free-flowing spheres composed of biodegradable or non-biodegradable proteins or synthetic polymers with ideal particle sizes of 1 - 1000 µm. There are two types of microspheres: microcapsules and micromatrix. Microcapsules refer to microspheres in which the embedded material is surrounded by clearly distinct capsule walls. Particles embedded in the micromatrix are dispersed or dissolved by the particle matrix, the release of which can be controlled medicine. They are made from polymers, waxes or other protective materials (e.g. biodegradable synthetic polymers and substitute natural products). Deploying it to an appropriate tool helps increase product security [1].

Unlike drug distribution, the new term is something sought out of necessity. When the half-life of the drug is short, the drug must be used more frequently, which may reduce patient compliance. To overcome the above problems, people have developed and modified different types of drugs to ensure patients' compliance with long-term treatment and reduce adverse effects by lowering blood pressure. Microspheres are defined as "monolithic spheres or medicinal substances distributed throughout the matrix according to the molecular distribution of the substance" (or) can be defined as structures with continuous phases of one or more miscible polymers in which chemicals are broken down into molecules or at the macroscopic level[2]. Many new drug delivery systems are available, and microspheres are one of the most common DDSs.

Microspheres are particle dispersion systems formed by adsorbing or dispersing drugs in a polymer matrix. DDS has many advantages due to its rich structure and functionality. It can be used in a variety of ways, including subcutaneous or intratumoral injection and transpulmonary administration as an inhalant [3]. More than 90% of available painkillers are administered by oral administration, which is the most popular and easiest route [4]. However, oral administration always has limited clinical efficacy due to the need for frequent administration to achieve stable plasma concentrations and patient compliance is not good. This pharmacokinetic limitation can be overcome by changing the formulation to release the drug slowly upon long-term administration. When a new drug site is discovered, the first challenge pharmaceutical companies face is how to produce

the dosage form. Additionally, by encapsulating the active pharmaceutical ingredient (API) in a polymer matrix, microspheres protect the API from environmental degradation (temperature, pH and oxidation) cause irritation and mask the unpleasant odor of the API. The fact that the drug is loaded into polymer microspheres shows that the treatment is only in the target area. Microspheres can be divided into two groups, depending on the carrier biodegradable and non-biodegradable. Non-biodegradable microspheres may accumulate in the body after application and cause adverse effects. Biodegradable microspheres can be broken down into products that are non-toxic to the human body [3]. The most important feature of this material is that it is biodegradable. The products produced by human metabolism do not harm the human body and the environment. There are many types of biodegradable polymer materials, both naturally derived and synthetic.

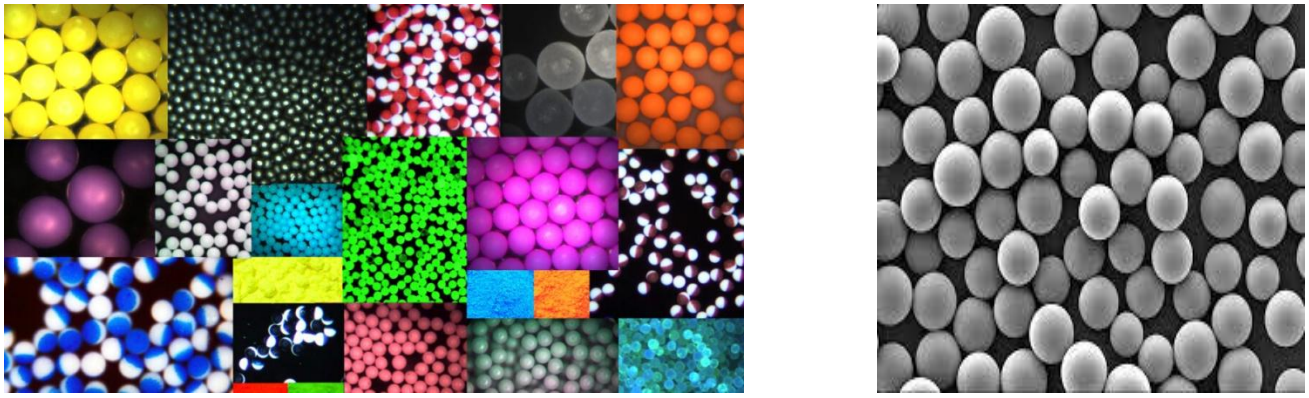

Figure 01: Microsphrers

Microspheres have a high surface area to volume ratio and provide sufficient space for cell growth. Additionally, microspheres with functional structures (e.g., hollow, core–shell) can be easily customized and formed to effectively deliver cells and bioactive molecules. However, small microspheres (diameter <20 μm) are not suitable as cell carriers because when cells adhere and spread on biomaterials, the diameter of the cells is usually larger than 20 μm. At the same time, large-sized microspheres (diameter > 200 μm) are difficult to inject through a conventional (18-gauge or higher) needle[5].

In recent years, microspheres have become a research hotspot. Microspheres were initially designed as drug delivery vehicles in which bioactive substances could be stably released while maintaining their properties. With their improved physicochemical and biological properties, microspheres have the potential to become important components. Microspheres made of natural polymers, synthetic polymers, or composite materials can be used as individual units or aggregates [6].

HISTORY OF MICROSPHERE [7]

The original dermal filler, Zyderm, was first introduced in 1982 to critical acclaim. We have all been waiting for this product and it has finally arrived. Although it is still one of the safest drugs injected into the dermis, initial excitement has diminished due to its short duration. According to the senior author's three decades of experience with all types of autografts, including dermal, fat, cartilage, bone and muscle, they can be isolated from sites where they do not retain their biological activity. To find a solution to this problem, he studied various microspheres made from various synthetic materials currently used in medicine.

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LIMITATION [8]:

1. Update the production model.

2. The release rate of controlled-release tablets will vary depending on many factors, such as food and bowel movements.

3. Difference in output from one series to another.

4. Anti-release agents generally contain more drug, so any loss in the integrity of the form's release properties will increase the potential for toxicity.

5. This medicine should not be crushed or chewed.

TYPES OF MICROSPHERES [9]:

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

The adhesion of the solution to the membrane using a binder can be defined as the adhesion of a water-soluble polymer. These types of microspheres exhibit longer residence time at the application site. For example, apply the medicine to mouth, eyes, anus, nose, etc. Do not use in areas with mucous membranes.

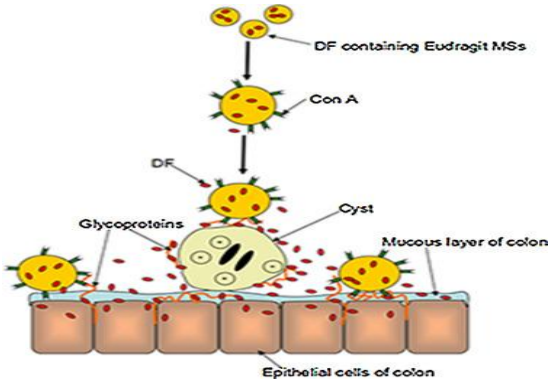

Figure 02: Bioadhesive microspheres

(2) Magnetic microspheres

This type of delivery is important for local application of drugs to diseased areas, where large amounts of free drug can be replaced by small doses of magnetically applied drugs. Magnetic carriers receive a magnetic response to the magnetic field.

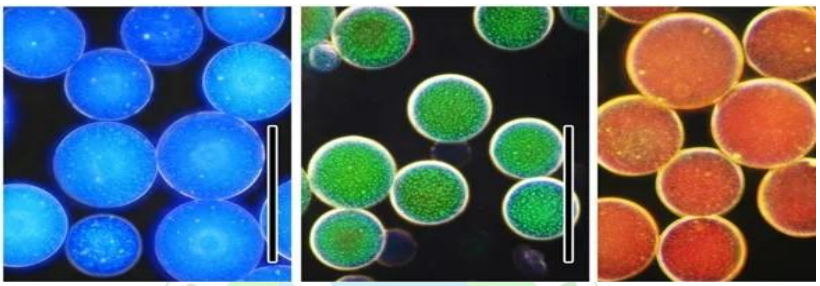

Figure 03: Magnetic microspheres

(3) Floating microspheres

The volume of floating microspheres is less than the liquid in the stomach; they remain in the stomach without affecting the digestive system. The drug is slowly released to where it is needed. It also reduces the risk of accidents and disposable drug products.

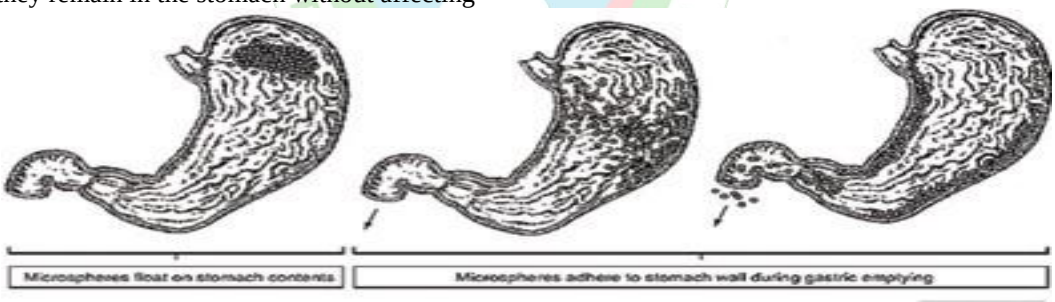

Figure 04: Floating microspheres

(4) Radioactive microspheres

Radiofixed therapeutic microspheres, 10-30 nm in size, are larger than microvessels. They are injected into blood vessels to stimulate the tumor. The radiation cloud kills all tumor cells. Overlapping radiation to ensure no tumor cells survive. These radio microspheres deliver high doses of radiation to areas without causing tissue damage. Areas of tumor cells that were able to survive and grow that did not receive sufficient XRT were lost. Different types of radioactive microspheres are α emitters, β emitters, γ emitters.

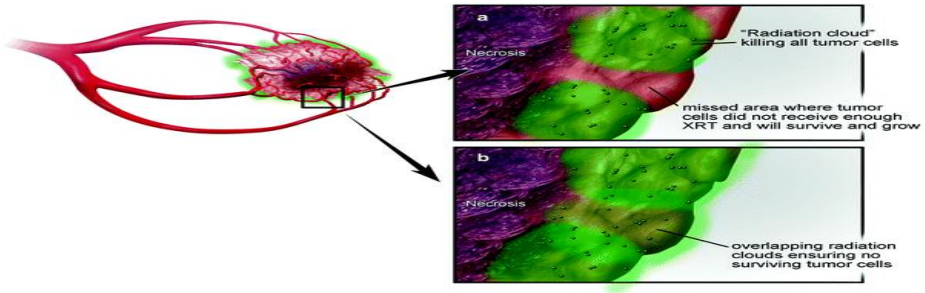

Figure 05: Radioactive microspheres

(5) Polymeric microspheres

The different types of polymeric microspheres classified as

i. Biodegradable polymeric microspheres

Natural polymers such as starch are considered biodegradable, biocompatible, and naturally bioadhesive. These polymers cause gel formation by prolonging their contact time with the mucosa due to their swelling properties in aqueous media.

ii. Synthetic polymeric microspheres

Synthetic polymer microspheres are widely used in medicine and are also used as containers, containers, embolization materials and drug carriers, etc. They can also be used and have been proven to be safe and biocompatible. Displacement of the injection and risk of embolism and other organ damage.

METHOD OF PREPERATION

Solvent evaporation method

The solvent evaporation method is a method for preparing microspheres by removing the volatile solvent from the dispersed phase in the emulsion. The size of microspheres can be controlled in the nanometer range. Generally, the solvent evaporation process produces oil/water (O/W), oil/water/oil (O/W/O), water/oil (W/O), water/oil/water, solvent and polymer (W/O/W) and emulsion systems. Once a stable emulsion is formed, the organic solvent is dispersed into the continuous phase by heating, removed by reduction or continuous stirring, and evaporated by the interaction of the phase and air. At the same time, the microspheres gradually solidify, and after filtering, washing and drying, the final microspheres and drug-loaded microspheres can be obtained. Generally speaking, organic solvents can be removed from emulsion systems into the gas phase by evaporation or into the continuous phase by extraction. For the solvent to evaporate, the carrier solvent must be dissolved in the continuous phase before evaporation occurs[10].

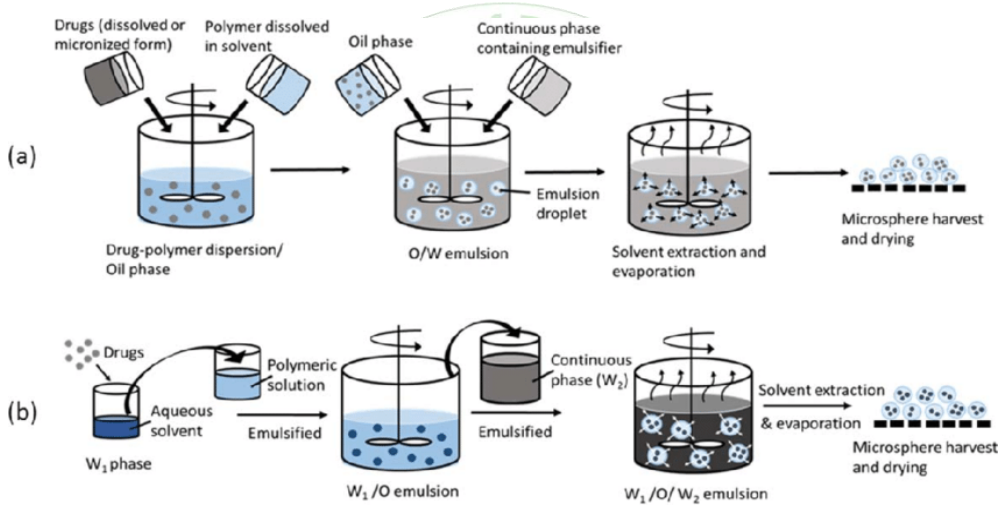

Figure 06: Solvent evaporation method the preparation of microspheres

Single emulsion technique

This method has been used to prepare protein and carbohydrate microspheres based on natural polymers. First, the polymer is dissolved in an aqueous medium and then dispersed as an oil in a non-aqueous solvent. The dispersion is then crosslinked by heat or using a chemical cross linking agent such as glutaraldehyde. The type of surfactant tends to influence the size, particle size, surface morphology, drug transport, drug release, and biological properties of microspheres[11].

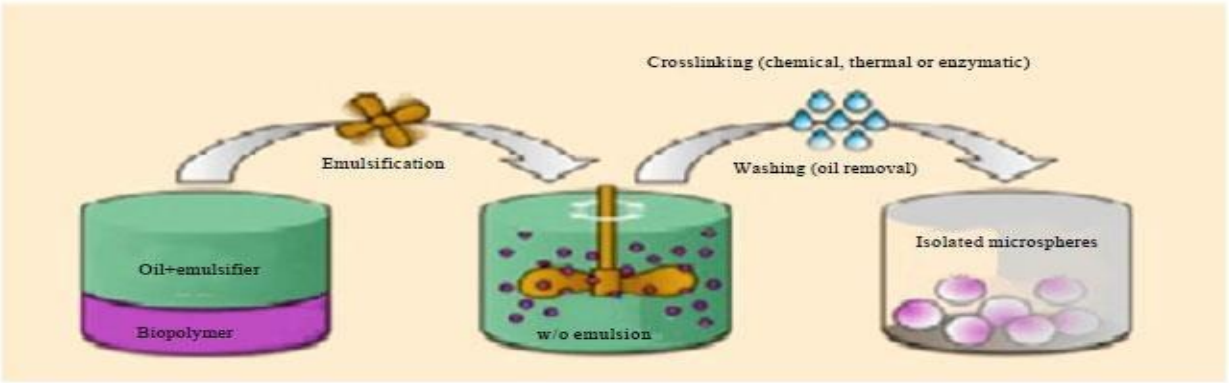

Figure 07: Single emulsion technique the preparation of microspheres

Double emulsion technique

Double emulsion systems involve the formation of water-in-oil (w/o/w) or oil-in-water (o/w/o). w/o/w double emulsion for water-soluble drugs, peptides, proteins, vaccines, etc[11]. The w/o/w double emulsion method is suitable for encapsulation of hydrophilic molecules. The main steps include forming primary and secondary emulsions and using washing/evaporation techniques to remove organic solvents. Microspheres prepared by two emulsification methods have high encapsulation efficiency and high yield and are suitable for temperature-sensitive drugs. However, water-soluble substances from the polymer phase into the external aqueous phase will limit the encapsulation of hydrophilic substances[12].

The stability of the initial emulsion is important for the success of proteins or peptides in double emulsion technology. Effect of emulsion stability on the properties (morphology and porosity) of microspheres prepared using a w/o/w double emulsion system with two different molecular weights. The functional properties of microspheres can be modified by various modifications, including polymer, emulsifier, organic solvent, drug/polymer ratio, lack of emulsification, extraction or evaporation process[12].

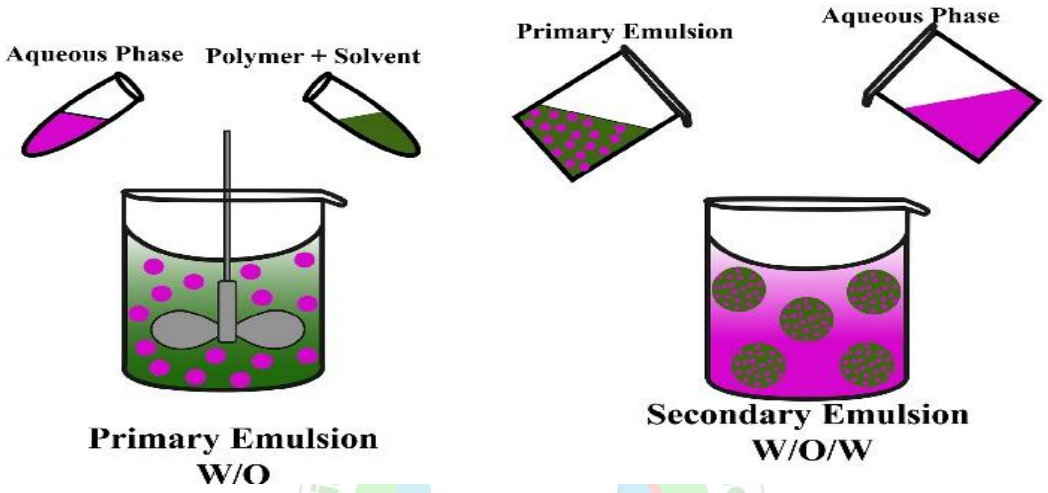

Figure 08: Double emulsion technique for the preparation of microspheres

Polymerization Technique [13]

Preparation of Microspheres by this method can be done by 2 types:

I. Ordinary polymerization: This type of polymerization includes bulk polymerization, suspension polymerization, precipitation polymerization, emulsion polymerization, etc. In the case of polymerization, monomers are heated along with the catalyst to initiate polymerization. The resulting polymer is molded into microspheres and can be used as a chemical carrier during the polymerization process. Bulk polymerization has the advantage of producing pure polymer. In the case of suspension, the monomer or monomer mixture is heated together with the active substance as a dispersion of water droplets in a continuous aqueous phase. Suspension polymerization, also known as pearl polymerization, is carried out at low temperatures. In the case of emulsion polymerization, an initiator is present in the aqueous phase and then diffuses onto the micelle surface.

II. Interfacial polymerization: It involves the reaction of various monomers at the interface of two immiscible liquid phases, essentially forming a polymer film surrounding the dispersed phase.

Spray drying technique [11,12]

Both the polymer and the drug are dissolved in a volatile organic solvent and homogenized in a high-speed homogenizer. The resulting dispersion is then sprayed into a stream of hot air, where the solvent instantly evaporates, producing microsphere-free particles.

Microspheres prepared by spray drying have been reported to encapsulate proteins to improve protein stability. The spray drying method can overcome the problem of large amounts of solvents associated with the emulsion-based microencapsulation process. However, drying requires a smaller size than the emulsion method. Therefore, spray drying is generally not suitable for the early development of microsphere formulations. The spray drying process can be divided into:

- The emulsion is transported to the atomizer at a certain speed through the pipeline, and the liquid feed is atomized into droplets by the atomizer.
- The atomized droplets will dry, and the atomized droplets and drying medium (nitrogen) will be mixed in the drying chamber.
- Climate change completes solvent evaporation, resulting in rapid evaporation of water and subsequent particle formation.
- Separation of dry material from the drying medium using cyclones or bagged screens. Air and dry material enter the cyclone separator tangentially, and the air follows the vortex force, forming a vortex. To speak louder or bigger, to follow the flow of the wind. Due to centrifugal force, the words will hit the glass and fall into the container.

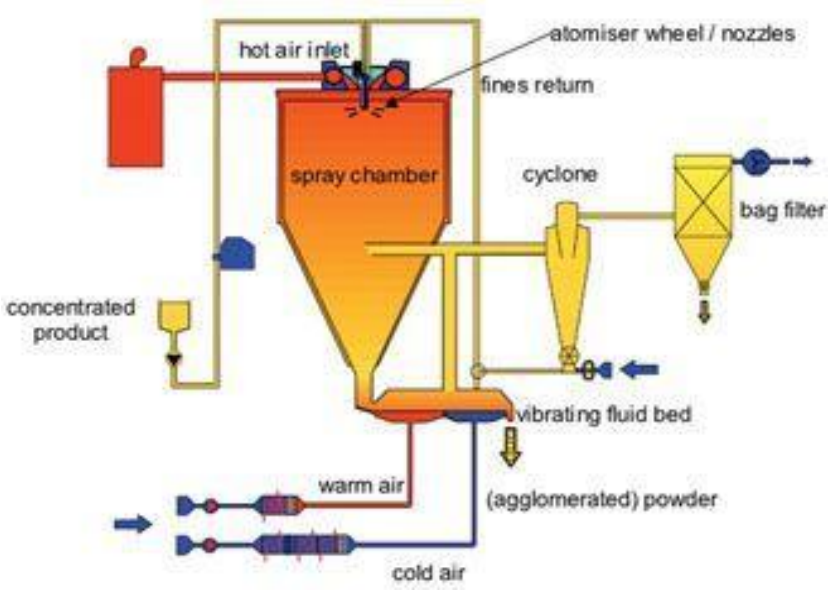

Figure 09: Spray drying technique for the preparation of microspheres

Phase separation coacervation technique [11]

This technology mainly prepares hydrophilic substances such as peptides and proteins with water. The principle is based on reducing the solubility of polymers in the organic phase and creating a polymer-rich phase called coacervate. A third part is added to the system to separate the coacervates, creating two phases: the supernatant phase and the polymer-rich phase (Figure 10). Additionally, phase separation can be achieved by different methods, such as the addition of salts, different solvents, or different polymers.

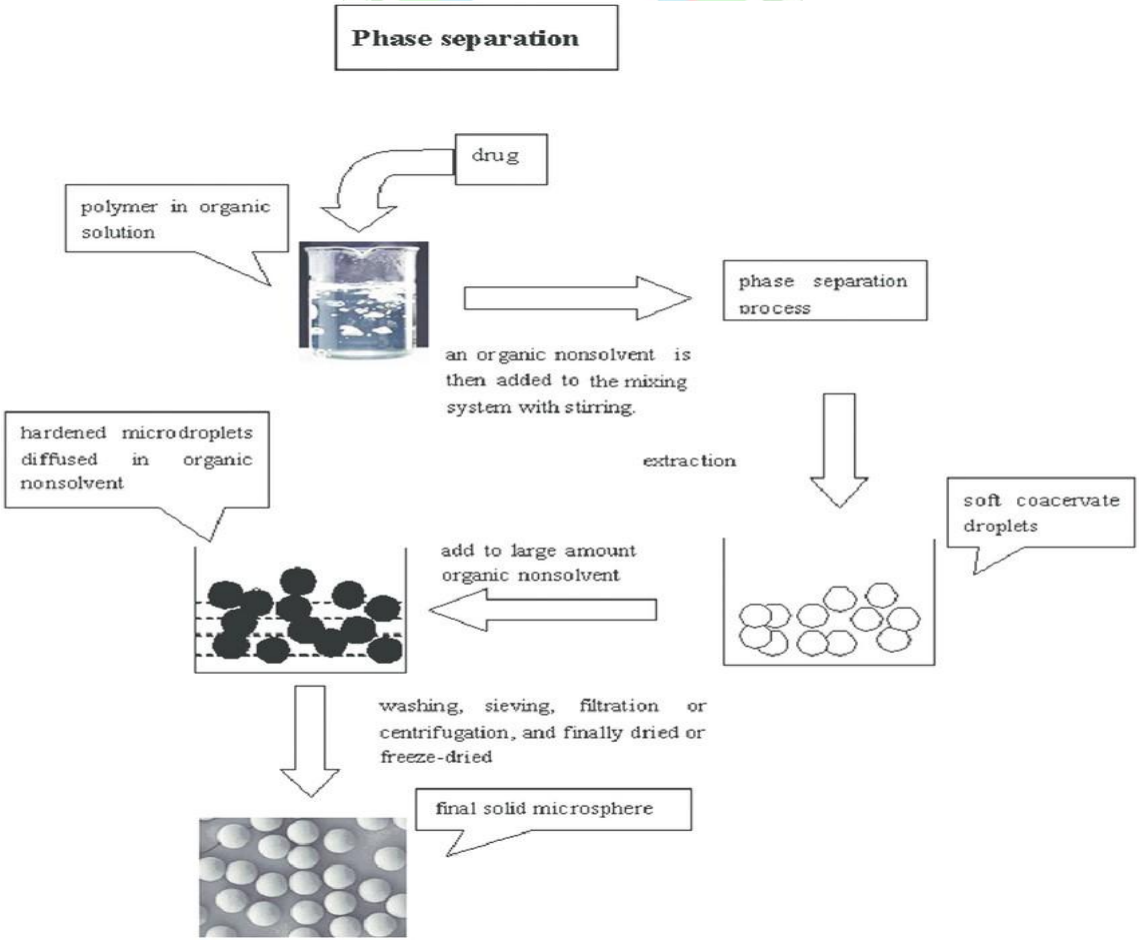

Figure 10: Phase separation coacervation technique for the preparation of microspheres

Ionotropic gelation technique [14]

This method was developed by Lim and Moss. Using this method, a gel-type polymer (such as alginate) is dissolved in a liquid, the active ingredients are suspended in the mixture, and the drug is squeezed through a needle to form microdroplets that fall into the chlorinated chemicals. The calcium in the curing solution thus forms microspheres. Mix on low speed. Divalent calcium ions present in the curing solution cross-link the polymer to form gel microspheres.

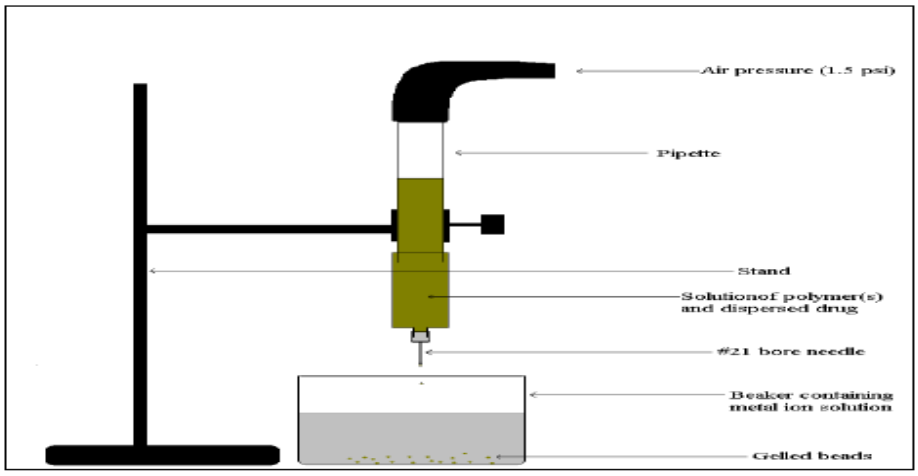

Figure 11: Ionotropic gelation technique for the preparation of microspheres

Multiple emulsion method

The multiple emulsion technique may be the best way to increase the activity of target molecules in microspheres. In this model, the first emulsion (oil in water) (aqueous solution containing the target molecule in chitosan solution) is the first. This initial emulsion is then added to the external oil phase to form a multiple emulsion (water in oil). Hydrophobic reagent-loaded microspheres prepared by various emulsion methods has good morphological properties and yield. Microspheres are prepared in different steps according to different thermal conditions. Example Citric acid was added to a solution of chitosan in acetic acid (2.5% w/v), then cooled to 0°C, and then added to corn oil. After stirring for 2 minutes, the temperature was maintained at 120°C and the emulsion was added drop wise to the corn oil. The synthesis was then carried out in a powerful mixer (1000 rpm) for 40 min, and the resulting microspheres were filtered, washed, dried and sieved.

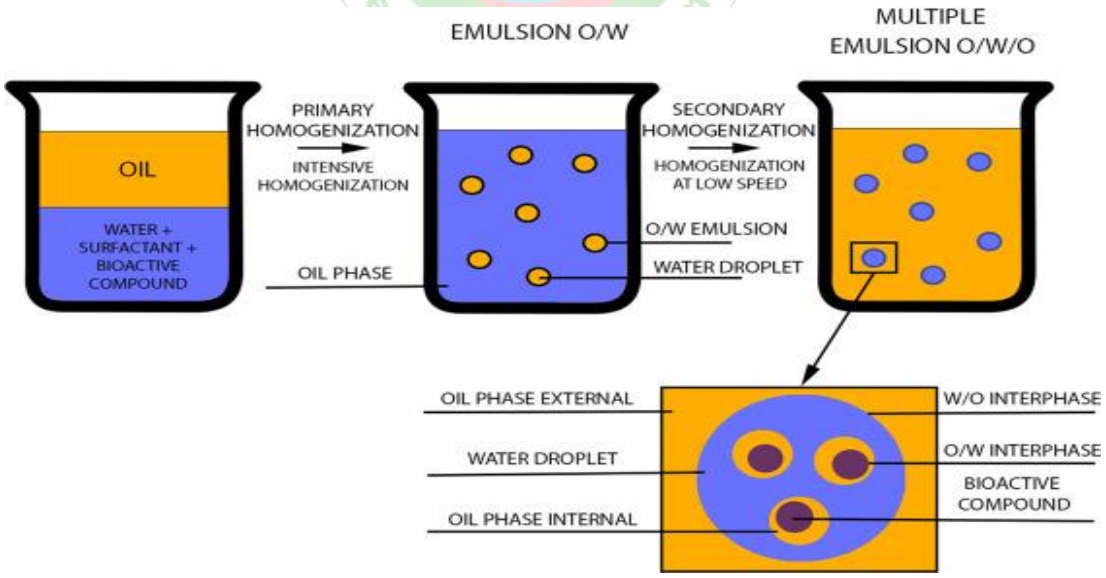

Figure 12: Multiple emulsion method for the preparation of microspheres

ADVANTAGES [4]

Better patience compliance

Because microspheres can release the drug slowly over a longer period of time, the frequency of administration is reduced, thus improving patient compliance, especially for children, the elderly, and the mentally ill.

Enhance bioavailability

The size of microspheres is in the micron range, so the smaller it is, the larger the surface area, which makes the

soluble drug not well, hence the bioavailability of the drug increases.

Constant drug plasma concentration

Microspheres allow controlled drug release over an extended period of time; Therefore, the drug concentration in the body does not change and reaches a constant Cmax value.

Reduction in adverse effects

Biodegradable polymer microspheres are biocompatible with the in vivo environment. They do not require surgical removal. Since the drug is released in a controlled manner, its toxicity is also reduced.

Enhance stability

Liquid drug can be converted into microspheres to ensure drug stability and maintain clinical shelf life.

Parenteral formulation

Microspheres are spherical and high doses can be used as microsphere parenteral depots.

Targeted drug delivery

Microspheres are used in diseases, especially cancer, when the concentration in tissues is still low.

DISADVANTAGES [4]

Production cost

The production costs of prescription drugs are much higher than the production costs of prescription drugs.

Reproducibility

Microspheres are difficult to reproduce because their construction requires special skills and technology.

Potential toxicity

Because microspheres carry large amounts of drug, drug waste may occur, leading to potential toxicity.

Polymeric toxicity

Depending on the formulation, additional polymer materials such as plasticizers, stabilizers, and antibiotics may also be used, and these polymers can hydrolyze, oxidize, or react with bacteria, causing toxicity.

Swallowing

Microspheres used for oral administration should be swallowed rather than chewed or crushed because they are designed for sustained release.

Maintaining conditions

Microsphere processing conditions such as pH, temperature, mixing, solvent evaporation, and heat will affect the stability of the drug to be encapsulated.

CHARACTERIZATION OF MICROSPHERES

Mean particle size [15]

The average size of the preparation was evaluated by the sieving method, in which the average size of the microspheres was calculated. Additionally, the fluidity of the microspheres, expressed as the angle of repose, was also evaluated. The criteria for this decision are as follows:

$$\text{Mean particle size} = \frac{\sum (\text{Mean particle size of the fraction} \times \text{Weight fraction})}{\sum \text{Weight fraction}}$$

Production yield [15]

Calculate the weight of the raw materials used in the preparation and the final weight of the microspheres produced. The percentage of microspheres was calculated as follows:

$$\text{Production yield (\%)} = \frac{\text{Weight of microspheres}}{\text{Total expected weight of drug and polymers} \times 100}$$

Determination of bulk density and tapped density [16]

Place the microspheres (1g) into the 10 ml graduated cylinder and fill the starting volume. Using a USP bulk density meter, tap the graduated cylinder 100 times. Use the following formula to determine bulk density and tap density:

$$\text{Bulk density} = \frac{\text{Weight of the microspheres}}{\text{Initial volume}}$$

$$\text{Tapped density} = \frac{\text{Weight of the microspheres}}{\text{Final volume after tapping}}$$

Determination of Hausner ratio [16]

Hausner ratio is determined by the formula:

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Carr's (compressibility) index [17]

The material's compressibility index should be a secondary measure of the material's density, size and shape, surface area, moisture content and viscosity.

$$\text{\% Compressibility index} = \frac{\text{Tapped density-Bulk density} \times 100}{\text{Tapped density}}$$

Determination of angle of repose [16]

To determine the stance angle, microspheres are poured into the funnel, the lower end of which is fixed at a height of 2 cm from the surface. Pour microspheres until the tip of the surface of the microsphere cluster touches the funnel. The tan-1 ratio of the pile height to the pile base radius gives the angle of repose. The stance angle is determined by the following formula:

$$q = \tan^{-1} h/r$$

Where,

h = Height, r = Radius

Drug entrapment or capture efficiency [14]

The encapsulation efficiency or percent encapsulation of microspheres can be determined by keeping the microspheres in sterile solution and allowing lysis. The resulting lysate is filtered or centrifuged and the active ingredients determined as required by the monograph. Calculate the percentage of effective interference using the formula below

$$\text{Entrapment efficiency} = \frac{\text{\% Drug loading}}{\text{\% Theoritical loading} \times 100}$$

where

$$\text{\% Drug loading} = \frac{\text{Weight of drug in microsphere}}{\text{Weight of microsphere}}$$

Degree of swelling [14]

The degree of swelling defines the ability of mucoadhesive microspheres to swell at the suction point by absorbing the fluid present in the suction zone; this is important for inducing mucoadhesion. The degree of swelling can be calculated from the change in polymer content (Wg-Wi).

$$\text{Degree of swelling} = \frac{Wg - Wi \times 100}{Wg}$$

Where,

Wi - Initial weight of microspheres,

Wg - Final weight of microspheres

Density Determination [13]

The density of microspheres can be measured using a multi-volume pycnometer. Place the correct sample into the container multi-volume pycnometer. Helium gas is introduced into the chamber at constant pressure and allowed to expand. This expansion causes the pressure in the room to decrease. Record two consecutive readings of the shock value of the first difference. From the two pressure readings, the volume and density of the microsphere carrier can be determined.

Isoelectric Point [13]

The isoelectric point can be measured by measuring the electrophoretic mobility of microspheres using microelectrophoresis equipment. The average velocity of the pH difference between 3 and 10 is calculated by measuring the time required for the particles to move 1 nm.

COMPATIBILITY STUDY [17]

Fourier transfor-infrared spectroscopy (FT-IR)

FT-IR spectra of pure drugs, polymers, and polymerized drugs were recorded in a spectrophotometer using the KBr particle method and reported as wavenumbers (cm^{-1}). The scanning range is 4000 to 450 cm^{-1}. FT-IR spectra support the identification of functional groups present in compounds. FT-IR spectra were also used to compare with standard FT-IR spectra of pure substances to demonstrate physical differences between substances and different substances.

Surface morphology

Scanning electron microscopy (SEM) was used to characterize the surface and cross-sectional morphology of the formed floating microspheres. The SEM sample was mounted directly on the double-sided tape fixed on the aluminum rod by gently brushing the dust. The billets are then coated with gold/palladium to a thickness of approximately 20 nm by a gold sputtering module in a high vacuum evaporator under argon atmosphere. Feel free to scan and photograph the coated pattern afterwards.

Powder X-ray diffraction (PXRD)

Sample runs were performed at a current of 30 mA, a voltage of 40 KV, and a measurement rate of 8 degrees/minute using steps of 0.02° per second over a theta range of 5-80°. Therefore, it is used to determine the properties of pure substances, whether crystalline or amorphous, and to check whether the properties of substances change with the use of polymers.

Differential scanning calorimetry (DSC)

Differential scanning calorimetry was used to perform thermal measurements using argon as an inert gas to examine the crystallization difference between the solution and the microspheres. Weighted samples were placed in aluminum pans and sealed. The sample is heated from 20 to 200°C at a rate of 5°C per minute in an argon atmosphere with a gas flow rate of 100 mL/min. Use an empty pot with a lid as a reference. Record the results from the heat.

RECENT ADVANCEMENT IN MICROSPHERE [8]

1. Important utilizations of polymer.

Chitosan and cellulose are used as examples of fibers with high, medium and low bile acid binding capacity, respectively. In control mice fed a high-fat/high-cholesterol diet for 3 weeks, serum cholesterol increased approximately 2-fold to 4.3 mM, and adding 7.5% of this fiber to the diet prevented this increase. Additionally, by being treated with these fibers, cholesterol levels in high stores due to the HFHC diet can also be reduced. Three fibers have been shown to work to lower cholesterol; however, cholestyramine has the greatest effect on liver cholesterol. The mechanism by which cholestyramine reduces cholesterol:

1) Reduce cholesterol intake,

2) Reduce cholesterol absorption,

3) Increase bile acid and cholesterol levels.

The latter effect may be attributed to the bile acid potential of cholestyramine. In contrast, adding chitosan or fiber to the diet reduced cholesterol intake but did not affect intestinal absorption or fecal sterol excretion. This study provides strong evidence that satiety and satiety effects reduce cholesterol.

2. Increase Stability of Drug

To ensure the stability of the drug, chitosan polymer mixes the drug with chitosan into slurry and kneads for 45 minutes until a ball is formed. Granules produced by passing through 1. 16 mesh is stable under most conditions.

3. Orthopaedic Patients

Chitosan is a biopolymer with osteoconductive, wound healing and antimicrobial properties and is ideal for use as a bioactive layer to improve osseointegration of orthopedic and craniofacial implant devices. It has been shown to promote tissue growth in tissue repair, wound healing, and bone regeneration.

4. Cosmetics industry

Cosmetics for hair or skin treatment are offered, containing new quaternary ammonium chitosan derivatives of the formula. It has been determined that chitosan derivatives have a particularly strong effect on hair keratin, strengthening the hair and cooling the hair. For example, Styling lotions, oxidative hair dye compositions, toning compositions, skin cream, hair texture, gel form.

5. Dental Medicine

Chitosan has been shown to improve wound healing, improve the appearance and function of the skin, and prevent excessive scarring. In dentistry, chitosan is also used as a dressing for mouth wounds and as a tampon after radical treatment of maxillary sinusitis. It is also being investigated as an absorbent membrane in periodontal surgery. Chitosan prevents many diseases, arthritis, cancer, diabetes, disease suppression, etc. It has many activities and supports as a healthy food that can heal and/or treat.

6.Wound Healing Properties [2]

Chitosan's ability to promote wound healing was first revealed in 1978. Chitosan acetate film has advantages such as oxygen permeability, high water absorption, hardness and protective properties.

APPLICATIONS IN DRUG DELIVERY SYSTEM [2]

Ophthalmic Drug Delivery

The polymer exhibits good behaviors such as bioadhesion, permeation-enhancing properties, and interesting physicochemical properties, making it a unique material for ocular drug delivery vehicles. Due to their elastic properties, polymeric hydrogels are more acceptable as solids or semisolids for distribution such as suspensions or ointments. Microparticulate drug carriers (microspheres) appear to be a promising method for topical application of acyclovir to the eye.

Gene delivery

Delivery systems include viral vectors, polycationic complexes, and microencapsulation systems. Viral vectors are useful for gene delivery due to their high efficiency and general cell targeting. However, when used in the body, they can cause immune system disruption and cancer formation. To overcome the limitations of viral diseases, non-viral diseases have been considered in gene therapy. Non-infectious bacteria have advantages such as easy preparation, cell/tissue targeting, inertness, no plasmid size limitation, and large production capacity. Polymers have been used as DNA vectors in gene delivery applications. Additionally, the polymer may be a useful oral material due to its stickiness and loading into the gastrointestinal tract.

Intratumoral and local drug delivery

Intratumoral and local drug delivery strategies have recently gained momentum as promising cancer treatments. Polymer films were prepared to deliver paclitaxel to the tumor in the relevant clinical area. Paclitaxel can be loaded onto a translucent film and has a 31% (w/w) conversion. Studies have shown that paclitaxel-containing polymer films are obtained in high yield by the casting method and the chemical properties of the molecules do not change during preparation.

Oral drug delivery

The oral drug delivery ability of polymer films containing diazepam was examined in rabbits. The results show that the film with a 1:0.5 drug-polymer mixture would be an effective paper equivalent to a paper capsule. The pH sensitivity combined with the reactivity of the primary amine group makes the polymer particularly suitable for oral administration.

Nasal drug delivery

The nasal mucosa is an ideal site for bioadhesive drug delivery systems. Polymer-based drug delivery systems, such as microspheres and gels, have been shown to have good bioadhesion properties and swell easily upon contact with the nasal mucosa, increasing the residence time and bioavailability of the drug in the nose.

Buccal drug delivery

Oral tablets based on microspheres containing chlorhexidine diacetate can increase the release time of the drug in the oral cavity, thereby enhancing the antibacterial effect of the drug. Polymer particles that are not combined with the drug have antimicrobial activity due to the polymer. Buccal bilayer device (double layer) using a mixture of anionic cross-linked polymers (polycarbophil, sodium alginate, gellan gum) membrane, drugs (nifedipine and propranolol hydrochloride) and chitosan, with or without PAVI tablet, has a form widely applied in control.

Gastrointestinal drug delivery

Polymer particles with internal cavities prepared by deacidification have been shown to be buoyant and provide controlled release of prednisolone when added to acidic and neutral media. Floating melatonin hollow microcapsules demonstrate the gastric retention control release system. Drug release from these microcapsules is slow and is released in the gastric fluid for 1.75 to 6.7 hours. Most mucoadhesive microcapsules, such as metoclopramide and glipizide-loaded chitosan microspheres, remain in the stomach for more than 10 hours.

Peroral drug delivery

Due to the mucoadhesive properties of the polymer and many of its derivatives, presystemic metabolism of the peptide may increase the bioavailability of many oral peptide drugs such as insulin, calcitonin, and buserelin.

Vaginal drug delivery

For modification, thioglycolic acid is added to the first amino group of the polymer, creating clotrimazole and benzimidazole derivatives that are widely used to treat genitourinary fungal diseases. By adding the thiol group, the mucoadhesive properties of the polymer are greatly improved and this has been shown to increase the residence time on the mucous membrane (26 times longer than the corresponding polymer) to achieve control in the treatment of fungal infections. Polymeric vaginal tablets containing metronidazole and acriflavine have been shown to have adequate release and good adhesion.

Transdermal drug delivery

The polymer has a good film. The drug released from the device is affected by and through the membrane. Polymeric gel beads are a promising biocompatible and biodegradable carrier for the treatment of local inflammation with drugs such as prednisolone, demonstrating a release that will improve treatment. Drug release rate was observed depending on the membrane type used.

Colonic drug delivery

Polymers are used specifically to deliver insulin to the intestine. It was determined that the capsule disintegrated especially in the intestine. This damage has been shown to be due to lower pH in the large intestine than in the terminal or the presence of bacterial enzymes that degrade the polymer. The powder mixture was extruded between different powders using water and dilute acetic acid. When dilute acetic acid is used for the granulation step, the mass fraction of chitosan in the container will increase to 100%.

Imaging [9]

The diameter of the microsphere plays an important role in determining the target area for imaging using radiolabeled microspheres. Microspheres injected through a vein other than the portal vein usually enter the lungs. This phenomenon has been specifically developed for scintigraphy of lung tumors using human serum albumin microspheres.

Monoclonal Antibodies [13]

Monoclonal antibodies directed against microspheres are anti-viral microspheres. This site is used to fulfill specific site purposes. Monoclonal antibodies are highly specific molecules. Samples can be added to microspheres by either:

Ø Nonspecific adsorption and specific adsorption

Ø Direct incorporation

Ø Coupling with reagents

FUTURE CHALLENGES [18]

Future challenges for microspheres are particularly in medicine due to their broad applications in molecular biology. For example: microsphere-based genotyping platform for detection of six single nucleotide polymorphisms, Yttrium 90 microspheres for advanced methods to prevent post-liver tumor transplantation and distribution.

CONCLUSION:

This review article discusses microspheres as a better drug delivery system than other types of drug delivery. Microspheres are safer than other forms of drug delivery because they benefit from improved patient efficiency and target accuracy. Microsphere drug delivery system has the advantages of sustained release control, improved stability, reduced drug use frequency, separation rate and bioavailability, and is the most effective drug delivery system. Microspherical drug delivery system is an effective and safe drug delivery system that can be used in many applications such as drug targeting, flotation and drug resistance. Methods for the preparation and evaluation of microspheres are comprehensive and useful. Microspheres are used not only for drug delivery but also to image tumors, detect biomolecular interactions, and treat cancer.

Table 1: Drug involved in microspheres in various category

Sr. No	*Drug*	*Category*	*Method of preparation*	*References*
1	Glipizide	Antidiabetic	Solvent evaporation method	22
2	Salbutamol Sulphate	Bronchodilators	Solvent evaporation method	23
3	Zidovudine	Antiretroviral	Double emulsion solvent diffusion method	24
4	Levocetirizine dihydrochloride	Antihistamine/ Antiallergic	Spray drying technique	25
5	Ranitidine	Antacid	Spray drying technique	26
6	Cefixime trihydrate	Antibiotic	Phase separation coacervation technique	27
7	Ketorolac tromethamine	Anti-inflammatory	Phase separation coacervation technique	28
8	Ofloxacin	Antimicrobial	Ionotropic gelation technique	29
9	Ibuprofen	Anti-inflammatory	Ionotropic gelation technique	30
10	Maraviroc	Antiviral	Ionotropic gelation technique	31

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