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Review Article on Novel Drug Deliversystem of Microsphere

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ABSTRACT
Targeted drug delivery aims to concentrate the drug in the tissue of interest while simultaneously reducing the relative concentration of the drug in the remaining tissues. This localizes the drug to the target site. The evolution of existing drug molecules from traditional forms to new delivery systems significantly improves their performance in terms of patient compliance, safety, and efficacy. Existing drug molecules can be given new life in the form of new drug delivery systems. Properly designed new drug delivery systems can provide significant advances in solving the problems associated with releasing drugs at specific locations and at specific rates. Microspheres are free-flowing powders, typically composed of proteins or synthetic polymers, that are naturally biodegradable and ideally have a particle size of less than 200 µm. Microspheres have applications in the delivery of novel drugs, particularly in the selection of diseased cells, diagnostic agents, genes and genetic material, safe, targeted and effective in vivo drug delivery, and nutrition as miniature versions of diseased organs and tissues within the body. It will play a central role in the delivery of supplements. .

Keywords: Microspheres, Controlled drug delivery system , Target site ,specificity, Novel Drug Delivery

I. INTRODUCTION

controlled drug delivery systems are used to overcome some of the problems associated with traditional treatments and improve the therapeutic efficacy of certain drugs. To achieve maximum therapeutic efficacy, active ingredients must be delivered to the target tissue in optimal amounts and duration, with low toxicity and minimal side effects. There are various approaches to delivering therapeutic substances to target sites in a sustained controlled release manner**.**New drug delivery systems deliver therapeutic substances to target sites in well-controlled and sustained models.Microspheres or microparticles are defined as free-flowing spherical particles composed of a polymer matrix and drug. They are composed of biodegradable proteins or synthetic polymers with particle sizes less than 200 µm2.Microspheres can be described as small spherical particles with diameters in the micrometer range (usually 1 µm to 1000 µm). Microspheres are also called as particulates. Microspheres have been extensively studied for use in drug delivery, and a variety of polymers have been used to formulate microspheres and, as a result, have been evaluated for specific purposes. Microsphere play an important role to the bioavailability improve of convetional drugs. A constant plasma concentration is maintained, ultimately reducing total dosage and some side effects **.**There are two types of microspheres. Microcapsules and micromatrices. A microcapsule is one in which the entrapped substance is surrounded by a separate capsule wall, and a micromatrix is one in which the entrapped substance is dispersed throughout the microsphere matrix. [1-3]

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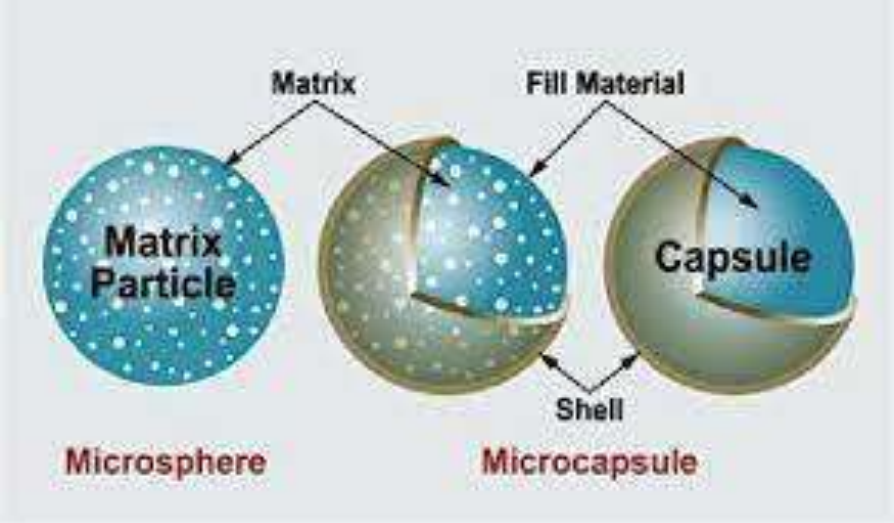

Fig.1:Microsphere and microcapsule

1.1. Advantages of microspheres

- Microspheres provide consistent and long-lasting therapeutic effects.
- Increased patient compliance due to less frequent dosing.
- Microspheres are spherical and small in size, allowing them to be inserted into the body.
- Improved drug utilization increases bioavailability while reducing the risk of side effects.
- Microsphere morphology allows controlled variation in drug release and degradation
- Turns liquids such as oil into solids, making them easier to handle.[3]

1.2. Disadvantages of microspheres

- When microspheres are used parenterally, it is difficult to completely remove the carrier from the body.
- This drug has some harmful toxic effects.
- The release rate of controlled-release dosage forms can depend on a variety of factors, including diet and rate.
- How it passes through the intestines.
- Differences in release rate from one dose to another.
- Controlled-release formulations generally contain higher amounts of active ingredient, which can result in potential toxicity if the integrity of the release characteristics of the dosage form is compromised.
- Do not crush or chew this type of dosage form. [1]

1.3. Characteristics of microsphere

S. No.	Property	Consideration
1	Size	Diameter Uniformity/distribution
2	Composition	Density Refractive index Hydrophobicity/hydrophilicity Nonspecific binding Autofluorescence
3	Surface chemistry	Reactive groups Level of functionalization Charge
4	Special properties	Visible dye/fluorophore Super-paramagnetic

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1.4. Polymers Used in Microsphere Preparation

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

- Synthetic Polymers and
- Natural polymers

Synthetic polymers are divided into two types:[4,5]

- Non-biodegradable polymers
  - Poly methyl methacrylate (PMMA)
- Acrolein
  - Glycidyl methacrylate
- Epoxy polymer
- Biodegradable polymers
  - Lactides, Glycolides &their co polymer
  - Poly alkyl cyano Acrylates
  - Poly anhydrides

Natural polymers are obtained from different sources like Proteins, carbohydrates and chemically modified carbohydrates.[6,7]

- Proteins:
- Albumin
- Gelatin 9
- Collagen

- Carbohydrates
- Agarose
- Carrageenan
- Chitosan10
- Starch

- Chemically modified carbohydrates:
- Poly dextran 11
- Poly starch.

II. TYPES OF MICROSPHERES

Microspheres are classified into different types. They are of following

1. Bioadhesive microspheres
2. Magnetic microspheres
3.Therapeutic magnetic microspheres

Floating microspheres

Radioactive microspheres

4.. Polymeric microspheres

I. Biodegradable polymeric microspheres

II. Synthetic polymeric microspheres

1.5. Bioadhesive microspheres

Adhesion refers to the fact that drugs adhere to membranes using the water solubility of water-soluble polymers. The attachment or adhesion of drug delivery systems to mucosal membranes, such as the cheeks, nose, eyes, rectum, etc., is sometimes referred to as bioadhesion. This type of microspheres allows for a longer residence time at the target site, ensuring better therapeutic efficacy. [8]

2.2. Magnetic microspheres

This type of delivery system localizes the drug to the target site. In this type of delivery system, a drug or therapeutic radioisotope bound to a magnetic component is injected into the systemic circulation and then stopped at the disease/target site by a strong magnetic field. Magnetic microspheres are molecular particles (4 μm) small enough to travel through capillaries without causing esophageal obstruction, but are so sensitive (ferromagnetic) that they can be trapped in micro -vessels and moved by magnetic fields to adjacent is drawn through the tissue . [7-9]

- Therapeutic magnetic microspheres
- Diagnostic microsphers

2.3. Therapeutic magnetic microspheres

2.3.1.Floating microspheres

The floating type has a lower bulk density than the density of gastric fluid, so it remains buoyant in the stomach without affecting the rate of gastric emptying. The drug is released slowly at the desired rate and the system is found to float above the gastric contents, reducing gastric residence time and increasing plasma concentration variability. Additionally, the potential for dose dumping is also reduced. The effect lasts longer, so the frequency of administration is reduced. [10]

2.3.2. Radioactive microspheres

Radio embolization microspheres with a size of 10–30 nm are larger than the diameter of the capillary bed upon impact. In all of these diseases, radioactive microspheres deliver high doses of radiation to the target area without damaging normal surrounding tissue, as they are injected into the artery that carries the target tumor. Radioactivity is not emitted from the microsphere, but acts within the radioactive isotope at a normal distance. The different types of radioactive microspheres include α-emitters, β-emitters, and ϒ-emitters. [11-12]

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2.4.Polymeric microspheres

Polymer microspheres can be classified into biodegradable polymer microspheres and synthetic polymer microspheres.[13]

2.4.1. Biodegradable polymer microspheres

Natural polymers such as starch are used because they are biodegradable, biocompatible, and bioadhesive. Biodegradable polymers have a high ability to swell in aqueous media, thus increasing residence time when in contact with mucous membranes.

That leads to the formation of a gel. The rate and extent of drug release are continuously controlled by the polymer concentration and release pattern. This type of microsphere has a longer residence time at the application site.

2.4.2. Synthetic polymeric microspheres

Synthetic polymer microspheres are widely used in clinical applications. Additionally, it has been used as a bulking agent, filler, embolic particle, drug delivery carrier, etc., and has proven safety and biocompatibility. However, the main drawback of this type of microspheres is that the microspheres tend to migrate away from the injection site, leading to a potential risk of embolism and further organ damage.

III. MECHANISM OF MICROSPHERES

The majority of drug delivery through microparticles prevents the formation of matrix-like internal solid-dispersion morphology structures. The active ingredients may be insoluble in the polymer matrix and are released by erosion. First, water diffuses into the matrix and removes the water that forms near the surface of the device. By creating channels to the surface and releasing a certain amount of drug during the initial burst of drug, the resulting osmotic pressure is reduced [2].

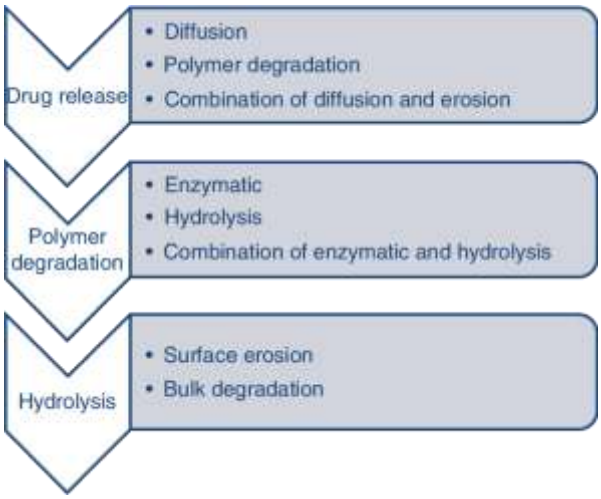

Fig.3:Mechanism of microspheres

IV. TECHNIQUES OF PREPARATION OF MICROSPHERES

Methods used for the preparation of microspheres are:

- Single emulsion techniques
- Double emulsion techniques
- Polymerization
- Phase separation coacervation technique
- Spray drying
- Emulsion crosslinking method
- solvent evaporation
- Air suspenation

4.1. Single emulsion technique

This technology is primarily used to produce various carbohydrates and proteins. In this technique, natural polymers are first dissolved in an aqueous medium and then dispersed in a non-aqueous medium (oil phase). The next step is to crosslink the dispersed beads. This he can achieve in two ways.

By heating: The dispersion liquid is added to heated oil. But this method Not suitable for heat-labile drugs.

By chemical crosslinking Agent :use of glutaraldehyde, Formaldehyde, acid chloride, etc.

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as a cross -linking agent. Chemicals . .[17] Networking has the downside of overexposure

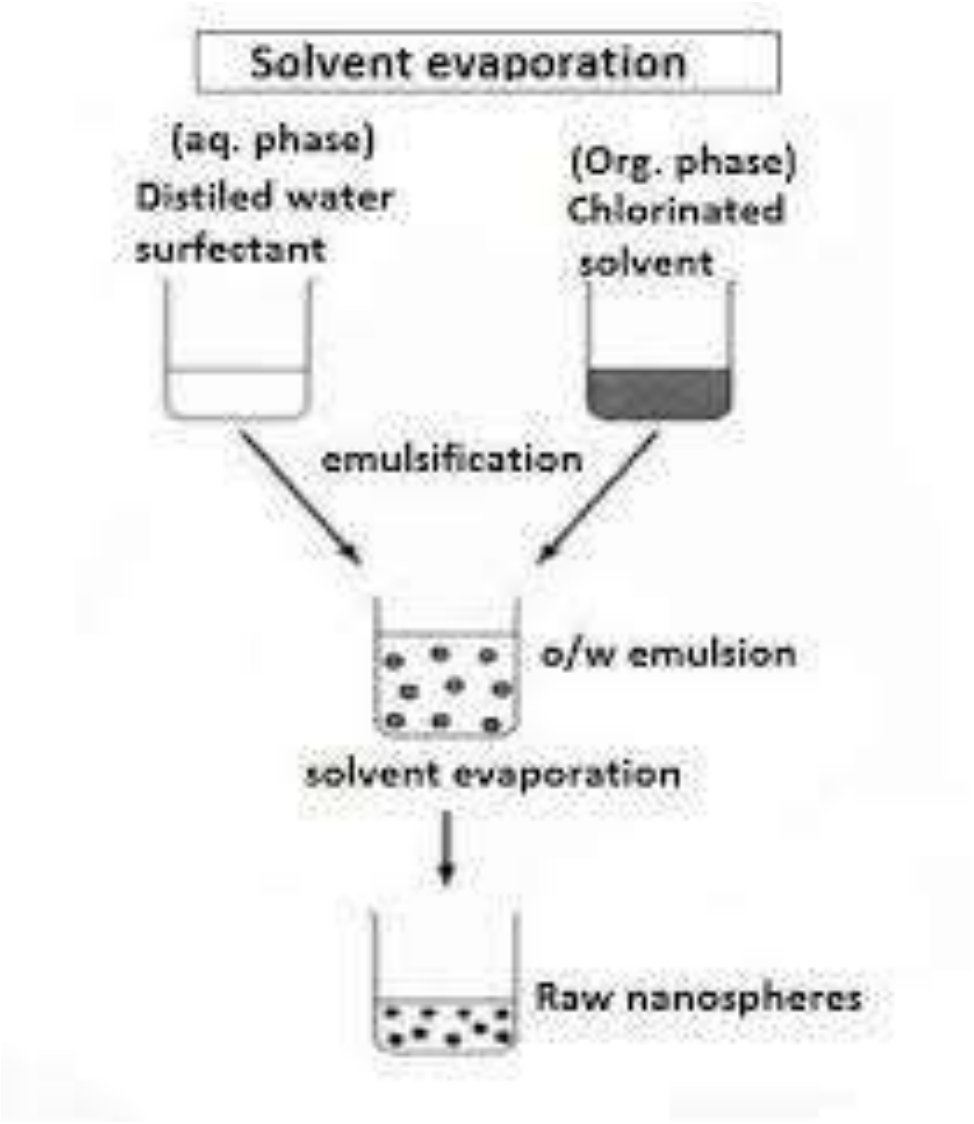

Fig.4.1:Singleemulsion Technique

4.2.Double emulsion techique

This includes the production of some emulsions. H. W/O/W is prepared by pouring the primary W/O emulsion into an aqueous polyvinyl alcohol solution. This W/O/W emulsion is constantly stirred for 30 minutes. Add water little by little to the emulsion over 30 minutes. Collection of microcapsules by filtration and drying under vacuum. Ideal for water-soluble drugs, peptides, proteins, and vaccines. Both natural and synthetic polymers can be used in this process. The aqueous protein solution is dispersed in a continuous lipophilic organic phase. This protein solution contains the active ingredients .Dispersing in oil/homogenizing the organic phase/vigorously, i.e. Formulation of the first emulsion, then addition of an aqueous solution of PVA (polyvinyl alcohol), etc.Multiple emulsions are formed by adding extensive aqueous phase modification/curing after this separation, washing, drying and collection of microspheres are prepared using O/W/O multiple emulsion process [19-20]

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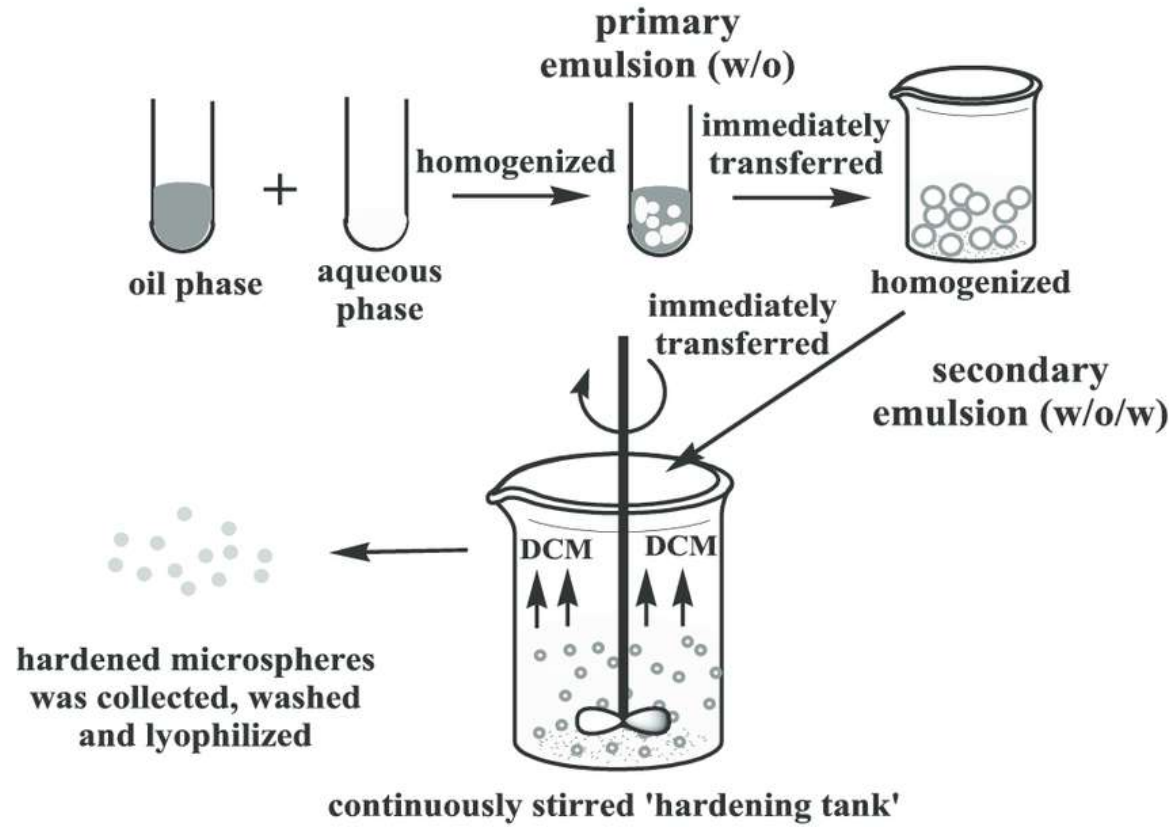

Fig.4.2:Double emulsion technique

4.3.Polymerization techniques

Two techniques are mainly used for the formulation of microspheres are as follow:

4.3.1.Normal polymerization

In bulk polymerization, a monomer or mixture of monomers is typically heated with an initiator or catalyst to initiate polymerization. The polymer thus obtained can be formed into microspheres. The active ingredient can be prepared by adding the active ingredient during the polymerization process. Although this is a pure polymer formation technology, the heat of reaction is very difficult to dissipate, which affects the thermal instability of the active ingredient. Suspension polymerization is carried out at low temperatures and is also known as bead polymerization, in which a monomer mixture containing the active ingredient is heated as a droplet dispersion in a continuous aqueous phase [21]

4.3.2.Interfacial polymerization

The reaction of different monomers at the interface between two immiscible liquid phases forms a polymer film that essentially envelops the dispersed phase. This technique uses two reactive monomers. One is dissolved in the continuous phase and the other is dispersed in the continuous phase (aqueous in nature) in which the second monomer is emulsified [21]

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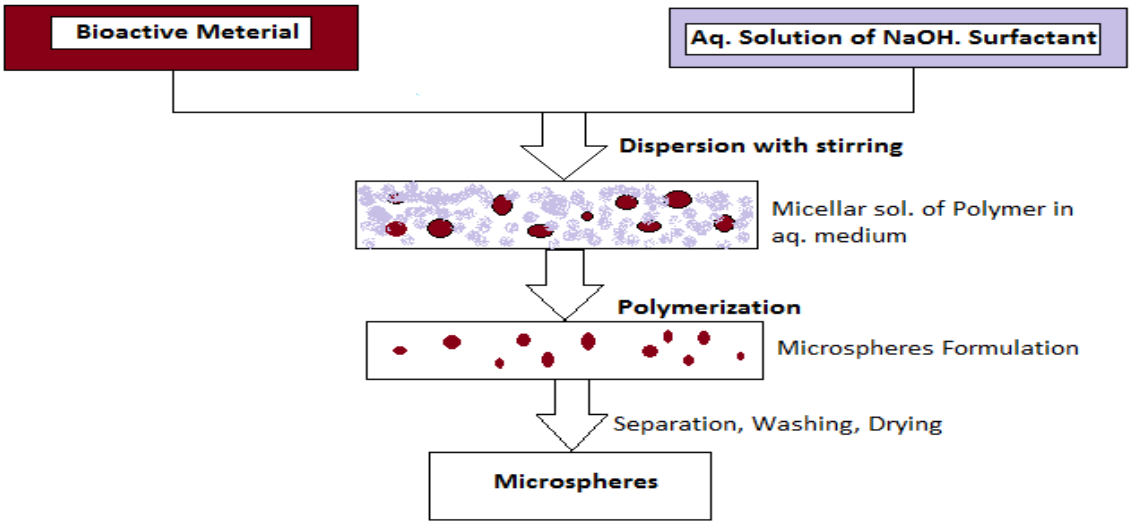

Fig.4.3:Polymerization techniques

4.4.Spray drying technique

In this technique, the polymer is dissolved in a volatile organic solvent such as dichloromethane or acetone, etc.and the active ingredient (solid) is dispersed in the polymer solution using high-speed homogenization. The dispersion is then sprayed into a stream of hot air. The spray forms small droplets from which the solvent evaporates instantly. This results in the formation of microspheres in the size range 1–100 µm. The prepared microparticles are separated by hot air using a cyclone separator, and traces of solvent are removed by vacuum drying[13-14]

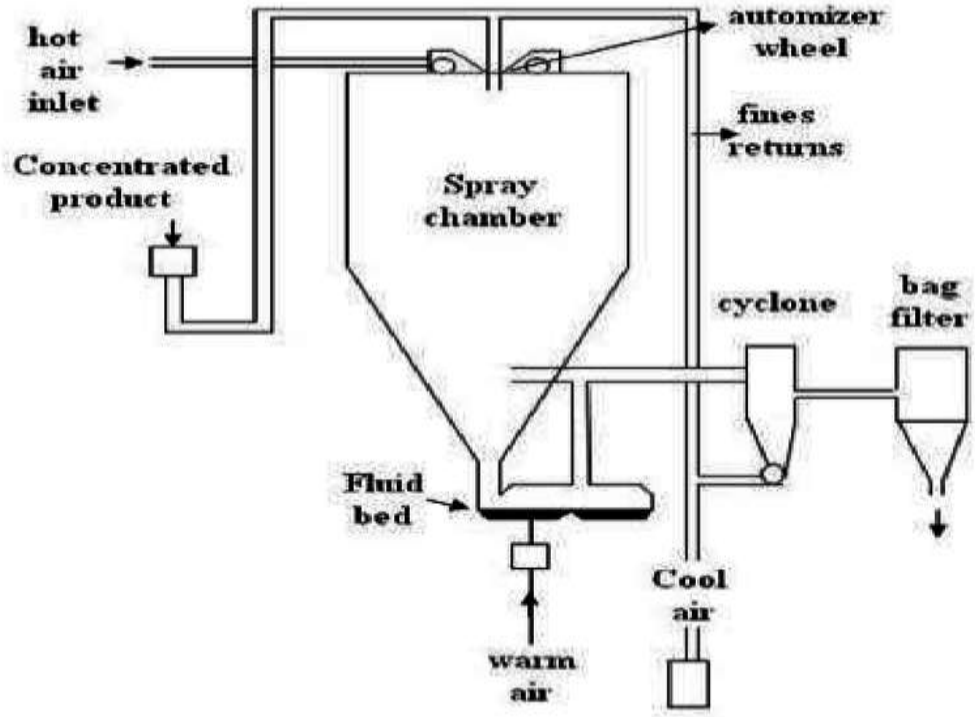

Fig.4.4:Spray drying technique

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4.5.Emulsion cross linking method

This method utilizes the reactive functional groups of the polymer to crosslink with the aldehyde groups of the cross-linked. In this method, a water-in-oil (W/O) emulsion was prepared by emulsifying an aqueous polymer solution in an oil phase. Water droplets were stabilized with appropriate surfactants such as Span 80 and sodium dioctyl sulfosuccinate. The stable emulsion was cross linked using a suitable cross linker such as glutaraldehyde to harden the droplets. Microspheres were filtered and washed repeatedly with hexane or petroleum ether to remove traces of oil. Finally, they were washed with water to remove the cross linker and dried at room temperature for 24 h [24]

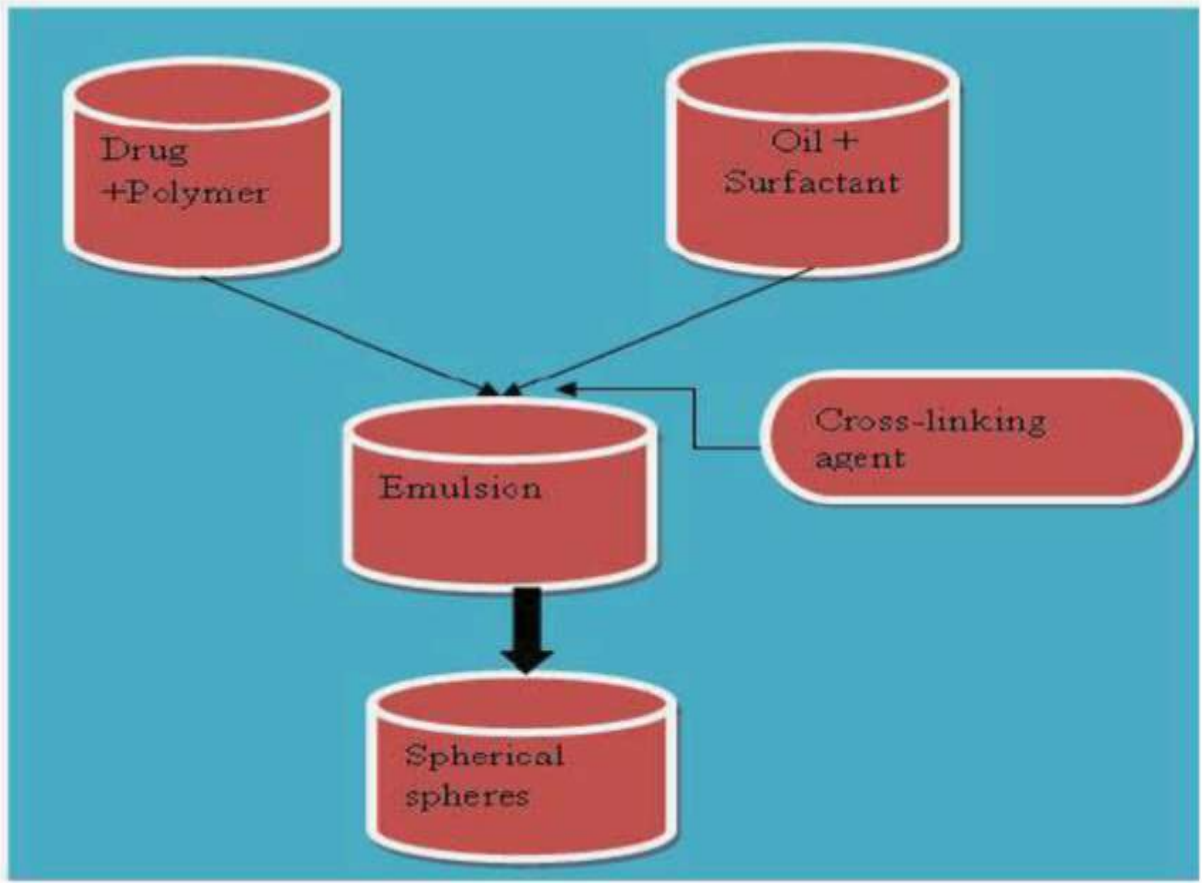

Fig.4.5: crosslinking Emulsion method

4.6.Solvent Evaporation technique

The process is carried out in a liquid production medium. Microcapsules are dispersed by volatile solvents that are immiscible with the liquid phase of the manufacturing process. The core material to be microencapsulated is dissolved or dispersed in the polymer coating solution. While stirring, the core material mixture is dispersed throughout the vehicle liquid manufacturing process to obtain microcapsules of the required size. The mixture is then heated, if possible, to evaporate the solvent of the base polymer dispersed in the polymer solution. The polymer contracts around the core. When the core material is dissolved in the polymer coating solution, a matrix is created in the form of microcapsules. Core materials can be either water-soluble or water-insoluble. The core material can be either water-soluble or water-insoluble. During the evaporation of the solvent, aqueous (O/W) or non-aqueous formation occurs [25].

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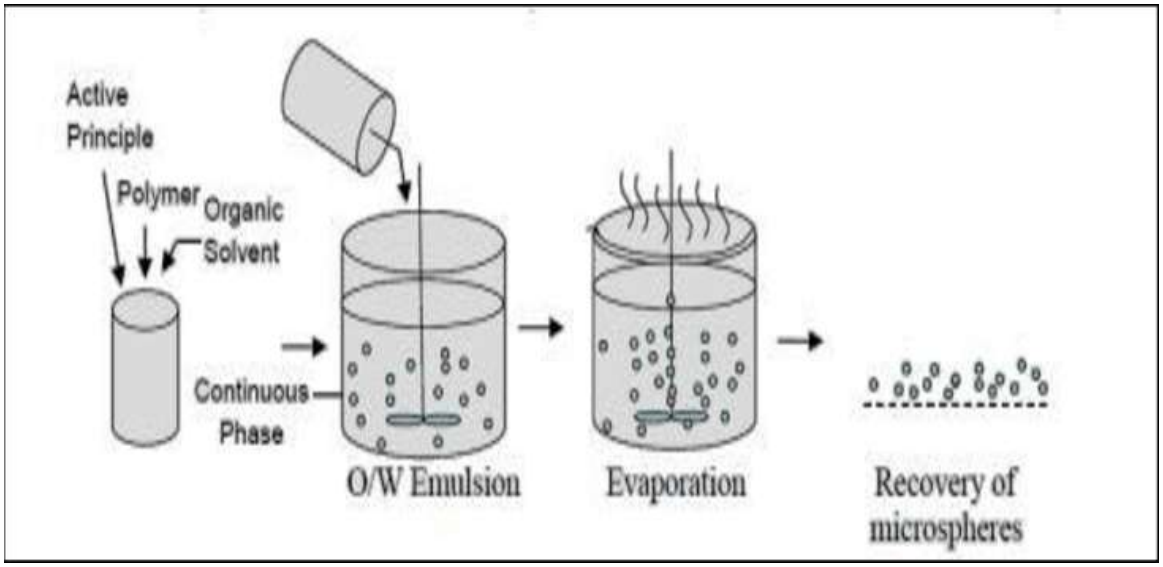

Fig.4.6:Solvent Evaporation technique

4.7.Air suspension:

Microencapsulation using an air suspension process consists of dispersing solid and particulate core materials into a supporting air stream and spraying them onto air suspension particles (Figure). Inside the coating chamber, particulate core material is suspended in an upwardly moving air stream. The design of the chamber and its operating parameters influence the recirculation flow of particles through the coating zone portion of the coating chamber where coating material is sprayed onto the moving particles. With each pass through the coating zone, the core material receives a layer and this circular process is repeated depending on the purpose of microencapsulation. The supplemental air flow also serves to dry the product during encapsulation. The drying rate is directly related to the temperature of the supporting air stream used.[34]

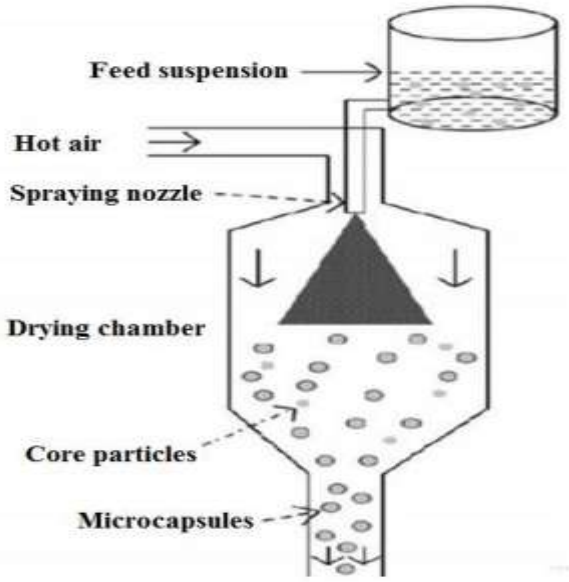

Fig.4.7: Air suspension

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4.8.Coacervation phase separation:
Microencapsulation via coacervation phase separation consists of three steps.

i) Formation of three immiscible phases: a liquid production phase, a core material phase and a coating material phase.
ii) Deposition of a liquid polymer coating onto the core material.
iii) Curing of the coating, usually by thermal, crosslinking or desolvation techniques, to form microcapsules. Depositing a liquid polymer coating around the interface between the core material and the liquid carrier phase. Often, physical or chemical changes are induced in the coating polymer solution, which can lead to phase separation of the polymer. Droplets of concentrated polymer solution form and coalesce to form a two-phase liquid-liquid system. If the coating material is an immiscible polymer, it can be added directly. Monomers can also be dissolved in the liquid vehicle phase and polymerized at the interface. The key equipment required for microencapsulation by coacervation phase separation method is a jacketed tank equipped with a variable speed stirrer. [22]

V. EVALUATION PARAMETEROF MICROSPHERES

5.1.Characterization

Characterization of particulate carriers is an important phenomenon that aids in the development of suitable carriers for the delivery of proteins, drugs, or antigens. The microstructures of these microspheres are different. Carrier release and stability are determined by these microstructures [23]

5.2.Particle size and shape

The most well-known methods for visualizing microparticles are conventional light microscopy (LM) and scanning electron microscopy (SEM). Both can be used to analyse the shape and external structure of particles. For double-walled microspheres, LM allows control over coating parameters. The microsphere structure can be seen before and after coating, and its changes can be measured using a microscope. In contrast to LM, SEM offers higher resolution. SEM images allow inspection of the surface of microspheres and can also be used to inspect the double-walled structure of the particle cross-section[26].

5.3.Electronspectroscopy forchemical analysis

The surface chemistry of the microspheres can be determined using electron spectroscopy for chemical analysis (ESCA) [27]

5.4.Density measurement

The density of microspheres can be calculated using a multivolume hydrometer accurate weight sample in cup is the placed into the multi volume pycnometer.helium is at constant pressure in chamber and allowed. [28].

5.5.Isoelectric point

Micro electrophoresis is used to calculate the electrophoretic mobility of microspheres, from which the isoelectric point can be calculated. The calculated by weiging the time of particle movement of a distance of 1nm.**[**29**]**

5.6.Contact angle

To determine the wetting properties of particulate carriers, the contact angle is determined . microspheres heap that formed area of free standing after making microspheres flow the glass funnel.[30]

5.7.In vitro method

Release studies of certain types of microspheres are often performed using a rotating paddle apparatus (USP/BP) using another suitable dissolution medium .[2]

5.8.Effectiveness of drug encapsulation

The capture efficiency or percent capture of microspheres can be determined by keeping the microspheres in a buffer and dissolving them. The resulting lysate is filtered or centrifuged and active ingredients determined according to monograph requirements. Drug entrapment efficiency can be calculated using the following formula: % inclusion = actual content/theoretical content x 100.[31]

5.9.Percentage Yield rate

It is calculated by multiplying the weight of the microspheres obtained from each batch by the total weight of drug and polymer used to prepare that batch by 100.[31]

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5.10.Swelling index

The swelling index of the microspheres was determined using the following formula:
Swelling index = (mass of swollen microspheres – mass of dry microspheres/mass of dry microspheres) [2]

VI. FLOW PROPERTIES

6.1.Bulk density

To measure, pour a sample of microspheres of known weight into a graduated cylinder without tapping, measure the length, and divide the weight by the volume.
Bulk density = weight of microsphere/bulk volume

6.2.Tap density

To determine this, pour a sample of microspheres of known weight into a graduated cylinder, tap well, measure the volume, and divide the weight by the volume.
Tap density = weight of microsphere/volume after tapping

6.3.Hausner ratio

The Hausner ratio is the ratio of the tap density to the bulk density of the microsphere and can be used to predict the flow of the microsphere. A low Hausner ratio of 1.2 indicates free-flowing microspheres.

Hausner ratio = bulk density – tapped density

6.4.Angle of repose

This is defined as the maximum angle to the horizontal that can be achieved by a microsphere cluster. Fixed height cones and fixed base cones can be used to calculate the angle of repose.
Angle of rest = tan-1 h/r
R = radius of the base of the microsphere cluster
h = height of the microsphere cluster

6.5.Zeta potential

The polyelectrolyte shell is constructed by solidifying chitosan with different atomic charges in the W2 stage, and the subsequent particles are determined by estimating the zeta potential.[31,32,33]

VII. APPLICATIONS OF MICROSPHERES

- Taste and odour masking
- Delay volatilization
- Safe handlings of the toxic effect

Increase the stability of drug against the external condition.

7. 1.Microspheres in vaccine delivery

A prerequisite for vaccines is protection against microorganisms or their toxic substances. An ideal vaccine must meet the requirements of efficacy, safety, ease of use, and cost. The aspects of safety and minimizing side effects are complex issues. The safety aspects and the degree of induction of antibody responses are closely related to the type of application. Biodegradable delivery systems for parenteral vaccines have the potential to overcome the shortcomings of traditional vaccines. Interest in parenteral (subcutaneous, intramuscular, intradermal) carriers is that they offer certain advantages, such as:

- Improvement of antigen city by adjuvant effect
- Regulation of antigen release.
- Antigen stabilization.

7.2.Targeting with particulate carriers

The concept of targeting, or. site-specific drug delivery, is a well-established dogma and is receiving increasing attention. The therapeutic efficacy of drugs depends on their access and specific interactions with candidate receptors. Being able to evacuate the pool in a reproducible, efficient and specific manner is a prerequisite for drug effects mediated by the use of delivery systems.

7.3.Monoclonal antibodies facilitate targeting of microspheres

Monoclonal antibodies that target microspheres are immuno microspheres. This targeting is used to selectively target specific websites. Monoclonal antibodies are highly specific molecules. This extremely high specificity of monoclonal antibodies (Mabs) can be exploited to deliver bioactive molecules packed into microspheres to target sites. Mabs can be directly attached to microspheres through covalent bonds. Free aldehyde, amino, or hydroxyl groups on the surface of the microspheres can bind antibodies.[15,16]

- Non-specific adsorption and specific adsorption

Cards can be attached to microspheres
One of the following methods:

- Direct coupling
- Reagent-mediated coupling

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7.4.Imaging

Microspheres have been extensively studied and used for targeting purposes. Radiolabeled microspheres can be used to image a variety of cells, cell lines, tissues, and organs. The particle size range of microspheres is an important factor in determining the imaging of a specific location. Particles injected intravenously outside the portal vein become trapped in the capillary beds of the lungs. This phenomenon has been exploited for scintigraphic imaging of lung tumor masses using labelled human serum albumin microspheres [17,18]

7.5.Topical porous microspheres

Microsponges are porous microspheres with numerous interconnected cavities with particle sizes ranging from 5 to 300 µm. These Microsponges contain a wide range of active ingredients such as emollients, fragrances, and essential oils and are used as topical delivery systems. Additionally, these porous microspheres containing active ingredients can be incorporated into formulations such as creams, lotions, and powders. Microsponges consist of an unfolded structure with a porous surface from which active ingredients are released in a controlled manner.

7.6.Nasal administration of drugs

Intranasal (IN) administration offers many theoretical and practical advantages for local and systemic administration of various therapeutic compounds. IN delivery is needle-free, non-invasive, essentially painless, does not require sterile preparations, and can be self-administered. The large surface area of the nasal mucosa, formed by the presence of a large number of microvilli, a porous endothelial membrane, and a highly vascularized epithelium, ensures a rapid onset of therapeutic effect. Describes various systems, devices, formulations, and methods for administering drugs into the nose or nasal cavity. Depending on the therapeutic purpose, intranasal drugs can be used specifically for local treatment or systemic effects. For nasal drug delivery, the attachment of bioadhesive properties to microspheres is of great importance due to other advantages. Reducing the frequency of drug administration due to efficient absorption and increased bioavailability of the drug, closer contact with the mucosal layer, and less frequent administration of the drug. Mucociliary drug removal A drug delivery system that adheres to the nasal mucosa.

7.7.Gastroretentive controlled delivery system

Floating systems are low-density systems that float above the stomach contents and remain in the stomach for a longer period of time than traditional dosage forms. Gastric emptying of dosage forms is a highly variable process, and the ability to control emptying time is a valuable advantage for dosage forms. However, there are some difficulties in developing controlled release systems for better absorption and improved bioavailability. When the system hovers over the stomach contents, the drug is slowly released at the desired rate, resulting in longer gastric residence times and reduce fluctuations in drug concentrations in the plasma. Several polymers such as cellulose acetate, chitosan, Eudragit, acriquat, methocyl, Polyacrylates, polyvinyl acetate, carbopol, agar, polyethylene oxide, polycarbonate, acrylic resins, and polyethylene oxide have been used in gastric retention controlled delivery systems. [22]

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7.8.Implantable devices

Microencapsulation is also used medically to encapsulate living cells and vaccines. Biocompatibility can be improved by encapsulating artificial cells and biomolecules such as peptides, proteins, and hormones, preventing unnecessary immune reactions that can lead to inactivation and rejection. Microspheres are used to isolate substances until their activity is needed. The biotechnology industry uses microspheres to contain microorganisms and their recombinant products and to aid in the isolation of these products

.

7.9.Application to pharmaceuticals

There are currently a large number of microencapsulated medicines on the market, including aspirin, theophylline and its derivatives, vitamins, pancrelipase, antihypertensive agents, potassium chloride, progesterone, and combinations of contraceptive hormones. Microencapsulated KCL is used to prevent gastrointestinal complications associated with potassium chloride. The dispersibility of microcapsules and controlled release of ions minimizes the possibility of localized high salt concentrations that can cause ulcers, bleeding, and perforation. Microspheres have also found potential use as injectable or inhaled products. The

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number of products on the market does not reflect the amount of research conducted in this area or the benefits that can be achieved with this technology. Economic considerations were an important factor in determining the number of microencapsulated drugs. Most encapsulation processes are expensive and require large capital investments in equipment. Pan coating or spray coating and spray drying are exceptions, as the necessary equipment may already exist in-house. Most microencapsulation processes are patent protected and therefore incur additional costs.

7.10.Other uses

Fluorescent microspheres can be used in membrane-based techniques for flow cytometry, cell biology, microbiology, and fluorescence-coupled immunosorbent assays. Yttrium can be used in the primary treatment of hepatocellular carcinoma and can also be used to treat his HCC before transplantation with promising results. There are many applications for microencapsulation in other industries. The most well-known microencapsulated products are carbonless copy paper, photosensitive paper, microencapsulated fragrances such as "scent strips" (also known as "snap and bursts"), and microencapsulated flavour's (``scratch and sniff''). '). All these products are typically produced by gelatin-acacia complex coacervation. Scratch and sniff is used in children's books and in advertising for food and cosmetic flavors. Microcapsules are also commonly used in diagnostics. For example, temperature-sensitive microcapsules for thermographic detection of tumors. In the biotechnology industry, microencapsulated microbial cells are used for the production of recombinant proteins and peptides.

VIII. CONCLUSION

.Microspheres are an innovative and advanced approach to drug delivery. Compared to other forms of drug delivery, patient compliance and target accuracy are improved, making drug delivery safer. Microspheres are the most popular drug delivery technology due to their advantages of sustained and controlled release, increased stability, reduced dosing frequency, and reduced dissolution rate and bioavailability. As a versatile drug delivery system, microsphere drug delivery systems can be used for various purposes such as targeted drug delivery, floating delivery, and vaccine delivery. There are many efficient methods to prepare and evaluate microspheres after manufacture. In addition to drug delivery, microspheres are also used to diagnose bio molecular interactions, scan tumors, and treat cancer. With all their important properties, microspheres are undoubtedly promising candidates for delivering drugs and related substances in a novel and absolutely beneficial way, and will have an even greater impact on medicine in the future. There is a possibility.

REFERENCES

[1]. Vyas S.P. and Khar R.K., Targeted and Controlled drug delivery, 07 Edition, Vallabh Prakashan, New Delhi India, 420-445.

[2]. Alagusundaram M, Chetty MSC, Umashankari K, Badarinath AV, Lavanya C, Ramkanth S. Microspheres as a Novel Drug Delivery System-A Review. International Journal of Chem Tech Research 2009 1 526-34

[3]. Varma N.K., Alam G, Vishwakarma D.K., Mishra J.N., Khan W.U., Singh A.P., Roshan A. Recent Advances in Microspheres Technology for Drug Delivery. International Journal of Pharmaceutical Sciences and Nanotechnology. 2015 May 31; 8(2):2799-813

[4]. Dandagi P.M., Mastiholimath V.S, Patil M.B., Gupta M.K., Biodegradablemicro particulate system of captopril. International Journal of Pharmaceutics. micro particulate system of captopril. International Journal of Pharmaceutics. 307, 2006, 83-88.

[5]. Chinna G. B., Shyam S. R., V. K. Varma. M., Sleeve Raju M., Sai Kiran M, Formulation and Evaluation of Indomethacin Microspheres using natural and synthetic polymers as Controlled Release Dosage Forms. International Journal of Drug Discovery, 2(1), 2010, 8-16.

[6]. Mazumder. R., Nath L. K., Anwarul, Haque, Tarasankar. M., Chaudhary P. K., Shrestha B., Formulation and in vitro evaluation of natural polymers based microsphere for colonic drug delivery, International journal of pharmacy and pharmaceutical sciences, 2(1), 2010, 211-219

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 5 Sep-Oct 2023, pp: 1407-1421 www.ijprajournal.com ISSN: 2249-7781

[7]. Kavitha K, Chintagunta.P., Kumar A.S. N., Tamizh M. T, Formulation and evaluation of trimetazine hydrochloride loaded gelatin microsphere. International Journal of Pharmacy and Pharmaceutical Sciences, 2(3), 2010, 67-70

[8]. Chaware P, Sharma S, Bhandari A, Garud A, Garud N. Bioadhesive Microspheres: A Review on Preparation and In-Vitro Characterization. World Journal of Pharmaceutical Research. 2014;4(2):423-36.

[9]. Farah Hamad Farah, et. al., Magnetic Microspheres: A Novel Drug Delivery System, Analytical and Pharmaceutical Research. 2016;3(5):1-10. DOI: 10.20959/wjpps20179-10054.

[10]. Jagtap Yogesh Mukund, et. al., Floating microspheres: a review, Brazilian Journal of Pharmaceutical Sciences, 2012;48(1):17-30.

[11]. Urs Hafeli, et. al., Review: Radioactive Microspheres for Medical Applications, Cleveland Clinic Foundation, Radiation Oncology Department T28, page 1-29.

[12]. Lachman LA, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. Varghese Publishing House, Mumbai, India: 1991, 3rd edition; P-414-415.

[13]. Ketie Saralidze, et. al., Polymeric Microspheres for Medical Applications, Materials, 2010, 3, Page 3537- 3564

[14]. Nair R, Reddy B. Application of chitosan microspheres as drug carriers: a review. J Pharm Sci Res 2009;1:1-12

[15]. Kadam NR, Suvarna V. Microsphere a brief review. Asian J Biomed Pharm Sci 2015;5:13-9.

[16]. Kataria S, Middha A. Microsphere a review. Int J Res Pharm Chem 2011;1:2237-781

[17]. Pradeesh TS, Sunny MC, Varma HK, Ramesh P. Preparation of microstructured hydroxyapatite microspheres using oil in water emulsions. Bull Materials Sci 2005;28:383-90.

[18]. Jayaprakash S, Halith SM, Mohamed Firthouse PU, Kulaturanpillai K. Preparation and evaluation of biodegradable microspheres of methotrexate. Asian J Pharm 2009;3:26-46.

[19]. Kumar. A, Jha .S, Rawal. R, Chauhan P.S. and Maurya S.D. Mucoadhesive microspheres for novel drug delivery system: A Review. American Journal of Pharm Tech Research. 2013; 3(4):197- 13.

[20]. Meena K.P., Dangi J.S., Samal P.K., Namedo K.P. Recent advances in microsphere manufacturing technology. International Journal of Pharmacy and Technology. 2011; 3(1):854-855.

[21]. Kadam N.R., Suvarna.V. Microsphere: a brief review. Asian Journal of Biomedical and Pharmaceutical Sciences.2015 Aug 1; 5(47):13.

[22]. Pavan Kumar B., Chandiran I. S., Bhavya B., Sindhuri M., Microparticulate drug delivery system: A Review, Indian journal of pharmaceutical science & research, 2011;1(1):19-37.

[23]. Dhakar R. C., Maurya S. D., Sager B. PS., Bhagat S., Prajapati ,S. K., Jain C. P., Variables influencing the drug entrapment efficiency of microspheres: A pharmaceutical review, Der Pharmacia Lettre, 2010;2(5):102-116.

[24]. Parmar H, Bakliwal. S, Gujarathi. N, Rane. B, Pawar.S., Different method of formulation and evaluation of Mucoadhesive microsphere. International Journal of Applied Biology and Pharmaceutical Technology. 2010; 1(3):1157-1167

[25]. Moy A.C, Mathew S.T, Mattapan. R, Prasanth V.V. Microsphere-An Overview. International Journal of Pharmaceutical and Biomedical Sciences. 2011; 2(2):332-338.

[26]. Singh .C, Purohit. S, Singh .M, Pandey.B.L. Design and evaluation of microspheres: A Review, Journal of Drug Development and Research 2013; 2(2):18-27.

[27]. Sahil K, Akanksha M, Premjeet S, Bilandi A, Kapoor B. Microsphere: A review. International Journal of Research in Pharmacy and Chemistry 2011; 1(11):84-98.

[28]. Pavan.K. B, Chandiran. I.S, Bhavya. B, Sindhuri. Microparticulate drug delivery system: A Review. Indian journal of pharmaceutical science & research. 2011; 1(1):19- 37

[29]. Dhakar. R.C, Maurya. S.D, Sager. B.P.S, Bhagat. S, Prajapati. S.K, Jain.C.P.

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 5 Sep-Oct 2023, pp: 1407-1421 www.ijprajournal.com ISSN: 2249-7781

Variables influencing the drug entrapment efficiency of microspheres: A pharmaceutical review. Der Pharmacia Lettre. 2010; 2(5):102-116.

[30]. Gogu.P.K. Preparation & in vivo characterization of spray dried Microspheres Formulation Encapsulating 4- chlorocurcumin. Indian Journal of Pharmaceutical sciences. 2010; 72:346-352.

[31]. Patel N.R, Patel D.A, Bharadia P.D, Pandya. V, Modi.V. Microsphere as a novel drug deliver. International Journal of Pharmacy & Life Sciences. 2011; 2(8).

[32]. Thadanki .M, Chadalawada P.K, Lavanya.P., Umashankar. D, Formulation and evaluation of sustained release saxagliptin microspheres by ionotropic gelation method. International Journal of Bioassays. 2017; pg. no. 5328- 5333.

[33]. Dupinder. K, Saini S.S: Variable Effecting Drug Entrapment Efficiency of Microspheres: A Review. International Research Journal of Pharmaceutical and Applied Sciences (IRJPAS); 2013; 3(3):24-28.

[34]. NOVEL DRUG DELIVERY SYSTEMS (NDDS) (B.Pharmacy - Semester 7 - All Indian Universities - As Per PCI Syllabus) (Paperback, Dr. Rajesh Kumar Nema, Dr. Harish Sharma, Dr.Gyanesh Kumar Sahu, Ms. PreranaSahu)

[35]. https://journals.indexcopernicus.com/api/file/viewByFileId/724587.pdf

[36]. https://www.researchgate.net/figure/Evaluation-parameters-of-microspheres_tbl3_326912995

[37]. https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.researchgate.net%2Ffigure%2FSchematic-diagram-of-two-step-double-emulsion-solvent-evaporation-method-of-F-LM_fig1_305340084&psig=AOvVaw19nEioP0ovIeSvs4tWe3T_&ust=1698290996177000&source=images&cd=vfe&opi=89978449&ved=0CBMQjhxqFwoTCOi3yI6hkIIDFQAAAAAdAAAAABAE[38] https://www.researchgate.net/figure/Drug-release-mechanism-from-microspheres_fig5_266086935

[38]. https://www.researchgate.net/publication/266086935_Long-Term_Delivery_of_Protein_Therapeutics

[39]. https://www.researchgate.net/publication/334645337_Microsphere-A_Novel_Drug_Delivery_System

[40]. https://www.researchgate.net/publication/351675421_A_Novel_Drug_Delivery_System_Review_on_Microspheres

[41]. https://www.researchgate.net/publication/353637803_FLOATING_MICROSPHERE_AS_NOVEL_APPROACH_DRUG_DELIVERY_SYSTEM

[42]. https://journals.innovareacademics.in/index.php/ijcpr/article/view/38326#:~:text=Microspheres%20are%20normally%20free%2Dflowing,uniformly%20dispersed%2C%20dissolved%20or%20suspended.