*DOI: 10.55522/jmpas.V14I2.6841* **ISSN NO. 2320 – 7418**

International peer reviewed open access journal

**Journal of Medical Pharmaceutical and Allied Sciences**

Journal homepage: www.jmpas.com CODEN: JMPACO

Review article

# Microspheres: a novel drug delivery approach

**Rupajit Bhattacharjee[1], Kuntal Manna*[2], Sinha Ashutosh Kumar[1]**

[1]Department of Pharmaceutics, Bir Bikram College of Pharmacy, Old Agartala, Tripura, India
[2]Department of Pharmacy, Tripura University (A Central University), Agartala, Tripura, India

**Corresponding author:** Kuntal Manna, ✉ k_manna@tripurauniv.ac.in, **Orcid Id**: https://orcid.org/0000-0001-5327-365X

Department of Pharmacy, Tripura University (A Central University), Agartala, Tripura, India

© The author(s). This is an open access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by-nc/4.0/). See https://jmpas.com/reprints-and-permissions for full terms and conditions.

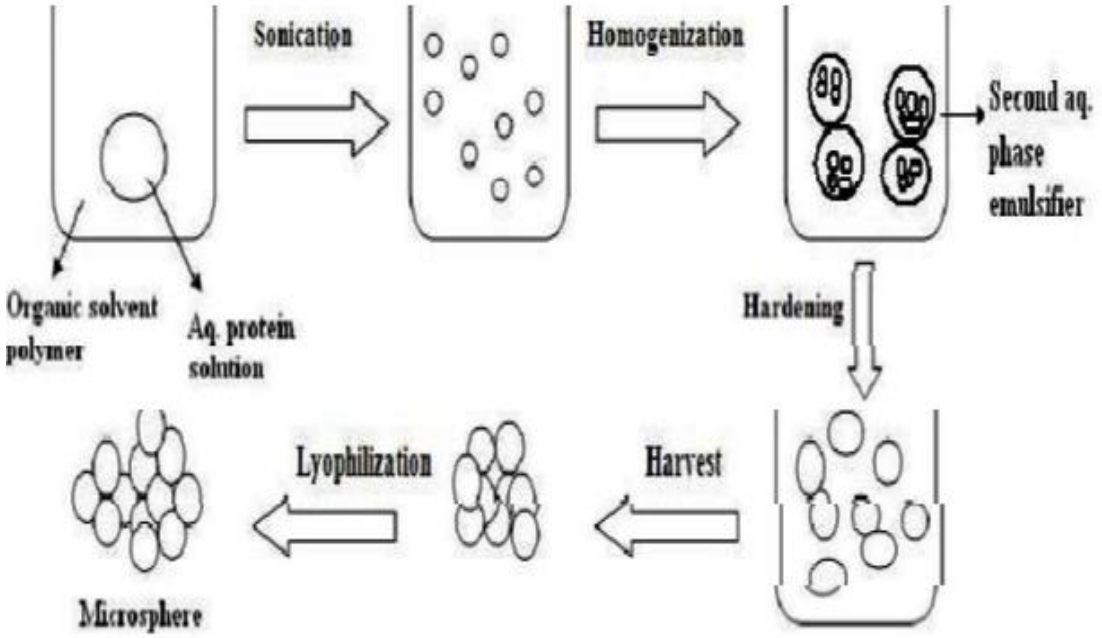
**Received** - 01-02-2025**, Revised** - 26-03-2025, **Accepted** - 22-04-2025 **(DD-MM-YYYY)**

Refer This Article

Rupajit Bhattacharjee, Kuntal Manna, Sinha Ashutosh Kumar, 2025. Microspheres: a novel drug delivery approach. Journal of medical pharmaceutical and allied sciences, V 14 - I 2, Pages - 42 – 54. Doi: https://doi.org/10.55522/jmpas.V14I2.6841.

## ABSTRACT

Advancements in biotechnology, genetics, and combinatorial chemistry are facilitating the development of a diverse array of novel, more effective and targeted therapies. The efficacy and commercialization potential of many new medications can be significantly influenced by drug delivery methods due to prevalent issues such limited solubility, high potency, and/or poor stability. Consequently, there is a want for safer and more efficient medication delivery systems and equipment. Drug delivery systems are engineered to administer a therapeutic agent in the requisite dosage, at the appropriate time, to the correct site within the body, thereby enhancing efficacy, improving compliance, and reducing side effects. Microspheres are typically free-flowing powders composed of proteins or biodegradable synthetic polymers, with an optimal particle size of less than 1000 µm. An effectively designed controlled drug delivery system can address some issues associated with conventional therapy and improve the therapeutic efficacy of a certain medicine. Multiple methodologies exist for administering a therapeutic agent to the target location in a sustained and controlled release manner. One method involves utilizing microspheres as medication carriers.




**Keywords:** Microspheres, Classifications of microspheres, Synthesis, Characterization, Applications.

## INTRODUCTION

Controlled release systems for drug delivery are being established to mitigate various challenges linked to conventional management methods. Devices like hydrogels, rods, pellets, micro particles; liposomes and polymer-based disks are used in controlled release drug delivery. These devices encapsulate the medication and release the therapeutic agents at regulated rates over extended periods of time, ranging from days to months [1, 2]. Microspheres serve as a medium for delivering drugs to the site of action at a controlled rate. These materials typically consist of biodegradable proteins or synthetic polymers, presented as powders with specific diameters ranging from 1 to 1000 µm. The application of microspheres offers numerous advantages in areas including drug delivery, bone tissue engineering, and the absorption/desorption of contaminants through regeneration. Polyethylene microspheres are frequently utilized as either permanent or temporary fillers. The reduced melting temperature of polyethylene microspheres facilitates the formation of porous structures in ceramics and other materials. Charged polyethylene microspheres are utilized in electronic paper digital displays. Glass microspheres serve mainly as fillers for weight reduction, retro-reflectors for highway safety, and additives in cosmetics and adhesives, with few applications in medical technology. Microspheres represent a widely studied drug delivery system for the targeted and sustained release of therapeutic agents. These materials exhibit biocompatibility, biodegradability, and the ability for surface modifications. A range of polymers has been investigated for their ability to encapsulate drugs with diverse physicochemical properties [1].

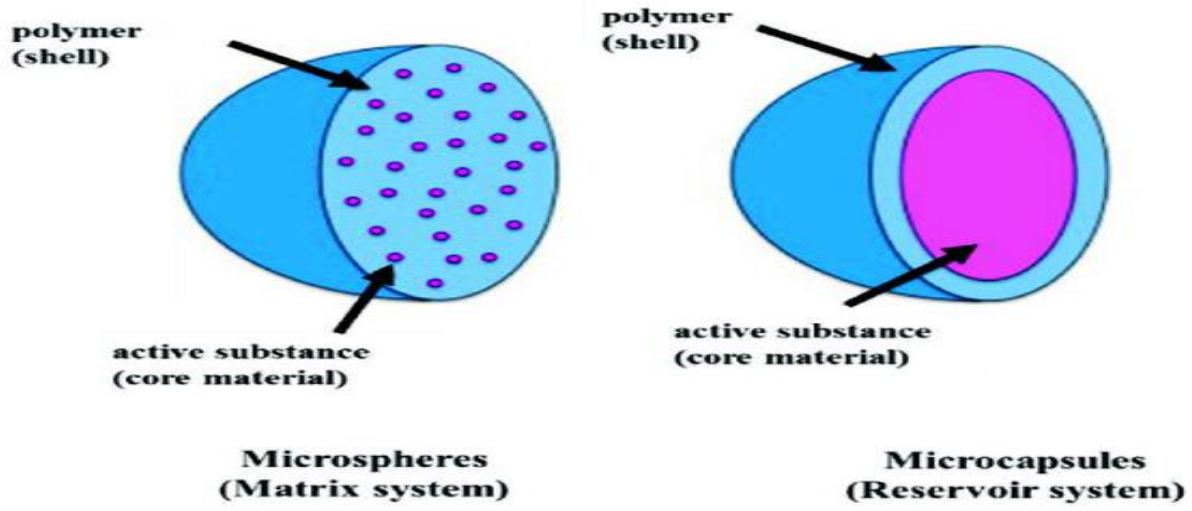
Microcapsules possess a unique capsule wall encasing the entrapped material, whereas micro matrices feature the entrapped substance distributed throughout the microsphere's matrix. The controlled release of a medicine can be achieved through the utilization of solid biodegradable microspheres containing the drug dispersed or dissolved inside a particle matrix. They consist of biodegradable synthetic polymers, modified natural goods, and polymeric, waxy, or other protective substances. They are manufactured utilizing polymers and waxes derived from both natural and manmade components. The polymer utilized in the fabrication of microspheres influences their stability, solubility, and drug release characteristics. The predominant types of polymeric microspheres are polyethylene, polystyrene, and expandable microspheres. Microspheres exist in both solid and hollow variants. Hollow microspheres serve as additions to decrease a material's density. Microsphere-based topical preparations have acquired attention for their prolonged therapeutic efficacy. Microparticulate medication delivery methods have gained prominence in recent years [3-8].

**Microspheres**

Microspheres represent the micro-particulate modality of drug administration. Microspheres as drug carriers represent a state-of-the-art method for sustaining and regulating pharmacological effects in a targeted area. Microspheres are minute particles measuring between 1 and 1000 micrometers. Microspheres facilitate transient embolization. These are eliminated from the body through natural metabolic processes after achieving their clinical objective without disrupting the operation of other organs. Microspheres are fabricated using natural and synthetic polymers. Various procedures are employed for the creation of microspheres, including single emulsion, double emulsion, polymerization, phase separation, spray drying, solvent extraction, and emulsion solvent evaporation [9-14].

The solid biodegradable microspheres included the drug either disseminated or dissolved inside the particle matrix, and they possess the potential for controlled drug release. Microspheres as drug carriers represent a highly successful innovative method for sustaining and regulating drug action at a specific region (e.g., tissue). Microspheres are classified into two categories: Microcapsules and Micro matrices.

**Figure 1:** Type of Microspheres



**Microcapsules**

These are structures in which the entrapped substance is completely enclosed by a defined capsule wall.

**Micro Matrices**

A system in which the entrapped substance is distributed throughout the matrix of the microsphere.

Their function includes the manipulation of the drug's in vivo action, pharmacokinetic profile, tissue distribution, and cellular interactions. They facilitate the controlled release of pharmaceuticals. Examples include narcotics, antagonists, and steroid hormones.

**Mechanism of Microspheres**

The predominant method of drug delivery through micro particles inhibits the development of a matrix-like internal solid dispersion morphology structure. The medication may be insoluble within the polymeric matrix, leading to its release during the erosion process. Initially, water permeates the matrix, dissolving the material that forms near the device's surface. The osmotic pressure is alleviated by creating a pathway to the surface and dispensing a specified quantity of medication during the initial drug release.

**Advantages of Microspheres drug delivery**

A reliable method of medication delivery guarantees that the drug arrives to the target location with specificity, if altered, and sustains the required concentration at the place of interest without negative effects.

Microsphere decreases the dose frequency, hence enhancing patient compliance.

Owing to their spherical morphology and diminutive dimensions, they can be administered inside the body.

Improving drug use will increase bioavailability while reducing the likelihood of unwanted effects.

The benefit of biodegradable microspheres over big polymer implants is that they can be installed and removed without the need for surgery.

Liquids, such as oils, are solidified to enhance their manageability.

The morphology of microspheres enables regulated drug release and alterations in degradation rates.

Targeting via the Use of Micro Particulate Carriers.

Chemo-embolization.

Topical porous microspheres Microsponge are porous microspheres featuring a network of interconnected spaces of between 5 and 300 µm.

Fluorescent microspheres have additional uses in cell biology, membrane-based technologies, flow cytometry, and Immuno sorbent tests connected to fluorescence [15-19].

## MATERIALS AND METHODS

**Materials used in Microspheres Formulation**

Microspheres are usually polymers containing drug encapsulated delivery system [15- 19].

**Figure 2:** Types of Polymer used for formulation of Microspheres

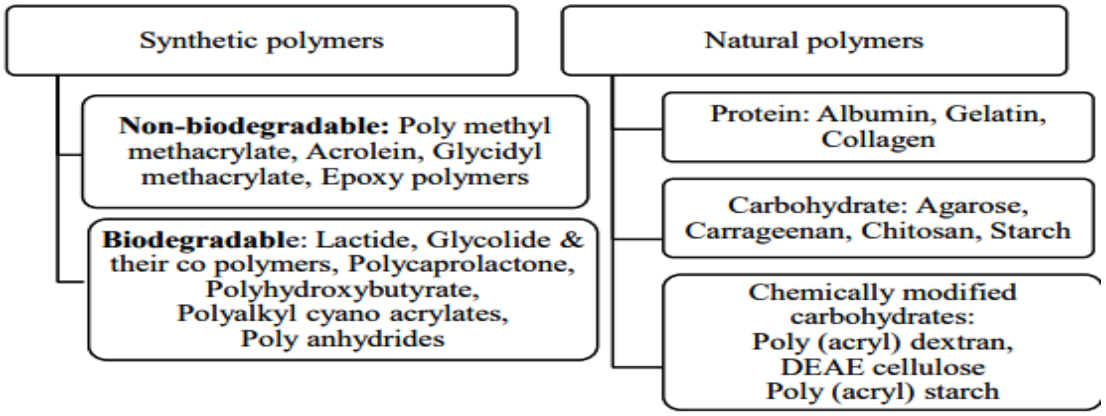



**Figure 3:** Types of Biodegradable Polymer used for formulation of Microspheres

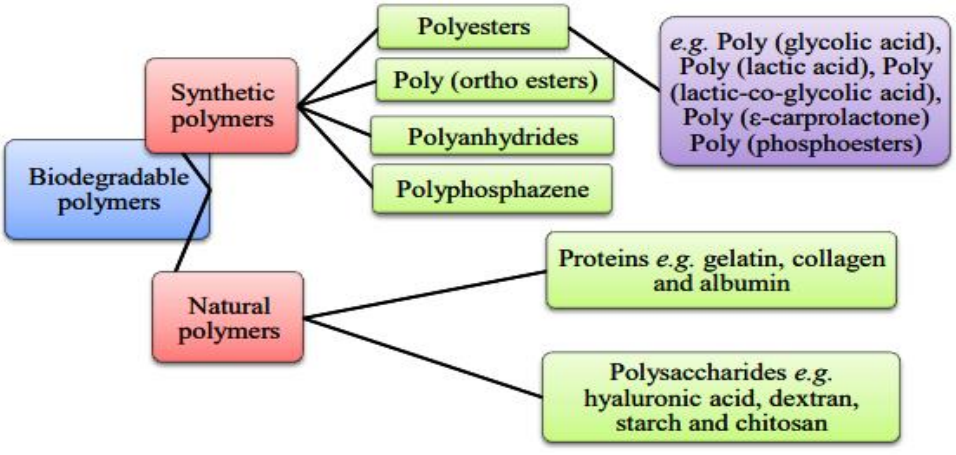
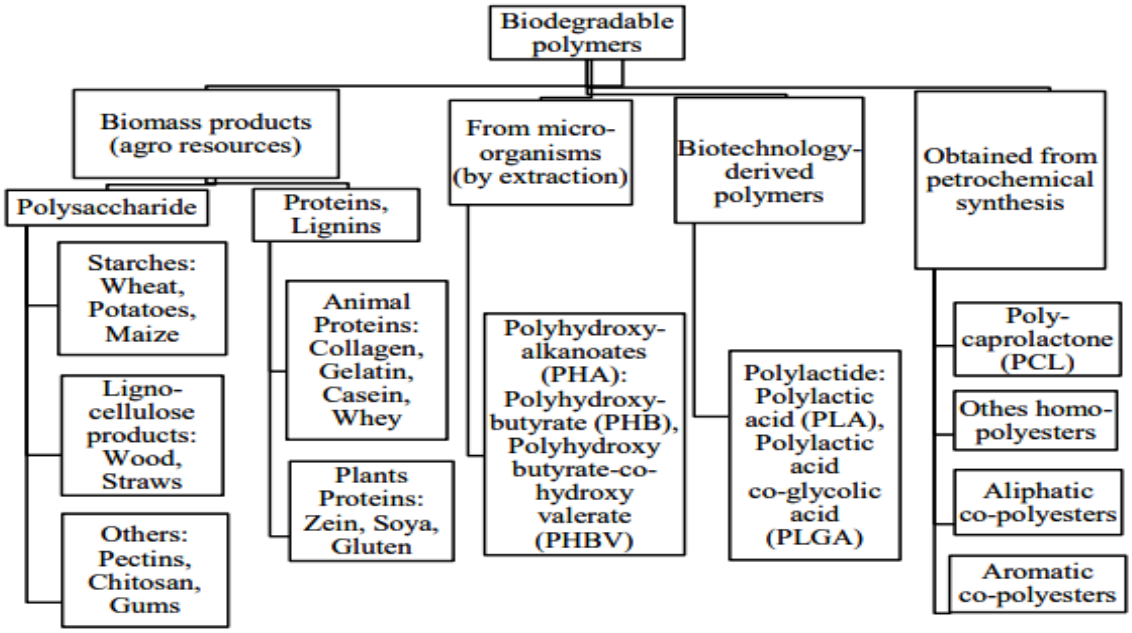


**Figure 4:** Types of Biodegradable Polymer on Basis Resources




**Types of Microspheres**

**Bioadhesive Microspheres**

Using the adhesive qualities of water-soluble polymers, adhesion is the technique of securing a medication to a membrane. Bioadhesion refers to a drug delivery system's adherence to a mucosal membrane, including buccal, ocular, rectal, nasal, and other mucosal membranes. These microspheres exhibit extended residence duration at the application site, leading to enhanced absorption and therapeutic efficacy.

**Magnetic Microspheres**

This delivery mechanism is essential as it enables the medicine to be delivered precisely at the necessary location. A less quantity of magnetically focused medication will supplant a greater quantity of freely circulating medication in this scenario. The included ingredients (e.g., chitosan, dextran, etc.,) implemented for magnetic microspheres, transmit magnetic responses to magnetic carriers via a magnetic field. Magnetic microspheres are categorized into two types:

**Therapeutic Magnetic Microspheres**

To target liver cancers with a chemotherapeutic medication, these are utilized. Proteins and peptides are potentially potential drug targets using this method.

**Diagnostic Microspheres**

These serve the purpose of diagnosis. Through the synthesis of nano-scale particles composed of paramagnetic iron oxides, it becomes feasible to visualize liver metastases and differentiate bowel loops from adjacent abdominal structures.

**Floating Microspheres**

The bulk density of these microspheres is lower than that of gastric fluid, allowing them to float in the stomach without influencing the rate of gastric emptying. The medication is released gradually and at the intended rate when the system is buoyant in gastric contents, which improves stomach residency and variability in plasma concentration. Strikes and dose dumping are less probable. The therapeutic effect is prolonged, resulting in reduced dosing frequency.

**Radioactive Microspheres**

Radio embolization therapy Microspheres with diameters ranging from 10 to 30 nm exceed the size of capillaries and become trapped in the initial capillary bed they encounter. They are introduced into the arteries, leading to the formation of a tumor of interest. In these conditions, radioactive microspheres effectively deliver a high radiation dose to targeted areas while preserving the integrity of adjacent normal tissues. This drug delivery system is distinct from others in that the radioactive substance is not released from the microsphere; instead, it exerts its effects from within a radioisotope. Examples: α, β, γ emitters.

**Polymeric Microspheres**

These are categorized into two classes:

**Biodegradable polymeric microspheres**

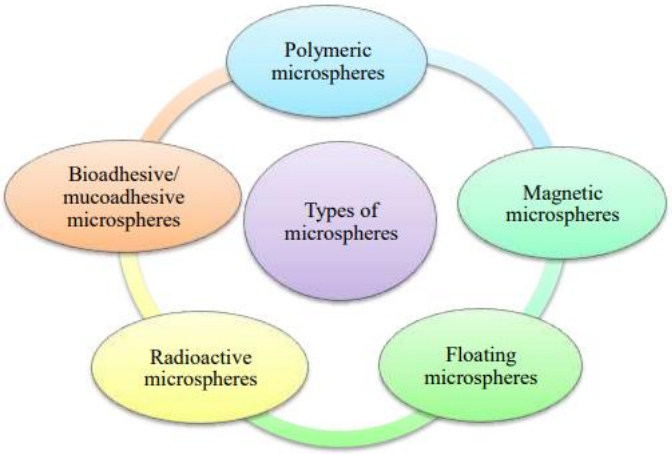
Natural polymers, including starch, are utilized for their biodegradable, biocompatible, and bioadhesive properties. Biodegradable polymers exhibit a high degree of swelling in aqueous environments, which prolongs their residence time in contact with mucous membranes and facilitates gel formation. The polymer concentration and temporal release pattern govern the rate and extent of medication release. The primary disadvantage is that the drug loading efficiency of biodegradable microspheres in clinical use is complex and challenging to regulate regarding drug release.

**Synthetic polymeric microspheres**

Synthetic polymeric microspheres are extensively utilized in clinical applications, including bulking agents, fillers, embolic particles, and drug delivery systems. Synthetic polymeric microspheres exhibit safety and biocompatibility. The primary drawback of these microspheres is their propensity to migrate from the

injection site, posing a risk of embolism and resultant organ damage [20 – 25].

**Figure 5:** Types of Microspheres




**Optimal Microspheres Carriers**

The fabrication of microspheres necessitates materials that exhibit the following properties:

Control over content dissemination;

Ensure the safeguarding of pharmaceuticals;

Extended duration of effect;

Solubility in water or dispensability;

Sterilization capability;

Non-toxic;

Biodegradability;

Enhancement of therapeutic efficacy;

Vulnerable to chemical alteration;

Regulated particle dimensions [26].

**Techniques for Microsphere Fabrication**

The following techniques are employed for fabrication of Microsphere:

Single emulsion techniques,

Double emulsion techniques

Polymerization

Phase separation coacervation technique

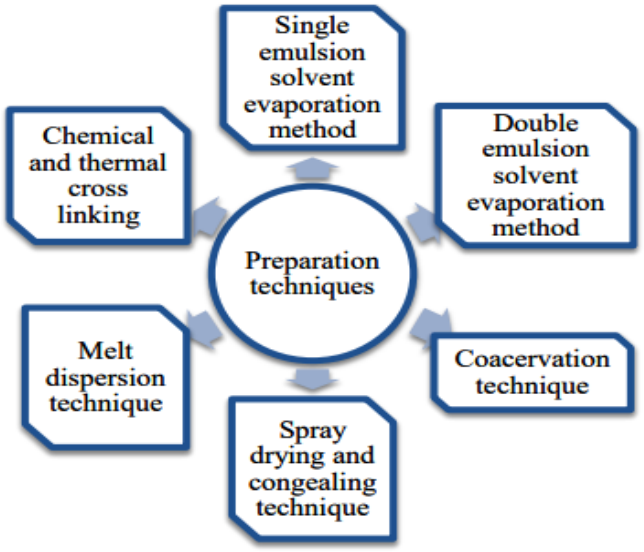
Spray drying and spray congealing

Solvent extraction

Quassi emulsion solvent diffusion

Ionic gelation method

**Figure 6:** Techniques for Microsphere Fabrication




**Single Emulsion Techniques**

A variety of proteins and carbohydrates can be prepared by first dissolving natural polymers, such as proteins and carbohydrates, in an aqueous medium and then dispersing them in a non-aqueous oil phase. Two approaches are employed to facilitate cross-linking in the subsequent stage as follows:

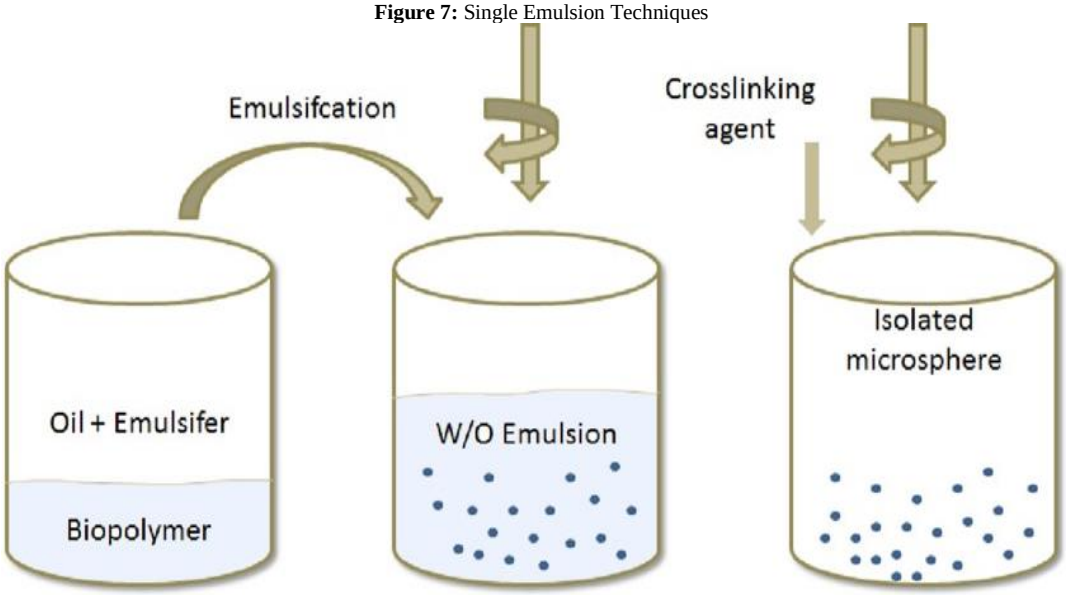
**Cross-linking via heat**

Nevertheless, heat denaturation is inappropriate for thermo labile pharmaceuticals, as this process necessitates the incorporation of the dispersion into preheated oil.

**Chemical cross-linking**

Involves the use of agents such as Glutaraldehyde, formaldehyde, terephthaloyl chloride, and diacid chloride [27-40].

**Figure 7:** Single Emulsion Techniques



**Double Emulsification Method**

This method outlines a procedure for the preparation of double emulsions, specifically of the water-in-oil-in-water (w/o/w) type. This method is frequently employed to encapsulate water-soluble drugs, peptides, proteins, and vaccines in polymer matrices. The process is outlined as follows:

**Formation of Multiple Emulsions (W/O/W)**

The procedure commences with the dispersion of an aqueous protein solution containing active components into a lipophilic organic continuous phase. This constitutes the primary emulsion, wherein the protein solution is spread inside the organic phase.

**Homogenization of Sonication:** The first emulsion is subsequently treated to homogenization or sonication to fragment droplets and attain a more uniform dispersion of the aqueous phase inside the organic phase.

**Addition of Polyvinyl Alcohol (PVA)**

The homogenized or sonicated emulsion is subsequently incorporated into an aqueous solution of polyvinyl alcohol (PVA). The incorporation results in the creation of a double emulsion, whereby the aqueous protein solution is disseminated inside the continuous aqueous phase containing PVA.

**Solvent Removal**

The double emulsion undergoes solvent extraction. This can be accomplished by techniques such as solvent evaporation or solvent extraction. Solvent evaporation may require sustaining the emulsion under reduced pressure or agitating it to facilitate the evaporation of the organic phase.

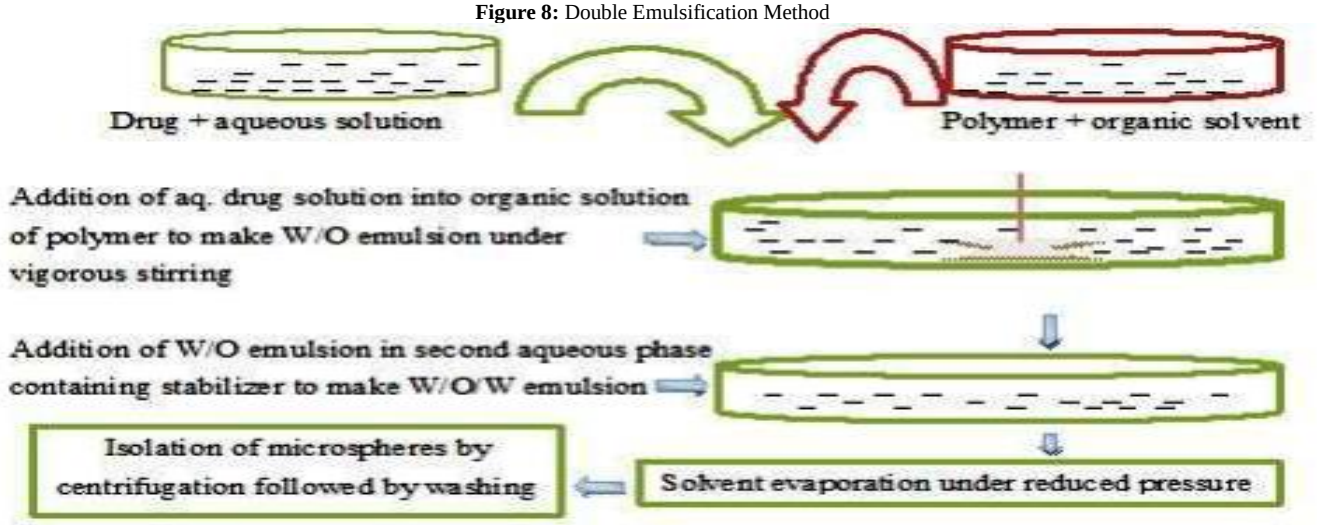
**Phase Separation**

Subsequent to solvent elimination, the emulsion is introduced into a substantial volume of water. This results in the organic phase diffusing into the surrounding water, leaving solid microspheres that contain the encapsulated protein and are encased in the polymer matrix.

**Filtration and Washing**

The solid microspheres are subsequently acquired using filtering, isolating them from the adjacent liquid. Cleaning with organic solvents like n-hexane or acetone effectively eliminates any residual oil from the microsphere surfaces, resulting in purified microspheres prepared for subsequent processing or application.

**Figure 8:** Double Emulsification Method




This technique enables the encapsulation of water-soluble molecules within polymer matrices, facilitating controlled release and safeguarding the contained materials. This approach is adaptable and utilized in pharmaceuticals, biotechnology, and other domains necessitating regulated delivery systems.

**Polymerization**

The standard polymerization procedures for microsphere preparation are essentially categorized into two types:

**Normal Polymerization & Interfacial Polymerization**

**Normal Polymerization**

Normal polymerization includes several approaches, namely bulk, suspension, precipitation, emulsion, and micellar polymerization procedures.

Conducted in the liquid phase.

Bulk polymerization entails the thermal activation of a monomer or a combination of monomers using an initiator or catalyst to commence polymerization.

The resultant polymer can be shaped into microspheres, with drug loading potentially occurring during the procedure.

Suspension polymerization, referred to as bead or pearl polymerization, is the heating of monomer or monomer combinations in droplet dispersion within a continuous aqueous phase, typically incorporating initiators and additives.

Emulsion polymerization contrasts with suspension polymerization in that the initiator resides in the aqueous phase, subsequently spreading to the surface of micelles.

Bulk polymerization offers the benefit of producing pure polymers.

**Interfacial Polymerization**

Engages the interaction of diverse monomers at the interface of two immiscible liquid phases to produce a polymer film that effectively encases the dispersion phase.

Conducted in the liquid phase.

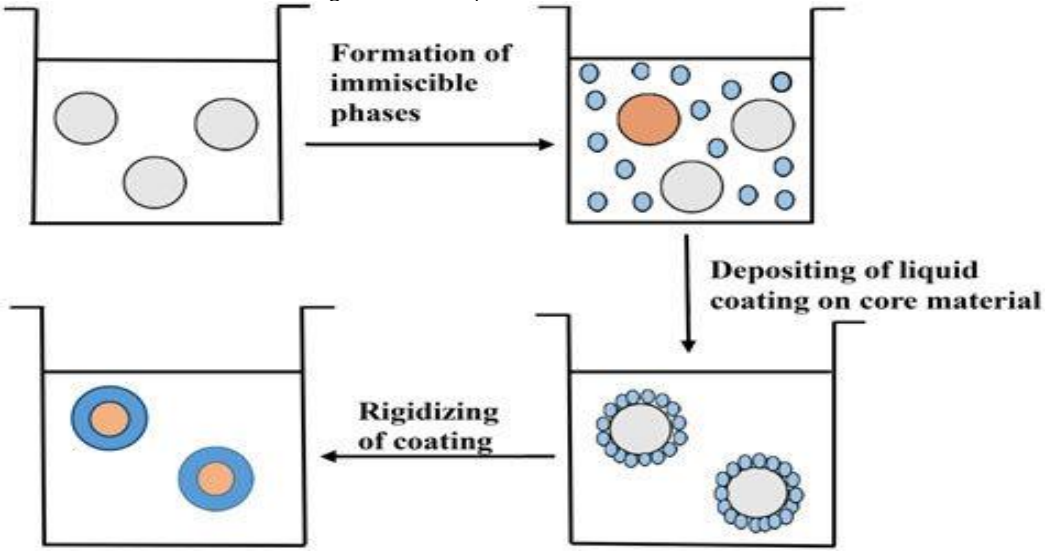
Normal and interfacial polymerization processes are essential in the

synthesis and development of microspheres, providing distinct methodologies and benefits for diverse applications in medicines, materials science, and biotechnology.

**Phase Separation Coacervation Method**

The phase separation process is specifically designed for the fabrication of reservoir-type systems. This method is utilized to encapsulate water-soluble pharmaceuticals, including peptides, proteins, and certain matrix-type formulations, particularly when the drug possesses hydrophobic properties, as exemplified by steroids. Coacervation is a procedure aimed at the creation of micrometer-sized biodegradable polymer encapsulating formulations through liquid-liquid phase separation techniques. The processing parameters, such as polymer concentration, quenching temperature, quenching duration, and solvent composition, influence the form and dimensions of the microsphere.

**Figure 9**: Phase Separation Coacervation Method




**Spray Drying and Spray Congealing**

These approaches depend on the evaporation of the polymer and drug aerosol in the atmosphere. The two procedures, designated based on the process of solvent removal or solution cooling, are termed spray drying and spray congealing, respectively. The polymer is first dissolved in a volatile organic solvent such as dichloromethane or acetone. The solid medication is subsequently distributed in the polymer solution using high-speed homogenization. Thereafter, this dispersion is atomized in a stream of heated air, resulting in the creation of small droplets or a fine mist, from which the solvent swiftly evaporates, yielding microspheres sized between 1 and 100 µm. Microparticles are extracted from the heated air utilizing a cyclone separator, while residual solvent traces are removed via vacuum drying. A significant benefit of this technique is its operability under aseptic conditions. In spray drying, different penicillins are encapsulated, whereas thiamine mononitrate and sulpha ethyl-thia-di-zole are encapsulated in a mixture of mono- and diglycerides of stearic and palmitic acids through spray congealing. Rapid solvent evaporation, however, results in the creation of porous microparticles.

**Figure 10:** Spray Drying Method

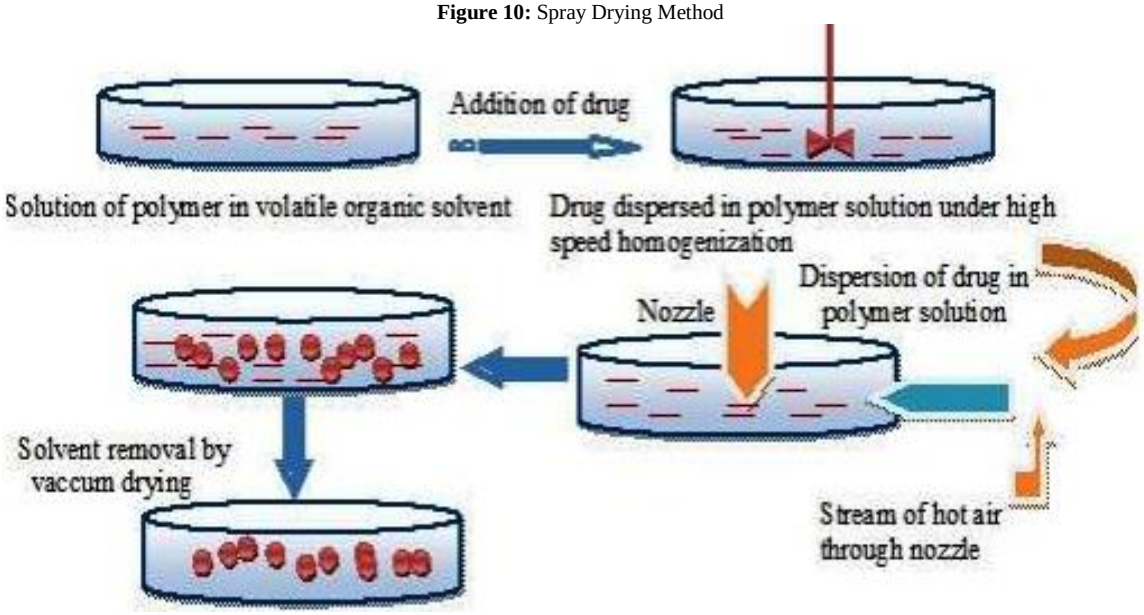


**Figure 11:** Spray Congealing Method

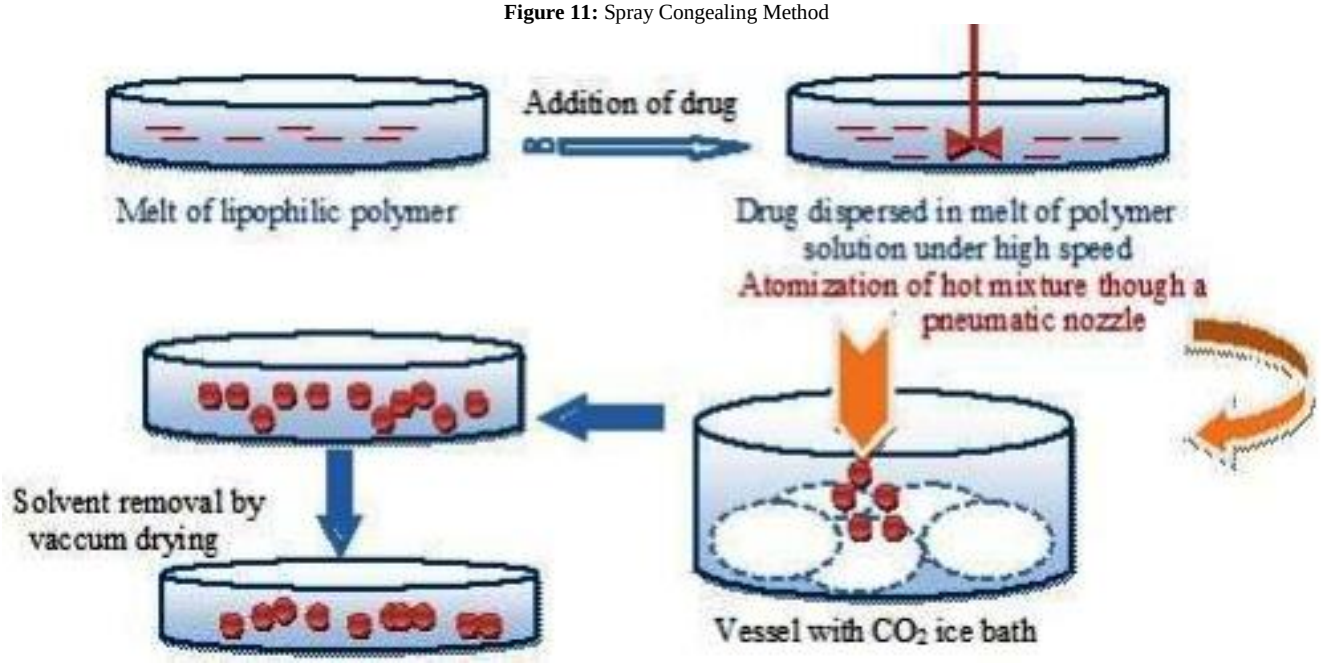
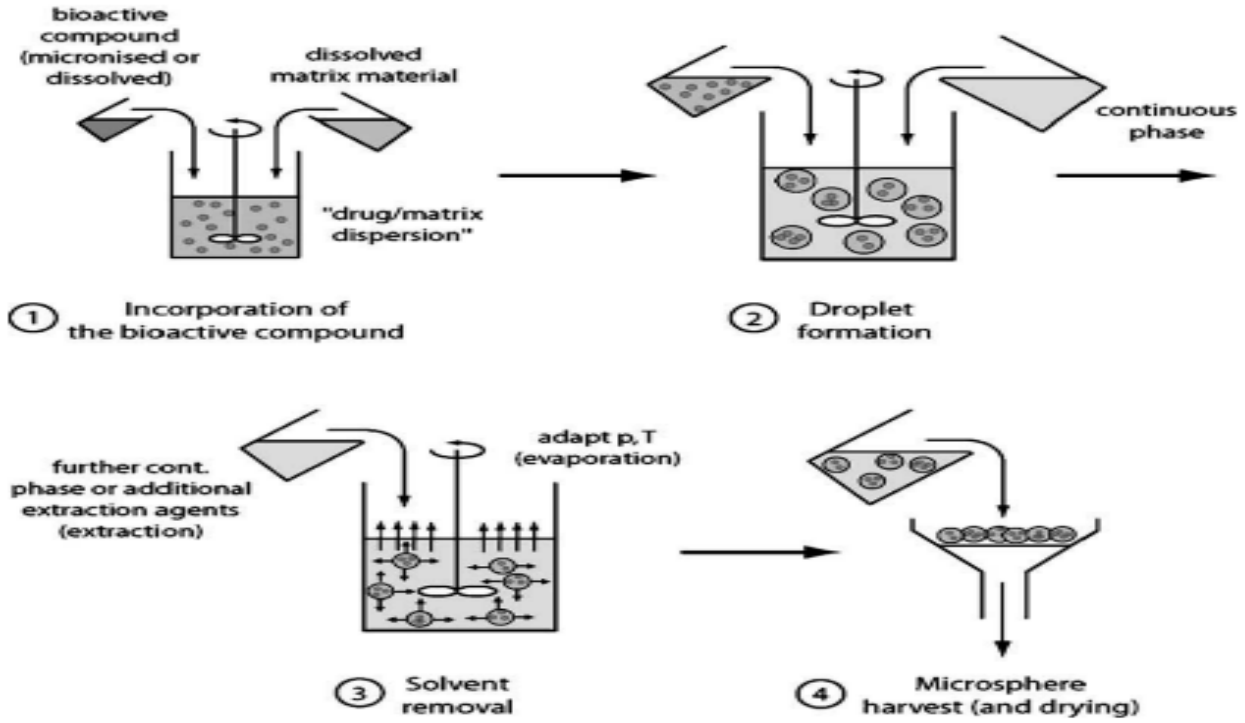



**Figure 12:** Solvent Extraction Method




**Solvent Extraction Method**

The preparation of micro-particles via the solvent extraction method involves the extraction of the organic phase to eliminate the organic solvent. This method employs water-miscible organic solvents such as isopropanol. The extraction of the organic phase is performed using water, which decreases the hardening time of the microspheres. The procedure entails the direct incorporation of the drug or protein into the polymer-organic solution. The rate of solvent removal through the extraction method is influenced by water temperature, the emulsion volume-to-water ratio, and the polymer's solubility profile.

**Quassi Emulsification Method**

The literature introduces a new quasi-emulsion solvent diffusion technique for the fabrication of controlled-release drug microspheres utilizing acrylic polymers. Microspheres are synthesized through a quasi-emulsion solvent diffusion technique, utilizing distilled water and polyvinyl alcohol (PVA) as the external phase. The internal phase comprises the drug, ethyl alcohol, and polymer, with the polymer incorporated at a concentration of 20% to improve plasticity. The internal phase is first prepared at 60ºC and then introduced to the external phase at room temperature. After emulsification, the mixture is stirred continuously for 2 hours, followed by filtration to isolate the Microsponge. The product is subjected to washing and subsequently dried in a vacuum oven at 40ºC for duration of 24 hours. This method

can be used to encapsulate Ibuprofen.

**Ionic Gelation Method**

This method facilitated the development of an alginate/chitosan particulate system for the controlled release of diclofenac sodium. The medication is first combined with an aqueous sodium alginate solution. Stirring is maintained until complete dissolution occurs, after which a $Ca^{2+}/Al^{3+}$ solution is added incrementally to create a homogeneous mixture. Internal gelation is achieved by permitting the microspheres to remain in the initial solution for 24 hours prior to filtration and separation. The optimal release of diclofenac sodium occurs within the pH range of 6.4 to 7.2, facilitating complete release. Nonetheless, the drug persists at acidic pH levels.

## RESULT AND DISCUSSION

**Physicochemical Characterization of Microspheres**

**Characterization**

Characterizing micro particulate carriers is essential for developing suitable carriers for the transport of proteins, medications, or antigens. The diverse microstructures of these microspheres govern the release and stability of the carriers.

**Particle Size and Shape**

The two most popular methods for observing microscopic particles are scanning electron microscopy (SEM) and conventional light microscopy (LM). Both methods enable the examination of the form and structure of micro particles. In the instance of double-walled microspheres, LM facilitates adjustments to the coating settings. Pre- and post-coating, the structures of microspheres can be observed, allowing for microscopic assessment of any differences. In contrast to LM, SEM boasts superior resolution. SEM facilitates the exploration of microsphere surfaces and can also delve into double-walled structures upon cross-sectioning of particles.

**Electron Spectroscopy for Chemical Analysis (ESCA)**

The surface chemistry of microspheres can be determined using it.

**Density Determination**

To find out how dense the microspheres are, you can use a multi-volume pycnometer.

**Iso-electric Point**

Micro-electrophoresis is utilized to measure the electrophoretic mobility of microspheres, which assists in identifying their iso-electric point.

**Angle of Contact**

Finding out whether microspheres are hydrophilic or hydrophobic can be done by measuring the contact angle, which is a measure of the wetting property of a micro particle carrier. Because adsorbed components affect this thermodynamic property, it is relevant only to solids. By placing a droplet in a circular cell that is placed above the objective of an inverted microscope, the contact angle at the solid/air/water interface may be determined, along with the receding angle. Within one minute of microsphere deposition, measurements of the contact angle are taken at a temperature of 20°C.

**Swelling Index**

The swelling index was ascertained by quantifying the degree of swelling of microspheres in the supplied buffer solution. To achieve total equilibrium, a meticulously measured quantity of microspheres was permitted to expand in the specified buffer. Excess liquid adhering to the surface was eliminated using blotting, and the enlarged microspheres were weighed with a microbalance. Thereafter, the hydrogel microspheres were subjected to drying in an oven at 60°C for 5 hours until the mass of the dried sample stabilized. The swelling index of the microspheres was determined utilizing the formula:

$$\textbf{Swelling index} = \frac{\text{Mass of swollen microspheres} - \text{Mass of dry microspheres}}{\text{Mass of dried microspheres}} \textbf{ X100}$$

**Hausner Ratio**

The Hausner ratio denotes the relationship between the tapped density and the bulk density of microspheres, functioning as a measure of their flow characteristics. A Hausner ratio below 1.2 indicates that the microspheres exhibit free-flowing characteristics.

**Angle of Repose**

The greatest angle that a pile of microspheres can reach with respect to the horizontal is known as the angle of repose. The fixed base cone and fixed height cone methods are two ways to measure the angle of repose. Microspheres with a low angle of repose appear to be free-flowing, while those with a high angle are poor-flowing.

$$\textbf{Angle of Repose } (\theta) = \tan^{-1} h/r.$$

r = the radius of the base of the heap of microsphere

h = height of the heap of microsphere

**Surface Charge Analysis**

The assessment of surface charge can be conducted through micro-electrophoresis, a specialized apparatus that measures the electrophoretic mobility of microspheres, thereby enabling the determination of the iso-electric point. The mean velocity at different pH values, generally between 3 and 10, is calculated by recording the time required for particle displacement over a specified distance, commonly 1 mm. It is possible to determine the particle's electrical mobility using this data. Both the ion absorption properties and the surface-contained charge of the microspheres are intimately related to the electrophoretic mobility.

***In Vitro* Methods**

Determining a drug's permeability and release properties through membranes requires experimental techniques. In response to this requirement, numerous in vitro and in vivo methodologies have been established. The quality control processes of in vitro drug release investigations are essential in pharmaceutical manufacture and product development. In vitro release profiles have frequently been studied using standard USP or BP dissolving machines, which use both

rotating components like paddles and baskets. The dissolving medium employed in these investigations generally spans from 100 to 500 ml, with rotational speeds fluctuating between 50 and 100 rpm.

**Determination of Microspheres Drug Content or Entrapment Efficiency**

A glass mortar and pestle are used to crush a certain number of microspheres after they have been precisely weighed. The powdered microspheres are suspended in a defined volume of an appropriate solvent. Following a 12-hour suspension period, the solution is filtered, and the resulting filtrate is analysed for drug content utilizing a UV-Visible spectrophotometer. The ratio of the real to theoretical drug content is used to compute the drug content, also referred to as entrapment efficiency. This calculation assesses the efficacy of drug retention within the microspheres throughout the manufacturing process.

**Zeta Potential**

The polyelectrolyte shell is created by consolidating chitosan of different molecular weights into the W2 stage, followed by the assessment of following particles using zeta potential testing. This technique likely entails the integration of chitosan, a polycationic polymer sourced from chitin, into a water-in-oil (W2) emulsion system. The selection of chitosan with varying molecular weights influences the characteristics of the polyelectrolyte shell surrounding the particles. The measurement of zeta potential characterizes the surface charge of particles, which is essential for comprehending their stability and interactions with other system components [41-45].

**Applications of Microspheres**

**Microspheres in Vaccine Delivery**

An optimal vaccine must meet essential characteristics, such as efficacy, safety, user-friendliness, and cost-effectiveness. Biodegradable vaccine delivery technologies intended for parenteral injection present potential answers to the limitations of traditional vaccines. These systems provide benefits including improved antigenicity via adjuvant activity, regulated modulation of antigen release, and stability of the antigen.

**Targeting using Microparticulate Carriers**

The theory of site-specific medication delivery, sometimes referred to as targeting, is a well-established concept that is garnering heightened interest. The therapeutic efficacy of a medicine depends on its ability to access and interact with certain target receptors. The capacity to exit the drug pool consistently, efficiently, and accurately is fundamental to drug activity, enabled by a carrier system.

**Monoclonal Antibodies (mAbs) Mediated Microspheres Targeting**

Monoclonal antibodies aimed at microspheres generate immune-microspheres, a technique utilized for the precise targeting of specific locations. Monoclonal antibodies demonstrate exceptional specificity, allowing for precise targeting. This particularity can be utilized to guide microspheres infused with bioactive compounds to targeted locations. Monoclonal antibodies may be directly conjugated to the microspheres via covalent coupling, establishing a connection to free aldehyde groups, amino groups, or hydroxyl groups present on the surface of the microspheres. The monoclonal antibodies may be conjugated to microspheres through any of the subsequent methodologies:

Nonspecific adsorption, Specific adsorption, Direct coupling, coupling via reagent

**Chemo-embolization**

Chemo-embolization is an endovascular technique utilized for the treatment of tumours. The procedure involves the precise embolization of tumor arteries combined with the localized administration of a chemotherapeutic agent either concurrently or subsequently.

**Microspheres in Gene Delivery**

Recombinant adenoviruses are commonly utilized for gene delivery owing to their excellent efficacy and extensive cell target range. Nevertheless, there in vivo application frequently elicits immunological responses and carcinogenic potential. Moreover, many gene therapy sessions may be required utilizing viral vectors. Conversely, non-viral gene delivery techniques employ microspheres to encapsulate genes, providing prolonged gene delivery. Microspheres are stable, readily fabricated and capable of targeting specific cells or tissues, induce minimal immunological responses, and facilitate large-scale reproducible manufacture.

**Topical Porous Microspheres**

Micro sponges are characterized by their porous microspheres, which exhibit an intricate network of voids with dimensions varying from 5 to 300 µm. The micro sponges serve as a sophisticated topical delivery system, adept at encapsulating a range of active compounds, including emollients, perfumes, and essential oils, among others.

**Medical Applications**

Microspheres are widely used in the delivery of vaccines against a variety of illnesses, including influenza, hepatitis, pertussis, and diphtheria. They are employed in multiple medical fields for the sustained release of proteins, hormones, and peptides. Microspheres demonstrate significant efficacy in the delivery of DNA plasmids and insulin for therapeutic purposes. Microspheres are essential for both dynamically targeting tumor cells and antigens and passively targeting leaky tumor arteries in intravenous and intra-arterial therapies.

**Microspheres for Delivery of Protein and Peptides**

Biodegradable polymer microspheres have been studied for their capacity to regulate the release of proteins and peptides. They help maintain stable plasma concentrations of proteins or peptides over long periods of time. Biodegradable substances including polylactic acid, polylactic-co-glycolic acid, and chitosan are frequently employed in the development of microspheres for protein and peptide pharmaceuticals. Peptide pharmaceuticals such as triptorelin,

lanreotide, buserelin, and abarelix employ microsphere-based delivery mechanisms.

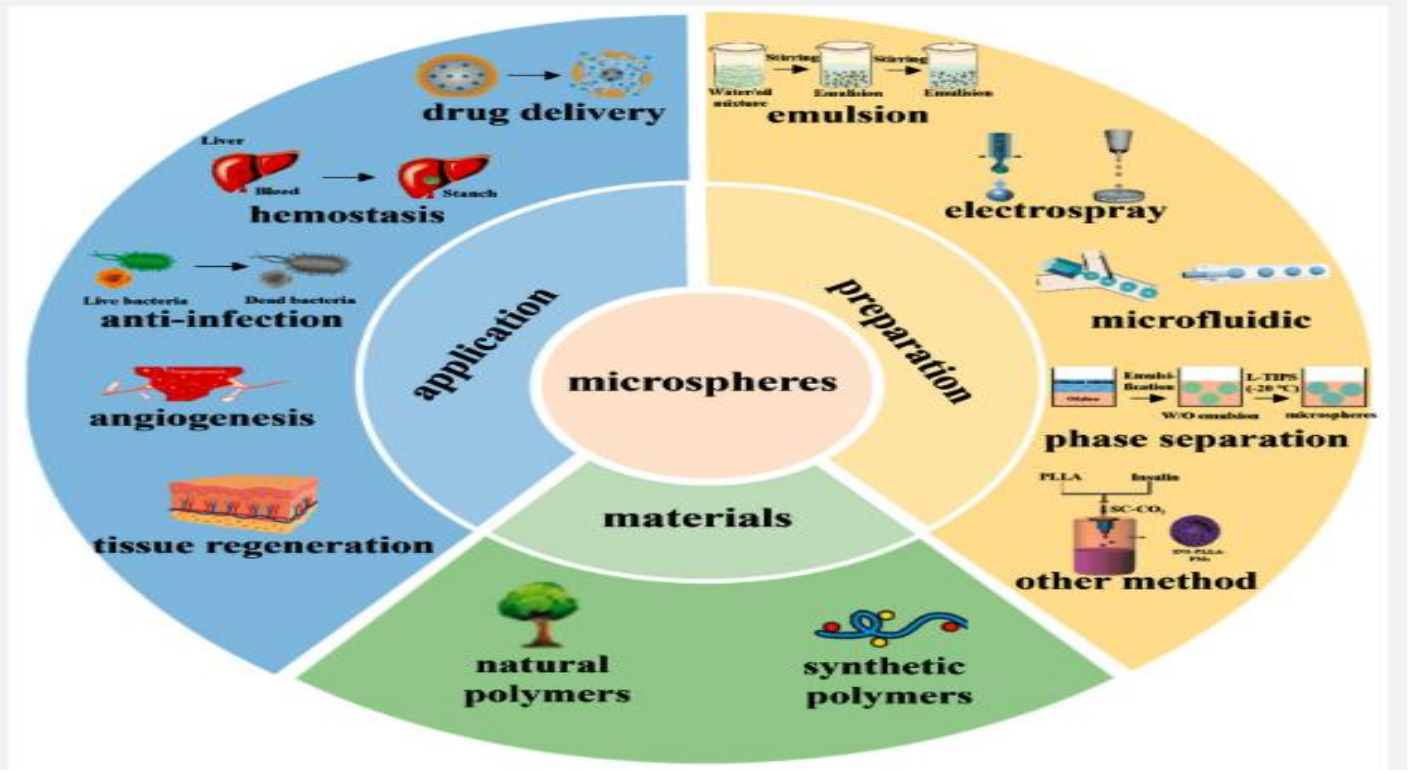
**Radioactive Microspheres Applications**

It can be employed for radioembolization of hepatic and splenic tumors, radio synovectomy of rheumatic joints, localized radiation, and interventional treatment. Imaging of the liver, spleen, bone marrow, lung, and the thrombus itself may be conducted in instances of deep vein thrombosis.

**Other Application**

Fluorescent microspheres are used in fluorescent immunoassays, cell biology, and membrane-based flow cytometry, among other applications. According to encouraging findings, yttrium-90 can be used to treat hepatocellular carcinoma (HCC) both primary and pre-transplant [21-35].

**Figure 13:** Applications of Microspheres




## CONCLUSION

Compared to other medication delivery systems, microspheres are safer because they have better patient enforcement and more accurate targeting. Because of its benefits—such as improved stability, decreased dose frequency, dissolving rate, bioavailability, and continuous and controlled-release action—microspheres are the most widely used drug delivery technology. An effective and safe drug delivery method, the microsphere system can be applied to a number of tasks, including vaccine distribution, floating, and precise medication targeting.

## REFERENCES

1. Darafsheh A, Limberopoulos NI, Derov JS, et al, 2014. Advantages of microsphere-assisted super-resolution imaging technique over solid immersion lens and confocal microscopies. Appl Phys Lett. 104(2), Pages 11-14. Doi: https://doi.org/10.1063/1.4864760

2. Adepu S, Ramakrishna S, 2021. Controlled drug delivery systems: Current status and future directions. Molecules. 26(19), Pages 5905- 5915. Doi: https://doi.org/10.3390/molecules26195905

3. Ranade VV, Hollinger MA, 2004. Drug Delivery Systems. 2nd Edition, CRC Press, Boca Raton, London, New York, Washington. Pages 319- 389.

4. Jain KK, 2014. Drug Delivery System in Methods in Molecular Biology. 2nd Edition, Jain PharmaBiotech Basel. Pages 46-57. Doi: 10.1007/978-1-4939-0363-4.

5. Katz LC, Iarovici DM, 1990. Green Fluorescent Latex Microspheres: A New Retrograde Tracer. Neuroscience. 34 (02), Pages 511- 520. https://doi.org/10.1016/0306-4522(90)90159-2

6. Rodríguez Villanueva J, Bravo-Osuna I, Herrero-Vanrell R, et al, 2016. Optimising the controlled release of dexamethasone from a new generation of PLGA-based microspheres intended for intravitreal administration. Eur J of Pharm Sci., 20(92) Pages 287–297. Doi: 10.1016/j.ejps.2016.03.012.

7. Ohiagu FO, Chikezie PC, Chikezie CM, 2021. Pathophysiology of diabetes mellitus and its Complications: Metabolic events and control. Biomedical Research and Therapy. 8(3), Pages 4243–4257. Doi: 10.15419/bmrat.v8i3.663.

8. Kessler RC, Tat Chiu W, Demler O, et al, 2005. Prevalence, Severity and Comorbidity of 12-Month DSM-IV Disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 62(6), Pages 617-627. Doi: 10.1001/archpsyc.62.6.617.

9. Virmani T, Gupta J, 2017. Pharmaceutical application of Microspheres: An Approach for the treatment of various diseases. Int J Pharm Sci Res. 8(8), Pages 3252–3260. Doi: http://dx.doi.org/10.13040/IJPSR.0975-8232.8 (8).3252-60.

10. Anupam KS, Ankita G, Mona A, 2016. Formulation & Characterization of nanostructured lipid carrier (NLC) based gel for topical delivery of Etoricoxib. Journal of Drug Delivery & Therapeutics. 6(2), Pages 4–13.

11. Wischke C, Schwendeman SP, 2018. Principles of encapsulating hydrophobic drugs in PLA/PLGA microparticles. Int. J. Pharm. 364(2), Pages 298-327. Doi: 10.1016/j.ijpharm.2008.04.042.

. 12. GU B Sun X, Papadimitrakopoulos F, Burgess DJ, 2017. Seeing is believing, PLGA microsphere degradation revealed in PLGA microsphere/PVA hydrogel composites. J. Control Release. 228, Pages 170–178. Doi: 10.1016/j.jconrel.2016.03.011.

13. Zhang Z, Bi X, Huang G, 2011. Enhanced targeting efficiency of PLGA microspheres loaded with Lornoxicam for intra-articular administration. Drug Deliv. 18(7), Pages 536–44. Doi: 10.3109/10717544.2011.596584.

14. De Bodinat C, Guardiola-Lemaitre B, Mocaër E, et al, 2010. Agomelatine, the first melatonergic antidepressant: Discovery, characterization and development. Nat Rev Drug Discov. 9(8), Pages 628-42. Doi: 10.1038/nrd3140.

15. Venkatesan P, Manavalan R, Valliappan K, 2009. Microencapsulation: A Vital Technique in novel drug delivery system. J. Pharm. Sci. & Res. 1(4), Pages 26-35.

16. Ramazani F, Chen W, Van Nostrum CF, et al, 2016. Strategies for encapsulation of small hydrophilic and amphiphilic drugs in PLGA microspheres: State-of-the-art and challenges. Int J Pharm. 29(1-2), Pages 358-367. Doi: 10.1016/j.ijpharm.2016.01.020.

17. Raj H, Sharma S, Sharma A, et al, 2021. A Novel Drug Delivery System: Review on Microspheres. Journal of Drug Delivery and Therapeutics. 11(2-S), Pages 156–161. Doi: 10.22270/jddt.v11i2-S.4792.

18. Arshady R, 1993. Microspheres for biomedical applications: preparation of reactive and labelled microspheres. Biomaterials. 14(1), Pages 5-15. Doi: 10.1016/0142-9612(93)90015-t.

19. Jagtap SC, Karale AA, Ambekar AW, 2014. Microsponge: A novel topical drug delivery system. Journal of drug delivery research. 3 (4), Pages 1-9.

20. Bharti N, Dhatt GS, Gautam SP, et al, 2016. An incisive review on Microspheres as drug delivery system. International Journal of Pharmaceutics & Drug Analysis. 4(11), Pages 486–493.

21. Rastogi V, Shukla SS, Singh R, et al, 2016. Microspheres: A promising drug carrier. Journal of Drug Delivery and Therapeutics. 6(3), Pages 18-26. Doi: 10.22270/jddt.v6i3.1196.

22. Kumar SS, Reddy J, Chandra SKB, 2012. A review on Microsphere for Novel drug delivery System. J Pharm Res. 5(1), Pages 420–424.

23. Vyas SP, Khar RK, 2003. Targeted and Controlled Drug Delivery: Novel Carrier Systems. Int J Pharm. 267(1–2), Pages 157. Doi: 10.1016/S0378-5173(03)00356-9.

24. Vasir JK, Tambwekar K, Garg S, 2003. Bioadhesive microspheres as a controlled drug delivery system. Int J Pharm. 255(1-2), Pages13-32. Doi: 10.1016/s0378-5173(03)00087-5.

25. Patil SB, Sawant KK, 2008. Mucoadhesive Microspheres: A Promising Tool in Drug Delivery. Curr Drug Deliv. 5(4), Pages 312-318. Doi: 10.2174/156720108785914970.

26. Wang X, Wang X, Liu L, et al, 2011. Preparation and characterization of carbon aerogel microspheres by an inverse emulsion polymerization. Journal of Non-Crystalline Solids. 357(3), Pages 793-797. Doi: https://doi.org/10.1016/j.jnoncrysol.2010.11.015.

27. Yang Z, Peng H, Wang W, et al, 2010. Crystallization behavior of poly (ε-caprolactone)/ layered double hydroxide nanocomposites. J Appl Polymer Sci. 116(5), Pages 2658–2667. Doi: https://doi.org/10.1002/app.31787.

28. Sharma J, Chaudhary A, Kumar I, 2022. Microspheres: A Novel Drug Delivery System. Ijppr. Human. 24 (2), Pages 47-67.

29. Lee J, Ha JU, Choe S, et al, 2006. Synthesis of highly monodisperse polystyrene microspheres via dispersion polymerization using an amphoteric initiator. J Colloid Interface Sci. 298(2), Pages 663–671. Doi: 10.1016/j.jcis.2006.01.001.

30. Alam S, Hasan MK, Neaz S, et al, 2021. Diabetes Mellitus: Insights from Epidemiology, Biochemistry, Risk Factors, Diagnosis, Complications and Comprehensive Management. Diabetology. 2(2), Pages 36-50. Doi: https://doi.org/10.3390/diabetology2020004.

31. Sharma B, Singh I, Sharma J, 2022. Microspheres: A Novel Drug Delivery System. Ijppr Human. 24 (2), Pages 47-67.

32. Pradeesh TS, Sunny MC, Varma HK, et al, 2005. Preparation of microstructured hydroxyapatite microspheres using oil in water emulsions. Bull Mater Sci. 28(5), Pages 383–390.

33. Sharma N, Purwar N, Chandra Gupta P, 2015. Microspheres as drug carriers for controlled drug delivery: A review. Int J Pharm Sci Res. 6(11), Pages 45-79. Doi: http://dx.doi.org/10.13040/IJPSR.0975-8232.

34. Arshady R, 1993. Microspheres for biomedical applications: preparation of reactive and labelled microspheres. Biomaterials. 14(1), Pages 5-15. Doi: 10.1016/0142-9612(93)90015-t.1993.

35. Brar V, Kaur G, 2014. Biopolymers as Carriers for Nasal Drug Delivery. Polymer - Plastics Technology and Engineering. 53(14), Pages 1518–1531.

36. Dolder CR, Nelson M, Snider M, 2008. Agomelatine treatment of major depressive disorder. Ann Pharmacother. 42(12), Pages 1822-1831. Doi: 10.1345/aph.1L296.

37. Rathore B, Yadav A, Nayak G, et al, 2012. A review on microspheres as drug delivery carriers for management of diabetes mellitus. Int J of Pharm & Life Sci (IJPLS). 3(10), Pages 2064–2070.

39. Lyke KE, Ishizuka AS, Berry AA, et al, 2017. Attenuated PfSPZ Vaccine induces strain-transcending T cells and durable protection against heterologous controlled human malaria infection. Proc Natl Acad Sci. 114(10), Pages 2711-2716. Doi: 10.1073/pnas.1615324114.

40. Garcia-Cebrian A, Bauer M, Montejo AL, et al, 2007. Factors influencing depression endpoints research (FINDER): Study

design and population characteristics. Eur Psychiatry. 23(1), Pages 57-65. Doi: 10.1016/j.eurpsy.2007.10.002.

41. Dubovsky SL, Warren C, 2009. Agomelatine, a melatonin agonist with antidepressant properties. Expert Opin Investig Drugs. 18(10), Pages 1533-1540. Doi: 10.1517/13543780903292634.

42. San L, Arranz B, 2008. Agomelatine: A novel mechanism of antidepressant action involving the melatonergic and the serotonergic system. Eur Psychiatry. 23(6), Pages 396-402. Doi: 10.1016/j.eurpsy.2008.04.002.

43. Ferrari AJ, Charlson FJ, Norman RE, et al, 2013. Burden of Depressive Disorders by Country, Sex, Age, and Year: Findings from the Global Burden of Disease Study 2010. PLoS Med., 10(11), Pages 1001547. Doi: 10.1371/journal.pmed.1001547.

44. Kennedy SH, 2009. Agomelatine Efficacy at Each Phase of Antidepressant Treatment. CNS Drugs. 23(2), Pages 41-47. Doi: 10.2165/11318660-000000000-00000.

45. Kockisch S, Rees GD, Tsibouklis J, et al, 2005. Mucoadhesive, triclosan-loaded polymer microspheres for application to the oral cavity: Preparation and controlled release characteristics. Eur J Pharm Biopharm. 59(1), Pages 207-216. DOI: 10.1016/j.ejpb.2004.07.007