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REVIEWING THE DESIGN AND IDENTIFICATION TECHNIQUES OF MICROSPHERES

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ABSTRACT
The distribution mechanism for microparticles is acknowledged as dependable. a method for precisely delivering the medication to the intended location. The medication should be administered at a rate and concentration that maximizes therapeutic efficacy while minimizing negative effects to a specific target site. Microspheres are spherical particles that are empty and have a diameter of less than 200 mm. Microspheres are a free-flowing powder made of both synthetic and natural polymers. They may have a medicine with controlled release. The most crucial components of pharmacological drug delivery are polymers. These days, a wide variety of polymers with various characteristics are accessible for usage in many pharmaceutical applications. Both natural and synthetic polymers are used in the creation of microspheres. Acrolein, polyanhydrides, lactides, glycosides, and methyl methacrylate are examples of synthetic polymers. Albumin, gelatin, collagen, agarose, chitosan, and carrageenin are examples of natural polymers. The free-flowing powders known as microspheres are made of artificial polymers and proteins with a particle size distribution of 1 to 1000 micrometers. There are various ways to create microspheres, however the method of preparation varies depending on the medication. The polymers utilized and the necessary duration of action. Micromeritic qualities, including particle size and shape, swelling index, tapped density, and drug loading efficiency, are the metrics used to evaluate microspheres. In the upcoming days, we will discover the microspheres in innovative medication delivery by mixing several additional scenarios. With regard to disease cell sorting diagnostics, gene and genetic materials, safe, targeted, and efficient in vivo delivery, as well as supplements that enhance a microscopic understanding of a sick organ.
KEYWORDS: *Microparticle, Drug delivery system, microspheres, Synthetic polymers.*

INTRODUCTION

Delivery methods utilizing microparticles are acknowledged as a dependable way to precisely administer medication to the intended location. Drug delivery has grown in significance mostly as a result of increased knowledge of the challenges posed by traditional drug delivery methods. A medicinal chemical can be delivered to the target place in a number of ways using controlled or continuous release techniques (1). One method is the use of polymers in the development of microparticulate drug delivery systems through the microencapsulation technique, which produces uniformly sized, spherical microscopic particles or microspheres with a diameter of 1 to 1000 µm by enclosing or enveloping a solid, liquid, or gaseous active ingredient (core material) with a polymeric material. If dosages could be maintained for controlled release, the benefits to patients would be increased. The medication should be administered at a rate and concentration that maximizes therapeutic efficacy while minimizing negative effects to a specific target site. The size of a microsphere is less than 200 mm, and they are spherical, empty particles. Microspheres are particles that may flow freely and are made of either synthetic or natural polymers (2). They could be a controlled release medication. By allowing the medicine to be localised at the site of action and extending its release, homogenous monolithic particles called microspheres enhance patient care. Natural polymer-based microsphere carrier systems have garnered significant interest in recent years due to their potential for long-term medication delivery. These days, dosage formulations with target-specificity and controllable release rates have a significant influence on the creation of innovative drug delivery systems. Recently, there has been a lot of interest in innovative dosage forms that can target the active drug molecule to a specific spot and manage the release rate. A well-crafted controlled drug delivery system can improve a particular medicine's therapeutic efficacy and solve many of the issues with traditional therapy. In order to achieve optimal therapeutic efficacy, the drug must be delivered to the target tissue in the ideal amount during the appropriate time frame, resulting in low toxicity and negligible side effects. There are several methods for getting a medicinal drug to the intended location in a sustained controlled release trend. Using microspheres as drug carriers is one such method. Microspheres can be characterized as a structure composed of

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one or more miscible polymers in which drug particles are scattered at the molecular or macroscopic level. Alternatively, they can be defined as monolithic spheres or therapeutic agent distributed throughout the matrix either as a molecular dispersion of particles (3).

BENEFITS

1. Microspheres have a long-lasting and consistent therapeutic impact.
2. enhances patient compliance by lowering the frequency of dosing.
3. Because of their tiny size and spherical shape, they may be injected into the body.
4. Increased drug use will increase bioavailability and decrease the frequency or severity of side effects.
5. The shape of the microsphere permits controlled variability in medication release and breakdown.

LIMITATION

Some of the disadvantages were found to be as follows

1. The modified release from the formulations.
2. The release rate of the controlled release dosage form may vary from a variety of factors like food and the rate of transit though gut.
3. Differences in the release rate from one dose to another.
4. Controlled release formulations generally contain a higher drug load and thus any loss of integrity of the release characteristics of the dosage form may lead to potential toxicity.
5. Dosage forms of this kind should not be crushed or chewed

Materials

For the creation of microspheres, a variety of materials both biodegradable and non-biodegradable have been studied. These materials comprise modified natural compounds as well as polymers derived from both synthetic and natural sources. Methyl methacrylate, acrolein, lactide, glycoside, and related copolymers, ethylene vinyl acetate copolymer, polyanhydrides, etc. are examples of synthetic polymers used as carrier materials. The natural polymers starch, collagen, albumin, gelatin, and carrageenan are employed for this purpose (4).

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

1. Synthetic Polymers:

a. non-biodegradable polymers.

E.g., Poly methyl methacrylate (PMMA), Acrolein, Glycidyl methacrylate Epoxy polymers

b. Biodegradable polymers

E.g., Lactides, Glycosides & their copolymers 3 Poly alkyl cyano acrylates Poly anhydrides

2. Natural Polymers can be obtained from different sources like proteins, carbohydrates, and chemically modified carbohydrates.

Proteins: Albumin, Gelatin and Collagen

Carbohydrates: Agarose, carrageenan, Chitosan, Starch

Chemically modified carbohydrates: Poly dextran, poly starch

TYPES OF MICROSPHERES

1. Bio adhesive microspheres

Adhesion is defined as the drug's capacity to cling to a membrane by means of the sticky characteristic of water-soluble polymers. The term "bio adhesion" refers to the attachment of a drug delivery device to a mucosal membrane, such as the buccal, ocular, nasal, or rectal. Because these specific microspheres stay at the application site for a longer amount of time, they come into close contact with the absorption site and enhance the therapeutic impact (5).

2. Floating microspheres

Floating types float in the stomach without slowing down the rate at which food is discharged since their bulk density is lower than that of gastric fluid. The medicine is released gradually at the intended pace if the stomach content is floating in the system, increasing gastric residency and causing fluctuations in plasma concentration. It also reduces the possibility of dose dumping and striking. Another strategy is to produce a long-lasting therapeutic effect, which reduces the frequency of dose (6)

3. Magnetic microspheres

This type of medication delivery method is essential since it precisely addresses the illness's location. A smaller amount of a magnetically targeted medication can replace a larger amount of the drug that is freely circulating. Magnetic carriers react magnetically to a magnetic field when they are combined with chitosan, dextran, and other materials into magnetic microspheres. There are two types of magnetic microspheres: therapeutic and diagnostic (7).

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4. Polymeric microspheres

The different types of polymeric microspheres can be classified as follows and they are biodegradable polymeric microspheres and synthetic polymeric microspheres.

A. Biodegradable polymeric Microspheres

The idea behind using natural polymers like starch is that they are biodegradable, biocompatible, and naturally sticky. Biodegradable polymers have a high degree of swelling property with aqueous medium, which causes gel formation and extends the residence period when in contact with mucous membranes. The polymer concentration and the sustained release pattern regulate the drug's release rate and extent. The primary disadvantage of biodegradable microspheres in clinical usage is its complex drug loading efficiency, which makes it challenging to regulate drug release (8).

B. Synthetic polymeric microspheres

Synthetic polymeric microspheres have shown great promise in clinical applications, where they are utilized as embolic particles, bulking agents, fillers, drug delivery vehicles, and other applications. They are also safe and biocompatible. However, the primary drawback of these microspheres is their propensity to disperse from the injection site, which increases the risk of embolism and additional organ damage (9).

5. Radioactive microspheres

Radiological immobilization When microspheres of the size of 10–30 nm are encountered, they tap into the first capillary bed because they are larger than capillaries. In order to treat all these problems, radioactive microspheres are injected into the arteries that flow to the tumors of interest. This allows for a high radiation dose to be delivered to the targeted area without causing harm to the normal surrounding tissues. Unlike medicine delivery systems, it operates from a radioisotope-typical distance rather than releasing radioactivity from microspheres. The various types of radioactive microspheres include emitters, ß emitters, and α-emitters (10).

METHODS OF PREPARATION

1. Single emulsion technique

The single emulsion method is used to create the microparticulate carriers of natural polymers, such as proteins and carbohydrates. After being dissolved or dispersed in an aqueous media, the natural polymers are then distributed in a non-aqueous medium, such as oil. The process of cross-linking scattered globules is done in the second step of preparation. There are two ways to accomplish cross-linking: using heat or chemical cross-linking agents like formaldehyde, glutaraldehyde, diacid chloride, etc (11).

2. Hot Melt Microencapsulation

This approach was initially used to manufacture microspheres of polyanhydride copolymer of poly bis (p-carboxy phenoxy) propane anhydride with sebacic acid19. This method involves melting the polymer first, then continuously mixing in the solid drug particles. To obtain a stabilized emulsion, the produced mixture is next heated to a temperature over the polymer's melting point while being continuously stirred and suspended in a non-miscible solvent, such as silicone oil. The resulting emulsion is chilled to solidify the polymer particles, and then petroleum ether is used to filter and wash the microspheres **(12).**

3. Complex Coacervation

The basic idea behind this technique is that, given the right circumstances, mixing solutions of two hydrophilic colloids would separate the liquid precipitate. This process involves dissolving the immiscible polymer in an appropriate vehicle to prepare the coating material phase, and dispersing the core material in a coating polymer solution while stirring continuously. One of the phase separation techniques—that is, adjusting the polymer solution's temperature, adjusting the medium's pH, adding a salt, an incompatible polymer, or a nonsolvent—was used to achieve microencapsulation. Another method involved inducing a polymer-polymer interaction. To create a self-sustaining microsphere, the coating is often toughened using thermal cross-linking procedures. (13).

4. Double Emulsion Method

The most popular technique for microencapsulation was initially presented by Ogawa Y et al. in 1988 (20). To obtain the primary water-in-oil emulsion, this process involves adding an aqueous solution of the medication and polymer to the organic phase while vigorously stirring. To create the various emulsions (w/o/w), this emulsion was then added to a large volume of water containing an emulsifier such as polyvinyl alcohol or polyvinylpyrrolidone, while being stirred continuously until the majority of the organic solvent evaporated and solid microspheres were left behind. After that, the microspheres are dried and cleaned (14).

5. Spray Drying

The polymer is first dissolved in an appropriate volatile organic solvent, such as acetone or dichloromethane, before being sprayed dried. After that, the medication is homogenised at a fast speed and distributed throughout the polymer solution in its solid state. A hot air stream is then used to atomize this dispersion. As a result of atomization, tiny droplets or fine mists are formed, and when the solvent instantly evaporates, microspheres with sizes between one and one hundred micrometres are created. A cyclone separator is used to separate microparticles from hot air, and vacuum drying is used to eliminate any solvent residue. The process's ability to function under aseptic circumstances is one of its main advantages; it moves quickly, which results in the formation of porous micro particles (15).

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6. Solvent Evaporation

The operations are performed within a liquid production apparatus. A volatile solvent that is immiscible with the liquid production vehicle phase is used to disseminate the microcapsule coating. In the coating polymer solution, a core material to be microencapsulated is dissolved or distributed. To create the right size microcapsule, the core material mixture is agitated and distributed throughout the liquid manufacturing vehicle phase. After the combination is heated, if needed, to evaporate the solvent, the polymer shrinks around the core and becomes dispersed in the polymer solution. Matrix-type microcapsules are generated if the core material dissolves in the covering polymer solution. Either water soluble or water in soluble materials could make up the main components (16).

7. Polymerization techniques

The polymerization techniques conventionally used for the preparation of the microspheres are mainly classified as:

I. Normal polymerization

II. Interfacial polymerization.

Both are carried out in liquid phase.

Normal polymerization

Several methods, including bulk, suspension, precipitation, emulsion, and micellar polymerization processes, are used to carry it out. To start polymerization in bulk, a monomer or combination of monomers combined with an initiator or catalyst is often heated. The resulting polymer can be shaped into microspheres. During the polymerization process, drugs may be loaded. Bead or pearl polymerization is another name for suspension polymerization. In this case, the monomer or mixture of monomers is heated while dispersing as droplets in an ongoing aqueous phase. Other additives and an initiator might also be included in the droplets. Because the initiator is present in the aqueous phase and diffuses to the micelle surface subsequently, emulsion polymerization differs from suspension polymerization (17).

Interfacial polymerization

In order to create a polymer film that effectively envelops the dispersed phase, it entails the interaction of different monomers at the interface between the two immiscible liquid phases.

DRUG LOADING IN MICROSPHERE

There are two main ways to load the medications into the microspheres: either during the microsphere preparation process or after the microsphere preparation process by incubating them with the drug solution. There are three possible ways to load the active ingredients: chemical bonding, surface absorption, and physical trapping. Maximum drug loading in microspheres was discovered to be possible when the drug was added during the preparation process, although many other process variables, such as the presence of additives, the preparation method, the polymerization heat, the degree of agitation, etc., may also have an impact. After the microspheres are prepared, they can be incubated with a high concentration of the drug in an appropriate solvent to accomplish drug loading. Here, the medicine may be incorporated into the microspheres by absorption through the microspheres' surface or by penetrating or diffusing through their pores. Following the solvent's removal, the drug-loaded microsphere is left behind (18).

Evaluation of Microspheres

- **Particle size analyzer**
  In order to prevent microsphere aggregation, 50 mg of microspheres are suspended in 5 mL of distilled water with 2% w/v of tween 80. The aforementioned suspension is then sonicated in a water bath, and the particle size is expressed as volume mean diameter in micrometers (19).
- **Entrapment efficiency**
  5mg of medication-containing microspheres are crushed, dissolved in distilled water for 3 hours with the aid of an ultrasonic stirrer, filtered, and then subjected to UV-Visible spectroscopic analysis. The ratio of real drug content to theoretical drug content is known as entrapment efficiency (20).
  % Entrapment = Actual content/Theoretical content x 100
- **Scanning electron microscopy (SEM)**
  The SEM method determines surface morphology. Using double-sided sticky tape, the microcapsules are directly placed on the SEM sample slab, covered with gold film at low pressure, and examined. (21).
- **Swelling index**
  The characterization of sodium alginate microspheres is done using this method. Alginate microspheres (100 mg) are placed in a wire basket and stored on top of a different solution (100 mL), such as distilled water or a buffer solution of pH (1.2, 4.5,

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7.4), while swelling is permitted at 37 °C. Therefore, by periodically measuring weight and soaking with filter paper, variations in weight variance between the initial weight of microspheres and weight owing to swelling are measured (22).

- **Optical microscopy**
  Using an optical microscope, this technique measures the size of the particles (Meizer OPTIK) measured under 450x (10x eye piece and 45x objective), and the results show that there are 100 particles (23).
- **Thermal analysis**
  Thermal analysis of microcapsule and its component can be done by using
  Differential scanning calorimetry (DSC)
  Thermo gravimetric analysis (TGA)
  Differential thermometric analysis (DTA)
  Accurately the sample is weighed and heated on alumina pan at constant rate of 10oc/min under nitrogen flow of 40 ml/min.
- **Stability studies**
  Stability Studies are done by placing the microspheres in screw capped glass container and storing them at following conditions.
  1. Ambient humid condition
  2. Room temperature (27+/-2 ℃)
  3. Oven temperature (40+/-2 ℃)
  4. Refrigerator (5 0+/-8 ℃).

  It was carried out of for 60 days and the drug content of the microsphere is analyzed.
- **Isoelectric point**
  An instrument called a micro electrophoresis is used to measure the electrophoretic mobility of microspheres in order to identify their isoelectric point. The time of particle travel across 1 mm is used to calculate the mean velocity at various Ph values, which range from 3 to 10. This information can be used to calculate the particle's electrical mobility. The surface contained charge, ionizable behavior, or ion absorption nature of the microspheres can all be related to the electrophoretic mobility (24).
- **Angle of repose**
  The funnel method was used to determine the microspheres' angle of repose (q). The microspheres were transferred via a vertically adjustable funnel, allowing for the creation of a maximum cone height. The angle of repose and the radius of the heap were computed.
  Tan θ = h/r
  Where h is the height of the granules above the flat surface, θ is the angle of repose, and r is the radius of the circle the granule heap forms.

- **Density determination**
  A multivolume pycnometer can be used to determine the microspheres' density. The multi volume pyrometer is filled with a precisely weighed sample that is placed in a cup. The chamber is filled with constant pressure helium, which is then allowed to expand. The pressure inside the chamber drops as a result of this expansion. There are two sequential pressure reduction readings recorded, each at a different initial pressure. The volume and subsequently the density of the microsphere carrier are calculated from two pressure readings (25).
- **Bulk density**
  It is the blend's mass to bulk volume ratio. Powder was added to a measuring cylinder, and the volume the powder occupied was measured.
  Microsphere mass divided by bulk volume equals bulk density.
  Tapped density
  It is the ratio of mass of the blend to tapped volume. It was measured by digital tap densitometer by measuring the volume occupied by powder after 100 standard tapping.
  Tapped density=mass of microspheres/volume of microspheres after tapping
- **Carr's (compressibility) index**
  The following equation was used to calculate the microparticles' compressibility index (C.I.) or Carr's index value.
  100% compressibility is equal to Tapped density minus Bulk density. tapped-out density
  A powder that often results in good flow characteristics has a score below 15%, whereas a number above 25% indicates poor flowability (26).

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Application of Microspheres

- **I.** I. stomach retentive floating microspheres are particularly helpful in reducing the main negative effects of stomach irritation; for example, NSAID floating microspheres, such as indomethacin, are good for rheumatoid arthritis patients.
- **II.** Because this system can stay in the stomach for extended periods of time, the medication can be released gradually. These technologies thereby solve the issue of the short gastric residence time that arises when using an oral controlled release formulation.
- **III.** These systems provide an easy way of maintaining constant blood level with an ease of administration and better patient compliance.
- **IV.** Recently, intertumoral and local drug delivery techniques have gained popularity as a potentially effective cancer therapeutic modality. Polymer films were created to deliver paclitaxel at the tumor's location in a therapeutically appropriate concentration. Transparent and flexible films with a 31% (w/w) loading capacity for paclitaxel were possible. The study found that the casting approach produced polymer films containing paclitaxel's with good loading efficiencies while maintaining the chemical integrity of the molecule throughout preparation.
- **V.** Polymer is a unique material for the construction of ocular drug delivery vehicles because of its favorable biological behavior, which includes bio adhesive, permeability-enhancing capabilities, and intriguing physio-chemical qualities. Polymer hydro gels are more aesthetically pleasing than solid or semisolid formulations when it comes to ocular distribution, such as ointments or suspensions, because of their elastic qualities. Ophthalmic chitosan gels increase precorneal drug residence durations, indicating a reduction in drug removal by the lachrymal flow, and better adherence to the mucin that coats the corneal surface of the eye and the conjunctiva. Furthermore, the improvement of its penetration results in a more focused effect and permits the use of lower drug dosages.
- **VI.** Clotrimazole, an imidazole derivative, is embedded in a polymer that has been changed by adding thioglycolic acid to its core amino groups. This polymer is commonly used to treat mycotic infections of the genitourinary tract. The polymer's mucoadhesive qualities are significantly enhanced by the addition of thiol groups, and this is observed to lengthen the vaginal mucosa tissue polymer's residence period.
- **VII.** It has been shown that chitosan can both prevent excessive scar formation and hasten wound healing to provide a skin surface that is cosmetically acceptable. In dentistry, chitosan is also used as a tampon after extreme therapy for maxillary sinusitis and as a bandage for mucous lesions in the mouth. It is being researched for use as a periodontal surgical absorbent membrane. With its diverse range of biological activities, chitosan is promoted as a nutritious meal that can help treat and/or alleviate several illnesses, such as hepatitis, diabetes, cancer, and arthritis.

CONCLUSION

Ionotropic gelation-produced microspheres show promise as a possible stomach retention strategy. In the future, by fusing different approaches, microspheres will play a major role in novel drug delivery, specifically in the areas of diseased cell sorting, diagnostics, gene & genetic materials, safe, targeted, and efficient in vivo delivery, and supplements as tiny replicas of the body's diseased organs and tissues.

REFERENCE

1. *Patra, J.K., Das, G., Fraceto, L.F. et al. Nano based drug delivery systems: recent developments and future prospects. J Nanobiotechnol 16, 71 (2018). https://doi.org/10.1186/s12951-018-0392-8*
2. *Singh MN, Hemant KS, Ram M, Shivakumar HG. Microencapsulation: A promising technique for controlled drug delivery. Res Pharm Sci. 2010 Jul;5(2):65-77. PMID: 21589795; PMCID: PMC3093624.*
3. *Senapati, S., Mahanta, A.K., Kumar, S. et al. Controlled drug delivery vehicles for cancer treatment and their performance. Sig Transduct Target Ther 3, 7 (2018). https://doi.org/10.1038/s41392-017-0004-3*
4. *Jaspreet Kaur Vasir, Kaustubh Tambwekar, Sanjay Garg, Bio adhesive microspheres as a controlled drug delivery system, International Journal of Pharmaceutics, Volume 255, Issues 1–2,2003, Pages 13-32,ISSN 0378-5173, https://doi.org/10.1016/S0378-5173(03)00087-5..*
5. *Bhise M, Shukla K, Jain S, Bhajipale N, Sudke S, Burakle P. Development and Evaluation of Floating Microspheres of Anticonvulsant Drug by 3^2 Full Factorial Design. Turk J Pharm Sci. 2022 Oct 31;19(5):595-602. doi: 10.4274/tjps.galenos.2021.53050.*
6. *Satinder Kakar, Deepa Batra, Ramandeep Singh, Ujjwal Nautiyal, Magnetic microspheres as magical novel drug delivery system: A review, Journal of Acute Disease, Volume 2, Issue 1,2013, Pages 1-12, ISSN 2221-6189, ://doi.org/10.1016/S2221-6189(13)60087-6.*
7. *Harjit Tamber, Pål Johansen, Hans P. Merkle, Bruno Gander, Formulation aspects of biodegradable polymeric microspheres for antigen delivery, Advanced Drug Delivery Reviews,Volume 57, Issue 3,2005,Pages 357-376, ISSN 0169-409X, https://doi.org/10.1016/j.addr.2004.09.002.*
8. *Kohane DS, Tse JY, Yeo Y, Padera R, Shubina M, Langer R. Biodegradable polymeric microspheres and nanospheres for drug delivery in the peritoneum. J Biomed Mater Res A. 2006 May;77(2):351-61. doi: 10.1002/jbm.a.30654. PMID: 16425240.*

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EPRA International Journal of Research and Development (IJRD)
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9. *Saralidze K, Koole LH, Knetsch MLW. Polymeric Microspheres for Medical Applications. Materials (Basel). 2010 Jun 7;3(6):3537–64. doi: 10.3390/ma3063537. PMCID: PMC5521755.*
10. *Sinha VR, Goyel V, Trehan A. Radioactive microspheres in therapeutics. Pharmazie. 2004 Jun;59(6):419-26. PMID: 15248454.*
11. *Nava-Arzaluz MG, Piñón-Segundo E, Ganem-Rondero A, Lechuga-Ballesteros D. Single emulsion-solvent evaporation technique and modifications for the preparation of pharmaceutical polymeric nanoparticles. Recent Pat Drug Deliv Formul. 2012 Dec;6(3):209-23. doi: 10.2174/187221112802652633. PMID: 22734869.*
12. *E. Mathiowitz, R. Langer, Polyanhydride microspheres as drug carriers I. Hot-melt microencapsulation, Journal of Controlled Release, Volume 5, Issue 1, 1987, 13-22, ISSN 0168-3659, https://doi.org/10.1016/0168-3659(87)90033-2.*
13. *Yakindra Prasad Timilsena, Taiwo O. Akanbi, Nauman Khalid, Benu Adhikari, Colin J. Barrow, Complex coacervation: Principles, mechanisms and applications in microencapsulation, International Journal of Biological Macromolecules, Volume 121, 2019,Pages 1276-1286, ISSN 0141-8130, https://doi.org/10.1016/j.ijbiomac.2018.10.144.*
14. *Muhammad Iqbal, Nadiah Zafar, Hatem Fessi, Abdelhamid Elaissari, Double emulsion solvent evaporation techniques used for drug encapsulation, International Journal of Pharmaceutics, Volume 496, Issue 2, 2015, Pages 173-190, ISSN 0378-5173, https://doi.org/10.1016/j.ijpharm.2015.10.057.*
15. *Sosnik A, Seremeta KP. Advantages and challenges of the spray-drying technology for the production of pure drug particles and drug-loaded polymeric carriers. Adv Colloid Interface Sci. 2015 Sep; 223:40-54. doi: 10.1016/j.cis.2015.05.003. Epub 2015 May 22. PMID: 26043877.*
16. *Urbaniak T, Musiał W. Influence of Solvent Evaporation Technique Parameters on Diameter of Submicron Lamivudine-Poly-ε-Caprolactone Conjugate Particles. Nanomaterials (Basel). 2019 Aug 31;9(9):1240. doi: 10.3390/nano9091240. PMID: 31480469; PMCID: PMC6780331.*
17. *Shutova, M.S., Alexandrova, A.Y. Normal and transformed fibroblast spreading: Role of microfilament polymerization and actin-myosin contractility. Cell Tiss. Biol. **4**, 25–35 (2010). https://doi.org/10.1134/S1990519X10010037.*
18. *Li, W., Chen, J., Zhao, S. et al. High drug-loaded microspheres enabled by controlled in-droplet precipitation promote functional recovery after spinal cord injury. Nat Commun **13**, 1262 (2022). https://doi.org/10.1038/s41467-022-28787-7.*
19. *J. Cornillault, "Particle Size Analyzer," Appl. Opt. 11, 265-268 (1972).*
20. *Yue PF, Lu XY, Zhang ZZ, Yuan HL, Zhu WF, Zheng Q, Yang M. The study on the entrapment efficiency and in vitro release of puerarin submicron emulsion. AAPS PharmSciTech. 2009;10(2):376-83. doi: 10.1208/s12249-009-9216-3. Epub 2009 Apr 21. PMID: 19381837; PMCID: PMC2690779.*
21. *P. Allan-Wojtas, L. Truelstrup Hansen, A.T. Paulson, Microstructural studies of probiotic bacteria-loaded alginate microcapsules using standard electron microscopy techniques and anhydrous fixation,*
22. *V. Ramesh Babu, Malladi Sairam, Kallappa M. Hosamani, Tejraj M. Aminabhavi, Preparation of sodium alginate–methylcellulose blend microspheres for controlled release of nifedipine, Carbohydrate Polymers, Volume 69, Issue 2, 2007,Pages 241-250, ISSN 0144-8617, https://doi.org/10.1016/j.carbpol.2006.09.027.*
23. *Chen X, Zheng B, Liu H. Optical and digital microscopic imaging techniques and applications in pathology. Anal Cell Pathol (Amst). 2011;34(1-2):5-18. doi: 10.3233/ACP-2011-0006. PMID: 21483100; PMCID: PMC3310926.*
24. *Glynn JR Jr, Belongia BM, Arnold RG, Ogden KL, Baygents JC. Capillary Electrophoresis Measurements of Electrophoretic Mobility for Colloidal Particles of Biological Interest. Appl Environ Microbiol. 1998 Jul 1;64(7):2572-7. doi: 10.1128/AEM.64.7.2572-2577.1998. PMID: 9647832; PMCID: PMC106428.*
25. *Wolfgang Zauner, Neil A Farrow, Adrian M.R Haines, In vitro uptake of polystyrene microspheres: effect of particle size, cell line and cell density, Journal of Controlled Release, Volume 71, Issue 1, 2001, Pages 39-51, ISSN 0168-3659, https://doi.org/10.1016/S0168-3659(00)00358-8.*
26. *Khonsari F, Zakeri-Milani P, Jelvehgari M. Formulation and Evaluation of In-vitro Characterization of Gastic-Mucoadhesive Microparticles/Discs Containing Metformin Hydrochloride. Iran J Pharm Res. 2014 Winter;13(1):67-80. PMID: 24734057; PMCID: PMC3985245.*