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Microparticulate Drug Delivery Systems: Formulation Strategies and Applications

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ABSTRACT
Because of its distinctive properties and wide-ranging uses in a variety of fields, microparticles manufacturing particles represent an intriguing class of microscopic systems. This abstract explores the complex world of microparticles particles with a focus on the various varieties, manufacturing processes, and characterization methods. Materials with substantial technical promise in a variety of domains, such as energy, imaging, medicine, and ecological uses, are microscopic particles and nanotechnology. Because of their amazing capacity to spontaneously form and saturate both hydrophilic and hydrophobic substances, microparticles are indispensable in a variety of commercial and academic undertakings. Its types may included here, key characteristics and applications of micro-particles, emphasizing their significance in drug delivery, enhanced oil recovery, and nanotechnology. The versatile nature of micro-particles positions them as promising candidates for addressing complex challenges and driving innovation across numerous industries. This paper provides a concise overview of micro-particles, highlighting their potential to revolutionize materials science, pharmaceuticals, and beyond.
Keywords: *Micro-particle Formulation, Targeted Delivery, Drug and Gene Delivery*

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INTRODUCTION

Drug delivery is an approach or technique of administering a pharmacological ingredient that produces a beneficial impact on humans or creatures (1).When converting a medication that comes in standard shape into a novel method of administration, its regulation, protection, and effectiveness are all able to be significantly increased (2). A drug's regulation, safeguarding, as well as efficacy are all likely to be much improved when it is changed from its conventional form into a novel way of delivery. The development of improvements and modifications in compositions is also aided through multiple technical advancements in manufacturing processes including being dried, purification, and combining (3). The ADDS can revolutionize how problems using customized drug administration are handled through the appropriate innovation. The creation and application of microparticle formulas has evolved into a game-changing discovery with broad ramifications in the fields of medications and sophisticated material science (4). Microparticles, which are extremely tiny fragments with sizes usually between several micrometers are what to a several centimeters, have opened up new possibilities for medicine the delivery process, substance engineering as a career and other fields. The complex process of packaging drugs, such as medications, vaccinations, or beneficial substances, inside carefully designed small-scale containers is known as microparticle formulation (5,6). The exact management of certain medicines' discharge rate, strength, and selectivity made possible by this methodology has an essential effect on how effectively they treat disease. Furthermore, microscopic particles might be designed to meet particular needs, such as prolonged drug absorption, increased accessibility, or increased stability (7). Microparticle compositions have a wide range of applications that are fluid. They provide remedies to problems in therapeutics such the necessity for delayed release of medication or the quick destruction of highly volatile medications (8). Microparticle formulation, a subfield of materials science and pharmaceutical technology, has gained significant prominence in recent years due to its potential to revolutionize drug delivery, materials engineering, and various other applications (9,10). The size of microscopic particles is normally in the range of several microns to a couple of millimeters. Microscopic particles comprise entities that range in diameter from 0.1 to 100 µm. The dynamics of small particles can differ significantly from that of microparticles due to its significantly greater surface-to-volume proportion. Within the context of biology,

a microparticle is equivalent to an exterior vesicle known as a microvesicle (11,12). It usually comprises a single active component incorporated within the matrix of polymers. There are actually two main kinds of microscopic particles, which fluctuate based on how the medicine circulates inside the polymers: microspheres and microcapsules. When it comes to microspheres is that their active component and polymer itself are mixed uniformly throughout the whole particle. In contrast, the pharmaceutical material inside micro-capsules is covered in a polymeric coating. The ingredient that acts can divide into distinct parts, and the particulate core may be either solid or liquid, or possibly gaseous (13). Several single-stranded or polymers vehicles as well as manufacturing procedures, such as aggravation, spray drying, emulsification, and freeze-drying, may be utilized to manufacture those microscopic structures (14). In order to make sure that the ingredient that acts is well embedded in the structure of the matrix, the element utilized to produce the tiny particles needs to have certain properties (15). In addition, it must to offer excellent pharmaceutical stability, regulate the dispensing of drugs, and guide the medicine to the intended location in the human body (16,17). The micro-particle dispersion methodology is a relatively recent and effective approach for creating small particles, which additionally may be applied to create nano-particles from polymeric materials (18,19). A different approach for creating microscopic particles for medicinal purposes is by hydrodynamic manufacturing (20,21,22). This approach creates microscopic particles / nano-materials that have a limited distribution of dimensions using droplet shape nanotechnology. There are many uses for micro-particle dispersion techniques, such as the delivery of medications, encapsulating formulations as well as other biomedical ones (23).

Principles of Micro-particle Formulation

Encapsulation and Controlled Release:

The process of encasing the API (Active Pharmaceuticals Ingredients) inside of small amounts containers forms the basis of microparticle synthesis (24). Its encapsulates may increase the ability to be absorbed of delicate substances, prevent them from rapidly degrading, and regulate how they circulate gradually. It's crucial for the administration of drugs, because focused and long-lasting administration can improve the efficacy of therapy (25,26).

Particle Engineering:

Extensive modification of a microscopic's dimensions, form, and chemical composition is required for its engineering (27). These variables affect a number of traits, including the loading of drugs ability, systemic interactions, & releasing timings (28). Microscopic particles are accurately engineered to suit specifications using methods such as drying by spraying method, emulsifying and solvent removal (29).

Bio-compatibility:

Biologically compatible microscopic particles compositions are necessary ensure safe administration in healthcare settings. In order to assure compliance in the body of humans, bio-degradable substances like PLGA, which (poly(lactic-co-glycolic acid)) are frequently utilized in the manufacturing of micro-particles (30,31).

Targeted Delivery:

Targeting particular human organs or cells constitutes one of the main benefits of microparticle compositions (32). Microscopic particles can have their surfaces altered so that they are capable of binding to sensors or attach to particular biological settings, assuring that the medicine or active ingredient can reach exactly where it will be required (33).

Milling Gas Condensation :

Physical procedures such as gas condensing and milling are employed to create both microparticles and nanoparticles (34). Whereas gas condensing requires substance evaporating as an initial point in an environment of inert gases and then condensing into nanocrystals in the workings of the chamber's cooler sections, milling entails lowering the dimensions of the origin material. (35,36). Gas condensation is a based on bottom- technique that may be used to create substances having tiny structures and is an exciting method to produce microparticles with particular characteristics. The method is very adaptable in that it allows for regulation of particle dimensions and shape distributions over a wide variety of processes and variable changes, including both temperatures and pressures (37,38,39). In the development and manufacturing of tiny materials, gas condensate has proven to be a highly advantageous approach. It enables the manufacturing of a variety of substances, including intermetallic substances, ceramics but one alloys, metals, electronic components, and composites (40,41).

Electro- spraying method:

A flexible technique for creating both micro- and nanomaterials is electro-spraying. In order to create microscopic particles, a conducting fluid is poured into a sprayer and subjected to a powerful voltage (42). The method, which has been extensively employed in biopharmaceutical and medication delivery uses, depends on the electro-hydrodynamic preparation of polymeric melts away, approaches, or dispersion forms (43.44). The idea behind electro-spraying is to compel the polymer mixture to come out of the

syringes in the form of beads by applying an extremely high voltage to it. The droplets will then vaporize along their path, leave behind a solid remains of positively charged particles that are collected in a collectors (45,46). This method makes it possible to produce tiny particles with constrained agglomerate and narrower size variations (47). Particulate size and shape can be adjusted for specific uses by adjusting variables including current, voltage humidity, and concentration of polymers (48,49). Electrical spraying is being utilized to generate uniformly sized soluble micro or nanostructures for a range of biological uses (50,51). The technique is an intriguing option for micro-particle production in drugs and other industry because it has benefits in terms of reliability, controllable dimension, and the capacity to manufacture nanoparticles with a broad spectrum of materials (52).

Thermal Decomposition method;

A process called thermal decay breaks down a compound's chemical attachments by applying heat to it. This process is utilized to create tiny particles (53,54). This method has been used to create nanoscale and small particles made of different substances, such as metallic and composites. One benefit of thermal decay technologies is their simplicity and capacity to yield microparticles with certain characteristics. But control over particle form and size might be restricted, and more study is required to maximize the synthesized technique for a range of compounds and uses (55,56).

Lipid microparticle characterization:

Drug Loading:

The percentage of substance absorbed by the matrix of fatty acids is known as medication / drug loading (57). Based with the following formula, the dose of the pharmaceutical substance measured inside the LMs divided by the entire mass of each nanoparticle sampling represents the medication loading:

$$\text{Dr loading (\%)} = \frac{\text{mass of drug in microparticles.}}{\text{mass of microparticles recovered}} \times 100$$

Based with the below formula, the amount of active substance that is included in its liquefied fatty acids stage throughout unit manufacturing and the amount that is encapsulated in the microscopic particles is what determines the encapsulation effectiveness:

$$\text{Entrapment efficiency (\%)} = \frac{\text{mass of drug in microparticles}}{\text{Mass of microparticles recovered}} \times 100$$

The benefit of preparations containing elevated loaded values lies in the fact fewer fragments are needed to reach the optimal medication dose (58,59,60).The estimated value & loaded rise as a more potent substance is added throughout production, however the effectiveness of containment declines due to the fact that is less phospholipid weight accessible to the therapeutic ingredient to get contained (61).

The effectiveness of medicinal product dosing and encapsulated is assessed on the LMs following either centrifugation or filtration to remove the stage of water. To remove drugs that have been bound onto the exterior of particulates, they are able to be sprayed by solvent. They might additionally be sterilized to produce fluid-free microscopic particles (62).

The integrated medication is extracted via the the LMs by heated the material over its lipid's temperature of melting, subsequently undergoing mixing or sonication. The acquired samples is analyzed using spectrophotometric or chromatographic procedures after being diluted according to volume and filtered (63).

1) Particle size:

The dimension of the particles is affected by a number of factors, including the constituents of LMs (matrix material, surfactants type or amount, and integrated medication), the process of manufacturing, and environmental factors (for example, faster mixing velocity results in a decrease in LM average diameters) (64,65). The mean dimension of particles is a measure utilized to convey the variation in particle sizes. The dimension of the particles beneath where half of the material being studied (in terms of either proportion or weight) fits is known as either the mass or the average diameters (D50) in the outcome. Additionally, the D10 and D90 (particle sizes beyond whose 10 and 90% of a samples, respectively, are measured in terms of volumes or weight) (66).

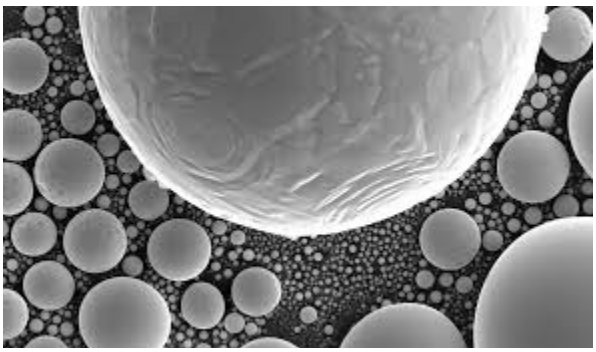

Fig:1 prepared microparticle

The resulting formula determines how to determine the polydispersity index (P.I.), a valuable indicator of the breadth of the dimension of the allocation:

P. I.= D90 - D10 / D50

Small P.I. values (ca. < 0.3) indicate narrow particle size distribution.

Optical microscopy and scanning electron microscopy (67,68):

Granular dimensions and form are able to be determined using visible as well as scanning electron microscopy techniques. The properties of the exterior structure are additionally ascertained using the aforementioned method. This size variation of few micrometer is where the optical microscope's technology becomes fewer precise. The primary drawback of the method is the relatively low sample size (300–500 particles), which reduces the statistically significant nature of the findings. The process is also drawn out and laborious. The immediate assessment of each particle 17 structure and the existence of aggregates is made possible by both of them, and this makes them both very helpful.

Coulter counter (69):

A solution consisting of electrolyte-containing nanoparticles flows via a tiny opening on both sides wherein a pair of electrodes are submerged in order to determine changes in the resistance to electricity throughout the detection area. The equipment's capacity to measure an enormous quantity of nanoparticles in a brief amount of period constitutes the technique's key benefit.

Laser diffraction (70,71):

The theory behind this approach is based on the observation that there is a direct relationship among the dimension of particles & the position at which the laser's beam is dispersed by it. Complicated techniques involving Fraunhofer and/or Mye equations are used to determine the particulate sizes using the way light scatters angle. Light scattering can be utilized using dried powder or suspended matter and has an extensive size range ranging from around 0.1 m to 1000 m. The frequently used approach for the investigation of particle dimension dispersion, it provides a quick and easy way to size materials.

Dynamic light scattering (72):

The frequency of changes in the laser's beam brightness that are dispersed by nanoparticles as they pass by the water in the specimen cell is measured by optical dispersion. The amount of light will fluctuate more quickly depending on how tiny the particles are and more quickly that they disperse. It only measures sizes from a couple of nanometers to roughly three micron. As a result, the technique is not frequently used to gauge LM size.

2) Crystallinity and Polymorphism:

Characterizing the level of lipids crystallization and altering the composition of the crystallographic structure throughout nanoparticle manufacturing or preservation are crucial factors as they affect the extent of drug integration. There are discrepancies in entrapped effectiveness and releasing behavior because thermo-dynamically unsteady crystal structures have reduced densities, which result in greater movement of the entrapped material (73). dditionally, medication solid-status changes in LMs (whether crystallized or granular) can reveal details on how the medication will disperse or mix into the phospholipid substrate as well as react with excipients. Among the most popular methods for LM solid-state drives research are powdered diffraction of X-rays and the application of differential scanning calorimetry (DSC) (74). A thermodynamic technique called DSC evaluates the reaction of the heat of the specimen to a specific temperature gradient, allowing for the determination of transformation energies and the associated temperature gradients (glass transition temperatures, solidifying and melting points). The basis for DSC evaluation is the observation that various polymorphism forms have varying melting degrees and enthalpies. For example, tristearin is capable of crystallizing in the solid b-form, which has a temperature at which it melts of around 65 °C, as well as its unstable a and b' shapes, which have melting points of about 48 °C and 62 °C, respectively. When the material being studied is heated or cooled, it is likely

that the solidification state of the lipids vehicle or integrated component will change (75,76). Since the X-ray wavelengths are similar to the spacing among crystallized elements, powdered X-ray dispersion studies takes advantage of the inherent scattering of the radiation by crystalline. By correlating the orientation and magnitude of the peak values for diffraction against those of a recognized material or polymorphism form, the results of X-ray diffraction analysis can also be used to study a powdered substance. This approach has the benefit of examining the material exactly as it is supplied. The existence of scattering waves at several locations and with variable strengths can be used to identify polymorphism changes. Furthermore, it is widely accepted that the absence of a substance's crystallographic peak signifies that it has become heterogeneous since unstructured forms result in large and dispersed maximal in diffract bands (77,78). Regarding solidstate investigation of LMs, Fourier transform infrared and Raman spectroscopy were additionally used. The intricacy of the spectrum with substantially overlapping bands limits the utility of infrared imaging, despite the fact that it is employed to identify polymorphs. Since there is minimal preparation of the material required, Raman spectroscopy is an especially helpful technology. Raman spectra of lipids have been demonstrated to be highly sensitive to alterations in chemical strand configuration, packaging, and dynamics (79,80).

3) Interaction with biological systems:

Biocompatibility:

LMs are generally accepted because they are primarily made of naturally occurring and biodegradable phospholipid. Though physiologically suitable emulsification (such as phosphatidylcholine and bile acids) were additionally used to prepare LMs, it is still important to take into account the surfactant's neurotoxicity. The viability of cells experiments have been used to examine the tolerance of LMs in vitro (81). In this method, unloading microscopic particles are suspended in an appropriate environment and incubated with the cultures of cells. When cells are exposed to foreign elements, their vitality is evaluated utilizing a variety of readily accessible testing, including the ejection of lactate dehydrogenase (82). A broad spectrum of component intensities was utilized to perform this in vitro method with murine macrophage J774, humans types lungs pulmonary (A549) as epithelium (Calu-3) lines of cells, however none substantial cytotoxic effects were seen, indicating the acceptable tolerance of LMs (83). In diverse cell strains (293 juvenile kidney cells and murine macrophages cells), neutrality LMs had no cytotoxic properties, whereas negative LMs showed influenced by concentration cytotoxic similar to those of the negative lipid. The minimal damage of nanoparticles made of lipids on various cell lines has also been shown in a variety of in vitro experiments, and these findings could be appropriately extended to LMs (84).

Biodegradation:

Since the LM framework is made up of organically produced lipids, there are in vivo biological channels for their metabolization. Esterases and lipases were the primary organisms involved in the 24 breakdown of LMs. Since lipases are found throughout the human body, particularly in the gut, dermal and muscular tissues, and systemic liquids, biological degradation of lipid fragments can take place irrespective of their mode of distribution (85). LMs have been demonstrated to degrade after being incubated in conditions that are physiological including lipases in vitro (80% mass loss after 48 days). Yet, additional research should be done to confirm whether these findings may be applied to the more complicated in vivo scenario. It ought to be emphasized that the process of in vivo release of drugs will be impacted by both diffusion and the enzyme-mediated breakdown of the LM matrix (86). The nanoparticles of lipids have been the subject of much research regarding the impact their chemical constitution on the rate of lipolytic breakdown of enzymes. It is logical to presume that the acquired data may also be pertinent for the LMs.

Interaction with cells:

Although LM production and characterisation have received extensive study, their influence on cellular has largely gone unnoticed. Although biological impediments are generally impossible to be overcome by microscopic particles, however dependent upon their dimensions and kind of membranes, nanomaterials may be able to do so (87). Microscopic particles can penetrate cells capable of scavenging (such as neutrophils and macrophages), which allows them to absorb nanoparticles up to 10 m in diameter. In contrast, nearly all types of cells can conduct the cytokines absorption method for sub-micron substance, allowing for the widespread interior delivery of nanomaterials. Erni et al. in vitro showed that the human main monocytes are capable of internalizing both neutrality and electrically loaded LMs. The quick (24 h) interior particles disintegration that accompanied phagocytosis made LMs an ideal vehicle for the immediate introduction of medicines to these particular cells (88). While quercetin became encased in the LMs as opposed to being present in its purified form, the intracellular movement of the flavonoids was dramatically improved across both types of cells. Because of less quercetin disintegration following encapsulating and improved contact among the encased quercetin and the living thing's surface, the LMs were able to increase cellular absorption. To fully comprehend the dynamics of the LMs' interactions with cell membranes both in vivo and in vitro, more research is necessary (89).

4) Administration routes:

The subsequent parts will investigate how LMs are being utilized to deliver different kinds of medications via different ROA.

Oral administration:

Through oral administration, the LM could supply prolonged absorption and defense over biochemical and enzyme-mediated breakdown of unstable medicines (such as proteins and peptides) within the digestive tract. Particularly, lipids frameworks are considered more biodegradable and offer peptides as well as proteins a less harmful microenvironment then polymers that are synthetic. Insufficiently soluble in water medicines' bioavailability in the mouth has also been demonstrated to be improved using lipid-based microparticulate methods. Since only 2–3% of unbroken particles are absorbed through the digestive tract, this impact can be attributed to the activation of inherently occurring solubility mechanisms and the inclusion of 26 surfactants, which increases stability (90). The fact that LMs are nontoxic post administration by mouth is another benefit. Yet, it is important to confirm that the lipid carriers are stable in the gastrointestinal and digestive juices. Serratiopeptidase, a type of peptides medication and proteolytic digestive enzyme, can be delivered orally via LMs since they can entrap large amounts of peptides and provide prolonged releases (91,92).

Applications:

Physiological uses, therapeutic regeneration, and delivery of drugs are the main areas in which microparticles find use.

- **Drug and Gene Delivery:** Uses of microparticles in medication and transmitting genes have been thoroughly investigated. In order to provide regulated releasing and specialized delivery to particular tissues or cells, they are employed for encasing medications, peptides, amino acids, or other chemicals that are bioactive.
- **Biomedical Applications:** Flexible gelatin tiny particles and little particles generate interest in the medical community as vaccine adjuvants to and for pharmaceutical delivery methods. Because of their advantages, which include pores, elastic modulus, and biological compatibility, these small particles may capture molecules that are bioactive with little to no loss of biologic activity.
- **Novel Drug Delivery Systems:** Because of their tiny dimension and potent transportation capability, emboli and microparticles are essential components of innovative systems for delivering medicines. They are used as drug carriers to deliver medications to specific locations with delayed and targeted discharge.

CONCULSION

Small particles are materials that can be used in a variety of fields, including vitality, scans, technological innovation in the environment, and medicine administration. Physically and chemically techniques are used in the production of small particles, and each has benefit of its own. Physical approaches include milling, gas condensation, electro-spraying, and thermal decomposition. With the use of these techniques, it is possible to modify the size, composition, form, and size distribution of particles to fit particular needs. The composition of microparticles manufacturing particles has special qualities such a wide interface area, low interfacial tension, and the capacity to distribute and disintegrate polar medicines. Because of the inter-particle connections, which call for statistical adjustment when determining drop dimension, the description of tiny emulsion is difficult. A potential technique for creating micro- and nanoparticles for numerous purposes is microparticles manufacturing particles production.

REFERENCES

1. Bhattacharya S, Rodriques P, Prajapati B. (2023). Introductory Chapter: Advanced Drug Delivery Systems. In Advanced Drug Delivery Systems . DOI: 10.5772/intechopen.109337
2. Caprasse J. (2016). Microfluidic formulation: offering new biomedical perspectives to poly (phospho) ester microparticles. https://hdl.handle.net/2268/307056
3. Elsayed I, AbouGhaly MH. (2016). Inhalable nanocomposite microparticles: preparation, characterization and factors affecting formulation. Expert Opinion on Drug Delivery. 13(2):207-22.
4. Lee YS, Johnson PJ, Robbins PT, Bridson RH. (2013). Production of nanoparticles-in-microparticles by a double emulsion method: A comprehensive study. European Journal of Pharmaceutics and Biopharmaceutics. 1;83(2):168-73.
5. Sarmadi M, Behrens AM, McHugh KJ, Contreras HT, Tochka ZL, Lu X, Langer R, Jaklenec A. (2020). Modeling, design, and machine learning-based framework for optimal injectability of microparticle-based drug formulations. Science advances. 8;6(28):eabb6594.
6. Han FY, Thurecht KJ, Whittaker AK, Smith MT. (2016). Biodegradable PLGA-based microparticles for producing sustained-release drug formulations and strategies for improving drug loading. Frontiers in pharmacology. 28;7:185.

7. Burgain J, Gaiani C, Cailliez-Grimal C, Jeandel C, Scher J. Encapsulation of Lactobacillus rhamnosus GG in microparticles: Influence of casein to whey protein ratio on bacterial survival during digestion. Innovative Food Science & Emerging Technologies. 2013 Jul 1;19:233-42.
8. Volodkin DV, Schmidt S, Fernandes P, Larionova NI, Sukhorukov GB, Duschl C, Möhwald H, von Klitzing R. One-Step Formulation of Protein Microparticles with Tailored Properties: Hard Templating at Soft Conditions. Advanced Functional Materials. 2012 May 9;22(9):1914-22.
9. Amidi M, Pellikaan HC, de Boer AH, Crommelin DJ, Hennink WE, Jiskoot W. Preparation and physicochemical characterization of supercritically dried insulin-loaded microparticles for pulmonary delivery. European Journal of Pharmaceutics and Biopharmaceutics. 2008 Feb 1;68(2):191-200.
10. Leonardi D, Salomón CJ, Lamas MC, Olivieri AC. Development of novel formulations for Chagas' disease: optimization of benznidazole chitosan microparticles based on artificial neural networks. International journal of pharmaceutics. 2009 Feb 9;367(1-2):140-7.
11. Battaglia L, Ugazio E. Lipid nano-and microparticles: an overview of patent-related research. Journal of Nanomaterials. 2019 Jan 15;2019.
12. Martín-Sabroso C, Fraguas-Sánchez AI, Aparicio-Blanco J, Cano-Abad MF, Torres-Suárez AI. Critical attributes of formulation and of elaboration process of PLGA-protein microparticles. International journal of pharmaceutics. 2015 Mar 1;480(1-2):27-36.
13. Campos E, Branquinho J, Carreira AS, Carvalho A, Coimbra P, Ferreira P, Gil MH. Designing polymeric microparticles for biomedical and industrial applications. European Polymer Journal. 2013 Aug 1;49(8):2005-21.
14. Wischke C, Schwendeman SP. Principles of encapsulating hydrophobic drugs in PLA/PLGA microparticles. International Journal of pharmaceutics. 2008 Dec 8;364(2):298-327.
15. Li RG, Lindland K, Tonstad SK, Bønsdorff TB, Juzeniene A, Westrøm S, Larsen RH. Improved formulation of 224Ra-labeled calcium carbonate microparticles by surface layer encapsulation and addition of EDTMP. Pharmaceutics. 2021 Apr 29;13(5):634.
16. Acarturk FÜ, Takka SE. Calcium alginate microparticles for oral administration: II: effect of formulation factors on drug release and drug entrapment efficiency. Journal of microencapsulation. 1999 May 1;16(3):291-302.
17. Wong CY, Al-Salami H, Dass CR. Microparticles, microcapsules and microspheres: A review of recent developments and prospects for oral delivery of insulin. International journal of pharmaceutics. 2018 Feb 15;537(1-2):223-44.
18. Yoo J, Won YY. Phenomenology of the initial burst release of drugs from PLGA microparticles. ACS Biomaterials Science & Engineering. 2020 Oct 9;6(11):6053-62.
19. Gómez JM, Csaba N, Fischer S, Sichelstiel A, Kündig TM, Gander B, Johansen P. Surface coating of PLGA microparticles with protamine enhances their immunological performance through facilitated phagocytosis. Journal of Controlled Release. 2008 Sep 10;130(2):161-7.
20. Naha PC, Kanchan V, Panda AK. Evaluation of parenteral depot insulin formulation using PLGA and PLA microparticles. Journal of biomaterials applications. 2009 Nov;24(4):309-25.
21. Momoh MA, Kenechukwu FC, Attama AA. Formulation and evaluation of novel solid lipid microparticles as a sustained release system for the delivery of metformin hydrochloride. Drug Delivery. 2013 Apr 1;20(3-4):102-11.
22. Jordan F, Naylor A, Kelly CA, Howdle SM, Lewis A, Illum L. Sustained release hGH microsphere formulation produced by a novel supercritical fluid technology: in vivo studies. Journal of Controlled Release. 2010 Jan 25;141(2):153-60.
23. Reddy JR, Gnanaprakash K, Badarinath AV, Chetty CM. Formulation and evaluation of microparticles of metronidazole. Journal of Pharmaceutical Sciences and Research. 2009 Dec 1;1(4):131.
24. Duncanson WJ, Lin T, Abate AR, Seiffert S, Shah RK, Weitz DA. Microfluidic synthesis of advanced microparticles for encapsulation and controlled release. Lab on a Chip. 2012;12(12):2135-45.
25. Mazzara JM, Ochyl LJ, Hong JK, Moon JJ, Prausnitz MR, Schwendeman SP. Self-healing encapsulation and controlled release of vaccine antigens from PLGA microparticles delivered by microneedle patches. Bioengineering & translational medicine. 2019 Jan;4(1):116-28.
26. Sopeña F, Maqueda C, Morillo E. Controlled release formulations of herbicides based on micro-encapsulation. Ciencia e investigación agraria. 2009 Apr;36(1):27-42.
27. Vehring R. Pharmaceutical particle engineering via spray drying. Pharmaceutical research. 2008 May;25:999-1022.
28. Silva AS, Tavares MT, Aguiar-Ricardo A. Sustainable strategies for nano-in-micro particle engineering for pulmonary delivery. Journal of nanoparticle research. 2014 Nov;16:1-7.
29. Chow AH, Tong HH, Chattopadhyay P, Shekunov BY. Particle engineering for pulmonary drug delivery. Pharmaceutical research. 2007 Mar;24:411-37.
30. Link DP, van den Dolder J, van den Beucken JJ, Cuijpers VM, Wolke JG, Mikos AG, Jansen JA. Evaluation of the biocompatibility of calcium phosphate cement/PLGA microparticle composites. Journal of Biomedical Materials Research Part A: An Official Journal of The Society for Biomaterials, The Japanese Society for Biomaterials, and The Australian Society for Biomaterials and the Korean Society for Biomaterials. 2008 Dec 1;87(3):760-9.
31. El-Sherbiny IM, Smyth HD. Controlled release pulmonary administration of curcumin using swellable biocompatible microparticles. Molecular pharmaceutics. 2012 Feb 6;9(2):269-80.
32. Lassalle V, Ferreira ML. PLA nano-and microparticles for drug delivery: an overview of the methods of preparation. Macromolecular bioscience. 2007 Jun 7;7(6):767-83.
33. Lagreca E, Onesto V, Di Natale C, La Manna S, Netti PA, Vecchione R. Recent advances in the formulation of PLGA microparticles for controlled drug delivery. Progress in biomaterials. 2020 Dec;9:153-74.

34. Kale SN, Deore SL. Emulsion micro emulsion and nano emulsion: a review. Systematic Reviews in Pharmacy. 2017;8(1):39.
35. Hsu CH, Cui Z, Mumper RJ, Jay M. Preparation and characterization of novel coenzyme Q 10 nanoparticles engineered from microemulsion precursors. AAPS PharmSciTech. 2003 Sep;4:24-35.
36. Pan Z, Cui B, Zeng Z, Feng L, Liu G, Cui H, Pan H. Lambda-cyhalothrin nanosuspension prepared by the melt emulsification-high pressure homogenization method. Journal of nanomaterials. 2015 Jan 1;16(1):263-.
37. Abramov S, Ruppik P, Schuchmann HP. Crystallization in emulsions: A thermo-optical method to determine single crystallization events in droplet clusters. Processes. 2016 Aug 11;4(3):25.
38. Tesfai A, El-Zahab B, Bwambok DK, Baker GA, Fakayode SO, Lowry M, Warner IM. Controllable formation of ionic liquid micro-and nanoparticles via a melt–emulsion–quench approach. Nano letters. 2008 Mar 12;8(3):897-901.
39. Aher SS, Malsane ST, Saudagar RB. Nanosuspension: an overview. Asian Journal of Research in Pharmaceutical Science. 2017;7(2):81-6.
40. Geetha G, Poojitha U, Khan KA. Various techniques for preparation of nanosuspension-A Review. International Journal of Pharma Research & Review. 2014 Sep;3(9):30-7.
41. Szumała P. Structure of microemulsion formulated with monoacylglycerols in the presence of polyols and ethanol. Journal of surfactants and detergents. 2015 Jan;18(1):97-106.
42. Jaiswal J, Gupta SK, Kreuter J. Preparation of biodegradable cyclosporine nanoparticles by high-pressure emulsification-solvent evaporation process. Journal of Controlled Release. 2004 Apr 16;96(1):169-78.
43. Makadia HA, Bhatt AY, Parmar RB, Paun JS, Tank HM. Self-nano emulsifying drug delivery system (SNEDDS): future aspects. Asian Journal of Pharmaceutical Research. 2013;3(1):21-7.
44. Božič M, Elschner T, Tkaučič D, Bračič M, Hribernik S, Stana Kleinschek K, Kargl R. Effect of different surface active polysaccharide derivatives on the formation of ethyl cellulose particles by the emulsion-solvent evaporation method. Cellulose. 2018 Dec;25:6901-22.
45. Bouchemal K, Briançon S, Perrier E, Fessi H. Nano-emulsion formulation using spontaneous emulsification: solvent, oil and surfactant optimisation. International journal of pharmaceutics. 2004 Aug 6;280(1-2):241-51.
46. Rao JP, Geckeler KE. Polymer nanoparticles: Preparation techniques and size-control parameters. Progress in polymer science. 2011 Jul 1;36(7):887-913.
47. Yoon G, Park JW, Yoon IS. Solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs): recent advances in drug delivery. Journal of Pharmaceutical Investigation. 2013 Oct;43:353-62.
48. Texter J. Precipitation and condensation of organic particles. Journal of dispersion science and technology. 2001 Aug 31;22(6):499-527.
49. Nagavarma BV, Yadav HK, Ayaz AV, Vasudha LS, Shivakumar HG. Different techniques for preparation of polymeric nanoparticles-a review. Asian J. Pharm. Clin. Res. 2012 Jun;5(3):16-23.
50. Naik JB, Lokhande AB, Mishra S, Kulkarni RD. Development of sustained release micro/nanoparticles using different solvent emulsification technique: A review. Int J Pharm Bio Sci. 2012 Oct;3(4):573-90.
51. Macsik Z, Hudston LA, Wurth KN, Meininger D, Jesinghaus C, Tenner TJ, Naes BE, Boswell M, Shozugawa K, LaMont SP, Steiner RE. Identification, isolation, and characterization of a novel type of Fukushima-derived microparticle. Journal of Radioanalytical and Nuclear Chemistry. 2022 Dec;331(12):5333-41.
52. Aher SS, Malsane ST, Saudagar RB. Nanosuspension: an overview. Asian Journal of Research in Pharmaceutical Science. 2017;7(2):81-6.
53. Pistel K, Kissel T. Effects of salt addition on the microencapsulation of proteins using W/O/W double emulsion technique. Journal of microencapsulation. 2000 Jan 1;17(4):467-83.
54. Maa YF, Hsu CC. Effect of primary emulsions on microsphere size and protein-loading in the double emulsion process. Journal of microencapsulation. 1997 Jan 1;14(2):225-41.
55. Mehrnia MA, Jafari SM, Makhmal-Zadeh BS, Maghsoudlou Y. Crocin loaded nano-emulsions: Factors affecting emulsion properties in spontaneous emulsification. International journal of biological macromolecules. 2016 Mar 1;84:261-7.
56. Zhu Q, Qiu S, Zhang H, Cheng Y, Yin L. Physical stability, microstructure and micro-rheological properties of water-in-oil-in-water (W/O/W) emulsions stabilized by porcine gelatin. Food chemistry. 2018 Jul 1;253:63-70.
57. Reithmeier H, Herrmann J, Göpferich A. Development and characterization of lipid microparticles as a drug carrier for somatostatin. International journal of pharmaceutics. 2001 May 7;218(1-2):133-43.
58. Rosita N, Ambarwati N, Erawati T, Hariyadi DM. Characterization and in vitro release of inhalation quercetin solid lipid microparticles: Effect of lipid. Journal of Advanced Pharmaceutical Technology & Research. 2022 Jan;13(1):11.
59. Scalia S, Young PM, Traini D. Solid lipid microparticles as an approach to drug delivery. Expert opinion on drug delivery. 2015 Apr 3;12(4):583-99.
60. Di Sabatino M, Albertini B, Kett VL, Passerini N. Spray congealed lipid microparticles with high protein loading: Preparation and solid state characterisation. European journal of pharmaceutical sciences. 2012 Aug 15;46(5):346-56.
61. Bunjes H. Characterization of solid lipid nano-and microparticles. Lipospheres in drug targets and delivery. 2004 Nov 29:41-66.
62. Üner M. Preparation, characterization and physico-chemical properties of solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC): their benefits as colloidal drug carrier systems. Die pharmazie-an international journal of pharmaceutical sciences. 2006 May 1;61(5):375-86.

63. Nnamani PO, Ibezim EC, Attama AA, Adikwu MU. Surface modified solid lipid microparticles based on homolipids and softisan® 142: preliminary characterization. Asian Pacific Journal of Tropical Medicine. 2010 Mar 1;3(3):205-10.
64. Reithmeier H, Herrmann J, Göpferich A. Development and characterization of lipid microparticles as a drug carrier for somatostatin. International journal of pharmaceutics. 2001 May 7;218(1-2):133-43.
65. Sanna V, Kirschvink N, Gustin P, Gavini E, Roland I, Delattre L, Evrard B. Preparation and in vivo toxicity study of solid lipid microparticles as carrier for pulmonary administration. AAPS pharmscitech. 2004 Jun;5:17-23.
66. El-Kamel AH, Al-Fagih IM, Alsarra IA. Testosterone solid lipid microparticles for transdermal drug delivery. Formulation and physicochemical characterization. Journal of microencapsulation. 2007 Jan 1;24(5):457-75.
67. Van Der Pol E, Hoekstra AG, Sturk A, Otto C, Van Leeuwen TG, Nieuwland R. Optical and non-optical methods for detection and characterization of microparticles and exosomes. Journal of Thrombosis and Haemostasis. 2010 Dec 1;8(12):2596-607.
68. Issman L, Brenner B, Talmon Y, Aharon A. Cryogenic transmission electron microscopy nanostructural study of shed microparticles. PLoS One. 2013 Dec 26;8(12):e83680.
69. Higashi A, Fujii Y. Studies on microparticles contained in medium-depth ice cores retrieved from east Dronning Maud Land, Antarctica. Annals of Glaciology. 1994;20:73-9.
70. Darakis E, Khanam T, Rajendran A, Kariwala V, Naughton TJ, Asundi AK. Microparticle characterization using digital holography. Chemical Engineering Science. 2010 Jan 16;65(2):1037-44.
71. Amidi M, Pellikaan HC, de Boer AH, Crommelin DJ, Hennink WE, Jiskoot W. Preparation and physicochemical characterization of supercritically dried insulin-loaded microparticles for pulmonary delivery. European Journal of Pharmaceutics and Biopharmaceutics. 2008 Feb 1;68(2):191-200.
72. Labrie A, Marshall A, Bedi H, Maurer-Spurej E. Characterization of platelet concentrates using dynamic light scattering. Transfusion Medicine and Hemotherapy. 2013 Apr 1;40(2):93-100.
73. Kogan A, Popov I, Uvarov V, Cohen S, Aserin A, Garti N. Microemulsion-facilitated crystallization of Carbamazepine. Journal of dispersion science and technology. 2007 Aug 1;28(7):1008-19.
74. Kogan A, Popov I, Uvarov V, Cohen S, Aserin A, Garti N. Crystallization of carbamazepine pseudopolymorphs from nonionic microemulsions. Langmuir. 2008 Feb 5;24(3):722-33.
75. Devaraj S, Munichandraiah N. Electrochemical supercapacitor studies of nanostructured α-MnO2 synthesized by microemulsion method and the effect of annealing. Journal of the Electrochemical Society. 2006 Dec 19;154(2):A80.
76. Yang SM, Zhang D, Chen W, Chen SC. A flow-free droplet-based device for high throughput polymorphic crystallization. Lab on a Chip. 2015;15(12):2680-7.
77. Doktorovová S, Araújo J, Garcia ML, Rakovský E, Souto EB. Formulating fluticasone propionate in novel PEG-containing nanostructured lipid carriers (PEG-NLC). Colloids and Surfaces B: Biointerfaces. 2010 Feb 1;75(2):538-42.
78. Lu CH, Wu WH, Kale RB. Microemulsion-mediated hydrothermal synthesis of photocatalytic TiO2 powders. Journal of Hazardous Materials. 2008 Jun 15;154(1-3):649-54.
79. Jovani M, Domingo M, Machado TR, Longo E, Beltrán-Mir H, Cordoncillo E. Pigments based on Cr and Sb doped TiO2 prepared by microemulsion-mediated solvothermal synthesis for inkjet printing on ceramics. Dyes and Pigments. 2015 May 1;116:106-13.
80. Müller RH, Runge SA, Ravelli V, Thünemann AF, Mehnert W, Souto EB. Cyclosporine-loaded solid lipid nanoparticles (SLN®): Drug–lipid physicochemical interactions and characterization of drug incorporation. European journal of pharmaceutics and biopharmaceutics. 2008 Mar 1;68(3):535-44.
81. Formariz TP, Sarmento VH, Silva-Junior AA, Scarpa MV, Santilli CV, Oliveira AG. Doxorubicin biocompatible O/W microemulsion stabilized by mixed surfactant containing soya phosphatidylcholine. Colloids and Surfaces B: Biointerfaces. 2006 Aug 1;51(1):54-61.
82. Szczepanowicz K, Bazylińska U, Pietkiewicz J, Szyk-Warszyńska L, Wilk KA, Warszyński P. Biocompatible long-sustained release oil-core polyelectrolyte nanocarriers: From controlling physical state and stability to biological impact. Advances in Colloid and Interface Science. 2015 Aug 1;222:678-91.
83. Rhyaf A, Naji H, Al-Karagoly H, Albukhaty S, Sulaiman GM, Alshammari AA, Mohammed HA, Jabir M, Khan RA. In Vitro and In Vivo Functional Viability, and Biocompatibility Evaluation of Bovine Serum Albumin-Ingrained Microemulsion: A Model Based on Sesame Oil as the Payload for Developing an Efficient Drug Delivery Platform. Pharmaceuticals. 2023 Apr 12;16(4):582.
84. Ali MK, Moshikur RM, Wakabayashi R, Moniruzzaman M, Kamiya N, Goto M. Biocompatible ionic liquid surfactant-based microemulsion as a potential carrier for sparingly soluble drugs. ACS Sustainable Chemistry & Engineering. 2020 Mar 4;8(16):6263-72.
85. Kumari A, Yadav SK, Yadav SC. Biodegradable polymeric nanoparticles based drug delivery systems. Colloids and surfaces B: biointerfaces. 2010 Jan 1;75(1):1-8.
86. Martins AF, de Oliveira DM, Pereira AG, Rubira AF, Muniz EC. Chitosan/TPP microparticles obtained by microemulsion method applied in controlled release of heparin. International journal of biological macromolecules. 2012 Dec 1;51(5):1127-33.
87. Lin G, Cortez-Jugo C, Ju Y, Besford QA, Ryan TM, Pan S, Richardson JJ, Caruso F. Microemulsion-assisted templating of metal-stabilized poly (ethylene glycol) nanoparticles. Biomacromolecules. 2020 Dec 18;22(2):612-9.
88. Sethuram L, Thomas J, Mukherjee A, Chandrasekaran N. Eugenol micro-emulsion reinforced with silver nanocomposite electrospun mats for wound dressing strategies. Materials Advances. 2021;2(9):2971-88.

89. Patil S, Sandberg A, Heckert E, Self W, Seal S. Protein adsorption and cellular uptake of cerium oxide nanoparticles as a function of zeta potential. Biomaterials. 2007 Nov 1;28(31):4600-7.
90. Sahu GK, Sharma H, Gupta A, Kaur CD. Advancements in microemulsion based drug delivery systems for better therapeutic effects. Int J Pharm Sci Dev Res. 2015;1(008).
91. Shukla T, Upmanyu N, Agrawal M, Saraf S, Saraf S, Alexander A. Biomedical applications of microemulsion through dermal and transdermal route. Biomedicine & Pharmacotherapy. 2018 Dec 1;108:1477-94.
92. Cilek A, Celebi N, Tırnaksız F, Tay A. A lecithin-based microemulsion of rh-insulin with aprotinin for oral administration: Investigation of hypoglycemic effects in non-diabetic and STZ-induced diabetic rats. International Journal of Pharmaceutics. 2005 Jul 14;298(1):176-85.

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