Biopolymer Applications Journal (BAJ)
e-ISSN : 2800-1729
Lamia TAOUZINET et al. Vol 1, N° 2, 2022, pp. 24-29

Nano-Encapsulation Systems Improve Drug Delivery and Solubility

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Received: 05 May 2022; Accepted: 05 June 2022; Published: 20 July 2022

Abstract

Size reduction is one of the most often utilized and important unit processes in pharmaceutical manufacture. It contributes to increased medicine safety and bioavailability, decreased toxicity, improved drug release, and improved drug formulation possibilities. Nanoencapsulation is a process that involves encapsulating a bioactive molecule in liquid, solid, or gaseous form within a matrix of inert material in order to preserve the coated component. The size of nanoencapsules can range from 1 to 1,000 nm. They have a multitude of different shapes, depending on the materials and methods used to prepare them. The main reason for nanoencapsulation species is to ensure that the encapsulated material reaches the area of action without being adversely affected by the external environment through which it passes. This research concentrated on current breakthroughs in nanoencapsulation drug systems, production, and characterization methodologies.

Keywords *Nanoencapulation, Drug delivery, Solubility.*

I. Introduction

Nanotechnology can enable improved medication delivery methods for better disease management and treatment by manipulating the properties of materials like polymers and fabricating nanostructures.

The most important application of clinical nanotechnology, it is predicted, will be in pharmaceutical development within a short period of time [1]. From the micro to the nanoscale, drug delivery research is now progressing. Novel approaches for controlled release, targeted delivery, and enhanced bioavailability have been associated with the technology of nanoparticles (NPs) as drugs or constituents of drugs [2]. Polymer capsules made at the nanoscale provide advantages such as drug breakdown, controlled drug release, and excellent absorption at the target location [3]. Scientists across the world are now working to develop novel polymers, refine existing ones, and test particular polymer-drug combinations. Nanocapsules, for example, have been made from monomers or by simple nano deposition of a polymer that has been accomplished [4].Through diagnostic and therapeutic agent transportation, nanomaterials are formulated in a unique way to make contact with molecules, interact with them, and detect any changes at the molecular level [1, 5]. Fabrication of nanoscale materials and devices can be done from the bottom up or from the top down. Bottom-up methods fabricate nanomaterials or structures from a controlled buildup of atoms or molecules, which is regulated by thermodynamic means such as self-assembly [6]. Microtechnologies, on the other hand, can be used to fabricate nanoscale structures and devices. Photolithography, nanomolding, dip-pen lithography, and nanofluids are examples of top-down nanofabrication technologies [7]. As a result, advancements in this field will lead to improved drug delivery, as well as other applications in medicine and pharmacy, as well as methods of preparation.

II. Nanotechnology-based drug delivery systems

Several nanoparticles and nanomaterials have been studied and authorized for usage in therapeutic settings. The following sections go over some of the most prevalent forms of nanoparticles.

Micelles: Micelles are lipid- and amphiphilic-molecule-based amphiphilic surfactant molecules. Micelles spontaneously aggregate and self-assemble into spherical vesicles with a hydrophilic outer monolayer and a hydrophobic core in aqueous circumstances, allowing hydrophobic medicinal substances to be included. Micelles' unique characteristics allow for increased solubility of hydrophobic medicines, resulting in improved bioavailability. Micelles have a diameter of 10 to 100 nm. Micelles are used as drug delivery agents, imaging agents, contrast agents, and therapeutic agents, among other things [8].

Liposomes: Liposomes are vesicular structures made up of one or more lipid bilayers and an equal number of aqueous compartments [9]. Liposomes range in size from the tiniest vesicle (diameter 20nm) to liposomes with a diameter of 1m or larger, about comparable to the dimensions of live cells, and may be observed under a light microscope. One or three compartments in a liposome can carry medicines (water

soluble agents in the central aqueous core, lipid soluble agents in the membrane, peptide and small proteins at the lipid aqueous interface) [10]. Phospholipids, which are molecules with a head group and a tail group, are commonly used to make membranes. The head is attracted to water, whereas the tail, which is made up of a long hydrocarbon chain, is repelled by if. A liposome is a self-forming structure made up of one or more concentric lipid bilayers separated by water buffer compartments and is a lipid bilayer-based artificially produced spherical vesicle [11].

Dendrimers: Dendrimers are a new type of polymer with a controlled structure and nanometric dimensions. Dendrimers, which are utilized in drug administration and imaging, are typically 10 to 100 nm in diameter and have numerous functional groups on their surface, making them suitable drug carriers [12]. Dendrimers have been extensively researched in terms of their structure and function. Dendrimers nowadays can be extremely specialized, encasing functional molecules [therapeutic or diagnostic agents) within their core [13]. They can be manufactured into metallic nanostructures and nanotubes, as well as having an encapsulating capability, and they are compatible with organic structures such as DNA. Dendrimers are used extensively in the medical and biological areas because they have various reactive surface groups [nanostructure) and are compatible with organic structures such as DNA. Nonsteroidal anti-inflammatory formulations, antibacterial and antiviral medicines, anticancer agents, pro-drugs, and screening agents for high-throughput drug discovery are among the medicinal applications of dendrimers [14] Because of their propensity to break cell membranes due to a positive charge on their surface, dendrimers may be hazardous [15].

Carbon nanotubes: Carbon nanotubes are cylinders made up of single-layer carbon atoms wrapped together into sheets [graphene). They can be single walled, multi walled, or made up of several concentrically interconnected nanotubes [16]. Carbon nanotubes can reach extremely high loading capacities as drug carriers due to their large exterior surface area. Carbon tubes are also useful as imaging contrast agents [17] and biological sensors due to their unique optical, mechanical, and electrical characteristics [18].

Metallic nanoparticles: Iron oxide and gold nanoparticles are examples of metallic nanoparticles. A magnetic core (45 nm) and hydrophilic polymers, such as dextran or PEG [16], make up iron oxide nanoparticles. Gold nanoparticles, on the other hand, have a gold atom core surrounded by negative reactive groups on the surface, which may be functionalized by adding a monolayer of surface moieties as ligands for active targeting [18]. Metallic nanoparticles have been used as imaging contrast agents [19], in laser‑based treatment, as optical biosensors and drug delivery vehicles [20].

Quantum dots: Quantum dots (QDs) are fluorescent semiconductor nanocrystals with a diameter of 1100 nm that have showed promise in a variety of biological applications, including medication delivery and cellular imaging [21]. Quantum dots have a shellcode structure, which is generally made up of elements from the II-VI or III-V groups of the periodic table. Quantum dots have been used in medical imaging because of their unusual optical characteristics and size, as well as their great brightness and stability [21].

III. Preparation methods

High-pressure homogenization technique

On a big scale, this method is employed. It can be done in one of two ways: cold homogenization or hot homogenization. Stress is given to the lipid by applying high pressure through extremely high shear, and it is pushed through a specially constructed homogenization valve to produce suspended particles with a homogeneous size distribution. It's crucial to understand that, depending on the nature of the medication and excipients, both raised and below room temperature can be utilized [22].

Supercritical Fluid Technology

Supercritical fluids are non-hazardous to the environment. Supercritical antisolvent (SAS), rapid expansion of supercritical solution (RESS), and precipitation with compressed antisolvent process (PCS) are all typical supercritical fluids techniques. Two fully miscible solvents are used in the SAS technique: one is supercritical liquid and the other is a fluid solvent. While the solutes are insoluble in supercritical liquid, nanoparticulates are generated as a result of the rapid precipitation of solutes formed as a result of the supercritical fluid's extraction of the fluid solvent. The solutes are dissolved into the supercritical liquid in the RESS method, which results in a considerable loss of solvent power and therefore precipitation of the solutes owing to fast extension of solutes through tiny nozzle into the area of reduced pressure. Meziani et al. (2004) used a supercritical fluid method to make nanoparticles of Poly (heptadecafluorodecyl acrylate) with a diameter of >50nm. Although organic solvents are not required in the RESS approach for nanoparticle production, the main disadvantage is that the products formed at the primary step are microscaled rather than nanoscaled. However, a newer supercritical fluid technique known as RESOLV is presently in use, in which a fluid solvent inhibits particle development in the expansion jet nozzle, resulting in the creation of nanoscaled particulates in their early stages [23].

Emulsion-Solvent Evaporation Method

One of the most common ways for preparing nanoparticles is this approach. There are two processes to emulsification-solvent evaporation. The polymer solution must first be emulsified into an aqueous phase in the first stage.

The polymer solvent is evaporated in the second stage, causing the polymer to precipitate as nanospheres. The nano particles are collected by ultracentrifugation and then washed with distilled water to eliminate any remaining stabilizers or free drugs before being lyophilized for storage). The highpressure emulsification and solvent evaporation technique is a variation of this process . This process begins with the creation of an emulsion, which is then homogenized under high pressure before being stirred to remove the organic solvent. The size may be adjusted by altering the stirring rate,

dispersion agent type and quantity, organic and aqueous phase viscosity, and temperature . This method, on the other hand, can be used to make liposoluble drugs, with the scale-up issue posing a limitation [24].

Solvent Displacement / Precipitation Method

In the presence or absence of surfactant, solvent displacement entails the precipitation of a preformed polymer from an organic solution and the diffusion of the organic solvent into the aqueous medium. In a semipolar water miscible solvent like acetone or ethanol, polymers, drugs, and/or lipophilic surfactants are dissolved. Under magnetic stirring, the solution is emptied or injected into an aqueous solution containing stabilizer. Rapid solvent diffusion produces nanoparticles very instantly [24].

Double Emulsion and Evaporation Method

To encapsulate hydrophilic medicines, the double emulsion approach is used, which includes adding aqueous drug solutions to organic polymer solutions while vigorously swirling to produce w/o emulsions. This w/o emulsion is continuously stirred into the second aqueous phase to create the w/o/w emulsion. The emulsion is subsequently evaporated to remove the solvent, and nano particles may be separated using high-speed centrifugation. Before lyophilization, the formed nanoparticles must be thoroughly washed [25]. The amount of hydrophilic drug to be integrated, the stabilizer concentration, the polymer concentration, and the volume of the aqueous phase are the factors that influence nano particle characterisation in this approach [26].

IV.Different advantages of nano sized drug delivery system over conventional dosage forms

In comparison to conventional dosage forms or drug delivery techniques, we got the following benefits using nanotechnology [27, 28]:

• Higher bioavailability for drugs having low solubility.
• Nanotechnology offers a wide range of applications (I.V, Oral, dermal etc.)
• There is a well-established method of preparation for large-scale manufacturing, namely high-pressure homogenization.
• Improved bioavailability, sustained and controlled release characteristics, and environmental hazard protection for medicinal molecules.
• Vaccines, anticancer drugs, and other biological products are good candidates for delivery.
• Nanotechnology might be used to conduct tissue editing on a nan size.

V. Characterization of Nanoparticles

Particle size: The most significant factors in nanoparticle characterisation are particle size distribution and shape. Electron microscopy is used to determine morphology and size. Nanoparticles are most commonly used in medication delivery and targeting. It has been discovered that particle size has an impact on medication release. The surface area of smaller particles is greater. As a result, the majority of the drug placed onto them will come into contact with the particle surface, resulting in rapid drug release. Drugs, on the other hand, slowly diffuse inside bigger particles. Smaller particles tend to agglomerate during storage and transit of nanoparticle dispersion, which is a disadvantage. As a result, there is a compromise between nanoparticle size and optimum stability [29]. The particle size has an impact on polymer degradation. In vitro, for example, the breakdown rate of poly (lactic-co-glycolic acid) increased with increasing particle size [30]. As mentioned below, there are many techniques for measuring nanoparticle size.

Dynamic light scattering (DLS),
Scanning electron microscopy (SEM)
Transmission electron microscope (TEM)
Atomic force microscopy (AFM)

Surface Charge: The type and strength of a nanoparticle's surface charge is critical since it influences how it interacts with the biological environment as well as how it interacts electrostatically with bioactive substances. The zeta potential of nanoparticles is used to assess colloidal stability. This potential is a proxy for the charge on the surface. It is the difference in potential between the outer Helmholtz plane and the shear surface. The measurement of the zeta potential allows for predictions about the storage stability of colloidal dispersion. High zeta potential values, either positive or negative, should be achieved in order to ensure stability and avoid aggregation of the particles. The zeta potential measurements can then be used to determine the amount of surface hydrophobicity. The nature of the substance contained within the nanocapsules or coated onto the surface may also be determined using the zeta potential [31].

Surface hydrophobicity: Several methods, such as hydrophobic interaction chromatography, biphasic partitioning, probe adsorption, and contact angle measurements, can be used to evaluate surface hydrophobicity. Several advanced analytical methods for surface examination of nanoparticles have recently been published in the literature. The detection of particular chemical groups on the surface of nanoparticles is possible using X-ray photon correlation spectroscopy [32].

Drug Release: Understanding the way and amount to which drug molecules are released is essential since one of the main reasons for studying nanotechnology is to deliver medicines. Most release techniques need the separation of the medication and its delivery vehicle in order to get this information. The quantity of drug bound per mass of polymer (typically moles of drug per mg polymer or mg drug per mg polymer) is referred to as nanoparticle drug loading. It can also be expressed as a percentage of the polymer. Classic analytical techniques such as UV spectroscopy or high-performance liquid chromatography (HPLC) following ultracentrifugation were employed for this analysis. UV spectroscopy or HPLC are used for quantification. Drug release assays are comparable to drug loading assays, which are used to determine the mechanism of drug release over time [33].

VI. Application nanotechnology examples

Nanotechnology and cancer treatment

A staggering number of people worldwide are affected by cancer, underlining the need for a more precise diagnosis technique as well as a revolutionary medication delivery system that is more targeted, efficient, and has fewer adverse effects [34]. Anticancer therapies are frequently seen to be preferable if the therapeutic agent is able to reach the precise target spot without causing any adverse effects. The surface of nanoparticle carriers might be chemically modified to facilitate the needed targeted delivery. The inclusion of PEG, or polyethylene oxide, at the surface of nanoparticles is one of the greatest instances of surface modifications. These changes improve not just the selectivity of medication absorption, but also the capacity to target tumors. PEG prevents the body's immune system from recognizing nanoparticles as foreign objects, allowing them to circulate in the bloodstream until they reach the tumor. Hydrogel's use in breast cancer treatment is also an excellent illustration of this cutting-edge technology. Herceptin is a monoclonal antibody that targets the human epidermal growth factor receptor 2 (HER2) on cancer cells in the treatment of breast cancer. With just a single dosage of Herceptin, a vitamin E-based hydrogel has been created that can transport the drug to the target location for several weeks. The hydrogel-based drug delivery is more efficient than traditional subcutaneous and intravenous drug administration modalities because Herceptin is retained better within the tumor, making it a superior anti-tumor agent [35- 37]. Through the use of nanotechnologies, nanoparticles may be changed in a variety of ways to extend circulation, improve drug localization, boost therapeutic effectiveness, and perhaps reduce the development of multidrug resistance. Several studies have used FDA-approved nano medicines as adjuvants in combinatory cancer treatment, a nanoparticle formulation of paclitaxel albumin stabilized [nab paclitaxel), has been authorized for the treatment of metastatic breast cancer [38]. According to ClinVar, there are over 900 active clinical studies utilizing nab paclitaxel as an anticancer drug. Furthermore, when utilized in combination with 5 chloro 2.4 dihydrooxypyridine, tegafur, and oteracil potassium for the treatment of HER2 negative breast cancer patients, nab paclitaxel showed good outcomes [39].

Nanotechnologies for the treatment of cardiovascular diseases

The properties of nanoparticles can also be used to treat cardiovascular disorders. Cardiovascular illnesses are the main cause of mortality worldwide, and rates are rising at an alarming rate because of sedentary lifestyles [40]. Stroke, hypertension, and a limitation or blockage of blood circulation in a specific location are common instances of cardiovascular illnesses that affect several people. These illnesses are the leading causes of long-term disability and mortality [40]. Nanotechnologies provide up new therapeutic and diagnostic possibilities for cardiovascular disease treatment. The majority of cardiovascular risk factors (such as hypertension, smoking, hypercholesterolemia, homocystinuria, and diabetes mellitus) are linked to decrease NO endothelium production. The initial stage in the development of atherosclerosis is endothelial dysfunction. NO bioavailability occurs when gold and silica nanoparticles are combined [41]. The 17E loaded CREKA-peptide-modified-nanoemulsion system has been shown to reduce the levels of pathological contributors to early atherosclerosis by reducing lesion size, lowering circulating plasma lipids, and decreasing gene expression of inflammatory markers associated with the disease when administered systemically [42]. Furthermore, innovative formulations of block copolymer micelles made with PEG and poly[propylene sulphide) have been shown to decrease the levels of proinflammatory cytokines [43], indicating that they have great promise for atherosclerosis treatment [43].

For the prevention of platelet aggregation, atherosclerosis, and thrombosis, drug administration through liposomes has been shown to be effective. Vasodilation, platelet aggregation inhibition, leukocyte adhesion, and anti-inflammatory characteristics are all pharmacological features of prostaglandin E1 (PGE1). Liposomal PGE1 medication delivery (LiprostinTM) is now in phase III clinical studies for the treatment of a variety of cardiovascular conditions, including restenosis after angioplasty [44]. The use of liposomes encapsulating the thrombolytic drug urokinase has also been investigated; cyclic arginylglycylglycylaspartic acid (cRGD) peptide liposomes encapsulated with urokinase can preferentially attach to the GPIIb/IIIa receptors, improving the thrombolytic effectiveness of urokinase by approximately [44]. Novel nanotherapeutic methods can also improve the efficacy and efficiency of traditional thrombolytic medicines. Drugs can be mechanically activated within blood arteries to specifically target vascular blockage locations based on the high fluid shear stresses existing within them In vivo and in vitro investigations have been positive, indicating that this method may be used to dissolve blood clots while requiring a considerably lower dose of thrombolytic medication [41-45]. The usage of dendrimers is one example of this technique. Dendrimers have been utilized to deliver medicinal medicines in a variety of illnesses. Plasminogen activator (rtPA) has been effectively linked to dendrimers, resulting in an alternative drug delivery method that allows for precise tuning of the rtPAdendrimer complex concentration over time by varying the dilution proportions of each member of the complex [45]. Another possible use for nanoparticles is to reduce haemorrhaging, which is a common adverse effect of thrombolytic drugs. Targeted thrombolysis using rtPA bound to polyacrylic acid coated nanoparticles reduces intracerebral hemorrhage and improves target site retention [46]. The use of nanotechnologies has helped to reduce medication adverse effects while also needing lower drug dosages to treat cardiovascular illnesses. Drugs may now be transported to target locations with more carrier capacity, specificity, and stability because to recent advancements in nanotechnology research for drug delivery systems, notably in terms of their water insoluble characteristics. Researchers have been able to design formulations that can enhance medication efficiency while lowering costs because to continuous developments in nanoparticle drug delivery technologies [47].

Nanotechnologies for sperm cryoprotection

Several nanoparticle compositions with significant antioxidant, anti-inflammatory, and antibacterial activities have been developed as a result of recent developments in

nanoparticle technology [7–9]. This certainly offers up a lot of possibilities for improving reproductive functioning in vitro or in vivo [10]. Nanoparticles with antioxidative characteristics may be especially useful for sperm function and male fertility. Semen cooling and cryopreservation have been shown to enhance oxidative stress in spermatozoa, lowering their fertilization ability significantly [11]. After 48 hours and up to 96 hours of incubation, CeO_2 supplementation in the semen extender enhanced motility metrics and boosted sperm cell velocity. Treatment of sperm from several species with cyclodextrins pre-loaded with an appropriate therapeutic molecule [antioxidants, essential oil) before cryopreservation has been shown to enhance sperm quality following the freezing-thawing process. PEGs have a beneficial effect when used in sperm cryopreservation. Treatment of rabbit sperm with vitamin E distributed in PEG 6000 (PEG/Vit E) protected sperm cells after freezing at 4 °C, according to Amokrane et al. (2020) [48]. Recent research has sparked interest in utilizing liposomal formulations as preservation diluents, lowering the danger of egg yolk contamination and raising the value of sperm quality through improved sperm protection [38, 39]. After 48 hours of cooling, the liposome/vitamin E combination also improves motility metrics.

VII. Conclusions

Nanotechnology has emerged as a critical technique for overcoming drug flaws and enabling medicines to target specific cells or tissues passively or actively. The benefits of nanotechnology systems as drug delivery vehicles in cancer, cardiovascular disorders, and sperm cryoprotection were highlighted in this paper. Future research should concentrate on the effects of therapeutic nanomedicine on performance, molecular mechanisms, and possible toxicity during treatment.

Acknowledgements
The authors thank the General Directorate of Scientific Research and Technological Development (DGRSDT/MESRS-Algeria) for their financial support.

Conflict of interest. The authors report no conflict of interest.

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