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Review Article

Nanoparticles as a Drug Delivery System: A Comprehensive Review

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Abstract

The field of nanotechnology is emerging as one that is expected to provide significant medicinal benefits. Pharmaceutical formulation researchers have a number of challenges, one of which is developing effective nanodelivery systems that can safely and precisely transport a drug to the intended site of action. They are trying to give the existing blockbuster drugs new indications and a new structure in order to maintain encouraging scientific findings and clinical developments. In nanodelivery systems, liposomes, lipid or polymeric nanoparticles, and nanoemulsions are the main constituents. The use of particulate vesicle systems as medication carriers for both small and big molecules has been extensively studied in recent years. Numerous biotechnology and medical tools and procedures could be totally changed by it, becoming more accessible, portable, safe, and easy to use. Medical treatments, industrial production in solar and oxide energy batteries for power storage, and prominent integration into a variety of common place materials like clothes, beauty products, optical equipment, catalytic, bactericidal, digital, technology for sensors, biological labeling, and the treatment of specific cancers are just a few of the many uses for nanoparticles. Recently, nanoparticles have attracted a lot of attention due to their exceptional properties, such as exceptional heat conductivity, antibacterial activity, and resistance to oxidation. Drug adverse effects have been reduced and the therapeutic efficacy has been enhanced by nanoparticles. In general, a variety of methods have been used to create nanoparticles, including ionic gelation or co-acervation of hydrophilic polymers, polymerization of monomers, and dispersion of preformed polymers. Additionally, this paper will discuss the varieties, properties, manufacturing processes, applications, and potential future developments of nanoparticles.

Keywords: Particulate system, Polymeric Nanoparticles, Nanoparticles, Nanotechnology, and Nanodelivery.

Introduction

Nanoparticles can be found in a Nanotechnology's fundamental building blocks are nanoparticles. Nanoparticles size vary from 1 to 100 nm and can be composed of organic material, metal, metal oxide, or carbon. In addition to their content, nanoparticles differ in size, shape, and dimension. One-dimensional graphemes can have only three-dimensional gold nanoparticles can have all three dimensions, two-dimensional carbon nanotubes can have both

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length and width, and zero-dimensional nanodots can have all three dimensions (length, width, and height) fixed at a single point.

The range of shapes, sizes, and configurations, such as conical, hollow core, spherical, cylindrical, tubular, spiral, flat, etc. [1]. Nanotechnology involves designing, producing, and using materials at the molecular, atomic, and macromolecular levels to create new nanoscale materials. Pharmaceutical nanoparticles are submicron (less than 100 nm in diameter) solid drug carriers.

The word "nanoparticle" refers to both nanospheres and nanocapsules. Nanospheres are a matrix system where the medicine is equally distributed, as opposed to nanocapsules, which have a unique polymeric membrane enclosing the drug.

The study of little items is called nanotechnology. It entails manipulating and using matter. The Latin term nanus, which really translates to "dwarf" and consequently " incredibly tiny," is source of prefix from the Greek word vavoc [2]. because of their size at the nanoscale and enormous surface area. NPs have unique chemical and physical characteristics. These qualities that make them suitable for a variety of home, industrial uses, including energy-based research, environmental, imaging, medicinal, and catalytic applications [3]. Nanoparticles have a complex structure. Each of them has two or three layers.

1. Various tiny compounds, metal ions, surfactants, or polymers have functionalized a surface layer.
2. Intentionally adding the shell layer is possible since it differs chemically from the core.
3. The essential elements; the core of NPs [4].

Numerous shapes, sizes, and structures, including spherical, cylindrical, tubular, conical, hollow core, spiral, flat, wire, and more, can be found in nanoparticles (NPs). It may also have an uneven form. There are two types of NP surfaces: uniform and irregular. They can either be crystalline or amorphous, and they can be single- or multi-crystal solids. Multi-crystal solids can aggregate or be loose. The main factor affecting these NPs' size and shape changes are physio-chemical features. NPs have proved successful in a number of sectors, including imaging, energy-based investigation, medicine, the environment, chemical and biological detection, gas sensing, and more, because of their special physical and chemical characteristics.

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Since the nanotechnology is seen as being among the key components of a renewable and environmentally friendly future, investigators are becoming increasingly interested in it.

Advantages of NPs

A few advantages of nanoparticles are as:

1. The simplicity of altering the dimensions and surface properties of nanoparticles to target medications both passively and actively following parenteral administration [2].

2. Labeling certain bacteria using immunofluorescence-based nanosized quantum dots, which facilitates their identification and elimination [5].

3. Nanotechnology has several uses in fields like nutrition and is a developing field in many industries, including aquaculture.

4. Fishing, illness prevention, water purification, reproduction, and lowering toxicity and adverse consequences [6].

5. Drug release can be sustained at the target site for days or even weeks when nanoparticles are prepared using biodegradable materials.

6. Drug accumulation at the body's target areas is made possible by the tiny size of nanoparticles, which allowed them to easily pass through tiny capillary which can be absorbed by cells [7].

7. Nanotechnology can improve the durability of textiles because NPs have an enormous surface area to volume proportion and a high surface energy [8].

8. Incorporating nano materials to facilitate efficient pharmaceutical and nutritional delivery is made easier by the method of encapsulation.

9. Food goods are labeled for safety and their distribution is tracked using nanobarcodes [9].

10. After parenteral distribution, nanoparticles' surface characteristics and particle size can be easily changed to allow for both passive and active drug targeting.

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11. To achieve great therapeutic efficacy and fewer side effects, they alter the drug's distribution and subsequent elimination. Additionally, they regulate and maintain the drug's release at the site of localization and during travel.

12. Administration routes of the system include oral, intraocular, parenteral, and nasal.

13. Nanoparticles are a superior way to deliver drugs to small parts of the body.

14. Thanks to engineering, researchers can operate precisely on this scale and have previously manipulated the physical properties of polymers and biomaterials.

15. Because the size of the particles directly affects the resistance provided by the body's physiological barriers, nanoparticles effectively deliver drugs to different sections of the body.

16. By boosting the bioavailability for specific medication targeting and regulated drug molecule release, as well as the aqueous solubility of poorly soluble medications, nanoparticles can aid in efficient drug delivery.

17. For targeted drug delivery, the surface properties of nanoparticles loaded with proteins, small molecules, peptides, and nucleic acids can be altered. This is because the immune system is unable to recognize and effectively target the nanoparticles to certain tissue types.

18. It is possible to decrease drug toxicity and provide more effective drug distribution by concentrating on nanomedicine carriers.

19. Nanocarriers possess promise for blood brain barrier (BBB) and other anatomical extremities of the body.

Disadvantages of Nanoparticles

Nanoparticles do have certain disadvantages in spite of these advantages, including the following:

1. In the biological milieu, nanoparticles are extremely reactive because of their enormous surface area and size.

2. Nonbiodegradable particle may be build up at the drug delivery site during use, resulting in a persistent inflammatory reaction [2].

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3. The restricted targeting capabilities of nanoparticles make it impossible to halt the therapy.

4. The cost of nanotechnology is high and can be substantially higher during development.

5. The employment of atomic bombs has become more destructive, more powerful, and easier to procure [7].

Nanoparticle's Type

Silver: Due to its strong antibacterial activity against microbes, viruses, as well as other eukaryotic microorganisms, silver has been shown to be the most effective [12,13]. Popular applications for nanomaterials include antimicrobials, sunscreen lotions, water treatment, and the textile sector [14,15]. The plants Capsicum annuum [16], Azadirachta indica [17], and Carica papaya [18] have been effectively used to biosynthesize silver nanoparticles.

Gold: In immunochemical studies, gold nanoparticles (AuNPs) are used to detect protein interactions. In DNA fingerprinting, which locates DNA in a sample, they act as a lab tracer. These nanoparticles can also be used to identify aminoglycoside medications including neomycin, gentamycin, and streptomycin. Gold nanorods are used in the identification of various bacterial types, cancer diagnosis, and cancer stem cell detection. [19,20]

Alloy: The alloy nanoparticles' structural characteristics differ from those of the bulk samples [21]. The highest electrical conductivity of silver flakes makes them the most widely used metal filler; their oxides also have comparatively higher conductivity [22]. Bimetallic alloy nanoparticles exhibit more benefits due to their characteristics, which are impacted by both metals and typical metallic nanoparticles[23].

Magnetic: The biocompatibility of magnetic nanoparticles like magnetite and magnethemite is well established. Treatment with genes, MR imaging (MRI), guided administration of medicines, specific therapy for cancer (magnetic hyperthermia), stem cell sorting and tampering and DNA sequencing have all been extensively investigated [24].

NPs Fabrication [25]

Among the materials meant to be utilized in the production of nanoparticles are proteins, polysaccharides, and synthetic polymers. Several aspects determine the selection criteria for matrix materials, such as:

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(a) The required nanoparticle size;

(b) Drug's inherent properties, such as stability and solubility in water;

(c) Surface properties, including permeability and charge;

(d) The degree of harmful effects, biologic compatibility, and biological degradation

(e) Desired drug release profile;

(f) Final product's antigenicity.

Popular Process for producing NPs as follows:

(1) Preformed polymer dispersion;

(2) Polymerizing monomers; and

(3) Gelation of ions or coacervation of hydrophilic polymers.

Alternative methods for creating nanoparticles, such as particle replication in non-wetting frameworks and supercritical liquid technologies, have also been published in the literature. It was claimed that latter had complete control over the size, shape, and composition of the particles, that could serve as a model for future industrial mass production of nanoparticles.

Preformed polymer dispersion [26,27]

A popular method for creating biodegradable nanoparticles from PLG, poly (D,L-glycolide), poly (lactic acid) (PLA), poly (D,Llactide-coglycolide) (PLGA), and poly (cyanoacrylate) (PCA) is the dispersion of premade polymers. This method can be applied in a number of ways, as explained below:

Method of solvent evaporation [28]

This method entails dissolving the polymer in an organic solvent that also dissolves the hydrophobic drug, such as ethyl acetate, dichloromethane, or chloroform. An oil in water (o/w) emulsion is created by emulsifying polymer and drug solution mixture in an aqueous solution that contains a surfactant or emulsifying agent. The organic solvent is evaporated by lowering the pressure or stirring continuously when a stable emulsion has developed. It was demonstrated that kind and amount of stabilizers, a mixer speed, and the concentration of

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polymers all affected particle size. High-speed homogenization or ultrasonication are frequently used to create tiny particle sizes.

The technique of spontaneous emulsification or solvent diffusion [29]

This method of solvent evaporation has been changed. The anoil phase in this process consists of a water-insoluble organic solvent. Solvents spontaneously diffuse between the two phases, creating an interfacial turbulence,which causes tiny particles to develop. A reduction in particle size is possible when the concentration of the watermiscible solvent rises. Drugs that are hydrophilic or hydrophobic can be handled utilizing the solvent evaporation or solvent diffusion methods. The medication must be dissolved in the internal aqueous phase to generate a multiple w/o/w emulsion when dealing with hydrophilic drugs.

Method of polymerization [30–32]

This process creates particles in a water-based solution by polymerizing monomers. Drug is integrated either by adsorption onto nanoparticles following the completion of polymerization or by dissolution in the polymerization solvent. The nanoparticle suspensions is re-suspended in an isotonic surfactant-free medium after being purified by ultracentrifugation to eliminate different stabilizers and surfactants employed during polymerization. This process has been used to create polybutylcyanoacrylate or poly (alkylcyanoacrylate) nanoparticles.

Ionic gelation or coacervation [33]

To prepare the nanoparticles, biodegradable hydrophilic polymers such sodium alginate, gelatin, and chitosan are used. creating a technique for ionic gelation to produce hydrophilic chitosan nanoparticles. This process creates coacervates that are in the nanoscale range by interacting the chitosan's positively charged amino group and the negatively charged tripolyphosphate.

Using supercritical fluid technologies to produce Nanoparticles [34–35]

Organic solvents are required for methods such as solvent extraction-evaporation, solvent diffusion, and organic phase separation, that is harmful for both the environment and human health. Due to the environmental safety of supercritical fluids, this method has been explored as a substitute for creating biodegradable micro- and nanoparticles. A solvent at a temperature

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higher than its critical temperature, when it maintains its single phase under all pressures, is called as a supercritical fluid. Supercritical CO2 (SC CO2) are widely utilized supercritical fluid due to its moderate critical conditions (Tc = 31.1 °C, Pc = 73.8 bars), nontoxicity, nonflammability, and affordability. Supercritical antisolvent (SAS) and rapid expansion of critical solution (RESS) are the most often used processing methods. SAS uses a solvent, like methanol, that are totally miscible with the supercritical fluid (SC CO2) to dissolve the solute to be micronized. Due to the solute is insoluble in the supercritical fluid under process conditions, solute precipitates quickly and forms nanoparticles when the supercritical fluid extracts the liquid solvent. Unlike SAS, RESS dissolves its solute in a supercritical fluid (such supercritical methanol) and then rapidly expands the solution into a lower pressure area via a small nozzle.

The solute eventually precipitates as a result of a sharp decline in the solvent power of supercritical fluids. This procedure is clean since the precipitate is practically solvent-free. Polymeric nanoparticles have been produced using RESS and its modified technique. The supercritical fluid technology technique is more costly and requires specialized equipment, despite being ecologically beneficial and ideal for large manufacturing.

Parameters for NPs Characterization

Modern nanoparticles are identified using microscopic parameters like atomic force microscopy, transmission electron microscopy, and scanning electron microscopy based on their size, shape, and surface charge. The charge, the distribution of sizes and average particle diameter all affect the nanoparticles' in vivo distribution and physical stability. Nuclear magnetic resonance, optical microscopy, atomic force microscopy, dynamic light scattering, and electron microscopyare among techniques used to assess particle size [36].

1.NMR

The size and qualitative parameters of NPs can be ascertained via nuclear magnetic resonance. Selectivity that chemical shift offers to reveal the physicochemical state of the constituents within the nanoparticles complements the sensitivity to molecular mobility [36].

2. **The DSC**

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The DSC measurement was used to determine the native medication's physical state within the nanoparticles. All the NPs, polymer, and natural medication weighed around 2 mg. These were scanned between 25°C and 300°C in various sealed standard aluminum pans while being heated at a rate of 10°C per minute in a nitrogen environment. As a guide, utilize a vacant metal pan [37].

3. Particles Size

The NPs' particle sizes were examined with a scanning electron microscope and were found to vary depending on the amount of polymer present, ranging from 350 nm to 600 nm [37]. Particle size and shape are the two factors that have the biggest effects on NPs. The primary goals of nanoformulation are drug release and targeted drug delivery, and the evidence gathered indicates that particles have an impact on the drugs released. Consequently, the particle's surface will come into contact with the loaded drug, hastening its release. Smaller particles can become foam clumps during storage. Thus, establish a connection between decreased particle size and stability. It was shown that as particle size grew, so did the rate of PLGA breakdown [38].

4. Zeta Potential

NPs' zeta potential is frequently used to describe their surface charge characteristics. It reflects the particles' electrical potential and is affected due to both their makeup and the medium in which they are dispersed. Because the surface charge stops the particles from aggregating, it has been shown that NPs with a zeta potential greater than + 30 mV can be suspended [39].

5. Spectroscopy of UV-visible Absorption

The optical characteristics of a solution are ascertained via absorbance spectroscopy. After the sample solution is lighted, the amount of light it absorbs is measured. when the wavelength is changed and absorbance is measured at multiple wavelengths. Beer-Lambert's law can be used to determine a solution's concentration based on absorbance.

6. SEM, or Scanning Electron Microscopy

This NP characterization method allows us to learn about the materials' morphology, size, shape, chemical makeup, and orientation. The secondary electrons and backscattered electrons

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released when the NPs solution is ground into a dry powder and put on a sample holder for SEM examination will reveal the surface of the sample. The elevation and depression of the surface can be used to determine the form of nanoparticles (NPs) since the release of electrons from NPs varies depending on their surface [41].

7. DLS

Examination of the generated particles' average volume diameters and polydispersity index in relation to their size and size distribution was done using a particle size analyzer, dynamic light scattering at a fixed angle of 173 at 25 c, and photon correlation spectroscopy. Three of the samples were performed [42].

Applications of NPs

The potential for nanomedicine to enhance human disease diagnosis and therapy is astounding. Using microorganisms to biosynthesize nanoparticles is an environmentally acceptable process. Numerous biotechnological tools could be transformed by nanotechnology, which would make them more accessible, customizable, safe, portable, and easy to use.

Drug Release Timing

Until the particle binds to the target, the drug must stay encapsulated and not disperse from the particle while it remains in the bloodstream to avoid nonspecific toxicity. Nanoparticles have the potential to be highly effective in targeted medicine delivery at the site of disease, which has some significant effects, including:

1. Nanoparticles can be used to increase the bioavailability of medications.

2. Medication directed at a particular location

3. To enhance poorly solubility medication absorption

4. Nanomaterials have proven to be an effective way to synthesize chemotherapy drugs including doxorubicin 5-fluorouracil, paclitaxel, and dexamethasone [43].

Specificity of cells

Conjugation of antibodies to carbon nanotubes with fluorescent or radiolabelling to improve cell specificity [44].

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Internalization

Surface-functionalized carbon nanotubes have the ability to internalize within mammalian cells.

Delivery of vaccines

Peptide conjugation could be employed as a vaccine delivery system. Silencing genes is necessary for cancer treatment, which involves specifically modifying tumor cells. In this instance, gene silencing has been accomplished using short interfering RNA. It is possible to suppress specific gene expression in the targeted cell by using siRNA to target functionalized single-walled carbon nanotubes [45].

In Diagnostics

According to reports, chemicals attached to nanotubes improve the effectiveness of diagnostic techniques. Effective biosensors can be designed with the help of this functionalization feature and the high surface to volume ratio that results from the high length to diameter aspect ratio [46]. Compared to alternative medication delivery and diagnostic systems, carbon nanotubes have a number of intriguing physicochemical characteristics. The physicochemical characteristics include high mechanical strength, high electrical conductivity, high mechanical conductivity, ultra-light weight, ordered structure with high aspect ratio, and semimetallic behavior [47].

Medical Applications of Nanotechnology

Delivery of Drugs

Delivering drugs, heat, light, or other elements to certain cell types (such cancer cells) in the form of nanoparticles is one application of nanoparticles in medicine that is presently under development. Disease cells can be directly treated thanks to nanoparticles that are designed to attract them. In addition to reducing harm to the body's healthy cells, this method will make it possible to identify illnesses early. Applying heat and administering chemotherapeutic medications to cancer cells is another method of treating cancer cells [48]. Gold nanorods are attached to DNA strands by researchers, which act as a scaffolding to hold the drug and the nanorod together. The gold nanorod absorbs infrared light and transforms it into heat when the

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cancer tumor is exposed to it. The chemotherapy medication is released as a result of the heat, which helps kill the cancer cells [49].

Diagnostic Methods

A nanoparticle is being developed by researchers to aid in the extremely early detection of cancerous tumors. The nanoparticles emit "biomarkers" molecules, which are peptides, when they come into contact with cancerous tumors. The idea states that because each nanoparticle includes several peptides, there is a high concentration of these biomarkers even in the early stages of cancer, enabling early sickness detection. The color of the nanorods changes when proteins accumulate on them. In order to detect problems early, the test is designed to be quick and inexpensive [50].

Antimicrobial Methods

A lotion containing nanoparticles and nitric oxide gas, which is known to destroy bacteria, can be used to treat staph infections. According to research on mice, applying a lotion containing nanoparticles to create nitric oxide gas at the site of staph abscesses significantly reduced the infection. Burn dressings will open if an infection is caused by pathogenic microorganisms that release antibiotics through nanocapsule coating. The frequency of dressing changes is decreased when an infection is treated more quickly [51].

Silver Nanoparticle application as an antimicrobial

For a variety of functions, ultrasonography creates images using sound waves. Following their passage through the body, these sound waves reflect off of tissue before returning to a receiver. In order to translate the sound wave into an electrical signal that the computer can use to create an image, the time it takes for the wave to reflect and return to its initial position is measured by this receiver.

Usage of this kind of medical imaging is widespread, ranging from oncology to obstetrics. Unfortunately, because ultrasonography's image quality may be subpar, little features may be overlooked [52].

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