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Review Article

A REVIEW: NANOPARTICLE IN PHARMACEUTICAL DRUG DELIVERY SYSTEM

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ABSTRACT:
Nanotechnology" is the most recent development in the field of pharmaceutical sciences. Nanopharmaceuticals are made up of goods that are nanoscale and can be altered in a variety of ways to enhance their properties. The use of nanoparticles in tissue engineering, medication transport, imaging, sensing, disease diagnostics, and treatment holds great promise for understanding fundamental biological processes. The use of nontechnology in medicine and drug administration has created new avenues and opened numerous doors to offer safer and more individualised treatment options. High stability, high specificity, high drug-carrying capacity, controlled delivery, targeted release, flexibility in using different routes of administration, ability to deliver both hydrophilic and hydrophobic drug molecules, and site-specific targeting are just a few of the many benefits that make nanoparticles more promising and efficient than traditional drug delivery systems. Drug delivery systems and numerous other sectors have seen revolutionary advances as a result of nanomaterials such as polymeric nanoparticles, magnetic nanoparticles, liposomes, carbon nanotubes, quantum dots, dendrimers, metallic nanoparticles, and polymeric nanoparticles. In order to administer medications over longer periods of time with less frequent doses, as well as with greater precision and penetration in tissues that are difficult to reach, researchers can manipulate molecule size and surface features. This chapter provides an overview of the various kinds of nanopharmaceuticals, including their characteristics, preparation techniques, benefits, and uses in the pharmaceutical and medical industries.
Keywords: Nanotechnology, Preparation, Nanoparticles, Characterization, Applications

INTRODUCT ION

Many industries, most notably the pharmaceutical sector, have been greatly impacted by the development of nanoscience and nanotechnology, which is the production and application of materials and instruments at the nanoscale. Since last century, nanotechnology has been a recognised area of study. One of the main challenges in treating many diseases is getting therapeutic compounds to the right place. Poor biodistribution, limited efficacy, undesired side effects, and lack of selectivity are characteristics of conventional drug use. By delivering the medication to the site of action, controlled drug delivery may be able to get around these restrictions, protecting the drug delivery system from quick clearance or degradation. Lower dosages of the medication are needed because it also increases the concentration of the medicine in the target tissues. A more basic and effective use of nanotechnology is the reduction of the size of the targeted formulation and the creation of an appropriate medication delivery system [1]. Recent advances in nanotechnology have demonstrated the enormous potential on nanoparticles as drug delivery systems. Different nanostructures with distinct physicochemical and biological characteristics that improve performance in a range of dosage forms are produced using size reduction techniques and technologies. The crucial aspect of nanoparticles is that their size can affect a substance's physiochemical characteristics. With their varied sizes and shapes, these nanoparticles displayed distinctive colours and characteristics that may be applied to bioimaging [2]. Nanotechnology is a multidisciplinary scientific field utilizing engineering and manufacturing techniques at the molecular level. The preferred size for nanomedical applications is less than 200 nm, whereas nanoparticles are solid, colloidal particles with sizes ranging from 10 nm to less than 1000 nm. The word "nano," which signifies midget in Latin, is its root. One thousand millionth of a unit is the ideal size range provided by nanotechnology; therefore, a nanometer is one thousand millionth of a meter (1 nm = 10−9 m).Being complex molecules, nanoparticles are made up of three layers: (a) the surface layer, which can be functionalised with metal ions, polymers, surfactants, and a variety of small molecules. (c) The core, which is basically the centre part of the nanoparticle and typically refers to the nanoparticle itself; (b) The shell layer, which is made of a

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completely different material chemically from the core[3]. In this review article, we aim to focus on different types, advantages, preparation, characteristics and applications with future scope of nanoparticles.

VARIOUS TYPES OF PHARMACEUTICAL NANOSYSTEMS

1)Liposomes:

Liposomes are spherical vesicles that self-assemble in aqueous solutions and include one or more bilayered lipid structures. They are between 50 and 100 nm in size. Liposomes' numerous different compositions, capacity to transport and shield a wide variety of biomolecules, and biocompatibility and biodegradability are all advantages. Additionally, their entrapment efficiency is high. They are longcirculating, provide both passive and active gene, protein, and peptide delivery, and can be functionalised with targeting ligands to enhance the build-up of therapeutic and diagnostic substances in specific cells[1].

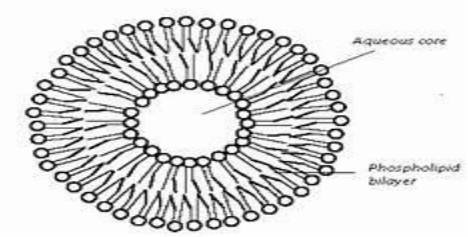

Figure.1 Liposomes

2)Solid lipid nanoparticles:

Solid lipid nanoparticles, which range in size from 50 to 1000 nm and are composed of solid lipids (a high melting fat matrix), are being used and expanded in the pharmaceutical industry because they are a suitable and alternative system to traditional colloidal carriers like emulsions, liposomes, and polymeric micro and nanoparticles. (4) They were created to overcome the drawbacks of polymer degradation and cytotoxicity, lack of a suitable large-scale production method, poor stability, drug leakage and fusion, phospholipid degradation, high production costs, and sterilisation issues. Their goals are to provide biocompatibility, storage stability, and to stop the incorporated drug from degrading [5].Solid lipid nanoparticles have a hydrophobic solid core with a monolayer coating of phospholipids, and the drug is typically dissolved or dispersed within the core. These nanoparticles are widely used as adjuvants for vaccines, topical application, cosmetics, anti-tubercular chemotherapy, and targeted brain drug delivery.(6)

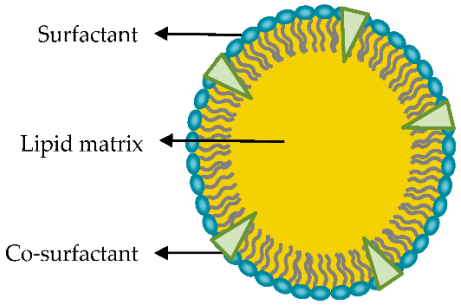

Figure.2 Solid lipid nanoparticles

3)Carbon nanotubes:

These molecules are cylindrical and range in size from 0.5 to 3 nm in diameter and 20 to 1000 nm in length. Carbon sheets in their third allotropic crystalline state can be single-layer or multilayer nanotubes. In addition to their exceptional strength, they feature special mechanical, thermal, and electrical qualities (insulating, semi-conductive, or conducting). Their roles include improved solubility, penetration into the nucleus and cytoplasm of cells, and delivery of genes and peptides. They are employed as an early-stage cancer diagnosis technique. (7)

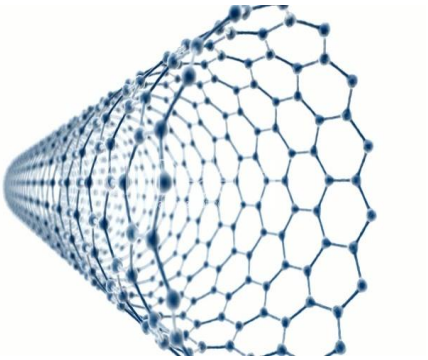

Figure.3 Carbon nanotubes:

4)Fullerenes :

Any molecule made completely of carbon that takes the shape of a hollow tube, ellipsoid, or sphere is called a fullerene. Cylindrical fullerenes are known as carbon nanotubes or buck tubes, while spherical ones are also known as buck balls. In addition to sharing structural similarities with graphite, which is made up of stacked grapheme sheets of connected hexagonal rings, fullerenes can also have pentagonal (or occasionally heptagonal) rings, which could result in potentially porous molecules. Commonly referred to as endohedral fullerenes, buckyball clusters or buck balls made up of fewer than 300 carbon atoms include the most prevalent fullerene, buckminsterfullerene, C60[6,7].

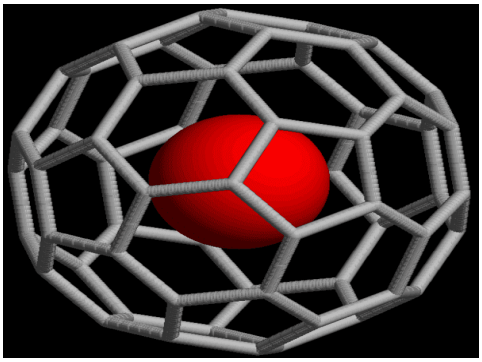

Figure.4 Fullerenes

5)Nano shells

A shell or outer covering of a thin layer of another substance, a few 1–20 nm thick, envelops the spherical cores of a certain compound (concentric particles), which are also known as core-shells. Compared to their single component counterparts or nanoparticles of the same size, highly functional materials known as nanoshell particles exhibit altered and enhanced capabilities. Their characteristics can be altered by altering the core-to-shell ratio or the constituent materials. Metals, insulators, and semiconductors (dielectric materials like silica and polystyrene) can all be used to create nanoshell materials. Due of their excellent stability, dielectric materials like polystyrene and silica are frequently utilized as cores. A new kind of composite spherical nanoparticles known as metal nanoshells is made up of a thin metallic shell, usually made of gold, encasing a dielectric core. Nanoshells have very advantageous optical and chemical characteristics for therapeutic and biomedical imaging uses. Other benefits of nanoshells over traditional organic dyes include enhanced optical characteristics and decreased vulnerability to thermal or chemical denaturation[6,7].

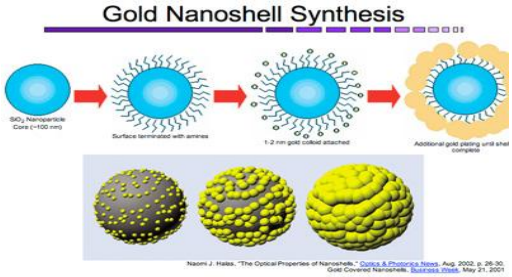

Figure.5 Nano shells

6)Dendrimers:

Branched macromolecules called dendrimers are composed of natural or synthetic components such as sugars, nucleotides, and amino acids. They have an outer surface, layers of branches inside, and a central core. Controlled polymerization creates this highly branched, almost monodisperse polymer structure. Dendrimers are loaded with small molecules from the core cavities via hydrophobic contact, hydrogen bonding, or chemical bonding. Their size is less than 10 nm. They are helpful for liver targeting, focused delivery of bioactives to macrophages, and regulated delivery of bioactives. (1)

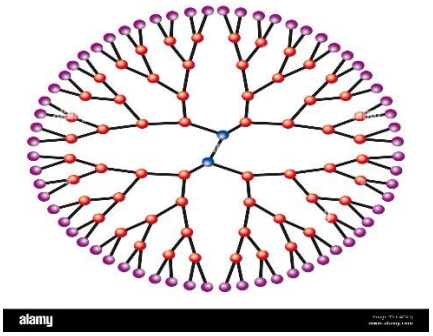

Figure.6 Dendrimers

7)Quantum dots:

Semiconductor particles known as quantum dots have a diameter of 2–10 nm. They are classified as "small crystals with a variable number of electrons that occupy well-defined, discrete quantum states and have electronic properties intermediate between bulk and discrete fundamental particles" in technical terms. They have a semiconductor core, a shell covering it, and a cap that improves solubility in aqueous buffers.Drug delivery, gene therapy, and medical diagnostics are just a few of the multipurpose applications for quantum dots. When thinking about quantum dots for different biomedical applications, toxicity is a significant barrier.

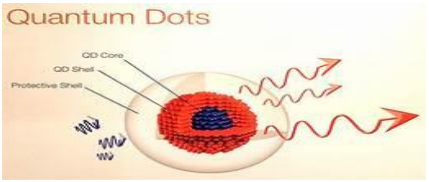

Figure.7 Quantum dots

PROPERTIES OF NANOPARTICLES

- Decrease drug resistance
- Decrease toxicity
- Increase oral bioavailability
- Enhance rate of dissolution
- Enhance solubility
- Increase the stability of drug and formulation
- Increase drug targeting ability
- Decreased patient-to-patient variability and increase Patient compliance
- Increase surface area
- Less amount of dose required [8].

CHARACTERIZATION OF NANOPARTICLE DRUG FORMULATIONS

Nanoparticles can enter the human body, by three main route, direct injection, inhalation and oral consumption. If anything is recognized as foreign, macrophages will engulf and eliminate it from the body. This is typically the problem with drug administration using nanoparticles; however, the

size and surface properties of the particles might affect clearance, which is covered in the subsection that follows.

Surface properties:

Appropriate targeting ligands, surface curvature, and reactivity are crucial for addressing stability, aggregation prevention, receptor binding, and the drug's following physiological effects in order to design the best possible nanoparticle drug delivery system. Particularly in physiological settings, surface characteristics mainly identify the aggregation state of particles and colloidal characteristics, which determine their effective size.[9]

Surface Charge :

The interaction of nanoparticles with the biological environment and their electrostatic interaction with bioactive compounds are determined by their surface charge and intensity. The stability of colloidal material is typically assessed using the nanoparticles' zeta potential, which is an indirect indicator of surface charge.[8]

Particle size:

The ratio of a particle's surface area to volume increases with decreasing particle size. This would suggest that, in comparison to a larger molecule, more of the medicine is near the particle's surface. The medicine would release more quickly if it were at or close to the surface. The distribution, toxicity, and targeting ability of nanoparticles are determined by their size and form, which also influences how the body's cells respond to them.[3]

Drug loading capacity and release

To maximize bioavailability, reduce clearance, and boost stability, researchers have studied the size and surface characteristics of nanoparticles. By regulating these features, the drug can be delivered to the body's tissues, but the entire process is pointless if the drug cannot be released from the nanoparticle matrix. The release of the drug will vary depending on the type of nanoparticle. [10]

METHODS OF PREPARATION OF NANOPARTICLES

The polymer's and the drug's physicochemical characteristics determine which technique is best for creating nanoparticles. Numerous substances, including proteins, lipids, polysaccharides, and both natural and manufactured polymers, can be used to create nanoparticles. The following criteria determine which matrix material is used.[8]

•Surface characteristics (charge and permeability)
• Aqueous solubility and stability of the drug
• Size of nanoparticles required
• Biocompatibility and toxicity
• Antigenicity of the final product
• Drug release profile desired
• Degree of biodegradability

1)Emulsification-Diffusion Method :

First, partially water-miscible solvents are used in equilibrium with another immiscible solvent, usually water (saturation), according to the thermodynamic principles of the Emulsification-Diffusion Method. In order to prevent mass transference during the procedure, this step is carried out.[11] There are two methods for carrying out the diffusion. The first is rapid diffusion through water dilution. Depending on the solvent's boiling point, the second step involves quickly moving the solvent from the internal into the external phase through evaporation at lower pressure. In this scenario, the amount of water needed should be enough to dissolve the inner-organic phase. This technique is sometimes referred to as "emulsification-solvent displacement." In both situations, assuming the stabilizing effect is appropriate, the presence of a nonsolvent medium causes polymer aggregation in nanoparticles.[12]

This technique provides several advantages, such as

• High encapsulation efficiencies (generally 70 %)
• No need for homogenization
• Highbatch-to-batch reproducibility
• Ease of scale-up
•Narrow size distribution [13]

2)Solvent Emulsification-Evaporation Method:

There are two steps in this procedure. The polymer solution is first emulsified into an aqueous phase, and then the polymer solvent evaporates, causing polymer precipitation.Since both the polymer and the hydrophobic medicine dissolve in an organic solvent, this technique is predicated on their solubility. The polymer and drug solution mixture is subsequently emulsified in an aqueous solution. An emulsifying agent or surfactant is present in this aqueous solution to create an oil in water (o/w) emulsion.[14] Drugs with lipophilic properties are then added to the organic phase after the organic solvent is evaporated under the right circumstances by constant stirring or pressure reduction, which causes polymer aggregation in the form of nanoparticles. Ultrasonication or high-speed homogenization may frequently be used to create small particle sizes.[15] Purification phases can be achieved by recovering polymer nanoparticles by ultracentrifugation and consecutive washing with distilled water to remove the stabilizer and release the medication[16]

3)Double Emulsion and Evaporation Method:

Double emulsion, also known as emulsion double emulsion, is a complicated system in which even tiny dispersed phase droplets are part of the dispersed phase itself. The size of double emulsion (DE) droplets is primarily polydispersed. The double emulsion approach is used to get around the problem of hydrophilic medicines' poor entrapment. Double emulsions come in two typical

varieties: oil-water-oil (o/w/o) and water-oil-water (w/o/w).[17]A change in the kind and concentration of stabilizer used in the system can significantly improve the stability and release qualities of double emulsions. Evaporation is used to remove the solvent from the emulsion, and high-speed centrifugation can be used to extract nanoparticles. This technology has several drawbacks, including large, irregular particles (polydisperse), a two-step procedure, hydrophilic active leakage into the external aqueous phase, and difficulty scaling up.[18]

4) Solvent Displacement/Precipitation Method:

A simple, repeatable, quick, and cost-effective one-step manufacturing approach for creating monodisperse, polymeric nanoparticles with a size range of roughly 50–300 nm is the solvent displacement method. For medications that are poorly soluble, this approach works better. Amphiphilic organic solvents, such as acetone, that are perfectly miscible with water are needed for this procedure. Colloidal particles are created when a polymer dissolved in acetone is gradually added to an aqueous phase while being stirred. After this, the solvent is extracted from the suspensions using lowered pressure.[19]

5) Coacervation or Ionic Gelation Method:

Calvo was the first to disclose the inotropic gelation technique, which Janes has since extensively studied and modified. Gelatin and sodium alginate are examples of biodegradable polymers that are now being studied to create biodegradable nanoparticles with low toxicity and biocompatibility. It is possible to dissolve chitosan in acetic acid with or without a stabilizing agent, like poloxamer, which can be added to the chitosan solution either before or after the polyanion is added.[20] After adding polyanion or anionic polymers, nanoparticles started to develop on their own. Strong electrostatic interactions between two aqueous phases result in the formation of coacervates. Ionic gelation, on the other hand, is the process by which a substance changes from a liquid to a gel at normal temperature as a result of ionic interactions.[21]A few drawbacks of this approach include flaws like poor surface morphology, a delicate particle system, a high dispersibility index, and an absence of suitable surface modification sites to attach functional moieties.[22]

APPLICATIONS OF NANOPARTICLES IN PHARMACEUTICAL DEVELOPMENT AND DRUF DELIVERY SYSTEM

1)Nanoparticles for Gene Delivery :

Gene therapy is a method of treating illness that involves either infusing genetic material, or DNA, into the cells to replace a damaged gene or alter its expression. Because of their size, shape, surface, and biological activities, nanoparticles have become the most promising vehicles for clinical gene therapy. Numerous gene-associated human disorders, including cancer, hemophilia, hypercholesterolemia, neurodegenerative diseases, and autoimmune diseases, have garnered considerable interest in gene therapy as a potentially effective treatment approach. In order to treat or stop the progression of the associated disease, this technique involves introducing genes into the target diseased tissues or cells by changing the expression of the endogenous genes.[23]A variety of nanoparticle types, including lipid-based, polymer-based, and inorganic nanoparticles, have been evaluated as gene carriers in order to overcome the challenges of gene delivery, which include encapsulation efficiency, stability of nanoparticles, degradation in blood circulation and endocytosis by target cells, endosomal escape, delivery efficiency, and pharmacological toxicity. A recent example of a polynucleotide vaccine that produces the antigenic protein close to professional antigen-presenting cells to elicit an immune response[24]

2)Nanoparticles for targeted imaging:

The creation of molecular probes for the visualization of cellular function, characterization, and measurement of molecular processes in living organisms at the cellular and molecular level without disturbing them is known as molecular imaging. Nanoparticles can be effectively used as tumor-specific probes with high specificity when conjugated with tumor targeting ligands (such as peptides, small organic molecules, antibodies, etc.). As imaging modalities are developed rapidly to aid in disease detection, emerging nanoparticle technologies are joined by the rapid advancement of imaging modalities.[25]For successful transport to the intended target, nanoparticles' charge, size, shape, and hydrophilicity continue to be crucial characteristics. In biological imaging applications, nanomaterials like dendrimers, iron oxide nanoparticles, gold nanoparticles, and quantum dots are frequently utilized. Direct detection of bacterial or viral DNA is feasible when gold nanoparticles are used as ultrasensitive fluorescence probes to identify cancer biomarkers in human blood. Because of their strong X-ray absorption and low toxicity profiles shown in animals over brief periods of time, metallic nanoparticles have enormous potential as X-ray contrast imaging agents[26]

3)Nanoparticles for Drug Delivery into the Brain:

The BBB's presence makes it difficult for medications to enter the brain efficiently, which is one of the most difficult barriers to treating illnesses related to the central nervous system.The brain is shielded against undesirable substances and invasive organisms by the dynamic barrier known as the blood-brain barrier (BBB). By passive diffusion, small hydrophilic molecules with masses

under 150 Da and extremely hydrophobic compounds with masses under 400–600 Da can pass through the blood-brain barrier. The creation of nanoparticles is crucial to achieving this. Nanoparticles ought to be non-inflammatory, non-immunogenic, biodegradable, and biocompatible. [27] Numerous illnesses, such as neurodegeneration (such as amyotrophic lateral sclerosis, Alzheimer's, Parkinson's, Huntington's, and Prion disease), hereditary deficits, and several forms of brain cancer, lack effective treatments. With its prolonged release profile and brain target delivery, nanotechnology has proven to be a valuable tool for bridging the bloodbrain barrier, which is essential for the successful treatment of neurodegenerative diseases.[28]

4)Nanoparticle delivery to subcellular organelles:

The potential area for drug delivery is targeting of the drug to cells or tissue of choice. In delivery systems, targeting refers to the capacity to guide the drug-loaded system to a desired location. Targeted nanoparticles can attach to targets located on the cell surface and enter the cell through endocytosis. This process involves two mechanisms. [8] 1)The preferential accumulation of chemotherapeutic agents in solid tumors is an example of passive targeting, which involves changing the size, shape, and composition of the nanoparticles to target them to a specific organelle.2) Active targeting enables the surface functionalization of drug carriers with ligands that are selectively recognized by receptors on the surface of the cells of interest. Nanoparticles can be used extensively in targeted drug delivery at the site of disease to improve the drug bioavailability, targeting of drugs to a specific site, and uptake of poorly soluble drugs.[29]

5)Nanoparticles in ocular delivery systems:

A lot of research has been done on using nanoparticles to release drugs to the eye for a long time. The main issue with ophthalmologic formulation is that they are quickly removed from the eye, which means that the drug is cleared through the nose. It could be demonstrated that nanoparticles have a higher adhesiveness, which leads to higher drug levels at the desired site of action. However, the main issue was that the nanoparticles have limited toxicological acceptance. Gasco demonstrated that SLN have a prolonged retention time at the eye, which was verified by using radiolabeled formulations and γ-scintigraphy. The lipids in SLN are easily metabolized, opening up new avenues for ophthalmological drug delivery without affecting vision.

6)Nanoparticles as per-oral drug delivery:

Aqueous dispersions or SLN-loaded conventional dosage forms, such as tablets, pellets, or capsules, can be administered orally. The stomach's acidic environment and high ionic strength encourage particle aggregation, so it makes sense that food would significantly affect SLN function.[29]

CONCLUSION :

There are many uses for nanotechnology and nanoparticles in biology and medicine. As previously mentioned, nanoparticles allow for new imaging and sensing techniques and are best suited to developing systems that can better deliver drugs to small parts of the body. Drug delivery systems enabled by nanotechnology will help to reduce drug toxicity, lower treatment costs, and improve bioavailability. Additionally, nanoenabled drug delivery allows drugs to pass through cell walls, which is crucial for the anticipated growth of genetic medicine in the coming years. However, some recently discovered health risk evidence restricts their use in the pharmacy and medical field, and some concerning issues such as safety, bioethical concerns, toxicity hazards, and physiological and pharmaceutical challenges should be resolved. n future expansion of nanotechnology is likely to affect just about every route of administration from oral to injectable and offer significant impact on drug delivery sector.

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