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Nanoparticles in Pharmaceutical Science

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Abstract: ***The development of particle size reduction technologies over the past 30 years has transformed them from a research approach to an established commercial drug delivery platform. Since a growing number of research substances for poor aqueous solubility, nanotechnology methods have gained particular significance. The term "nanotechnology" refers to the development and application of materials whose components are, by standard, no larger than 100 nm in size. Nanotechnology investigates structural behavior at the molecular, and sub-molecular levels. It has the potential to transform several medical and biotechnology instruments and processes into ones that are transportable, less expensive, safer, and simpler to use. Nanoparticles are used for a variety of things, including medical treatments, energy storage in solar and oxide fuel batteries, optical devices, bactericidal agents, electronic devices, biological labeling, and in the treatment of some cancers. They are also widely incorporated into a variety of materials used in everyday life. This paper seeks to provide an overview of nanoparticles, paying attention to the current innovations and future aspects.***

Keywords: Nanoparticles, Types, Synthesis, Applications, Etc.

1. INTRODUCTION

The most important development in recent years, nanotechnology, has modernized medicine. The market for nanotechnology products is steadily expanding. The revolutionary science of nanotechnology will have an impact on our attempts to enhance human health. The lifespan, effectiveness, toughness, adaptability, and unique physicochemical properties of nanoparticles have all been explored by the medical sector. They are used in a variety of therapeutic methods, including the focused administration of drugs, predictive visual monitoring of therapy, and even tumor diagnosis. 1,2

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The synthesis and creation of diverse nanomaterials are included in the burgeoning scientific topic known as nanotechnology. The longest and shortest axes of a nanoparticle are not significantly different in length, according to the International Organization for Standardization (ISO), which defines nanoparticles as nano-objects having all exterior dimensions in the nanoscale. Objects between 1 and 100 nm in size that may differ from the bulk material due to their size are referred to as nanoparticles. The most popular and commercially successful technology that strives to enhance the effectiveness of healthcare methods is nanotechnology or nanomedicine. Despite significant drawbacks, a lot of pharmaceutical and medical device businesses have already used medical nanotechnology. Nanotechnology has the potential to improve the safety profile of the administration of some medications with a high risk for toxicity, such as cancer chemotherapy medicines.

It is crucial to remember that living cells function as microscopic virtual machines that participate in all biological processes, such as nutrition transport, energy production, metabolism, and cell signaling. In light of this, it can be said that this technique is a strong contender for use in therapeutic biology and medicine. We talk about the value of nanoscience in this review as various nanotechnology platforms are applied in other areas of medicine. Additionally, we are talking about the potential applications of nanotechnology in human health in the future.3

However, prolonged exposure to nanoparticles by people at work might affect their health in different ways. Additionally, inhaling nanoparticles in the form of air pollutants may result in subsequent exposure to nanoparticles. Sometimes these inhaled nanoparticles get through the immune system and spread throughout the body, causing a risk to overall health.

Nanoparticles

Colloidal formations made of synthetic or partially synthetic polymers are known as polymeric nanoparticles. The drug is either absorbed, immobilized, encapsulated, or bonded using a nanoparticle matrix. Depending on the preparation method, nanoparticles, nanospheres, or nanocapsules can be produced. In contrast to nanocapsules, which retain the medication in a cavity and are sealed off by a specific polymer membrane, nanospheres are matrix systems in which the drug is physically and evenly distributed.9

NPs can have a variety of forms, dimensions, and structures. They might be irregular.10 or spherical, cylindrical, conical, tubular, hollow core, spiral, etc. NPs can range in size from 1 to 100 nm. Atom clusters is generally recommended if the size of NPs is less than 1 nm. NPs can be amorphous or crystalline, having single or many crystal solids. NPs can be agglomerated or loose.11

Need for developing nanoparticles

To achieve the drug's site-specific effect at a particular rate and dose, controlling particle size, surface properties, and the release of pharmacologically active substances are the main goals when developing nanoparticles as a delivery system.4 Polymeric nanoparticles have some unique advantages such as targeted drug delivery systems, an increase in stability of proteins and medications with that controlled release capabilities, and improved solubility of the API.5

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Advantages

The following are some benefits of employing nanoparticles as a drug delivery mechanism;

1. To target therapeutics passively and actively after parenteral administration, it is simple to modify the surface properties and particle size of nanoparticles.

2. Nanoparticle surfaces are modifiable to change how medications are biodistributed and then cleared, resulting in maximal therapeutic efficacy and minimal drug adverse effects.6

3. The variation of matrix ingredients can easily influence the features of controlled release and particle deterioration.

4. Polymer and liposome-based nanoparticles are typically biodegradable, do not accumulate within the body, and may thus be risk-free.

5. To achieve site-specific targeting, targeting ligands can be attached to particle surfaces, or magnetic guidance can be applied.

6. Drug activity must be maintained since drug loading is relatively high and may be absorbed into the systems without any chemical interactions.

7. Since smaller capillaries may be penetrated by smaller nanoparticles, this may enable effective drug accumulation at the target regions.

8. Several delivery methods are available, including intraocular, nasal, parenteral, and oral.7

Limitations

Despite these benefits, nanoparticles do have certain drawbacks, such as:

1. Physical handling of nanoparticles in liquid and dry forms is challenging due to their small size and large surface area changes that can lead to particle aggregation.

2. The nanoparticle is more reactive in the cellular environment the greater the surface area and the smaller the particle size.

3. The smaller particle size restricts the drug loading and burst release. Several practical problems must be overcome before nanoparticles can be used in clinical settings or approved for sale.8

Nanomaterial classification

Nanomaterials are the main components of nanotechnology. Materials that have at least one dimension that is in the nanoscale, or less than 100 nm, are referred to as nanomaterials 12. Nanomaterials are categorized into four groups based on their dimensions, as shown in Fig. 1.

(1) Zero-dimensional nanomaterials (0-D): Nanomaterials in this class have all three of their dimensions in the nanoscale range and are classified as zero-dimensional nanomaterials (0-D). Nanoparticles, fullerenes, and quantum dots are a few examples.

(2) One-dimensional nanomaterials (1-D): These materials are classified as nanomaterials and have one dimension that is not nanoscale. Nanotubes, nanofibers, nanorods, nanowires, and nanohorns are a few examples.

(3) Extra-nanoscale two-dimensional nanomaterials: The nanomaterials in this class have two dimensions. Nanosheets, nanofilms, and nanolayers are a few examples.

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(4) Three-dimensional nanomaterials (3-D): - Three-dimensional nanomaterials (3-D), also known as bulk nanomaterials, are materials that are not, in any way, restricted to the nanoscale. This class includes bulk powders, nanoparticle dispersions, nanowires, and nanotube arrays.

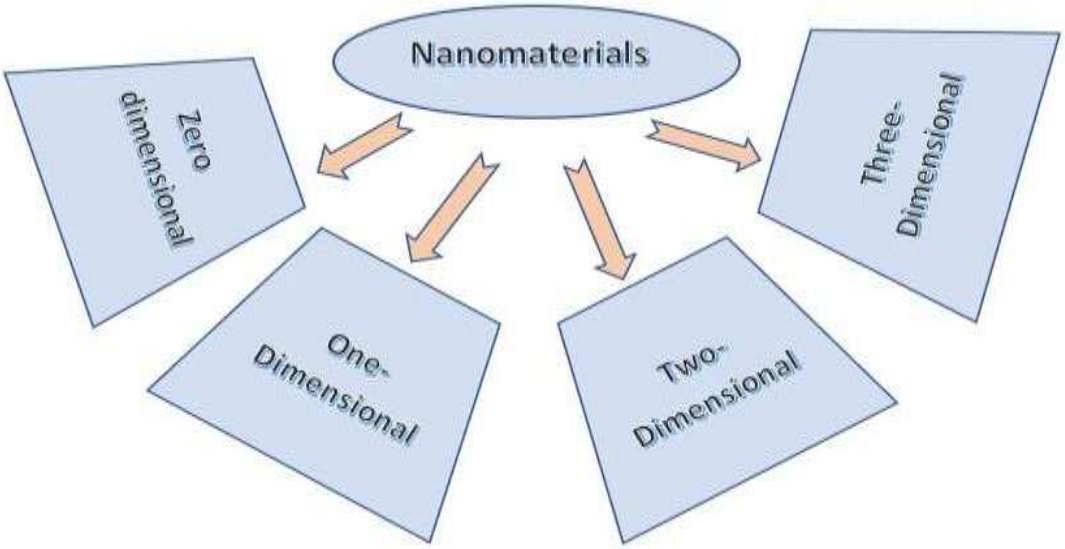

Figure 1: An overview on Nanomaterials

Nanoparticles: Types

Nanomaterials are divided into four primary categories depending on their structural configurations: metallic nanomaterials, carbon-based nanomaterials, dendrimers, and composites.

Nanoparticles can display different characteristics and functionalities than typical bulk materials, and as a result, scientists are currently quite interested in them. The most crucial element that makes it possible to create nanostructures with the necessary size, shape, and characteristics and allows for their use in diverse domains is the diminishing influence of classical physics and the activation of quantum physics. The limitation of load carriers, size-dependent electronic structures, the increased surface-to-volume-to-volume ratio, and other factors brought on by the special properties of atoms are additional reasons for the different behavior of nanoparticles in physical, chemical, optical, electrical, and magnetic behavior 13

1. Silver: Silver nanoparticles are the most effective due to their potent antimicrobial property against bacteria, viruses, and other eukaryotic microorganisms. Perhaps the most frequently used nanomaterials, are used in sunscreen lotions, water treatment, antimicrobials in the textile industry, and other applications (15,16,17,18). According to studies, plants like Capsicum annuum, Carica papaya, and Azadirachta indica can biosynthesize silver nanoparticles.

2. Gold: To identify protein interactions in immunochemical experiments, gold nanoparticles (AuNPs) are utilized. To identify the presence of DNA in a sample, they are utilized as lab tracers in DNA fingerprinting. They are also employed in the detection of antibiotics known as aminoglycosides, such as streptomycin, gentamycin, and neomycin. Gold nanorods are

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useful for identifying various bacterial groups, detecting cancer stem cells, and diagnosing cancer.

3. Alloy: Alloy nanoparticles exhibit structural properties that are unique from those of their bulk constituent components19. Because they have the highest electrical conductivity of all metal fillers and because their oxides have considerably higher conductivities compared to many other metals, silver flakes are the most widely used metal filler. Bimetallic alloy nanoparticles are more beneficial than conventional metallic NPs in that both metals influence their features.20

4. Magnetic: Biocompatibility research has been done on magnetic nanoparticles like Ferrous oxide (magnetite) and Ferric oxide (maghemite), two magnetic nanoparticles. For guided administering drugs, targeted cancer therapy (magnetic hyperthermia), gene therapy, DNA analysis, and magnetic resonance imaging, they have undergone thorough research (MRI).

5. Collagen: For the transfer of diverse substances including DNA, medicines, proteins, and growth factors, collagen functions as an effective carrier. Due to collagen's adaptability, it is feasible to modify it to create materials with a variety of durability, shapes, and morphologies. Additionally, collagen may form complexes with several physiologically active and therapeutic compounds.14

Synthesis of Nanoparticles:

The synthesis of nanoparticles can be classified in different ways: In first, it can be classified as:

1. Bottom-up technique
2. Chemical reaction technique
3. Top-down technique

1. Bottom-up strategies

The second approach, referred to as "bottom-up," relies on collecting and fusing gas or liquid atoms or molecules. 21

2. Chemical Reactions:

Nanoparticles can be created using chemical processes such as polymerizations, however, they are not often employed to create drug nanoparticles that contain just pure API. For the production of aqueous dispersions used in pharmaceutical coating materials, for example, these procedures are crucial from a commercial standpoint. Additionally, chemical processes can be employed to create polymeric nanoparticles with an API contained in a matrix-forming polymer. Such particles must be recognized from drug nanoparticles made using conventional particle size reduction procedures since their drug content is often much lower than 100%.

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3. Top-down strategies

The "top-down" method, which is the first strategy, allows for using an external force to break apart solid materials into smaller bits. This method uses a variety of physical, chemical, and thermal approaches to supply the energy required for nanoparticle production.21

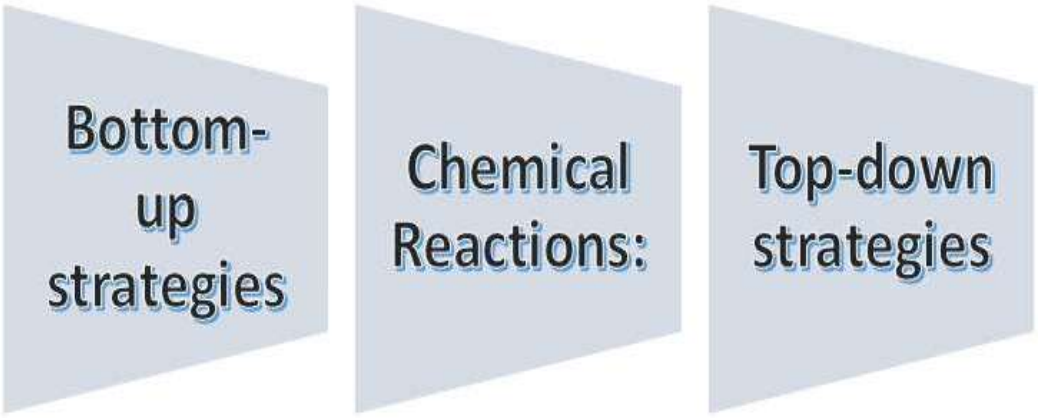

Figure2: A summary of various methods for creating nanoparticles

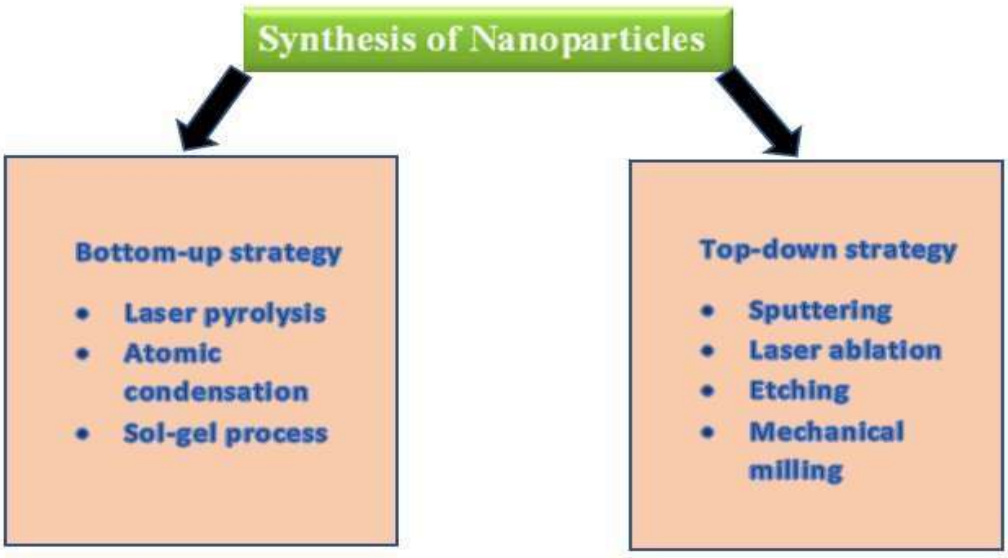

Figure3: Preparation of Nanoparticles

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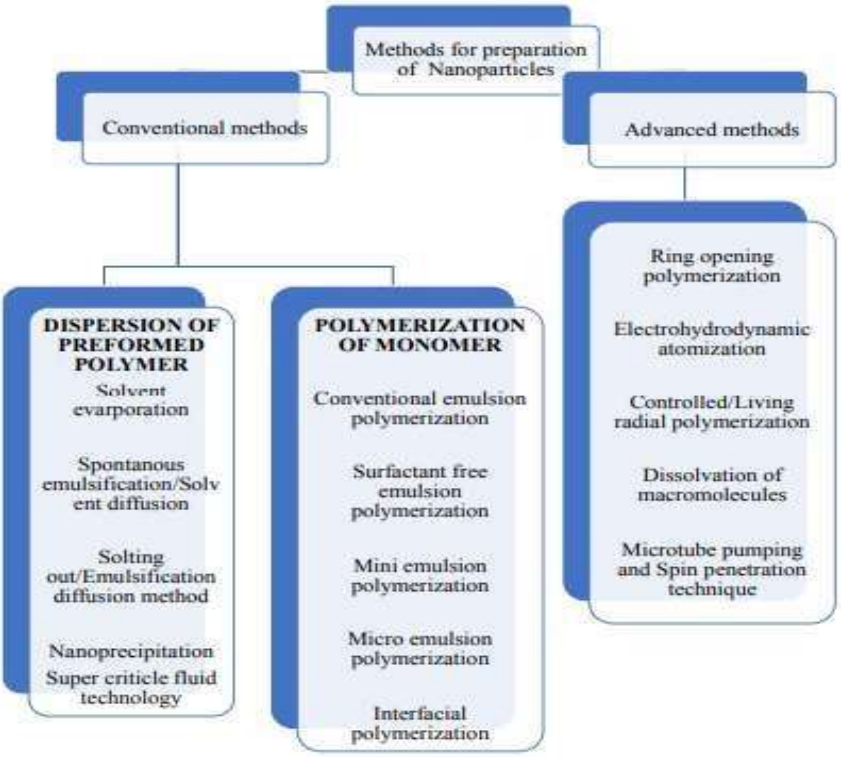

Figure4: Methods of preparation of Nanoparticles

1. **Solvent evaporation method:** Organic solvents like dichloromethane, chloroform, or ethyl acetate are utilized to dissolve the polymer, which also serves as the solvent to dissolve the hydrophobic medicine. To create an oil-in-water emulsion, the medication that has been dissolved or dispersed in a polymer solution is next emulsified in an aqueous solution that contains a surfactant or emulsifying agent. The organic solvent is evaporated after a stable emulsion has been established, either by lowering the pressure or by constant stirring. Ultrasonication or a high-speed homogenizer can be used to produce tiny, uniform-sized particles.22

2. **Spontaneous emulsification or solvent diffusion method:** A variant of the solvent evaporation method is the solvent diffusion method, also referred to as spontaneous emulsification. In this method, a little quantity of a water-immiscible organic solvent is used as an oil phase combined with a water-miscible solvent. Small particles arise as a result of the spontaneous diffusion of immiscible liquids, creating interfacial turbulence between the two phases. Particle size reduction is possible by boosting the concentration of water-miscible solvents. Hydrophobic or hydrophilic medicines can be processed using the solvent diffusion technique or the solvent evaporation method. A multiple w/o/w emulsion must be created for hydrophilic drugs, with the medication dissolved in the internal aqueous phase.23

3. **Polymerization method:** this method involves the polymerization of drug-soluble monomers to produce nanoparticles in an aqueous solution. The medicine may eventually be integrated through adsorption onto the nanoparticles when polymerization is finished.

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Different stabilizers and surfactants used for polymerization are subsequently eliminated by ultracentrifuging the nanoparticle solution, and the particles are then resuspended in an isotonic surfactant-free medium. It has been described to produce poly (alkyl cyanoacrylate) or poly (butyl cyanoacrylate) nanoparticles.24,25

4. Supercritical fluid technology: Traditional methods require using large amounts of hazardous organic solvents that are harmful to both people and the environment, such as solvent extraction-evaporation, solvent diffusion, and organic phase separation. Characterization of Nanoparticles. Toxic solvents and/or surfactants are used in conventional procedures (solvent evaporation, coacervation, and in situ polymerization). The use of supercritical fluids is the latest eco-friendly strategy. This process is environmentally safe and makes use of CO2 in its supercritical form, which offers the benefits of both liquid and gas. The advantages of this technique include simple temperature and pressure control, better NP purity, and little to no solvent residue [26]

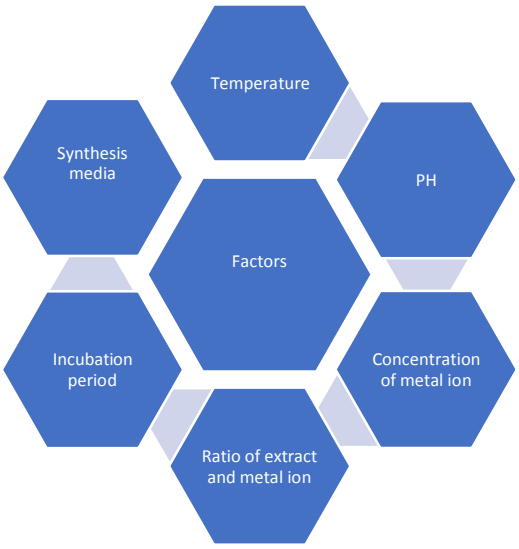

Figure5: Factors influencing the synthesis of various Nanoparticles

Characteristics of Nanoparticles

1. Particle size

In determining a nanoparticle's shape and particle size distribution is necessary, Electron microscopy is used to measure the size and morphological characteristics. The primary applications for nanoparticles are drug delivery and targeting. It has been discovered that particle size influences how quickly a drug is released. Larger surface areas are provided by smaller particles. A drawback of nanoparticle dispersion is that smaller particles have a tendency to cluster together when stored and transported. As a result, an exchange is made between a nanoparticle's microscopic size and its optimum stability.27

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2. Scanning Electron microscopy

Scanning electron microscopy (SEM), which uses direct vision, offers morphological analysis. In terms of morphological and sizing investigations, the approaches based on electron microscopy have a number of advantages, but they offer little insight into the size distribution. A nanoparticle solution should be dried down and placed on a sample holder for SEM examination before being coated with a conductive metal, such as gold, using a sputter coater. The sample is then scanned using an electron beam that has been precisely focused.28 The surface characteristics of the sample are determined using the secondary electrons released from the sample surface. The nanoparticles must be able to withstand a vacuum and the electron beam can damage polymers. The outcomes of dynamic light scattering are similar to the SEM's mean size determination.

3. Transmission electron microscope

Though operating according to different principles, TEM and SEM typically generate the same sorts of data. The preparation of samples for TEM is challenging and time-consuming since samples must be very thin for electron transmission. Nanoparticle dispersion is employed to support films or grids. To assist them to withstand the instrument vacuum and facilitating handling, nanoparticles are either fixed using a negative staining material, such as phosphotungstic or derivatives, uranyl acetate, etc., or by plastic embedding. After being encased in vitreous ice, the sample can also be heated to liquid nitrogen temperatures. The surface characteristics of the sample are recovered when an ultra-thin sample is sent through, interacting with the sample as it travels through. 37 29

4. Surface Charge

It is essential to understand the nature and magnitude of surface charges on nanoparticles in order to manage how they interact electrostatically with the biological environment and with bioactive substances. The zeta potential of nanoparticles is used to assess the colloidal stability. The surface charge is indirectly indicated by this potential. It pertains to the possible discrepancy between the shear surface and the outer Helmholtz plane. Using the zeta potential measurement, predictions about the colloidal dispersion's storage stability may be formed. High zeta potential levels, whether positive or negative, should be obtained to ensure stability and avoid particle aggregation. The degree of hydrophobicity of the surface may then be predicted using the measurements of zeta potential. The nature of the substance contained within the nanocapsules or deposited onto the surface may also be determined using the zeta potential. 30

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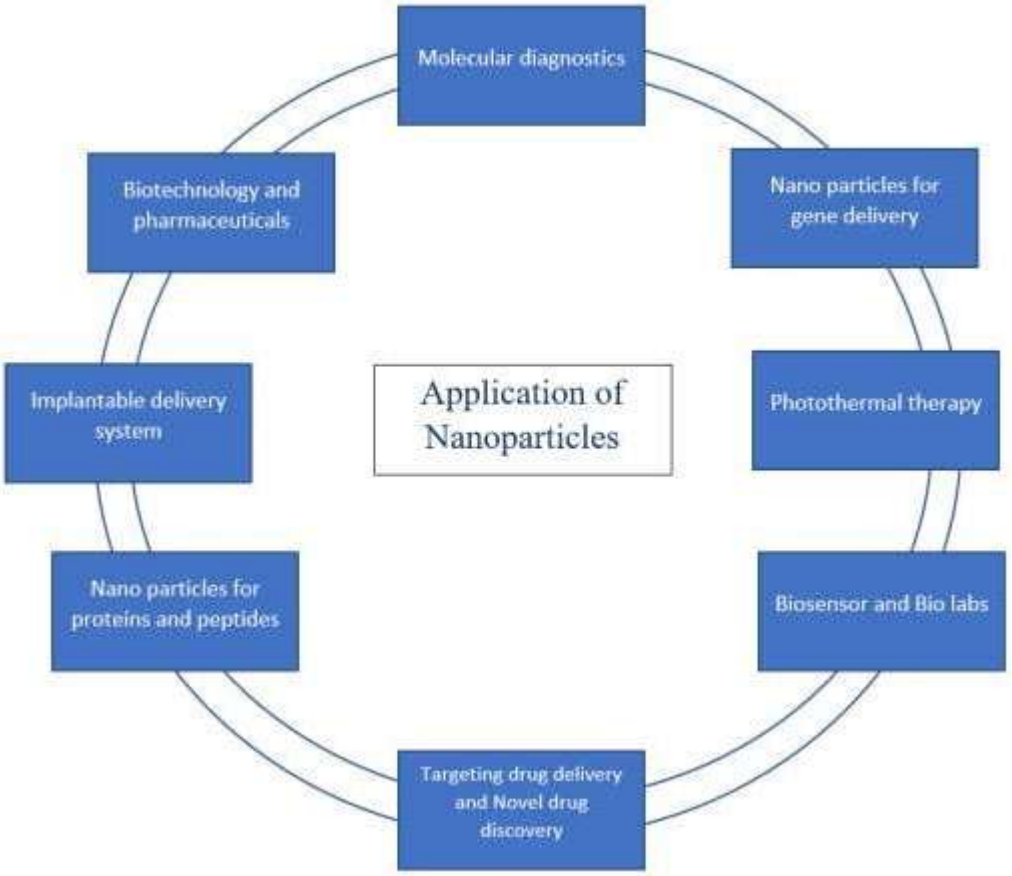

Figure6: Applications of Nanoparticulate Delivery Systems

Future opportunities and challenges

Nanoparticles and nanoformulations have already been employed as medicine-delivery devices with considerable effectiveness. Even more applications for nanoparticulate drug delivery systems exist, including radiation, gene therapy, AIDS therapy, anti-tumor therapy, protein delivery, antibiotic administration, vaccine delivery, and blood-brain barrier crossing using vesicles.

2. CONCLUSION

One of the novel drug delivery techniques that may be employed in targeted and regulated drug delivery systems is nanoparticles. Nanoparticles serve a as very attractive platform for a variety of biological applications. The surface and core properties of these systems may be tuned for single- and multimodal applications such as biosensing, tissue engineering, medication delivery, and bioimaging. The aforementioned shows that nanoparticulate systems have great promise for converting unstable, ineffectively soluble, and ineffectively absorbed physiologically active chemicals into potentially deliverable pharmaceuticals. The hydrophilic coating that prevents recognition by the reticuloendothelial system means that the core of this

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system, which is characterized by a prolonged circulation duration, may comprise a variety of drugs, enzymes, and genes.

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