



## Nanoparticles: Catalysts of progress in technology and health

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### Abstract

Nanoparticles have become a crucial component in technological advancements due to their superior performance and adaptability compared to their parent materials. These tiny particles are created by reducing metal ions to uncharged nanoparticles using hazardous reducing chemicals or biological agents such as bacteria, fungi, and plants. They have a wide range of therapeutic applications, including gene delivery and tumor cell targeting in the respiratory and digestive systems. Additionally, NPs have been increasingly utilized in industrial and environmental fields, making them highly relevant. This article provides a comprehensive overview of the classification, preparation process, and application of NPs, including their significant varieties, characteristics, synthesis processes, and environmental applications.

**Keywords:** metal nanoparticles, surface atom, quantum dot, biosensors, and nanotechnology

### Introduction

The use of nanotechnology has become increasingly popular over time. Nanoparticles are the fundamental component of nanotechnology, measuring one out of 100 nanometers in size. These particles can be made of carbon, metal, metal oxides, or organic substances<sup>[1]</sup>. Nanoparticles have unique physical, chemical, and biological properties that differ from those of comparable particles at larger scales. This is due to their substantially higher surface area to volume ratio, greater chemical reactivity or stability, and superior mechanical strength<sup>[2]</sup>. Nanoparticles have inherent qualities that make them useful in a wide range of applications. In addition to their composition, the nanoparticles' sizes, shapes, and diameters vary<sup>[3]</sup>. One-dimensional nanoparticles, like graphene, have only one parameter, while two-dimensional nanoparticles, like carbon nanotubes, have both length and breadth. Three-dimensional nanoparticles, like gold nanoparticles, have all three parameters, and zero-dimensional nanoparticles have all three parameters fixed at one location.

Certain nanoparticles are aggregated or loosely distributed and contain one or more single or multiple crystal solids<sup>[4]</sup>. The majority of nanoparticles are used in the production of new drugs that may be insoluble in water or have limited water solubility, which can harm the pharmaceutical business. The complex molecular structure of drugs is one of the primary reasons for their insolubility. Over sixty-five percent of newly developed active pharmaceutical ingredients (APIs) are considered to be poorly soluble in water or non-soluble. The Biopharmaceutics Classification System (BCS) identifies Class II pharmaceuticals based on their low water solubility and high permeability. BCS states that the dissolution phase is the rate-limiting step in the absorption of medicines. The current problem faced by pharmaceutical companies is the increasing number of medications that are not water-soluble, which reduces drug bioavailability. Nanoparticles can aid in the improvement of drug/protein stability and offer excellent controlled release characteristics.

### Nanotechnology's emergence

In the 1980s, experimental developments led to the rise of nanotechnology. The book *Engines of Creation*, published in 1986, established a conceptual framework for nanotechnology objectives.

#### 1. Early development of NPs

Pottery discovered in the Keeladi region of India, dating back to approximately 600 to 300 BC, has been found to contain carbon nanotubes<sup>[5, 6]</sup>. Additionally, "Damascus steel" from over 900 AD has cementite nanowires present in it, although the origin and production technique of this steel remains unknown.

#### 2. Identification of C, Ag, Zn, Cu, and Au nanoparticles

In 1991, carbon NPs were discovered by Iijima and Ichihashi, who later published a report on the production of single-wall carbon nanotubes in 1993<sup>[7]</sup>. These nanotubes, also known as Bucky tubes or CNTs, are made of a two-dimensional hexagonal carbon atom lattice. Recent research on the manufacture of nanosilver using silver nitrate and citrate has shown similarities in size and citrate stabilization<sup>[8]</sup>. It has been known since 1902 that proteins can maintain nanosilver<sup>[9, 10]</sup>. Commercial production of "Collargol" nanosilver, used for therapeutic purposes, began in 1897 with a size of 10 nm. In 1953, Moudry formulated a novel variety of 2-20 nm-diameter silver nanoparticles stabilized with gelatin, which was made using a different technique than Collargol. According to a patent declaration, "The necessity for nanoscale silver was realized by the developers of nanosilver formulations decades ago. For maximum efficiency, the silver must be disseminated as particles of colloidal size less than 25 nm in crystallite size<sup>[11]</sup>. In 1857, Michael Faraday researched the processes involved in creating and influencing colloidal suspensions of "Ruby" gold, which have distinct optical and electrical characteristics that qualify them as magnetic nanoparticles. Faraday demonstrated how specific types of illumination can cause gold nanoparticles to produce a range of colored solutions<sup>[12]</sup>.

## Nanometallic Particles

Metallic nanoparticles are defined as metals that measure between 1-100 nm in length, breadth, and thickness. The first investigation on metallic nanoparticles in solution was conducted by Faraday in 1857, and in 1908, Mie provided a numerical study of their hue. Nanomaterials are created and utilized with a range of chemical functional groups to link drugs, ligands, and antibodies. Metallic nanoparticles have a wide range of applications in the medical field, biotechnology, and as delivery systems for drugs and genes.

Platinum, lead, silver, and gold nanoparticles have optical properties due to a phenomenon called localized surface Plasmon resonance (LSPR), which is the resonant oscillation of their free electrons in the presence of light. Silver was once more valuable than gold and was seen as a symbol of purity. It has numerous therapeutic benefits and can treat a wide range of illnesses <sup>[13]</sup>. Noble metals were used to create stained glass and drinkware with stunning colors like the Lycurgus cup



**Fig 1:** shows images of the renowned Lycurgus cup, which changes color depending on whether it is lit from the inside or the outside. The Lycurgus Cup, the British Museum, and the Art of Glass.

## 1. Metallic nanoparticles have particular properties.

### 1.1. Subsurface Atom

The composition of atoms in the full-shell cluster structure can explain the percentage of surface atoms, as they are grouped by the magic number. This number refers to the number of protons or neutrons required to organize the atoms into full shells within the atomic nucleus. Magic numbers are determined using rare gas clusters. The full-shell cluster structure can be used to explain the percentage of surface atoms, and clusters can be classified as either dispersed or aggregated. Aggregated clusters have a smaller surface area than dispersed clusters if the number of atoms in each cluster is equal. The rate of reactions is influenced by the surface area of the reactant, making the reactant formed of dispersed clusters more reactive than the reactant made up of consolidated clusters.

### 1.2. Atomic Dot

Nanometers are made up of numerous atoms, and semiconductors like germanium or silicon are used to create them. Quantum dots can be explained using band theory in semiconductors. The band gap is the difference in energy between the top conduction band and the bottom valence band. Band gaps are a property of electronic semiconductor metals that divide the partially filled band from the empty conduction band. Molecular orbitals deal with HOMO and LUMO. HOMO is the highest energy-occupied molecular orbital, and LUMO is the lowest energy-unoccupied molecular orbital. The nearest energy-wise HOMO and LUMO orbitals in the two molecules allow for the strongest contact <sup>[14]</sup>. These orbitals are also known as "Frontier orbitals" because they are located at the outermost points of

the molecule's electron boundaries. Therefore, the energy of the metal nanoparticles can be described using quantum mechanics.

## 2. Metallic nanoparticle characteristics

- Substantial surface energies
- They have a large surface area to volume ratio when compared to bulk.
- Quantum confinement
- Plasmon stimulation
- Growing number of kinks

## 3. Nanoparticles: Categories

**3.1. Silver:** Silver nanoparticles have proven to be highly effective in combating bacteria, viruses, and other eukaryotic microbes, making them a popular choice in various industries. The textile industry, for instance, utilizes them as antibacterial agents, while they are also used in water purification and sunscreen creams <sup>[15]</sup>. These versatile nanomaterials are widely used due to their effectiveness. Interestingly, certain plants such as *Capsicum annum*, *Azadirachta indica*, and *Carica papaya* have been found to naturally biosynthesize silver nanoparticles.

**3.2. Gold:** Gold nanoparticles (AuNPs) are commonly used in immunochemical research to detect protein interactions and serve as laboratory tracers for identifying DNA through fingerprints <sup>[16]</sup>. Additionally, aminoglycoside medications like gentamycin, streptomycin, and neomycin can also be identified using AuNPs. Gold nanorods have proven to be valuable in identifying different bacterial species, locating cancer stems, and diagnosing cancer <sup>[17]</sup>.

**3.3. Alloy:** According to research [18], alloy nanoparticles exhibit distinct structural characteristics compared to their bulk counterparts. Among all metals, silver boasts the highest electrical conductivity, and its oxides conduct electricity more efficiently than most other metals [19]. As a result, silver flakes are frequently utilized as metal fillers. The properties of both metals play a role, but bimetallic alloy nanoparticles offer more benefits than traditional metallic NPs.

**Table 1:** Different Microorganisms Produce Metallic Nanoparticles

Microorganism	Type	Location	Size
Phoma sp.	Ag	Extrinsic Extracellular	71.06–74.46
Fusarium oxysporum	Au	Extrinsic Extracellular	20-40
Verticillium species	Ag	Intracellular	25 ± 12
Fumigates Aspergillus	Ag	Extrinsic Extracellular	5–25
Trichoderma asperellum	Ag	Extrinsic Extracellular	13–18
Chrysosporium phaenerochaete	Ag	Extrinsic Extracellular	50-200

#### 4. Information regarding nanoparticles

Nanoparticles act as a bridge between the atoms and molecules of a substance and its bulk form. While bulk materials exhibit consistent physical behaviors regardless of their size, nanoscaled materials have size-dependent features that differ from their bulk counterparts. This is because the physical characteristics of materials change when their size approaches the nanoscale and the surface-to-volume ratio increases. In bulk materials, the relationship between surface area and material volume is negligible [20], but in nanoscaled materials, the increased surface area controls their behavior. Nanoparticles have unique optical properties due to their small size, which causes quantum phenomena. For example, gold nanoparticles can range in color from deep red to black depending on their size. The melting temperatures of gold nanoparticles are also much lower than those of solid gold, at about 300 °C for nanoparticles with diameters of 2.5 nm. Nanoparticles have higher solar radiation absorption coefficients than thin films of bulk materials, and changing the particles' size, shape, and composition can alter the solar absorption of a substance. Recent research has focused on core-shell (dielectric) nanoparticles, which exhibit increased forward scattering and no reverse scattering. Unlike pure metallic nanoparticles, core-shell nanoparticles have special

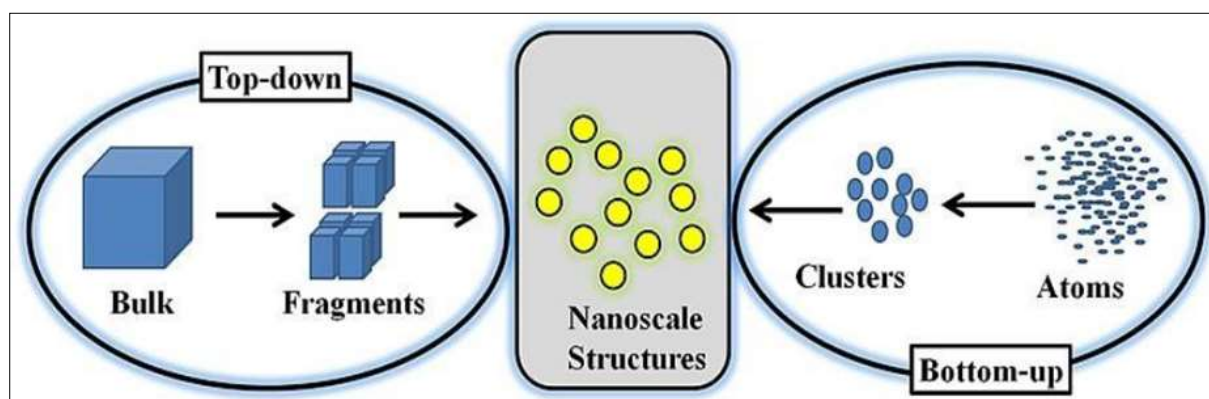
properties and can support both electric and magnetic resonances. Nanoparticles' size can change due to quantum confinement in semiconductor-based nanoparticles, surface Plasmon resonance in some metallic nanoparticles, and the evolution of paramagnetism in magnetic materials. While nanoparticles have many advantageous modifications at the nanoscale, some unfavorable alterations may also occur. For example, ferromagnetic nanoparticles (10 nm) can change the direction of their magnetization using heat energy at ambient temperature, making them unsuitable for information storage applications [21]. Nanoparticles can form suspensions in solvents, allowing components to remain evenly distributed. Adding clay nanoparticles to polymers can increase the strength of produced plastics and raise glass transition temperatures in some polymers, resulting in high rigidity. Nanoparticles are also crucial in textile manufacturing for creating fashionable and useful clothing. Nanoparticles can be made from a variety of materials, including metals, dielectrics, and semiconductors. Core-shell hybrid nanoparticles have also been created. Semiconductor nanoparticles that are small enough to exhibit quantization of energy levels (typically 10 nm) are sometimes referred to as quantum dots (QDs) [22]. These nanoparticles have various medical applications, such as imaging agents or medication carriers. Soft and semi-solid nanoparticles, such as liposomes, can also be created and used to deliver vaccines and anticancer medications to specific areas of the body.

#### 5. Analogue of Nanoparticles

Two primary methods for synthesizing nanoparticles are top-down and bottom-up approaches. These approaches are divided into various groups based on the operations and reaction circumstances.

##### A. Utilizing Top-Down Methodology

Top-down processing involves breaking down bulk materials into nanosized particles. While this approach can be effective, it can also be harmful. Top-down techniques rely on eliminating, dividing, and miniaturizing bulk manufacturing processes to achieve the desired structure and characteristics [23, 24]. However, these techniques are easier to implement. Popular methods for creating nanoparticles using top-down methodology include mechanical milling, thermal breakdown, sputtering, laser ablation, and nanolithography.



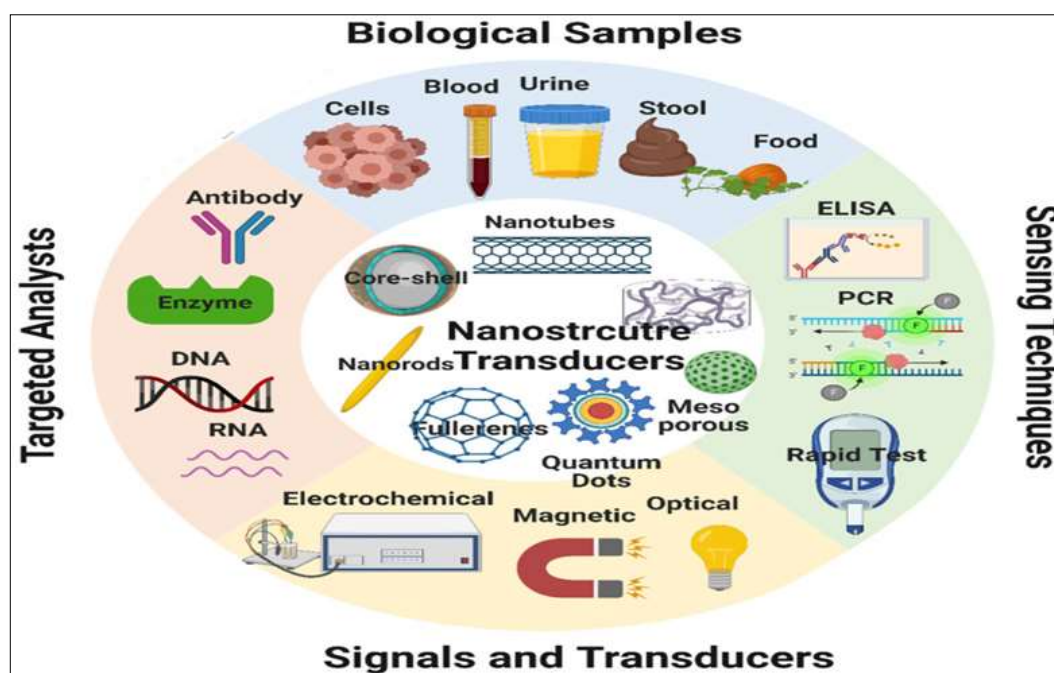
**Fig 2:** Provides a visual representation of both top-down and bottom-up approaches.

## B. Employing Bottom-Up Methodology

The bottom-up or constructive technique is an alternative strategy that builds nanoparticles from clusters, which are constructed from atoms. This approach often involves sedimentation and reduction procedures and is expected to be more cost-effective. Examples of this methodology include sol-gel, spinning, green synthesis, chemical vapor deposition (CVD), pyrolysis, and biosynthesis.

## Biosensors

Biosensors utilize organic components, including enzymes and antibodies, in conjunction with an electrical element to generate a measurable signal [25]. When an organic component interacts with a chemical or biological material, a physiological shift occurs, which is detected by the electrical components. A conventional biosensor consists of five essential components, as depicted in Figure 3. Analytes are chemicals whose concentration and presence can be determined, while receptors are organic molecules that can recognize analytes.



**Fig 3:** provides a schematic illustration of a typical biosensor, including the various bioreceptor and transducer types.

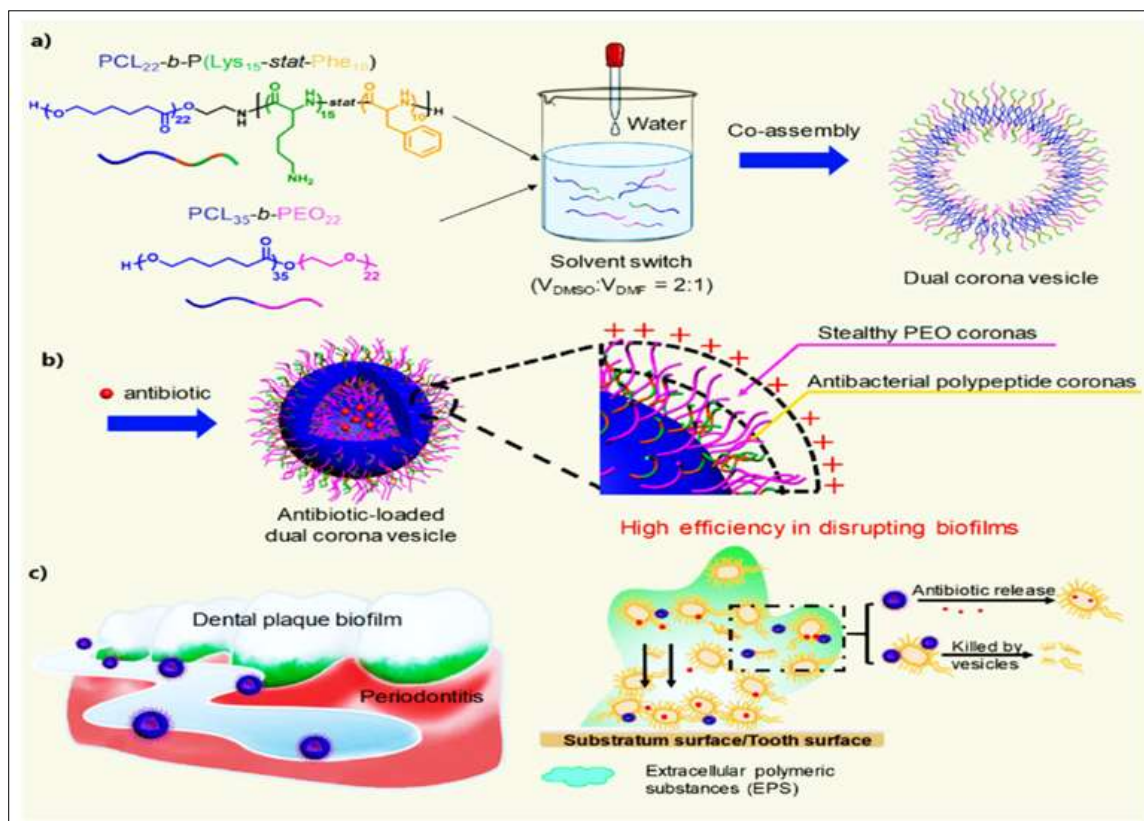
The transducer converts the physiological change resulting from the interaction between an analyte and a receptor into an optical or electrical signal that can be quantified in terms of quantity. The electrical device receives and measures the transducer's signals, while the computer and printer serve as the display and interpretation system, presenting the response's output in a user-friendly manner. Numerous nanomaterials, such as graphene, carbon nanotubes, semiconductor quantum dots, nanodiamonds, and polymer nanofibers, have been extensively studied for biosensing applications. Carbon can be used to conjugate biomolecules, such as enzymes, antibodies, DNA, and cells, to improve biosensor performance by lowering the detection limit and increasing sensitivity. The efficacy of biosensors can be influenced by nanomaterials with different properties, such as diffusivity, mechanical strength, chemical activity, effective surface-to-volume ratio, and electrocatalytic properties [26]. The development of biosensors that track DNA, bacteria, viruses, and other biomolecules also relies heavily on the biocompatibility of nanomaterials.

## Bioengineering of Tissue

Tissue engineering is a highly interdisciplinary approach that involves the use of biomaterials and biological components (such as cells and stimulatory chemicals) to

create structures that can mimic natural organs or tissues. This innovative technique has the potential to replace traditional organ/tissue transplant procedures, thereby reducing the financial burden [27]. Thanks to recent advancements, a variety of biocompatible nanomaterials, including nanoporous scaffolds and nanofiber membranes, can now be employed in tissue engineering. These nanomaterials have been successfully used in a range of tissues, including skin, bone, and brain. By carefully controlling the release of bioactive compounds such as growth factors, cytokines, inhibitors, genes, and pharmaceuticals, nanomaterials can be used to fine-tune the mechanical strength of the scaffold. As periodontal tissue loses its ability to self-repair with age, there is a growing need for innovative treatments in dental tissue engineering to reconstruct damaged tissue.

Nanomaterials offer a promising solution in this field, as they can be used as dental implants with nanocoatings, nanofillers to enhance biomaterials' mechanical properties, antibacterial substances to prevent oral infections, and components of toothpaste and other personal care products. Xi *et al.* co-assembled poly (ethylene oxide)-block-poly (caprolactone) and poly (lysine-stat-phenylalanine) to create multifunctional vesicles that carry ciprofloxacin hydrochloride (Fig. 4).



**Fig 4:** Showcases vesicles that can effectively treat biofilm-induced periodontitis by exhibiting antibacterial activity and efficient antibiotic delivery capacity. The vesicles are made by co-assembling multipurpose corona vesicles, which are then used to encapsulate the antibiotic ciprofloxacin. These multifunctional corona vesicles can break down dental plaque biofilms caused by bacteria.

These vesicles have been shown to effectively treat periodontitis by removing *Staphylococcus aureus* and *Escherichia coli* biofilms in both in vitro and in vivo studies.

## Nanocrystals have various applications in medication delivery methods.

### 1. Gastrointestinal tract

There are various ways in which drugs can be absorbed into the body, including through the gastrointestinal and dermal systems. The absorption kinetics of particles in the GI tract are influenced by post-translocation events, cellular barriers, and their initial interaction with enterocytes. The rate at which particles diffuse through GI secretion to reach colonic enterocytes determines how quickly they are disseminated throughout the body [28]. Nanoparticles are absorbed by the GI tract before being transferred to the bloodstream and dispersed throughout the body. To address the nonspecific absorptive mechanism and selective binding of ligands or receptors, techniques have been developed to enhance NPC interactions with absorptive locations such as enterocytes and M-cells in Peyer's patches. Enterocytes and M-cells have surface-specific carbohydrates that allow drug-carrying nanoparticles with the right ligands to attach to them and release their contents. Glycoproteins and lectins bind to this type of surface through a particular receptor-mediated process.

### 2. Respiratory tract

Nanoparticles can enter the body through the respiratory tract, bypassing its usual defenses and reaching the central nervous system. As a result, using nanoparticles as drug carriers for aerosol therapy is becoming increasingly important. Colloidal carriers, or nanocarrier systems, offer

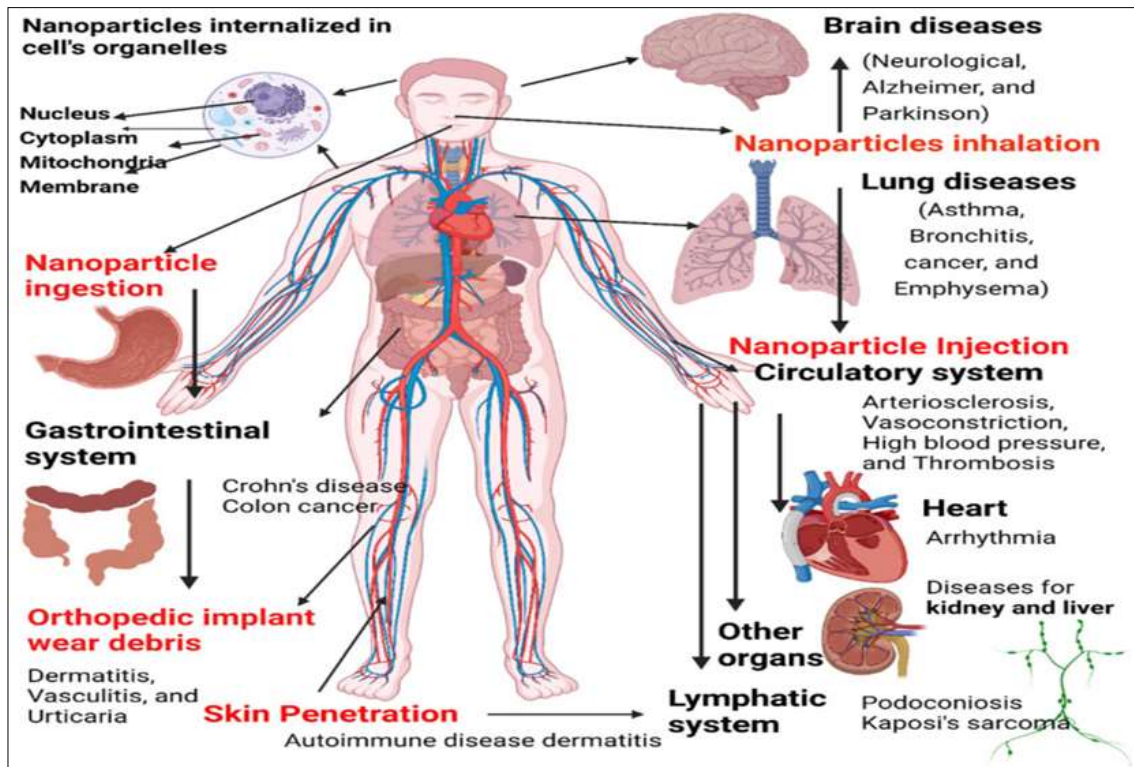
several advantages in pulmonary drug delivery, including a more uniform distribution of drug doses within the alveoli, enhanced drug stability, sustained drug delivery, and improved patient compliance. However, the blood-brain barrier presents a significant challenge for drug treatment in the brain. To overcome this obstacle, surface-modified poly (butyl cyanoacrylate) (PBCA) nanoparticles are used for modified drug delivery to the brain.

### 3. For the transfer of genes

The swift movement of plasmid-loaded nanoparticles from the endolysosomal breakdown to the cytoplasmic compartment renders them an effective means for gene delivery with sustained-release capabilities. This implies that the DNA discharged by the nanoparticles upon cellular uptake and escape from the endo-lysosomal compartment can result in gene expression that lasts for an extended period. By integrating therapeutic genes, such as bone morphogenic protein, into PLGA nanoparticles, this gene delivery technique can expedite the absorption of medication by cells and amplify the efficacy of bone healing.

### 4. Negative effects of nanomaterial Exposure

It's important to be aware of the potential negative effects of exposure to nanomaterials, despite their many benefits. Nanoparticles have been linked to various risk factors, including harm to physiological organs and tissues, as well as diseases such as lung cancer, asthma, bronchitis, thrombosis, atherosclerosis, arrhythmia, Parkinson's, and Alzheimer's. Furthermore, exposure to nanoparticles can also cause skin issues like urticaria, dermatitis, and skin irritation.



**Fig 5:** Illustrates the illness brought on by nanoparticle exposure and the entry of nanoscale elements into the body by ingestion, cutaneous exposure, and inhalation, which can result in a variety of risks.

The toxicity of certain nanomaterials can be influenced by various factors, including exposure period, dose, aggregation, concentration effects, size, aspect ratio, crystal structure, and surface characteristics. To calculate exposure dosage, one can divide the medium's molar content of nanoparticles by the exposure period [29]. However, it's important to note that aggregation and concentration effects can also impact the toxicity of the nanoparticle. Some nanoparticle types can aggregate, and these tiny aggregates may not easily enter the body, reducing their toxicity. Smaller nanoparticles can pass through cell membranes and have a higher potential for toxicity than larger ones. Additionally, the aspect ratio of nanoparticles may also impact their toxicity. For example, asbestos fibers larger than 10 nm in diameter are known to cause lung cancer, while those less than 10 nm are known to cause mesothelioma and asbestosis. On the other hand, the nanoparticle effect has an inverse relationship with nanoparticle size and a direct association with surface area. The crystal structure can affect oxidative processes, subcellular localization, and cell uptake. For instance, the oxidation of just one of two polymorphous  $\text{TiO}_2$  NP structures can cause DNA damage. The surface characteristics of the nanoparticles can potentially help toxify them through oxidation and translocation mechanisms.

### Conclusion

The field of nanotechnology is truly captivating and has the potential to transform our daily lives. By utilizing nanoparticles, we can enhance the performance and efficiency of everyday objects. These tiny particles are especially valuable because they can convert unstable and poorly soluble compounds into useful deliverable chemicals. Our review paper provides a comprehensive overview of nanoparticles, including their structure, classification,

production process, and applications in various domains. One of the most significant challenges in nanobiotechnology is to increase the therapeutic effectiveness of nanoparticles while minimizing their toxicity. Noble metal nanoparticles, with their unique atomic and supramolecular characteristics, hold promise as therapeutic and diagnostic tools. Encapsulation techniques have also been explored for delivering various bioactive cytotoxic chemicals. Additionally, nanoparticles can be utilized in tissue reengineering for a variety of tissue repairs. In agriculture and healthcare, carbon and metal-based nanoparticles can be used to create biosensors. Nanotechnology is a powerful and eco-friendly technology that has a bright future ahead.

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