

A NEW TECHNOLOGY: NANOPARTICLES

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Article Received on 13/02/2025

Article Revised on 04/03/2025

Article Accepted on 24/03/2025

ABSTRACT

The importance of nanoparticles in technological progress stems from their adaptable characteristics and improved performance compared to their original material. NPs are often created by reducing metal ions to uncharged nanoparticles using harmful reducing agents. However, there have been numerous recent efforts to develop green technology that utilizes natural resources rather than hazardous chemicals for nanoparticle production. In green synthesis, biological methods are utilized for NP synthesis due to being eco-friendly, clean, safe, cost-effective, straightforward, and highly efficient. Many biological organisms, such as bacteria, actinomycetes, fungi, algae, yeast, and plants, are employed for the green synthesis of NPs. About its application in medicine, nanotechnology has the potential to greatly improve current therapies and diagnostics, as well as pave the way for unprecedented advancements due to its ability to work at a nanoscale level.

KEYWORD:- Green-synthesis, Nanoparticles, Nanotechnology, Biological Synthesis, Microbial Nanotechnology, Bio-nanotechnology.

INTRODUCTION

Nanotechnology has emerged as a significant scientific achievement in the 21st century. It encompasses the synthesis, management, and application of materials with a size smaller than 100 nm. Nanoparticles play a crucial role in various sectors including the environment, agriculture, food, biotechnology, biomedical, and medicine. The exceptional properties of nanoparticles (NPs), including their natural origins, biocompatibility, anti-inflammatory, and antibacterial activity, efficient drug delivery, bioactivity, bioavailability, tumor targeting, and bio-absorption, have fueled significant advancements in biotechnological and applied microbiological applications. NPs are revolutionizing wastewater treatment, environmental monitoring, functional food additives, and antimicrobial agents.^[1,2,3]

A particle of matter with a diameter of one to one hundred nanometers (nm) is commonly referred to as a nanoparticle or ultrafine particle. Nanoparticles often display unique size-dependent characteristics due to their small size and large surface area. When the size of a particle approaches the nano-scale with a characteristic length scale close to or smaller than the de Broglie wavelength or the wavelength of light, the periodic boundary conditions of the crystalline particle are disrupted. Consequently, many of the physical properties of nanoparticles vary significantly from those of bulk

materials, opening up a wide range of new and innovative applications.^[4,5]

On the basis of dimensions NPs can be classified into four types^[6]

1. Zero-dimensional (0D) objects have length, breadth, and height, with the corresponding author fixed at a single point. For example, nano dots.
2. One-dimensional (1D) objects possess only one parameter. For example, graphene.
3. Two-dimensional (2D) objects possess only two parameters, i.e., length and breadth. For example, carbon nanotubes.
4. Three-dimensional (3D) objects possess all three parameters, namely length, breadth, and height. For example, gold nanoparticles.^[6,7]

Nanoparticles (NPs) can take on various shapes, sizes, and structures, such as spherical, cylindrical, tubular, conical, hollow core, spiral, flat, wire, and irregular forms. Their surfaces can be uniform or irregular, and they can exist in crystalline or amorphous forms, as single crystal solids or agglomerated multi-crystal solids. The physicochemical properties of these NPs are primarily influenced by their size and shape variations. With exceptional physical and chemical properties, NPs have demonstrated significant success in diverse applications, including medicine, environmental

preservation, energy research, imaging, and chemical and biological sensing. Nanotechnology is increasingly recognized as a crucial factor for a clean and sustainable future, garnering significant attention from researchers.^[6,7]

Structure of nanoparticles^[8,9]

Nanoparticles (NPs) possess a sophisticated structure, consisting of two or three layers: (i) a functionalized surface layer, modified by a variety of small molecules, metal ions, surfactants, or polymers, (ii) a purposefully added shell layer, chemically distinct from the core, and (iii) the core material, serving as the central component of the NPs.

The characteristic properties of NPs are generally due to the core material. Hence, NPs are often referred to by their core material only.

Nanoparticles (NPs) are typically categorized into various classes based on their morphology, size, and physical and chemical properties. They are mainly grouped as organic, inorganic, and carbon-based NPs.

A. Organic nanoparticles^[8]

Organic nanoparticles, ranging from 10 nm to 1 μ m in diameter, consist of solid particles made of organic compounds like lipids or polymers.

Some commonly known organic nanoparticles include dendrimers, liposomes, micelles, and ferritin. These organic nanoparticles are environment-friendly, biodegradable, non-toxic, and more suitable in the biomedical field. Both micelles and liposomes have a hollow core, also known as nanocapsules, and are sensitive to thermal and electromagnetic radiation. These unique properties make organic nanoparticles an ideal choice for drug delivery as they are highly efficient in targeted drug delivery.

B. Inorganic nanoparticles^[8,9]

Inorganic nanoparticles are the particles that are not made of carbon. It includes metal and metal oxides. As compared with organic NPs, inorganic NPs enormous research and commercial investments have been made.

1) Metal based nanoparticles^[8]

Organic nanoparticles (NPs) like dendrimers, liposomes, micelles, and ferritin offer numerous advantages. These environment-friendly, biodegradable, and non-toxic NPs are cost-effective and well-suited for biomedical applications. With unique properties such as a hollow core, sensitive to thermal and electromagnetic radiation, these NPs are ideal for efficient drug delivery to targeted areas. Metal-based nanoparticles (NPs) ranging from 10 to 100 nm in size exhibit unique properties such as high surface area to volume ratio, pore size, surface charge and charge density, crystalline and amorphous structures, high reactivity, and sensitivity to environmental factors like air, moisture, heat, and sunlight. These exceptional

properties make them highly promising for applications across various research areas.

2) Metal oxides based nanoparticles^[8,9]

Metal-based nanoparticles can be transformed into their corresponding oxides, known as metal oxide-based nanoparticles. Metal oxide-based nanoparticles have exceptional properties compared to their metal counterparts. Some examples of metal oxide-based nanoparticles include iron oxide (Fe₂O₃), magnetite (Fe₃O₄), aluminum oxide (Al₂O₃), cerium oxide (CeO₂), silicon dioxide (SiO₂), titanium oxide (TiO₂), and zinc oxide (ZnO). These metal oxides based NPs found to be more reactive and efficient.

C. Carbon based nanoparticles^[9]

Carbon-based nanoparticles (NPs) are composed of carbon and can take on various shapes, including tube-shaped, horn-shaped, spherical, or ellipsoidal. The two main classes of carbon-based NPs are fullerene and carbon nanotubes (CNTs). Other classes include graphene, nanofibers, and carbon black.

Advantage of nanoparticles^[10-15]

1. Modifying the surface characteristics and size of nanoparticles to target pharmaceuticals passively or actively following parenteral injection is a simple process.
2. Tagging certain bacteria with nanoscale quantum dots based on immunofluorescence to facilitate their identification and elimination.
3. Aquaculture is one of the many industries where nanotechnology is expanding. It has several uses in fields including nutrition.
4. Reproduction, fishing, disease prevention, water purification, and a decrease in toxicity and adverse effects.
5. Long-lasting medication release at the target location over several days or even weeks is made possible by the use of biodegradable ingredients in the creation of nanoparticles.
6. Due to their small size, nanoparticles are quickly absorbed by cells and can easily travel through tiny capillaries, allowing drugs to accumulate effectively at the body's target sites.
7. Because NPs have a high surface energy and a big surface area to volume ratio, nanotechnology can increase the durability of fabrics.
8. The encapsulation technology makes it simple to incorporate nano supplements for efficient medication and nutrient delivery.
9. Food products are labeled with nanobarcodes to ensure their safety and to monitor their distribution.

Disadvantage of nanoparticles^[8,9,10]

Despite these benefits, nanoparticles do have some drawbacks, such as the following

1. In the cellular milieu, nanoparticles exhibit strong reactivity due to their small size and large surface area.

2. Non-biodegradable particles may build up at the medication delivery site when they are utilized, which could result in a persistent inflammatory response.^[2]
3. The therapy cannot be stopped because of the restricted targeting capabilities of nanoparticles.
4. The cost of nanotechnology is high, and its development can be considerably more costly.
5. Nowadays, atomic weapons are more readily available, more powerful, and more devastating to use.

Nanoparticles preparation method^[10-21]

1. **The bottom-up, or constructive**, method is the process of creating materials starting with atoms and working their way up to nanoparticles. The most often used bottom-up techniques to create nanoparticles are:
 - A. Sol-gel method
 - B. Chemical vapour deposition
 - C. Pyrolysis
 - D. Spinning

A. Sol-gel method

A colloidal dispersion of solid particles in liquid is called a sol. A solvent and solid macromolecules are combined to create the gel. This wet chemical method makes use of a chemical solution that acts as a precursor for an integrated system of discrete particles. Metal oxides and chlorides are commonly employed as precursors in the sol-gel process. A liquid and solid phase are generated with the use of shaking, stirring, or sonication to combine the precursor with the host liquid.^[10]

B. Chemical vapour deposition (CVD)

The well-known CVD technique involves a chemical reaction between the gaseous and vapor phases and deposits a solid on a heated surface. A temperature that is higher than 900 °C in thermal CVD initiates the reaction. Powdered nano-composite has been produced via CVD. Using SiH₄, CH₄, WF₆, and H₂ as gas sources, SiC/Si₃N composite powder was produced at 1400 degrees Celsius.^[11]

C. Pyrolysis

To prepare fine particles for spray pyrolysis, a starting solution is usually made by dissolving the product's metal salt in the solvent. The droplets are atomized from a starting solution and then added to the furnace. Within the furnace, operations including solvent evaporation, solute diffusion drying, precipitation, reaction between the precursor and ambient gas, pyrolysis, or sintering may occur in order to produce the final furnace.^[12]

D. Spinning

The process of spinning generates a continual forced conversion in the vapor above the substrate. The evaporation rate in spin coating is usually rather uniform. The homogenous and ultrathin photoresist films must be spin-coated as a crucial stage in the semiconductor

production process¹⁵. Thus, the synthesis of NPs treated by an SDR with a revolving disk inside helps regulate physical parameters such as temperature. Usually, inert gases or nitrogen are filled with the reactor to stop chemical reactions within. The SDR revolved at different speeds and was pumped with precursor and water. The atoms fuse, precipitate, gather, and dry as a result of the spinning. Factors influencing the synthesis of NPs¹⁶ include liquid flow rate, disc rotation speed, liquid precursor ratio, feed position, and disc surface.^[12]

2. Top-down method

Destructive synthesis is employed in this process. The bigger molecules broke down into smaller ones, and these smaller ones then changed into nanoparticles.

- a. Thermal decomposition method
- b. Lithography
- c. Laser ablation
- d. Sputtering
- e. Mechanical milling

A. Thermal decomposition method

Chemical breakdown is driven by heat in an endothermic reaction. The chemical bond of a molecule is harmed by this heat. The decomposition temperature is the point at which an element starts to break down chemically.^[14]

B. Lithography

Size- and shape-controlled nanoparticles can be produced using top-down lithographic methods alone or in conjunction with other fabrication processes, such as reactive ion etching (RIE). One of all top-down methodologies, photolithography has been widely used in the conventional semiconductor sector and other fields needing micro and nano designs. Ion beam and e-beam lithography can be used to directly write incredibly fine patterns on ultra-small structural components and to make molds or masks that can be used with other lithography processes. However, these methods have extremely low costs and throughput. The previously noted issue with top-down fabrication process can be solved by nanoimprint lithography (NIL), which copies nano-patterns through a nanostructured master mold in a simple, parallel, and cost-effective manner.^[15]

C. Laser ablation

Pulsed lasers are frequently employed in the production of metals, ceramics, polymers, and glasses. They work by removing molecules off the surface of a substrate to generate microstructures. A substance is removed off a surface by focusing a laser beam, which absorbs energy and causes melting, evaporation, or vanishing ablation. Laser ablation is the technique that handles both vaporization and melt ejection, and it remains constant during the laser machining application.^[16]

D. Sputtering

Materials from the target's surface (a solid) can be evaporated by blasting it with extremely powerful argon ions, an inert gas, which causes the ejection of atoms and

clusters. As part of the sputtering process, a regulated inert gas is first introduced into the vacuum chamber. The cathode is then electrically charged to form self-sustaining plasma. A vapour steam is composed of the components that sputtered together. This vapour steam passes through the chamber and strikes the substrate to adhere to it and create a thin film or surface coating.^[17]

3. Mechanical milling method

In mechanical milling, a high energy mill is filled with a suitable milling medium and a steady powder charge. The objectives of milling are to reduce particle size and combine particles into new phases. The balls have two possible outcomes: either they fall freely and hit the balls and powder below, or they roll down the chamber's surface in a row of parallel layers. The dynamics of the operation determine how much energy is transferred from the balls to the powder during mechanical milling or alloying. Material milling plays a major role in the powder metallurgy, ceramics, and mineral processing sectors. Usually, the high energy ball mills—such as vibratory mills, planetary ball mills, and tumbler ball mills—have been employed for these uses.^[18,19]

Method of evaluation for release of drug^[18,19]

1. Adjacent diffusion cells with synthetic or natural membranes.
2. The diffusion method for dialysis bags.
3. The reverse hemodialysis bag method.
4. Agitation, then centrifugation or ultracentrifugation.
5. Centrifugal ultra-filtration methods or other forms of ultra-filtration.

Release investigations are typically carried out using centrifugation and controlled agitation. Because removing nanoparticles from release medium is a time-consuming and technically complex procedure, the dialysis technique is usually chosen. Five possible routes exist for the release of drugs: Drug delivery mechanisms include surface deposition, diffusion through the nanoparticle matrix, diffusion through the polymer wall of the nanocapsule, erosion of the nanoparticle matrix, and diffusion through both erosion and diffusion. The kinetic analysis of drug release from nanoparticles can be explained with the use of a bioexponential function.

$$C = Ae$$

where A and B are the system characteristic constants (A is utilized for the diffusion control system and B is used for the erosion control system), and C is the concentration of drug still present in the nanoparticles at time t.

Characterization parameters of NPs^[20-26]

Modern microscopic techniques such as atomic force microscopy (AFM), transmission electron microscopy (TEM), and scanning electron microscopy (SEM) are commonly used to identify nanoparticles based on their size, shape, and surface charge. The average particle diameter, size distribution, and charge of the nanoparticles affect their physical stability and in vivo

distribution. Particle size is measured using a variety of techniques, including as nuclear magnetic resonance, optical microscopy, electron microscopy, dynamic light scattering, and atomic force microscopy.

1. Nuclear magnetic resonance (NMR)

Nuclear magnetic resonance (NMR) can be used to determine the size and qualitative properties of NPs. The selectivity provided by chemical shift, in addition to the sensitivity to molecular mobility, allows information about the physicochemical status of the constituents inside the nanoparticles.^[27]

2. Differential scanning calorimetry (DSC)

The physical condition of the native medication inside the nanoparticles was ascertained using the DSC analysis. Each of the natural medication, polymer, and NPs weighed roughly 2 milligrams. They were placed individually into different sealed standard aluminum pans and heated between 25°C and 300°C at a rate of 10°C/min in a nitrogen atmosphere. Use an empty metal pan as a guide.^[28]

3. Particle size

The diameters of the NPs were examined using a scanning electron microscope, and it was discovered that they varied from 350 nm to 600 nm, depending on the quantity of polymer present³⁵. The two factors that have the biggest effects on NPs are morphology and particle size. Drug release and targeted drug delivery are the main objectives of nanoformulation, and the data collected has shown that particles have an effect on the pharmaceuticals released. As a result, the medication will release faster since the loaded drug will be exposed to the particle's surface. During storage, smaller particles frequently form foam aggregates. Draw a link, therefore, between stability and reduced particle size. It was shown that as particle size grew, so did the rate of degradation for PLGA.^[29-31]

4. Zeta potential

The zeta potential of NPs is often used to characterize their surface charge characteristic. It represents the electrical potential of the particles and is influenced by the composition of the particles as well as the medium in which they are distributed. It has been shown that because the surface charge keeps the particles from aggregating, NPs with a zeta potential exceeding + 30 mV can be suspended.^[32]

5. UV- visible absorption spectroscopy

Absorbance spectroscopy is used to determine the optical properties of a solution. The amount of light absorbed by the sample solution is measured after it is lit. when absorbance at each wavelength is measured and the wavelength is varied. The absorbance can be used to calculate the concentration of a solution using Beer-Lambert's law. There are several absorbance peaks in the optical measurement of the UV-visible spectrophotometer, including 410 nm.^[33]

6. Scanning electron microscopy (SEM)

We may learn about the morphology, shape, size, chemical composition, and orientation of the materials with the aid of this NP characterization technique. When the NPs solution is dried down and placed on a sample holder for SEM evaluation, secondary electrons and backscattered electrons are released, which identify the surface of the sample. Because the release of electrons from nanoparticles varies based on their surface, the shape of NPs can be ascertained by examining the depression and elevation of the surface.^[34]

7. Dynamic light scattering (DLS)

The produced particles' average volume diameters and polydispersity index were utilized to determine the particle size and size distribution using dynamic light scattering at a fixed angle of 173 at 25 °C and photon correlation spectroscopy. Three examinations were conducted on the samples.^[35]

Application of nanoparticles^[36-40]

Nanoparticles exhibit certain physical and chemical properties, such as mechanical, magnetic, optical, and thermal properties.

1. Medicine

The contributions of nanoparticles to medical imaging and medication and gene delivery have been very beneficial to clinical medicine. Iron oxide particles such as magnetite (Fe₃O₄) or its oxidized counterpart, hematite (Fe₂O₃), are most commonly used in biomedical applications. Ag NPs are becoming more and more common in home goods, wound dressings, and catheters due to their antibacterial action. Gold nanoparticles are showing considerable promise in cancer treatment as drug transporters, photothermal agents, and contrast agents. Over the past few decades, a lot of research has been focused on the creation of biodegradable nanoparticles as effective drug delivery vehicles. Many polymers have been used in drug delivery research because they effectively transfer drugs to their target site, enhancing therapeutic advantages while reducing unwanted effects.^[36]

2. Diagnostics

NPs can be employed as imaging agents to help visualize specific bodily parts. To enhance the visibility of organs and tissues during magnetic resonance imaging (MRI), iron oxide nanoparticles, or Fe₃O₄NPs, have been utilized as contrast agents. Au NPs have special optical, electrical, and catalytic capabilities and are being researched for use in diagnostics because they can accumulate in some malignant tumors.

3. Tissue engineering

NPs can encourage the growth and repair of tissues and organs. For example, titanium dioxide nanoparticles (TiO₂) have been studied for tissue engineering applications because of their ability to stimulate bone cell development.^[36]

4. Antimicrobials

Some nanoparticles (NPs), such as silver NPs (Ag NPs) and copper nanoparticles (CuNPs), have strong antibacterial properties and are being researched for use in bandages and other medicinal goods. All things considered, NPs are the subject of current research for a wide range of uses and hold great promise for the medical industry. However, it is crucial to carefully consider the advantages and potential hazards of doing so in order to ensure the safe and responsible use of NPs in medicine.^[37]

5. Cosmetic and sunscreens

The conventional UV sunscreen does not contain long-lasting medications. There are several advantages to sunscreen that contains nanoparticles, such as titanium dioxide. Titanium oxide and zinc oxide nanoparticles have been used in sunscreens because of their dual properties of being transparent to visible light and able to absorb and reflect ultraviolet radiation. A pigment called iron oxide nanoparticles is found in certain lipsticks.^[37]

6. Time release of the drug^[36]

To avoid nonspecific toxicity, the drug must remain encapsulated until the particle attaches to the target. While the particles are still in the circulatory system, it cannot diffuse them out. Targeted medication administration at the site of disease is a huge prospective application for nanoparticles, which has various crucial consequences, such as:

1. The bioavailability of drugs can be improved by using nanoparticles. medication that is intended for a specific area.
2. To improve the absorption of poorly soluble drugs.
3. Nanomaterials have been used to successfully formulate chemotherapeutic
4. Medications, such as paclitaxel, doxorubicin
5. Fluoro-uracil, and dexamethasone.

7. Cell specificity

Conjugation of antibodies to carbon nanotubes with fluorescent or radiolabelling to increase cell specificity.^[38]

8. Protein detection

For human cells to continue developing, it is imperative that we comprehend the roles played by proteins, which are fundamental to the language, mechanism, and structure of cells. Gold nanoparticles are widely used in immunohistochemistry to identify protein-protein interactions. surface enhanced Raman scattering spectroscopy to identify and detect individual dye molecules is a widely acknowledged method. Combining the two methods into a single NPs probe can greatly boost the multiplexing power of protein probes. The NPs are coated with hydrophilic oligonucleotides that have a Raman dye at one end and a small molecules recognition element terminally capped.^[39,40]

9. Cancer therapy

The cytotoxic atomic oxygen generated by lasers, which kills cancer cells, is the cornerstone of photodynamic cancer therapy. Cancer cells absorb more of a certain dye—which is used to create atomic oxygen—than do healthy cells. So, the only radiation coming from cancerous cells. Unfortunately, the residual dye molecules migrate to the patient's skin and eyes, making them extremely sensitive to sunshine. It could take up to six weeks for this effect to go away. To avoid this negative effect, the hydrophobic color molecules were encapsulated in porous nanoparticles. The dye stayed confined inside the cromosil NPs and did not spread to other parts of the body.^[41,42]

10. Biological application

Nanoparticles have been demonstrated to initiate both intrinsic and extrinsic apoptotic pathways for the killing of malignant cells, and copper has demonstrated potential in the fight against cancer. Hela cells, Md A-MB-231 human breast cancer cell lines, Caco-2 human colon cancer cells, HepG2 human liver cancer cells, and McF-7 human breast cancer cells are all susceptible to the anticancer effects of copper and copper oxide nanoparticles. Copper nanoparticles demonstrated their anti-inflammatory and anti-arthritis capabilities in rats administered Complete Freund's adjuvant (CFA), which mimics the course of human arthritis. These nanoparticles boosted antioxidant enzymes and lowered pro-inflammatory indicators. In an in vivo investigation on mice, the capacity of CuNPs to heal wounds was demonstrated by a significant increase in the concentration of fibrocytes that finally generated collagen for.^[41,42]

11. Nanobiosensors

Some examples of organic chemicals that have been used as antimicrobial packaging materials are essential oils, organic acids, and bacteriocins. Nanobiosensors are used in the food sector to identify infections during processing. Antimicrobial characteristics are exhibited by a variety of nanoparticles (NPs), such as Ag, chitosan, copper, and metal oxide NPs such as titanium oxide (TiO₂). Conventional techniques of diagnosing infectious diseases are sluggish, tedious, and require a lot of work, especially during an emergency. The rapid, inexpensive, and accurate identification of infectious pathogens, hormone imbalances, and DNA has been made possible by the development of microbial biosensors. In forensic identification, microbial biosensors have been used to examine bodily fluid traces that contain DNA and miRNA as proof.^[42]

12. Future perspectives

Nanotechnology has been rapidly advancing and is useful in a wide range of industries. NPs can cause a range of health problems with the kidneys, lungs, and other organs in both humans and animals. However, more work has to be done to address the lack of awareness about the risks associated with prolonged usage. A safe

technique for producing non-toxic NPs with additional beneficial features is green synthesis. Currently, one of the most fascinating areas of research is nanomedicine, which includes therapeutic alternatives, medication delivery, and cancer diagnosis. Producing NPs with uniform sizes, characteristics, biocompatibility with drug loading, and restricted release to the targeted cells is essential. It is acknowledged that NPs have significantly advanced the disciplines of diagnosis and therapy. Other areas, such the control of parasite infections and the reaction to cancer therapy, which has been reduced and is still insufficient, need to be included in their expectations.^[42-47]

CONCLUSION

Nanoparticles offer an incredibly attractive platform for a variety of biological applications. Nanomaterials are fascinating materials because of their superior and versatile physical, chemical, and biological capabilities over bulk materials. In this overview, we covered nanoparticles in brief, covering both their advantages and disadvantages. NPs are prepared using many methods, including top-down and bottom-up synthesis. Targeted drug delivery is being studied using a variety of nanomaterials, including carbon-based, gold, titanium, dendrimers, and liposomes. Because of their greater surface-area-to-volume ratio, nanostructured scaffolds can be used as selective substrates to absorb specific proteins and promote cell adhesion. There are several uses for NPs based on metal and carbon in the biomedical and agricultural industries for the development of biosensors. Different nanomaterials are discussed individually with regard to their many characteristic properties, antibacterial activities, protein detector, drug release time, and waste water treatment activities.

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