

Nanoparticles in Modern Science: From Design to Application**Chanchal¹, Krati^{2*}, Esha Vatsa², Nidhi Chaudhary², Amandeep Singh³**¹*Student, School of Pharmaceutical Sciences, Jigyasa University, Dehradun, Uttarakhand, India*²*Assistant Professor, School of Pharmaceutical Sciences, Jigyasa University, Dehradun, Uttarakhand, India*³*Principal & Professor, School of Pharmaceutical Sciences, Jigyasa University, Dehradun, Uttarakhand, India***Correspondence***Krati,**

Assistant Professor, School of Pharmaceutical Sciences, Jigyasa University, Dehradun, Uttarakhand, India.

E-mail: krati@jigyasauniversity.edu.in**Abstract**

Recent advances in nanotechnology have positioned nanoparticles as versatile and transformative materials across biomedical, environmental, and industrial sectors. Their unique physicochemical properties—arising from high surface area, tunable size, and surface functionality—enable enhanced performance compared with bulk materials. Between 2020 and 2025, significant progress has been made in eco-friendly green synthesis, microfluidic-assisted fabrication, hybrid nanostructures, and advanced surface engineering strategies. These developments have expanded the scope of nanoparticles in drug delivery, bioimaging, theranostics, clean energy production, water purification, and regenerative medicine. Innovations in characterization techniques such as real-time *in situ* analysis and improved surface-specific spectroscopies have strengthened the understanding of nanoparticle stability, protein corona behaviour, and nano–bio interactions. Despite substantial growth, challenges persist in large-scale production, long-term biocompatibility, regulatory acceptance, and reproducibility of synthesis and characterization. Addressing toxicity, immune interactions, and environmental impact remains crucial for clinical and industrial translation. Future perspectives emphasize personalized nanomedicine, AI-assisted nanoparticle design, sustainable manufacturing, and integrated nano–bio systems. This review compiles recent developments and emerging trends to provide an updated understanding of nanoparticle research and its broad interdisciplinary applications.

Keywords: Nanoparticles synthesis, Characterization technique, Biomedical applications, Metal and metal oxide nanoparticles, Therapeutic efficiency

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Introduction

In the past decade, nanotechnology has evolved from a niche scientific concept into one of the most transformative disciplines of modern research. Among its numerous innovations, nanoparticles have emerged as dynamic materials with extraordinary physical, chemical, and biological characteristics distinct from their bulk counterparts.

Recent years have witnessed an explosive growth in nanoparticle research, driven by the demand for efficient drug delivery systems, smart diagnostic tools, sustainable energy solutions, and environmental remediation techniques. The Novel synthesis techniques such as microfluidic-assisted fabrication, green synthesis using biological extracts, and advanced chemical reduction routes have improved precision,

reproducibility, and eco-friendliness. Despite these advances, challenges remain in understanding nanoparticle toxicity, large-scale production, and regulatory acceptance.

Unlike earlier reviews that primarily addressed traditional synthesis and applications, the present paper highlights recent innovations (2020–2025) in nanoparticle design, advanced characterization techniques, and evolving interdisciplinary applications. This review aims to provide an updated and comprehensive overview of current developments in nanoparticle research.



Fig. 1: Picture of Nanoparticle

DEFINITION

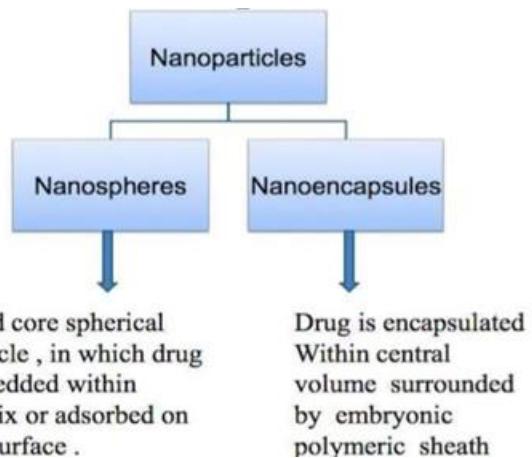


Fig. 2: Types of Nanoparticles

Nanoparticle is defined as particulate dispersion or solid particles with a size (range 10-1000nm). The drug is dissolved, entrapped, encapsulated, or attached to a nanoparticles matrix. Nanoparticles, nanospheres or nanocapsules can be obtained by the different methods of Preparation. In the system of nanocapsules, the drug is confined to a cavity surrounded by a unique polymer membrane while nanospheres are matrix systems in which the drug is uniformly dispersed [1]

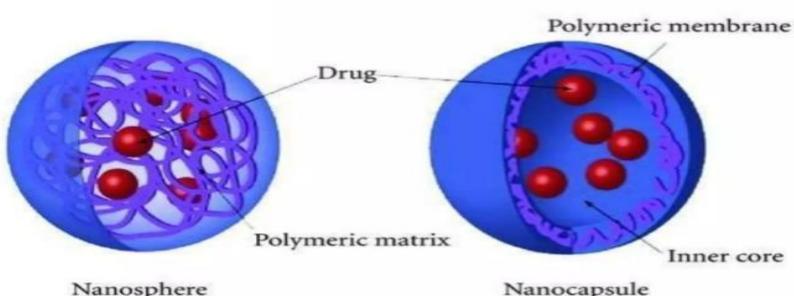


Fig. 3: Visual diagram of Nanospheres and Nanocapsules

SCOPE

- Personalized nanoparticle-based delivery systems will advance precision medicine through tailored size, surface chemistry, and targeting ligands.
- Green synthesis using waste-derived materials and eco-friendly reactions will promote sustainable large-scale nanoparticle production.
- Bridging lab-scale synthesis to clinical and industrial use requires stronger regulatory, toxicity, and scalability frameworks.
- Multifunctional hybrid nanoparticles integrating therapy, imaging, and biosensing offer vast potential in future theranostic applications.
- Expanding nanoparticle use in agriculture, environment, and energy demands cost-effective synthesis, reproducibility, and safety standardization.

IDEAL CHARACTERISTICS OF NANOPARTICLES

- Optimal particle size (10–200 nm):Ensures stability, enhanced permeability, and efficient cellular uptake for drug delivery.
- High surface area-to-volume ratio:Improves drug loading, controlled release, and interaction with target tissues.
- Biocompatibility and biodegradability:Prevents immune reactions and toxicity, allowing safe clearance from the body.
- Surface functionalization and targeting ability:Functional groups and ligands enable selective binding to diseased cells or tissues.

(1) CLASSIFICATION OF NANOPARTICLES

1. BY COMPOSITION

- Controlled and sustained drug release:Ensures prolonged therapeutic effect and reduces dosing frequency.
- Stability and reproducibility:Nanoparticles should maintain their structure, size, and drug activity during storage and physiological conditions.

SIGNIFICANCE

Enhanced Drug Delivery Efficiency:Nanoparticles improve solubility, bioavailability, and site-specific delivery of poorly soluble drugs, reducing systemic side effects.⁽¹⁾

Targeted and Controlled Release:Surface-modified nanoparticles enable targeted drug transport to diseased tissues with controlled release for prolonged therapeutic action^[2]

Improved Diagnostic and Imaging Techniques:Metallic and fluorescent nanoparticles enhance sensitivity in imaging and biosensing, aiding in early disease detection^[2,3]

Versatility in Multifunctional Applications:Nanoparticles serve in combined therapeutic, imaging, and biosensing platforms (“theranostics”), integrating diagnosis and treatment.

Sustainability and Environmental Impact:Green-synthesized nanoparticles reduce chemical waste and toxicity, supporting eco-friendly technological development^[3]

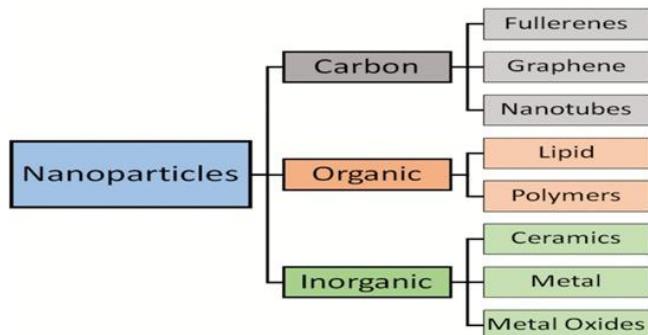


Fig. 4: Classification of nanoparticles on the basis of composition

• Organic nanoparticles

Made from carbon-based/organic materials (polymers, lipids) and designed to encapsulate or conjugate drugs/biomolecules. Generally biodegradable and biocompatible, often used for controlled release.

Examples: Polymeric nanoparticles (PLGA, PEG-based), liposomes, solid-lipid nanoparticles (SLNs), dendrimers, micelles.

Why important: Low toxicity, tunable degradation, easy surface functionalization for targeting[3].

• Inorganic (metal & metal-oxide) nanoparticles

Metals (Au, Ag) and metal oxides (Fe_3O_4 , TiO_2 , ZnO) provide optical, electronic, catalytic, or magnetic

2. BY DIMENSION

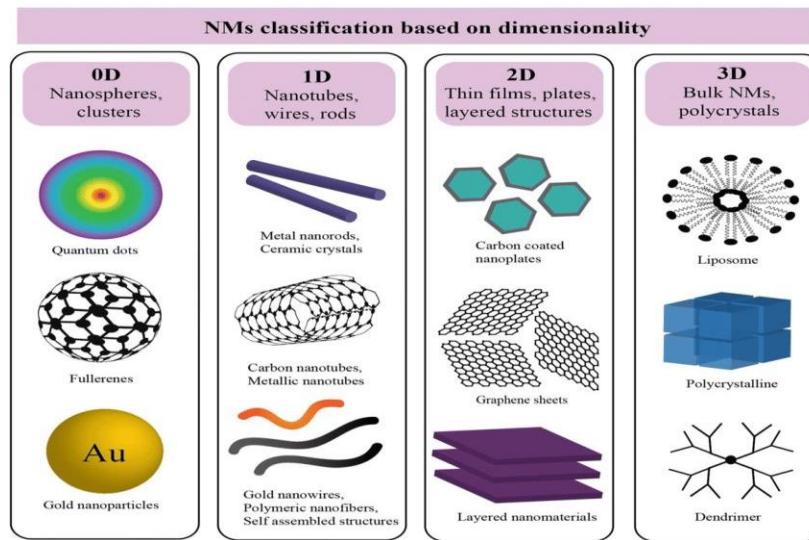


Fig. 5: Classification of nanoparticle on the basis of dimension

Nanomaterials (including nanoparticles) are often classified by how many of their spatial dimensions lie in the nanoscale (typically < 100 nm). This classification helps understand their confinement effects, electron mobility, and how they behave in applications.

• Zero-Dimensional (0D) Nanomaterials

All three external dimensions (length, width, height) are in the nanoscale. Electrons and other physical phenomena are highly confined in all directions.

Examples: Quantum dots, fullerenes, small spherical nanoparticles or metal clusters.

Properties: Strong quantum confinement effects; size-dependent optical and electronic behaviours.

• One-Dimensional (1D) Nanomaterials

functions. Widely used in imaging, diagnostics, antimicrobial formulations, and catalysis.

Examples: Gold nanoparticles (plasmonics), silver nanoparticles (antimicrobial), iron oxide (magnetic resonance & hyperthermia), TiO_2/ZnO (photocatalysis/UV filters)[4]

• Carbon-based nanoparticles

Particles composed of carbon allotropes — graphene oxide (GO), carbon nanotubes (CNTs), fullerenes, carbon dots. They offer high surface area, electrical conductivity, and distinctive surface chemistry.

Examples: GO/CNTs for drug/gene delivery and biosensing; carbon dots for bioimaging and fluorescence applications[4]

Two dimensions are in the nanoscale, while the third is larger (often significantly). This means the material is “nanoscale” in cross-section but elongated in one direction.

Examples: Nanotubes (like carbon nanotubes), nanowires, nanorods, nanofibers[5]

Properties: High aspect ratio, directional conductance, efficient pathways for electron/phonon transport.

• Two-Dimensional (2D) Nanomaterials

One dimension (thickness) is on the nanoscale, while the other two are not. This yields ultrathin sheet- or layer-like structures.

Examples: Nanosheets, thin films, graphene, nanolayers.

Properties: High surface area, strong surface interactions, often used in membranes, sensors, and electronics.

- **Three-Dimensional (3D) Nanomaterials**

None of the three dimensions are confined to the nanoscale as a whole structure, even though they may be built from nanoscale building blocks. For example, bulk nanostructured materials.

Examples: Nanoporous materials, nanocomposites, bundled nanowires, or arrays that form a 3D network.[5]

Properties: Combine nanoscale building block advantages (like high surface area) with bulk mechanical properties.

Synthesis of Nanoparticles

Nanoparticle synthesis methods are broadly grouped into top-down and bottom-up approaches. Top-down

methods break bulk materials into nanoscale pieces, while bottom-up approaches assemble atoms/molecules into nanostructures. Choice of method influences particle size, shape, crystallinity, surface chemistry, scalability, reproducibility, and environmental impact — all critical for downstream applications.

Top-down approaches

- Ball milling / mechanical milling
- Lithography / etching / milling (top-down lithographic methods)

Bottom-up approaches[6]

- Chemical reduction (wet chemical synthesis)
- Co-precipitation
- Sol-gel and hydrolysis-condensation routes
- Hydrothermal / solvothermal synthesis
- Thermal decomposition & hot-injection
- Microemulsion / reverse micelle methods.
- Template-assisted synthesis (hard & soft templates).

Physical/vapor-phase methods[6]

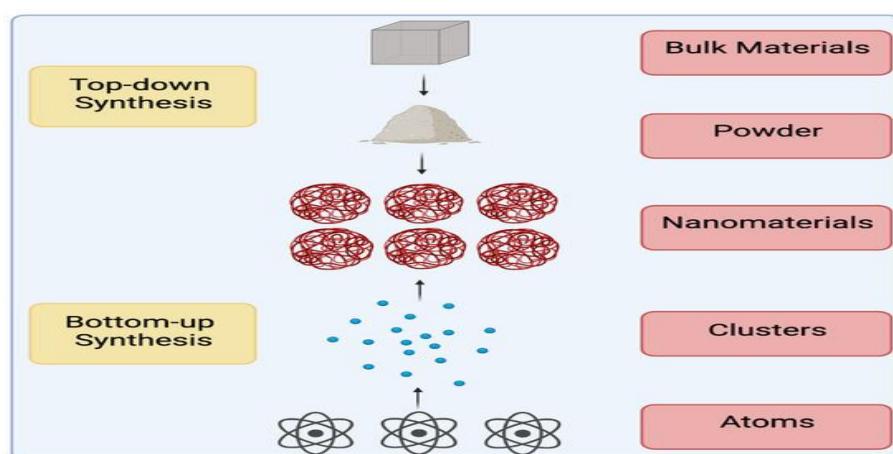


Fig. 6: Method of synthesis

- Chemical vapor deposition (CVD) & physical vapor deposition (PVD)
- Laser ablation in liquids / pulsed laser deposition

Biological / green / biogenic synthesis

- Plant-mediated synthesis
- Microbial / enzymatic synthesis

Emerging & advanced manufacturing methods

- Microfluidic / flow-reactor synthesis
- Aerosol / flame spray pyrolysis

CHARACTERIZATION TECHNIQUES

Table 1: Showing different characterization techniques

S.No	Technique	Purpose/Information Provided	Strengths	Common Pitfalls
1.	TEM(Transmission Electron Microscopy) [24]	Size, shape, internal structure, crystallinity	High-resolution imaging at nanometer scale	Sample prep artifacts, electron-beam damage, limited statistical sampling
2.	SEM(Scanning Electron Microscopy) [25]	Surface morphology, topography	3D-like surface visualization	Lower resolution than TEM, conductive coating may alter non-conductive NPs.
3.	DLS(Dynamic Light Scattering)	Hydrodynamic size, polydispersity	Fast measurement in suspension	Sensitive to aggregates, concentration, medium; measures hydrodynamic not actual size
4.	XRD(X-ray Diffraction)	Crystal structure, phase identification, crystallite size	Phase and crystallinity info	Peak broadening from strain vs size, not good for amorphous NPs
5.	FTIR(Fourier-Transform Infrared Spectroscopy) [25]	Surface functional groups, ligand binding	detects chemical bonds	Overlapping peaks, weak signals for small/low-concentration NPs
6.	UV-Vis Spectroscopy [26]	Optical properties, plasmon resonance, aggregation	Quick, non-destructive	Scattering vs absorption ambiguity, limited for non-plasmonic NPs
7.	Zeta Potential [27]	Surface charge, colloidal stability	Predicts dispersion stability	Sensitive to pH, ionic strength; doesn't guarantee long-term stability
8.	XPS(X-ray Photoelectron Spectroscopy) [24]	Surface elemental composition, chemical state	Detailed surface chemistry	Very surface-sensitive (~few nm), charging issues for insulators
9.	EDX/ EDS (Energy-Dispersive X-ray Spectroscopy) [26]	Elemental composition	Coupled with SEM/TEM for spatial info	Overlapping peaks, limited resolution, quantitative analysis needs standards

SURFACE FUNCTIONALIZATION AND MODIFICATION OF NANOPARTICLES

A. Fundamental Role of Surface Ligands

- Organic ligands (e.g., thiols, amines, carboxyls) form a crucial interface between the nanoparticle core and its environment, providing colloidal stability, controlling solubility, and preventing aggregation.
- Ligand design can modulate physicochemical properties, like hydrophobicity, charge, and reactivity, to suit specific applications.
- Multivalent or layer-by-layer ligand shells ("ligand shells") can be used to fine-tune surface functionality and responsiveness.

B. Importance of Surface Functionalization

- Controls nanoparticle interaction with biological and environmental systems.
- Enhances stability, prevents aggregation, and improves dispersion.
- Increases biocompatibility and reduces undesired interactions.
- Enables targeting, controlled release, and improved therapeutic efficiency.

C. Polyethylene Glycol (PEG) Functionalization

- PEGylation is widely used to reduce nonspecific protein binding (opsonization), thereby increasing circulation time in biological systems.
- The conformation of PEG on the nanoparticle surface (brush vs. dense layer) critically affects targeting efficiency: optimally

designed PEG layers can minimize protein corona while maintaining ligand accessibility.

- PEG functionalization is also used in high atomic number nanorods (e.g., Bi_2S_3), improving biocompatibility and stability in physiological media[8]

D. Electrostatic Functionalization / Adsorption

- Surface charge modification (positive or negative) is exploited to bind biomolecules (proteins, nucleic acids) via electrostatic adsorption, enabling reversible and stimuli-responsive loading.
- Layer-by-layer assembly or polymer coatings (e.g., polyelectrolytes) can further stabilize these associations while maintaining functionality.
- Such strategies improve loading efficiency but require careful balancing to prevent aggregation or premature desorption.

E. Targeting via Surface Modification

- Functionalization of metal nanoparticles (e.g., gold) with targeting ligands (antibodies, peptides, aptamers) enhances selective delivery to specific cells or tissues.
- Tailored surface engineering, such as combining PEG shielding with exposed ligand domains, improves targeting while reducing non-specific uptake.
- Surface modification strategies are also being optimized for immune system evasion or immune cell-specific targeting in drug delivery systems[7-9]

F. Carbon Dot-Based Functionalization

- Carbon dots (CDs) are increasingly used for multifunctional surface modification because of their small size, photoluminescence, and biocompatibility.
- CDs can be conjugated to nanoparticle surfaces to give additional properties: fluorescence, biocompatibility, or targeting.
- Their surface chemistries can be tuned for different applications (e.g., sensing, imaging, drug delivery) by modifying functional groups on the carbon dot[9]

G. Advanced and Emerging Functionalization Strategies

- Oleate-capped nanoparticle re-functionalization:** For example, nano-emitters can be re-functionalized using

- methacrylate monomers to improve dispersion in 3D-printable polymers.
- Click-chemistry conjugation:** Bio-orthogonal click reactions (e.g., azide-alkyne) enable precise, stable, and efficient attachment of biomolecules.
- Mixed-charge surface modification:** Using zwitterionic or pseudo-zwitterionic coatings reduces nonspecific protein adsorption and immune cell uptake, improving “stealth” behaviour.

H. Applications Enhanced by Surface Engineering

- Drug delivery:** Functionalization enables the loading of therapeutics (drugs, siRNA), targeting moieties, and controlled release.
- Biomedical imaging and therapy:** Surface-modified metal nanoparticles (e.g., Au, Bi_2S_3) are used in diagnostics (imaging) and radiotherapy enhancing.
- Sensing and diagnostics:** Functionalized surfaces (with carbon dots or charged polymers) improve sensor sensitivity, selectivity, and biostability[9]
- Implant coatings:** Surface modification improves biocompatibility and corrosion resistance in implantable biomaterials.

I. Design Principles & Characterization

- Rational ligand design requires understanding of nanoparticle-ligand and ligand-solvent interfaces[10,11]
- Characterization techniques such as FTIR, XPS, zeta potential, and DLS are essential to confirm successful functionalization and to assess stability in relevant environments.
- Surface modification must balance between functional density (for targeting) and “stealth” properties (to avoid rapid clearance)[10]

J. Biocompatibility and Safety

- Modified surfaces (PEG, charged ligands) can reduce cytotoxicity and immune clearance, improving therapeutic index.⁽¹¹⁾
- Functionalization strategies are being developed to minimize formation of a harmful protein corona and to control biological identity.
- Long-term in vivo stability and potential degradation of surface coatings are active areas of research; functionalization must be validated under physiologically relevant conditions.

K. Surface Chemical Modification

- Nanoparticles can be chemically modified by grafting functional groups (e.g., amines, carboxyls, phosphonates) or silanes, which alters surface charge, hydrophilicity, and reactivity.
- Example: Mixed-charge pseudo-zwitterionic mesoporous silica nanoparticles (MSNs) were engineered using amino- and phosphonate-silane grafting, which significantly reduced protein adsorption and cell uptake for better biocompatibility[11,13]
- Such surface modification helps in tailoring how nanoparticles interact with biological molecules, improving targeting, reducing fouling, and enhancing circulation time.

L. Polymer Coating / Encapsulation

- Polymers like PEG, chitosan, and other biocompatible polymers are often used to coat nanoparticle surfaces to improve stability, prevent aggregation, and provide "stealth" behavior in vivo.
- For example, metal/hydrogel nanocomposites have been modified through PEGylation to improve solubility and reduce nonspecific interactions[12]
- Coating also enables controlled drug loading and release, protecting drugs from premature degradation and providing sustained delivery.

M. Bio-conjugation (Biomolecule Attachment)

- Nanoparticles are frequently modified by conjugating biomolecules such as peptides, antibodies, DNA, or proteins to enable specific targeting and biological functionality.
- A promising strategy is clicking chemistry: for example, a universal click-chemistry approach has been developed to conjugate DNA to silica, silicon, and other nanoparticles, enabling high-density, stable DNA loading.
- This approach permits precise and stable functionalization, which is vital for biosensing, diagnostics, and therapeutic applications.

N. Inorganic and Metal-Based Modifications

- In the context of metallic nanoparticles, functionalization might involve introducing shell layers, silanization, or other surface treatments to improve their utility for drug delivery or targeting.

- For example, **surface modification of metallic nanoparticles** (like gold or iron oxide) has been reviewed for drug targeting: tailoring their surface improves biocompatibility and targeting efficiency.^[13]
- Iron oxide nanoparticles also see extensive research in how their surface is modified to favor medical applications[13]

O. Application-Specific Surface Modification

- In environmental or remediation contexts, modifying nanoparticles on biomass surfaces enhances their catalytic or adsorptive performance for pollutant degradation.
- For up conversion nanoparticles (UCNPs), novel surface modification methods are being developed to make them hydrophilic and stable in aqueous environments, which is essential for their use in bioimaging[12,13]
- In dental implants, nanoparticles are used to modify implant surfaces to promote bone revascularization and regeneration[14,15]

P. Biological Applications and Safety

- Modifying nanoparticle surfaces with biocompatible molecules reduces immunogenicity and improves circulation time in the body. Ly et al. (2024) summarize how different nanoparticle types (polymeric, inorganic) are modified for better performance in drug delivery[15,16]
- Specifically, silver nanoparticles require careful surface modification to balance antimicrobial properties with toxicity; recent research investigates how functionalization can make them safer for biomedical applications[16]
- Rational design of surface modification is complemented by detailed characterization (e.g., using FTIR, XPS, zeta potential) to validate modification and ensure stability.

Q. Design Principles for Modification

- Effective surface modification must consider the trade-off between functional density (for targeting) and colloidal stability: too many ligands may cause steric hindrance, but too few may reduce functionality.
- The modification process should be validated under relevant conditions (e.g., physiological pH, ionic strength) to ensure the modified nanoparticles remain stable and functional in real-world applications.

- Scale-up and reproducibility are key: surface modification strategies that work at lab scale must be optimized for production to maintain consistency of functionalization and performance.

APPLICATION OF NANOPARTICLES

- **Photocatalytic Water Purification**- Nanoparticles (especially semiconductor ones like ZnO) are used to degrade pharmaceutical pollutants(chloroquine) and organic contaminants in water under sunlight via advanced oxidation.
Benefits- Provides eco-friendly water treatment using sunlight; potentially low-cost; efficient removal of persistent organic pollutants.
- **Magnetic Nanomaterials for Targeted Drug Delivery**- Magnetic nanoparticles (e.g., iron oxide) are used in drug delivery systems, allowing for guided delivery via magnetic fields, controlled release, and possibly hyperthermia-based therapies[18,19]
Benefits- Spatial targeting, remote control, reduced systemic toxicity.
- **Clean Energy & Photocatalysis**- Nanoparticles (like metal-oxide nanostructures or MOF-based nanomaterials) are used in photocatalytic processes for clean energy generation and chemical production.
Benefits- Helps in sustainable catalysis, hydrogen production, and environmental remediation.
- **Environmental Remediation / Pollutant Removal**- Nanomaterials are used to remove or neutralize hazardous pollutants from wastewater, including heavy metals, dyes, and organic toxins[20]
Benefits- High surface area, strong reactivity, potential reusability of nanocatalysts.
- **Energy Storage and Conversion**- Nanoparticles are used in batteries, supercapacitors, and energy conversion devices, boosting performance due to their high surface area and tunable properties.
Benefits- Enhanced charge/storage efficiency, scalability with green synthesis.
- **Biomedical and Antimicrobial Nanocomposites**- Combining silver nanoparticles with polymers creates nanocomposites with potent antimicrobial properties suitable for wound healing, coatings, and biosensors.
Benefits- Combines mechanical stability with antimicrobial efficacy, potentially safer and more effective for clinical use.
- **Antimicrobial, Anticancer, and Wound Healing**- Silver nanoparticles (AgNPs) have

potent antimicrobial activity and are used in wound dressings, coatings, and as anti-infective agents[22,23]

- **Environmental Applications**-Nanoparticles synthesized via green (biological) methods are used for environmental remediation, pollution control, and sustainable catalysis. These green-synthesized nanoparticles are also used in biosensing environmental contaminants.⁽²³⁾
- **Biomedical Imaging and Diagnostics**- Quantum dots (QDs) are used for high-resolution bioimaging, fluorescence tagging, and biosensors.More generally, nanoparticles are key in molecular imaging, enabling precision diagnostics.
- **Regenerative Medicine / Tissue Engineering**- Nanotechnology is applied in regenerative medicine, for example, using nanoparticles to enhance tissue growth, scaffold design, or cell signaling.Nanoparticles can also be used as coatings or delivery systems to support stem-cell therapies or wound healing[24]
- **Theranostics (Therapy + Diagnostics)**- Nanoparticles are increasingly used in “theranostic” platforms, combining therapeutic payloads with imaging agents for simultaneous treatment and monitoring.These systems can release drugs in response to stimuli (pH, light, enzymes) while enabling real-time imaging.

7. CHALLENGES AND LIMITATIONS

A. Biological and Safety Challenges

- **Toxicity and dose-dependent adverse effects** — Metal-based and some engineered nanoparticles show size-, shape-, surface-chemistry- and dose-dependent cytotoxicity, oxidative stress, and organ accumulation; understanding long-term toxicity remains incomplete[25]
- **Protein corona formation and altered biological identity** — Immediately upon contact with biological fluids, nanoparticles adsorb proteins and biomolecules forming a “protein corona” that changes cellular uptake, biodistribution, efficacy, and immunogenicity. The corona is highly dynamic and context-dependent (biofluid, species, disease state), complicating translation[26]
- **Immunogenicity and unintended immune modulation** — Surface chemistries intended to improve targeting (e.g., certain ligands or adjuvants) can provoke complement activation or other immune responses, which may reduce safety or therapeutic index. Discussing immune assays

and relevant biomarkers is necessary when reviewing biomedical applications.

B. Characterization, Standardization, and Reproducibility Incomplete or non-standardized characterization

Many studies report limited characterization (e.g., only TEM or DLS) rather than a battery of orthogonal methods (TEM/SEM, DLS, XRD, XPS, FTIR, zeta). Lack of standardized protocols leads to poor reproducibility and conflicting reports of size, charge, and surface chemistry.[27]

•Analytical limitations for complex/biological environments — Techniques used in simple buffers often fail to capture nanoparticle behavior in complex biological matrices (changes in aggregation, corona formation, or dissolution), and in-situ / real-time methods are still emerging but not yet routine.

•Data reporting and metadata gaps — Inconsistent reporting of critical metadata (precise synthesis conditions, storage, dispersion protocol, assay details) prevents meaningful comparison across studies and meta-analysis. Calls for minimum reporting standards are increasing.[28]

C. Manufacturing, Scale-up, and Quality Control

- Scale-up and batch reproducibility** — Methods that work at lab scale (small-batch nanoprecipitation, green biosynthesis, microemulsion) may not translate to industrial production with consistent particle size, surface coverage, or loading; process control and critical process parameters (CPPs) remain active challenges.
- Stability, storage, and shelf-life** — Industrial products must remain stable (no aggregation, loss of functionalization, or payload leakage) for months/years under storage conditions — a requirement many experimental formulations have not yet demonstrated.

D. Limited targeting efficiency and endosomal escape — For drug-delivery and gene-delivery systems (e.g., lipid nanoparticles), cellular uptake does not always translate to functional delivery because of inefficient endosomal escape and intracellular trafficking barriers. New strategies are under study but represent a persistent limitation.

Cost, scalability, and accessibility — Complex surface chemistries, expensive raw materials, or multi-step functionalization may limit affordability and global accessibility of nanoparticle-based products. Consider economic analyses alongside technical performance.

FUTURE PERSPECTIVE AND OUTLOOK

Future directions in nanomedicine are rapidly evolving toward greater personalization, safety, and translational efficiency. Personalized and precision nanomedicine aims to engineer nanoparticles according to an individual's molecular profile — including tumor biomarkers, immune signatures, and microbiome characteristics — to improve therapeutic efficacy while limiting off-target interactions. Parallel to this, artificial intelligence and machine-learning models trained on high-quality, standardized datasets are expected to transform nanoparticle discovery by predicting synthesis outcomes, stability, and toxicity with minimal trial-and-error. Another major focus will be on in-situ and real-time characterization methods capable of monitoring nanoparticle aggregation, dissolution, and protein-corona dynamics directly in complex biological or environmental media, improving the reliability of in-vivo predictions. Sustainability will also guide future development through safe-by- design principles and greener, scalable manufacturing strategies using biological templates and waste-derived materials. Multifunctional theranostic and stimuli-responsive nanoparticles are anticipated to advance toward clinical prototypes, enabling combined imaging and therapy with controlled, on-demand activation. Progress in the field will further depend on regulatory harmonization, robust reporting standards, and the adoption of quality-by-design frameworks to facilitate scale-up and reproducibility. Additionally, precision engineering of the nano-bio interface will allow refined immune modulation for vaccines and regenerative applications. Environmental considerations, including life-cycle assessment and material circularity, will become essential for assessing long-term ecological impacts. Finally, deeper convergence with microfluidics, biosensors, organ-on-chip platforms, and engineered cells will create integrated diagnostic-therapeutic systems that enhance clinical translation[28]

CONCLUSION

Nanoparticles have rapidly evolved into one of the most influential components of modern scientific innovation, with advancements between 2020 and 2025 significantly expanding their technological relevance. Their unique nanoscale characteristics—controllable size, high surface area, and customizable surface chemistry—form the foundation for their diverse applications in medicine, diagnostics, catalysis, environmental remediation, and clean energy systems. Recent progress in green synthesis, microfluidic technologies, hybrid nanostructures, and advanced functionalization strategies has improved nanoparticle

precision, biocompatibility, and performance across these fields. Furthermore, enhanced characterization techniques have deepened our understanding of nanoparticle behavior in complex environments, especially regarding aggregation, dissolution, and protein corona formation. However, despite these strides, key limitations remain. Long-term toxicity, dose-dependent biological effects, and interactions with the immune system continue to pose significant concerns for clinical translation. Industrial-scale manufacturing, reproducibility, and storage stability also challenge commercialization. Variability in reporting standards and incomplete characterization often limit comparability between studies, highlighting the need for harmonized protocols and quality-by-design frameworks. Addressing these issues is essential for transitioning nanoparticles from laboratory innovation to real-world solutions. Looking ahead, the future of nanoparticles lies in personalized nanomedicine, AI-driven material optimization, sustainable and scalable synthesis, and multifunctional theranostic platforms capable of simultaneous diagnosis and therapy. Interdisciplinary convergence with biosensors, organ-on-chip models, and microfluidics will create more effective and reliable nano-enabled systems. Emphasizing environmental safety, regulatory clarity, and life-cycle assessment will further support responsible development. Overall, nanoparticles hold immense potential, and continued advancement in engineering, characterization, and translational science will determine their transformative impact in the coming decades.

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Source of Support: Nil

Conflict of Interest: Nil