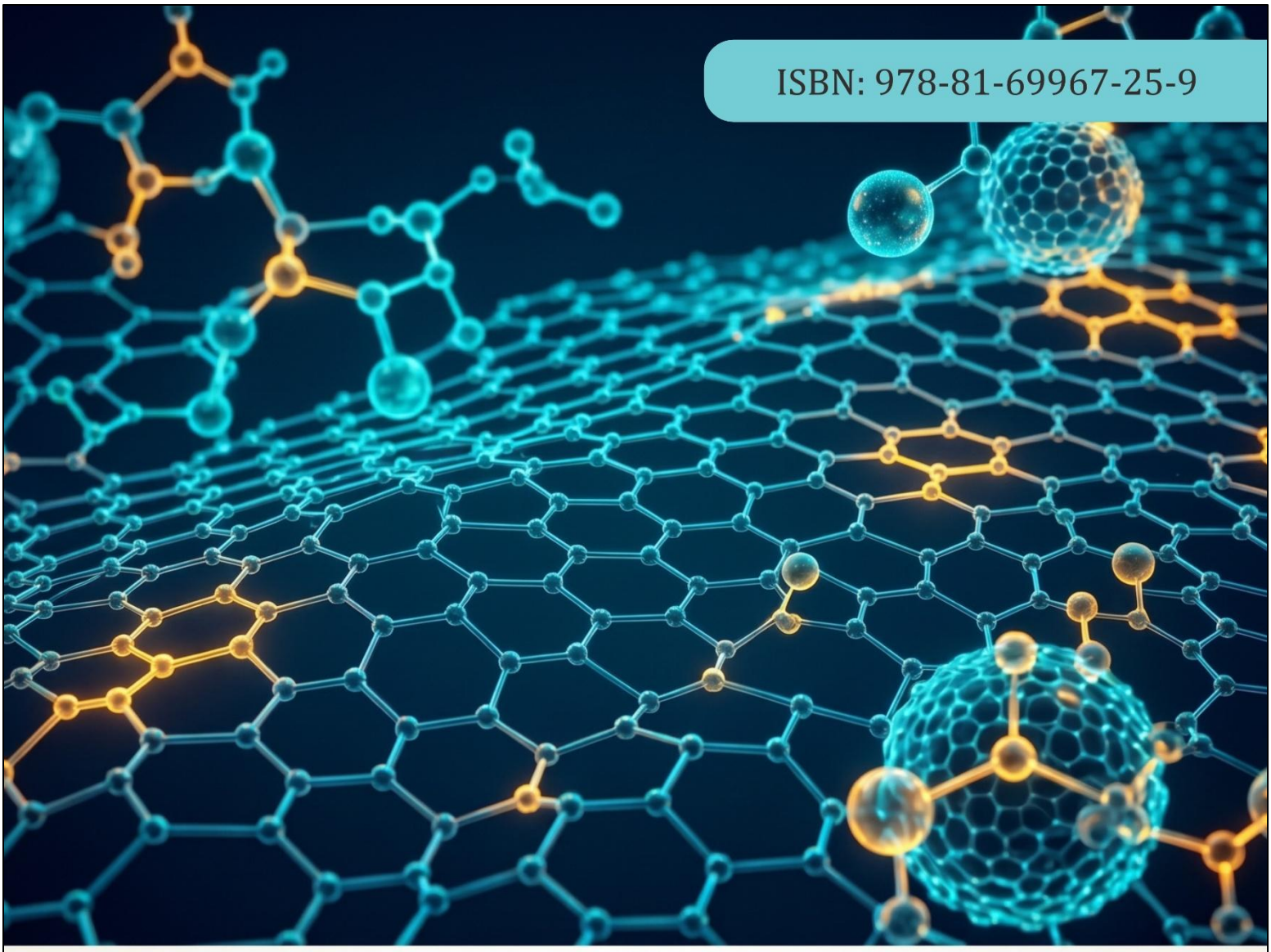
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CURRENT TRENDS OF NANOTECHNOLOGY

in Basic Sciences, Pharmaceutical and Engineering | Volume III

Editors:
Dr. Mohd Ayub Ansari
Prof. (Dr.) Shahanaz Ayub
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Dr. Kok Singh Dadoriya

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PREFACE

Nanotechnology continues to reshape the landscape of scientific research and technological innovation by enabling the design, development, and application of materials and systems at the nanoscale. Its interdisciplinary nature has created remarkable opportunities across basic sciences, pharmaceutical research, and engineering, contributing to advances in healthcare, materials development, environmental protection, and industrial applications. Current Trends of Nanotechnology in Basic Sciences, Pharmaceutical and Engineering – Volume III presents contemporary research perspectives and emerging developments that highlight the expanding scope and significance of nanoscale science.

This volume explores recent advancements in nanomaterials, nanoparticle synthesis, nanocomposites, characterization techniques, and innovative nanoscale applications. In basic sciences, nanotechnology provides new approaches to understanding material properties, molecular interactions, and fundamental scientific processes. In pharmaceutical sciences, developments in nanomedicine, targeted drug delivery, nanoformulations, diagnostics, and therapeutic systems are opening promising avenues for improved healthcare. Engineering applications encompass advanced functional materials, energy storage, electronics, sensors, environmental remediation, and the development of efficient technological systems.

The contributions emphasize the importance of interdisciplinary collaboration, innovative research methodologies, and the translation of fundamental scientific discoveries into practical solutions. They also highlight emerging opportunities and challenges associated with scalability, environmental sustainability, nanomaterial safety, characterization, and responsible technological development. Integrating scientific knowledge with engineering and pharmaceutical applications remains essential for advancing the field.

This book is intended for researchers, academicians, scientists, teachers, students, engineers, and pharmaceutical professionals interested in contemporary nanotechnology research. It aims to facilitate knowledge exchange, encourage interdisciplinary exploration, and provide insights into emerging scientific and technological possibilities.

The editors hope that this volume will serve as a valuable academic resource and inspire further investigation into nanoscale innovations. It aspires to strengthen research collaboration and contribute to scientific advancement, technological progress, improved healthcare, and sustainable development.

- Editors

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Chapter 1

PHARMACEUTICALS APPLICATIONS IN NANOMATERIALS

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INTRODUCTION

Nanotechnology involves the design and manipulation of materials at dimensions where size-dependent physicochemical properties become important. Nanomaterials are commonly associated with structures having dimensions in approximately the 1–100 nm range, although regulatory considerations may extend beyond this range when engineered nanoscale properties are present. The United States Food and Drug Administration (FDA) emphasizes that nanomaterials may exhibit altered physicochemical or biological characteristics compared with conventional materials and therefore require product-specific consideration of quality, safety, and effectiveness (U.S. Food and Drug Administration [FDA], 2014, 2022).

Pharmaceutical science has benefited considerably from nanoscale engineering. Conventional drugs may suffer from poor aqueous solubility, rapid degradation, limited absorption, short biological half-life, nonspecific distribution, or systemic toxicity. Nanomaterials can address some of these limitations by functioning as carriers, protective matrices, solubility-enhancing systems, imaging agents, or therapeutic agents themselves. Their large surface-area-to-volume ratio and ability to be engineered with specific surface characteristics facilitate interactions with biological membranes, proteins, cells, and tissues.

Nanomedicine therefore represents an interdisciplinary field connecting pharmaceutical sciences, materials science, molecular biology, biotechnology, medicine, and engineering. Recent reviews describe applications extending from drug delivery and cancer therapy to nucleic-acid therapeutics, vaccines, imaging, wound management, and regenerative medicine.

MAJOR TYPES OF PHARMACEUTICAL NANOMATERIALS

A variety of nanomaterial platforms have been investigated for pharmaceutical applications.

LIPID-BASED NANOMATERIALS

Liposomes, solid lipid nanoparticles, nanostructured lipid carriers, and lipid nanoparticles are important lipid-based systems. Liposomes consist of phospholipid bilayers surrounding an aqueous compartment and can encapsulate both hydrophilic and hydrophobic compounds. Lipid nanoparticles have become particularly important for nucleic-acid delivery because their composition can protect RNA from degradation and facilitate cellular uptake. A typical lipid nanoparticle contains an ionizable lipid, phospholipid, cholesterol, and a polyethylene glycol

(PEG)-containing lipid. The relative proportions and chemical structures of these components influence particle stability, cellular uptake, biodistribution, and intracellular release (Wu *et al.*, 2024).

POLYMERIC NANOPARTICLES

Polymeric nanoparticles are prepared from biodegradable or biocompatible polymers such as poly (lactic-co-glycolic acid) (PLGA), polycaprolactone, and related materials. Their size, surface charge, morphology, polymer composition, and functional groups can be modified according to the therapeutic objective. These systems can provide sustained or controlled drug release and are especially useful for compounds requiring protection from premature degradation.

Recent research emphasizes the ability to control the size, architecture, charge, and surface functionality of polymeric nanoparticles, allowing their properties to be tailored to particular delivery requirements (Polymeric Nanoparticles for Drug Delivery, 2024).

METALLIC AND METAL OXIDE NANOPARTICLES

Gold, silver, iron oxide, zinc oxide, titanium dioxide, and other inorganic nanoparticles possess distinctive optical, magnetic, catalytic, and antimicrobial properties. Gold nanoparticles have attracted attention in imaging and photothermal therapy, while iron oxide nanoparticles have applications in magnetic resonance imaging and magnetically guided systems. Silver nanoparticles are extensively studied for antimicrobial applications.

DENDRIMERS

Dendrimers are highly branched, three-dimensional macromolecules with a defined architecture and numerous surface functional groups. Their internal cavities can accommodate therapeutic molecules, while their external groups can be modified for targeting or improved biological compatibility. Dendrimers have therefore been investigated for drug, gene, and diagnostic-agent delivery.

MESOPOROUS SILICA NANOPARTICLES

Mesoporous silica nanoparticles contain ordered pores that provide a high internal surface area and substantial drug-loading capacity. Their surfaces can be chemically functionalized to control interactions with drugs and biological molecules. Stimuli-responsive silica systems have been investigated for pH-, temperature-, enzyme-, and light-responsive drug release.

NANOGELS AND NANOCRYSTALS

Nanogels are nanosized cross-linked polymeric networks capable of incorporating substantial amounts of water and therapeutic molecules. Nanocrystals, in contrast, consist predominantly of the drug itself in nanosized crystalline form. Drug nanocrystals can increase dissolution rate and apparent solubility, making them useful for poorly water-soluble active pharmaceutical ingredients.

NANOMATERIALS IN DRUG DELIVERY

Drug delivery is one of the most extensively investigated pharmaceutical applications of nanomaterials. The basic objective is to transport an active pharmaceutical ingredient to the desired biological site while maintaining adequate drug concentration and reducing unwanted exposure.

Nanocarriers can improve drug delivery through several mechanisms:

[1]. Enhancement of aqueous solubility;
[2]. Protection against enzymatic or chemical degradation;
[3]. Controlled and sustained drug release;
[4]. Modification of pharmacokinetic behaviour;
[5]. Improved cellular uptake;
[6]. Tissue-specific or cell-specific targeting;
[7]. Co-delivery of multiple therapeutic agents; and
[8]. Delivery of biological macromolecules.

The physicochemical properties of nanomaterials influence their interaction with biological systems. Particle size, surface charge, shape, composition, hydrophobicity, and surface functionalization can affect circulation time, protein adsorption, cellular uptake, and tissue distribution (Egwu *et al.,* 2024).

CONTROLLED AND SUSTAINED DRUG RELEASE

Conventional formulations may release a drug relatively rapidly after administration. Nanocarriers can act as reservoirs from which the active compound is released gradually. This can reduce dosing frequency and maintain therapeutic concentrations for longer periods.

Polymeric nanoparticles are particularly useful for controlled release because degradation of the polymer matrix can be adjusted through polymer composition, molecular weight, crystallinity, and particle characteristics. Lipid systems can similarly regulate drug release through lipid composition and structural organization.

TARGETED DRUG DELIVERY

Targeting strategies can be classified broadly as passive and active targeting. Passive targeting exploits physiological characteristics of diseased tissues. In cancer, for example, differences in vascular architecture and tissue permeability may facilitate nanoparticle accumulation in tumours. Active targeting involves attaching ligands such as antibodies, peptides, proteins, sugars, or other recognition molecules to the nanoparticle surface. These ligands may interact with receptors expressed at elevated levels on specific cells. However, targeting should not be regarded as an automatic property of every nanoparticle. Biological barriers, protein corona formation, heterogeneous receptor expression, clearance by the mononuclear phagocyte system, and variability between patients can influence actual targeting performance.

PHARMACEUTICAL APPLICATIONS IN CANCER THERAPY

Cancer is one of the major areas in which nanomaterials have been extensively investigated. Conventional chemotherapy may damage healthy tissues because anticancer drugs can distribute throughout the body rather than exclusively within malignant tissues.

Nanoparticles can potentially improve the therapeutic index of anticancer drugs by modifying their distribution, protecting them from premature degradation, and facilitating accumulation or uptake at tumour sites. Nanotechnology-based systems have been investigated for chemotherapy, immunotherapy, gene therapy, photothermal therapy, photodynamic therapy, and combination treatment (Al-Thani *et al.,* 2024).

NANOCARRIER-BASED CHEMOTHERAPY

Drugs such as poorly soluble cytotoxic compounds can be incorporated into lipid or polymeric nanoparticles. Encapsulation can alter pharmacokinetics and potentially reduce exposure of normal tissues. Liposomes are particularly important in pharmaceutical oncology because they can encapsulate therapeutic molecules and modify their distribution. Polymeric systems offer another route for prolonged release and combination therapy.

PHOTOTHERMAL THERAPY

Certain nanoparticles absorb light and convert electromagnetic energy into heat. Gold nanoparticles are prominent examples investigated for photothermal cancer therapy. When appropriately localized, light-induced heating can damage malignant cells.

PHOTODYNAMIC THERAPY

Nanomaterials can also carry photosensitizers that generate reactive oxygen species after irradiation. These reactive molecules can damage tumour cells and intracellular structures.

CANCER THERANOSTICS

The combination of diagnosis and therapy within a single Nano platform is known as **theranostics**. Nanoparticles can simultaneously carry therapeutic agents and imaging components, facilitating visualization of disease and treatment response. Recent reviews describe applications involving MRI, CT, fluorescence imaging, photothermal therapy, and targeted drug delivery (Al-Thani *et al.,* 2024).

NANOMATERIALS FOR GENE AND NUCLEIC-ACID DELIVERY

Nucleic-acid therapeutics includes DNA, messenger RNA (mRNA), small interfering RNA (siRNA), microRNA, and other RNA-based molecules. Their pharmaceutical application is limited by instability, enzymatic degradation, poor cellular penetration, and difficulty crossing biological membranes. Nanomaterials can protect nucleic acids from extracellular degradation and facilitate cellular internalization.

LIPID NANOPARTICLES

Lipid nanoparticles represent one of the most significant recent developments in pharmaceutical nanotechnology. Their clinical importance increased substantially following the successful use of LNPs for mRNA vaccines.

The lipid components help encapsulate and protect mRNA, facilitate cellular uptake, and promote intracellular release. Current research is expanding toward cancer vaccines, genetic disorders, immunotherapy, and delivery to tissues beyond the liver (Wang *et al.,* 2024; Kim *et al.,* 2024). An important challenge is that many LNP formulations preferentially accumulate in the liver. Consequently, researchers are investigating approaches for organ-selective delivery to tissues outside the liver (Nele *et al.,* 2024; Wu *et al.,* 2024).

GENE SILENCING

Nanocarriers can transport siRNA to target cells. Once internalized, siRNA can participate in RNA interference and reduce expression of selected genes. This strategy has potential applications in cancer, metabolic disorders, inflammatory diseases, and genetic conditions.

Nanoparticle-mediated nucleic-acid delivery therefore represents an important transition from traditional small-molecule pharmacotherapy toward molecularly targeted treatment.

NANOMATERIALS IN VACCINE DEVELOPMENT

Nanotechnology has contributed to modern vaccine development by improving antigen delivery, immune stimulation, and nucleic-acid protection.

Lipid nanoparticles are particularly important for mRNA vaccine delivery because mRNA is inherently susceptible to degradation. Encapsulation within lipid nanoparticles protects the nucleic acid and facilitates its delivery into cells.

Recent research is examining LNPs for infectious disease vaccines beyond COVID-19, as well as cancer vaccines and therapeutic immunization. The technology is also being optimized through modification of lipid chemistry, particle composition, tissue targeting, and manufacturing approaches (Zhang *et al.,* 2024; Wu *et al.,* 2024).

Nevertheless, LNP formulations may stimulate innate immune responses, and their immunogenicity and reactogenicity require careful assessment. The composition of the nanoparticle and chemical structure of its lipid components can influence these responses (Sharma *et al.,* 2024).

ANTIMICROBIAL AND ANTI-INFECTIVE APPLICATIONS

Antimicrobial resistance has increased the need for alternative approaches to infection management. Nanomaterials can contribute to antimicrobial therapy through direct antimicrobial activity or by serving as delivery vehicles for antimicrobial drugs.

Silver nanoparticles, for example, have demonstrated antimicrobial activity against a broad range of microorganisms. Other metal and metal oxide nanoparticles can generate reactive oxygen species or interact with microbial membranes.

Nanocarriers can also deliver antibiotics in a controlled manner and potentially improve drug concentration at infection sites. This approach may be useful in treating biofilm-associated infections, in which bacteria can exhibit increased resistance to conventional antimicrobial treatment. Nanomaterial-based wound dressings are an emerging application. Recent studies have examined metallic nanoparticles, metal oxides, MXene materials, and metal-organic frameworks for antimicrobial activity, drug delivery, inflammation control, and tissue regeneration (Faghani *et al.,* 2024).

NANOMATERIALS IN WOUND HEALING AND REGENERATIVE MEDICINE

Wound healing involves inflammation, cell proliferation, extracellular matrix formation, angiogenesis, and tissue remodelling. Nanomaterials can influence several of these processes.

Nanostructured wound dressings can act as physical barriers while simultaneously delivering antibiotics, anti-inflammatory agents, growth factors, or other therapeutic molecules. Some nanomaterials possess intrinsic antimicrobial activity, whereas others function primarily as drug reservoirs. Two-dimensional nanomaterials such as graphene derivatives, MXenes, black phosphorus, and related materials have been investigated for wound healing because of their distinctive surface, mechanical, electrical, and biological characteristics (Advancements in Employing Two-Dimensional Nanomaterials, 2024).

The integration of nanomaterials with hydrogels and polymeric scaffolds may further support tissue regeneration by providing a three-dimensional environment for cellular growth.

NANOMATERIALS IN DIAGNOSTIC IMAGING AND THERANOSTICS

Nanomaterials have important applications beyond drug delivery. Their magnetic, optical, electrical, and catalytic characteristics can be exploited for diagnostic purposes.

Iron oxide nanoparticles have been investigated as magnetic imaging agents. Gold nanoparticles can provide strong optical signals, while quantum dots have been investigated for fluorescence-based imaging.

The combination of imaging and therapy is particularly attractive because it may enable clinicians to monitor disease while administering treatment. Nanomaterials may therefore act as multifunctional platforms carrying drugs, imaging probes, targeting molecules, and stimuli-responsive components.

Such systems could contribute to personalized medicine by enabling treatment strategies based on individual disease characteristics. However, clinical translation requires careful assessment of toxicity, stability, biodistribution, clearance, and manufacturing reproducibility.

NANOMATERIALS FOR IMPROVING BIOAVAILABILITY

Poor aqueous solubility is a major challenge during pharmaceutical development. A drug with low solubility may exhibit inadequate dissolution and absorption despite having pharmacological activity.

Nanocrystals can increase dissolution rates by reducing drug particle size and increasing effective surface area. Lipid-based nanoparticles and polymeric nanocarriers can also improve apparent solubility by incorporating hydrophobic compounds within suitable matrices.

Nanotechnology may consequently reduce the amount of drug required to achieve a particular therapeutic effect. FDA guidance recognizes potential nanotechnology-related improvements such as increased bioavailability and changes in drug potency or dosage requirements, while emphasizing that these effects must be evaluated for the individual product.

NANOMATERIALS IN BRAIN DRUG DELIVERY

The blood–brain barrier (BBB) restricts the passage of many therapeutic compounds into the central nervous system. Consequently, treatment of neurological diseases remains a major pharmaceutical challenge.

Nanoparticles are being investigated as potential carriers for drugs, proteins, peptides, and nucleic acids intended for neurological applications. Surface modification with appropriate ligands may facilitate interactions with receptors involved in cellular transport across the BBB.

Potential applications include Alzheimer's disease, Parkinson's disease, brain tumours, and other neurological disorders. Nevertheless, achieving reproducible and clinically meaningful transport across the human BBB remains challenging.

NANOMATERIALS IN OPHTHALMIC DRUG DELIVERY

Ocular delivery is another area where nanotechnology may overcome conventional pharmaceutical limitations. Topically administered drugs can be rapidly removed by blinking, tear production, and nasolacrimal drainage.

Nanoparticles, nanogels, liposomes, and related systems can improve drug retention on the ocular surface and potentially provide sustained release. These systems have been investigated for treatment of infections, inflammation, glaucoma, and posterior-segment disorders.

Nanocarriers may also reduce the frequency of administration, thereby improving treatment adherence.

CONCLUSION

Nanomaterials have become important tools in modern pharmaceutical science because their size-dependent properties provide opportunities to modify drug delivery, bioavailability, pharmacokinetics, cellular uptake, and therapeutic specificity. Liposomes, lipid nanoparticles, polymeric nanoparticles, dendrimers, nanocrystals, metallic nanoparticles, mesoporous silica, nanogels, and emerging two-dimensional materials each provide distinct pharmaceutical possibilities.

The successful application of lipid nanoparticles for nucleic-acid delivery has demonstrated the clinical potential of nanotechnology and has accelerated research into vaccines, gene therapies, cancer treatment, and immunotherapy. At the same time, nanomaterials are being investigated for antimicrobial treatment, wound healing, imaging, ophthalmic delivery, neurological therapy, and regenerative medicine.

Future development should focus on designing nanomaterials that combine therapeutic effectiveness with predictable pharmacokinetics, acceptable toxicity, scalable manufacturing, and long-term stability. Rather than treating nanotechnology simply as a new drug carrier technology, pharmaceutical development increasingly views nanomaterials as multifunctional platforms capable of integrating diagnosis, targeting, controlled release, and therapy. Continued collaboration among pharmaceutical scientists, biologists, materials scientists, clinicians, engineers, and regulatory authorities will be essential for converting promising laboratory discoveries into safe, effective, and clinically useful nanomedicines.

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Chapter
2

SUSTAINABLE AND GREEN NANOTECHNOLOGY

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ABSTRACT

Green nanotechnology and sustainable nanotechnology are emerging fields that combine nanoscale science with environmental protection, resource conservation, and sustainable development. Nanotechnology involves the design and application of materials with dimensions typically ranging from 1 to 100 nanometers. At this scale, materials exhibit distinctive physical, chemical, optical, electrical, and biological properties that enable applications in electronics, healthcare, agriculture, renewable energy, and environmental remediation. However, conventional nanomaterial synthesis may require hazardous chemicals, energy-intensive processes, and generate potentially harmful waste. Green nanotechnology seeks to overcome these challenges by employing environmentally benign reagents, renewable biological resources, and energy-efficient synthesis methods. Sustainable nanotechnology extends this approach by evaluating the environmental, economic, and social impacts of nanomaterials throughout their life cycle. This chapter discusses the fundamental principles of nanotechnology, the environmental and health risks associated with conventional synthesis, green synthesis approaches, and the importance of life-cycle assessment. It also highlights the challenges and future prospects of developing safer, resource-efficient, and environmentally responsible nanotechnologies.

KEYWORDS: Green Nanotechnology, Nanomaterials, Green Synthesis, Sustainability, Environmental Safety, Life-Cycle Assessment.

INTRODUCTION

Nanotechnology is an interdisciplinary field concerned with the design, synthesis, characterization, and application of materials at the nanoscale, generally between 1 and 100 nanometers. At this scale, materials may exhibit properties that differ considerably from those of their bulk counterparts. These differences arise partly from the increased surface-area-to-volume ratio and, in some materials, quantum-size effects. Consequently, nanomaterials may demonstrate enhanced chemical reactivity, modified optical behavior, improved catalytic performance, and distinctive electrical and mechanical properties (Nel *et al.,* 2006).

The distinctive characteristics of nanomaterials have expanded their applications across numerous scientific and industrial sectors. In electronics and photonics, nanomaterials contribute to the development of miniaturized devices, advanced sensors, and improved

semiconductor technologies. In renewable energy, they are investigated for applications in solar cells, batteries, fuel cells, and catalytic energy conversion. Environmental applications include water purification, pollutant detection, wastewater treatment, and catalytic degradation of contaminants. In medicine, nanotechnology supports drug delivery, diagnostic imaging, biosensing, and the development of advanced therapeutic materials. Agricultural applications include nutrient-delivery systems, nanosensors, and formulations designed to improve resource efficiency.

Despite these advantages, the production and use of nanomaterials raise concerns about chemical consumption, energy requirements, waste generation, and possible adverse effects on living organisms. Responsible nanotechnology therefore requires approaches that integrate scientific innovation with environmental protection and human safety.

ENVIRONMENTAL AND HEALTH RISKS OF CONVENTIONAL NANOMATERIAL SYNTHESIS

Conventional nanomaterial synthesis includes physical and chemical methods such as sol–gel processing, chemical vapor deposition, hydrothermal synthesis, solvothermal reactions, and flame pyrolysis. Although these methods can provide useful control over particle size, shape, composition, and surface properties, they may involve hazardous precursors, strong reducing agents, organic solvents, elevated temperatures, or high pressures.

The use of such materials and conditions can increase energy consumption and produce chemical residues, contaminated wastewater, and other potentially hazardous by-products. Additional environmental burdens may arise from raw-material extraction, purification, transportation, and waste management. Consequently, the environmental performance of nanomaterial production depends not only on the final product but also on the resources and processes required to manufacture it.

Engineered nanomaterials may also present risks when released into terrestrial or aquatic environments. Their environmental behavior depends on characteristics such as particle size, shape, surface chemistry, concentration, aggregation, and chemical transformation. Exposure may affect microorganisms, plants, aquatic organisms, and other components of ecosystems. For example, silver nanoparticles possess antimicrobial properties that can affect beneficial microorganisms under certain exposure conditions. Some engineered nanomaterials have also been associated with oxidative stress and other biological responses in experimental systems (Nel *et al.*, 2006).

However, the presence of nanoparticles does not automatically imply that a material is harmful. Toxicity varies with the material, dose, exposure route, duration, and surrounding environmental conditions. Understanding these factors is essential for evaluating potential risks and developing appropriate safety measures. A comprehensive assessment should consider exposure during manufacturing, use, recycling, and disposal rather than focusing exclusively on the properties of the finished material (Alvarez *et al.*, 2024).

GREEN NANOTECHNOLOGY: CLEANER AND SAFER APPROACHES

Green nanotechnology applies the principles of green chemistry and sustainable engineering to the design, synthesis, use, and disposal of nanomaterials. Its central objective is to maintain the functional advantages of nanotechnology while reducing hazardous chemical inputs, energy consumption, waste generation, and potential harm to human health and the environment.

Green chemistry emphasizes the prevention of pollution at its source rather than relying exclusively on waste treatment after production. It promotes safer chemical substances, efficient resource utilization, reduced energy requirements, and the development of products that minimize environmental impacts (Anastas & Warner, 1998).

BIOLOGICAL SYNTHESIS OF NANOMATERIALS

Biological synthesis is an important approach in green nanotechnology. It uses renewable biological materials, including plant extracts, algae, bacteria, fungi, enzymes, and naturally occurring biomolecules, to facilitate nanoparticle formation and stabilization.

Plant extracts may contain polyphenols, flavonoids, sugars, proteins, and other compounds capable of participating in reduction and stabilization reactions. These substances can help convert metal ions into nanoparticles and influence their growth and surface characteristics. Depending on the synthesis system, biological materials may reduce the need for conventional chemical reducing agents and synthetic stabilizers.

Microorganisms and microbial products can also support nanoparticle formation through biological processes. Such methods have attracted research interest because they may operate under comparatively mild conditions and utilize renewable resources. Nevertheless, the properties of biologically synthesized nanoparticles depend on factors such as the composition of the biological material, pH, temperature, reaction time, and precursor concentration.

Biological synthesis should not automatically be considered environmentally harmless. The cultivation or collection of biological resources, purification requirements, energy consumption, and toxicity of the resulting nanoparticles must also be evaluated.

ENERGY-EFFICIENT SYNTHESIS METHODS

Green nanotechnology also encourages the adoption of synthesis techniques that reduce energy requirements and improve material efficiency. Microwave-assisted synthesis, ultrasonic processing, and mechanochemical methods may shorten reaction times or reduce the need for high-temperature processing in suitable systems.

The environmental advantages of these approaches depend on the particular materials and operating conditions. Energy consumption, solvent requirements, product yield, purification, and equipment demands should be considered when comparing alternative synthesis routes.

ADVANTAGES OF GREEN SYNTHESIS

Green synthesis can offer several potential benefits, including reduced dependence on hazardous reagents, improved utilization of renewable resources, lower waste generation, and opportunities to use agricultural or biological by-products as raw materials. Naturally derived surface compounds may also influence nanoparticle stability and interactions with biological

systems. However, these advantages must be demonstrated through systematic measurements. Comparisons of chemical inputs, energy intensity, product yield, waste production, and environmental impacts are more reliable indicators of sustainability than simply labeling a synthesis method as green (García-Quintero & Palencia, 2021).

SUSTAINABLE NANOTECHNOLOGY AND LIFE-CYCLE ASSESSMENT

Sustainable nanotechnology extends beyond cleaner synthesis to consider the overall environmental, economic, and social consequences of nanomaterials. It adopts a life-cycle perspective, examining impacts from raw-material extraction and processing through manufacturing, transportation, product use, recycling, and final disposal.

Life-cycle assessment (LCA) is a systematic methodology for evaluating environmental impacts associated with a product or process throughout its life cycle. International standards ISO 14040 and ISO 14044 provide principles and requirements for conducting such assessments (International Organization for Standardization, 2006, 2006).

For nanomaterials, LCA can help identify energy-intensive production stages, resource consumption, emissions, waste streams, and potential environmental trade-offs. It can also compare alternative synthesis methods and determine whether the benefits of a nano-enabled product outweigh the burdens associated with its production and disposal.

For example, a nanomaterial used in water purification may improve contaminant removal and reduce the need for certain treatment chemicals. However, its overall environmental benefit also depends on the energy required for synthesis, the durability of the purification system, the possibility of nanoparticle release, and the methods used to manage spent materials.

APPLICATIONS OF GREEN AND SUSTAINABLE NANOTECHNOLOGY

Green and sustainable nanotechnology has potential applications in several sectors.

- **Environmental protection:** Nanomaterials are being investigated for water purification, wastewater treatment, pollutant detection, and the removal or transformation of contaminants. Their effectiveness and environmental safety must be evaluated together, particularly where materials may enter natural ecosystems (Alvarez *et al.*, 2024).
- **Renewable energy:** Nanostructured materials can contribute to the development of solar-energy technologies, batteries, fuel cells, and catalysts. Improving their durability, manufacturing efficiency, and recyclability may strengthen their contribution to sustainable energy systems.
- **Agriculture:** Nano-enabled fertilizers, sensors, and crop-protection systems may offer opportunities to improve nutrient delivery and monitor agricultural conditions. Their adoption requires careful evaluation of soil accumulation, impacts on beneficial organisms, and potential movement into food chains.
- **Healthcare:** Nanomaterials support research into drug delivery, medical imaging, diagnostics, and therapeutic technologies. Sustainable development in this sector requires attention to biocompatibility, exposure, manufacturing waste, and the safe handling of materials throughout their life cycles.

- **Industrial manufacturing:** Green nanotechnology can encourage resource-efficient catalysts, improved coatings, and functional materials with longer service lives. The environmental value of these applications depends on their performance relative to conventional alternatives and the impacts associated with their production and end-of-life management.

CHALLENGES AND FUTURE PERSPECTIVES

Despite significant progress, several challenges limit the widespread adoption of green and sustainable nanotechnology.

- **Standardization:** Differences in synthesis procedures and characterization methods can make it difficult to reproduce results and compare studies. Consistent reporting of particle size, morphology, composition, surface properties, yield, and process conditions is essential.
- **Regulation and safety:** Uncertainties concerning nanoparticle exposure, environmental transformation, long-term effects, and waste disposal highlight the need for appropriate safety assessment and regulatory oversight.
- **Industrial scalability:** Biological synthesis may encounter challenges involving batch-to-batch variability, reaction control, purification, and large-scale production. Industrial implementation requires reliable methods that maintain material quality while controlling costs and environmental impacts.
- **Environmental fate:** More research is needed to understand nanoparticle persistence, transport, aggregation, transformation, and interactions with organisms under realistic environmental conditions.
- **Sustainability evaluation:** Quantitative assessments should integrate life-cycle impacts, resource use, energy demand, waste generation, and relevant safety indicators. Renewable or biological raw materials alone do not guarantee that a process is sustainable (García-Quintero & Palencia, 2021).

Future research should prioritize safer-by-design nanomaterials, reproducible green synthesis protocols, renewable feedstocks, resource recovery, and improved recycling and waste-management strategies. Interdisciplinary collaboration among chemists, biologists, environmental scientists, engineers, toxicologists, and policymakers will be important for translating laboratory advances into responsible industrial applications.

CONCLUSION

Green nanotechnology and sustainable nanotechnology provide complementary approaches to responsible nanoscale innovation. Green nanotechnology emphasizes cleaner synthesis, safer reagents, energy efficiency, and reduced waste, whereas sustainable nanotechnology evaluates broader environmental, economic, and social impacts throughout the life cycle of materials and products. Although nanomaterials offer important opportunities in healthcare, agriculture, energy, electronics, and environmental remediation, their benefits must be balanced against potential risks and resource requirements. Biological synthesis, energy-efficient processing, life-

cycle assessment, and safer material design can help improve the sustainability of nanotechnology. Continued research, standardized characterization, effective regulation, and reliable environmental assessment will be essential to ensure that future developments contribute meaningfully to environmental protection and sustainable development.

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Chapter 3

NANO-APPLICATIONS IN SOIL, RHIZOSPHERE, PLANT PROTECTION, AND STRESS MANAGEMENT

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INTRODUCTION

Nanotechnology involves the design and application of materials with dimensions generally within the nanoscale range, commonly about 1–100 nm in at least one dimension. At this scale, materials can display physicochemical properties that differ substantially from their bulk forms. High surface-area-to-volume ratio, adjustable surface chemistry, optical behaviour, magnetic properties and the ability to interact with biological molecules make nanomaterials valuable in biotechnology, agriculture and environmental science. The source document identifies metallic nanoparticles, metal oxide nanoparticles, carbon-based nanostructures, lipid-based carriers and polymeric nanoparticles among the major classes of nanomaterials investigated for biological applications.

Agriculture is an important area in which these properties can be exploited. Crop productivity depends not only on the supply of nutrients but also on soil quality, root–microbe interactions, protection against pathogens and insects, and the ability of plants to tolerate drought, salinity, temperature extremes and toxic substances. Conventional fertilizers and pesticides can be inefficient when nutrients or active compounds are lost before reaching their intended targets. Nano-enabled formulations offer possibilities for improving delivery, regulating release and increasing the effectiveness of agricultural inputs. The uploaded source specifically describes nanofertilizers as formulations containing nutrients in nanoscale forms or delivered through nanostructured carriers, and nanopesticides as systems that can protect active ingredients and regulate their release.

The agricultural use of nanomaterials should nevertheless be considered as an emerging technology rather than a universally risk-free solution. Their behaviour depends on particle size, concentration, surface characteristics, chemical composition and environmental conditions. Excessive exposure can produce oxidative stress in plant cells, while released nanoparticles may interact with soil microorganisms and other non-target organisms. Therefore, agricultural nanotechnology requires both technological development and careful environmental assessment.

NANO-APPLICATIONS IN SOIL

Soil is the principal medium that supplies plants with water and mineral nutrients and provides habitat for a diverse microbial community. Nanotechnology can contribute to soil management

through improved nutrient delivery, controlled release of agrochemicals, remediation of contaminated soils and monitoring of soil-associated pollutants.

NANOFERTILIZERS AND NUTRIENT MANAGEMENT

Nanofertilizers are among the most investigated agricultural applications of nanotechnology. They may contain nutrients in nanoscale formulations or use nanostructured carriers to transport essential elements. Zinc oxide nanoparticles and nanoscale hydroxyapatite are examples mentioned in the source material. Because nanostructured materials provide a large surface area, nutrients can be associated with carrier surfaces and, in suitable formulations, released in a controlled manner. This approach may improve nutrient-use efficiency and reduce losses through leaching or other pathways.

The concept of controlled release is particularly important. Conventional fertilizer nutrients can become unavailable because of fixation, leaching, volatilization or chemical transformation. A nano-enabled carrier can be designed to modify the timing and rate at which nutrients become available. Such delivery does not automatically guarantee improved plant nutrition; effectiveness depends on particle properties, soil chemistry, crop species and application rate. Therefore, field validation is necessary before a formulation is considered broadly useful.

SOIL REMEDIATION

Nanomaterials are also relevant to the remediation of contaminated soils. Their high surface area provides numerous sites for adsorption or interaction with contaminants. Iron-based nanoparticles and other nanostructured materials are being investigated for immobilizing or transforming pollutants. The environmental section of the source describes iron oxide nanoparticles that can bind toxic metal ions and facilitate their removal by magnetic separation in water treatment; related principles can inform research on contaminated soil systems.

Nanomaterials may be used either to reduce the mobility of a contaminant or to promote its removal or transformation. For example, surface-modified nanoparticles can interact with specific metal ions. However, remediation must be designed carefully because the introduced material itself becomes part of the soil environment. Its persistence, movement and effects on microorganisms must therefore be evaluated.

SOIL MICROBIAL COMMUNITY

The soil contains bacteria, fungi and other microorganisms that participate in decomposition, nutrient cycling and plant growth. Nanomaterials released into soil may interact with these organisms. At appropriate concentrations, some materials may influence microbial activity, whereas excessive exposure can have undesirable effects. The source document emphasizes that environmental risks can arise when nanoparticles interact with soil microorganisms, aquatic organisms and other living systems. Thus, maintaining beneficial soil biological activity is an important consideration in nano-enabled soil management.

NANO-APPLICATIONS IN THE RHIZOSPHERE

The rhizosphere is the narrow zone of soil influenced by plant roots. It is a highly active environment in which roots, soil particles, nutrients and microorganisms interact continuously.

Because the rhizosphere directly controls many aspects of nutrient acquisition and plant health, it represents an important target for precision agriculture.

TARGETED NUTRIENT DELIVERY

Nano-carriers can potentially concentrate nutrients around the root zone and regulate their release. Instead of allowing a nutrient to disperse rapidly throughout the soil, a suitably designed carrier may provide a more controlled supply near roots. This can be especially relevant for micronutrients required in small quantities but essential for plant metabolism.

ROOT GROWTH AND NUTRIENT UPTAKE

Certain nanomaterials, when used at appropriate concentrations, have been investigated for their effects on root development and nutrient uptake. Improvements may arise from changes in nutrient availability, interactions with root surfaces or stimulation of physiological processes. However, plant responses are concentration-dependent. A material that is beneficial at a low concentration can become phytotoxic at a higher concentration.

INTERACTION WITH RHIZOSPHERE MICROORGANISMS

Beneficial rhizosphere microorganisms can contribute to nutrient cycling and plant growth. Nano-enabled agricultural systems therefore need to distinguish between target pathogens and useful microbial populations. Nanomaterials with antimicrobial activity may suppress undesirable organisms, but indiscriminate antimicrobial activity could also disturb beneficial microorganisms. Consequently, future formulations should aim for greater selectivity and environmentally compatible concentrations.

NANO-ENABLED DELIVERY OF BIOLOGICAL MOLECULES

The general principle of nanocarriers—protecting a biological molecule and transporting it to a desired site—can also be considered for plant biotechnology. Nano-enabled systems may be investigated for delivery of bioactive molecules, nucleic acids and other compounds to plant tissues or the root environment. Such approaches remain dependent on the ability of the carrier to remain stable, reach the target and release its cargo under suitable conditions.

NANO-APPLICATIONS IN PLANT PROTECTION

Plant protection is a major application area for nanotechnology because crop losses can result from fungal, bacterial and viral pathogens as well as insect pests. Nano-formulations may improve the stability, delivery and controlled release of active compounds.

NANOPESTICIDES

Nanopesticides can use nanomaterials as carriers for pesticide molecules. The source document notes that these systems can protect active ingredients from premature degradation and allow their release to be regulated. Improved stability and controlled release may increase the period during which an active ingredient remains available and may potentially reduce the quantity or frequency of application under appropriate conditions.

Nano-formulation can also modify the physical properties of an agricultural chemical. For poorly soluble compounds, a nanoscale formulation may increase effective dispersion. A carrier can improve adhesion to a plant surface or help protect the active ingredient from

environmental degradation. These advantages should be assessed experimentally rather than assumed for every nanoparticle system.

NANO-FUNGICIDES AND ANTIMICROBIAL NANOPARTICLES

Metallic and metal oxide nanoparticles have attracted attention because of their antimicrobial properties. Silver nanoparticles, for example, can interact with microbial surfaces, disturb membrane organization and promote oxidative damage. The source material describes these mechanisms in relation to antimicrobial applications. Similar principles have encouraged research into nanoparticle-based protection against plant-associated microorganisms.

Copper-, zinc- and silver-containing nanomaterials have been investigated for antimicrobial applications, but their concentration and exposure conditions are critical. A formulation that suppresses a pathogen may also affect beneficial microorganisms or plant cells if applied excessively. Therefore, selectivity, dose and persistence are important factors in the development of nano-fungicides.

NANO-BASED DISEASE DETECTION

Early identification of disease is essential for effective crop management. Nanomaterial-based biosensors can help detect pathogen-associated molecules at low concentrations. Gold nanoparticles, for example, can be incorporated into diagnostic systems that generate visible colour changes when specific biological targets are recognized. Such approaches can support rapid diagnosis before symptoms become severe.

Nanostructured sensing surfaces can provide a large area for immobilizing recognition molecules such as antibodies, enzymes or nucleic acids. The resulting interaction can be converted into an optical or electrical signal. This provides a basis for portable and potentially rapid plant disease diagnostics.

ADVANTAGES FOR INTEGRATED PLANT PROTECTION

The combination of nano-pesticides and nano-sensors could support a more targeted plant-protection strategy. Sensors can identify a pathogen or stress condition, while a controlled-release formulation can deliver an appropriate active ingredient. Such precision approaches may reduce unnecessary chemical applications and contribute to more efficient crop management, although their practical use requires appropriate field testing and regulatory evaluation.

NANO-APPLICATIONS IN STRESS MANAGEMENT

Plants experience numerous abiotic stresses, including drought, salinity, high and low temperature, heavy-metal exposure and nutrient imbalance. These stresses can disturb photosynthesis, water relations, membrane stability and cellular metabolism. Nanomaterials are being investigated as tools that may improve plant responses to some of these adverse conditions.

DROUGHT STRESS

Water deficiency can reduce cell expansion, photosynthesis and nutrient transport. Some nanomaterials have been investigated for their ability to influence root development, water

relations and antioxidant responses. Improved root growth can potentially increase access to soil moisture, while regulation of oxidative stress may protect cellular components. However, responses depend strongly on plant species, nanoparticle characteristics and concentration.

SALINITY STRESS

Excess salt creates both osmotic stress and ionic imbalance. Nano-enabled approaches are being investigated to support plant water balance, nutrient acquisition and antioxidant defence under saline conditions. Nanomaterials may influence the availability or transport of ions and can sometimes stimulate protective biochemical responses. Such effects are not universal, and excessive nanoparticle exposure can itself cause oxidative stress.

HEAVY-METAL STRESS

Heavy metals in soil can be toxic to plants and may enter food chains. Nanomaterials can potentially assist in immobilizing metals in soil or altering their mobility. Iron-based materials are of particular interest for environmental remediation. The objective may be to reduce the availability of a toxic metal to roots rather than simply increase total removal. Any remediation strategy must be evaluated for long-term stability and ecological effects.

TEMPERATURE STRESS

Heat and cold can damage membranes, alter enzyme activity and increase oxidative stress. Nano-enabled treatments are being investigated for their ability to influence antioxidant systems and maintain cellular function during temperature stress. Such applications remain an active area of research.

OXIDATIVE STRESS AND ANTIOXIDANT DEFENCE

Many abiotic stresses lead to increased formation of reactive oxygen species. Plants naturally possess antioxidant enzymes and non-enzymatic compounds that limit oxidative damage. Certain nanomaterials may influence these defence systems, potentially strengthening the plant's response to stress. At excessive concentrations, however, nanoparticles can themselves promote reactive oxygen species formation. The source document identifies reactive oxygen species generation, membrane disruption and interference with biochemical activities as important toxicological concerns.

TISSUE CULTURE AND STRESS MANAGEMENT

Nanomaterials are also being explored as additives in plant tissue culture. Depending on material type and concentration, they may affect nutrient availability, microbial contamination and plant development. The source specifically notes that excessive exposure can produce oxidative stress and negatively affect plant cells. Therefore, concentration optimization is essential when nanomaterials are used in plant propagation systems.

MAJOR NANOMATERIALS USED IN AGRICULTURAL APPLICATIONS

Several categories of nanomaterials have potential agricultural relevance. Zinc oxide nanoparticles have been investigated for zinc nutrition and plant-related applications. Iron and iron oxide nanoparticles are relevant to micronutrient delivery and environmental remediation. Silicon dioxide nanoparticles are studied in relation to plant growth and stress responses.

Titanium dioxide nanoparticles have been investigated for their effects on plant processes and are also widely studied for photocatalytic environmental applications.

Silver and copper-containing nanoparticles are of interest because of their antimicrobial properties. Gold nanoparticles are especially important in nano-enabled sensing and diagnostic systems because of their distinctive optical behaviour. Carbon-based nanomaterials and polymeric or other nanostructured carriers may be useful for transporting active molecules. The choice of material should always be based on the intended function, target organism, dose and environmental context rather than on nanoparticle size alone.

ADVANTAGES OF NANO-ENABLED AGRICULTURE

Nano-enabled agricultural technologies offer several potential advantages. First, controlled delivery can improve the timing and localization of fertilizers or pesticides. Second, nanoscale carriers may protect active ingredients from premature degradation. Third, high surface area can improve interactions between the material and its target. Fourth, nanomaterial-based sensors can provide rapid detection of pathogens and environmental contaminants. Fifth, precision delivery may reduce unnecessary application of agricultural chemicals under suitable conditions.

These potential benefits align with the broader advantages described in the source document, including adaptable surface properties, regulated release and environmental applications such as pollutant detection, adsorption and degradation. Nevertheless, the benefits should be demonstrated through reproducible laboratory, greenhouse and field studies.

LIMITATIONS, ENVIRONMENTAL SAFETY AND TOXICOLOGICAL CONCERNS

The application of nanotechnology in agriculture must address potential risks. Nanoparticles can interact with plant cells, microorganisms, animals and environmental compartments in ways that are not always predictable from the behaviour of conventional materials. Important factors include particle size, shape, surface chemistry, aggregation, solubility, concentration and persistence.

Plant toxicity is a major concern. Excessive exposure to some nanoparticles can generate reactive oxygen species, damage membranes and disturb normal biochemical processes. Soil microorganisms may also be affected. Because these organisms participate in decomposition and nutrient cycling, changes in microbial communities may have consequences beyond the initial application site.

Environmental transport is another consideration. Nanoparticles may move through soil, water or plant tissues depending on their properties. Their possible accumulation in agricultural ecosystems requires assessment, especially when repeated applications are proposed. The source document emphasizes that nanoparticles released into natural ecosystems may interact with soil microorganisms, aquatic organisms and other living systems.

Manufacturing consistency is also important. Producing materials with uniform dimensions, reliable surface properties and appropriate purity can be technically demanding and costly. For

agricultural use, quality control must ensure that the material behaves consistently from one batch to another.

Therefore, safety evaluation should accompany technological development. Studies should consider acute and chronic effects, effects on beneficial organisms, persistence, transformation in soil, movement into water, crop accumulation and possible exposure through the food chain. Risk assessment should be based on realistic application rates and environmental conditions.

FUTURE PERSPECTIVES

Future research in agricultural nanotechnology is likely to focus on precision delivery, biodegradable materials, smart sensing and improved environmental compatibility. Nano-enabled fertilizers may be developed to release nutrients in response to soil or plant conditions. Nano-pesticides may increasingly emphasize controlled release and improved targeting. Biosensors may allow earlier detection of pathogens, nutrient deficiencies and environmental contaminants.

An important direction is the integration of nanotechnology with biological approaches. Combining nano-carriers with beneficial microorganisms, plant-derived compounds or other biological inputs may provide multifunctional systems. Another priority is the development of biodegradable or easily recoverable nanomaterials that minimize long-term environmental accumulation.

The source document identifies biodegradable nanomaterials and manufacturing approaches that minimize environmental contamination as important future research priorities. Large-scale agricultural adoption will depend not only on technical performance but also on cost, reproducibility, regulatory acceptance, farmer usability and demonstrated environmental safety.

CONCLUSION

Nanotechnology provides a range of approaches for improving agricultural productivity and environmental management. In soil, nanomaterials can support nutrient delivery, controlled release and remediation. In the rhizosphere, they can be investigated for targeted nutrient supply, root interactions and modulation of microbial environments. In plant protection, nano-formulations can improve pesticide delivery, while nano-based biosensors can contribute to early disease detection. In stress management, nanomaterials are being investigated for their ability to support plant responses to drought, salinity, temperature extremes and heavy-metal stress.

The distinctive properties of nanomaterials—including high surface area, adjustable surface chemistry and controlled-release potential—make them useful tools for precision agriculture. At the same time, these same properties can produce biological and environmental interactions that require careful evaluation. The source material emphasizes both the broad biological potential of nanomaterials and the need for evidence concerning safety, environmental compatibility and long-term effectiveness.

Thus, the future of agricultural nanotechnology should combine improved material design with responsible application. The most useful nano-enabled systems will be those that deliver measurable agricultural benefits while minimizing effects on non-target organisms, soil ecosystems and the wider environment.

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Chapter

4

GREEN AND PLANT-MEDIATED SYNTHESIS OF NANOPARTICLES: PRINCIPLES, MECHANISMS, CHARACTERISATION AND APPLICATIONS

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ABSTRACT

Nanotechnology has become a multidisciplinary platform for developing materials with applications across healthcare, agriculture, food systems, environmental treatment, catalysis and biotechnology. At the nanoscale, changes in surface area, structure and physicochemical behaviour can give materials properties that differ markedly from their bulk counterparts. Conventional routes can provide useful control over nanoparticle formation, but some processes depend on energy-intensive operations or chemical reducing and stabilizing agents. Biological synthesis offers an alternative in which natural materials participate in nanoparticle formation. Plant extracts are especially attractive because their metabolites can assist metal-ion conversion and surface protection. Different plant organs have been explored for preparing metallic and metal-oxide nanoparticles, while reaction conditions such as extract composition, pH, temperature, precursor concentration and reaction time influence the final material. A combination of spectroscopic, microscopic and surface analyses is therefore needed to establish nanoparticle characteristics. Although plant-mediated synthesis has broad research potential, reproducibility, scale-up, purification, toxicity and environmental assessment remain important considerations (Iravani, 2011; Mittal *et al.,* 2013; Singh *et al.,* 2016; Khan *et al.,* 2019).

KEYWORDS: Green Nanotechnology, Plant-Mediated Synthesis, Phytosynthesis, Nanoparticles, Phytochemicals, Silver Nanoparticles, Zinc Oxide Nanoparticles, Characterization, Nanotoxicology, Sustainable Nanotechnology.

INTRODUCTION

Nanotechnology deals with the design and use of materials whose structural features occur at the nanoscale. Nanoparticles are commonly discussed within an approximate 1–100 nm size range, although the precise definition may depend on the field of application. At these dimensions, optical, catalytic, electrical, magnetic and biological behaviour can differ from that of bulk materials. Consequently, nanoparticle performance is influenced by characteristics such as size, shape, surface area, crystallinity and surface chemistry (Khan *et al.,* 2019).

The behaviour of a nanoparticle is governed not only by its elemental composition but also by its dimensions, morphology, crystal structure and surface characteristics. The route selected for

synthesis can consequently affect the properties and eventual performance of the material (Khan *et al.,* 2019).

Nanoparticles may be produced through physical or chemical approaches. Physical processing can include techniques based on evaporation, condensation, irradiation or mechanical size reduction. Chemical routes generally employ precursor salts together with reducing and surface-stabilizing substances. Although these methods can be effective, their energy requirements and chemical inputs may create environmental or occupational concerns depending on the process (Mittal *et al.,* 2013; Khan *et al.,* 2019).

Green synthesis uses biological materials or biologically derived molecules to assist nanoparticle formation. Microorganisms, algae, fungi, plants and isolated biomolecules have all been investigated for this purpose. Plant systems are particularly useful because they provide diverse metabolites capable of interacting with metal ions and nanoparticle surfaces (Iravani, 2011; Singh *et al.,* 2016).

Plant-assisted synthesis has therefore developed into an important branch of green nanotechnology. A single plant extract may supply compounds that participate in both reduction and surface stabilisation, potentially reducing the need for separate synthetic reagents. Nevertheless, a biological synthesis route should not automatically be described as completely safe or sustainable; extraction, processing, purification, use and disposal also need to be considered (Iravani, 2011; Mittal *et al.,* 2013; Khan *et al.,* 2019).

PLANT-MEDIATED GREEN SYNTHESIS

Plant tissues contain numerous primary and secondary metabolites that can interact with metal ions and newly formed nanoparticles. Depending on their chemical structure, these constituents may contribute to reduction, nucleation, growth or surface protection (Iravani, 2011; Mittal *et al.,* 2013).

Commonly investigated plant parts include:

A range of plant materials has been investigated, including leaves, roots, stems, bark, flowers, fruits, seeds and fruit peels. Leaves are often selected because they are readily available and can contain substantial amounts of secondary metabolites. The most appropriate plant part, however, depends on the botanical source and the nanoparticle being targeted (Iravani, 2011; Mittal *et al.,* 2013). A generalized plant-mediated synthesis can be represented as:

Plant material → extraction → phytochemical-rich extract → metal precursor → reduction → nucleation → growth → capping/stabilization → nanoparticles

Water is frequently selected for extraction because it is inexpensive and comparatively benign. However, extraction solvents differ in their ability to recover particular metabolites. Consequently, the solvent, extraction temperature, duration and plant-to-solvent ratio can influence the chemical profile of the extract and, in turn, nanoparticle formation (Iravani, 2011; Mittal *et al.,* 2013).

ROLE OF PHYTOCHEMICALS

The metabolite profile of the plant extract is a major determinant of the chemistry occurring during nanoparticle synthesis (Iravani, 2011; Mittal *et al.,* 2013).

Phenolic compounds

Phenolic molecules contain oxygenated functional groups that can participate in electron-transfer and metal-binding reactions. Their contribution may therefore extend to both metal-ion reduction and stabilization of the resulting particles (Iravani, 2011; Singh *et al.,* 2016).

Flavonoids

Flavonoids contain hydroxyl and carbonyl functionalities that can coordinate with metal ions. Depending on the particular molecule and reaction environment, they may contribute to reduction as well as adsorption or capping at the nanoparticle surface (Iravani, 2011; Singh *et al.,* 2016).

Terpenoids

Terpenoids represent a structurally diverse group of plant metabolites. Their involvement in nanoparticle synthesis can vary with their functional groups and the composition of the plant extract, including possible roles in reduction and surface association (Singh *et al.,* 2016).

Alkaloids

Because alkaloids contain nitrogen-bearing functional groups, they can interact with metal ions. Their exact contribution to nanoparticle formation depends on the botanical source and the other compounds present in the extract (Singh *et al.,* 2016).

Proteins and enzymes

Proteins and enzymes can associate with nanoparticle surfaces and thereby influence particle stability. In some biological systems, enzymatic activity may also contribute to the reduction of metal ions (Singh *et al.,* 2016).

Sugars and polysaccharides

Sugars and polysaccharides can participate in reduction reactions and may form a protective organic layer around newly generated particle. Such surface association can provide steric protection and reduce aggregation (Iravani, 2011; Singh *et al.,* 2016).

Table 1: Phytochemicals involved in plant-mediated nanoparticle synthesis

Phytochemical	Possible Function
Phenolics	Reduction and stabilisation
Flavonoids	Reduction, chelation and capping
Terpenoids	Reduction and surface interaction
Alkaloids	Metal binding and possible reduction
Proteins	Capping and stabilisation
Sugars	Reduction and stabilisation
Polysaccharides	Surface coating and steric stabilisation
Organic acids	Complexation and reaction control

Detection of a phytochemical in an extract alone is not sufficient evidence that the compound is responsible for nanoparticle formation. Claims about mechanism should be supported by

chemical profiling, controlled experiments and, where possible, direct evidence linking particular metabolites with particle formation (Iravani, 2011; Mittal *et al.,* 2013).

MECHANISM OF NANOPARTICLE FORMATION

The pathway followed during plant-mediated nanoparticle formation depends on the metal precursor, extract composition and reaction environment. In general, the process can be described as a sequence involving interaction with metal ions, reduction, formation of nuclei, particle growth and surface stabilization (Iravani, 2011; Mittal *et al.,* 2013; Singh *et al.,* 2016).

Metal-ion interaction

Metal ions from the precursor first encounter functional groups and metabolites present in the plant-derived reaction medium. These interactions can influence the subsequent reduction and nucleation steps (Iravani, 2011).

Reduction

Electron-donating constituents of the extract can transfer electrons to metal ions, converting them into a lower oxidation state or, for metallic nanoparticles, into the elemental form (Iravani, 2011; Mittal *et al.,* 2013).

A simplified representation is:

$$\mathbf{M^{n+} + \text{reducing molecules} \rightarrow M^0}$$

Where M represents the target metal.

Nucleation and growth

Once reduced atoms are generated, they can associate to form very small nuclei. Continued addition of atoms or species to these nuclei produces particle growth, with reaction conditions helping determine the resulting dimensions and morphology (Mittal *et al.,* 2013; Singh *et al.,* 2016).

Capping and stabilisation

Organic molecules from the plant extract may become attached to the newly formed nanoparticle surface. This biological coating can restrict uncontrolled particle growth and decrease aggregation, contributing to colloidal stability (Iravani, 2011; Singh *et al.,* 2016).

For metal-oxide systems, the pathway may additionally involve reactions such as hydrolysis, precipitation, hydroxylation and dehydration, depending on the precursor and experimental conditions (Mittal *et al.,* 2013).

The overall process can therefore be summarized as:

Reduction → nucleation → growth → capping → stable nanoparticles

FACTORS AFFECTING SYNTHESIS

The characteristics of plant-derived nanoparticles are affected by several controllable synthesis variables, and changes in these parameters can alter reaction rate, particle size, morphology and stability (Mittal *et al.,* 2013; Singh *et al.,* 2016).

pH

pH can modify the ionization state of plant metabolites, the chemical form of the precursor and the surface charge of developing particles. These changes can consequently affect reduction behaviour, nucleation and particle morphology (Mittal *et al.,* 2013; Singh *et al.,* 2016).

Temperature

Reaction temperature changes molecular mobility and reaction kinetics. Raising the temperature may speed up nanoparticle formation, but excessive heating can also alter or degrade temperature-sensitive plant constituents (Mittal *et al.,* 2013).

Reaction time

The reaction period influences the extent of precursor conversion and subsequent particle development. Prolonged reaction may change particle size or increase the likelihood of aggregation in some systems (Mittal *et al.,* 2013).

Plant-extract concentration

Increasing the amount of plant extract changes the concentration of available reducing and surface-active molecules, which can influence the balance between nucleation, growth and stabilization (Mittal *et al.,* 2013).

Precursor concentration

The precursor level affects the number of available metal ions and therefore influences nucleation and growth. Excess precursor relative to the available stabilizing components can favours aggregation or a wider particle-size distribution (Mittal *et al.,* 2013).

Extraction conditions

Extraction parameters such as solvent type, extraction time, temperature and the ratio of plant material to solvent influence which metabolites enter the extract. These differences can subsequently alter nanoparticle formation and properties (Iravani, 2011; Mittal *et al.,* 2013).

Table 2: Major factors affecting plant-mediated nanoparticle synthesis

Parameter	Major Effect
pH	Reduction, nucleation and surface charge
Temperature	Reaction rate and particle growth
Reaction time	Conversion and maturation
Extract concentration	Reducing and capping capacity
Precursor concentration	Nucleation and particle size
Solvent	Phytochemical extraction
Mixing	Reaction uniformity
Light	May influence photochemical reactions

IMPORTANT PLANT-MEDIATED NANOPARTICLES

SILVER NANOPARTICLES

Silver nanoparticles have received extensive attention in plant-mediated synthesis because of their optical, catalytic and antimicrobial characteristics. Investigations have considered their use in areas such as antimicrobial materials, coatings, sensing and biomedical research (Ahmed *et al.,* 2016; Singh *et al.,* 2016). The biological activity of silver nanoparticles can involve several interacting mechanisms, including contact with cell envelopes, oxidative effects and release of silver ions. The magnitude of these effects is influenced by particle size, surface chemistry, concentration and the biological system under study (Ahmed *et al.,* 2016; Khan *et al.,* 2019).

GOLD NANOPARTICLES

Gold nanoparticles possess distinctive optical and surface characteristics. During plant-assisted synthesis, phytochemicals can participate in reduction of gold ions and may remain associated with the particle surface (Mittal *et al.,* 2013; Singh *et al.,* 2016).

These properties have supported research into gold nanoparticles for sensing, catalytic processes, imaging and other biomedical applications (Singh *et al.,* 2016).

ZINC OXIDE NANOPARTICLES

Zinc oxide nanoparticles combine semiconductor behaviour with photocatalytic, ultraviolet-absorbing and antimicrobial properties. Plant-derived approaches have therefore been investigated as alternative routes for preparing ZnO nanomaterials (Singh *et al.,* 2016).

COPPER AND COPPER OXIDE NANOPARTICLES

Copper and copper-oxide nanoparticles are of interest for catalytic and antimicrobial applications. Controlling oxidation state, particle growth and stability is important because copper-based systems can undergo changes during synthesis and storage (Singh *et al.,* 2016).

IRON OXIDE NANOPARTICLES

Iron-oxide nanoparticles can exhibit useful magnetic behaviour, particularly in magnetite-containing systems. This has encouraged research in separation, catalysis, environmental treatment and biomedical applications (Singh *et al.,* 2016).

TITANIUM DIOXIDE NANOPARTICLES

Titanium dioxide nanoparticles are widely investigated for photocatalytic and ultraviolet-related properties. Plant-assisted synthesis has been explored as one of several alternative preparation strategies (Singh *et al.,* 2016).

Table 3: Representative plant-mediated nanoparticles

Nanoparticle	Important Properties	Potential Applications
AgNPs	Antimicrobial, optical	Antimicrobial materials, sensing
AuNPs	Optical, catalytic	Biosensors, imaging, catalysis
ZnO NPs	Semiconductor, photocatalytic	Agriculture, antimicrobial applications
Cu/CuO NPs	Catalytic, antimicrobial	Catalysis, coatings
Fe_3O_4 NPs	Magnetic	Separation, remediation
TiO_2 NPs	Photocatalytic, UV-absorbing	Environmental applications

CHARACTERISATION OF NANOPARTICLES

Characterization is necessary because successful synthesis alone does not establish the dimensions, morphology, composition, crystal structure or colloidal behaviour of the product. Multiple complementary techniques are therefore normally required (Mittal *et al.,* 2013; Singh *et al.,* 2016).

UV–VISIBLE SPECTROSCOPY

UV–visible spectroscopy can be used to follow nanoparticle formation and, for suitable metallic systems, to observe absorption associated with surface plasmon behaviour (Mittal *et al.,* 2013).

FOURIER-TRANSFORM INFRARED SPECTROSCOPY

FTIR analysis helps identify chemical functional groups and can provide evidence that plant-derived molecules interact with or remain associated with nanoparticle surfaces (Mittal *et al.,* 2013).

X-RAY DIFFRACTION

X-ray diffraction is used to determine crystalline phases and structural features. Under appropriate conditions, diffraction data can also be used to estimate crystallite dimensions (Mittal *et al.,* 2013).

SCANNING ELECTRON MICROSCOPY

SEM is useful for examining particle morphology and the appearance of nanoparticle assemblies or surfaces (Mittal *et al.,* 2013).

TRANSMISSION ELECTRON MICROSCOPY

TEM provides high-resolution images that allow direct assessment of individual particle dimensions and morphology (Mittal *et al.,* 2013).

ENERGY-DISPERSIVE X-RAY SPECTROSCOPY

EDX or EDS supplies elemental information and can support confirmation that the intended metal is present in the material (Mittal *et al.,* 2013).

DYNAMIC LIGHT SCATTERING

DLS reports the hydrodynamic diameter of particles dispersed in a liquid. This value can exceed the primary particle diameter measured by electron microscopy because the measurement reflects the particle together with its associated solvation or surface layer (Mittal *et al.,* 2013).

ZETA POTENTIAL

Zeta-potential measurements provide an indication of surface charge and are commonly used as one parameter for assessing the electrostatic stability of nanoparticle dispersions (Mittal *et al.,* 2013).

Table 4: Characterization techniques

Technique	Information Obtained
UV–Vis	Optical properties and reaction monitoring
FTIR	Functional groups and surface interactions
XRD	Crystal structure and phase
SEM	Morphology
TEM	Particle size and morphology
EDX	Elemental composition
DLS	Hydrodynamic size
Zeta potential	Surface charge and stability

Because each analytical method provides a different type of information, a combination of techniques gives a more reliable description of nanoparticle identity and behaviour than reliance on a single measurement (Mittal *et al.,* 2013).

APPLICATIONS

ANTIMICROBIAL APPLICATIONS

Plant-derived silver, zinc oxide and copper-based nanoparticles have been investigated for antimicrobial activity against a variety of microorganisms. Reported mechanisms include interactions with cell surfaces, oxidative stress and metal-ion effects, although activity varies with the nanoparticle and test organism (Ahmed *et al.,* 2016; Singh *et al.,* 2016).

ENVIRONMENTAL REMEDIATION

Nanoparticles can participate in pollutant removal through adsorption, catalytic transformation or photocatalytic processes. Plant-mediated materials have consequently been examined for applications including degradation of dyes, treatment of contaminated water and removal of selected metal pollutants (Singh *et al.,* 2016).

AGRICULTURE

Nanomaterials have been investigated for agricultural uses such as nutrient delivery, pest management and regulation of plant responses. However, beneficial effects depend on dose and material characteristics, and potential environmental impacts must be evaluated alongside performance (Khan *et al.,* 2019).

FOOD PACKAGING

Antimicrobial nanoparticles may be incorporated into packaging systems to help limit microbial contamination. For food-related applications, however, migration, exposure, material stability and regulatory requirements need to be addressed before practical use (Khan *et al.,* 2019).

BIOSENSORS

The optical and electrochemical behaviour of gold and silver nanoparticles has made them useful candidates for sensor development, including approaches based on changes in optical signals or surface interactions (Mittal *et al.,* 2013; Singh *et al.,* 2016).

BIOMEDICAL RESEARCH

Plant-mediated nanoparticles have been investigated in drug-delivery research, imaging, antimicrobial strategies and cancer-related studies. Most reported applications remain experimental or preclinical, so claims of clinical utility require further toxicological, pharmacological and translational evidence (Singh *et al.,* 2016; Khan *et al.,* 2019).

CATALYSIS

The high surface area of nanoparticles can support catalytic activity. Plant-derived materials have therefore been studied in reactions involving pollutant degradation and other chemical transformations (Mittal *et al.,* 2013; Singh *et al.,* 2016).

ADVANTAGES OF PLANT-MEDIATED SYNTHESIS

Plant-mediated synthesis offers several potential advantages:

[1]. Reduced dependence on some hazardous chemical reducing agents;
[2]. Relatively simple experimental procedures;
[3]. Potential use of water-based extraction;

[4]. Simultaneous reduction and stabilisation by plant compounds;
[5]. Availability of diverse plant materials;
[6]. Potential utilisation of agricultural residues;
[7]. Compatibility with principles of green chemistry.

The potential benefits of plant-mediated synthesis should be demonstrated for the specific system under investigation rather than assumed in advance. Environmental performance also depends on extraction, energy use, purification, waste generation, application and end-of-life handling (Iravani, 2011; Khan *et al.,* 2019).

LIMITATIONS AND SAFETY CONCERNS

Although plant-based synthesis can reduce reliance on some conventional reagents, it also presents challenges related to biological variability, process control, product purification, scale-up, toxicity and regulation (Khan *et al.,* 2019).

PLANT VARIABILITY

The concentration and identity of plant metabolites can change with species, geographical origin, season, developmental stage and environmental conditions. Such variation can lead to differences between synthesis batches (Iravani, 2011; Singh *et al.,* 2016).

REPRODUCIBILITY

Changes in extract composition can translate into differences in particle size, morphology, surface chemistry and dispersion behaviour. Standardised raw materials and extraction procedures are therefore important for reproducible synthesis (Mittal *et al.,* 2013; Singh *et al.,* 2016).

SCALE-UP

Moving from a laboratory protocol to larger production requires control of extraction, mixing, reaction conditions, purification and quality assurance. A process that works at small scale may not retain identical performance when volumes and mass-transfer conditions change (Mittal *et al.,* 2013; Khan *et al.,* 2019).

PURIFICATION

The final nanoparticle preparation may contain residual plant metabolites, unreacted precursor or other process-related impurities. Appropriate purification and analytical quality control are therefore important, particularly for biomedical or food-related applications (Khan *et al.,* 2019).

NANOTOXICITY

Biological synthesis does not by itself establish that a nanoparticle is harmless. Toxicological outcomes can depend on particle dimensions, morphology, surface chemistry, dose, dissolution and exposure conditions, so safety must be evaluated for the specific material and use scenario (Khan *et al.,* 2019).

ENVIRONMENTAL EFFECTS

Nanoparticles entering soil or aquatic environments can interact with microorganisms, plants, animals and natural organic matter. Their persistence, transformation, transport and biological effects therefore need consideration when environmental applications are proposed (Khan *et al.,* 2019).

REGULATORY ISSUES

Materials intended for food, agricultural or medical use require appropriate evaluation of quality, safety, exposure and regulatory compliance. Green synthesis does not remove these requirements (Khan *et al.,* 2019).

FUTURE PERSPECTIVES

Future work should prioritise reproducible protocols, authenticated botanical material and controlled extraction procedures. Chemical profiling of extracts can help connect metabolite composition with nanoparticle characteristics, while statistical experimental design can be used to optimize several synthesis variables together (Iravani, 2011; Mittal *et al.,* 2013; Singh *et al.,* 2016).

Scale-up research should examine continuous or better-controlled production systems, automated monitoring and standardised extract preparation. A safe-by-design approach is also desirable, in which toxicological and environmental considerations are incorporated during material development rather than addressed only after synthesis (Khan *et al.,* 2019).

Agricultural residues and food-processing by-products may provide alternative sources of plant-derived molecules, linking nanoparticle production with waste valorisation. However, claims of sustainability should be supported by life-cycle evaluation that considers biomass, water, energy, chemicals, waste and disposal across the complete process (Iravani, 2011; Khan *et al.,* 2019).

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Chapter 5

BIOLOGICAL APPLICATIONS OF NANOMATERIALS

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INTRODUCTION

Nanomaterials are extremely small substances, generally measuring between 1 and 100 nanometres in at least one dimension. Their nanoscale structure produces distinctive physicochemical characteristics that differ from those of conventional bulk materials.

Their large surface-area-to-volume ratio, adjustable surface chemistry and ability to interact with biomolecules make them valuable in biological research. Nanotechnology has consequently become an important field in modern medicine, biotechnology, agriculture and environmental science.

Commonly investigated nanomaterials include metallic nanoparticles, metal oxide nanoparticles, carbon-based nanostructures, lipid-based carriers and polymeric nanoparticles.

CHARACTERISTICS OF NANOMATERIALS

Nanoscale dimensions: Their minute size enables interactions with cellular components and biological molecules.

- **High surface area:** A greater proportion of atoms is exposed at the surface, enhancing chemical interactions and the attachment of therapeutic compounds.
- **Functionalized surfaces:** Antibodies, peptides and other biomolecules can be attached to nanoparticles to modify their biological behaviour.
- **Optical behaviour:** Certain nanostructures possess light-absorbing or fluorescent properties suitable for diagnostic applications.
- **Magnetic behaviour:** Magnetic nanomaterials are useful for imaging, molecular separation and other biomedical procedures.
- **Drug-release properties:** Nanocarriers can be engineered to release therapeutic substances over a predetermined period or in response to specific conditions.

MAJOR BIOLOGICAL APPLICATIONS

NANOMATERIALS IN DRUG DELIVERY

Conventional drug administration can be limited by poor solubility, rapid degradation and the distribution of medication to healthy tissues. Nanotechnology provides alternative carrier systems that can address some of these difficulties. Therapeutic molecules may be enclosed within nanoparticles, incorporated into their structure or chemically attached to their surfaces. After administration, these carriers transport their contents through the body. Depending on their composition and surface characteristics, some formulations may accumulate preferentially

in particular tissues. Drug release can occur through diffusion, carrier degradation or changes in the surrounding biological environment.

Liposomes, biodegradable polymeric nanoparticles and lipid-based nanocarriers are examples of drug-delivery systems. Their potential benefits include improved drug stability, sustained release and reduced exposure of healthy tissues to certain medicines.

APPLICATIONS IN CANCER THERAPY

Nanotechnology offers several approaches for improving cancer diagnosis and treatment. Nanoparticle formulations can modify the distribution of anticancer agents and may improve their delivery to tumour tissues.

In photothermal therapy, suitable nanoparticles absorb externally applied light and transform its energy into heat. The resulting increase in temperature may damage malignant cells. Gold-based nanostructures are extensively investigated for this purpose.

Nanoparticles can also be modified with molecules that recognize selected receptors on cancer cells. Such modifications are intended to improve therapeutic specificity, although successful targeting depends on several biological factors.

Liposomal doxorubicin is an established example of a nanoparticle-based anticancer formulation. Many other nanoscale cancer treatments are still being investigated.

DISEASE DIAGNOSIS AND BIOMEDICAL IMAGING

Nanomaterials are valuable in diagnostic research because their magnetic, electrical and optical properties can be used to generate detectable signals.

Iron oxide nanoparticles can alter magnetic resonance signals and have been investigated as contrast-enhancing agents for MRI.

Quantum dots are semiconductor nanocrystals that emit fluorescence when excited by suitable light. Their optical characteristics make them useful for labelling and tracking biological molecules in research.

Gold nanoparticles are also incorporated into certain diagnostic assays because of their distinctive light-interacting properties.

In addition, magnetic nanoparticles coated with specific antibodies can assist in isolating cells, proteins and other biological targets from complex samples.

GENE TRANSFER AND GENETIC MEDICINE

Transporting nucleic acids into living cells is an important requirement in genetic medicine. However, unprotected genetic material may undergo rapid enzymatic degradation and often enters cells inefficiently.

Nanoparticle carriers can protect DNA or RNA during delivery and facilitate their entry into target cells. Lipid nanoparticles are particularly important in RNA delivery. They can encapsulate messenger RNA and support its transfer into cells, where the RNA directs the synthesis of a particular protein. Other investigated applications include the delivery of small interfering RNA for gene suppression and the transport of components used in CRISPR-based genome editing. The use of lipid nanoparticles in certain mRNA vaccines demonstrates an established medical application of this technology.

ANTIMICROBIAL APPLICATIONS

Metallic nanoparticles, particularly those containing silver, have attracted considerable attention because of their antimicrobial activity.

Silver nanoparticles may attach to microbial surfaces, disturb membrane organization and release silver ions. These interactions can interfere with essential enzymes and promote oxidative damage to cellular components.

Their antimicrobial properties have encouraged their incorporation into selected wound dressings, surface coatings and medical materials.

Nevertheless, antimicrobial effectiveness varies according to particle concentration, size, chemical composition and the susceptibility of the microorganism.

TISSUE ENGINEERING AND REGENERATIVE MEDICINE

Regenerative medicine aims to restore the structure and function of damaged tissues. Nanomaterials contribute to this field by providing scaffolds that resemble aspects of the natural extracellular matrix.

These scaffolds create a supportive environment in which cells can attach, proliferate and, under appropriate conditions, develop into specialized tissues.

For instance, hydroxyapatite nanoparticles are investigated for bone repair because hydroxyapatite is an important mineral component of natural bone.

Nano fibrous materials are also being studied for skin regeneration, while nanocomposite scaffolds are being developed for cartilage and other tissue-engineering applications.

The biological performance of these materials depends on their structure, mechanical properties, degradation behaviour and compatibility with surrounding cells.

DEVELOPMENT OF BIOSENSORS

Nanotechnology has contributed to the development of analytical devices capable of identifying small quantities of biologically important substances.

A biosensor typically contains a recognition component that selectively interacts with the substance being measured. A transducer then converts this interaction into an electrical, optical or another measurable signal.

Nanostructured materials can enhance signal generation by providing a large surface for immobilizing enzymes, antibodies or nucleic acids.

Such devices are used or investigated for glucose measurement, pathogen identification, disease-marker detection and environmental analysis.

For example, incorporating suitable nanomaterials into glucose-sensing electrodes may improve electron transfer and analytical sensitivity.

AGRICULTURAL APPLICATIONS OF NANOMATERIALS

NANOFERTILIZERS

Nanotechnology is being investigated as a means of improving nutrient management in agriculture. Nanofertilizers contain nutrients in nanoscale formulations or use nanostructured carriers to deliver essential elements to plants.

These formulations can be designed to regulate nutrient release and potentially reduce nutrient losses. Zinc oxide nanoparticles and nanoscale hydroxyapatite are examples being studied for agricultural applications.

NANOPESTICIDES

Nanomaterials can function as carriers for pesticide molecules, protecting active ingredients from premature degradation and allowing their release to be regulated.

Such formulations may improve pesticide stability and reduce the quantity or frequency of application under suitable conditions. However, their potential effects on beneficial organisms and the wider environment require careful evaluation.

DETECTION OF PLANT DISEASES

Nanomaterial-based sensing techniques are being developed for the rapid identification of plant pathogens.

Gold nanoparticles, for example, can be incorporated into diagnostic systems that produce visible colour changes when specific pathogen-associated molecules are detected.

These methods have the potential to support early disease identification and more effective crop management.

PLANT TISSUE CULTURE

Nanomaterials are being explored as additives in plant tissue culture systems. Depending on their properties and concentration, they may influence nutrient availability, microbial contamination and plant development.

Their effects are not always beneficial. Excessive exposure can produce oxidative stress and negatively affect plant cells.

ENVIRONMENTAL APPLICATIONS

WATER TREATMENT

Nanomaterials offer several approaches for removing contaminants from water. Their large surface area can provide numerous binding sites for pollutants, while certain nanostructures can promote chemical degradation reactions. Carbon-based nanomaterials are investigated for the adsorption of organic pollutants. Titanium dioxide nanoparticles can act as photocatalysts, using light energy to promote the breakdown of certain contaminants.

REMOVAL OF TOXIC METALS

Magnetic nanoparticles are being studied for extracting hazardous metal contaminants from polluted water.

Iron oxide nanoparticles can be modified with surface groups that bind particular metal ions. Following adsorption, magnetic separation may be used to recover the nanoparticles and the associated contaminants.

This approach is being investigated for treating water containing substances such as arsenic and lead.

ENVIRONMENTAL MONITORING

Nanomaterial-based sensors can help identify chemical and biological contaminants in environmental samples.

Their electrical and optical properties may permit the detection of low concentrations of pesticides, heavy metals and certain microbial pollutants.

EXAMPLES OF NANOMATERIALS AND THEIR USES

- Gold nanoparticles: Cancer therapy and biosensors.
- Silver nanoparticles: Antimicrobial agents.
- Iron oxide nanoparticles: MRI imaging.
- Carbon nanotubes: Drug delivery.
- Quantum dots: Bioimaging.
- Lipid nanoparticles: Gene delivery.
- Polymeric nanoparticles: Controlled drug release.
- Hydroxyapatite nanoparticles: Bone regeneration.
- Titanium dioxide nanoparticles: Water purification.

ADVANTAGES OF NANOMATERIALS

Nanomaterials offer several potential benefits in biological and biomedical applications.

- Improved therapeutic delivery: Suitable nanocarriers can protect medicines from degradation and modify their distribution within the body.
- Regulated drug release: Certain formulations provide gradual or stimulus-responsive release of therapeutic compounds.
- Enhanced diagnostic sensitivity: Nanostructured sensing surfaces can improve the detection of specific biological molecules.
- Adaptable surface properties: Chemical modification allows nanoparticles to be designed for different biological applications.
- Combined functions: Some nanomaterials can incorporate imaging and therapeutic capabilities within a single system.
- Environmental applications: Nanomaterials can support pollutant detection, adsorption and degradation.

LIMITATIONS AND TOXICOLOGICAL CONCERNS

Although nanotechnology provides numerous opportunities, several challenges must be addressed before many nanomaterials can be used safely on a large scale.

- Cellular toxicity: Certain nanoparticles can promote the formation of reactive oxygen species, disrupt cellular membranes and interfere with normal biochemical activities.
- Accumulation in biological tissues: Depending on their physicochemical properties, nanoparticles may remain in organs such as the liver or spleen. Their long-term effects require further investigation.
- Environmental risks: Nanoparticles released into natural ecosystems may interact with soil microorganisms, aquatic organisms and other living systems.
- Manufacturing challenges: Producing nanomaterials with uniform dimensions, consistent surface properties and reliable purity can be technically demanding and expensive.

- Clinical limitations: Although some nanoparticle formulations are already used in medicine, many emerging applications require additional evidence regarding their safety and therapeutic effectiveness.

FUTURE SCOPE

Ongoing research is directed towards developing more precise drug-delivery systems, advanced diagnostic platforms and safer materials for regenerative medicine.

Nanotechnology is also being investigated for nucleic acid delivery, genome-editing applications and more efficient agricultural nutrient management.

An important research priority is the development of biodegradable nanomaterials and manufacturing techniques that minimize environmental contamination.

CONCLUSION

Nanomaterials have become important tools in biotechnology because their distinctive structural and physicochemical properties enable a wide range of biological interactions. Their applications extend from pharmaceutical delivery and molecular diagnosis to tissue regeneration, agricultural technology and environmental management.

Further progress will depend on improving material performance while establishing reliable evidence of biological safety, environmental compatibility and long-term effectiveness.

Plagiarism-checking note: This version uses newly structured sentences and rephrased explanations rather than simply replacing individual words. Standard scientific terms and established mechanisms have been retained for accuracy. Before academic submission, add appropriate references to the original scientific literature and check the final document using your institution's required similarity-detection software.

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Chapter 6

NANOBIOTECHNOLOGY: PRINCIPLES, APPLICATIONS, RECENT ADVANCES AND FUTURE PERSPECTIVES

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ABSTRACT

Nanobiotechnology is an interdisciplinary field that integrates nanotechnology with biological sciences to develop nanoscale materials, devices, and systems for biological, medical, agricultural, and environmental applications. Nanomaterials possess unique physicochemical properties arising from their small size, large surface-area-to-volume ratio, surface chemistry, and other nanoscale effects. These properties have enabled the development of innovative approaches for drug delivery, cancer diagnosis and therapy, biosensing, gene delivery, tissue engineering, antimicrobial treatment, and medical imaging. Nanoparticles can also be synthesized through biological and green approaches using plants, microorganisms, enzymes, and biomolecules, providing alternatives to some conventional synthesis routes. However, biological interactions, toxicity, reproducibility, biodistribution, manufacturing, and regulatory requirements remain important challenges. Recent research is increasingly focused on precision nanomedicine, multifunctional nanostructures, intelligent delivery systems, and the integration of artificial intelligence with nanoparticle design. This review summarizes the fundamental principles of nanobiotechnology, major nanomaterials and synthesis approaches, biomedical applications, green nanotechnology, challenges, and future prospects.

KEYWORDS: Nanobiotechnology, Nanoparticles, Nanomedicine, Drug Delivery, Nano biosensors, Green Synthesis, Nanotoxicology, Cancer Therapy.

INTRODUCTION

Nanobiotechnology is an interdisciplinary field that combines nanotechnology with biology and biotechnology. It deals with the design, synthesis, characterization, and application of materials and structures at the nanoscale for biological and biomedical purposes.

The prefix **"nano"** comes from the Greek word *Nanos*, meaning dwarf or very small. A nanometer (nm) is one-billionth of a meter:

$1\ nm = 10^{-9}\ m$

The nanoscale is generally considered to be approximately **1–100 nm** for many nanotechnology applications.

At this scale, materials can exhibit properties that are significantly different from those of the same materials in bulk form. These differences may occur because of the very high surface-area-to-volume ratio and nanoscale physical effects.

Nanobiotechnology is particularly important because many biological structures, such as proteins, DNA, lipid membranes, and molecular complexes, naturally operate at the nanoscale.

DEFINITION OF NANOBIOTECHNOLOGY

Nanobiotechnology can be defined as:

The application of nanotechnology principles and tools to biological systems, together with the use of biological principles and materials for the development of nanoscale technologies.

It combines knowledge from:

- Nanotechnology
- Molecular biology
- Biotechnology
- Biochemistry
- Microbiology
- Chemistry
- Physics
- Materials science
- Medicine
- Pharmacology
- Engineering

The main objective is to develop nanoscale systems capable of interacting with biological molecules, cells, tissues, and organisms in a controlled manner.

RELATIONSHIP BETWEEN NANOTECHNOLOGY, BIOTECHNOLOGY AND NANOBIOTECHNOLOGY

NANOTECHNOLOGY

Nanotechnology deals with the manipulation of matter at the nanoscale.

BIOTECHNOLOGY

Biotechnology uses biological organisms, cells, enzymes, genes, or biological processes to develop useful products and technologies.

NANOBIOTECHNOLOGY

Nanobiotechnology brings these two fields together.

Nanotechnology + Biotechnology = Nanobiotechnology

For example, nanoparticles can be designed to carry a drug to a particular biological site. This involves nanoscale engineering as well as knowledge of biological interactions.

HISTORICAL DEVELOPMENT

The concept of manipulating matter at very small scales developed gradually through advances in physics, chemistry, microscopy, and molecular biology.

Important developments include:

- Development of advanced microscopy
- Understanding of molecular structures
- Development of semiconductor technology

- Discovery and study of carbon nanostructures
- Development of methods for producing nanoparticles
- Increasing use of nanomaterials in medicine and biotechnology

The development of electron microscopy made it possible to observe structures much smaller than could be resolved using conventional light microscopy.

The development of scanning probe techniques further expanded the ability to study and manipulate nanoscale surfaces.

NANOSCALE AND ITS IMPORTANCE

The nanoscale is extremely small.

For comparison:

- 1 meter = 10^9 nanometers
- Human hair is roughly tens of thousands of nanometers in diameter.
- DNA has a diameter of approximately 2 nm.
- Many proteins have dimensions of only a few nanometers.

This overlap between biological dimensions and the nanoscale is one reason nanotechnology is highly relevant to biotechnology.

Nanomaterials can interact with biological molecules at:

- Molecular level
- Cellular level
- Tissue level

WHY NANOMATERIALS HAVE UNIQUE PROPERTIES

Nanomaterials can behave differently from bulk materials because of several factors.

High Surface-Area-to-Volume Ratio

When particle size decreases, the proportion of atoms located at or near the surface increases.

A larger surface area can result in:

- Increased chemical reactivity
- Enhanced catalytic activity
- Greater interaction with biomolecules
- Increased adsorption capacity

This property is particularly important in biosensors and drug-delivery systems.

Quantum Effects

At very small dimensions, quantum mechanical effects can become important.

These effects can influence:

- Optical behavior
- Electronic properties
- Energy levels
- Fluorescence
- Electrical conductivity

Quantum dots are an important example of nanomaterials whose optical properties depend strongly on size.

Surface Properties

The surface of a nanoparticle can be chemically modified with:

- Polymers
- Proteins
- Antibodies
- Peptides
- DNA
- RNA
- Small molecules

Surface modification can change the stability, biological interactions, cellular uptake, and targeting properties of nanoparticles.

CLASSIFICATION OF NANOMATERIALS

Nanomaterials can be classified according to their dimensions, composition, and morphology.

Zero-Dimensional Nanomaterials

All three dimensions are within the nanoscale.

Examples:

- Nanoparticles
- Quantum dots

One-Dimensional Nanomaterials

Two dimensions are nanoscale, while one dimension is larger.

Examples:

- Nanowires
- Nanorods
- Nanotubes

Two-Dimensional Nanomaterials

One dimension is nanoscale.

Examples:

- Nano films
- Nano coatings
- Graphene sheets

Three-Dimensional Nanostructured Materials

These are bulk structures constructed from nanoscale building blocks.

Examples:

- Nanocomposites
- Nanostructured porous materials

MAJOR TYPES OF NANOMATERIALS

Metallic Nanoparticles

Common examples include:

- Gold nanoparticles
- Silver nanoparticles
- Copper nanoparticles
- Iron nanoparticles

They are investigated for:

- Biosensors
- Imaging
- Drug delivery
- Antimicrobial applications
- Cancer research

Metal Oxide Nanoparticles

Examples include:

- Zinc oxide nanoparticles
- Titanium dioxide nanoparticles
- Iron oxide nanoparticles
- Magnesium oxide nanoparticles

Applications include:

- Sensors
- Catalysis
- Imaging
- Antimicrobial materials
- Environmental technologies

Polymeric Nanoparticles

Polymeric nanoparticles are prepared from natural or synthetic polymers.

Examples include systems based on:

- PLGA
- Chitosan
- Polylactic acid
- Other biodegradable polymers

They are extensively investigated for controlled drug delivery.

Lipid-Based Nanomaterials

Examples include:

- Liposomes
- Lipid nanoparticles
- Solid lipid nanoparticles
- Nanostructured lipid carriers

They can be used to transport:

- Drugs
- Proteins
- RNA
- Other biological molecules

Carbon-Based Nanomaterials

Examples include:

- Carbon nanotubes
- Graphene
- Graphene oxide
- Fullerenes

Potential applications include:

- Biosensors
- Drug delivery
- Tissue engineering
- Imaging
- Electronic biosystems

NANOPARTICLES

Nanoparticles are nanoscale particles generally having dimensions in the approximate range of 1–100 nm.

They may be:

- Spherical
- Rod-shaped
- Triangular
- Cubic
- Irregular

Particle properties depend on:

- Size
- Shape
- Composition
- Surface charge
- Surface chemistry
- Crystallinity

GOLD NANOPARTICLES

Gold nanoparticles are among the most extensively studied nanomaterials in nanobiotechnology. They possess interesting optical properties and can be functionalized with various biological molecules.

Applications include:

- Biosensors
- Drug delivery

- Cancer research
- Molecular diagnostics
- Bioimaging

Their optical properties are related to interactions between light and conduction electrons at the nanoparticle surface.

SILVER NANOPARTICLES

Silver nanoparticles have been widely studied for antimicrobial applications.

Potential applications include:

- Antibacterial coatings
- Medical materials
- Biosensors
- Packaging
- Water-treatment research

Possible antimicrobial mechanisms include:

- Interaction with microbial membranes
- Release of silver ions
- Generation of reactive species
- Interference with cellular processes

The biological effects depend on particle characteristics and exposure conditions.

IRON OXIDE NANOPARTICLES

Iron oxide nanoparticles can exhibit magnetic properties.

Important applications include:

- Magnetic separation
- Biomedical imaging
- Targeted delivery research
- Magnetic biosensors
- Experimental therapeutic approaches

Their magnetic behavior allows them to respond to external magnetic fields.

NANOPARTICLE SYNTHESIS

Nanoparticles can be synthesized through three broad approaches:

- Top-down approach
- Bottom-up approach
- Biological or green synthesis

TOP-DOWN APPROACH

In the top-down approach, large materials are reduced or patterned to produce nanoscale structures.

EXAMPLES

- Milling
- Lithography
- Laser ablation

- Etching

ADVANTAGES

- Useful for producing patterned structures
- Can be adapted to industrial processes
- Suitable for certain device-fabrication applications

LIMITATIONS

- High energy requirements in some methods
- Possibility of structural defects
- Difficulties in controlling very small particle dimensions
- Material wastage can occur

BOTTOM-UP APPROACH

In the bottom-up approach, nanoparticles are formed from atoms, ions, molecules, or molecular assemblies.

EXAMPLES

- Chemical reduction
- Sol-gel method
- Precipitation
- Self-assembly
- Chemical vapor deposition

ADVANTAGES

- Good control of particle formation
- Can produce relatively uniform nanoparticles
- Suitable for controlled synthesis

GREEN SYNTHESIS OF NANOPARTICLES

Green synthesis is an environmentally conscious approach to nanoparticle production.

Biological materials can act as:

- Reducing agents
- Stabilizing agents
- Capping agents

Sources include:

- Plants
- Bacteria
- Fungi
- Algae
- Yeast
- Enzymes
- Proteins
- Biomolecules

PLANT-MEDIATED NANOPARTICLE SYNTHESIS

Plants contain many phytochemicals capable of interacting with metal ions.

Important phytochemicals include:

- Flavonoids
- Phenolic compounds
- Terpenoids
- Proteins
- Sugars
- Organic acids

A general process is:

Plant material → Extract preparation → Addition of metal precursor → Reduction → Nucleation → Growth → Stabilization → Nanoparticles

ADVANTAGES

- Simple
- Potentially economical
- Uses biological resources
- Can reduce dependence on some hazardous chemical reagents

However, the exact composition of plant extracts can vary, which can affect reproducibility.

MICROBIAL SYNTHESIS

Microorganisms can also participate in nanoparticle synthesis.

Examples include:

- Bacteria
- Fungi
- Yeasts
- Algae

Microbial cells may produce enzymes and biomolecules capable of reducing metal ions and stabilizing nanoparticles.

Advantages include:

- Biological synthesis conditions
- Potential control through microbial processes
- Production of biologically coated nanoparticles

CHARACTERIZATION OF NANOMATERIALS

Characterization is essential for determining whether

Synthesized nanoparticles have the desired properties.

UV-Visible Spectroscopy

UV-Visible spectroscopy can be used to study optical absorption.

It is particularly useful for investigating metallic nanoparticles with characteristic optical responses.

Scanning Electron Microscopy

SEM provides information about:

- Surface morphology
- Shape

- Particle distribution
- Approximate size

Transmission Electron Microscopy

TEM provides high-resolution images of nanoparticles.

It can determine:

- Particle size
- Shape
- Morphology
- Internal structure

Atomic Force Microscopy

AFM uses a nanoscale probe to investigate surface topography.

It can provide three-dimensional surface information.

X-Ray Diffraction

XRD is used to study:

- Crystal structure
- Crystallinity
- Phase composition

Dynamic Light Scattering

DLS measures the hydrodynamic size distribution of particles suspended in a liquid.

Fourier Transform Infrared Spectroscopy

FTIR helps identify functional groups and chemical interactions associated with nanoparticles.

NANOBIOTECHNOLOGY IN MEDICINE

Nanomedicine is one of the most important areas of nanobiotechnology.

Major applications include:

- Drug delivery
- Cancer treatment
- Medical imaging
- Diagnostics
- Gene delivery
- Vaccine-related technologies
- Tissue engineering
- Biosensing

NANOTECHNOLOGY-BASED DRUG DELIVERY

Drug delivery is the process of transporting a therapeutic substance to its site of action.

Conventional drugs may sometimes have problems such as:

- Poor solubility
- Rapid degradation
- Low bioavailability
- Non-specific distribution
- Unwanted side effects

Nanocarriers can be designed to address some of these challenges.

NANOCARRIERS

Important nanocarriers include:

LIPOSOMES

Spherical vesicles consisting of lipid bilayers.

POLYMERIC NANOPARTICLES

Nanoparticles made from polymers that can encapsulate or associate with therapeutic agents.

MICELLES

Structures formed by amphiphilic molecules.

DENDRIMERS

Highly branched nanoscale polymers.

SOLID LIPID NANOPARTICLES

Nanoparticles containing a solid lipid matrix.

LIPID NANOPARTICLES

Nanoscale lipid-based delivery systems widely studied for nucleic-acid delivery.

ADVANTAGES OF NANOPARTICLE DRUG DELIVERY

Potential advantages include:

- Improved drug solubility
- Controlled release
- Protection of therapeutic molecules
- Altered pharmacokinetics
- Improved cellular delivery
- Possibility of targeting particular tissues
- Reduced exposure of healthy tissues in some systems

The actual benefit depends on the nanoparticle design and biological context.

TARGETED DRUG DELIVERY

Targeted delivery aims to increase the concentration of a therapeutic agent at a desired biological site.

Targeting can be broadly divided into:

PASSIVE TARGETING

Uses differences in tissue physiology to influence nanoparticle accumulation.

ACTIVE TARGETING

Uses molecules such as:

- Antibodies
- Peptides
- Aptamers
- Ligands

On the nanoparticle surface to interact with specific cellular targets.

Targeting does not automatically guarantee delivery only to the intended cells; biological barriers and particle clearance can strongly influence outcomes.

NANOBIOTECHNOLOGY AND CANCER

Cancer is one of the most important fields of nanomedicine research.

Nanotechnology can contribute to:

- Cancer detection
- Imaging
- Drug delivery
- Targeted therapy
- Combination therapy
- Photothermal therapy
- Diagnostic biosensors

CANCER DIAGNOSIS

Nanoparticles can be incorporated into diagnostic systems for detecting:

- Tumor biomarkers
- Proteins
- DNA
- RNA
- Other disease-associated molecules

Because some nanomaterials have strong optical, magnetic, or electrical properties, they can improve signal generation in certain diagnostic platforms.

CANCER DRUG DELIVERY

Nanocarriers can transport anticancer agents.

The objectives may include:

- Increasing drug accumulation at tumors
- Improving drug solubility
- Protecting drugs
- Controlling drug release
- Reducing systemic exposure where possible

However, tumor biology is highly complex, and nanoparticle delivery to tumors is not always efficient.

PHOTOTHERMAL NANOTHERAPY

Some nanoparticles can convert absorbed light energy into heat.

When appropriately designed and activated, this property can be investigated for cancer treatment.

The general principle is:

Light → Nanoparticle absorption → Energy conversion → Heat → Therapeutic effect

NANOBIOSENSORS

A biosensor is an analytical device containing a biological recognition element and a signal-transduction mechanism.

A typical biosensor consists of:

Biological recognition element → Transducer → Signal processing → Output

Nanomaterials can improve biosensor properties by increasing surface area and providing useful optical or electrical characteristics.

TYPES OF NANOBIOSENSORS

Nano biosensors can be based on:

- Optical detection
- Electrochemical detection
- Electrical detection
- Magnetic detection
- Mechanical detection

APPLICATIONS OF NANOBIOSENSORS

They are investigated for detecting:

- Glucose
- Pathogens
- DNA
- RNA
- Proteins
- Hormones
- Cancer biomarkers
- Toxins
- Environmental pollutants

Nano biosensors have potential applications in:

- Clinical diagnosis
- Food safety
- Environmental monitoring
- Point-of-care testing
- Biotechnology research

NANOTECHNOLOGY IN GENE DELIVERY

Gene delivery involves transporting genetic material into cells.

Nanotechnology can provide carriers for:

- DNA
- RNA
- siRNA
- mRNA
- Other nucleic acids

Nucleic-acid molecules can be protected from degradation and delivered to cells using appropriately designed nanocarriers.

Major challenges include:

- Cellular uptake
- Endosomal escape
- Stability

- Targeting
- Toxicity
- Efficient intracellular release

NANOTECHNOLOGY IN TISSUE ENGINEERING

Tissue engineering aims to restore, replace, or regenerate damaged tissues.

Nanomaterials can be incorporated into scaffolds.

Important properties include:

- Surface roughness
- Mechanical properties
- Porosity
- Biocompatibility
- Degradation rate

Nanostructured surfaces can influence:

- Cell adhesion
- Cell proliferation
- Cell differentiation

Applications include:

- Bone
- Cartilage
- Skin
- Nerve tissue
- Dental tissue

NANOTECHNOLOGY IN REGENERATIVE MEDICINE

Regenerative medicine attempts to stimulate or support the repair of damaged tissues.

Nanomaterials can be used to:

- Deliver growth factors
- Deliver genes
- Provide structural scaffolds
- Control cellular environments
- Support stem-cell-based approaches

ANTIMICROBIAL NANOTECHNOLOGY

Certain nanoparticles possess antimicrobial activity.

Examples include:

- Silver nanoparticles
- Zinc oxide nanoparticles
- Copper-based nanoparticles

Possible mechanisms include:

- Damage to microbial membranes
- Release of metal ions
- Generation of reactive oxygen species

- Interaction with proteins
- Disruption of metabolic processes

NANOBIOTECHNOLOGY IN AGRICULTURE

Nanobiotechnology has potential applications in agriculture.

MAJOR APPLICATIONS

- Nano-fertilizers
- Nano-pesticide delivery
- Plant disease detection
- Nanosensors
- Controlled nutrient delivery
- Crop monitoring

Nanotechnology may help improve the controlled delivery of agricultural inputs.

However, environmental fate and effects on beneficial organisms must be carefully evaluated.

NANOBIOTECHNOLOGY IN FOOD TECHNOLOGY

Potential applications include:

- Food packaging
- Food safety sensors
- Detection of pathogens
- Controlled release of preservatives
- Encapsulation of nutrients
- Improvement of food-storage systems

Nanostructured materials can be incorporated into packaging or sensing systems.

Safety evaluation is essential before widespread food applications.

ENVIRONMENTAL NANOBIOTECHNOLOGY

Nanomaterials can be used for environmental applications.

WATER PURIFICATION

Nanomaterials can help remove:

- Heavy metals
- Organic pollutants
- Microorganisms
- Other contaminants

ENVIRONMENTAL SENSORS

Nanosensors can detect low concentrations of environmental contaminants.

WASTE TREATMENT

Nanomaterials can participate in adsorption, catalysis, and other treatment processes.

NANOTOXICOLOGY

Nanotoxicology is the study of the potential harmful effects of nanomaterials.

The toxicity of a nanomaterial may depend on:

- Size
- Shape

- Surface area
- Surface charge
- Chemical composition
- Solubility
- Dose
- Exposure route
- Exposure duration

Potential biological effects may involve:

- Oxidative stress
- Inflammation
- Membrane damage
- Cellular stress
- Organ accumulation

Not every nanoparticle is necessarily toxic, and toxicity cannot be predicted solely from the fact that a material is nanoscale. Detailed material-specific evaluation is required.

NANO-BIO INTERACTIONS

When nanoparticles enter a biological environment, they interact with:

- Proteins
- Lipids
- Carbohydrates
- Cells
- Blood components
- Extracellular matrices

Proteins can adsorb onto nanoparticle surfaces and form what is often called a protein corona.

The protein corona can influence:

- Particle identity in biological fluids
- Cellular uptake
- Biodistribution
- Clearance
- Biological activity

Understanding nano-bio interactions is therefore essential for developing safe and effective nanomedicines.

ADVANTAGES OF NANOBIOTECHNOLOGY

Major advantages include:

- Molecular-scale interaction
- High surface-area-to-volume ratio
- Improved detection sensitivity
- Controlled drug delivery
- Potential targeted delivery
- Unique optical properties

- Unique magnetic properties
- Potential for multifunctional systems
- Wide range of biomedical applications

LIMITATIONS OF NANOBIOTECHNOLOGY

Despite its potential, nanobiotechnology has several limitations:

- Possible toxicity
- High production cost
- Complex manufacturing
- Difficulty in reproducibility
- Stability problems
- Unpredictable biological interactions
- Regulatory challenges
- Environmental concerns
- Difficulties in large-scale production

FACTORS AFFECTING NANOPARTICLE PERFORMANCE

Nanoparticle behavior depends on several factors.

SIZE

Size affects:

- Cellular uptake
- Biodistribution
- Clearance
- Surface area

SHAPE

Shape can influence:

- Cellular interaction
- Transport
- Uptake

SURFACE CHARGE

Surface charge affects interactions with:

- Proteins
- Cell membranes
- Biological barriers

SURFACE CHEMISTRY

Surface functionalization can influence:

- Stability
- Targeting
- Protein adsorption
- Cellular uptake

COMPOSITION

Different materials can produce very different biological effects.

NANOMEDICINE

Nanomedicine refers to the use of nanotechnology in medicine.

Major areas include:

- Drug delivery
- Diagnostics
- Imaging
- Regenerative medicine
- Cancer therapy
- Biosensors
- Nucleic-acid delivery

Nanomedicine aims to improve diagnosis and treatment by controlling materials and therapeutic systems at very small scales.

NANOTECHNOLOGY AND PERSONALIZED MEDICINE

Personalized medicine aims to select treatment strategies based on individual biological characteristics.

Nanotechnology could support personalized medicine through:

- Patient-specific drug delivery
- Biomarker detection
- Molecular diagnostics
- Controlled therapeutic release
- Combination diagnostic-therapeutic systems

This field remains an active research area.

THERANOSTICS

The term theranostics combines:

Therapy + Diagnostics

Nanoparticles can potentially be designed to perform both functions.

For example, a multifunctional nanoparticle could theoretically:

- Identify a target
- Provide an imaging signal
- Deliver a therapeutic molecule
- Allow monitoring of treatment

Such systems are called theranostic Nano platforms.

NANOROBOTICS

Nanorobotics refers to the development of nanoscale or micro scale systems capable of performing controlled tasks.

Potential future applications include:

- Targeted drug delivery
- Diagnostic sensing
- Microenvironment monitoring
- Minimally invasive procedures

Many nanorobotics medical applications remain experimental.

ARTIFICIAL INTELLIGENCE IN NANOBIOTECHNOLOGY

Artificial intelligence and machine learning are increasingly being explored in nanobiotechnology.

AI can potentially help with:

- Nanoparticle formulation
- Prediction of particle properties
- Drug-loading optimization
- Toxicity prediction
- Image analysis
- Biomarker identification

Combining computational approaches with experimental nanotechnology may reduce trial-and-error during material development.

FUTURE PROSPECTS

The future of nanobiotechnology may include:

- Smart drug-delivery systems
- Precision nanomedicine
- Advanced biosensors
- AI-assisted nanoparticle design
- Sustainable green synthesis
- Improved gene delivery
- Multifunctional theranostic systems
- Advanced tissue-engineering materials
- Personalized medicine
- Improved environmental nanotechnology

The successful development of these technologies will require collaboration among biologists, chemists, physicists, engineers, medical researchers, toxicologists, and regulatory scientists.

CONCLUSION

Nanobiotechnology is an interdisciplinary field that combines nanoscale science with biological systems. The unique properties of nanomaterials provide opportunities for applications ranging from drug delivery and cancer therapy to biosensors, gene delivery, tissue engineering, agriculture, food technology, and environmental protection.

Nanoparticles can be engineered according to their size, shape, composition, and surface chemistry. Their surfaces can also be functionalized with biological molecules to modify their interactions with cells and tissues.

Green synthesis provides an attractive route for producing certain nanomaterials using biological resources, although reproducibility and safety must be carefully considered.

Despite its enormous potential, nanobiotechnology faces challenges related to toxicity, biological interactions, manufacturing, cost, reproducibility, environmental impact, and regulatory approval.

The future of nanobiotechnology will depend on the development of safe, effective, reproducible, sustainable, and biologically compatible nanomaterials**.**

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Chapter 7

NANOTECHNOLOGY IN WATER PURIFICATION

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ABSTRACT

Water pollution is one of the major environmental challenges affecting human health, ecosystems, agriculture, and industrial development. Conventional water-treatment methods are useful for removing many contaminants, but some persistent pollutants, heavy metals, microorganisms, dyes, pharmaceuticals, and other emerging contaminants can be difficult to remove efficiently. Nanotechnology provides new approaches to water purification through the development and application of nanoscale materials with high surface area, tunable surface chemistry, catalytic activity, and antimicrobial properties.

Nanomaterials such as metal and metal oxide nanoparticles, carbon nanotubes, graphene-based materials, nanocomposites, zeolites, metal-organic frameworks (MOFs), and nanoporous membranes have been investigated for water purification. These materials can remove contaminants through adsorption, membrane separation, photocatalytic degradation, catalytic reduction, antimicrobial action, and other processes. For example, TiO_2 and ZnO nanoparticles can act as photocatalysts, while graphene-based materials and other nanoadsorbents can interact with heavy metals and organic pollutants. Magnetic nanoparticles offer the additional advantage of potentially being recovered from treated water using an external magnetic field.

Despite their potential, nanotechnology-based water purification still faces challenges including production cost, nanoparticle aggregation, recovery, toxicity, environmental release, membrane fouling, scalability, and regulatory requirements. Future research is increasingly focused on green synthesis, recyclable nanomaterials, hybrid systems, intelligent materials, and integration with conventional treatment technologies.

KEYWORDS: Nanotechnology, Water Purification, Nanomaterials, Nanoparticles, Adsorption, Photocatalysis, Nanofiltration, Membrane Technology, Heavy Metals, Nanocomposites.

INTRODUCTION

Water is one of the most important natural resources required for life. Clean water is essential for drinking, food production, sanitation, industrial activities, and ecosystem stability. However, rapid industrialization, urbanization, population growth, agricultural activities, and improper waste disposal have increased the contamination of water resources.

Water pollutants may include:

- Heavy metals

- Organic pollutants
- Dyes
- Pesticides
- Pharmaceuticals
- Pathogenic microorganisms
- Nutrients
- Salts
- Suspended solids
- Emerging contaminants

Some contaminants are difficult to remove using conventional treatment processes. As a result, advanced technologies are being investigated to improve water purification.

Nanotechnology has emerged as an important research area because nanoscale materials can possess properties that differ substantially from their bulk counterparts. Their high surface-area-to-volume ratio, surface reactivity, tunable chemistry, and catalytic properties can be advantageous for pollutant removal. Recent reviews describe nanomaterials as promising adsorbents, photocatalysts, membrane components, and antimicrobial agents for water treatment.

DEFINITION OF NANOTECHNOLOGY

Nanotechnology is the science and engineering of designing, producing, characterizing, and applying materials and structures at the nanoscale.

The prefix **nano** represents a factor of 10^{-9}.

Therefore:

1 nanometer (nm) = 10^{-9} meter

At the nanoscale, materials can exhibit distinctive:

- Physical properties
- Chemical properties
- Optical properties
- Electrical properties
- Magnetic properties
- Catalytic properties

These characteristics make nanomaterials useful for environmental applications.

NANOTECHNOLOGY IN WATER PURIFICATION

Nanotechnology in water purification involves the use of nanoscale materials and processes to:

- Remove pollutants
- Destroy contaminants
- Separate dissolved substances
- Inactivate microorganisms
- Detect contaminants
- Improve membrane performance
- Produce safer water

The major mechanisms are:

Adsorption → Photocatalysis → Membrane filtration → Catalytic degradation → Antimicrobial action → Sensing

Recent literature emphasizes adsorption, photocatalysis, membrane filtration, and antibacterial applications as major areas of nanotechnology-based water treatment.

WHY NANOMATERIALS ARE USEFUL FOR WATER PURIFICATION

HIGH SURFACE-AREA-TO-VOLUME RATIO

Nanomaterials have a large surface area relative to their volume.

This provides many active sites for interaction with pollutants.

Therefore, nanomaterials can be highly effective for adsorption and surface reactions.

HIGH CHEMICAL REACTIVITY

Many nanomaterials have high surface reactivity.

This property can help in:

- Pollutant degradation
- Catalytic reactions
- Oxidation-reduction processes

TUNABLE SURFACE CHEMISTRY

The surface of a nanomaterial can be modified using:

- Functional groups
- Polymers
- Biomolecules
- Other nanoparticles

Surface modification can improve selectivity toward specific pollutants.

PHOTOCATALYTIC PROPERTIES

Some nanomaterials can interact with light and generate reactive species capable of degrading organic pollutants.

Examples include:

- Titanium dioxide
- Zinc oxide
- Other semiconductor nanomaterials

ANTIMICROBIAL PROPERTIES

Some nanomaterials can damage microorganisms or inhibit their growth.

This makes them potentially useful for water disinfection and antimicrobial membrane surfaces.

TYPES OF NANOMATERIALS USED IN WATER PURIFICATION

METAL NANOPARTICLES

Examples include:

- Silver nanoparticles
- Gold nanoparticles
- Copper nanoparticles
- Iron nanoparticles

Potential applications include:

- Antimicrobial treatment
- Catalysis
- Pollutant removal
- Detection

METAL OXIDE NANOPARTICLES

Important examples include:

- TiO_2
- ZnO
- Fe_2O_3
- Fe_3O_4
- MgO
- CuO

These materials have been widely investigated for adsorption, photocatalysis, antimicrobial activity, and related applications.

CARBON-BASED NANOMATERIALS

Examples include:

- Carbon nanotubes
- Graphene
- Graphene oxide
- Reduced graphene oxide
- Carbon quantum dots
- Fullerenes

These materials can provide large surface areas and tunable surface chemistry.

They are particularly interesting for adsorption and membrane applications.

NANOCOMPOSITES

Nanocomposites combine nanoscale materials with another material.

Examples include:

- Polymer–nanoparticle composites
- Magnetic nanocomposites
- Graphene-based nanocomposites
- Metal oxide composites

The objective is often to combine several properties in one material.

For example:

Adsorption + Photocatalysis + Magnetic Recovery

Can be combined in a multifunctional nanocomposite.

METAL-ORGANIC FRAMEWORKS

Metal-organic frameworks, or **MOFs**, are porous materials constructed from metal centers or clusters connected by organic ligands.

Their properties include:

- High surface area

- Tunable pore structure
- Adjustable surface chemistry
- Potentially high adsorption capacity

MOFs are being investigated for removing heavy metals, organic pollutants, dyes, and other contaminants.

NANOTECHNOLOGY-BASED WATER PURIFICATION MECHANISMS

ADSORPTION

Adsorption is one of the most important mechanisms.

During adsorption, contaminants present in water attach to the surface of a nanomaterial.

The contaminant is called the **adsorbate**, while the material is called the **adsorbent**.

Possible interactions include:

- Electrostatic attraction
- Hydrogen bonding
- π–π interactions
- Ion exchange
- Surface complexation
- Van der Waals interactions

Surface functionalization can improve the selectivity of nanomaterials toward particular pollutants.

REMOVAL OF HEAVY METALS

Heavy-metal contamination is a major water-quality problem.

Important heavy metals and metalloids include:

- Lead
- Cadmium
- Mercury
- Chromium
- Arsenic
- Nickel

Nanomaterials can remove these contaminants through:

- Adsorption
- Reduction
- Ion exchange
- Surface complexation
- Precipitation

Carbon-based nanomaterials, metal oxides, zero-valent metals, MOFs, and nanocomposites have all been studied for heavy-metal removal.

REMOVAL OF DYES

Textile and related industrial effluents can contain large amounts of synthetic dyes.

Examples include:

- Methylene blue
- Congo red

- Rhodamine B
- Methyl orange

Nanomaterials can remove dyes by:

Adsorption or **Photocatalytic degradation**

Graphene-based materials, activated carbon nanocomposites, TiO_2, ZnO, and other nanomaterials have been investigated for dye removal.

PHOTOCATALYSIS

Photocatalysis is an important nanotechnology-based process.

A photocatalyst absorbs light and produces reactive species that can transform or degrade contaminants.

A simplified process is:

Nanophotocatalyst + Light → Electron–Hole Pairs → Reactive Species → Pollutant Degradation

Reactive species may include:

- Hydroxyl radicals
- Superoxide-related species
- Photogenerated electrons
- Photogenerated holes

These reactive species can attack organic pollutants.

TITANIUM DIOXIDE NANOPARTICLES

Titanium dioxide (TiO_2) is one of the most extensively investigated photocatalytic nanomaterials.

Important characteristics include:

- Photocatalytic activity
- Chemical stability
- High surface activity
- Relative photostability

TiO_2 has been investigated for degradation of:

- Organic dyes
- Pharmaceutical compounds
- Pesticides
- Other organic pollutants

Recent reviews continue to identify TiO_2 as a major material in photocatalytic water treatment.

ZINC OXIDE NANOPARTICLES

ZnO is another important semiconductor nanomaterial.

Potential applications include:

- Photocatalytic degradation
- Antimicrobial treatment
- Pollutant removal
- Water-treatment membranes

ZnO can generate reactive species under suitable irradiation conditions.

MAGNETIC NANOPARTICLES

Magnetic nanoparticles are particularly attractive because they may be separated from water using a magnetic field.

For example:

Contaminated water + Magnetic nanoparticles

↓

Pollutant adsorption

↓

External magnetic field

↓

Nanoparticle separation

↓

Cleaner water

This approach can potentially improve nanoparticle recovery and reuse.

Iron oxide nanoparticles are particularly important in this area.

NANOFILTRATION

Nanofiltration is a membrane-based separation technology.

Nanofiltration membranes can remove:

- Organic molecules
- Multivalent ions
- Dyes
- Some pharmaceuticals
- Other dissolved contaminants

Nanoporous membranes are being investigated for desalination, heavy-metal removal, organic pollutant removal, and pathogen control.

NANOMATERIALS IN MEMBRANE TECHNOLOGY

Nanomaterials can be incorporated into membranes to improve:

- Water permeability
- Selectivity
- Hydrophilicity
- Antifouling properties
- Antimicrobial activity
- Mechanical properties

Examples include membranes containing:

- TiO_2
- ZnO
- Silver nanoparticles
- Carbon nanotubes
- Graphene oxide
- Silica nanoparticles

GRAPHENE-BASED MEMBRANES

Graphene and graphene oxide have attracted significant interest in water purification.

Graphene-based materials may provide:

- High surface area
- Tunable surface chemistry
- Thin separation layers
- Potentially selective transport pathways

Graphene oxide can also interact with various pollutants through surface functional groups.

Recent reviews identify graphene-based composites and carbon nanotubes as important nanomaterials for water purification.

ANTIMICROBIAL NANOTECHNOLOGY

Water may contain pathogenic microorganisms such as:

- Bacteria
- Viruses
- Protozoa
- Fungi

Certain nanomaterials can contribute to microbial inactivation.

Silver nanoparticles are among the most studied antimicrobial nanomaterials.

Possible mechanisms include:

- Interaction with microbial membranes
- Release of metal ions
- Generation of reactive species
- Damage to proteins
- Disruption of cellular metabolism

The actual antimicrobial effect depends on nanoparticle composition, size, surface properties, concentration, and environmental conditions.

NANOTECHNOLOGY FOR DESALINATION

Desalination involves removing dissolved salts from saline water.

Nanotechnology is being investigated to improve membrane-based desalination.

Potential advantages include:

- High water permeability
- Selective ion rejection
- Reduced membrane thickness
- Improved surface properties

Nanoporous membranes with nanoscale pores are an active research area for desalination.

REMOVAL OF PHARMACEUTICALS

Pharmaceutical residues can enter water through:

- Domestic wastewater
- Hospitals
- Pharmaceutical industries
- Improper disposal

Examples include:

- Antibiotics
- Analgesics
- Anti-inflammatory drugs
- Hormonal compounds

Nanomaterials can potentially remove pharmaceuticals through:

- Adsorption
- Photocatalysis
- Membrane separation
- Advanced oxidation

REMOVAL OF PESTICIDES

Agricultural runoff can introduce pesticides into surface and groundwater.

Nanomaterials may help remove pesticides through:

- Adsorption
- Catalytic degradation
- Photocatalysis
- Membrane separation

Functionalized nanomaterials can potentially be designed to improve selectivity toward particular pesticide molecules.

REMOVAL OF PATHOGENS

Nanotechnology can contribute to microbial removal through:

- Antimicrobial nanoparticles
- Nanocomposite membranes
- Photocatalytic systems
- Nano-enabled filtration

However, the release of antimicrobial nanoparticles into treated water must be carefully controlled.

NANOTECHNOLOGY FOR WATER QUALITY MONITORING

Nanotechnology is not limited to pollutant removal.

Nanosensors can be used to detect:

- Heavy metals
- Pathogens
- Organic pollutants
- Chemical contaminants
- Biological markers

Thus, future water-treatment systems may combine:

Detection + Purification + Monitoring

In one integrated platform.

GREEN NANOTECHNOLOGY

Green nanotechnology focuses on producing and using nanomaterials in ways that reduce environmental impacts.

Biological sources can include:

- Plants
- Bacteria
- Fungi
- Algae
- Enzymes
- Agricultural residues

Green synthesis may reduce dependence on certain hazardous chemical reagents.

However, green synthesis does not automatically mean that a nanomaterial is safe. Toxicity, reproducibility, scalability, and environmental fate still need to be evaluated.

ADVANTAGES OF NANOTECHNOLOGY IN WATER PURIFICATION

Major advantages include:

- High surface area
- High adsorption capacity
- High reactivity
- Potential selective pollutant removal
- Photocatalytic activity
- Antimicrobial properties
- Potential multifunctionality
- Possibility of combining several treatment mechanisms

Recent reviews emphasize the combination of adsorption, photocatalysis, membrane separation, and antibacterial activity as a major strength of nanomaterial-based treatment.

LIMITATIONS OF NANOTECHNOLOGY

Despite its advantages, several challenges remain.

High Cost

Some nanomaterials require expensive raw materials and sophisticated production methods.

Aggregation

Nanoparticles can aggregate, reducing their effective surface area.

Recovery

Free nanoparticles can be difficult to recover after treatment.

Toxicity

Some nanomaterials may have toxic effects on aquatic organisms or humans.

Environmental Release

Nanoparticles escaping from treatment systems may enter natural ecosystems.

Membrane Fouling

Nanomaterial-based membranes can still experience fouling.

Scale-Up

High laboratory removal efficiency does not necessarily guarantee successful large-scale operation.

Cost, scalability, toxicity, recovery, and long-term stability are repeatedly identified as important barriers to practical implementation.

NANOTOXICOLOGY

Nanotoxicology is the study of the potential harmful effects of nanomaterials.

Important factors include:

- Particle size
- Shape
- Surface charge
- Chemical composition
- Surface coating
- Concentration
- Exposure duration
- Environmental conditions

Potential concerns include:

- Oxidative stress
- Cellular damage
- Inflammation
- Effects on aquatic microorganisms
- Bioaccumulation
- Release of toxic ions

Therefore, safety assessment must be an integral part of nanotechnology-based water purification.

RECOVERY AND REUSE

For practical applications, nanomaterials should ideally be recoverable and reusable.

Potential methods include:

- Magnetic separation
- Membrane separation
- Immobilization
- Filtration
- Sedimentation

Magnetic nanomaterials are especially attractive because an external magnetic field can potentially facilitate their recovery.

HYBRID NANOTECHNOLOGY SYSTEMS

Hybrid systems combine different treatment mechanisms.

For example:

Adsorption + Photocatalysis

A pollutant can first be concentrated on the surface of an adsorbent and then degraded photocatalytically.

Recent research describes hybrid adsorption–photocatalysis composites as a promising approach for treating persistent organic pollutants.

Other combinations include:

- Nano adsorption + membrane filtration
- Photocatalysis + membrane filtration

- Adsorption + magnetic separation
- Antimicrobial nanoparticles + membrane filtration

NANOTECHNOLOGY AND WASTEWATER REUSE

Treated wastewater can potentially be reused for:

- Irrigation
- Industrial processes
- Groundwater recharge
- Landscaping
- Other non-potable applications

Advanced nanotechnology-based treatment may contribute to the removal of contaminants that remain after conventional treatment.

However, treatment objectives should be based on the intended reuse and applicable water-quality standards.

ROLE OF ARTIFICIAL INTELLIGENCE

Artificial intelligence and machine learning are increasingly being investigated in nanotechnology-based water treatment.

AI can potentially help predict:

- Pollutant removal
- Adsorption capacity
- Optimal operating conditions
- Nanomaterial properties
- Membrane performance
- Toxicity

Recent reviews identify AI-assisted optimization and intelligent nanomaterials as emerging directions.

FUTURE PERSPECTIVES

Future research is expected to focus on:

- Green synthesis of nanomaterials
- Low-cost nanomaterials
- Recyclable and reusable nanomaterials
- Magnetic nanocomposites
- Advanced nanoporous membranes
- Solar-driven photocatalysis
- Multifunctional nanocomposites
- AI-assisted material design
- Real-time nanosensors
- Integrated treatment systems
- Life-cycle assessment
- Long-term environmental safety

The development of multifunctional and sustainable materials is particularly important for moving nanotechnology from laboratory research toward practical water-treatment systems.

PROPOSED WATER PURIFICATION SYSTEM

A conceptual nanotechnology-based purification system can be represented as:

Contaminated Water
↓
Pre-treatment
↓
Nano adsorption
↓
Nanofiltration
↓
Photocatalytic Treatment
↓
Disinfection
↓
Nanomaterial Recover
↓
Final Water Quality Testing
↓
Purified Water

This integrated approach can combine several technologies instead of depending on a single treatment process.

COMPARISON OF NANOTECHNOLOGY-BASED METHODS

Method	Major Function	Suitable Contaminants	Main Advantage
Nano adsorption	Surface removal	Heavy metals, dyes, organics	High surface area
Photocatalysis	Pollutant degradation	Organic pollutants	Can destroy contaminants
Nanofiltration	Physical separation	Salts, ions, organics	Selective separation
Antimicrobial nanoparticles	Microbial inactivation	Bacteria and other microbes	Antimicrobial activity
Magnetic nanoparticles	Adsorption + recovery	Metals and organics	Magnetic separation
Nanocomposites	Multifunctional treatment	Mixed pollutants	Multiple mechanisms
Nanosensors	Detection	Various contaminants	Rapid monitoring

RESEARCH GAPS

Important research gaps include:

- Long-term environmental effects
- Standardized toxicity testing
- Nanoparticle recovery
- Material regeneration

- Large-scale manufacturing
- Cost reduction
- Real wastewater studies
- Membrane fouling control
- Long-term membrane stability
- Life-cycle assessment
- Regulatory frameworks

Laboratory experiments often use simplified water samples, while real water contains many competing substances. Therefore, more studies using real wastewater and realistic operating conditions are needed.

CONCLUSION

Nanotechnology has significant potential for improving water purification. Nanomaterials possess unique properties such as high surface area, tunable surface chemistry, catalytic activity, and antimicrobial behavior, making them useful for removing a wide range of contaminants.

The major applications include:

Adsorption → Photocatalysis → Nanofiltration → Desalination → Disinfection → Sensing

Important nanomaterials include:

TiO_2 → ZnO → Iron oxide → Silver nanoparticles → Carbon nanotubes → Graphene/graphene oxide → MOFs → Nanocomposites

However, successful commercialization requires more than high pollutant-removal efficiency. The nanomaterial must also be affordable, stable, recoverable, reusable, scalable, and environmentally safe.

Future water purification systems are likely to combine nanotechnology with conventional treatment, renewable energy, advanced membranes, green synthesis, sensors, and artificial intelligence. Recent research particularly emphasizes hybrid systems, sustainable materials, intelligent treatment, and improved recovery and safety.

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Chapter
8

NANO-TOOLS IN PLANT METABOLOMICS AND PHYTOCHEMISTRY: PLATFORMS, APPLICATIONS AND PERSPECTIVES

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ABSTRACT

Plants synthesise an immense diversity of specialised metabolites that underpin human nutrition, medicine and crop resilience. Capturing this chemical diversity requires analytical tools that are sensitive, spatially resolved and tolerant of complex biological matrices. Engineered nanomaterials, defined by at least one dimension in the 1–100 nm range, have emerged as such tools. This chapter reviews how nanostructured surfaces, nanoparticles, nanosensors and nanocarriers are reshaping plant metabolomics and phytochemistry. Five areas are discussed: nanomaterial-assisted mass spectrometry and imaging, nano-enabled sample preparation, optical and electrochemical Nano sensing, nanocarrier-based delivery of phytochemicals, and plant-mediated nanoparticle synthesis. Limitations related to reproducibility, toxicity and data standardization are outlined, and future directions are proposed.

KEYWORDS: Nanotechnology, Plant Metabolomics, Phytochemistry, Mass Spectrometry Imaging, Nanosensors, Nanocarriers.

INTRODUCTION

Plants are remarkable chemical factories. Beyond the primary metabolites required for growth, a single species may produce thousands of specialised metabolites, including alkaloids, terpenoids, phenylpropanoids and glucosinolates, which mediate defence, signalling and environmental adaptation (Fiehn, 2002; Hall, 2006). Metabolomics aims to measure these small molecules comprehensively, whereas phytochemistry seeks to isolate, characterize and exploit those with biological activity. Both disciplines face shared analytical hurdles: wide concentration ranges, extensive structural isomerism, rapid metabolite turnover and strong spatial heterogeneity across tissues and cells (Saito & Matsuda, 2010; Alseekh *et al.,* 2021).

Liquid chromatography–mass spectrometry (LC-MS) and nuclear magnetic resonance spectroscopy are powerful, yet workflows built on them usually depend on tissue homogenisation, which erases spatial information, and they can struggle with low-abundance or poorly ionizing compounds (Dettmer *et al.,* 2007). Nanotechnology offers complementary solutions. Materials behave differently at the nanoscale, showing high surface-area-to-volume ratios and tunable optical, electronic and magnetic properties, so they can be engineered to

capture, ionize, amplify, transport or report on small molecules (Wang *et al.,* 2016). In this chapter, the term nano-tools denotes any engineered nanoscale material or device used to analyse, extract, deliver or generate plant metabolites. The following sections describe the main classes of nano-tools, explain their working principles, and discuss their promise and limitations.

NANOMATERIAL-ASSISTED MASS SPECTROMETRY AND IMAGING

Mass spectrometry is the cornerstone of plant metabolomics, but conventional matrix-assisted laser desorption/ionization (MALDI) performs poorly for metabolites below about 500 Da, because organic matrix ions create intense background signals in the same mass range. Inorganic nanomaterials address this problem. The concept dates to the late 1980s, when ultrafine cobalt particles suspended in glycerol were used to ionize proteins (Tanaka *et al.,* 1988), and it later developed through graphite-assisted (Sunner *et al.,* 1995) and porous silicon platforms (Wei *et al.,* 1999). Nanostructured surfaces absorb laser energy efficiently and generate little chemical noise, which makes them well suited to low-molecular-weight analytes.

Several nanomaterial families are now in use. Gold and platinum nanostructures promote ionization of small biomolecules such as amino acids, sugars and phenolic compounds (Kawasaki *et al.,* 2007). Silver deposition permits detection of olefins and other poorly ionizing lipids with high spatial resolution (Dufresne *et al.,* 2013). Graphene serves as a matrix with minimal interference for small-molecule analysis (Dong *et al.,* 2010). Nanostructure-initiator mass spectrometry (NIMS) traps a liquid initiator within a nanostructured silicon surface; the initiator is released on laser or ion irradiation, enabling both direct analysis and tissue imaging (Northen *et al.,* 2007; Yanes *et al.,* 2009).

Mass spectrometry imaging (MSI) is where these materials have the clearest impact on plant science. By rastering a laser across a tissue section coated with nanoparticles, researchers can map the distribution of flavonoids, alkaloids and lipids across roots, leaves, seeds and glandular structures (Boughton *et al.,* 2016). Nanoparticle-assisted imaging has reached cellular-scale resolution in tissue (Taira *et al.,* 2008), which matters in plants because specialised metabolites are often sequestered in particular cell types or compartments. Such maps can reveal biosynthetic sites, transport routes and localized defence responses that bulk extraction averages away.

The choice of nanomaterial depends on analyte polarity, ionization mode and the desired resolution. Particle size, shape, surface coating and deposition method (sputtering, spraying or sublimation) all influence signal intensity and homogeneity, so protocol standardization is essential for quantitative or comparative studies.

NANO-ENABLED SAMPLE PREPARATION AND SEPARATION

Extraction and clean-up often determine the quality of metabolomic data. Magnetic nanoparticles, typically iron oxide cores coated with silica, polymers or functional ligands, can be applied in magnetic solid-phase extraction, where analytes adsorb onto dispersed particles that are then recovered with an external magnet (Šafaříková & Šafařík, 1999). Compared with

packed cartridges, dispersed nanoparticles offer large surface area, rapid adsorption and simple handling, advantages that matter when many small plant samples must be processed in parallel.

Surface chemistry can be tailored to the target class: hydrophobic coatings for terpenoids, ion-exchange groups for alkaloids, or boronate affinity ligands for glycosylated compounds. Selective enrichment of this kind reduces matrix effects such as ion suppression, a persistent difficulty in plant LC-MS (Alseekh *et al.,* 2021). It also concentrates trace metabolites that would otherwise fall below detection limits. Carbon nanotubes, graphene and other nanostructured sorbents have likewise been explored as sorbents and as modifiers of chromatographic phases, although their routine use in plant studies is still developing.

A practical consideration is recovery. Strong adsorption can hinder elution of some analytes, and nonspecific binding may bias the metabolite profile. Validation with authentic standards and spiked plant matrices is therefore needed before nano-sorbents are adopted in untargeted workflows.

NANOSENSORS FOR DETECTION AND PROFILING

Optical and electrochemical nanosensors offer rapid, low-cost detection that complements mass spectrometry. Gold and silver nanoparticles display localized surface plasmon resonance, and their colour changes on aggregation or ligand binding provide the basis of colorimetric assays (Saha *et al.,* 2012). Such principles have been adapted to detect antioxidants, phenolics and contaminants in plant-derived products, giving results that can be read visually or with a handheld spectrometer.

Surface-enhanced Raman scattering (SERS) exploits the strong electromagnetic fields near roughened metal nanostructures to amplify the vibrational signature of adsorbed molecules, with sensitivity approaching the single-molecule level under optimal conditions (Kneipp *et al.,* 1997; Langer *et al.,* 2020). Because Raman spectra are rich in structural information, SERS can discriminate closely related phytochemicals and supports authentication and quality control of botanicals with minimal sample preparation. Its main limitations are uneven distribution of signal-enhancing hot spots, interference from plant pigments and fluorescence, and the difficulty of quantification in complex extracts.

Electrochemical sensors modified with carbon nanotubes, graphene or metal nanoparticles exploit the redox activity of polyphenols and flavonoids. They enable compact, portable measurements that are attractive for field phenotyping and for screening of crude extracts. Because they respond to groups of electro active compounds rather than to single molecules, they are best viewed as screening tools that direct, rather than replace, full metabolite profiling.

This overview outlines diverse nanoscale tools, their core physical principles, and specialized analytical and delivery functions. It highlights their utility across laser-assisted mass spectrometry, magnetic separation, surface-enhanced Raman fingerprinting, and controlled encapsulation, supported by benchmark literature for each application.

Table 1: Representative nano-tools in plant metabolomics and phytochemistry

Nano-Tool	Principle	Application	Example Source
Gold/platinum nanostructures	Laser energy absorption and ionization with low background	Small-molecule detection by LDI-MS	Kawasaki *et al.* (2007)
Silver nanoparticles	Silver-assisted ionization	High-resolution imaging of olefins and lipids	Dufresne *et al.* (2013)
NIMS surfaces	Initiator release from nanostructured silicon	Tissue imaging, direct analysis	Yanes *et al.* (2009)
Magnetic nanoparticles	Dispersive adsorption and magnetic recovery	Enrichment and clean-up of extracts	Šafaříková & Šafařík (1999)
SERS substrates	Plasmonic field enhancement of Raman signal	Fingerprinting, authentication	Langer *et al.* (2020)
Lipid and polymeric nanocarriers	Encapsulation and controlled release	Delivery of poorly soluble phytochemicals	Ezhilarasi *et al.* (2013)

NANOCARRIERS IN PHYTOCHEMISTRY

Many bioactive phytochemicals, including flavonoids, curcuminoids and terpenoids, suffer from poor aqueous solubility, chemical instability and limited oral bioavailability, which restrict their therapeutic use (Bilia *et al.*, 2014). Nanocarriers such as liposomes, polymeric nanoparticles, solid lipid nanoparticles and nanoemulsions encapsulate these compounds, shield them from degradation and can improve solubility, absorption and controlled release (Ezhilarasi *et al.*, 2013). Surface decoration with targeting ligands further allows delivery to specific tissues. From an analytical standpoint, nanoformulation shifts attention from chemical identity alone to physical form. Particle size, polydispersity, zeta potential, encapsulation efficiency and release profile become critical quality attributes, and they must be reported alongside conventional phytochemical characterization. Metabolomic approaches can in turn be used to follow how encapsulated phytochemicals are transformed in biological systems, linking formulation design to metabolic outcome.

PLANT-MEDIATED SYNTHESIS OF NANOPARTICLES

Plant extracts are rich in polyphenols, terpenoids, proteins and sugars that act as both reducing and capping agents, so metal salts can be converted into nanoparticles without harsh chemicals (Iravani, 2011; Mittal *et al.*, 2013). This green route links phytochemistry and nanotechnology in two directions: phytochemicals generate nanoparticles, and the resulting particles can then be used to analyse or deliver phytochemicals (Singh *et al.*, 2016).

Particle size, shape and stability depend on extract composition, pH, temperature and reaction time. The metabolite profile of the extract is therefore a determinant of nanoparticle quality. Metabolomic characterization of extracts can help explain batch-to-batch variability and identify

the compounds responsible for reduction and stabilisation, turning an empirical process into a more predictable one. Such an approach also encourages the use of agricultural residues and underused species as sustainable sources of reducing agents.

PLANT NANOBIONICS AND IN VIVO SENSING

A newer direction places nanomaterials inside living plants. Giraldo *et al.* (2014) showed that single-walled carbon nanotubes can cross chloroplast envelopes, enhance photosynthetic electron transport and, when functionalized, act as sensors for nitric oxide in living tissue. More broadly, nano-enabled strategies are being developed to deliver nutrients, protective agents and signalling molecules to crops (Kah *et al.,* 2019). Targeted delivery of elicitors could in principle modulate secondary metabolism, while embedded sensors could report metabolic status in real time, moving metabolomics from snapshots of extracted tissue towards dynamic monitoring.

CHALLENGES AND LIMITATIONS

Despite rapid progress, several obstacles limit wider adoption. Reproducibility is the most immediate: batch-to-batch variation in nanoparticle size, coating and deposition affects signal intensity, and laboratories rarely share harmonized protocols. Reporting standards for metabolomics, such as those summarized by Alseekh *et al.* (2021), should be extended to include nanomaterial characterization, covering size distribution, surface chemistry and storage conditions. Safety and environmental fate are equally important. Toxicity of nanomaterials depends on size, shape, composition and surface reactivity (Nel *et al.,* 2006), and nanoparticles introduced into plants or soils may be taken up, transformed or accumulated in unpredictable ways. Nanoparticles can also alter the plant metabolome itself, creating a risk that the tool changes the quantity it is meant to measure.

Analytical issues remain as well. Nanomaterials may form adducts, promote in-source fragmentation or bind selectively to certain compound classes, complicating annotation and quantification. Costs, scalability and regulatory acceptance, especially for Nano formulated phytochemicals intended for human use, add further barriers.

FUTURE PERSPECTIVES

Several developments are likely to shape the field. Integration of nano-tools with microfluidics and portable instruments may enable on-site profiling of medicinal and food crops. Higher-resolution imaging combined with nanomaterial matrices could move plant metabolomics toward single-cell analysis. Machine-learning methods applied to spectral and imaging datasets will help to interpret the large volumes of data these tools generate, and multi-omics integration will place spatial metabolite maps in the context of gene expression and protein activity. Finally, biodegradable and sustainably produced nanomaterials will be needed so that analytical gains do not come at an environmental cost.

CONCLUSION

Nano-tools are expanding what can be measured, mapped and delivered in plant science. Nanostructured surfaces improve mass spectrometric detection of small metabolites and enable imaging at cellular scale, magnetic and carbon-based nanomaterials streamline sample

preparation, plasmonic and electrochemical nanosensors provide rapid screening, and nanocarriers extend the practical value of poorly soluble phytochemicals. Green synthesis and plant nanobionics further blur the boundary between the plant as subject and the plant as partner in nanotechnology. Realizing this potential will depend on standardised protocols, rigorous safety assessment and close collaboration between analytical chemists, plant biologists and materials scientists.

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Chapter 9

NANOROBOTICS IN BIOMEDICINE: PRINCIPLES, MOLECULAR ACTUATION, AND TARGETED THERAPEUTIC APPLICATIONS

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ABSTRACT

Nanorobotics represents a convergence of nanotechnology, molecular biology, computer science, and robotics, enabling the design of autonomous devices at the sub-micron scale. Unlike macroscopic machines governed by classical mechanics, nanorobotic systems operate within regimes dominated by low Reynolds numbers, Brownian motion, and interfacial molecular forces. This review explores the foundational physics, fabrication strategies, and actuation mechanisms underpinning nanoscale machines, with specific emphasis on DNA nanotechnology and synthetic molecular motors. Furthermore, we examine their transformative biomedical utility—particularly in targeted drug delivery, minimally invasive microsurgery, and precision cancer therapy—addressing ongoing engineering challenges and translational pathways toward clinical implementation.

KEYWORDS: Nanorobotics, Nanotechnology, Nano Machines, Targeted Drug Delivery, DNA Nanotechnology, Biomedical Engineering, Molecular Motors, Cancer Therapy, Biotechnology.

INTRODUCTION

NANOROBOTICS

Nanorobotics is an interdisciplinary field that merges nanotechnology, robotics, computer science, and molecular biology. It deals with the design, fabrication, sensing, actuation, and control of robotic devices at or near the nanoscale (typically ranging from 1 to 1000 nanometers).

While traditional robotics deals with macro-scale systems operating in predictable environments governed by classical mechanics, nanorobotics operates in a realm dominated by molecular interactions, thermal fluctuations (Brownian motion), high surface-area-to-volume ratios, and quantum effects. At this scale, gravity is largely negligible, while viscous forces, electrostatic interactions, and Van der Waals forces dictate the physics of movement.

FABRICATION AND MANUFACTURING PARADIGMS

Building devices at the nanoscale requires innovative manufacturing approaches. Researchers typically categorize these methods into two main paradigms:

- **Top-Down Manufacturing:** Adapting conventional machining and lithographic techniques (such as electron-beam lithography, photolithography, and focused ion beam milling) to carve nanoscale features from bulk materials. This is highly effective for electronic components and nano-electromechanical systems (NEMS).
- **Bottom-Up Manufacturing:** Utilizing chemical synthesis, molecular self-assembly, and DNA origami. In DNA origami, long single-stranded DNA scaffolds are folded into complex 2D and 3D nanostructures using hundreds of short 'staple' strands. This allows for precise, programmable molecular architecture ideal for biological environments.

ACTUATION AND LOCOMOTION

Moving a robot through a fluid at the nanoscale presents unique challenges due to the Scallop Theorem, which states that reciprocal motion (like a single hinge opening and closing) yields no net displacement in a low Reynolds number (viscous) environment. To overcome this, nanorobots utilize non-reciprocal motions:

- **Magnetic Propulsion:** External rotating or oscillating magnetic fields exert torque on magnetic nanorods or helical flagella (inspired by bacteria like E. coli), driving them forward like corkscrews.
- **Chemical/Catalytic Propulsion:** Nano motors convert chemical energy from their surrounding environment (e.g., hydrogen peroxide or glucose in bodily fluids) into kinetic energy. For instance, catalytic platinum patches on micro/nanorods decompose hydrogen peroxide, ejecting oxygen bubbles to create jet-like propulsion.
- **Light and Electric Field Actuation:** Light-driven Nano machines use photo-thermal effects or photo-isomerization to alter shape and induce motion, while electric fields can induce electrophoresis and dielectrophoresis.

BIOMEDICAL APPLICATIONS

The most promising and heavily researched application domain for nanorobotics is biomedicine. Targeted nanorobotic systems have the potential to revolutionize diagnostics and therapeutics:

- **Targeted Drug Delivery:** Nanorobots can be engineered to navigate the circulatory system, locate diseased tissue (such as a tumor via surface-receptor binding), and release a therapeutic payload locally, minimizing systemic toxicity and side effects.
- **Minimally Invasive Surgery:** Swarms of nanorobots could be deployed to clear arterial plaque (atherosclerosis), remove blood clots, or repair cellular damage from within.
- **Diagnostics and Biosensing:** Functionalized nanorobots can detect single molecules, pathogens, or circulating tumor cells at exceptionally early stages of disease progression.

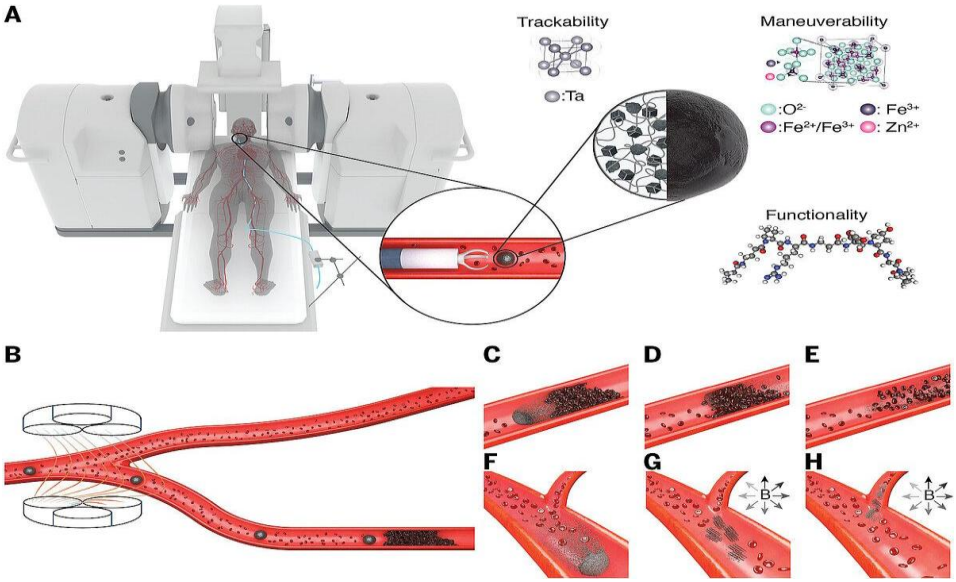


Figure 1: Diagnosing and Biosensing

Table 1: Major nanorobotic platforms and their biomedical potential

Platform	Operating Principle	Potential Application	Key Limitation
DNA-based	Base pairing and molecular switching	Programmable cargo release	Nuclease degradation
Magnetic	External magnetic actuation	Steered transport	Deep-tissue control
Catalytic	Chemical reaction-driven propulsion	Active transport	Fuel and by-product safety
Enzyme-powered	Biochemical energy conversion	Biocompatible propulsion research	Substrate dependence
Bio hybrid	Biological movement combined with engineered control	Localized delivery	Biological variability
Responsive polymer	Stimulus-induced structural change	Controlled release	Stability and degradation

CHALLENGES AND FUTURE DIRECTIONS

Despite remarkable advancements, several significant hurdles remain before nanorobotics can transition widely from laboratories to clinical and industrial settings:

- **Power and Communication:** Embedding batteries is impossible at the nanoscale. Wireless power transfer (via magnetic or ultrasound fields) and onboard chemical harvesting are active areas of development. Similarly, communicating with a nanorobot deep inside the human body remains extremely difficult.
- **Biocompatibility and Toxicity:** Materials used must be non-toxic, non-immunogenic, and biodegradable or safely cleared by the renal system after completing their task.
- **Control in Complex Environments:** Navigating turbulent blood flow, immune system clearance (phagocytosis by macrophages), and biological barriers (like the blood-brain barrier) requires sophisticated autonomous control algorithms.

Review Questions

1. How does the low Reynolds number environment affect the locomotion of nanorobots, and what is the significance of the Scallop Theorem?
2. Compare and contrast top-down and bottom-up manufacturing techniques in nanotechnology.
3. What is the primary power sources utilized for nanorobots operating within the human body?

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Chapter
10

NANOMATERIALS AT THE BIO-INTERFACE: EMERGING APPLICATIONS

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ABSTRACT

Nanomaterials are materials designed to function at the nanoscale, generally with at least one dimension between 1 and 100 nm. At this scale, materials can behave quite differently from their bulk counterparts. Their large surface area, tunable optical and magnetic properties, and high surface reactivity give them considerable value in biological and biomedical research. Over the past few decades, these properties have been increasingly exploited in drug delivery, medical diagnosis, imaging, tissue repair, antimicrobial treatment, and cancer therapy.

This chapter presents an overview of the major nanomaterials used in biological applications. These include organic nanocarriers such as liposomes, polymeric nanoparticles, dendrimers, and micelles; inorganic materials such as metallic and magnetic nanoparticles, quantum dots, and mesoporous silica; carbon-based materials; hybrid nanomaterials; and biologically derived systems such as exosomes. Their applications in targeted drug delivery, bioimaging, biosensing, tissue engineering, antimicrobial therapy, gene delivery, genome editing, and cancer treatment are discussed. Particular emphasis is placed on the ways in which nanoparticles can be modified to recognize specific cells, overcome biological barriers, and release therapeutic molecules in a controlled manner.

Despite the progress made in nanomedicine, several issues still need careful consideration. Toxicity, biocompatibility, long-term safety, manufacturing, cost, and regulatory approval remain important concerns. Moving promising nanomaterials from laboratory studies into practical medical applications will require continued collaboration among biologists, chemists, materials scientists, engineers, and medical researchers.

KEYWORDS: Nanomaterials, Nanomedicine, Drug Delivery, Bioimaging, Biosensors, Tissue Engineering, Antimicrobial Therapy, Nanotoxicology, Theranostics.

INTRODUCTION

Nanotechnology has opened up new possibilities for designing and using materials at extremely small dimensions, typically between 1 and 100 nm. Materials that appear familiar at the macroscopic level may show very different behavior when their dimensions are reduced to the nanoscale. One reason is the dramatic increase in surface area available for interaction with surrounding molecules. Changes in electronic structure at this scale can also influence optical, magnetic, and chemical properties.

These features are particularly relevant to biology. Nanoparticles can interact with proteins, DNA, cell membranes, and other biological structures because their dimensions are comparable to many of these components. This makes it possible to design nanoscale materials for specific functions within or around living cells.

The meeting of nanotechnology and biology has led to the development of fields such as nanobiotechnology and Bionanotechnology. Research in these areas has contributed to advances in drug delivery, medical imaging, biosensing, tissue engineering, antimicrobial treatment, gene delivery, and cancer therapy.

Another important feature of nanomaterials is their flexibility. Researchers can modify their size, shape, surface charge, chemical composition, and surface coating to suit a particular purpose. For instance, the properties required for a nanoparticle used in medical imaging may be very different from those needed for a nanoparticle designed to transport a therapeutic drug.

The following sections describe the major classes of nanomaterials used in biology and medicine and examine their applications in drug delivery, diagnosis, tissue regeneration, antimicrobial treatment, gene delivery, and cancer therapy. The safety concerns and practical challenges associated with these materials are also considered.

CLASSIFICATION OF NANOMATERIALS USED IN BIOLOGY

Nanomaterials used in biological research originate from a variety of chemical and biological sources. For convenience, they can be broadly grouped into organic, inorganic, hybrid or composite, and biologically derived materials.

ORGANIC NANOMATERIALS

Liposomes are small spherical vesicles surrounded by one or more phospholipid layers. Their structure contains both aqueous and lipid regions, allowing them to accommodate a wide range of drugs and other therapeutic molecules. Because of their relatively good biocompatibility, liposomes have been among the most extensively investigated nanocarriers.

Polymeric nanoparticles are prepared using polymers such as poly (lactic-co-glycolic acid) (PLGA), chitosan, and polyethylene glycol (PEG)-modified materials. An important advantage of these nanoparticles is that their degradation rate and drug-release behavior can be adjusted according to the requirements of a particular application.

Dendrimers are highly branched molecules with a characteristic tree-like architecture. Their well-defined structure and large number of surface functional groups allow them to interact with and carry different biological molecules.

Micelles form when amphiphilic molecules arrange themselves in an aqueous environment. They are particularly useful for improving the solubility and delivery of drugs that dissolve poorly in water.

INORGANIC NANOMATERIALS

Inorganic nanomaterials have attracted considerable interest because of their distinctive physical and chemical properties.

Metallic nanoparticles, particularly gold and silver nanoparticles, are valued for their optical and surface characteristics. Iron oxide nanoparticles, in contrast, are especially useful because of their magnetic properties. These features have encouraged their investigation in imaging, diagnosis, sensing, and therapy.

Quantum dots are semiconductor nanocrystals whose optical properties depend strongly on particle size. Their fluorescence can therefore be adjusted by controlling their size, making them useful for labeling and imaging biological structures.

Mesoporous silica nanoparticles contain numerous nanoscale pores, resulting in a large internal surface area. This porous structure makes them attractive carriers for drugs and other biological molecules.

Carbon-based nanomaterials, including carbon nanotubes, graphene oxide, fullerenes, and carbon dots, possess a combination of properties such as high strength, electrical conductivity, and distinctive optical behavior. These features have encouraged their investigation in biosensing, drug delivery, imaging, and regenerative medicine.

HYBRID AND COMPOSITE NANOMATERIALS

A single nanomaterial does not always provide all the properties required for a particular biological application. One way of addressing this limitation is to combine two or more materials to form hybrid or composite nanoparticles.

For example, magnetic nanoparticles can be coated with lipid layers, while gold nanoparticles can be modified with polymers. Such combinations allow researchers to bring together the biological compatibility of organic materials and the optical or magnetic properties of inorganic materials. These multifunctional systems are being explored for applications in both diagnosis and therapy.

BIOLOGICALLY DERIVED NANOMATERIALS

Biological systems themselves provide a number of nanoscale structures with potential biomedical applications.

Protein-based nanoparticles, including albumin nanoparticles and ferritin cages, can serve as biologically compatible platforms for carrying therapeutic molecules.

Viral nanoparticles and virus-like particles (VLPs) have highly organized structures that can be adapted for molecular delivery.

Exosomes and extracellular vesicles are naturally produced by cells and contain proteins, lipids, and nucleic acids. Their role in cell-to-cell communication has made them particularly interesting as possible systems for drug and gene delivery.

DRUG DELIVERY SYSTEMS

Drug delivery is one of the most extensively investigated applications of nanotechnology in medicine. Conventional drugs may have several limitations, including poor water solubility, rapid degradation, short circulation times, and unwanted effects on healthy tissues. Nanocarriers offer ways of addressing some of these problems by protecting therapeutic molecules and influencing where and when they are released.

ENHANCED PERMEABILITY AND RETENTION EFFECT

Some nanoparticles can accumulate in tumor tissues because the blood vessels associated with tumors may be more permeable than normal blood vessels, while lymphatic drainage may be inadequate. This phenomenon is referred to as the enhanced permeability and retention (EPR) effect. It provides one explanation for the passive accumulation of nanoparticles in certain tumors.

However, the EPR effect is not consistent across all tumors. Tumor characteristics vary between patients and between tumor types and passive targeting alone may therefore not always produce the expected therapeutic effect.

ACTIVE TARGETING

Active targeting provides a more specific way of directing nanoparticles toward particular cells. Molecules such as antibodies, peptides, aptamers, or folic acid can be attached to the nanoparticle surface because they recognize receptors that may be present at higher levels on certain diseased cells.

Once the nanoparticle reaches the target, the attached ligand can bind to its corresponding receptor and promote cellular uptake. The aim is to increase the concentration of the therapeutic compound at the intended site while limiting unnecessary exposure elsewhere.

CONTROLLED AND STIMULI-RESPONSIVE RELEASE

Nanocarriers can also be designed to release their contents in response to particular environmental conditions. Depending on their design, they may respond to changes in pH, temperature, enzyme activity, light, or magnetic fields.

For example, a pH-sensitive nanoparticle may remain relatively stable in the bloodstream but release its drug under acidic conditions, such as those found in some tumor environments or intracellular compartments. Controlled release of this kind may help reduce exposure of healthy tissues to the therapeutic compound.

IMPROVED PHARMACOKINETICS

Nanoparticles can protect drugs from premature degradation and may increase the time they remain in circulation. Surface modification with PEG, commonly known as PEGylation, has been used to reduce the rapid recognition and removal of nanoparticles by the immune system.

Several nanomedicines have already reached clinical use. Examples include liposomal doxorubicin, albumin-bound paclitaxel, and lipid nanoparticle systems for mRNA delivery. The successful application of lipid nanoparticles in mRNA vaccine technology has further demonstrated the practical value of nanocarrier systems.

BIOIMAGING AND DIAGNOSTICS

Nanotechnology has expanded the range of tools available for visualizing biological structures and disease processes. Nanomaterials can generate strong optical, magnetic, or other detectable signals, making them useful in medical imaging and diagnostic applications.

Quantum dots produce bright fluorescence and are relatively resistant to photobleaching. Because their emission properties depend on particle size, different quantum dots can be used to label and visualize different biological targets.

Super paramagnetic iron oxide nanoparticles (SPIONs) have been investigated as contrast agents for magnetic resonance imaging. Their magnetic properties can improve tissue visualization, and they have been studied in applications involving tumors, inflammation, and blood vessels.

Gold nanoparticles exhibit strong surface plasmon resonance. This property has led to their use in techniques such as photo acoustic imaging, computed tomography contrast enhancement, and surface-enhanced Raman spectroscopy.

Up conversion nanoparticles can absorb near-infrared radiation and emit visible light. Since near-infrared wavelengths can penetrate biological tissues relatively well, these particles are being investigated for imaging structures located deep within tissues.

A related development is **theranostics**, which combines diagnosis and treatment in a single Nano platform. In principle, such systems can provide information about a disease while simultaneously delivering therapy, creating opportunities to monitor treatment response.

BIOSENSORS

Biosensors are devices used to detect biological molecules or biological processes. The incorporation of nanomaterials can improve their sensitivity and response because of the large surface area and distinctive electrical, optical, and chemical properties of nanoscale materials.

Electrochemical biosensors incorporating graphene or carbon nanotubes can improve electron transfer and enhance detection sensitivity. Such systems have been investigated for detecting glucose, cholesterol, and other biologically important molecules.

Plasmonic biosensors commonly use gold or silver nanoparticles. When a target molecule interacts with the nanoparticle surface, changes in surface plasmon resonance can be measured. This provides a way of detecting target molecules without conventional labels.

Fluorescent nanosensors based on quantum dots or carbon dots can detect proteins, nucleic acids, and small molecules with high sensitivity.

Lateral flow assays use nanoparticles as labels to produce rapid diagnostic results. Their relatively simple design and low cost make them useful for point-of-care testing, particularly where sophisticated laboratory facilities are not readily available.

TISSUE ENGINEERING AND REGENERATIVE MEDICINE

Nanomaterials have become increasingly interesting in regenerative medicine because some nanoscale structures can reproduce features of the natural tissue environment. Cells interact closely with the extracellular matrix, and the physical characteristics of a surface at the nanoscale can influence cell attachment, growth, and differentiation.

Nano fibrous scaffolds produced through Electrospinning can resemble the fibrous organization of the natural extracellular matrix. Materials such as polycaprolactone and collagen have been used to develop these scaffolds.

In bone tissue engineering, **hydroxyapatite-containing nanocomposite scaffolds** are particularly useful. Hydroxyapatite resembles the mineral component of natural bone and can provide a suitable environment for bone-forming processes.

Carbon nanotubes and graphene have also been investigated in neural tissue engineering. Their electrical conductivity may be useful in supporting neuronal activity and influencing stem-cell differentiation.

Another approach involves using nanoparticles to deliver growth factors. Compounds such as bone morphogenetic protein-2 and vascular endothelial growth factor can be released gradually and locally, helping regulate processes such as bone formation and blood-vessel development.

ANTIMICROBIAL APPLICATIONS

The continuing rise of antimicrobial resistance has increased interest in alternative methods of controlling microorganisms. Nanomaterials are particularly attractive because they can affect microorganisms through several mechanisms rather than acting through a single conventional antibiotic target.

Silver nanoparticles can interact with microbial membranes, promote the formation of reactive oxygen species, and interfere with essential cellular components.

Zinc oxide and titanium dioxide nanoparticles can generate reactive oxygen species under suitable light conditions. These reactive molecules can damage microbial cells and contribute to their inactivation.

Chitosan nanoparticles can interact with negatively charged microbial surfaces. This interaction may disturb membrane integrity and interfere with normal microbial growth.

Nanoparticles can also be used to carry conventional antibiotics. By improving the penetration of antimicrobial agents into microbial biofilms, nanoparticle-based delivery systems may increase the local effectiveness of these drugs.

GENE DELIVERY AND GENOME EDITING

Efficiently introducing genetic material into cells remains a major challenge in gene therapy and genome editing. Nanomaterials provide several non-viral approaches for transporting DNA, RNA, and genome-editing components.

Lipid nanoparticles are among the most important non-viral systems currently used for RNA delivery. They protect fragile RNA molecules from degradation and help transport them into cells. Their successful use in mRNA vaccine technology has demonstrated the potential of this approach on a large scale.

Polymeric nanoparticles and dendrimers can bind nucleic acids and package them into compact structures. These complexes can subsequently be taken up by cells and used for the delivery of genetic material.

Gold nanoparticles have also been investigated as carriers for genome-editing components, including CRISPR-associated systems. Their surfaces can be modified to interact with particular biological molecules, making them potential candidates for controlled molecular delivery.

CANCER THERAPY

Cancer therapy is one of the major areas of interest in nanomedicine. Nanoparticles can function as carriers for anticancer drugs and can also be incorporated into therapeutic approaches that rely on physical or biological mechanisms.

PHOTOTHERMAL THERAPY

In photothermal therapy, nanoparticles such as gold nanorods absorb near-infrared light and convert the absorbed energy into heat. The resulting localized heating can damage cancer cells.

PHOTODYNAMIC THERAPY

Photodynamic therapy uses photosensitizing compounds that become active when exposed to light and generate reactive oxygen species. Nanoparticles can assist by carrying these photosensitizers and improving their delivery to the intended site.

MAGNETIC HYPERTHERMIA

Iron oxide nanoparticles can generate heat when exposed to an alternating magnetic field. This property has been investigated for producing localized heating in tumor tissues.

IMMUNONANOTECHNOLOGY

Nanoparticles are also being explored in cancer immunotherapy. They can be designed to transport tumor antigens, immune-modulating compounds, or adjuvants to specific immune cells. The overall aim is to stimulate an effective immune response against cancer while improving the precision with which therapeutic molecules are delivered.

BIOCOMPATIBILITY, TOXICITY, AND SAFETY CONSIDERATIONS

The potential benefits of nanomaterials must be considered together with their possible biological risks. Nanoparticles do not necessarily behave in the same way when their size, shape, surface chemistry, or concentration is changed. Consequently, safety assessment needs to be considered for each material and application.

CYTOTOXICITY

Some nanoparticles can cause oxidative stress, interfere with mitochondrial activity, or damage cellular membranes, particularly at high concentrations. Their potential toxicity therefore needs to be evaluated carefully before biological or medical use.

BIODISTRIBUTION AND CLEARANCE

After entering the body, nanoparticles can be distributed among different tissues and organs depending on factors such as size, shape, surface charge, composition, and surface coating. Some particles may be cleared relatively quickly, whereas others may remain in organs such as the liver and spleen.

IMMUNOGENICITY

Nanomaterials can interact with the immune system in different ways. Some may trigger unwanted immune responses, while others may avoid immune recognition. Such interactions can influence both the safety and effectiveness of a nanomaterial.

LONG-TERM EFFECTS

The long-term effects of exposure to some non-biodegradable nanomaterials are still being investigated. Possible accumulation and chronic biological effects are especially important when nanoparticles are intended for repeated or prolonged use.

Regulatory organizations such as the U.S. Food and Drug Administration and the European Medicines Agency have developed approaches for evaluating nanomedicine products. However, the considerable variation among nanomaterials makes it difficult to establish testing and characterization methods that can be applied universally.

CHALLENGES AND FUTURE DIRECTIONS

Nanotechnology has developed rapidly, but several scientific and practical challenges still need to be addressed before many laboratory discoveries can become routine clinical technologies.

Manufacturing and Reproducibility

Producing nanoparticles with precisely the same characteristics on a large scale remains difficult. Even small variations in particle size, shape, surface properties, or composition can influence biological performance.

Biological Barriers

Nanoparticles encounter several biological barriers after entering the body. Protein corona formation, uptake by immune cells, biological clearance, and differences in tissue environments can all reduce the efficiency of targeted delivery.

Safety Evaluation

A better understanding of both short-term and long-term toxicity is still needed. Standardized testing methods would also make it easier to compare the safety of different nanomaterials.

Cost and Accessibility

The synthesis, purification, characterization, and functionalization of advanced nanoparticles can be expensive. Reducing production costs will therefore be important if nanomedicine is to become more accessible.

Future research is likely to focus increasingly on multifunctional and “smart” nanomaterials that can sense their surroundings and respond to specific conditions. Artificial intelligence and computational modeling may assist researchers in predicting suitable nanoparticle compositions and optimizing their properties. Biologically derived systems such as exosomes are also receiving attention because of their natural biological compatibility. At the same time, advances in genomics and proteomics may allow nanocarriers to be designed with greater specificity for particular biological targets.

CONCLUSION

Nanomaterials have become an important part of contemporary biological and biomedical research. Their small size and adjustable properties provide opportunities that are difficult to achieve with conventional materials. They are being investigated for a wide range of applications, from drug and gene delivery to diagnostic imaging, tissue regeneration, antimicrobial treatment, and cancer therapy.

However, demonstrating biological activity is only one step toward successful medical application. The safety, biodistribution, degradation, long-term effects, manufacturing requirements, and regulatory aspects of each nanomaterial must also be understood. Careful evaluation of these factors is essential before promising laboratory findings can be translated into routine clinical use.

The future development of biological nanotechnology will depend on contributions from several disciplines. Biology, chemistry, materials science, engineering, pharmacology, and medicine each provide important perspectives for developing safer and more effective nanomaterials. Continued research, combined with careful evaluation and responsible development, could help transform promising nanoscale systems into reliable technologies for the detection, monitoring, and treatment of disease.

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Chapter

11

ARTIFICIAL INTELLIGENCE-ASSISTED NANOTECHNOLOGY: APPLICATIONS IN NANOMATERIAL DESIGN AND CHEMICAL ANALYSIS

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ABSTRACT

Nanomaterials show distinctive optical, electronic, catalytic, magnetic and biological properties, but their design, synthesis and characterization involve many interacting variables, which makes conventional trial-and-error work slow and resource-intensive. Artificial intelligence (AI), particularly machine learning (ML) and deep learning, offers a data-driven alternative. ML models can link synthesis parameters, structure and function; predict material performance before preparation; optimize reaction conditions; interpret spectroscopic and microscopic data; and strengthen nanosensors for chemical analysis. AI is also being applied in green nanotechnology, Nanotoxicology and pharmaceutical nanotechnology. This chapter reviews recent progress in AI-assisted nanotechnology, emphasizing nanomaterial design, synthesis, characterization and chemical analysis. Challenges concerning data quality, interpretability, reproducibility, standardization and responsible use are also discussed.

KEYWORDS: Artificial Intelligence, Machine Learning, Nanomaterials, Nanomaterial Synthesis, Chemical Analysis, Nanosensors, Nanotoxicology, Green Nanotechnology.

INTRODUCTION

Nanotechnology deals with materials and structures with dimensions of roughly 1–100 nm. At this scale, a high surface-to-volume ratio, quantum effects and size-dependent surface phenomena give materials properties that differ markedly from those of the bulk (Saleh, 2024). Metal and metal oxide nanoparticles, carbon-based nanomaterials, quantum dots, nanocomposites and polymeric nanoparticles are therefore used in catalysis, sensing, environmental remediation, energy storage, electronics and medicine.

Nanomaterial development traditionally relies on experimental optimization of precursor concentration, pH, temperature, reaction time, solvent, reducing agent, stabilizer and atmosphere (Namakka *et al.,* 2023). Small changes in these parameters can alter particle size, morphology, crystallinity and surface charge, so reaching a target material by trial and error can consume considerable time, reagents and effort.

Machine learning offers a complementary route. By learning from experimental datasets, ML algorithms can identify relationships between inputs and material properties, and recent reviews describe growing use of ML in property prediction, rational design, synthesis

optimization, image analysis and quality control (Yang *et al.,* 2024). This chapter surveys these developments with a chemistry-centred focus.

ARTIFICIAL INTELLIGENCE IN NANOTECHNOLOGY

AI refers broadly to computational methods that perform tasks normally requiring human intelligence. Machine learning, its main branch relevant here, learns patterns from data to make predictions or classifications. Common methods include linear regression, decision trees, random forests, support vector machines, artificial neural networks and clustering algorithms; deep learning uses multilayer neural networks, which are especially effective for images and spectra.

A typical workflow is:

Experimental data → preprocessing → feature selection → model development → prediction/optimization → experimental validation

Input features may include elemental composition, precursor concentration, pH, temperature, reaction time and surface chemistry. Outputs may include particle size, morphology, band gap, catalytic activity, adsorption capacity, stability or toxicity. When validated, such models can reduce the number of experiments needed and point researchers toward promising conditions.

AI-ASSISTED NANOMATERIAL DESIGN

A central application of AI is predicting structure–property relationships. The properties of a nanomaterial depend on several interconnected parameters, and ML can handle these simultaneously, revealing patterns that conventional statistics may miss (Yang *et al.,* 2024). For example, a model trained on composition, size, morphology and surface characteristics, with catalytic activity as the output, can estimate the performance of new candidate materials before they are made. The same logic applies to nanocomposites, whose mechanical, thermal, electrical and optical behaviour depends on the nanofiller, matrix and processing conditions. Predictive models can help select fillers and loadings, narrowing the search space before laboratory work begins. Table 1 summarizes representative roles of AI across nanotechnology.

Table 1: Examples of AI applications in nanotechnology

Activity	AI/ML Role	Potential Benefit
Nanomaterial design	Property prediction	Faster material discovery
Nanoparticle synthesis	Parameter optimization	Fewer experimental trials
Microscopy	Image recognition	Automated morphology analysis
Spectroscopy	Pattern recognition	Faster interpretation
Chemical sensing	Signal classification	Improved selectivity
Nanotoxicology	Toxicity prediction	Early safety assessment
Nanocomposites	Composition optimization	Improved performance

AI IN NANOPARTICLE SYNTHESIS AND OPTIMIZATION

Nanoparticles can be produced by physical, chemical and biological routes (Namakka *et al.,* 2023). Chemical synthesis is widely used but demands tight control of conditions to obtain the

desired size and shape. Green synthesis using plant extracts, microorganisms or biomolecules is increasingly attractive because it can reduce hazardous reagents, although the many biological variables involved make it harder to control.

Instead of varying one factor at a time, ML models can analyze many parameters together and identify combinations associated with desired particle characteristics. Gulevich *et al.* (2024) reviewed ML-assisted optimization of colloidal, hydrothermal, chemical-reduction and flow-reactor syntheses, showing that models can suggest optimal synthesis parameters and predict nanomaterial properties before experimental preparation. Coupling such models with automated laboratory equipment further allows iterative, closed-loop optimization.

AI FOR NANOMATERIAL CHARACTERIZATION

Characterization establishes size, morphology, composition, structure and surface properties. Standard techniques include UV–Visible spectroscopy, FTIR, XRD, SEM, TEM, dynamic light scattering (DLS) and zeta-potential measurement (Namakka *et al.,* 2023).

AI helps extract information from these often complex datasets. In microscopy, deep-learning models can detect particles, compute size distributions and classify morphology, greatly reducing the effort of manual image analysis (Yang *et al.,* 2024). In spectroscopy and diffraction, ML can resolve overlapping signals and support classification and quantitative prediction. Table 2 lists typical applications.

Table 2: AI applications in nanomaterial characterization

Technique	AI Application
UV–Visible spectroscopy	Spectral pattern classification
FTIR	Functional-group pattern recognition
XRD	Phase identification and prediction
SEM/TEM	Particle and morphology recognition
DLS	Size-distribution analysis
Fluorescence spectroscopy	Sensor signal interpretation
Electrochemical methods	Classification and quantitative analysis

AI-ASSISTED CHEMICAL ANALYSIS AND NANOSENSORS

High surface area and tunable surface chemistry make nanomaterials valuable sensing elements, improving sensitivity, selectivity and signal generation. AI adds value by converting complex, often overlapping signals into analytical information: ML algorithms can classify the responses of sensor arrays, identify analytes and build quantitative calibration models.

Mousavizadegan *et al.* (2023) reviewed ML in analytical chemistry, from the synthesis of luminescent nanostructures to their use in luminescence sensing, noting gains in sensitivity, selectivity and automated data interpretation. Potential targets include heavy-metal ions, pesticides, pharmaceutical residues, food contaminants and biomolecules. A particularly useful capability is distinguishing chemically similar analytes, a persistent difficulty in real samples where interferents and matrix effects are common.

AI FOR GREEN AND SUSTAINABLE NANOTECHNOLOGY

Green nanotechnology seeks to lower the environmental footprint of nanomaterial production and use. ML can compare reducing agents, solvents, temperatures and biological extracts to identify conditions that reduce energy demand, waste and hazardous chemicals, in line with the principles of green chemistry. AI may also support life-cycle assessment by integrating data on production, use and disposal. Combined with green synthesis, these tools could help develop safer nanoparticles from plant extracts, microorganisms and renewable resources, although such applications remain largely at an early stage.

AI IN NANOMATERIAL SAFETY AND TOXICITY PREDICTION

Widespread use of nanomaterials requires systematic evaluation of their effects on health and the environment. Toxicity can depend on composition, size, shape, surface charge, concentration, aggregation, exposure route and biological medium (Saleh, 2024). Because conventional testing is costly and slow, ML models offer a way to estimate toxicity early; for example, Masarkar *et al.* (2024) applied ML in a meta-analysis to predict nanoparticle cytotoxicity from physicochemical and experimental variables.

Such predictions can support risk assessment but cannot replace experiments. Zhou *et al.* (2024) stress dataset curation, descriptor selection, external validation, applicability domain and mechanistic interpretation as prerequisites for reliable nanotoxicology models.

APPLICATIONS IN WATER PURIFICATION, ENERGY AND PHARMACEUTICALS

- **Water purification.** Metal oxides, carbon materials and nanocomposites can adsorb pollutants or drive photocatalytic degradation. ML can predict adsorption capacity and optimize pH, pollutant concentration, contact time and temperature.
- **Energy.** Nanomaterials are central to batteries, supercapacitors, fuel cells, solar cells and photocatalysis. ML can screen candidates for conductivity, stability, surface area and electrochemical performance.
- **Pharmaceuticals.** Nanoparticles serve as carriers for controlled and targeted drug delivery. ML can relate particle characteristics to drug loading, release, cellular uptake and biological response, and it is being used to design nanotheranostics that combine diagnosis and therapy (Rao *et al.*, 2024).

CHALLENGES AND LIMITATIONS

- **Data quality:** reliable models need large, representative and consistent datasets; heterogeneous methods and small, positively biased datasets (failed experiments are rarely reported) limit performance.
- **Interpretability:** deep-learning models often act as black boxes, making it hard to extract chemical insight from predictions.
- **Reproducibility:** synthesis outcomes differ between laboratories because of instruments, reagents and conditions.
- **Standardization:** common formats for describing nanomaterials and reporting data are needed to build transferable models.

- **Experimental validation:** computational accuracy does not guarantee practical performance; predictions must be tested.
- **Safety and ethics:** AI should support, not replace, scientific judgment and established safety testing.

FUTURE PERSPECTIVES

Future progress is likely to combine computational prediction, automated experimentation and real-time characterization. Self-driving laboratories could integrate robotics, analytical instruments and ML to design experiments, synthesize materials, analyze results and select the next experiment autonomously. Explainable AI will be important so that chemists can relate.

Predictions to physical and chemical causes and coupling ML with quantum chemistry, molecular simulation and high-throughput experimentation may further accelerate discovery. Shared, standardized databases of composition, size, morphology, synthesis conditions, characterization and biological effects, together with collaboration among chemists, materials scientists, computer scientists and engineers, will be essential.

CONCLUSION

AI is becoming an enabling technology for nanoscience. ML can predict properties, optimize synthesis, interpret characterization data, improve chemical sensors and assess toxicity, and its integration with green synthesis, remediation, energy and pharmaceutical research can speed up materials development. For chemistry, it marks a shift from trial and error toward data-driven, predictive research. Reliable datasets, transparent models, standardized reporting and experimental validation remain essential if this potential is to be realized.

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Chapter

12

SAFETY, TOXICITY AND ENVIRONMENTAL IMPACT OF NANOMATERIALS: MECHANISMS, RISK ASSESSMENT AND SUSTAINABLE PERSPECTIVES

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ABSTRACT

Nanomaterials are used in sunscreens, paints, batteries, textiles, medicines and water-treatment systems. Their useful properties arise partly from nanoscale size, high surface area and distinctive surface reactivity, but these same features may alter interactions with cells and ecosystems. This chapter summarizes human exposure routes, mechanisms of toxicity, environmental fate and ecotoxicological effects, and approaches to risk assessment. Key mechanisms include oxidative stress, inflammation, genotoxicity, membrane damage and protein-corona formation. Nanomaterials may aggregate, dissolve or chemically transform after release, changing their mobility and toxicity. Assessment tools include standardized characterization, in vitro and in silico testing, grouping, read-across and nano-QSAR or machine-learning models. Persistent gaps include limited chronic-exposure data, inconsistent reporting and uncertainty about realistic environmental concentrations. Safe-and-sustainable-by-design, green synthesis, life-cycle assessment and transparent governance can help reduce avoidable risks while preserving beneficial applications.

KEYWORDS: Nanotoxicology, Engineered Nanomaterials, Oxidative Stress, Protein Corona, Environmental Fate, Ecotoxicity, Risk Assessment, Nano-QSAR, Nano Plastics, Safe-And-Sustainable-By-Design.

INTRODUCTION

Engineered nanomaterials (ENMs) have moved from laboratories into consumer products and medical technologies. Nanotoxicology studies their potential adverse effects on living organisms and ecosystems. At the nanoscale, a greater proportion of atoms are exposed at the surface, so reactivity and biological behavior may differ from those of the same bulk substance. Size, shape, surface chemistry, solubility and crystal structure all influence hazard; chemical composition alone is not enough to predict safety (Donaldson *et al.,* 2004; Nel *et al.,* 2006).

Studies of long, rigid multi-walled carbon nanotubes found asbestos-like inflammation in animal models, highlighting the importance of fiber geometry and bio persistence without demonstrating that all nanotubes are carcinogenic (Poland *et al.,* 2008; Takagi *et al.,* 2008). Other research showed that silver from textiles and titanium dioxide from building facades can enter wastewater and aquatic environments (Benn and Westerhoff, 2008; Kaegi *et al.,* 2008). Nano

safety therefore requires consideration of a material's full life cycle, from manufacture and use to disposal.

What makes nanomaterials different?

Nanomaterials are commonly discussed within the 1–100 nm size range, although size alone may not capture the point at which properties become relevant to health or the environment (European Commission, 2011; Auffan *et al.,* 2009). Five interacting characteristics are especially important:

- Size and surface area influence reactivity, deposition and cellular contact.
- Shape and aspect ratio matter because long, rigid, persistent fibers may resist macrophage clearance and cause frustrated phagocytosis.
- Surface chemistry, coatings and charge affect dispersion, protein binding and cellular uptake.
- Composition and solubility determine whether toxicity results from the particle itself or from released ions, as observed with silver, copper oxide and zinc oxide.
- Crystal structure and electronic properties can influence reactive oxygen species (ROS) generation.

Routes of exposure and biodistribution:

INHALATION

Inhalation remains the exposure route of greatest concern in workplaces. Deposition in the respiratory tract depends strongly on particle size and agglomeration state, and the biokinetics of inhaled nanoparticles, including clearance and limited translocation, has been reviewed in detail by Geiser and Kreyling (2010). Occupational exposure assessments across production and handling stages have shown that release is often highest during powder handling, sieving, cleaning and maintenance operations (Kuhlbusch *et al.,* 2018).

DERMAL AND ORAL EXPOSURE

Intact skin is generally an effective barrier, and most studies suggest that nanoparticles in sunscreens remain largely in the outer stratum corneum, though damaged or diseased skin and mechanical flexing remain open questions. Oral exposure, by contrast, is becoming more relevant as nanoparticles appear in food additives, supplements and packaging, and through the swallowing of particles cleared from the airways. Particle behavior in the gastrointestinal tract is shaped by pH changes, digestive enzymes and food-matrix interactions, so a nanoparticle seldom reaches the gut wall in the form in which it was manufactured.

PARENTERAL EXPOSURE

For nanomedicines, direct injection bypasses natural barriers. Here the main questions are biodistribution, accumulation in the liver and spleen, and immune recognition. Oberdörster (2010) emphasized that safety assessment for nanomedicine should be integrated with, but not replaced by, the concepts of general nanotoxicology, because intended systemic exposure raises its own questions about long-term retention and clearance.

MECHANISMS OF TOXICITY

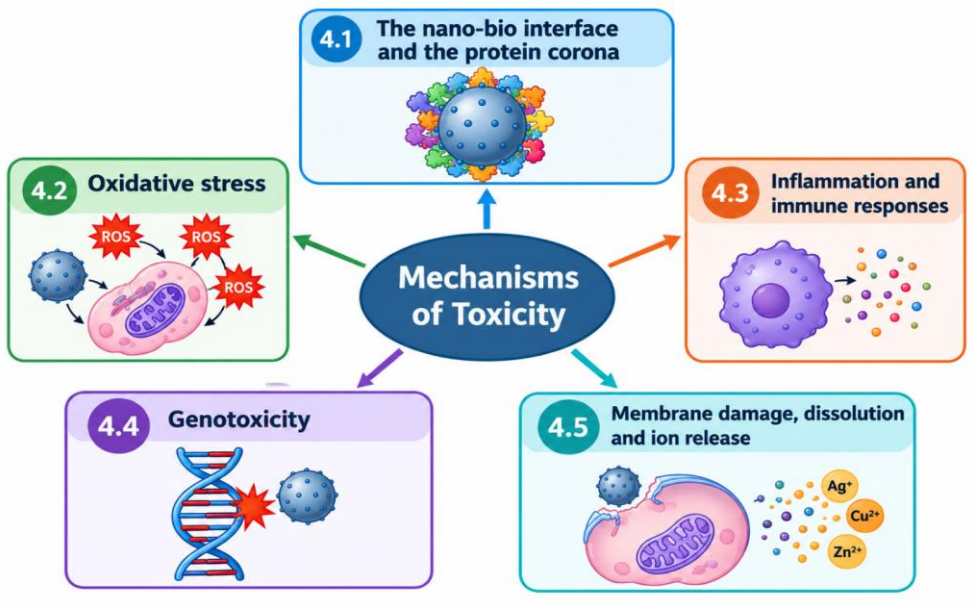


Figure 1: Mechanisms of Toxicity

THE NANO-BIO INTERFACE AND THE PROTEIN CORONA

The biological identity of a nanoparticle changes when it enters a biological fluid. Proteins and other molecules adsorb to its surface, forming a dynamic "protein corona" that influences cellular uptake, circulation and immune recognition. Thus, results obtained in simple laboratory media may not accurately predict behaviour in blood or lung fluid (Monopoli *et al.*, 2012; Walkey and Chan, 2012).

OXIDATIVE STRESS

Oxidative stress is one of the most consistently reported mechanisms. Particles may generate ROS directly, release redox-active ions or stimulate immune cells to produce ROS. Low levels can activate antioxidant defences; greater stress may promote inflammation, while severe stress can damage cells (Nel *et al.*, 2006; Xia *et al.*, 2006).

INFLAMMATION AND IMMUNE RESPONSES

Macrophages and epithelial cells recognize particles and release cytokines and chemokines. When the particle is bio persistent, as with long rigid fibers, this can turn into chronic inflammation, fibrosis and, in the worst case, tumor promotion, the sequence that made asbestos so dangerous (Poland *et al.*, 2008; Takagi *et al.*, 2008). Nanoparticles can also modulate immune function in subtler ways, either stimulating or suppressing responses depending on surface features, which matters for both safety and therapeutic design.

GENOTOXICITY

Genotoxicity may result directly from interaction with DNA or cell division, or indirectly through oxidative stress and inflammation. Testing requires caution because nanoparticles can absorb light, bind assay dyes or catalyse reactions, producing false-positive or false-negative results (Kroll *et al.*, 2009).

MEMBRANE DAMAGE, DISSOLUTION AND ION RELEASE

Some particles damage membranes or organelles, including mitochondria. Others dissolve after cellular uptake and release toxic ions—the "Trojan horse" mechanism. Studies of silver, copper oxide and zinc oxide indicate that dissolved ions explain much, but not necessarily all, of their toxicity, and effects differ among organisms (Bondarenko *et al.,* 2013).

ENVIRONMENTAL RELEASE, FATE AND TRANSFORMATION

HOW MUCH IS OUT THERE?

Measuring engineered nanoparticles in nature is difficult because natural particles and colloids are abundant and analytical techniques may not distinguish them from manufactured materials. Models have estimated surface-water concentrations commonly in the ng/L to μg/L range for several ENMs, while wastewater sludge, soils and landfills can receive substantial material flows (Gottschalk *et al.,* 2009; Keller *et al.,* 2013). Soils treated with biosolids may act as long-term reservoirs.

Transformations: the particle you release is not the particle you measure

Lowry *et al.* (2012) emphasized that ENMs undergo physical, chemical and biological transformations such as aggregation, dissolution, sulfidation, oxidation, photochemical reactions and surface-coating changes. Silver offers a clear example. In a pilot wastewater treatment plant, Kaegi *et al.* (2011) found that silver nanoparticles were largely transformed into silver sulfide, which is much less soluble and, in many studies, considerably less toxic than pristine particles. This reminds us that hazard data on pristine ENMs may overestimate or underestimate risk depending on how environmental ageing changes the particle. Navarro *et al.* (2008) and Klaine *et al.* (2008) similarly stressed that fate, bioavailability and effects are intertwined with water chemistry, natural organic matter, ionic strength and pH.

ECOTOXICOLOGICAL EFFECTS

Early reviews of nanoecotoxicology identified several consistent themes (Nowack and Bucheli, 2007; Handy *et al.,* 2008; Klaine *et al.,* 2008):

Microorganisms. Silver nanoparticles can inhibit nitrifying bacteria through ROS-related mechanisms and ion release, which raises concerns for biological wastewater treatment performance (Choi and Hu, 2008).

Algae and plants. Algae can be affected through shading, particle adhesion to cell walls and ion release, while terrestrial plants may show altered growth, root uptake and, in some cases, accumulation (Navarro *et al.,* 2008).

Invertebrates and fish. Filter feeders such as *Daphnia* and bivalves are exposed through ingestion, and effects include reduced reproduction, oxidative responses and gill damage in fish (Handy *et al.,* 2008).

Trophic transfer. Particles or released ions can move from lower to higher trophic levels, although the extent of biomagnification appears material-dependent and in many cases limited.

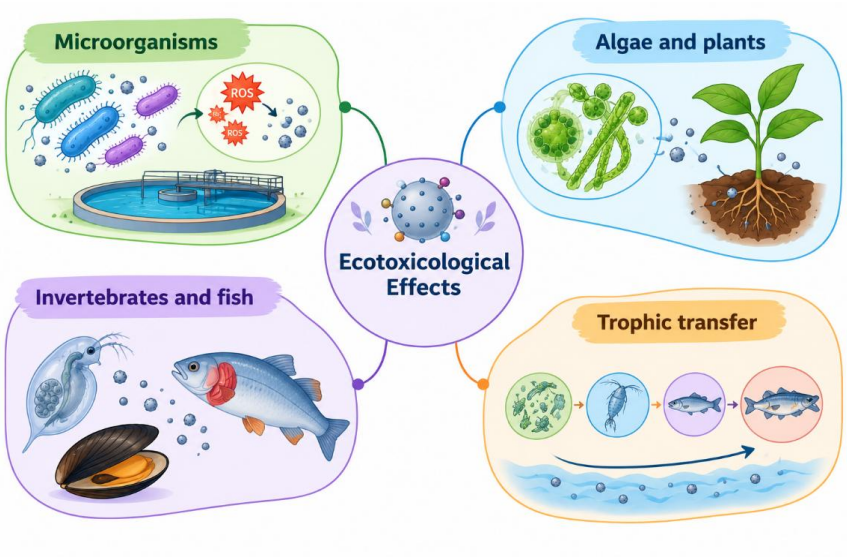


Figure 2: Ecotoxicological Effects

NANO PLASTICS: A NEW FRONTIER AT THE EDGE OF NANOTOXICOLOGY

Nano plastics form when larger plastic items weather, fragment or are processed. Gigault *et al.* (2018) suggested reserving the term for such incidental, colloidally behaving particles between about 1 nm and 1 μm, and cautioned that their messy, variable composition makes uniform lab-made polymer beads a weak model for them. Mitrano *et al.* (2021) then set nano plastics against the backdrop of global plastic pollution, pointing to the analytical difficulty of finding and counting such small particles in real samples.

Evidence that these particles are really out there has been accumulating. Ter Halle *et al.* (2017) reported nano plastics in water samples from the North Atlantic subtropical gyre, and Bouwmeester *et al.* (2015) argued that concepts from nanotoxicology could help evaluate the potential health impact of micro- and nano plastics entering the human food production chain. More striking, and more contested, are findings in human tissue: Ragusa *et al.* (2021) detected plastic particles in human placenta, and Marfella *et al.* (2024) reported micro- and nano plastics in carotid artery plaque, with their presence associated with a higher risk of later cardiovascular events in the patients studied.

For readers of this chapter, the practical message is that nano plastics inherit the toolbox of nanotoxicology: careful dosimetry, full characterization, awareness of the protein corona, and attention to ageing and transformation (Mitrano *et al.*, 2021). They also inherit its pitfalls, notably exposure concentrations far above environmental levels and test particles that do not resemble environmental ones. Nano plastics therefore serve as both a warning and a rehearsal: a reminder of what happens when a nanoscale contaminant is recognized late, and an opportunity to apply nano safety lessons early.

RISK ASSESSMENT OF NANOMATERIALS

THE CLASSICAL FRAMEWORK AND WHY IT STRAINS

Conventional risk assessment combines hazard identification, dose–response assessment, exposure assessment and risk characterization. For nanomaterials every step is complicated:

dose metrics (mass, surface area or particle number?) are debated, characterization requirements are extensive, and the same chemical composition can yield many nanoforms. The OECD guidance on sample preparation and dosimetry for the safety testing of manufactured nanomaterials was an important attempt to harmonize how test dispersions are prepared and reported (OECD, 2012). Hristozov *et al.* (2016) reviewed available frameworks and tools for nanomaterial risk assessment and found that, while many approaches exist, few have been broadly validated or applied in a regulatory setting.

TESTING STRATEGIES: IN VIVO, IN VITRO AND BEYOND

Animal inhalation studies remain the reference for pulmonary hazard, but are expensive, slow and ethically demanding, so there is strong interest in cell-based and alternative methods. As noted earlier, in vitro assays require careful controls for particle interference (Kroll *et al.,* 2009). More realistic models such as co-cultures, air–liquid interface exposures and three-dimensional tissue models are gradually improving predictive power. Integrated testing strategies combine physicochemical characterization, in vitro screening and targeted in vivo confirmation to reduce animal use while keeping relevance.

GROUPING, READ-ACROSS AND DECISION FRAMEWORKS

Grouping and read-across may reduce the need to test every nanoform separately. Frameworks such as DF4nanoGrouping consider intrinsic properties, behaviour in a particular system and biological effects. Data from one material should be applied to another only when the relevant similarities and mechanisms are well supported (Arts *et al.,* 2015; Oomen *et al.,* 2015).

COMPUTATIONAL APPROACHES

Nano-QSAR and machine-learning models use material descriptors to predict uptake or toxicity. Their promise is limited by small, inconsistent datasets and poor reporting. Useful models require descriptors relevant to nanoscale behaviour, transparent applicability domains and validation against realistic conditions. Mechanistic approaches, including adverse outcome pathways, can connect early molecular events to later adverse effects and strengthen predictions (Puzyn *et al.,* 2011; Li *et al.,* 2022; Halappanavar *et al.,* 2020).

EXPOSURE ASSESSMENT IN WORKPLACES AND FOR CONSUMERS

Exposure assessment should combine measurements with modelling and consider whether particles are free, embedded in a product or tightly bound within a matrix. Workplace controls should prioritise containment, engineering measures, safe handling and training (Maynard *et al.,* 2006).

REGULATORY AND METHODOLOGICAL GAPS

Several gaps recur in the literature and in practice.

Definitions and reporting. Differences in how "nanomaterial" is defined across jurisdictions complicate compliance and comparison (European Commission, 2011; Schwirn *et al.,* 2014).

Insufficient characterizations. Toxicity papers frequently omit information on dispersion state, coating, impurities, endotoxin contamination or ageing, which makes results hard to reproduce.

Dose relevance. Many in vitro and in vivo studies use concentrations well above realistic exposure, so hazard may be demonstrated without being linked to realistic risk.

Long-term and low-dose effects. Chronic exposure studies are scarce compared with acute ones.

Mixtures and real-world matrices. ENMs rarely occur alone; co-contaminants, organic matter and microplastics alter behavior.

Data sharing. Findable, accessible, interoperable and reusable data would accelerate modelling and read-across, but incentives for sharing remain weak (Jeliazkova *et al.*, 2015; Wilkinson *et al.*, 2016).

SUSTAINABLE PERSPECTIVES

SAFE-AND-SUSTAINABLE-BY-DESIGN

Safe-and-sustainable-by-design (SSbD) moves safety evaluation upstream, so potential hazards and environmental burdens are considered during material and product development. Design choices may include less hazardous compositions, controlled aspect ratios, coatings that reduce unwanted ion release and matrices that limit release during use and disposal. The European framework for SSbD has evolved through recommendations and revisions; it offers a structured approach to considering safety, sustainability, trade-offs and uncertainty, but should not be treated as automatic certification of safety (Caldeira *et al.*, 2022; European Commission, 2022, 2026).

GREEN SYNTHESIS

Green synthesis uses plant extracts, biological materials, benign solvents or milder conditions instead of more hazardous reagents. However, "green" synthesis does not guarantee a safe product. Biogenic particles can remain toxic, production may vary between batches, and scale-up may require substantial energy or land. Sustainability claims therefore need evidence (Iravani, 2011).

LIFE CYCLE THINKING

Life-cycle assessment (LCA) considers impacts from raw materials and manufacturing through use, recycling and disposal. Energy-intensive production, limited recyclability or persistent releases may offset benefits during product use. LCA for ENMs remains constrained by gaps in inventory data and nano-specific toxicity indicators (Hischier and Walser, 2012).

GOVERNANCE, TRANSPARENCY AND PUBLIC TRUST

Transparent communication is also necessary. Researchers, industry, regulators and communities should discuss benefits, uncertainties and risk-management measures early to support responsible innovation and public trust.

FUTURE DIRECTIONS

Priorities include standardized reporting of particle characteristics and test conditions; realistic chronic, low-dose and aged-material studies; validated high-throughput and mechanism-based methods; better datasets for computational prediction; and stronger validation of grouping and read-across. SSbD principles should be integrated into the training of scientists and engineers.

CONCLUSION

Nanomaterials are diverse and cannot be judged by chemical composition alone. Size, shape, surface properties, dissolution and environmental transformation influence their interactions with organisms and ecosystems. Oxidative stress, inflammation, ion release, genotoxicity and protein-corona formation are important mechanisms, while fiber-like persistent materials deserve particular attention. Environmental risk assessment remains limited by measurement challenges, uncertain exposure and incomplete long-term evidence. Combining improved testing, computational tools, transparent data, life-cycle thinking and ssbd can help society retain the benefits of nanotechnology while reducing avoidable harm.

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Chapter

13

BEAUVERIA BASSIANA-MEDIATED GREEN SYNTHESIS OF SILVER NANOPARTICLES: BIOLOGICAL PROPERTIES, CHARACTERIZATION AND EMERGING APPLICATIONS IN NANOCOSMECEUTICALS

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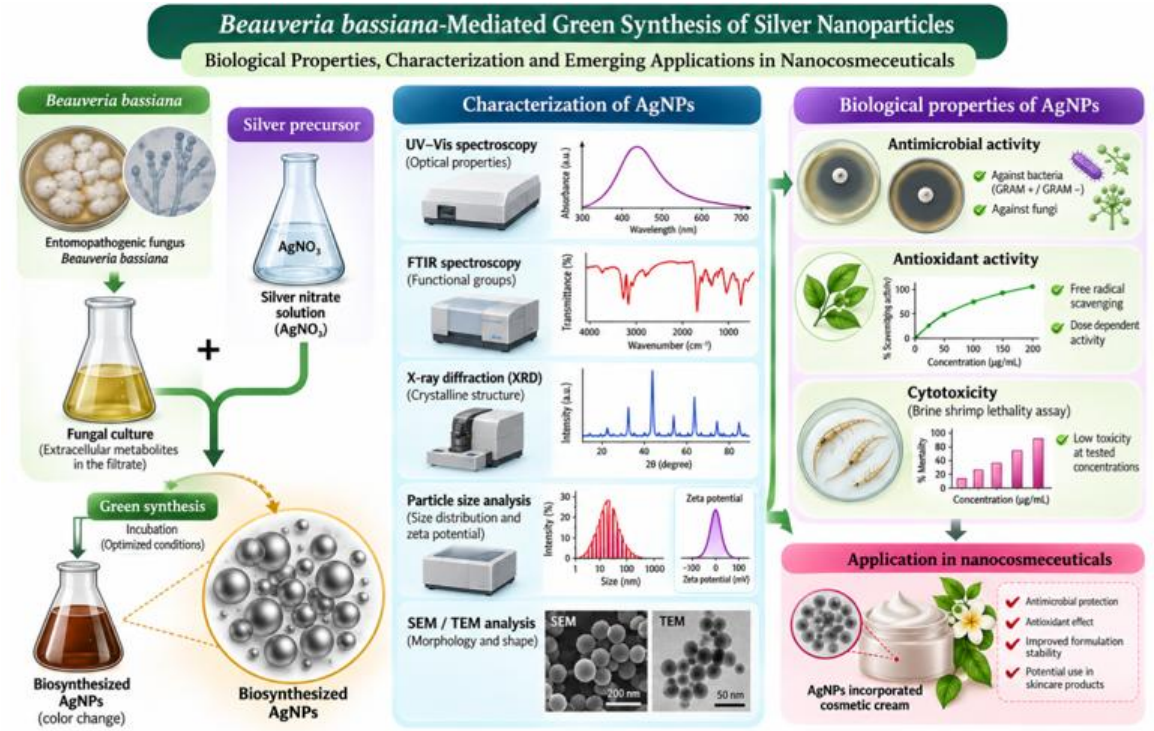
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ABSTRACT

Green synthesis of silver nanoparticles (AgNPs) using biological systems has gained considerable attention as an environmentally compatible approach to nanomaterial production. The entomopathogenic fungus *Beauveria bassiana* offers promising potential for nanoparticle synthesis due to its ability to produce extracellular enzymes, proteins, and secondary metabolites that facilitate the reduction of silver ions and stabilization of nanoparticles. This chapter highlights the synthesis, physicochemical characterization, biological properties, and emerging applications of *B. bassiana*-mediated silver nanoparticles in nanocosmeceuticals. The synthesis process is influenced by parameters such as pH, temperature, reaction time, silver nitrate concentration, and fungal extract concentration. Characterization techniques, including UV–Visible spectroscopy, Fourier-transform infrared spectroscopy, scanning electron microscopy, dynamic light scattering, zeta potential analysis, and X-ray diffraction, provide insights into nanoparticle formation, morphology, surface characteristics, and crystalline structure. Reported studies have demonstrated antimicrobial activity against selected bacterial and yeast species, along with antioxidant activity evaluated using the DPPH radical-scavenging assay. Furthermore, incorporation of these nanoparticles into cosmetic cream formulations has shown potential for enhancing sun-protection performance under experimental conditions. Despite these promising findings, further research is required to establish their safety, skin compatibility, formulation stability, and suitability for practical cosmetic applications. Overall, *B. bassiana*-mediated silver nanoparticles represent a promising research avenue connecting entomopathogenic fungi, green nanotechnology, and cosmetic biotechnology.

KEYWORDS: *Beauveria bassiana*, Silver Nanoparticles, Green Synthesis, Fungal Nanotechnology, Antimicrobial Activity, Antioxidant Activity, Nanocosmeceuticals, Cosmetic Formulations.

GRAPHICAL ABSTRACT



INTRODUCTION

Nanotechnology has emerged as one of the important interdisciplinary areas connecting biology, chemistry, physics, materials science, medicine and industrial biotechnology. The manipulation of materials at the nanoscale can produce distinctive optical, catalytic, electrical, magnetic and biological properties. Among the different nanomaterials investigated to date, metallic nanoparticles have received considerable attention because of their large surface-to-volume ratio and unusual physicochemical characteristics. Silver nanoparticles (AgNPs) are particularly important because of their antimicrobial, catalytic, optical and surface-reactive properties. These properties have encouraged research into applications ranging from antimicrobial materials and environmental technologies to biomedical products and cosmetics. In the cosmetic sector, AgNPs have been investigated particularly for antimicrobial and antifungal functions and as components of multifunctional nanocosmetic formulations (Paiya – santos *et al.*, 2021).

The properties of AgNPs are strongly influenced by particle size, morphology, surface charge, crystallinity, aggregation state and surface-associated molecules. Consequently, the method used for nanoparticle synthesis is an important determinant of their final biological performance. Traditional physical and chemical synthesis approaches can produce nanoparticles with desirable characteristics, but may require high energy inputs or chemical reducing and stabilizing agents. Biological synthesis has consequently attracted attention as a potentially more environmentally compatible approach (Fatima *et al.*, 2016).

Biological synthesis can involve plants, bacteria, fungi, algae, enzymes and isolated biomolecules. Among these systems, fungi are particularly attractive because of their ability to produce large amounts of extracellular metabolites and enzymes (Amobonye *et al.*, 2020). These

biomolecules may participate in both the reduction of metal ions and stabilization of the resulting nanoparticles. The entomopathogenic fungus *Beauveria bassiana* is an especially interesting candidate. It is widely recognized for its role as a biological control fungus and possesses considerable metabolic diversity. Previous studies have demonstrated that *B. bassiana* can participate in extracellular AgNP synthesis. A particularly relevant study by Pillay *et al.* (2024) investigated *B. bassiana*-mediated AgNPs as potential active nanocosmeceutical ingredients. The study optimized synthesis conditions, characterized the resulting nanoparticles, evaluated their antimicrobial and antioxidant activities, examined their toxicity using a brine-shrimp model, and investigated their incorporation into a cosmetic cream (Gajera *et al.*, 2022).

NANOTECHNOLOGY AND NANOCOSMECEUTICALS

The incorporation of nanotechnology into cosmetics has resulted in the development of the broader field of nanocosmeceuticals. Nanocosmeceuticals refer broadly to cosmetic or cosmeceutical formulations incorporating nanostructured materials to modify product characteristics or deliver functional ingredients. Nanotechnology can potentially improve: Ingredient dispersion, Stability, Controlled release, Skin deposition, Photoprotection, Antimicrobial performance, Antioxidant delivery and, Sensory characteristics (Badnore *et al.*, 2019). Several nanomaterial classes have been investigated in cosmetic formulations, including: Liposomes, Nanoemulsions, solid lipid nanoparticles, polymeric nanoparticles, gold nanoparticles, silver nanoparticles, metal oxide nanoparticles, and nanostructured lipid carriers. Silver nanoparticles have attracted particular interest because of their antimicrobial properties. However, the application of AgNPs to cosmetics also raises important questions concerning dermal exposure, particle penetration, silver-ion release and toxicological effects.

SILVER NANOPARTICLES

PHYSICOCHEMICAL PROPERTIES

AgNPs possess properties that differ from bulk silver because of nanoscale dimensions and surface effects. A) High surface-area-to-volume ratio: Smaller nanoparticles provide a greater proportion of atoms at the surface. This can increase interaction with microorganisms, biomolecules and surrounding media. B) Surface plasmon resonance: AgNPs exhibit characteristic optical behaviour arising from collective oscillation of conduction electrons. This produces surface plasmon resonance that can be detected using UV–Visible spectroscopy. C) Surface reactivity: The surface of AgNPs can interact with proteins, enzymes, membranes and other biological molecules. D) Silver-ion release: AgNPs can release Ag^{+} ions under appropriate environmental conditions. The released ions may contribute substantially to antimicrobial activity and toxicity (Balakumaran *et al.*, 2016).

GREEN SYNTHESIS OF SILVER NANOPARTICLES

Green synthesis aims to reduce dependence on potentially hazardous chemical reagents and environmentally intensive processes. Biological molecules involved proteins, enzymes, amino acids, polysaccharides, phenolic compounds, organic acids, terpenoid-like metabolites and other secondary metabolites.

FUNGI

Fungi have several characteristics that make them attractive for nanoparticle synthesis. High biomass production: Fungi can produce substantial quantities of mycelial biomass under controlled culture conditions. Extracellular secretion: Fungal cultures can release enzymes and metabolites into the surrounding medium, potentially enabling extracellular nanoparticle formation. Metabolic diversity: Fungi produce numerous primary and secondary metabolites. Ease of cultivation: Many fungal species can be maintained using relatively simple culture systems. Potential for extracellular synthesis: Extracellular production can simplify separation of nanoparticles from fungal biomass. Previous research has documented fungal-mediated AgNP synthesis using different genera, and *B. bassiana* has been specifically investigated for this purposed.

BIOLOGICAL SIGNIFICANCE OF *BEAUVERIA BASSIANA*

Beauveria bassiana is an entomopathogenic fungus with an established role in biological pest management. Its biological importance is associated with its ability to infect a broad range of insect hosts. The fungus produces various enzymes and secondary metabolites that facilitate interactions with its hosts and environment. These metabolites are also relevant to nanobiotechnology because molecules produced by the fungus may function as: reducing agents, nucleation-promoting molecules, stabilizers, capping agents, or surface-functionalizing molecules. Thus, *B. bassiana* can be viewed as a potential biological nanofactory (Banu and Bala Subramanian, 2014)

***BEAUVERIA BASSIANA*-MEDIATED AGNP SYNTHESIS**

Several studies have demonstrated the ability of *B. bassiana* to participate in AgNP formation. An earlier study reported extracellular transformation of silver nitrate into AgNPs using *B. bassiana* mycelial extract. Another study used extracellular metabolites of *B. bassiana* to synthesize AgNPs and reported nanoparticles around 24.8 nm, demonstrating that the fungus can generate nanoparticles with biological functionality. The study also investigated *B. bassiana*-derived AgNPs for biological control of mustard aphid, illustrating that the same fungal nanotechnology platform has applications beyond cosmetics. This previous work provides the background for investigating *B. bassiana*-mediated AgNPs in nanocosmetic formulations. Pillay *et al.*, 2024 reported that systematically optimized the synthesis conditions. The highest synthesis efficiency was obtained using the extracellular fungal extract at pH 10.0, 60 °C and 3 h (Bruna *et al.*, 2016)

Table 1: Major parameters affecting synthesis

Parameter	Possible Effect
pH	Influences reduction and particle stability
Temperature	Influences reaction rate and nucleation
Reaction time	Influences particle formation and growth
$AgNO_3$ concentration	Influences nanoparticle yield and size
Extract concentration	Influences availability of reducing/capping molecules
Fungal growth conditions	Influence metabolite composition

An important point for your chapter is that these should be described as optimized conditions for the reported experimental system, not as universally optimal conditions for *B. bassiana*.

CHARACTERIZATION OF BBAGNPS

The study employed several analytical techniques, including UV–Visible spectroscopy, FTIR, particle-size analysis, electron microscopy, thermogravimetric analysis and differential scanning calorimetry (Qamandar and Shafeeq 2018). A) UV–Visible spectroscopy: UV–Visible spectroscopy is commonly used for preliminary confirmation of AgNP formation. The appearance of a surface-plasmon-resonance band indicates formation of nanoscale silver structures. Changes in peak width and position may also provide information about: particle size, size distribution, aggregation and nanoparticle morphology. B) FTIR: FTIR can identify functional groups associated with biomolecules attached to the nanoparticle surface. This is important in biological synthesis because the biological extract can function as both a reducing and capping system. C) SEM: Scanning electron microscopy provides information about particle morphology and surface characteristics. The 2024 study reported predominantly spherical nanoparticles, with particles ranging approximately from 32.26 to 141.76 nm, while a substantial proportion had an average size around 41.5 nm. This is an important distinction: average particle size should not be interpreted as meaning every particle had exactly that size. D) DLS: Dynamic light scattering provides hydrodynamic particle size in suspension. It can differ from TEM/SEM measurements because hydrated surface layers and associated biomolecules contribute to hydrodynamic diameter. E) Zeta potential: The reported BbAgNP zeta potential was approximately: −23.2 ± 1.1 mV. This provides information about the surface charge and colloidal behaviour of the nanoparticles. F) XRD: X-ray diffraction provides information regarding crystalline structure. The reported BbAgNPs exhibited a face-centred crystalline structure.

ANTIMICROBIAL ACTIVITY

The broad antimicrobial activity of AgNPs is one of the major reasons for their investigation in cosmetic formulations (Soleimani *et al.,* 2022). The BbAgNP study evaluated activity against bacteria and yeasts. The reported minimum inhibitory concentrations were:

Test Organism	**Reported MIC**
Bacillus subtilis	156 μg/mL
Escherichia coli	156 μg/mL
Pseudomonas aeruginosa	312.5 μg/mL
Staphylococcus aureus	312.5 μg/mL
Candida albicans	312.5 μg/mL
Candida utilis	312.5 μg/mL

ANTIOXIDANT ACTIVITY

The antioxidant activity of BbAgNPs was evaluated using the DPPH radical-scavenging assay. The reported IC_{50} was approximately: 400.22 μg/mL under the conditions of the study. The antioxidant property is relevant to cosmetic research because oxidative stress is associated with

several processes involved in skin ageing and environmental damage. DPPH radical-scavenging activity demonstrates chemical antioxidant activity under an in-vitro assay; it does not by itself demonstrate anti-ageing efficacy in human skin (Hussain *et al.,* 2016).

PHOTOCATALYTIC ACTIVITY

The BbAgNPs showed relatively low photocatalytic activity, reported at approximately 4.66% in the assay used. Photocatalytic behaviour is relevant to nanoparticle characterization because excessive photo activity could potentially influence: formulation stability, degradation of organic ingredients, oxidative reactions, biological interactions. Therefore, photocatalytic characterization can contribute to a broader understanding of nanoparticle behavior (Prabakaran *et al.,* 2016).

COSMETIC CREAM FORMULATION

One of the strongest features of study is that it progressed from nanoparticle synthesis to actual cosmetic formulation (ong and Nyam 2022). BbAgNPs were incorporated into cream formulations at different concentrations. The reported SPF increased with increasing nanoparticle concentration, and the formulation containing BbAgNPs demonstrated improved sun-protection performance. The study reported a maximum SPF of approximately 4.74 and described approximately 2.6-fold improvement relative to the relevant control formulation. An SPF around 4.74 should not be presented as equivalent to a high-SPF sunscreen product. It is better described as evidence of SPF enhancement in the experimental formulation (Sethi 2024).

POTENTIAL APPLICATIONS

- Antimicrobial creams **t**he broad antimicrobial spectrum makes BbAgNPs a potential candidate for investigation in antimicrobial topical formulations.
- Cosmetic preservation and their antimicrobial properties may warrant investigation as part of microbial-control strategies, although compatibility with existing preservatives and regulatory requirements must be established (Tyagi *et al.,* 2019)
- Photoprotective formulations the SPF enhancement reported by Pillay *et al.* supports further investigation into BbAgNP-containing photoprotective formulations.
- Antioxidant formulations the DPPH activity provides a basis for further investigation of antioxidant formulations.
- Multifunctional nanocosmeceuticals the combination of antimicrobial, antioxidant and photoprotective characteristics represents an interesting direction for multifunctional products (Vijaram *et al.,* 2024).

CONCLUSION

Beauveria bassiana-mediated synthesis of silver nanoparticles offers several biological, technological and scientific advantages. Fungal metabolites can act as natural reducing agents, converting silver ions into nanoscale silver particles. Proteins, enzymes and other biomolecules present in the fungal extract may act as natural capping and stabilizing agents. The possibility of extracellular nanoparticle synthesis facilitates easier recovery and processing of the nanoparticles. The diverse metabolites produced by *B. bassiana* may also impart useful surface

functionality to the synthesized nanoparticles. Synthesis conditions such as pH, temperature, reaction time and precursor concentration can be optimized to obtain desirable nanoparticle characteristics.

The resulting nanoparticles can be characterized using established techniques such as UV–Vis spectroscopy, FTIR, XRD, SEM and TEM. Their nanoscale properties can contribute to antimicrobial and antioxidant activities. Furthermore, the synthesized nanoparticles can be incorporated into suitable cosmetic formulations such as creams and gels. Thus, this approach provides an interdisciplinary link between entomopathogenic fungi, green nanotechnology, biological activity and cosmetic biotechnology.

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Chapter
14

NANO FERTILIZERS, NUTRIENT DELIVERY AND POST HARVEST MANAGEMENT

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ABSTRACT

In the face of extraordinary population growth, the global agricultural sector hand-to-hand struggling with the challenge of sustaining food production while addressing environmental and resource constraints. Conventional fertilizers, though boosting crop yields, pose challenges just like nutrient losses and soil degradation, when applied for a long period of time. The concept of "nano-farming" is introduced as a paradigm shift innovation in agricultural, pest management and leveraging nanotechnology to optimize nutrient delivery. Implementation of nanotechnology in agriculture has the potential to ensure a sustainable 'farm to fork' journey by supporting increased food production, nutritional quality, and environmental conservation, thus addressing the challenges of modern agriculture and food security (Pandita, 2020) This study explores - The intricate dynamics between conventional agricultural practices and population growth, the transformative potential of nano-fertilizers (NFs) in shaping a sustainable future for agriculture. The review delves into the multifaceted world of NFs, emphasizing their potential to increase yields, revolutionize crop nourishment and preserve the environment. It discusses the advantages of NFs, including controlled nutrient release, improved nutrient uptake efficiency and reduced environmental impact. The mechanisms of NF uptake by plants, emphasizing their potential to enhance nutrient absorption, and their effects on the different plant processes, are also emphasized. This study also discusses the challenges that are expected to be faced by the incorporation of nanoparticles in agricultural sector. Nano-fertilizers enhance agricultural productivity by providing controlled-release nutrient delivery, while nano-scale post-harvest technologies preserve produce quality and extend self-life.

KEYWORDS: Nano-Fertilizers (NFs), Conventional Fertilizers, Soil Fertility, Food Security, Nutrient Quality, Nanoparticles.

INTRODUCTION

In an era marked by extraordinary population growth, the world faces an increasingly complex challenge of how to sustainably feed and provide for a planet, swelling with billions of people (Solanki *et al.*, 2015). With the collective food demand, the agricultural sector has to undergo the

maximum challenges in managing this critical issue. From changing dietary preferences to the demand for more sustainable farming practices, the dynamics between population growth and agriculture are reshaping our world in profound ways (Bernard and Lux, 2017). It has been estimated that the global agricultural crop production needs to improve by 70% to accommodate the increasing population demand by 2050 (Tiwari *et al.,* 2017). The multifaceted impact of a growing population on agriculture, exploring the pressures it places on food production, land use, resource management, and the quest for innovative solutions to ensure food security and environmental sustainability in the face of this demographic surge has become imperative in today's world (Kopittke *et al.,* 2019). The pervasive presence of nutrient deficiencies in soils has led to significant economic hardships for farmers, and notable reductions in both the nutritional value and overall quantity of grains available for both people and livestock (Daniel *et al.,* 2022). The relationship between population growth and agriculture is of fundamental concern, intertwined with intricate economic, social, and environmental dynamics (Sharma *et al.*, 2023).

Uses of fertilizers have been adopted as an important factor in boosting agricultural output (Olad *et al.,* 2018). Chemical fertilizers, when used in large quantities, continuously over a period of time, are viewed as double-edged swords, as they do augment crop yields but also disrupt soil mineral equilibrium and reduce soil fertility (Shang *et al.,* 2019). The concept and structure of agriculture changed over the years, with each technique being replaced by a more promising version. This shift in the agricultural practices is crucial because of the environmental challenges, which often stem from the unmanaged practices of traditional fertilization methods in various farming operations (Verma *et al.,* 2022).

SUSTAINABLE AGRICULTURE

Sustainable agriculture is the need of the time, in order to address the interconnected challenges of environmental conservation, resource scarcity, climate change, and food security, while promoting economic prosperity and social upliftment. One of the important concepts of sustainable agriculture is to limit the application of agrochemicals to a minimum level, with the ultimate goal of safeguarding the environment and preserving diverse species from the risk of extinction (Muhie, 2022). In quest of agricultural sustainability, a number of innovative methods are being explored, which have the potential to boost farm production, while preserving the environmental integrity. Utilization of nanohybrid constructs like Nano-fertilizers as means of smart agrochemical delivery systems, and to achieve enhanced crop productivity can play a significant role in achieving the targets of sustainable agriculture (Raliya *et al.,* 2017). Nano-fertilizers can be defined as synthesized or modified forms of traditional fertilizers or bulk fertilizer materials, or they are extracted from various plant parts using chemical, physical, mechanical, or biological methods with the aid of nanotechnology. They are designed to improve soil fertility, productivity, and the quality of agricultural produce by enhancing nutrient absorption, either by acting as carriers for conventional fertilizers or as direct nutrient sources (Ditta and Arshad, 2016). Recently, researchers have designed N-NFs by enclosing urea

within hydroxyapatite NPs, allowing for a controlled and gradual release of nitrogen to benefit plant growth (Kottegoda *et al.,* 2017). Similarly, Phosphorus based NFs enable crops to directly absorb phosphorus, resulting in a reduction of phosphorus losses (Basavegowda and Baek, 2021).

NANO-FERTILIZERS

Definition - "The advanced agricultural inputs engineered at the nanoscale (1 to 100 nm) to deliver essential nutrients directly to crops with much higher efficiency than conventional fertilizers known as Nano fertilizers"

N, K, P, Zn, Fe, Cu, Mn, Mo, and CNTs have shown exceptional targeted delivery when they are applied at a specific concentration for diverse crops. It is known that NPs are present in soil systems Nano-fertilizers have been categorised as macronutrient and micronutrient nano-fertilizers based on their nutrient content. In addition, nano-biofertilizers (nanomaterials that are combined with microorganisms) are emerging as an alternative approach

Macronutrients, such as N, K, P, Ca, Mg, and S, have been combined with nanomaterials in order to enable the delivery of a precise quantity of these nutrients to crops. The macronutrient-based nano-fertilizers consist of one or more nutrients that are encapsulated within a particular nanomaterial. The utilisation of NPK in agriculture is likely to increase in the coming years. Thus, research needs to be conducted in order to develop new fertilizers with high nutrient efficiency that is environmentally friendly in order to replace the conventional micronutrient fertilizers.

Nitrogen (N), which is categorised as a primary macronutrient, is one of the key nutrients; it is deficient in most agricultural soils. Although 78% of N is present in the atmosphere, plants cannot utilise the atmospheric form of N and require nitrogen in the form of nitrates and ammonium. Commercially, it is manufactured using the Haber–Bosch process. Nitrogen fertilizers influence plant growth and development and help to maintain an adequate supply of nutritious food. Due to rapid volatilization and leaching, these commercially available nano-fertilizers (urea) vanish after approximately 75% application. Therefore, the disadvantages of nitrogen fertilizers are their low utilisation and the loss of N to the environment, which contributes to eutrophication and high levels of greenhouse gas emissions. Recently, an advanced N nano-fertilizer has been developed using urea-coated hydroxyapatite NPs (rod-shaped structures with an average aspect ratio 10) for targeted delivery and slow release. These compound NPs were selected because of their rich N and P sources, as well as their chemical compatibility.

Phosphorus (P) Similar to N, P is also fundamental to all living organisms and 90% P is used for food production. Rock phosphate is the raw material for manufacturing most commercial phosphate fertilizers. The major drawbacks of P fertilizers are that they rapidly change from the utilizable form of P into the less accessible forms, they have a low usability and uptake efficiency, and they cause eutrophication (increased N and P levels in water). Previously, different biological approaches for enhancing P uptake by plants, such as phosphatase and

phytase-producing bacterial species and fungi, P-solubilizing bacteria, and vesicular–arbuscular mycorrhiza, have been investigated. However, P-mobilizing microorganisms were not beneficial because of the low soil organic carbon, limiting the energy supply to the P-mobilizing microorganisms, and the high evaporation of water from the soil surface. These factors negatively affect the survivability of the micro-organisms. Nanotechnology researchers are investigating methods that will improve the slow release and uptake efficiency of P fertilizers, maintains P in its usable form in the long-term, and allows the mobilisation of native P to plants. Tarafdar *et al.* used tricalcium phosphate as a precursor salt in order to synthesise fungal-mediated P NPs. Subsequently, Liu and Lal investigated the effect of carboxymethyl cellulose-stabilised hydroxyapatite NPs on soybeans. P nano-fertilizer showed promising results for seed treatment when natural raw phosphorite was applied using ultrasonic dispersion. Although P is often present in adequate amounts in the soil, the demand for P fertilizers by farmers is high because the amount of P is not stable for the plants. Zinc NPs were used in order to enhance the efficiency of the conversion of native P into plant-available P. Enzymes such as phosphatase and phytase require Zn as a cofactor. The addition of ZnO NPs increased the activities of these enzymes and P uptake by 11% in legumes and cereals, which also improved the plant growth, the yield, the biomass, and the nutritional significance of cereals and legumes. P-supplements, along with ZnO NP exposure, have also been observed in cotton plants. In cotton, this combination of ZnO supplemented with P increased the biomass, the proteins, and the photosynthetic pigments, which protect against oxidative damage. In order to improve P uptake, native P mobilisation is stimulated by either micronutrient-based NPs (for instance, Fe and Zn) or by generating P-based NPs. This will not only improve the plant growth but also help to address other issues, such as the ecological impacts of P-induced eutrophication and the limited P availability.

Micronutrients The elements that are necessary for the plant in trace/low quantities are called micronutrients. They are vital for plants to maintain metabolic processes.

Zinc (Zn) is a structural or regulatory cofactor for various enzymes and proteins that is required for plant growth. Zn is involved in defence responses against harmful pathogens, the regulation of auxins, the synthesis of carbohydrates, and the protein metabolism.

Boron (B) is not only involved in the biosynthesis of the cell wall and its lignification in plants, but it also plays a vital role in plant growth and other physiological processes. Therefore, the application of appropriate amounts of Zn and B is essential for achieving maximum production with high-quality horticultural crops. It was observed that the application of B or Zn nano-fertilizers (at three different concentrations) improved the fruit yield (30%) in pomegranate trees (*Punica gratatum* cv. Ardestani). The shoot and fruit yield were increased when rubber-type nanomaterials were used as a zinc source, compared with the usage of commercial Zn-sulphate fertilizer. Similar results were reported with a Zn NP-related nano-fertilizer, which considerably improved the grain yield (38%) of pearl millet (*Pennisetum americanum*). In addition, they were also related to the increase in the length of the root and shoot, the root area, the chlorophyll

content, the total soluble leaf protein, and the plant dry biomass, compared to those of the control in 6-week-old plants. A considerable increase in yield was also observed in sunflower, sugarcane, potato, rice, maize, and wheat using Zn NPs as a nutrient source. Moreover, stabilised maghemite NPs enhanced the growth rate and the chlorophyll content of *Brassica napus*.

Iron (Fe) is also essential in minute amounts in plants in order to maintain proper growth and development. Fe availability can lead to the destruction of key metabolic and physiological processes, leading to reduced plant yield.

Manganese (Mn) acts as a cofactor for many enzymes, providing the ability to withstand various environmental constraints. Furthermore, Mn is imperative for photosynthesis and the synthesis of ATP, chlorophyll, fatty acids, proteins, and secondary metabolites such as lignin and flavonoids. The effects of laboratory-prepared NPs, such as Zn, Cu, Mn, and iron oxide, on the germination of lettuce (*Lactuca sativa*) seeds were assessed at low concentrations (<50 mg/L), and the study revealed that CuO NPs were similar to Zn NPs. In addition, the growth of lettuce seedlings was enhanced by MnO and FeO NPs.

Silica (Si/SiO/SiO_2/Silicon) Silica NPs promote seedling growth and activate antioxidant enzymes in order to resist biotic and abiotic stresses. The two major hurdles in agriculture are salinity and drought, which reduce the crop production. Under salt stress, Si NPs increase the potassium uptake and reduce the sodium uptake. The advantages of silica and silicon NPs for plant growth and development can practically combat unfavourable climate changes, such as high temperatures and erratic rainfall (because silica can mitigate the evaporation of water from the soil surface.

Titanium TiO_2 has been utilised commercially as a pigment in paints and sunscreens, owing to its photocatalytic activity. TiO_2 is primarily used in NP studies that are related to plant growth, plant responses to seed germination, pest management, pesticide degradation, superior water purification, and sensor technology, in order to detect pesticide residues, because it converts light energy into electrical or chemical energy under sunlight. TiO_2 NPs have been used for numerous crops, such as spinach, watermelon, tomato, bean, millet, lettuce, *Lemna minor*, and wheat. These studies using TiO_2 NPs concluded that they increase the germination rate, the yield/biomass, the chlorophyll content, the photosynthetic activity, and the nutrient content. Moreover, physiological activities were also improved due to an increase in the nitrogen metabolism and RuBisCO. However, plant responses toward TiO_2 NPs depend on the plant type, the nanoscale properties, and the exposure concentration. Furthermore, plants that are exposed to TiO_2 NPs grow faster by capturing more sunlight.

KEY BENEFITS

- **High Absorption:** Ultra-small particle size allows easy entry through plant stomata, cuticular channels, and cell walls.
- **Reduced Volume:** One 500 ml bottle of IFFCO Nano Urea can replace at least one full 45 kg bag of conventional urea.

- **Lower Environmental Footprint:** Controlled or slow release minimizes nutrient leaching, groundwater runoff, and gaseous emissions.
- **Targeted Nutrition:** Available in liquid or solid formulations for nitrogen, phosphorus (such as Nano DAP), and micronutrients like iron or zinc.

HOW NANO-FERTILIZERS WORK ON SOIL FERTILITY

Traditional fertilizers need to be applied in large amounts, as they have low uptake efficiencies. The two main challenges for phosphorus- and nitrogen-based fertilizers are low nutrient uptake efficiency and rapid change into chemical forms that cannot be utilised by plants. This has had a negative impact on the soil and the environment, as the emission of dangerous greenhouse gases and eutrophication has increased.

Nano-fertilizers gradually release nutrients, which may aid in improving nutrient use efficiency without any related adverse effects. These nano-fertilizers are constructed in order to deliver nutrients slowly over an extended time period and to reduce nutrient loss considerably, thereby ensuring environmental safety. Traditional fertilizers are not only costly but may also be harmful to humans and the environment, whereas nano-fertilizers play a significant role in maintaining the soil fertility and improving the crop yield.

The organic and inorganic components of the soil can modify the effects of the applied nano-fertilizers, depending on their nature and their interactions with the soil. When nano-fertilizers are applied to the soil, aggregation occurs first, which reduces the area of action, and the aggregates become less mobile in porous materials as their size increases. Hence, the amount of organic matter in the soil, the surrounding environment, and the chemical properties of the nano-fertilizers can enhance or reduce the mobility of the NPs. Nano-fertilizers can influence the activity of the soil microorganisms in many ways. Nano-fertilizers can increase the nutrient use efficiency, thus being beneficial for nutrition management. These nutrients are bound to the nano-absorbents that are applied either alone or in combination and release the nutrients at a slower rate than that of conventional fertilizers. This approach would minimise nutrient leaching into groundwater and increase the nutrient use efficiency. In order to achieve considerable efficiency in food security, both the agriculture and horticulture sectors are under pressure to utilise alternative fertilizers rather than chemical fertilizers.

According to Kale and Gawade, in Zn-deficient soil, the addition of ZnO NPs to other fertilizers boosted barley productivity by 91% and improved the nutrient use efficiency when compared to that of the control; however, bulk $ZnSO_4$ increased the productivity by only 31% when compared to that of the control. Additionally, nano-composite fertilizers have shown positive effects on rhizosphere bacteria by stimulating the formation of secondary metabolites, which improved plant growth by promoting the colonisation of the root surface.

Moreover, research has shown that using “controlled release fertilizer” decreased nitrogen leaching and runoff loss by 25% and 22%, respectively, compared to those by the traditional fertilizers, while also increasing wheat yield and soil residual mineral nitrogen by 6% and 10%, respectively. The diverse nanomaterials include silver (Ag), gold (Au), aluminium (Al), single

or multi-walled nanotubes, magnetised iron NPs, zinc (Zn), zinc oxide (ZnO), copper (Cu), silica (Si), titanium dioxide (TiO_2), and cerium oxide (Ce_2O_3) .

Table 1: Mode of application – Foliar

Sr. No.	Crop Species	Nanomaterials	Duration of Treatments	Responses
1	*Cicer arietinum*	Zn, Fe and NPK	First Spraying at 4 to 6 leaf stage, second spraying at 30 days, and third spraying during pod filing	There was a significant increase in both biological and seed output
2	*Cyamopsis tetragonoloba*	ZnO	4–6 weeks	Increases in biomass accumulation and nutrient concentration, and enhancements to growth physiology
3	*Solanum lycopersicum*	CuO	11 days	Eliminated the spread of disease
4	*Moringa peregrina*	ZnO and Fe_3O_4	Watered every 3 days	Salinity levels reduced the growth parameters significantly
5	*Solanum lycopersicum*	Al_2O_3 NPs	20 days	Effectively counteract Fusarium as a biocontrol agent
6	*Punica granatum*	Zn and B NPs	Once every season and one week before the first full bloom	Increases in pomegranate fruit yield
7	*Oryza sativa*	TiO_2 and SiO_2	55 days	Better development and Cd translocation inhibition
8	*Triticum aestivum*	N, P and NPK NPs	on plant	Significant changes in plant growth parameters like shoot length, root length and others
9	*Triticum aestivum*	NPK NPs	On grains, Treatment after 21 days of the date of planting	Significant increase in total saccharide content of wheat grains
10	*Coffea arabica*	ZnO	40–45 days	Acceleration of net photosynthesis and increased biomass production
11	*Vigna unguiculata*	AgNPs	4–7 days	Growth inhibition of X. axonopodis pv. malvacearum and other harmful bacteria

Owing to the high receptivity of nanomaterials, plants are able to absorb the nutrients and essential chemicals effectively. These "smart fertilizers" are preferable to the conventional fertilizers. Several factors determine the efficiency of nano-fertilizers. Both intrinsic and extrinsic factors in crops are highly dependent on the absorption, the transportation, and the accumulation of nano-fertilizers, and the route of exposure. The major intrinsic factors determining the efficacy of NPs are the surface coatings and the particle size, whereas the extrinsic factors that strongly affect the potential application of nano-fertilizers in crops include the soil texture, the soil pH, and the organic matter.

MECHANISM OF NANO-FERTILIZERS UPTAKE BY PLANTS

Plant roots and leaf surfaces serve as the primary pathways for nutrient intake, exhibiting high porosity at the nanoscale. Due to their small size, Nano-fertilizers have the potential to enhance plant nutrient absorption through their microscopic pores. This process might involve the facilitation of complexation with molecular transporters or root exudates, by creating new pores, or leveraging endocytosis or ion channels to facilitate nutrient uptake (Mastronardi *et al.,* 2015). Studying the Effect of nano-fertilizers on biochemical and molecular processes in plants Nanoscale fertilizers can influence various metabolic pathways by modulating the activities of key enzymes and regulatory genes and, henceforth can impact a range of biochemical and molecular responses in plants. With the ability to permeate the seed coat and promote water absorption and utilization, Nano-fertilizers activate the enzymatic system within the seeds, thereby improving the seed germination and seedling growth. Seed nano-priming using Nano-fertilizers increases the accumulation of reactive oxygen species

ABSORPTION OF NANO-FERTILIZERS

Through the roots and leaves considerably influences their behaviour, bioavailability, and the absorption in crops. They control the accessibility of nutrients in the crops by slowing and controlling the release mechanisms, which is advantageous to growers. Nano-fertilizers should be synthesised in accordance with the need for the nutrient by the proposed crops, and biosensors should be added to the latest advanced fertilizer, which would control the supply of nutrients according to the requirement of the nutrient in the soil and the condition of the growth period of the plant. The availability of micronutrients during crop growth has a negative effect, as it results in the production of fruits and vegetables with poor nutritional value. NPs can effectively deliver deficient micronutrients, such as Zn and Fe, to crops and fresh food products.

NANO-FERTILIZERS AND CONVENTIONAL FERTILIZERS

The advent of the green revolution during the 1960s marked a significant shift towards intensive farming methods, resulting in a considerable rise in crop yields primarily facilitated by the increased use of agrochemicals, notably fertilizers (Morari *et al.,* 2011). This shifting notably helped in enhancing the agricultural productivity, particularly in developing countries of Asia and Africa. However, it also brought about adverse effects on soil system such as reduced nutrient efficiency,

KEY BENEFITS VS. CONVENTIONAL FERTILIZERS

- **Higher Nutrient Use Efficiency (NUE):** A much higher percentage of the applied nutrient is absorbed, reducing the total fertilizer requirement.
- **Reduced Environmental Loss:** Minimizes nitrogen runoff, ammonia volatilization, and phosphate fixation in the soil.
- **Stress Tolerance:** Helps plants manage abiotic and biotic stresses by improving water use and photosynthetic activity.

CHALLENGES OF NANO-FERTILIZERS IN AGRICULTURE INDUSTRY

Although the introduction of NF technology in agriculture presents a potential shift in crop cultivation, promising increased yields while minimizing the ecological footprints, it also presents a number of challenges, primarily regulatory hurdles that hinder swift integration. NFs can incur high costs due to the need for specialized storage facilities and transportation methods for large-scale production. It is essential for NF production economics to demonstrate to conventional fertilizer

NANO FERTILIZER NUTRIENT DELIVERY

- **High Surface Area and Bioavailability:** Nano-fertilizers (ranging from 1 to 100 nm) offer a high surface-area-to-volume ratio, significantly increasing solubility and plant uptake efficiency compared to conventional synthetic fertilizers.
- **Controlled and Slow Release:** Nutrients are encapsulated in nanomaterials—such as hydroxyapatite, zeolites, chitosan, or clay—or surface-adsorbed onto carrier nanoparticles. This allows a slow and steady release over 40–50 days, matching plant growth demands and raising Nutrient Use Efficiency (NUE) to 60–70% (compared to 30–40% for conventional nitrogen and 5–15% for phosphorus).
- **Targeted Uptake Routes:** They can be applied via root fertigation or foliar sprays, where nanoscale particles enter through stomata and cuticular pores directly, bypassing soil fixation, leaching, and volatilization losses.
- **Examples in Practice:** Products like Nano Urea and Nano-DAP reduce overall chemical application volumes while boosting crop yields and grain/fruit quality.

CORE MECHANISMS OF DELIVERY

- **High Surface Area-to-Volume Ratio:** The ultra-small size drastically increases contact area with leaf surfaces and root membranes, accelerating absorption rates.
- **Cellular Entry:** Particles enter plant leaves primarily through stomata and cell membranes via endocytosis or specialized nanocarrier transport.
- **Controlled and Stimuli-Responsive Release:** Unlike conventional granules that lose 60–70% of nutrients through leaching, volatilization, or soil fixation, nano-carriers release nutrients slowly and gradually. This release can be triggered by environmental factors such as soil pH, moisture, root exudates, or specific biological crop demands.
- **Foliar and Soil Application:** They are applied via foliar sprays (e.g., IFFCO Nano Urea Plus or Coromandel Gromor Nano DAP), soil amendment, or seed coating.

Table 2: Comparison of Nano Fertilizer Delivery Systems

Sr. No.	Delivery System / Product	Primary Mechanism / Carrier	Application Method	Key Nutrients Delivered	Main Advantage
1	Mesoporous Silica Nanoparticles	Inorganic porous silica framework	Soil / Seed Treatment	N, P, K & trace metals	High loading capacity and controlled diffusion-based release.
2	Nano Urea / Nano Urea Plus (e.g., IFFCO)	Nanoscale liquid formulation	Foliar Spray	Nitrogen	Replaces a significant portion of bulk soil urea with lower dosage.
3	Polymer-Encapsulated Nano DAP (e.g., Coromandel Gromor)	Polymer-encapsulated aqueous suspension (<100 nm)	Foliar Spray	Nitrogen (N), Phosphorus (P_2O_5)	Rapid absorption via stomata; supports ATP synthesis.
4	Chitosan / Alginate Nanocomposites	Biopolymer-based nano-carriers	Soil Amendment / Foliar	Macro- and micronutrients	Biodegradable matrix with pH-responsive slow release.

POST-HARVEST MANAGEMENT WITH NANOTECHNOLOGY

- **Edible Coatings and Thin Films:** Nanocomposite films, chitosan-SiO2, and biopolymer coatings enriched with nanoparticles provide an oxygen and moisture barrier that slows down respiration and ripening in fruits and vegetables.
- **Antimicrobial and Pathogen Control:** Silver nanoparticles (AgNPs), zinc oxide (ZnO), and titanium dioxide (TiO2) nanoparticles act as effective antimicrobial agents, preventing fungal decay, bacterial growth, and post-harvest rot.
- **Shelf-Life Extension:** These nano-interventions maintain post-harvest firmness, reduce weight loss, and preserve nutritional value during storage and transport.

KEY APPLICATIONS IN POST-HARVEST MANAGEMENT

- **Edible Nano-Coatings & Films:** Formulated from natural polymers like chitosan, alginate, pullulan, or starch combined with metal/silica nanoparticles, these ultra-thin layers coat fruits and vegetables. They slow down respiration, limit water loss, block oxidation, and suppress pathogens like *Botrytis cinerea* and *Colletotrichum gloeosporioides*.
- **Smart & Active Nano-Packaging:** Incorporates nanomaterials (such as silver, titanium dioxide, zinc oxide, or nano-clay silicates) into packaging films. This lowers gas and moisture transmission rates, improves mechanical and oxygen-barrier properties, and acts as an active antimicrobial shield.
- **Controlled-Release Systems:** Utilizes porous nanostructures or nano-emulsions to deliver active preservatives, antioxidants, and ethylene inhibitors (such as potassium permanganate-coated zeolite) in a slow, targeted manner.

- **Nano-Sensors & Biosensors:** Deploys nanoscale instruments and gas/pathogen sensors inside packaging or storage facilities for real-time monitoring of microbial spoilage, gas changes, and product freshness.
- **Cut Flower Preservation:** Uses silver nanoparticles (SNPs) to limit ethylene synthesis and prevent microbial blockages in vascular tissues, significantly extending vase life.

MAJOR CHALLENGES & CONSTRAINTS

- **Toxicity & Health Risks:** Potential migration of engineered nanoparticles into food raises concerns regarding cellular penetration, oxidative stress, and long-term consumer toxicity.
- **Environmental Impact:** Non-target interactions and the persistence of certain nanomaterials in ecosystems require eco-friendly, biodegradable alternatives (like chitosan or polylactic acid).
- **Cost & Scalability:** High production costs and a lack of standardized regulatory frameworks hinder widespread commercial adoption, particularly for small-scale agricultural producers.

Table 3: Technology Category and their Key Limitations

Sr. No.	Technology Category	Primary Nanomaterials Used	Main Function / Benefit	Key Limitations
1	Controlled-Release Carriers	Zeolites, polymer nanocapsules, porous silica	Slow, targeted release of antimicrobials and ethylene scavengers	Complex synthesis, risk of chemical residue
2	Nano-Sensors	Carbon dots, metallic nanoparticles, biosensors	Real-time tracking of spoilage, gases, and pathogens	High initial setup cost, technical calibration needs
3	Edible Nano-Coatings	Chitosan, pullulan, alginate, ZnO, AgNPs	Delays ripening, reduces water loss, inhibits fungi/bacteria	High formulation cost, potential changes to food texture/taste
4	Smart Packaging	Nanoclays, TiO_2, SiO_2, ZnO, AgNPs	Enhances oxygen/moisture barriers, provides antimicrobial action	Regulatory uncertainty, recycling challenges

CONCLUSION

There is still a need for in-depth quantitative research on the long-term effectiveness, energy and resource consumption, and environmental impact of nano-fertilizers. The successful implementation of novel nano-fertilizers in agriculture depends on public acceptance, which is affected by perceptions of risk and benefit. To successfully commercialize nano-fertilizers, a strategic marketing plan should be crafted in collaboration with a marketing agency, aimed at reaching potential customers like

The integration of nanotechnology-infused fertilizers marks a pivotal stride toward fostering a greener and more sustainable future in agriculture. These innovative nano-fertilizers stand as pillars of change, revolutionizing conventional farming practices in order to attain the urgently needed second green revolution of the world. Their nano-sized components pave the way for targeted nutrient absorption, minimizing environmental impact while maximizing crop yield. By attenuating nutrient

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Chapter

15

NANOBIOTECHNOLOGICAL RELEVANCE AGAINST CANCER AND ITS CLINICAL COMPLICATIONS MANAGEMENT: AN UPDATE

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ABSTRACT

Cancer is one of the major causes of mortality worldwide and advanced techniques for therapy are urgently needed. The development of novel nano materials and nano carriers has allowed a major drive to improve drug delivery in cancer. The major aim of most nano carrier applications has been to protect the drug from rapid degradation after systemic delivery and allowing it to reach tumor site at therapeutic concentrations, meanwhile avoiding drug delivery to normal sites as much as possible to reduce adverse effects. These nano carriers are formulated to deliver drugs either by passive targeting, taking advantage of leaky tumor vasculature or by active targeting using ligands that increase tumoral uptake potentially resulting in enhanced antitumor efficacy, thus achieving a net improvement in therapeutic index. The rational design of nanoparticles plays a critical role since structural and physical characteristics, such as size, charge, shape, and surface characteristics determine the biodistribution, pharmacokinetics, internalization and safety of the drugs. In this review, we focus on several novel and improved strategies in nanocarrier design for cancer therapy.

KEYWORDS: Nanoparticles, Nanomedicine, Drug Delivery, Pharmacokinetics, Cancer Therapy.

INTRODUCTION

Cancer is one of the top causes of morbidity and mortality worldwide and it is anticipated to be the major cause of death in the coming decades (Bray *et al.,* 2012). Despite the breakthroughs and considerable research on alternative approaches, existing treatments are still limited to surgery, radiation, chemotherapy, and immunotherapy. Treatment failure is attributed to either medication resistance, pharmacological or toxicological concerns in most instances. In opposite, employment of nanocarriers which leads to enhanced therapeutic index and tumor tissue concentrations of the medications and can enhance the efficacy of already utilized regimens by providing superior pharmacokinetic properties.

According to Bray *et al.* (2012), cancer is one of the main causes of morbidity and mortality globally and is predicted to become the leading cause of death in the upcoming decades. Surgery, radiation, chemotherapy, and immunotherapy are still the only available treatments, despite advancements and substantial research on new strategies. In most cases, drug

resistance, pharmacological problems, or toxicity difficulties are linked to treatment failure. On the other hand, the introduction of nanocarriers can improve the pharmacokinetic characteristics of existing regimens and boost the therapeutic index and drug concentrations in tumor tissue. In this chapter, we will focus on strategies of nanoparticle design and highlight the latest developments in cancer nanomedicine.

NANOPARTICLES AND PARTICLE INTERACTION

Jatzkewitz created a polymer-drug conjugate in the 1950s (Jatzkewitz, 1954), and Bangham developed liposomes in the middle of the 1960s (Bangham and Horne, 1964; Bangham *et al.*, 1965). Albumin-based nanoparticles, which served as the foundation for albumin-bound paclitaxel (Abraxane), were first described by Scheffel and associates in 1972 (Scheffel *et al.*, 1972). The US Food and Drug Administration (FDA) approved abraxane in 2005 to treat breast cancer (Gradishar *et al.*, 2005). More recently, it was approved to treat lung cancer (Casaluce *et al.*, 2012). The FDA licensed Abelcet, amphotericin B lipid complex, for the treatment of invasive fungal infections (Chonn and Cullis, 1995). It is also frequently used to treat systemic fungal illness, which causes significant morbidity in cancer patients.

Maeda and associates saw increased nanoparticle formation at the tumor site in the 1980s as a result of the tumor vasculature's changed shape (Matsumura and Maeda, 1986). Because of their aberrant and leaky construction, blood vessels in tumors differ from normal blood vessels. The "enhanced permeability and retention (EPR) effect" is caused by impaired blood vessel regulation (Maeda *et al.*, 2006). The EPR effect is influenced by decreased lymphatic derangement, larger fenestrations, and gaps between endothelial cells, which vary from 200 to 1200 nm, whereas normal endothelium has pores that are between 10 and 50nm.

Due to "passive targeting," this action has become a defining characteristic of the solid tumor vasculature, increasing the accumulation of nanoparticles at the tumor site. As a result, drug carriers' show improved therapeutic efficacy in tumors together by means of diminished toxicity and side effects.

Even though passive targeting techniques have many benefits, there are still a number of issues that need to be resolved. The permeability in blood arteries may vary within the same tumor since some cancers are difficult to administer because they do not have an EPR effect (Yuan *et al.*, 1995). In order to get beyond these restrictions, nanoparticles are made to bind to certain targets (active targeting) using ligands that identify specific receptors in target cells.

ACTIVE TARGETING

A Numerous receptor on the surface of tumor cells has been investigated as possible locations for selective administration. To attach particular receptor ligands, a range of conjugation chemistries can alter the surface of nanoparticles (Torchilin, 2005). After identifying and attaching to their destinations, nanoparticles are taken up via receptor-mediated endocytosis. The medication or payload is released in the cytoplasm or nucleus after internalization. Peptides, vitamins, antibodies, carbohydrates, and other chemical compounds can all function as receptor ligands. For example, nanoparticles conjugated with the ligands of these receptors

have been delivered by taking advantage of the over expression of transferrin and folate in some cancers (Yng *et al.,* 2010; Fernandes *et al.,* 2008).). Another example is the $\alpha v\beta 3$ integrin, which is over expressed in a wide range of tumors active targeting. Han *et al.* (2010) reported that the administration of chitosan nanoparticles conjugated with cyclic Arg-Gly-Asp (RGD) led to increased tumor delivery and enhanced anti-tumor activity in ovarian cancer models. The surface of nanoparticles can be modified by a variety of conjugation chemistries to attach specific receptor ligands.

To improve tumoral uptake of nanoparticles, a range of targeted agents, including nucleic acids (aptamers) and monoclonal antibodies (mAbs), are also employed. Milstein first reported using mAbs for targeting in cancer treatment (Warenius *et al.,* 1981). Since then, antibody-based targeting has advanced significantly as a viable cancer treatment approach. Rituximab (Rituxan) for the treatment of non-Hodgkin's lymphoma (James and Dubs, 1997), trastuzumab (Herceptin) for the treatment of breast cancer (Albanell and Baselga, 1999), and bevacizumab as an angiogenesis inhibitor for colorectal cancer (Ferrara, 2005) are examples of clinically authorized and commonly used mAbs. Twelve mAb-based treatments have been approved since 1997, and more antibody-based strategies are undergoing preclinical or clinical testing (Scott *et al.,* 2012). Direct conjugation of an antibody with a medicinal substance has also been investigated. The first clinically authorized formulation in this approach was Mylotarg. The CD33 antibody was coupled with the chemotherapeutic drug calicheamicin (Peer *et al.,* 2007). Approved for the treatment of non-Hodgkin's lymphoma, Zevalin and Bexxar are radio-immunoconjugates made with CD20 antibody (Grillo-López, 2002; Blagosklonny, 2004).

1	Rituximab (Rituxan)	for the treatment of non-Hodgkin's lymphoma	(James and Dubs, 1997)
2	trastuzumab (Herceptin)	for the treatment of breast cancer	(Albanell and Baselga, 1999),

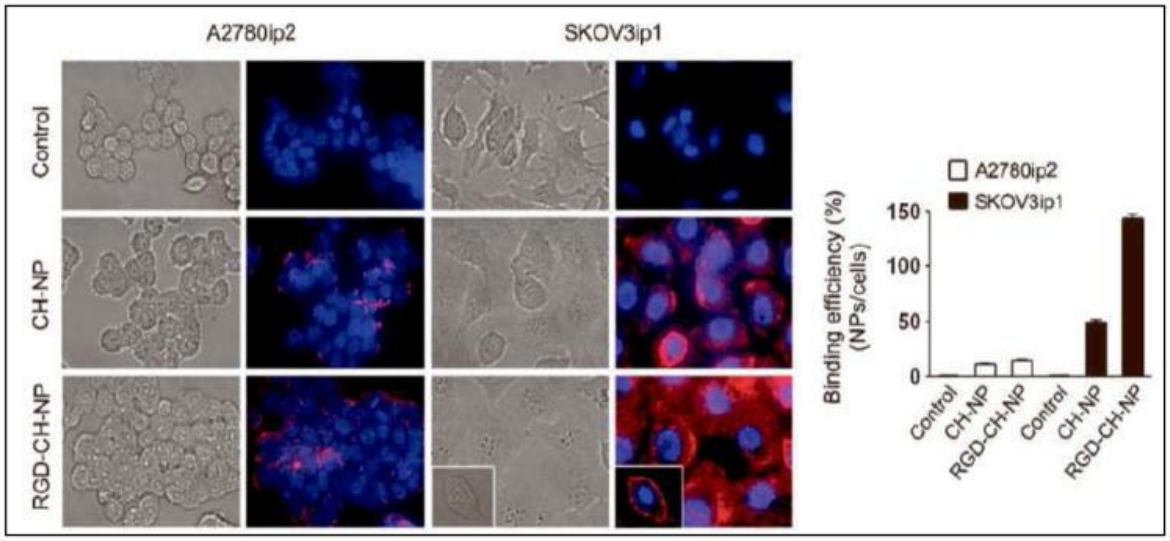


Figure 1: Targeted therapy with RGD-Chitosan Nanoparticles

Binding efficiency of Alexa555 siRNA (red fluorescence) incorporated chitosan nanoparticles (CH-NP)- conjugated with RGD peptide (RGD-CH-NP) in SKOV3ip1 or A2780ip2 ovarian cancer cells (blue for nuclei) by fluorescence microscopy (Han *et al.*, 2010).

Recently, nucleic acid aptamers have gained immediate attention after the *in vitro* selection of functional nucleic acids (termed SELEX) that was discovered in 1990 (Ellington and Szostak, 1990, Tuerk and Gold, 1990). Aptamers are single stranded oligonucleotides that can modulate molecular targets with high specificity and affinity through their three-dimensional structures. Aptamers exhibit significant advantages such as the technical possibility in selection and chemical modification, specificity to target any given molecule, its prosperous bio-activity in vivo, the low production costs, the simplicity in synthesis and storage for the marketing (Scaggiante *et al.*, 2013) There are currently several aptamers that are in clinical trials (Scott *et al.*, 2012). For instance, Pegaptanib was approved by FDA and used as a VEGF-specific aptamer that binds to VEGF and blocks the interaction with its receptor (VEGFR) thereby inhibiting its activity (Gragoudas *et al.*, 2004). Moreover, aptamers seem alluring to modify the surface of nanoparticles for the design of targeted drug delivery systems.

DRUG DELIVERY SYSTEMS

LIPOSOMES

Phospholipids with hydrophilic heads and hydrophobic anionic/cationic long chain tails disperse to create liposomes, which are self-assembling nanoparticles that form closed membrane structures (Fig. 2). Medications and siRNA are examples of hydrophilic agents that can be inserted into inner compartments, while hydrophobic medications can be incorporated into hydrophobic membranes. Currently, a number of liposomal anticancer medications are either being explored in advanced phases of clinical trials or are being employed as carriers in clinical settings with effectiveness. For example, the FDA approved PEGylated liposomal doxorubicin (Doxil) carriers for the treatment of Kaposi's sarcoma after doxorubicin-loaded liposomes were modified with polyethylene glycol (PEG), which changes the plasma pharmacokinetics and tissue distribution of doxorubicin (Patel, 1996). Non-pegylated liposomal doxorubicin (Myocet by Elan), liposomal daunorubicin (DaunoXome by Gilead), liposomal amphotericin B (abelcet), liposomal cytarabine (DepoCyte by SkyePharma/ Enzon/ Mundipharma), and liposomal cisplatin (Lipoplatin by Regulon) are among the approved liposomal formulations in addition to Doxil (Huwyler *et al.*, 2008). However, the use of antisense oligonucleotides in liposomal formulations for cancer treatment is equally appealing (Tari *et al.*, 1995). Antisense oligonucleotides have the ability to specifically block genes that cause disease, which prevents the synthesis of proteins linked to that disease. For example, it has been shown that liposomal formulation of bcl-2 oligos inhibits the creation of bcl-2 protein, which in turn inhibits the proliferation of follicular lymphoma cell lines (Tormo *et al.*, 1998). Additionally, the in vivo behavior in rodents was assessed using liposomal bcl-2 antisense oligos. Over the course of a 6-week intravenous therapy of liposomal Bcl-2 oligos, the liposomes were broadly dispersed and no appreciable toxicity was noted (Gutierrez-Puente *et*

al., 1999). Another illustration is the raf antisense oligonucleotide, which increases susceptibility to radiation and chemotherapy by inhibiting c-raf. In its Phase I research, LErafAON, a liposomal formulation of raf oligonucleotide, demonstrated efficacy for advanced solid tumors (McGinnis *et al.,* 2012).

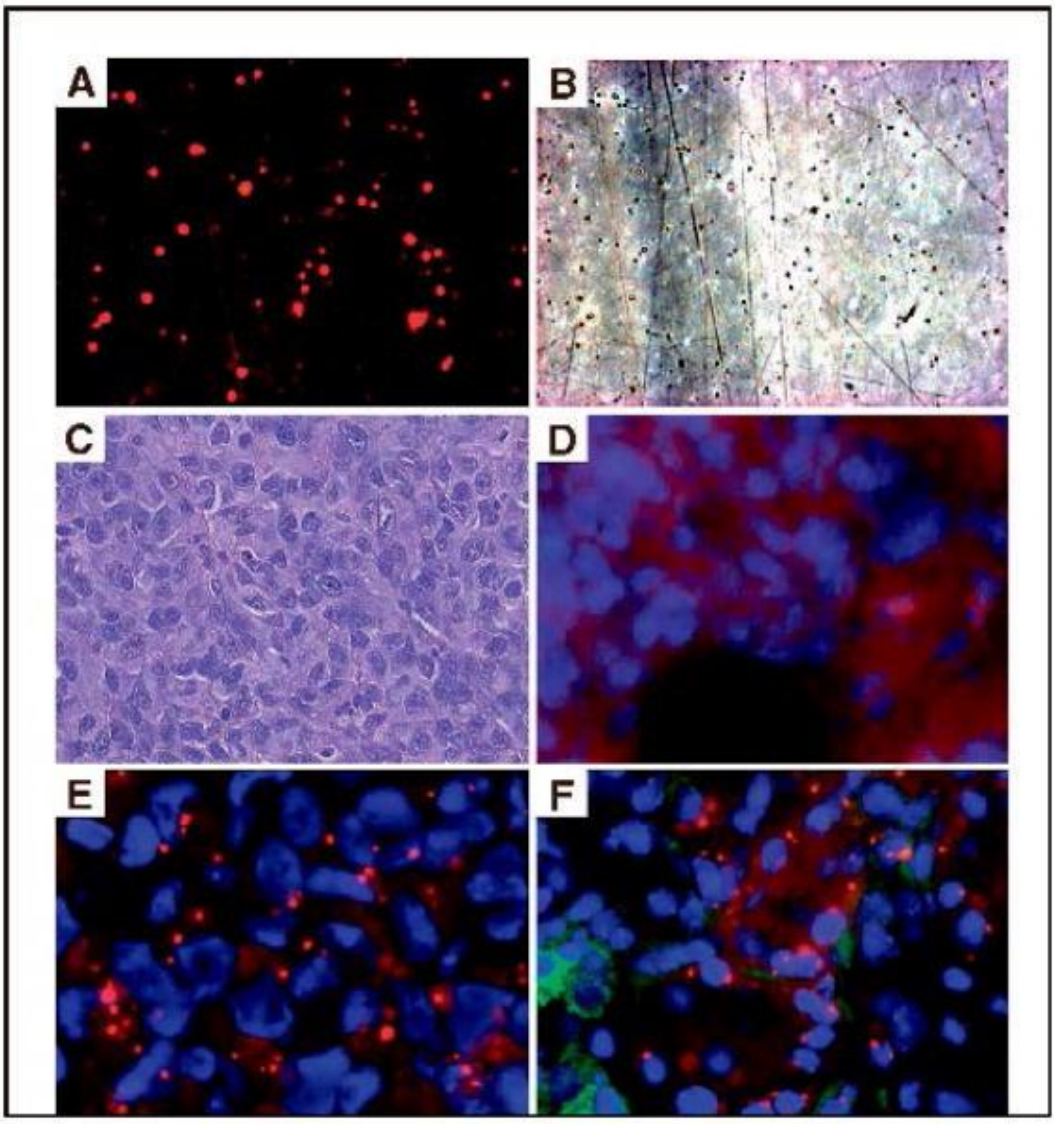


Figure 2: Accumulation of siRNA with DOPC nanoliposomes *in vivo*

Fluorescent **(A)** and phase **(B)** view of liposomes after siRNA incorporation.

C. Hematoxylin &Eosin stain of HeyA8 ovarian tumor.

D. Autofluorescence in tumor 48 hours after intravenous administration of nonfluorescent control siRNA.

E. Tumor accumulation of Alexa 555 siRNA (red fluoresce) incorporated in DOPC.

F. Alexa 555 siRNA is seen in both tumor cells and surrounding macrophages (green) (Landen *et al.,* 2005).

POLYMERIC NANOPARTICLES

The high biocompatibility and flexibility of polymer-based delivery systems, which allow for the engineering of multifunctional nanoparticles with desired size, shape, internal and external

morphology, and surface modifications, make them highly promising for biomedical applications. Polymers can be isolated from their natural sources, such chitosan, which is made from chitin, or they can be synthesized in the appropriate structure, like poly-lactic-co-glycolic acid (PLGA), during the nanoparticle manufacturing stage. Preclinical research on drug delivery has made extensive use of PLGA, arginine, chitosan, human serum albumin, alginate, and hyaluronic acid. Preclinical research on polymer-based nanoparticles has shown a lot of promise. For instance, one of the most extensively utilized polymeric delivery systems, especially for gene delivery, is chitosan nanoparticles. Because of their positive charge, chitosan nanoparticles are a desirable option for the transport of small interfering RNA (siRNA). Negatively charged siRNA and positively charged chitosan interact electrostatically to form a safe siRNA carrier in the bloodstream. Kim and colleagues used siRNA-incorporated chitosan nanoparticles to examine the therapeutic benefits of src and fgr inhibition in orthotopic models of ovarian cancer. Tumor development was significantly reduced when src and fgr were dual silenced in vivo using chitosan nanoparticles (Kim *et al.*, 2011).

The first polymeric formulation approved by the FDA for the treatment of metastatic breast cancer in clinical trials is albumin bound paclitaxel (abraxane) (Gradishar *et al.*, 2005). It was recently approved for the treatment of lung cancer. Abraxane took advantage of albumin's capacity to attach to the 60-kDa glycoprotein (gp60) receptor (albondin) (Miele *et al.*, 2009). Following this receptor-ligand contact, the albumin-gp60 complex initiates the absorption of protein-bound plasma molecules via caveolin-1. However, because of a sequence homology with gp60, albumin also binds to osteonectin (secreted protein acid rich in cysteine [SPARC]). In certain neoplasms, such as lung, breast, and prostate cancer, SPARC is abundantly expressed and contributes to intratumor. accumulation of all albumin-bound drugs (Hawkins *et al.*, 2008). In addition, Livatag (Doxorubicin Transdug) is a poly (isohexyl cyanoacrylate) nanoparticle formulation loaded with doxorubicin and approved for the treatment of multidrug-resistant protein-overexpressing hepatocellular carcinoma (Sultana *et al.*, 2013).

POLYMERIC MICELLES

Amphiphilic-block copolymers with sizes ranging from 10 to 100 nm self-assemble to create polymeric micelles. They consist of a hydrophilic corona and a hydrophobic core. Micelles can increase the bioavailability of hydrophobic medications and provide protection and inactivation when exposed to biological environments (Torchilin, 2001). In anticancer therapy, polymeric micelle formulations are employed for both passive and active targeting. For instance, Genexol-PM is presently being studied as a polymeric micelle formulation loaded with paclitaxel for the treatment of pancreatic, lung, and breast cancer. Doxorubicin-loaded micelle formulations Pluronic and NK911 are presently undergoing Phase I research (Sultana *et al.*, 2013). Early clinical trials are being conducted on NC-6004, a formulation laden with carboplatin, for the treatment of solid tumors (Wilson *et al.*, 2008). Additionally, polymeric micelle formulations that are modified with various ligands, such as folate (which binds to the folate receptor) and mAb C225 (which binds to the EGF receptor), are made for active targeting. Doxorubicin-loaded

PLGA-b-PEG polymeric micelle formulation has been demonstrated to enhance tumoral absorption and significantly reduce tumor growth in a nude mouse xenograft model (Yoo and Park, 2004).

DENDRIMERS

A core, branching units, and functionalized terminal groups make up dendrimers, which are hyperbranched nanoparticles. Multiple anticancer drugs can be integrated into the central core of dendrimers or conjugated to functional end groups, which is their main advantage (Lee *et al.,* 2005). Furthermore, the payload's release profiles can be altered by controlling the depolymerization of dendrimers (Wong *et al.,* 2012). For instance, polyamidoamine (PAMAM) dendrimers can be changed with anionic, neutral ligand molecules and PEGylated or acetylated to improve their biocompatibility and release characteristics (Cai *et al.,* 2013). For instance, to cause the release of doxorubicin in acidic environments, doxorubicin was attached to PEGylated PAMAM dendrimers via acid-sensitive links (Zhu *et al.,* 2010). Evaluations of pH-dependent payload release, cytotoxicity, cellular uptake and intracellular localization were performed using SKOV-3 ovarian cancer cell line. In addition, dendrimers with highest PEGylation degree showed the maximum- accumulation in SKOV3 tumor xenografts in mice. Conversely, polylysine dendrimers coupled with a fibronectin receptor ligand for $\alpha 5\beta 1$ were created for tumor targeting. Compared to non-transformed cells, activated $\alpha 5\beta 1$ is abundantly expressed in breast cancer cells and is essential for cancer invasion and metastatic pathways. A ligand called PHSCN peptide binds with a particular area of integrin's $\alpha 5$ subunit to prevent its function. This ligand can be used to modify polylysine dendrimers for tumor targeting, and treatment with this carrier significantly decreased the number of invasive human breast cancer cells (Yao *et al.,* 2011). Furthermore, when tumor bearing mice were treated with polylysine dendrimers modified with integrin ligand, lung colony formation was obviously inhibited. In conclusion, despite the fact that dendrimers are extensively used for the design and development of therapeutics, further research is needed to improve its immunogenicity to assure the safety of long-term administration in clinic.

FEATURES OF NANOPARTICLES

The in vivo biodistribution and cellular uptake of these drug carriers are significantly influenced by the physical and chemical properties of nanoparticles, such as size, charge, shape, and surface characteristics. The main factors that affect the nanoparticles' lifetime and delivery will be the main emphasis of this section.

One of the most important major elements influencing the nanoparticles' circulation time is their size. Following systemic injection, the reticulo-endothelial system (RES) eliminates nanoparticles that have accumulated in the spleen as a result of mechanical filtration. For instance, Kupffer cells, the primary component of RES, are crucial in the elimination of particles that have accumulated in the liver (Moghimi *et al.,* 2001). Since nanocarriers take advantage of the EPR effect in tumors and avoid filtration in the spleen while being large enough to avoid absorption in the liver, 100–200 nm is currently recognized as the ideal size for drug delivery

systems. (Petros and DeSimone, 2010). Particles with a smaller diameter than 5nm are rapidly cleared from blood circulation through renal clearance or extravasation (Wong *et al.,* 2008), (Alexis *et al.,* 2008), (Choi *et al.,* 2007). However, particles with a size up to 15 μm; accumulate in liver, spleen and bone marrow (Petros and DeSimone, 2010).

Furthermore, cellular internalization by phagocytosis, macropinocytosis, caveolar-mediated endocytosis, and clathrin-mediated endocytosis is greatly influenced by particle size. Size range has a significant impact on biodistribution and cellular internalization, as was previously mentioned. Furthermore, current research indicates that in terms of cellular internalization and distribution, particle shape is just as significant as size range (Geng *et al.,* 2007; Decuzzi *et al.,* 2010). Furthermore, Gratton and colleagues investigated the relationship between size and shape on the frequency of internalization in HeLa cells. It's noteworthy to note that particles with identical volumes but distinct forms internalized at wildly disparate rates (Gratton *et al.,* 2008). In a distinct study, Godin and coworkers demonstrated that the accumulation of discoidal particles in breast tumors were five times higher than spherical particles despite their similar diameters (Godin *et al.,* 2012). As a result, accumulating evidence shows that although size is a major parameter in the design of nanocarriers for decades, the shape as well, has a high impact along with the size.

FORM

It has been demonstrated that particle shape affects the degradation characteristics of nanoparticles and the consequent release of payload (Bawa *et al.,* 1985). Surface area and diameter were also shown to be crucial for the nanoparticles' cellular absorption (Panyam *et al.,* 2003; Dunne *et al.,* 2000). To accomplish zero-order, hemispherical particles were produced as sustained release devices. However, spherical particles can provide different degradation profiles due to their susceptibility to degradation (Champion *et al.,* 2007). Furthermore, because the spleen has asymmetric filtering units, spherical nanoparticles' deformability is crucial in preventing spleen filtration (Moghimi *et al.,* 2001). Therefore, nanoparticles, particularly those larger than 200 nm, should be either flexible enough to escape filtration even with a diameter of 10 μm, or deformable enough to prevent filtration in the spleen.

Decuzzi and colleagues investigated the impact of nanoparticle size and shape on biodistribution and tumor accumulation following intravenous administration in a sophisticated investigation. Spherical silica particles were produced in a variety of forms, including quasi-hemispherical, discoidal, and cylindrical silicon-based particles, and in sizes ranging from 700 nm to 3μm. Tumors and the major organs—liver, spleen, heart, lungs, kidneys, and brain—were examined for silicon content and histological assessment following a single intravenous particle injection to tumor-bearing animals. This study demonstrated the significance of nanoparticle shape characteristics in addition to size distribution, showing that the geometry of the particles influences opsonization, in vivo biodistribution, adhesion strength, and internalization rate in the cells (Decuzzi *et al.,* 2009).

SURFACE CHARACTERISTICS

The duration of nanoparticles in blood circulation after systemic delivery is significantly influenced by their surface characteristics. After administration, nanoparticles may be coupled with proteins which are known as 'opsonins', such as immunoglobulins and complement proteins that contribute to identification of nanoparticles by macrophages. As a result, opsonization plays a major role in determining the fate of nanoparticles in blood circulation. Nanoparticles' circulation time in blood and tissues can be increased or decreased by altering their surface. For example, RES are quickly removed from circulation by negatively charged nanoparticles (Zahr *et al.,* 2006). Cationic surfaces may stimulate cell membrane permeability and enhance cellular uptake (Chen *et al.,* 2009) yet, cationic nanoparticles prepared from polycationic polymers such as polyethyleneimine and diethylaminoethyl-dextran can induce disruption in the cell, through formation of holes, membrane thinning and membrane erosion in lipid bilayers (Leroueil *et al.,* 2008). On the other hand, the use of neutrally charged particles as well as particles coated with polyethylene glycol (PEG) lead to a major reduction of particle uptake by the RES (Torchilin and Trubetskoy, 1995, Otsuka *et al.,* 2003).

Rats' blood circulation was prolonged when PEGylated liposomes modified with rat serum albumin (RAS) were compared to unmodified PEGylated liposomes. Quantitative measurements of total blood protein levels were made both with and without RAS coating in order to do additional analysis. Consequently, the total number of serum proteins that can cause opsonization in serum was greatly decreased by RAS-modified liposomes (Furumoto *et al.,* 2007). In addition, doxorubicin-loaded and albumin-modified liposomes revealed better pharmacokinetics and tissue distribution of doxorubicin (Yokoe *et al.,* 2008). The therapeutic index and tumor accumulation of albumin-modified PEGylated liposomal doxorubicin were considerably greater than those of non-modified PEGylated liposomal doxorubicin indicating that surface modification of nanoparticles with albumin, enhances their safety and effectiveness. Additionally, ligands that identify and attach to particular receptors can be used to alter the surface of nanoparticles. Additionally, to add selectivity, monoclonal antibodies can be attached onto the surface of nanoparticles. For example, HER2-specific antibody-modified nanoparticles deliver the medication, especially to cells that express HER2 (Kirpotin *et al.,* 2006). Using liposomes and micellar delivery methods, Torchilin's team has also developed various strategies for active targeted delivery to the tumor. To improve the therapeutic effectiveness of the payload in brain tumor xenografts, they have created doxorubicin-loaded liposomes modified with monoclonal antibody 2C5 (Gupta and Torchilin, 2007). These results show that surface properties are essential for nanoparticles to prevent their quick clearance. From the blood circulation before reaching the tumor site, and to provide active targeting through surface modifications with antibodies or ligands.

FEATURES OF RELEASE

The effectiveness of the treatment at the target sites is determined by the release characteristics of the nanoparticles. Due to the quick rise and fall of plasma drug levels following systemic

delivery, which results in borderline dosages with ensuing adverse effects, conventional medications used in clinical settings have a limited therapeutic window. Drug delivery systems, on the other hand, seek to reduce side effects and patient pain by delivering the intended concentration of the medication within the therapeutic range at the target site. Zero-order release kinetics, which can be accomplished via osmotic pressure, mechanical pumping, and electrokinetic transportation, can achieve constant plasma drug levels over an extended period of time (Sakamoto *et al.,* 2010). Additionally, because of their lengthy biodegradation time, which can range from days to months, biocompatible polymeric nanoparticles are also employed to extend the duration of drug release. In particular, a key factor in the rate of polymer biodegradation is molecular weight. For example, the sustained release of docetaxel following intravenous treatment was investigated using poly lactide-co-glycolide (PLGA) and poly lactic acid (PLA) (Musumeci *et al.,* 2006). It has been demonstrated that the drug's release rate is strongly correlated with the polymers' molecular weight. Additionally, the high molecular weight polymer. Multistage delivery system is an additional alternative approach providing sustained release of the payload where mesoporous silicon particles (MSP) offer unique opportunities for drug delivery (Tanaka *et al.,* 2010). MSPs size, charge, shape, porosity are among the characteristics that can be tailored for particular applications and objectives of its use. We have used MSPs loaded with nanoliposomes carrying small interfering RNA (siRNA) that leads to target mRNA degradation. In this study, degradation of silicon particles allowed for the long term release of siRNA to the target site (Shen *et al.,* 2013, Tanaka *et al.,* 2010). (Fig. 3)

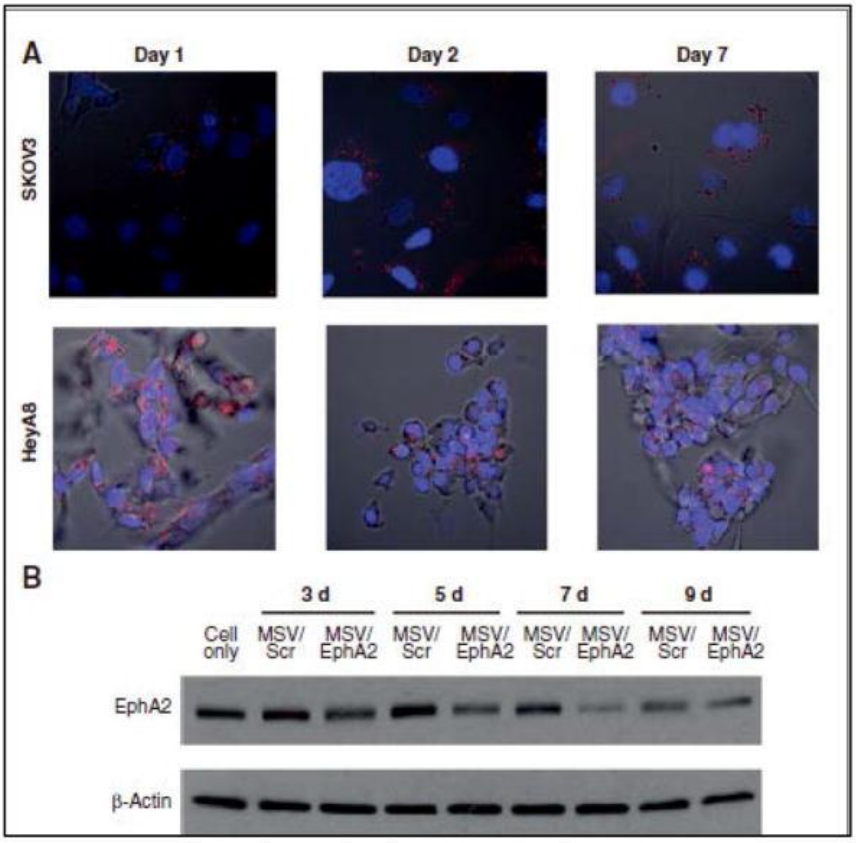


Figure 3: Sustained Release of Liposomal Epha2 Sirna in Tumor Cells

A. Alexa555-labeled siRNA oligos (red fluorescence) were packaged in DOPC nanoliposomes and loaded into Multistage Vector (MSV). Human ovarian tumor cells SKOV3ip2 and HeyA8 (nuclei in blue) were incubated with MSV/Alexa555 siRNA and release of Alexas555 siRNA from MSV was monitored by confocal microscopy over the next 7 days.

B. Western blot analysis of EphA2 expression in SKOV3 cells incubated with MSV/EphA2 siRNA indicating inhibition in protein expression more than 7 days (Shen *et al.,* 2013).

SHEN, H., RODRIGUEZ-AGUAYO, C., XU, R., GONZALEZ-VILLASANA, V., MAI, J., HUANG, Y., ZHANG, G., GUO, X., BAI, L. & QIN, G. 2013. Enhancing chemotherapy response with sustained EphA2 silencing using multistage vector delivery. *Clinical Cancer Research*.

Drug release was examined under various pH and temperature circumstances, including physiological conditions (pH 7.4), endosomal conditions (pH 6.6 and 6.0), and lysosomal conditions (pH 5.4). Reduced pH and elevated temperature were linked to doxorubicin release rate. Additionally, they have shown improved anticancer activity in tumor-bearing mice produced by HeLa cells administered subcutaneously. However, exogenous stimuli like ultrasound, a magnetic field, or a slight temperature increase might cause the release (MacEwan *et al.,* 2010). For example, ultrasound causes polymers to break down, slightly raises the temperature, and increases the permeability of cell membranes, all of which lead to the medicine being released at the intended location (Mitragotri, 2005). Schroeder and colleagues have proven the release of cisplatin following low frequency ultrasound. leagues (Schroeder *et al.,* 2009). In this study, cisplatin-loaded liposomes were intraperitoneally administered into tumor bearing mice and the release of cisplatin was triggered by ultrasound at tumor site. Despite the tremendous progress in the design and development of nanoparticles, further preclinical studies are still required to conduct clinical trials for cancer therapy.

CONCLUSION AND PROSPECTS FOR THE FUTURE

Nanomedicine developments present fresh chances to strengthen the anticancer arsenal. Currently in preclinical and clinical stages, targeted and nontargeted nanoparticles show how delivery strategies affect the field. Additional research in nanomedicine will enhance the therapeutic window of medications with significantly fewer side effects, improving patient outcomes.

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Chapter
16

ADVANCES IN SMART NANOMATERIALS

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ABSTRACT

Smart nanomaterials (SNMs) have emerged as superb, precise, and simple functional materials with usage that cut across academia (research), industrial (products), environmental, agricultural, and health sectors. They also have various technological applications and consumer products in both small- and large-scale systems. Their inevitability is evident in the number of adequate advantages or benefits associated with them due to the magnitude of functional sites, site arrangement comprehensivity, and the potential properties of the material's composition. In this era, tremendous advancement has been birthed in the nanotechnology field such that it has found enormous application in human treatment, aerospace, industries, and environmentally.

The need for functionalities of materials given their environmental changes while they possibly and automatically manifest in terms of their higher surface areas gives credence to understanding them better. Their excellent absorption, fluorescence nature, high electrical conductivity, exceptional magnetic and optical properties have all given imperativeness to their extensive characterization to give comprehensive insight into their properties. This chapter aims at the concise compilation of SNMs progress over the years including some of the various sensing devices that are commonly available. It also comprises the fundamentals of SNMs, the various synthetic procedures or routes for their fabrication, and the different characterization techniques, which reveal their embedded potential for practical applications.

KEYWORDS: Nanotechnology, Smart Nanomaterials, Characterization, Physical Mechanisms, Chemical Mechanisms, Biological Mechanisms.

INTRODUCTION

Smart nanomaterials represent a revolutionary breakthrough in science and engineering. These are advanced materials engineered at the nanoscale—typically between 1 and 100 nanometers—that possess the unique ability to dynamically alter their properties in response to specific external or environmental triggers. Because of this inherent ability to "sense" and "respond," they are often referred to as intelligent or stimuli-responsive materials.

KEY CHARACTERISTICS

- **Nanoscale Size:** Operates at 1 to 100 nm with a large surface-area-to-volume ratio.

- **Stimuli-Responsive:** Reacts dynamically to physical (temperature, light, electric/magnetic fields), chemical (pH, redox levels), or biological (enzymes, glucose) changes.
- **Multifunctional:** Capable of self-healing, targeted drug delivery, and adaptive sensing.

KEY TYPES OF SMART NANOMATERIALS

- **Carbon-Based:** Graphene, carbon dots and carbon nanotubes (CNTs), celebrated for their incredible mechanical strength and exceptional electrical and thermal conductivity.
- **Inorganic:** Quantum Dots and Metal-Organic Frameworks (MOFs), widely used in high-tech display screens, imaging, and gas storage.
- **Organic & Polymer-Based:** Nano-hydrogels and lipid nanoparticles, polymers, which excel at holding water and interacting safely within biological systems.

HOW DO THEY WORK? (STIMULI & RESPONSE)

Smart nanomaterials are highly sensitive to environmental changes. Their triggers generally fall into three main categories:

- **Physical Triggers:** Changes in temperature, light (such as UV or visible light), magnetic fields, or electric voltage cause the material to alter its structure or phase.
- **Chemical Triggers:** Variations in pH levels, moisture (humidity), or the presence of specific chemical species (like oxygen or carbon dioxide) spark a reaction.
- **Biological Triggers:** Exposure to specific enzymes, proteins, or glucose levels inside a living organism activates the material.

THE MECHANICS OF STIMULI-RESPONSE

Smart nanomaterials do not think—they react through predictable, pre-engineered physical and chemical transitions. When a trigger occurs, the material responds through specific scientific mechanisms.

PHYSICAL MECHANISMS

- **Photothermal/Photochemical (Light Trigger):** When metallic nanostructures (like gold nanoparticles) absorb specific light wavelengths, their electrons oscillate rapidly—a phenomenon known as Localized Surface Plasmon Resonance (LSPR). This converts light into intense localized heat. Polymer-based smart materials can also undergo *photo isomerization*, where light physically bends or reshapes the underlying molecules.
- **Phase Transitions (Temperature Trigger):** Thermo-responsive polymers possess specific thermal thresholds (known as LCST or UCST). When the temperature crosses this threshold, the polymer chains instantly flip from a hydrophilic (water-loving) state to a hydrophobic (water-repelling) state, causing the material to rapidly collapse or swell to release encapsulated payloads.
- **Proton Relaxation (Magnetic/Electric Trigger):** Under an external magnetic field, magnetic nanoparticles align their spins. In biomedical imaging, this triggers changes in proton relaxation times, creating sharp contrasts for MRI scans. In electronics, electrical voltage forces ionizable groups inside polymers to shift, converting electrical energy directly into physical movement (actuation).

Table 1: Examples of physical-responsive nanomaterials and their biomedical applications

Sr.	Stimuli	Nanomaterial	Application
1	Temperature	Poly(ethylene oxide)$_a$-poly(propylene oxide)$_b$-poly(ethylene oxide)$_a$ PEO-PPO-PEO	Oral drug delivery, wound healing
2	Temperature	Poly(N-isopropyl acrylamide-co-sulfobetaine methacrylate) nanogel PNS nanogels	Diagnosis/ chemotherapy
3	Temperature	Collegen or Citosen based	Drug delivery
4	Temperature	*Poly (N-isopropylacrylamide)- poly (N,N-dimethyl acrylamide)- poly(acrylic acid*) PNIPAM-PDMA-PAA	Drug delivery
5	Temperature	*Gold nanoparticles—Pluronic F127-Hydroxypropyl methylcellulose* AuNPs-PF127-HPMC	Drug delivery, photothermal platform, skin wound healing
6	Temperature	*Poly (oligo (ethylene glycol) methacrylate –co-poly (glycidal methacrylate) co polymers/poly (lactic acid-co-glycolic acid*) P(OEGMA-co-PGMA) copolymers/PLGA	Tissue engineering
7	Electrical	*Polyaniline/gold nanocomposite* PANI/AuNCs	Immunosensor detection of chronic kidney disease
8	Electrical	Polyaniline, poly(3,4-ethylenedioxythiophene) PANIP, PEDOT	Neural prostheses
9	Electrical	Poly(3,4-ethylenedioxythiophene)-coated poly(lactic acid-co-glycolic acid) nanofiber PEDOT-coated PLGA nanofiber	Drug delivery
10	Electrical	Fe_3O_4/Polyaniline Fe_3O_4/PANI	Antimicrobial, drug delivery
11	Magnetic	Trastuzumab (Tra, a humanized monoclonal antibody that specifically recognizes HER2)-12doxorubicin poly(vinyl alcohol)/ single-component thiol-functionalized poly (methacrylic acid) T-DOX PVA/PMASH magnetic nano capsules	Tumor therapy
12	Magnetic	3D collagen hydrogel	Directed neuronal regeneration
13	Magnetic	Fe_3O_4/methoxy poly-ethylene glycol)-poly-(lactide) composite nano capsuls Fe_3O_4/MePEG-PLA composite nano capsules	MRI
14	Light	poly(ethylene glycol) PEG	Switchable fluorescent probes
15	Light	Ruthenium-containing block copolymer Poly-Ru nanoparticles	*In vivo* photodynamic therapy and photochemotherapy

16	Electrochemical	Biosynthesized gold nanoparticles/ poly(catechol)/graphene sheets/glassy carbon electrode Bio AuNP/Pol/Gr/GCE	Biosensor, DNA mutation and acute lymphoblastic leukemia detection

CHEMICAL MECHANISMS

- **Ionization and Swelling (pH Trigger):** Materials designed for pH response contain acidic or basic functional groups. When the surrounding pH changes (e.g., the highly acidic environment inside a tumor or stomach), these groups gain or lose protons (H^+ ions). The resulting electrostatic repulsion forces the nanoparticle matrix to push apart and swell, allowing trapped drugs to escape.
- **Bond Cleavage (Redox Trigger):** Intracellular environments possess high concentrations of molecules like Glutathione (GSH). Smart nanocarriers are often built with *disulfide bonds* or acid-labile bridges that remain stable outside the cell but break apart instantly upon meeting GSH, dismantling the nanoparticle to deploy its treatment.

Table 2: Examples of chemical-responsive nanomaterials and their biomedical applications

Sr.	**Stimuli**	**Nanomaterial**	**Application**
1	**pH**	*polylactic acid-Resveratrol* PLA-RSV	Drug delivery
2	**pH**	*Ppoly (ethylene glycol)-Ag nanoparticle* PEG-Ag NPs	Antibacterial, wound healing
3	**pH**	Melanin-like nanoparticles	Photo acoustic imaging of tumors
4	**pH**	*Hybrid ultra-pH-sensitive (HyUPS) nanotransistor* HyUPS nanotransistors	Receptor-mediated endocytosis in tumor cells
5	**pH**	*Layered double hydroxides-zinc (II) phthalocyanine containing octa-sulfonate nanohybrid* LDH-$ZnPcS_8$ nanohybrid	Theranostics
6	**pH**	*Poly (carboxybetaine methacrylate)-nanodiamonds* PCBSA-@-NDs	Theranostics
7	**Redox**	*Poly (ethylene glycol) conjugated to paclitaxel* via *disulfide linkage* PEG_{2000}-S-S-PTX	Prodrug for breast cancer cells
8	**Redox**	*Prodrug/AgNPs hybrid nanoparticles*	Drug delivery
9	**Redox**	*P[(2-((2- (camptothecin)-oxy) ethyl) disulfanyl) ethylmethacrylate) -co- (2-(D-galactose) methylmethacryl-ate)] and silver nanoparticles* P(MACPTS-co-MAGP)@AgNPs nanoparticles	Drug release
10	**Redox**	*Poly (ethylene glycol)-Pluronic F68-nanoscale covalent organic frameworks* F68@SS-COFs	Cancer therapy
11	**Redox**	*Hyaluronic acid–chitosan–lipoic acid nanoparticles* (HACSLA-NPs)	Breast cancer therapy
12	**Redox**	*Folate redox-responsive chitosan nanoparticles* FTC-NPs	Anticancer drug delivery

BIOLOGICAL MECHANISMS

Enzymatic Cleavage: These nanomaterials are integrated with specific peptide sequences that act as locks. When they encounter specific biological enzymes (such as proteases or phospholipases secreted by bacteria at a wound site), the enzyme cleaves the peptide lock, triggering the material's functional breakdown.

Table 3: Examples of biological-responsive nanomaterials and their biomedical applications

Sr.	Stimuli	Nanomaterial	Application
1	**Glucose**	Chitosan/poly(gamma-glutamic acid) nanoparticles	Oral insulin delivery
2	**Glucose**	*Carboxymethyl chitosan-phenylboronic acid-Lvaline nanoparticles* (CMCS-PBA-LV) NPs	Oral administration of insulin
3	**Glucose**	*Chitosan-g-polyethylene glycol monomethyl ether nanocomplex* CS-g-(mPEG) NP	Oral insulin delivery
4	**Glucose**	*Hyaluronic Acid (HA)-coated calcium carbonate NPs*	Oral insulin delivery
5	**Glucose**	*Acetalated dextran nanoparticles* Ac-Dex Nps	Glycemic control
6	**Glucose**	*Boronic acid-derived polymers*	Drug delivery
7	**Glucose**	*Glycidyl methacrylated dextran/Concanavalin A* Dex-GMA/Con A ConA micro/nanospheres	Insulin treatment
8	**Enzyme**	*Adenosine triphosphate coated with silver nanoparticles* ATP-Ag nanoparticles	Participate in signal transduction and protein activity
9	**Enzyme**	*Activatable low-molecular weight protamine—poly(ethylene glycol) poly(ε-caprolactone) nanoparticles—loaded with paclitaxel* ALMWP-NP-PTX	Glioblastoma therapy
10	**Enzyme**	*Layer-by-layer assembly of poly(2-oxazoline)-based materials*	Therapeutic delivery
11	**Enzyme**	*Nanoplatform formed from Ti substrates modified with layer-by layer mesoporous silica nanoparticles-silver nanoparticles* LBL@MSN-Ag nanoparticles	Tissue growth *in vivo* and, simultaneously, treat implant-associated bacterial infection

MAJOR APPLICATIONS

HEALTHCARE & MEDICINE

This technology is transforming modern medicine by making treatments highly precise.

Targeted Drug Delivery: In cancer therapies, these smart nanoparticles detect the specific acidic pH or higher temperature of tumor cells. They release medicine exactly

Table 4: Examples of dual and multi-responsive nanomaterials and their biomedical applications

Sr.	Stimuli	Nanomaterial	Application
1	**UV light/redox/ pH**	*Six-arm star-shaped amphiphilic copolymer with poly (caprolactone) -bpoly (acrylic acid) -b-poly (poly (ethylene glycol) methyl ether methacrylate)*	Anticancer drug delivery
2	**Redox/pH/ temperature**	*Nanogels based on alginate and cystamine*	Anticancer drug delivery
3	**pH/redox /temperature**	*N,N0 -bis(acryloyl)cystamine, Poly(N-isopropylacrylamide), 2-hydroxyethylmethacrylate, Methacrylic acid, a disulfide bond contained cross-linker, and 4doxorubicin* SS-NPs@DOX	Drug delivery
4	**pH/light/enzyme**	*Copper sulfide nanoparticles* CuS NPs	Theranostics
5	**pH/redox**	*Thiol-modified polylysine- indocyanine green/ poly(ethylene glycol) nanoparticles* PLL-ICG/DPEG Nps	Photothermal and photodynamic therapy
6	**pH/redox**	*Poly (ethylene glycol) –polylacticacid-thioketal groups-Paclitaxel-(Maleimide thioether) Chlorin e6* mPEG-PLA-TKI-PTX nanoparticles and Ce6-(SS-mal-)-Ce6 (PNPCe6)	Chemotherapy, drug release
7	**pH/redox**	*Histidine -4 polyamidoamine dendrimer -Disulfide bonds-(poly (ethylene glycol)- Transferrin* (His-PAMAM-ss-PEG-Tf, HP-ss-PEG-Tf) nanocarrier	Anticancer drug delivery
8	**pH/redox**	*Lipoic acid ethylenediamine- Polyethylene glycol diglycidyl ether- L-lysine* poly(LAE-co-PGDE-co-Lys) core-crosslinked nano aggregate	Anticancer drug delivery
9	**pH/redox**	*Paclitaxel- poly(6-O-methacryloyl-d-galactopyranose)-gemcitabine/ N-acetyl-d-glucosamine(NAG)-poly(styrene-alt-maleic anhydride)-b-polystyrene* PTXL-ss-PMAGP-GEM/NAG NLCs	Anticancer drug delivery
10	**pH/magnetic field**	*Magnetic nanoparticles* MFNPs	Targeting, drug delivery, MRI
11	**pH/temperature**	Poly(NIPAM)nanogel @ Fe_3O_4 NPs/poly(acrylic acid) -graft—κ—carrageenan	Drug delivery
12	**Temperature/pH**	*Poly(N-isopropylacrylamide)* pNIPAM	Drug release
13	**Ultrasound/pH**	*Poly(ethylene oxide, 2-(diethylamino)ethyl methacrylate, (2-tetrahydrofuranyloxy)ethyl methacrylate* PEO_{43}-*b*-P(DEA_{33}-*stat*-TMA_{47})	Drug release

14	**Temperature/ magnetic field**	*Poly(N-isopropylacrylamide)- Magnetic nanoparticles* b-PNIPAM-mNPs	The isolation of diagnostic targets that can be used in point-of-care devices
15	**Light/pH**	rGO-PDA nanosheets	Drug delivery, phototherapy

At the cancer site, leaving healthy cells untouched and drastically reducing chemotherapy side effects.

- **Medicine:** Targeted cancer therapy and responsive drug carriers that release medication only inside tumor environments.
- **Smart Bandages:** Advanced wound dressings that can sense the onset of an infection (via pH or temperature shifts) and automatically release antibiotics into the wound.

ELECTRONICS & ENERGY

- **Next-Gen Displays:** Quantum dots are powering brighter, more energy-efficient and flexible screens for smartphones, televisions, and wearable tech.
- **Electronics:** Carbon-based circuits for faster, smaller, and more energy-efficient devices
- **Intelligent Sensors:** Ultra-sensitive nanoscale devices capable of instantly detecting trace amounts of toxic gases, pollutants, or pathogens.

ENVIRONMENT & AGRICULTURE

- **Environmental & Agriculture:** Responsive nano-adsorbents and filters that capture heavy metals and micro-pollutants from wastewater, changing properties to release the trapped toxins safely during recycling and controlled-release soil or plant management.
- **Smart Fertilizers:** In agriculture, nano-capsules release nutrients into the soil gradually, triggered only when the soil reaches a certain dryness or nutrient deficiency.
- Nano-adsorbents for wastewater purification, pollutant detection.

CHALLENGES AND THE WAY FORWARD

While smart nanomaterials hold immense promise, they face critical hurdles before widespread adoption. Manufacturing them on a commercial scale remains highly expensive and complex. Additionally, extensive research is still required to fully understand their long-term nano-toxicity and safety impacts on human health and the environment.

CONCLUSION

Smart nanomaterials are the backbone of future manufacturing and technology. As research matures, these adaptive materials will continue to bridge the gap between biology and engineering, making everyday solutions safer, more efficient, and deeply sustainable. With the increasing progress and the continuous innovation of science and technology, we have reason to believe that stimuli-responsive nanomaterials will surely lead to effective strategies and bring a substantial benefit in the biomedical field.

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Chapter 17

NANOTECHNOLOGY IN CANCER THERAPY

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ABSTRACT

Nanotechnology is now part of routine cancer care. More than a dozen nanomedicines are approved, beginning with liposomal doxorubicin in 1995. By packaging drugs in carriers of roughly 1–200 nm, nanotechnology changes where a drug goes in the body, how long it circulates and how it acts. This chapter reviews the main carrier platforms, the principles of tumour targeting, and the therapies nanotechnology makes possible, from safer chemotherapy to radio sensitization and mRNA cancer vaccines. It then summarizes approved products, explains why translation has been slow (a median of only about 0.7% of an injected dose reaches a solid tumour), and outlines the directions most likely to shape the field.

KEYWORDS: Nanomedicine, Drug Delivery, Liposomes, EPR Effect, Active Targeting, Theranostics, Lipid Nanoparticles, Cancer Immunotherapy.

INTRODUCTION

Cancer caused an estimated 20 million new cases and 9.7 million deaths worldwide in 2022 [1]. Systemic chemotherapy remains central to treatment, but most of each dose never reaches the tumour. Cytotoxic drugs spread through the body, are cleared quickly and damage healthy dividing tissue, which leaves a narrow therapeutic window.

Nanotechnology addresses this by engineering carriers in the 1–200 nm range. At this scale, materials have a very high surface-to-volume ratio, can carry thousands of drug molecules, and can be coated with polymers, targeting ligands or imaging agents. In oncology, these features serve five aims [2]:

- Solubilize and protect drugs such as paclitaxel, siRNA and mRNA.
- Prolong circulation and shift drug distribution towards tumours.
- Target cancer cells or trigger release inside the tumour.
- Enable new treatments, such as light- or radiation-activated killing.
- Combine diagnosis and therapy (theranostics).

The field gained a mechanistic basis in 1986, when Matsumura and Maeda described the enhanced permeability and retention (EPR) effect: large molecules accumulate in tumours because tumour vessels are leaky and lymphatic drainage is poor [3]. PEGylated liposomal doxorubicin (Doxil) became the first approved cancer nanomedicine in 1995 [4].

NANOCARRIER PLATFORMS

Organic carriers dominate the clinic because they are biodegradable and well characterized. Inorganic carriers add physical functions such as heating, magnetism and radiation enhancement.

Table 1: Main nanocarrier platforms

Platform	Size (nm)	Key Feature	Clinical Example
Liposomes	80–150	Lipid bilayer; PEG coating prolongs circulation	Doxil, Onivyde, Vyxeos
Lipid nanoparticles	60–120	Ionisable lipid core for siRNA and mRNA	Intismeran autogene (investigational)
Albumin nanoparticles	~130	Solvent-free drug bound to albumin	Abraxane, Fyarro
Polymeric nanoparticles and micelles	20–200	Biodegradable polymers; controlled release	Genexol-PM, Apealea
Polymer–drug conjugates	5–20	Drug covalently linked to polymer	Oncaspar
Gold nanoparticles	10–150	Near-infrared absorption for heating	AuroShell (pilot studies)
Iron oxide nanoparticles	10–100	MRI contrast; magnetic hyperthermia	NanoTherm
Hafnium oxide nanoparticles	~50	Amplifies local radiation dose	NBTXR3 (investigational)

- **Lipid carriers:** Liposomes hold water-soluble drugs in their aqueous core. A PEG coating reduces uptake by the liver and spleen and extends Doxil's half-life to about 2–3 days. Its main benefit is far less cardiotoxicity than free doxorubicin [4]. Vyxeos holds daunorubicin and cytarabine at a fixed 1:5 ratio; in older patients with secondary acute myeloid leukaemia, it raised median survival from 5.95 to 9.56 months [6]. Lipid nanoparticles (LNPs) contain an ionisable lipid that becomes charged in acidic endosomes, helping nucleic acids escape into the cytoplasm [10].
- **Protein carriers:** Nab-paclitaxel (Abraxane) formulates paclitaxel with albumin, removing the castor-oil solvent that causes hypersensitivity. In metastatic breast cancer it nearly doubled response rates compared with solvent-based paclitaxel (33% vs 19%) [5].
- **Polymeric carriers**: PLGA nanoparticles release drug as the polymer degrades and are easy to decorate with ligands. Micelles self-assemble from block copolymers and solubilize hydrophobic drugs. Dendrimers are highly branched polymers with many surface groups, but they remain mostly preclinical.

- **Inorganic and carbon carriers:** Gold nano shells convert near-infrared light to heat. Iron oxide particles are biodegradable and serve both imaging and hyperthermia. High-atomic-number particles such as hafnium oxide boost radiotherapy. Mesoporous silica offers high drug loading, while carbon nanotubes and graphene remain preclinical because of concerns about persistence and toxicity.

TUMOUR TARGETING AND DELIVERY BARRIERS

An injected nanoparticle must survive in blood, leave the vessel at the tumour, penetrate dense tissue, enter the target cell and release its cargo [9]. Losses compound at each step, so delivery efficiency is the field's central problem.

- **Passive targeting:** Tumour vessels are leaky and drain poorly, so particles of about 20–150 nm can leak in and stay (the EPR effect) [3]. Long circulation helps, which is why particles are sized above the kidney cut-off (about 5.5 nm) and coated with PEG. However, EPR is strong in fast-growing mouse tumours and highly variable in patients. A meta-analysis of 117 preclinical studies found a median of only 0.7% of the dose reached the tumour [7]. In 2020, Sindhwani and colleagues showed that up to 97% of nanoparticles entered tumours by active transport through endothelial cells, not through gaps [8].
- **Active targeting:** Ligands such as folic acid, transferrin, antibodies (for example against HER2), RGD peptides and PSMA-binding molecules can be attached to the particle surface. Ligands rarely raise total tumour accumulation; they mainly improve retention and cell uptake once particles arrive [9]. No actively targeted nanomedicine has yet been approved for cancer. BIND-014, a PSMA-targeted docetaxel particle, was discontinued after phase II [16].
- **Stimuli-responsive release:** Carriers can be designed to release drug in response to tumour acidity (pH 6.5–6.9, and lower in endosomes), high intracellular glutathione, tumour enzymes, or external heat, light, ultrasound and magnetic fields.
- **After extravasation:** Dense matrix and high interstitial fluid pressure keep large particles near vessels. Inside cells, most particles end up in lysosomes; typically, only a few percent of LNP-delivered RNA escapes to the cytoplasm [10].

THERAPEUTIC MODALITIES

Nanotechnology improves the delivery of existing drugs and also enables treatments that would not otherwise exist.

- **Nano formulated chemotherapy:** Most approved products reformulate known cytotoxics, and their gains are mainly in safety and dose intensity [2]. Liposomal irinotecan (Onivyde) with 5-fluorouracil extended median survival in previously treated metastatic pancreatic cancer from 4.2 to 6.1 months [17]. Carriers also allow co-delivery at a fixed synergistic ratio (Vyxeos) and pairing of a drug with a resistance inhibitor.
- **Nucleic acid therapies:** siRNA, mRNA and gene-editing tools are degraded in blood and cannot cross membranes alone. Nanocarriers protect them and carry them into cells

[10]. Delivery beyond the liver, where LNPs naturally accumulate, remains the key hurdle.

- **Photothermal and photodynamic therapy:** Gold nanoshells and similar particles turn near-infrared light into heat that kills tumour cells. In a pilot study, MRI-guided nanoshell ablation of prostate tumours was safe, and most men had no detectable cancer in the treated zone at 12 months [12]. Photodynamic therapy uses light-activated agents that generate reactive oxygen. Both are limited by light penetration of about 1 cm.
- **Radiosensitisation:** High-atomic-number particles absorb more X-rays than tissue and raise the local dose. NBTXR3, hafnium oxide nanoparticles injected once into the tumour, doubled the pathological complete response rate in soft-tissue sarcoma (16% vs 8%) [11]. Now licensed to Johnson & Johnson as JNJ-1900, it remains investigational and is in the phase III NANORAY-312 trial in head and neck cancer [18].
- **Magnetic hyperthermia:** Iron oxide particles heat up in an alternating magnetic field. With NanoTherm plus radiotherapy, patients with recurrent glioblastoma had a median survival of 13.4 months from first recurrence [13].
- **Immunotherapy:** Nanoparticles drain to lymph nodes and are taken up by immune cells, making them natural vaccine carriers. The leading example is intismeran autogene (mRNA-4157/V940), an LNP-delivered personalised mRNA therapy encoding up to 34 tumour neoantigens. After positive phase IIb results with pembrolizumab in resected melanoma [20], Merck and Moderna reported on 19 August 2026 that the phase III INTerpath-001 trial (1,137 patients) met its primary endpoint of recurrence-free survival [14]. Detailed figures await peer review. Other approaches include delivering immune adjuvants, reprogramming tumour macrophages, and generating CAR-T cells inside the body.

THERANOSTICS

Theranostic nanoparticles combine treatment and imaging, so clinicians can see where a carrier goes. Iron oxide particles provide MRI contrast. Radiolabelled particles allow whole-body tracking by PET, gold gives CT contrast, and optical probes guide surgery.

Imaging is especially valuable for selecting patients, because EPR varies widely between patients. In metastatic breast cancer, PET imaging of 64Cu-labelled HER2-targeted liposomes showed large differences in tumour uptake between patients, and higher uptake was associated with better response [19]. Imaging also guides externally activated treatments, ensuring that light, magnetic fields or radiation are applied where particles have gathered [12].

APPROVED NANOMEDICINES

About fifteen nanomedicines have been approved for cancer. Most are lipid, protein or polymer reformulations of known drugs.

Three patterns stand out. Every intravenous product is organic, while the inorganic ones are injected into the tumour and activated locally. Most products improve tolerability more than survival. And no actively targeted particle has yet been approved [16].

The pipeline is led by LNP-mRNA vaccines [14], radiation-activated particles [18], new formulations of existing drugs and nanoparticle immune agonists.

Table 2: Selected approved cancer nanomedicines (newest first)

Year	Product	Platform	Main indication
2021	Fyarro (sirolimus)	Albumin	Malignant PEComa
2019	Hensify (NBTXR3), EU	Hafnium oxide	Soft-tissue sarcoma
2017	Vyxeos (daunorubicin + cytarabine)	Liposome	Secondary AML
2015	Onivyde (irinotecan)	Liposome	Metastatic pancreatic cancer
2010	NanoTherm, EU	Iron oxide	Glioblastoma
2007	Genexol-PM (paclitaxel), Korea	Polymeric micelle	Breast, lung, ovarian cancer
2005	Abraxane (paclitaxel)	Albumin	Breast, lung, pancreatic cancer
1995	Doxil (doxorubicin)	PEGylated liposome	Ovarian cancer, myeloma, Kaposi sarcoma
1994	Oncaspar (pegaspargase)	Polymer conjugate	Acute lymphoblastic leukaemia

CHALLENGES IN CLINICAL TRANSLATION

The gap between strong results in mice and modest benefits in patients has several causes.

- **Low delivery and variable EPR:** Most of each dose ends up in the liver and spleen. Mouse tumours show uniform EPR, whereas human tumours vary widely [7].
- **Protein corona and immune reactions:** Plasma proteins coat particles within seconds, which can mask ligands and change where they go [15]. Some liposomes trigger complement-related infusion reactions, and repeated dosing can induce anti-PEG antibodies that speed clearance.
- **Toxicity and persistence:** Nanocarriers change a drug's side effects rather than removing them; Doxil, for example, causes hand–foot syndrome. Non-degradable inorganic particles can stay in the liver and spleen for months.
- **Manufacturing:** Small process changes alter size, loading and release, so reproducible large-scale production is difficult. Microfluidic mixing for COVID-19 vaccine lnps shows that scale-up is achievable when products are designed for it.
- **Regulation, cost and access**: Generic nanomedicines must prove equivalence in structure as well as content. High prices for products whose main benefit is tolerability limit uptake, especially in low- and middle-income countries.
- **Trial design:** Failures such as BIND-014 and CRLX101 reflect unselected patients and reliance on EPR that may not occur in humans [16]. The field is shifting to biomarker-driven trials and to approaches that do not depend on systemic delivery.

FUTURE DIRECTIONS AND CONCLUSION

The next decade is likely to be shaped less by new materials than by smarter use of proven ones:

- **Precision nanomedicine:** imaging and biomarkers to select the patients most likely to respond [19].
- **mRNA and nucleic acid therapies:** extending LNPs to more tumours, shared-antigen vaccines and tissues beyond the liver [14].
- **Nano-immunotherapy**: turning "cold" tumours responsive through adjuvant delivery, macrophage reprogramming and in vivo CAR-T generation.
- **Locally activated therapies:** radiosensitising, photothermal and magnetic particles combined with radiotherapy and checkpoint inhibitors.
- **Data-driven design:** machine learning and barcoded screening to predict how particles behave in the body.

Nanotechnology has changed cancer care more slowly than early optimism predicted. Its first products made toxic drugs safer. Its current generation fixes drug ratios, amplifies radiotherapy and delivers nucleic acids that could not otherwise reach cells. The central problem of delivery is now well understood. The field is answering it with patient selection, local activation and immune-focused strategies. The first positive phase III result for an LNP-delivered mRNA cancer therapy in 2026 marks the point at which nanomedicine's distinctive capabilities, and not only its ability to repackage old drugs, are being tested at scale.

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Chapter
18

NANOBIOTECHNOLOGY IN DIAGNOSTICS, THERAPEUTICS, AND BIOTECHNOLOGY

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ABSTRACT

Nanoparticles, generally defined as particles with at least one dimension between 1 and 100 nm, occupy the same size range as many biological macromolecules, including proteins, nucleic acids and viruses. Together with their high surface-area-to-volume ratio, size and shape-dependent optical, magnetic and electronic behaviour, and tunable surface chemistry, this overlap allows them to interact with cells, membranes and biomolecules in ways that bulk materials cannot, and has made them central to modern biotechnology and medicine. This chapter presents an overview of the physicochemical properties that govern the biological behaviour of nanoparticles and of the major lipid-based, polymeric, inorganic and biomimetic classes used in biomedicine. It then examines their principal applications: targeted and stimuli-responsive drug delivery; lipid nanoparticle carriers for siRNA, mRNA vaccines and genome-editing components; colorimetric, fluorescent and electrochemical diagnostics and biosensors; contrast agents for magnetic resonance, computed tomography, optical and photo acoustic imaging, photothermal, photodynamic, magnetic hyperthermia and radiosensitizing cancer therapies; antimicrobial agents against resistant pathogens and biofilms; scaffolds and delivery systems for tissue engineering; and uses in bioprocessing, agriculture, food safety and environmental remediation. Green synthesis using plants and microorganisms is discussed as a sustainable route to nanoparticle production. The chapter also considers the major obstacles to clinical translation, namely cytotoxicity and long-term accumulation, protein corona formation, immune recognition and rapid clearance, low delivery efficiency to solid tumours, scale-up and regulatory challenges, and environmental safety. It concludes with emerging directions, including biomimetic cell-membrane-coated particles, organ-selective nucleic acid delivery, personalized nanomedicine and artificial-intelligence-guided nanoparticle design.

KEYWORDS: Nanoparticles, Nanomedicine, Drug Delivery, Biosensors, Bioimaging, Antimicrobial Nanomaterials, Tissue Engineering, Green Synthesis.

INTRODUCTION

Nanobiotechnology brings together nanoscience and the biological sciences. Biological systems themselves operate at the nanoscale: a ribosome is roughly 20 to 25 nm across, an antibody about 10 nm, and the DNA double helix about 2 nm in diameter. Engineered nanoparticles can therefore interact with cells, membranes and biomolecules at a scale that bulk materials cannot reach (Barenholz Y. Doxil et al 2012). The field has moved from laboratory concept to clinical reality. Liposomal doxorubicin (Doxil), approved in the 1990s, was among the first nanomedicines, and lipid nanoparticle formulations of mRNA became widely known through the COVID-19 vaccines. Nanoparticles are now used to deliver drugs and nucleic acids, to detect disease markers at very low concentrations, to enhance imaging contrast, to kill tumour cells and resistant microbes, and to guide tissue regeneration (Mitchell et al 2021).

PROPERTIES THAT MAKE NANOPARTICLES USEFUL IN BIOLOGY

Size and surface area

As particle size falls, a larger fraction of atoms lies at the surface. This increases reactivity and provides a large area for loading drugs or attaching targeting molecules. Size also governs biological fate. Very small particles (below about 5 to 6 nm) are cleared rapidly by the kidneys, whereas particles of roughly 10 to 200 nm can circulate longer and accumulate in leaky tissues such as many solid tumours (Matsumurae *et al.*, 1986). Larger particles are more readily taken up by the mononuclear phagocyte system in the liver and spleen.

Shape

Spheres, rods, sheets, cubes and stars behave differently in circulation, cellular uptake and optical response. Gold nanorods, for example, absorb near-infrared light in a shape-dependent manner, which is exploited in photothermal therapy (Peer *et al.*, 2007).

Surface chemistry and charge

Surface charge influences colloidal stability, interaction with cell membranes and toxicity. Cationic particles bind cells and nucleic acids strongly but are often more cytotoxic. Coating particles with polyethylene glycol (PEGylation) reduces protein adsorption and prolongs circulation. Surfaces can also be functionalized with antibodies, aptamers, peptides, folate or carbohydrates for active targeting (Hou *et al.*, 2021).

Composition-dependent properties

Metallic nanoparticles show unique optical properties (surface plasmon resonance in gold and silver). Semiconductor quantum dots show size-tunable fluorescence. Iron oxide nanoparticles are superparamagnetic. Polymeric and lipid based particles are biodegradable and can encapsulate hydrophilic or hydrophobic cargo (Adams *et al.*, 2018).

MAJOR CLASSES OF BIOMEDICAL NANOPARTICLES

Lipid-based: liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers and lipid nanoparticles (LNPs). They are biocompatible and suited to both small molecules and nucleic acids.

Polymeric: poly (lactic-co-glycolic acid) (PLGA), polylactic acid, polycaprolactone, chitosan, alginate and albumin. They are biodegradable and allow tunable release.

Dendrimers and micelles: highly branched, monodisperse dendrimers such as PAMAM and self-assembled amphiphilic micelles, which solubilize poorly water-soluble drugs.

Inorganic: gold, silver, iron oxide, silica (including mesoporous silica), zinc oxide, titanium dioxide, carbon-based materials (carbon nanotubes, graphene, carbon dots) and quantum dots.

Biological and biomimetic: protein cages, virus-like particles, exosomes and cell membrane coated nanoparticles.

DRUG DELIVERY

Conventional drugs often suffer from poor solubility, rapid clearance, non-specific distribution and dose-limiting toxicity. Nanocarriers address these problems by protecting the drug, improving its pharmacokinetics and directing it to the site of action (Polack *et al.,* 2020).

PASSIVE TARGETING

Tumour blood vessels are often leaky and tumour lymphatic drainage is poor. Nanoparticles of suitable size therefore accumulate preferentially in tumours, a phenomenon described as the enhanced permeability and retention (EPR) effect. The magnitude of EPR varies considerably between tumour types and between patients, and this variability is a recognized limitation (Michalet *et al.,* 2005).

ACTIVE TARGETING

Ligands on the particle surface bind receptors overexpressed on target cells, for example folate receptor, transferrin receptor, HER2 or integrins. Antibodies, antibody fragments, aptamers and peptides such as RGD are commonly used. Active targeting typically improves cellular uptake once particles have reached the tissue, rather than increasing the amount that reaches it (Rai *et al.,* 2009).

STIMULI-RESPONSIVE AND CONTROLLED RELEASE

Smart carriers release their payload in response to internal stimuli (the acidic pH of tumours and endosomes, redox gradients, overexpressed enzymes) or external stimuli (light, heat, ultrasound, magnetic fields). This allows spatial and temporal control of release (Iravani *et al.,* 2011).

CLINICAL EXAMPLES

Liposomal doxorubicin (Doxil/Caelyx) reduces cardiotoxicity compared with free doxorubicin. Albumin-bound paclitaxel (Abraxane) avoids the solvents needed for conventional paclitaxel formulations (Monopoli *et al.,* 2012). Liposomal amphotericin B reduces nephrotoxicity in treating fungal infections. These products illustrate that the main clinical gains of nanocarriers have often been improved safety and formulation rather than dramatic increases in efficacy.

DELIVERY ACROSS BIOLOGICAL BARRIERS

The blood brain barrier, skin, mucosal surfaces and the gastrointestinal tract restrict drug entry. Nanoparticles coated with ligands such as transferrin or lactoferrin, or designed for transcytosis, are being explored for brain delivery. Mucoadhesive chitosan particles, microneedle assisted systems and inhaled nanoparticles are under investigation for mucosal, transdermal and pulmonary delivery (Wilhelm *et al.,* 2016).

GENE DELIVERY AND NANOPARTICLE-BASED VACCINES

Nucleic acids are large, negatively charged and easily degraded by nucleases, so they require protective carriers. Lipid nanoparticles composed of an ionizable lipid, phospholipid, cholesterol and a PEG-lipid encapsulate nucleic acids, are taken up by endocytosis, and release their cargo into the cytoplasm as the ionizable lipid becomes protonated in the acidic endosome (Price *et al.*, 2020).

siRNA: Patisiran (Onpattro), approved in 2018, was the first siRNA drug and uses an LNP carrier directed to the liver.

mRNA vaccines: The COVID-19 mRNA vaccines use LNPs to deliver nucleoside-modified mRNA encoding the SARS-CoV-2 spike protein.

Genome editing: LNPs and other nanocarriers are used to deliver CRISPR-Cas components, including Cas9 mRNA with guide RNA, as an alternative to viral vectors.

Non-viral vectors: Cationic polymers such as polyethylenimine, chitosan and dendrimers condense DNA into polyplexes for transfection.

Nanoparticles also serve as vaccine platforms in other ways. Virus-like particles display antigens in a repetitive, highly immunogenic array. Polymeric and inorganic nanoparticles can carry antigens and adjuvants together to the same antigen-presenting cell, strengthening and shaping the immune response.

DIAGNOSTICS AND BIOSENSING

Nanomaterials improve the sensitivity, speed and miniaturization of diagnostic assays.

Gold nanoparticles

Colloidal gold changes colour on aggregation because of shifts in its surface plasmon resonance, which forms the basis of colorimetric assays (Wang *et al.*, 2026). Gold nanoparticles are also the label in lateral flow immunoassays, including pregnancy tests and many rapid antigen tests.

Quantum dots

Quantum dots have broad absorption, narrow, size-tunable emission and high photostability. They permit multiplexed detection of several targets at once and long-term cell tracking. Concerns about heavy metal content (for example cadmium) have driven interest in carbon dots and other lower-toxicity alternatives (Chen, *et al.*, 2026).

Magnetic nanoparticles

Functionalized magnetic beads are used to capture and concentrate cells, proteins and nucleic acids from complex samples, simplifying purification and enhancing detection.

Nanobiosensors

Electrochemical and optical biosensors that use nanoparticles, nanowires, carbon nanotubes or graphene can detect cancer biomarkers, pathogens, toxins and metabolites such as glucose at very low concentrations (Thalluri *et al.*, 2026). Surface-enhanced Raman scattering (SERS) on gold or silver nanostructures can give molecular fingerprints with high sensitivity. Point of care devices based on these principles is a major goal for resource-limited settings.

BIOIMAGING AND CONTRAST AGENTS

Magnetic resonance imaging (MRI): Superparamagnetic iron oxide nanoparticles (SPIONs) shorten T2 relaxation and darken the tissues in which they accumulate. They have been used for

liver imaging and lymph node mapping, and ferumoxytol is used as an iron-based contrast agent in some settings.

Optical and fluorescence imaging: Quantum dots, dye-doped silica particles and upconversion nanoparticles allow deep-tissue and background-free imaging, since upconversion particles emit visible light under near-infrared excitation.

Computed tomography (CT): Gold nanoparticles have a high X-ray attenuation and long circulation time compared with small-molecule iodinated agents.

Photoacoustic imaging: Gold nanorods and other absorbing nanoparticles convert pulsed light into ultrasound signals, giving high-resolution images at depth.

Theranostics: A single nanoplatform can carry an imaging agent and a therapeutic agent, so that drug accumulation can be visualized and treatment monitored.

CANCER THERAPY

Beyond serving as drug carriers, some nanoparticles act directly as therapeutic agents.

Photothermal therapy (PTT): Gold nanorods, nanoshells and carbon-based nanomaterials absorb near-infrared light, a wavelength range that penetrates tissue well, and convert it to heat, causing localized thermal ablation of tumour cells.

Photodynamic therapy (PDT): Nanoparticles deliver photosensitizers that generate reactive oxygen species when illuminated. Nanocarriers improve the solubility and tumour accumulation of hydrophobic photosensitizers.

Magnetic hyperthermia: Iron oxide nanoparticles generate heat in an alternating magnetic field. An iron oxide formulation has been approved in Europe for treating glioblastoma.

Radiosensitization: High atomic number nanoparticles such as gold and hafnium oxide increase local radiation dose deposition within tumours. A hafnium oxide nanoparticle product has received regulatory approval in Europe for soft tissue sarcoma.

Immunotherapy: Nanoparticles can deliver tumour antigens, adjuvants, checkpoint inhibitors or cytokines and can reprogram the tumour microenvironment, for example by repolarizing macrophages.

Combination therapy: Co-loading two or more drugs, or combining chemotherapy with phototherapy, allows synergistic effects and may help overcome multidrug resistance.

ANTIMICROBIAL APPLICATIONS

Antibiotic resistance has renewed interest in nanomaterials as antimicrobial agents. Their activity commonly involves several mechanisms at once, which makes the development of resistance less likely than with single-target antibiotics (Sarkar, *et al.,* 2026).

- Disruption of cell wall and membrane integrity
- Release of metal ions (such as Ag+, Zn2+, Cu2+) that inactivate enzymes and proteins
- Generation of reactive oxygen species
- Interference with DNA replication and protein synthesis
- Inhibition of biofilm formation

Silver nanoparticles are the most widely studied and are used in wound dressings, burn care and coatings for catheters and medical devices. Zinc oxide, copper, copper oxide and titanium dioxide nanoparticles are also used the last under photocatalytic conditions. Nanocarriers can

improve delivery of conventional antibiotics into biofilms and intracellular bacteria, and nanoparticle-based antiviral and antifungal strategies are being explored (Bozkaya *et al.,* 2026). A limitation is that the same properties that damage microbes can harm host cells, so selectivity and dose must be examined carefully.

TISSUE ENGINEERING AND REGENERATIVE MEDICINE

Native tissue is organized at the nanoscale. The extracellular matrix, for example, is a network of collagen fibres tens to hundreds of nanometres thick. Nanomaterials can reproduce this architecture and influence cell adhesion, proliferation and differentiation (Jaritz, *et al.,* 2026).

Nanofibrous scaffolds: Electrospinning produces polymer nanofibre mats from materials such as polycaprolactone, PLGA, collagen and silk fibroin that mimic the ECM.

Bone regeneration: Nano-hydroxyapatite, bioactive glass nanoparticles and their composites resemble the mineral phase of bone and promote osteointegration.

Growth factor and gene delivery: Nanoparticles protect growth factors such as BMP-2 and VEGF and release them in a sustained way to guide healing.

Wound healing: Nanofibre dressings, silver-containing materials and nanoparticle-based delivery of antimicrobial and pro regenerative factors support wound closure.

Neural and cardiac applications: Conductive nanomaterials such as carbon nanotubes, graphene and gold nanowires are investigated to support electrical signalling in nerve and cardiac tissue constructs.

APPLICATIONS IN BIOTECHNOLOGY, AGRICULTURE AND THE ENVIRONMENT

Biotechnology and bioprocessing: Enzymes immobilized on magnetic or porous nanoparticles show better stability and can be recovered and reused. Magnetic nanoparticles simplify DNA, RNA and protein purification and nanoparticles are used for intracellular delivery in cell engineering and for long-term cell tracking (Abd Eltwab, et al.,2026).

Agriculture: Nano-fertilizers allow slow and targeted nutrient release, nano-pesticides and nano-formulated agrochemicals can reduce the quantity applied, and nanosensors can monitor soil conditions and plant pathogens. Nanoparticles and nanocarriers are also being investigated for delivering genetic material to plant cells. The long-term environmental behaviour of these materials requires careful assessment (Dhariwal, *et al.,* 2026).

Environmental biotechnology: Nanomaterials support water purification, adsorption and photocatalytic degradation of pollutants, detection of contaminants and enhancement of microbial bioremediation (El Alouani *et al.,* 2026).

Food science: Nanosensors and antimicrobial nanocomposite packaging aid in detecting spoilage and extending shelf life.

GREEN SYNTHESIS OF NANOPARTICLES

Conventional physical and chemical routes can require high energy, toxic reagents and stabilizers. Green or biological synthesis uses plant extracts, bacteria, fungi, yeast, algae or biomolecules as reducing and capping agents. Phytochemicals such as polyphenols, flavonoids, terpenoids, proteins and sugars reduce metal ions to nanoparticles and stabilize them in a single step (Dube, *et al.,* 2026).

Green synthesis is attractive because it is cost-effective, simple and generally uses mild conditions. Biomolecule coatings may also add biological activity (Kirubakaran *et al.,* 2026). Its limitations include batch-to-batch variability in extract composition, difficulty controlling size and shape, uncertain reaction mechanisms and challenges in scale-up. Rigorous characterization is therefore essential, using UV-visible spectroscopy, dynamic light scattering and zeta potential, electron microscopy (SEM, TEM), X-ray diffraction, FTIR and energy-dispersive X-ray spectroscopy (Prashanth, *et al.,* 2026).

CHALLENGES AND SAFETY CONSIDERATIONS

Toxicity and biodistribution: Nanoparticles may accumulate in the liver, spleen, lungs and kidneys. Possible effects include oxidative stress, inflammation, genotoxicity and organ damage. Toxicity depends on composition, size, shape, surface charge, dose and route of exposure, and long-term data are limited for many materials.

Protein corona: On entering biological fluids, nanoparticles adsorb proteins that form a corona. This changes the particle's effective identity, can mask targeting ligands, and alters uptake, clearance and immune recognition.

Immune responses and clearance: Opsonization and uptake by macrophages remove many particles from circulation. PEGylated particles can provoke anti-PEG antibodies, which may cause accelerated blood clearance or hypersensitivity reactions in some patients.

Delivery efficiency: Analyses of preclinical studies suggest that only a small percentage of the injected dose typically reaches solid tumours, which indicates that tumour delivery is harder than early EPR-based expectations implied.

Translation, manufacturing and regulation: Reproducible large-scale manufacturing, quality control, stability, standardized characterization and clear regulatory frameworks remain obstacles. Animal models often fail to predict human outcomes.

Environmental and ethical aspects: The release, persistence and ecological effects of engineered nanomaterials, along with equitable access to nanomedicine, require attention.

FUTURE PERSPECTIVES

Several directions are shaping the next generation of biological nanotechnology:

Biomimetic nanoparticles coated with red blood cell, platelet, leukocyte or cancer cell membranes to prolong circulation and improve targeting.

Stimuli-responsive and multifunctional systems that integrate sensing, imaging and therapy.

Personalized nanomedicine guided by patient-specific biomarkers and tumour characteristics.

Organ-selective LNPs extending nucleic acid delivery beyond the liver to lung, spleen, immune cells and other tissues.

In vivo gene editing using nanocarrier-delivered CRISPR systems.

Artificial intelligence and machine learning to design nanoparticles, predict biological behaviour and screen formulations more efficiently.

Sustainable nanotechnology that couples green synthesis with safe-by-design principles.

CONCLUSION

Nanoparticles have become versatile tools across the biological sciences. They improve drug solubility and targeting, enable nucleic acid therapeutics and vaccines, provide sensitive

diagnostics and imaging, offer new routes to treat cancer and resistant infections, and support tissue regeneration, agriculture and environmental protection. Realizing their full potential depends on resolving questions of safety, targeting efficiency, reproducible manufacturing and regulation. Interdisciplinary collaboration among biologists, chemists, materials scientists, clinicians and regulators will be essential to translate laboratory advances into safe and effective products.

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Chapter
19

NANOMATERIALS AS CATALYSTS IN CHEMICAL TRANSFORMATIONS: MECHANISMS, APPLICATIONS, AND SUSTAINABLE PERSPECTIVES

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ABSTRACT

Nanomaterials have become important in modern chemistry because their nanoscale dimensions provide opportunities to modify surface reactivity, electronic properties, and catalytic performance. Their high surface-area-to-volume ratios and adjustable surface structures make them attractive materials for promoting chemical transformations. Metal nanoparticles, metal oxides, carbon-based nanomaterials, and supported nanocatalysts have been investigated in organic synthesis, oxidation, reduction, hydrogenation, environmental remediation, and energy conversion. Their catalytic behaviour depends on several factors, including particle size, morphology, composition, surface defects, and interactions with supporting materials. Nanocatalysts may improve reaction efficiency and selectivity under suitable conditions and can sometimes facilitate catalyst recovery and reuse. Nevertheless, aggregation, catalyst deactivation, metal leaching, environmental risks, and difficulties associated with large-scale production remain significant challenges. This chapter examines the fundamental principles of nanocatalysis, the major classes of catalytic nanomaterials, their applications in chemical transformations, and their potential contribution to sustainable chemistry. Current challenges and future research directions are also discussed.

KEYWORDS: Nanomaterials, Nanocatalysis, Chemical Transformations, Metal Nanoparticles, Heterogeneous Catalysis, Green Chemistry, Sustainable Synthesis.

INTRODUCTION

Catalysis is fundamental to chemical science because catalysts accelerate reactions by providing alternative pathways with lower activation barriers. Catalytic processes are widely employed in pharmaceutical manufacturing, petrochemical industries, fine chemical synthesis, pollution control, and energy production. Conventional catalytic systems, however, may encounter limitations involving reaction selectivity, catalyst stability, separation, and energy consumption. Nanotechnology offers opportunities to develop catalytic materials with controllable structural and surface properties. Nanomaterials are commonly associated with dimensions in the approximate range of 1–100 nanometres, although the definition depends on their composition and structure.

At this scale, a substantial fraction of atoms may be located at the surface, where they can interact directly with reactant molecules. The resulting properties can influence adsorption, bond activation, reaction pathways, and product formation.

Nanocatalysts include metallic nanoparticles, metal oxide nanostructures, carbon-based materials, and hybrid systems containing catalytic particles supported on suitable substrates. Their performance is determined not simply by particle size but also by composition, morphology, surface chemistry, and the reaction environment.

The development of nanocatalysts therefore provides an important approach to designing catalytic systems for chemical synthesis, environmental applications, and sustainable industrial processes (Yentekakis *et al.*, 2023).

FUNDAMENTAL PRINCIPLES OF NANOCATALYSIS

Surface area and catalytic activity

One of the most important characteristics of nanomaterials is their high surface-area-to-volume ratio. Compared with larger particles of the same material, nanoparticles can expose a greater proportion of their atoms at the surface.

In heterogeneous catalysis, reactants interact with accessible surface sites before undergoing chemical transformation. Increasing the number of available sites can improve catalytic performance when the intrinsic activity of those sites and their accessibility remain favourable.

However, decreasing particle size does not always increase activity. Extremely small particles may exhibit different electronic properties, while aggregation can reduce accessible surface area. Consequently, the relationship between particle size and catalytic performance must be evaluated for each reaction.

Surface structure and active sites

Catalytic activity depends on the atomic arrangement of the material's surface. Edges, corners, crystal facets, vacancies, and other structural features may provide sites with different chemical properties.

These sites influence how strongly reactant molecules bind to the catalyst and how readily chemical bonds are activated. Adsorption that is too weak may prevent effective activation, whereas excessively strong adsorption can inhibit product formation by preventing intermediates or products from leaving the surface.

Effective nanocatalyst design therefore requires a balance between adsorption, reaction, and desorption.

Electronic and support effects

The electronic properties of nanomaterials can differ from those of their bulk counterparts. In metallic nanoparticles, particle dimensions and surface structure may influence the distribution of electronic states and the strength of interactions with adsorbed molecules.

Catalyst supports also play an important role. Materials such as silica, alumina, carbon, and selected metal oxides can improve particle dispersion and limit aggregation. Interactions

between the active particles and the support may additionally influence catalytic activity and stability.

Understanding these relationships helps researchers develop nanocatalysts with controlled properties and improved performance (Yentekakis *et al.,* 2023).

MAJOR CLASSES OF NANOCATALYSTS

Metal nanoparticles

Metal nanoparticles containing gold, silver, platinum, palladium, nickel, or copper are widely investigated for catalytic applications.

Their performance depends on particle size, morphology, oxidation state, and surface composition. Palladium-based nanoparticles, for example, are studied for carbon–carbon coupling reactions, while platinum and nickel catalysts are investigated for hydrogenation and other reduction processes.

Precious metals can provide high activity in selected reactions, whereas more abundant metals may offer cost advantages. The appropriate material must be selected according to the reaction mechanism, desired product, and operating conditions.

Metal oxide nanomaterials

Metal oxides such as titanium dioxide, cerium oxide, iron oxides, zinc oxide, and manganese oxides have important applications in oxidation, photocatalysis, and environmental catalysis.

Their activity can arise from surface acid–base properties, redox behaviour, oxygen vacancies, and interactions with reactants. Titanium dioxide is frequently investigated for photocatalytic reactions, while cerium oxide is studied in oxidation processes and catalysts involving oxygen storage.

Surface composition and defect concentration can influence performance, making material characterisation essential.

Carbon-based nanomaterials

Graphene, carbon nanotubes, and other nanostructured carbon materials can serve as catalyst supports or functional components of catalytic systems.

Their advantages may include chemical stability, adjustable surface chemistry, and the ability to disperse metal particles. Functional groups introduced onto their surfaces can improve interactions with catalytic components or reactant molecules.

However, the preparation, functionalisation, recovery, and environmental impact of carbon-based nanomaterials must also be considered.

Supported and hybrid nanocatalysts

Supported nanocatalysts combine active nanoparticles with a stabilising material. This approach can improve dispersion and reduce aggregation during operation.

Hybrid systems may contain metals, metal oxides, porous materials, polymers, or magnetic components. Magnetic nanocatalysts are particularly interesting when magnetic separation can simplify recovery from a reaction mixture.

Their practical performance depends on active-site accessibility, support stability, mass transfer, and the strength of interactions between the components.

APPLICATIONS IN CHEMICAL TRANSFORMATIONS

Hydrogenation and reduction

Hydrogenation involves the addition of hydrogen to suitable chemical compounds. It is widely used in organic synthesis, pharmaceutical manufacturing, and the preparation of industrial intermediates.

Metal nanoparticles can facilitate hydrogen activation and the subsequent transformation of adsorbed substrates. Depending on the catalyst, hydrogenation can be applied to carbon–carbon double bonds, carbon–carbon triple bonds, and selected other functional groups.

Catalyst composition and surface structure influence reaction rate and product selectivity. An important objective is to achieve the desired transformation while preserving other functional groups in the molecule.

Oxidation reactions

Oxidation reactions are essential for preparing aldehydes, ketones, carboxylic acids, and other oxygen-containing compounds.

Metal nanoparticles and metal oxide nanomaterials have been investigated for selective oxidation. Under appropriate conditions, these materials may promote the conversion of reactants while limiting unwanted side reactions.

The choice of oxidising agent is also important. Catalytic processes using suitable oxidants may reduce waste generation compared with certain conventional methods. Nevertheless, the overall environmental performance depends on reaction conditions, solvent selection, catalyst production, and the treatment of by-products.

Carbon–carbon coupling reactions

Carbon–carbon bond formation is central to organic chemistry because it enables the construction of complex molecular structures.

Palladium-containing catalytic systems are widely investigated for reactions such as Suzuki–Miyaura and Heck coupling. Nanostructured catalysts have attracted interest because their surface properties can influence activity and selectivity.

These transformations are relevant to the synthesis of pharmaceuticals, agrochemicals, and functional materials.

An important consideration is whether the reaction proceeds on the surface of the solid catalyst or involves metal species released into solution. Catalyst leaching must be assessed when evaluating reusability, product purity, and the true nature of the catalytic process.

Photocatalytic transformations

Photocatalysis uses light to initiate or facilitate chemical reactions. Semiconductor nanomaterials can absorb suitable photons and generate charge carriers that participate in surface oxidation and reduction reactions.

Titanium dioxide and zinc oxide are examples of materials investigated for photocatalytic applications. Research areas include pollutant transformation and selected light-driven chemical syntheses.

Photocatalytic efficiency depends on light absorption, charge separation, recombination, surface chemistry, and reaction conditions.

Although photocatalysis provides opportunities for using solar energy, its practical effectiveness depends on illumination requirements, catalyst stability, reaction selectivity, and the identification of final products.

Carbon dioxide conversion

Carbon dioxide conversion is an important research area because it offers possibilities for producing useful chemicals from a carbon-containing feedstock.

Nanostructured catalysts have been investigated for thermochemical, electrochemical, and photochemical conversion of carbon dioxide. Depending on the process, products may include carbon monoxide, formate, methanol, or other carbon-containing compounds.

Catalyst composition and surface structure influence reaction pathways and product selectivity. However, carbon dioxide conversion does not automatically result in a carbon-neutral process. Its environmental benefits depend on the energy source, the origin of other reactants, process efficiency, and the life cycle of the products (Yentekakis *et al.*, 2023).

NANOCATALYSTS AND GREEN CHEMISTRY

Green chemistry aims to minimise hazardous substances, reduce waste, and improve the efficiency of chemical processes.

Nanocatalysts may contribute to these goals by improving reaction selectivity, reducing the formation of unwanted products, and enabling some transformations under comparatively mild conditions. Heterogeneous catalysts may also be recovered and reused when their structure and activity remain sufficiently stable.

Another research direction involves plant-mediated nanoparticle synthesis. Plant extracts contain biomolecules that may participate in reducing metal precursors and stabilising the resulting particles.

Nevertheless, a synthesis method should not be considered environmentally superior solely because it uses biological materials. Solvent consumption, energy requirements, purification, waste generation, and the environmental fate of the resulting nanomaterial must also be evaluated.

A complete assessment should therefore consider the entire catalytic process rather than focusing only on the activity of the final material.

CHARACTERISATION OF NANOCATALYSTS

Characterisation is essential for connecting nanomaterial structure with catalytic behaviour.

Transmission electron microscopy provides information about particle size and morphology, while scanning electron microscopy can reveal surface structure. X-ray diffraction is used to identify crystalline phases and assess crystallinity.

X-ray photoelectron spectroscopy provides information about surface composition and chemical states. Energy-dispersive X-ray spectroscopy can help determine elemental composition, while Fourier-transform infrared spectroscopy can identify functional groups and investigate surface modifications.

Specific surface area can be estimated using gas adsorption methods. Where appropriate, researchers should also investigate pore structure, particle-size distribution, and changes in the material after catalytic use.

Catalytic evaluation should report relevant measurements, including conversion, yield, selectivity, reaction rate, and stability. Leaching and catalyst recovery should also be assessed when reusability is claimed.

Using complementary analytical methods provides a stronger understanding of catalytic performance than relying on a single measurement.

CHALLENGES AND LIMITATIONS

Despite their potential, nanocatalysts face several important limitations.

- **Aggregation and sintering:** Nanoparticles may combine or grow during preparation and use, reducing accessible surface area and changing catalytic behaviour.
- **Catalyst deactivation:** Surface poisoning, structural changes, and the accumulation of unwanted deposits can reduce activity over time.
- **Metal leaching:** Active components may dissolve or detach from supported catalysts, affecting stability and potentially contaminating products.
- **Reproducibility:** Small variations in synthesis conditions can produce materials with different particle sizes, morphologies, and surface properties.
- **Environmental and health concerns:** The risks associated with nanomaterials depend on their composition, exposure, persistence, and transformation. Their safety cannot be assumed from their small size or chemical usefulness.
- **Industrial scale-up:** Laboratory performance may not translate directly to industrial reactors because of differences in mass transfer, heat transfer, operating conditions, and material handling.

Addressing these challenges requires reproducible synthesis, appropriate characterisation, long-term testing, and realistic economic and environmental assessment.

FUTURE PERSPECTIVES

Future research will increasingly focus on designing nanocatalysts with controlled active sites, improved durability, and reduced dependence on expensive or scarce elements.

Single-atom catalysts, bimetallic nanoparticles, defect-engineered metal oxides, and multifunctional hybrid materials represent promising research directions. Their practical advantages must be established through reproducible experiments and comparison with suitable reference catalysts.

Advances in computational modelling and data-driven materials design may improve the identification of relationships between catalyst structure and reaction performance.

Sustainable manufacturing, safer synthesis methods, efficient catalyst recovery, and life-cycle assessment will also be important. Researchers should report standardised performance measures, including catalyst loading, conversion, selectivity, energy requirements, recyclability, and leaching.

Successful industrial application will depend not only on high catalytic activity but also on reliability, safety, cost-effectiveness, and environmental compatibility.

CONCLUSION

Nanomaterials have expanded the possibilities of catalytic design through their adjustable surface structures, distinctive electronic properties, and potential for controlling chemical transformations. Metal nanoparticles, metal oxides, carbon-based materials, and supported hybrid systems have been investigated in hydrogenation, oxidation, coupling reactions, photocatalysis, and carbon dioxide conversion.

Their potential contribution to sustainable chemistry depends on more than catalytic activity alone. Stability, selectivity, recovery, reproducibility, toxicity, and economic feasibility must also be considered.

Continued progress in nanomaterial synthesis, structural characterisation, mechanistic understanding, and process engineering may enable more efficient and sustainable chemical transformations.

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