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Review

Nanotechnology for Healthcare: Plant-Derived Nanoparticles in Disease Treatment and Regenerative Medicine

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Abstract: Nanotechnology has revolutionised biomedical research, offering innovative healthcare solutions. Plant-based nanotechnology is emerging as a sustainable alternative, minimising environmental impacts and enhancing therapeutic effectiveness. This paper explores the potential of plant-derived nanoparticles (PNPs) in medicine, highlighting their biocompatibility, multifunctionality, and eco-friendliness. PNPs, synthesised through green methods, have demonstrated promising applications in drug delivery, cancer therapy, antimicrobial treatments, and tissue regeneration. Their unique properties, such as a high surface area and bioactive components, enable improved drug delivery, targeting, and controlled release, reducing side effects and enhancing treatment efficacy. Additionally, plant-derived compounds' inherent antimicrobial and antioxidant properties, retained within platinum nanoparticles (PNPs), present innovative opportunities for combating antimicrobial resistance and promoting wound healing. Despite their potential, challenges remain in standardising PNP synthesis, ensuring consistency, and scaling up production for industrial applications. This review emphasises the need for further research on PNP toxicity, biocompatibility, and regulatory frameworks to fully harness their capabilities in clinical and commercial applications. Plant-based nanotechnology represents a promising, greener alternative for advancing healthcare solutions, aligning with global sustainability goals.

Keywords: plant-derived nanoparticles (PNPs); targeted drug delivery; antimicrobial properties; biocompatibility; sustainability; nanomedicine

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1. Introduction

Nanomaterials have significantly advanced biomedical research due to their remarkable loading capacity and enhanced protection of payloads, heralding a new era of innovation. Nanoparticles are promising in various fields, including biomedicine, bio-labelling, agriculture, and antimicrobial agents. The increasing interest in nanoparticle research stems from their diverse applications across several domains, such as diagnostics, biomarkers, cell identification, antimicrobial treatments, drug delivery, and cancer therapies [1–3]. Nanoparticles can be synthesised through various physical, chemical, and biological methods (Figure 1), with biological approaches gaining notable attention for their simplicity, cost-effectiveness, and ability to customise nanoparticles' shape, size, and functionalities [3].

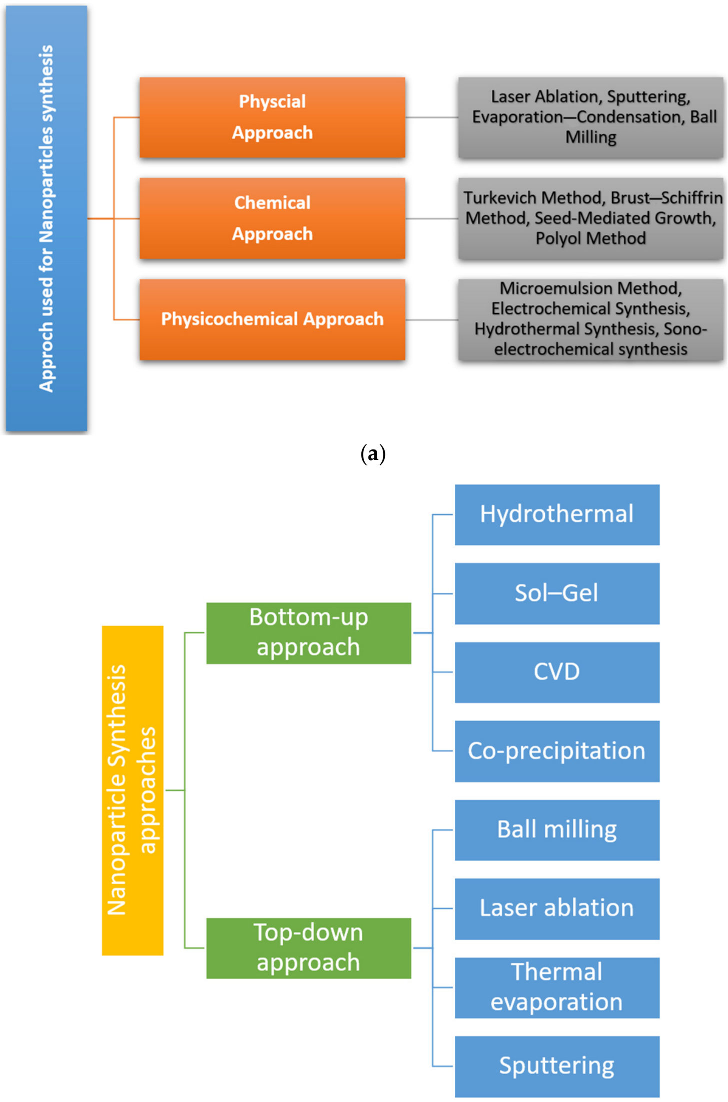

Figure 1. Methods commonly used for nanoparticle synthesis: (**a**) Physical, chemical, and physicochemical techniques employed in the production of nanomaterials; (**b**) nanoparticle fabrication through bottom-up and top-down approaches, which are widely recognised methods for creating nanoparticles.

The top-down approach involves physical processes like grinding, diffusion, thermal decomposition, and irradiation to reduce larger materials into smaller particles. Conversely, the bottom-up approach uses chemical and biological processes to synthesise nanoparticles. While the chemical agents in these processes can pose environmental risks, using ecologically hazardous substances may lead to toxic by-products [1,4]. Nanoparticles have become a focal point in biomedical research due to their unique properties that enable interaction with cells and tissues and their effectiveness in disease treatment [5,6]. Additionally, plant-derived nanoparticles have shown potential as novel therapeutic agents, emphasising the promise of green nanotechnology for synthesising metallic nanoparticles through plant-mediated processes. Several metal nanoparticles have demonstrated antimicrobial properties, offering innovative strategies to combat the rise in antimicrobial resistance [7,8]. Recent advancements in nanoparticle production have prioritised key factors such as size, shape, chemical composition, and structural content. The unique properties of nanomaterials, particularly their high surface area to volume ratio, differentiate them from bulk materials. This size-dependent characteristic influences the physicochemical properties of nanoparticles, often giving rise to unique quantum effects.

Integrating nanoparticles into the medical and healthcare sectors has led to significant advancements, particularly in diagnostics, therapeutics, and drug delivery systems (Figure 2). Nanoparticles have enabled the development of ultra-resolution imaging systems, facilitating early diagnosis and treatment monitoring [9]. Moreover, they serve as carriers in drug delivery systems, improving drug efficacy and minimising side effects. Nanoparticles also play a critical role in tissue engineering, wound management, and regenerative medicine [10,11]. Additionally, they contain active substances that contribute to creating effective agents for treating infectious diseases.

Figure 2. Different applications of nanoparticles (NPs) in the medical and healthcare industries. Nanoparticles are used in various ways, including in drug delivery systems for targeted and controlled release, improving the effectiveness of cancer treatments, enhancing diagnostic imaging techniques, and facilitating wound healing and tissue regeneration. They also play a role in antimicrobial therapies, helping combat infections and developing advanced medical devices. These diverse applications highlight the potential of NPs to revolutionise healthcare by improving patient outcomes and treatment precision.

The applications of nanoparticles in medicine are vast, ranging from enhanced imaging systems to more efficient drug delivery methods, all aimed at improving patient care and treatment outcomes [12]. Nanomaterials exhibit essential properties that make them multifunctional tools for exploring biological phenomena. Their size allows them to interact with and influence vital biological components in a remarkable way [13]. In recent decades, there has been a surge in research exploring the use of nanotechnology across various fields such as pharmaceuticals, cosmetics, environmental science, healthcare, and energy (Table 1).

In clinical medicine, the practical application of nanoparticles depends on adhering to specific size limitations. Larger nanoparticles are prone to rapid phagocytosis and are quickly removed from circulation, while smaller nanoparticles may present toxicity concerns and are quickly cleared from the body via the kidneys. Nanomedicine leverages the tools of nanotechnology to address medical challenges and effectively combat a range of diseases. It is essential to note that nanotechnology is an integrated approach encompassing various scientific disciplines, particularly biology, chemistry, physics, and materials science, all of which contribute significantly to developing these emerging technologies [14,15].

Table 1. A comprehensive overview of the various biomedical applications of plant-derived nanoparticles, emphasising their versatility and potential in different medical and healthcare fields, including drug delivery, cancer therapy, antimicrobial treatments, and wound healing, as highlighted in recent studies.

Biomedical Application	Description	Refs.
Cancer Treatment	Plant-derived NPs show promise in targeted drug delivery to cancer cells, reducing side effects and improving treatment efficacy.	[10,16]
Wound Healing	NPs derived from plant extracts possess antimicrobial and anti-inflammatory properties, accelerating wound healing and tissue regeneration.	[17–19]
Bone Regeneration	Plant-based NPs can stimulate osteogenesis and angiogenesis, promoting bone growth and regeneration in fractures or defects.	[20]
Antimicrobial Agents	NPs synthesised from plant compounds exhibit potent antimicrobial activity against various pathogens, including bacteria and fungi.	[11,21]
Drug Delivery Systems	Plant-derived NPs carry drug molecules, enabling controlled release, targeted delivery, and enhanced therapeutic outcomes.	[22,23]
Diagnostics	NPs functionalised with plant-derived ligands or biomolecules can be used for targeted imaging, early disease detection, and diagnostic assays.	[22,23]
Anti-Inflammatory Agents	Plant-based NPs possess anti-inflammatory properties, mitigating inflammation associated with various diseases, injuries, or chronic conditions.	[24,25]
Antioxidants	NPs derived from antioxidant-rich plants scavenge free radicals, protecting cells from oxidative damage and reducing the risk of oxidative stress-related diseases.	[26,27]
Immunomodulators	NPs derived from plant extracts modulate the immune response, enhancing immune function or suppressing excessive inflammation or immune activation.	[28]
Cardiovascular Health	Plant-based NPs may improve cardiovascular health by regulating blood pressure, lipid levels, and endothelial function, potentially reducing the risk of cardiovascular diseases.	[27,28]
Anti-Diabetic Agents	Plant-derived NPs show potential in managing diabetes by enhancing insulin sensitivity, reducing blood glucose levels, and protecting pancreatic β-cells.	[26,29]
Anti-Cancer Agents	NPs derived from plants exhibit anti-cancer properties, inducing apoptosis, inhibiting proliferation, and suppressing tumour growth and metastasis.	[30]
Tissue Engineering	Plant-based NPs incorporated into scaffolds or biomaterials facilitate tissue regeneration and engineering, promoting the growth of functional tissues or organs.	[20,31]
Antiviral Agents	NPs derived from plant extracts possess antiviral activity against various viruses, inhibiting viral replication and reducing viral infectivity.	[7,9,11]
Gene Delivery Systems	Plant-derived NPs can be functionalised for gene delivery, enabling targeted and efficient delivery of therapeutic genes for gene therapy applications.	[32]

Integrating nanotechnology into medicine has fostered the emergence of new fields of study and provided fresh perspectives on understanding biological systems. These advances enable specific parameters, such as improved solubility, controlled drug retention in the bloodstream, targeted drug delivery, and controlled release under various conditions [33–37]. The ability to manipulate substances at the nanometre scale also allows for the modification of their physiochemical properties and biological activity. Drug delivery systems utilising nanoparticles can enhance medications' effectiveness, increase absorption, and target specific tissues, ensuring precision and prolonged drug action at predetermined sites [22]. This review explores targeted drug delivery techniques, medicinal preparation, and diagnostic methods that harness the power of nanotechnology.

2. Different Types of Nanoparticles

Various processes are employed in the production of nanoparticles, each yielding a unique type of nanoparticle. Nanoparticles derived from botanical materials are widely recognised as the most suitable medium for nanoparticle synthesis.

When comparing different methods for synthesising nanoparticles, it becomes evident that using botanical sources offers distinct advantages. This approach is known for its simplicity, increased efficiency, and cost-effectiveness compared to chemical or physical nanoparticle production methods. Additionally, it consumes less energy and occurs in a more favourable working environment [26,38,39]. Different parts of plants, including roots, stems, latex, leaves, and bark, can be utilised to produce nanoparticles (Figure 3). Figure 3 illustrates the eco-friendly synthesis of nanoparticles from plant or microbial sources, emphasising the sustainability of this production method [40,41]. By harnessing the inherent properties of plants or microbes, this method offers a greener alternative to conventional synthesis approaches, thereby reducing environmental impacts. Understanding the process of plant-mediated nanoparticle generation is still a subject of ongoing research. Scientists have discovered that various biomolecules, including phenols and flavonoids, play a crucial role in reducing metal ions and aiding in the formation of nanoparticles [14,42]. Nanomaterial fabrication, specifically that of silver nanoparticles, has attracted significant interest due to their diverse capabilities and the bioactive reducing metabolites produced by the organisms involved.

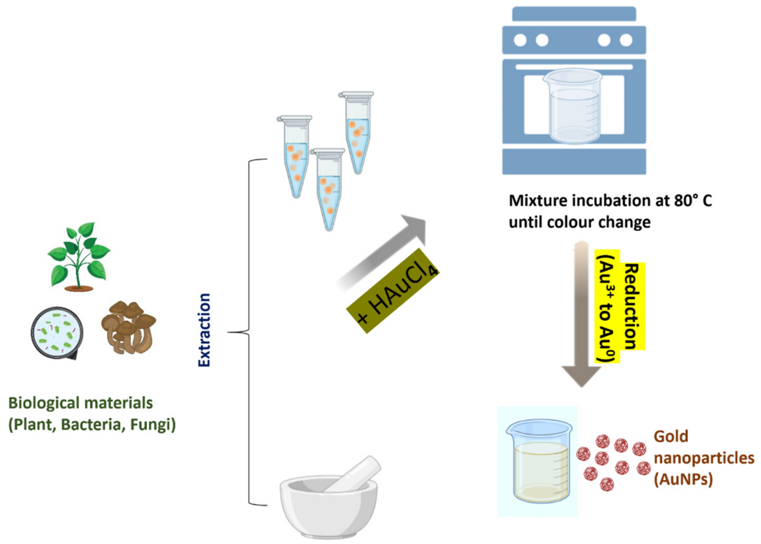

Figure 3. Eco-friendly synthesis of nanoparticles using plant and microbial resources, emphasising sustainable methods. This process utilises natural materials such as plant extracts and microorganisms to create nanoparticles, offering an environmentally friendly alternative to traditional chemical synthesis. These biological resources reduce the environmental impact and enhance the biocompatibility and functionality of the nanoparticles, making them ideal for applications in medicine and other industries.

2.1. Metallic Nanoparticles

Standard metallic nanoparticles, such as gold, silver, and iron oxide, exhibit unique properties that make them valuable across various applications [35]. Gold nanoparticles, for instance, are utilised in biomedical imaging, drug delivery, and cancer therapy due to their biocompatibility and surface plasmon resonance [43]. Silver nanoparticles have potent antimicrobial properties, making them effective in wound dressings, textiles, and water purification systems. Iron oxide nanoparticles are utilised in magnetic resonance imaging (MRI), targeted drug delivery, and hyperthermia cancer treatment, owing to their magnetic properties and biocompatibility. Zinc oxide nanoparticles (ZnO NPs) are widely used in industries like rubber, paint, coatings, and cosmetics. Known for their biocompatibility, affordability, and low toxicity, they have gained popularity in biomedicine, particularly in anticancer and antibacterial applications by generating reactive oxygen species (ROS), releasing zinc ions, and inducing apoptosis. Additionally, zinc plays a crucial role in maintaining insulin's structural integrity [44]. Each type of metallic nanoparticle offers specific advantages, contributing to advancements in diverse fields, from healthcare to environmental remediation (Table 2).

Table 2. A summary of common metallic nanoparticles, highlighting their unique properties and specific applications in various fields, as referenced in studies.

Metal	Nanoparticle Type	Applications	Key Properties	Refs.
Gold (Au)	Nanospheres, nanorods, nanostars	Drug delivery, biosensors, photothermal therapy	High biocompatibility, surface plasmon resonance (SPR)	[15,43]
Silver (Ag)	Nanoparticles, nanowires	Antimicrobials, wound healing, electronics	Broad-spectrum antimicrobial activity, electrical conductivity	[1,5,8]
Iron (Fe)	Oxide nanoparticles (Fe_3O_4)	Magnetic resonance imaging (MRI) contrast agents, drug delivery	Superparamagnetism, biodegradability	[37]
Palladium (Pd)	Nanoparticles, nanocatalysts	Catalysis (hydrogenation reactions), sensors	High catalytic activity, hydrogen absorption	[45]
Platinum (Pt)	Nanoparticles, nanocatalysts	Fuel cells, sensors, drug delivery	Excellent catalytic activity, high stability	[46]
Copper (Cu)	Nanoparticles, oxide nanoparticles (CuO)	Antimicrobials, antifungal agents, electronics	Antimicrobial activity, electrical conductivity, thermal conductivity	[24]
Zinc (Zn)	Oxide nanoparticles (ZnO)	Sunscreen, UV protection, electronics	UV absorption, semiconductivity	[7,47]
Titanium (Ti)	Dioxide nanoparticles (TiO_2)	Photocatalysis (pollutant degradation), drug delivery	Photocatalytic activity, biocompatibility	[48]
Gadolinium (Gd)	Oxide nanoparticles (Gd_2O_3)	MRI contrast agents	High paramagnetic properties	[6]
Cobalt (Co)	Nanoparticles, oxide nanoparticles (Co_3O_4)	Magnetic recording media, batteries	Magnetism, electrochemical properties	[6]
Nickel (Ni)	Nanoparticles	Magnetic recording media, catalysis	Magnetism, catalytic activity	[49]
Molybdenum (Mo)	Disulfide nanoparticles (MoS_2)	Lubricants, catalysis	Excellent lubrication properties, catalytic activity for hydrogen evolution reaction (HER)	[39]
Tungsten (W)	Oxide nanoparticles (WO_3)	Electrochromic devices, sensors	Electrochromic properties, gas-sensing ability	[39]
Bismuth (Bi)	Nanoparticles	Sensors, photothermal therapy	High thermal conductivity, photothermal ablation	[50]
Magnesium (Mg)	Nanoparticles	Biodegradable implants, drug delivery	Biodegradability, good mechanical properties	[51]

2.1.1. Silver Nanoparticles

As previously reported, the plant-mediated synthesis of silver nanoparticles from $AgNO_3$ is a relatively simple, eco-friendly, and biological method [16]. This approach opens up opportunities for producing silver nanoparticles, which can be used as therapeutics to address a wide range of human diseases. However, using chemical methods to synthesise silver nanoparticles also has inherent drawbacks, such as the risk of harming the environment, the general health of individuals, and exceptionally normal cellular processes [16]. Silver ions can easily penetrate the cell walls and cytoplasmic membranes due to their electrostatic attraction to sulphide proteins. To explain this, it can be stated that such an interaction assists in disrupting bacterial envelopes by raising the osmatic permeability of the cytoplasmic membrane (Figure 4). The authors of [52] utilised walnut tree green husk tissue to synthesise silver nanoparticles. The walnut green husk was extracted and added to water to facilitate both the reduction and stabilisation of synthesised silver nanoparticles. Table 3 illustrates the various applications of silver nanoparticles (AgNPs), including their use as antibacterial coatings in medical devices and their application in catalysis for environmental cleanup [53]. Due to their size and high surface area, AgNPs are effective antimicrobial agents; however, safety and environmental issues remain a concern.

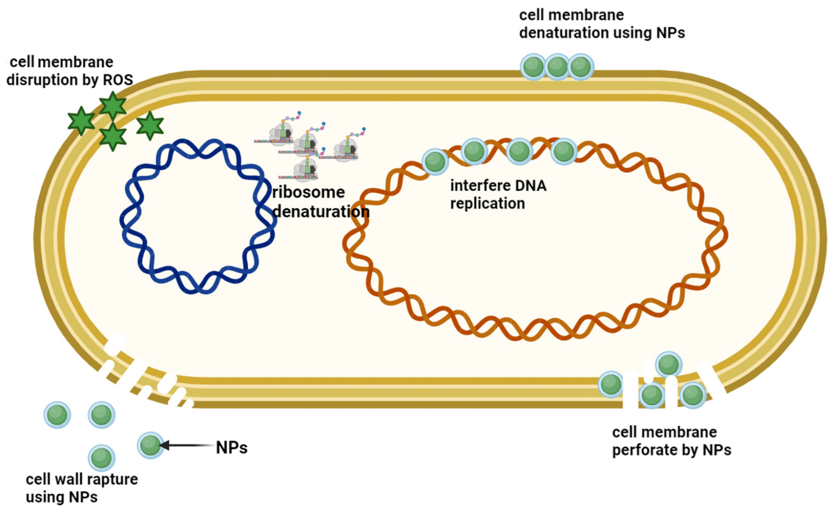

Figure 4. The antimicrobial effects of silver nanoparticles (AgNPs) involve several mechanisms: (1) Disruption of the cell wall and cytoplasmic membrane: silver ions (Ag^+) released from silver nanoparticles adhere to or penetrate the cell wall and cytoplasmic membrane. (2) Ribosome denaturation: silver ions disrupt ribosomes, hindering protein synthesis. (3) Membrane disruption by reactive oxygen species: reactive oxygen species, generated from the disrupted electron transport chain, can lead to membrane damage. (4) Interference with DNA replication: silver ions and reactive oxygen species bind to DNA, preventing its replication and cell division. (5) Membrane denaturation: silver nanoparticles accumulate in cell wall recesses, leading to membrane denaturation. (6) Membrane perforation: silver nanoparticles traverse the cytoplasmic membrane, potentially releasing cellular organelles.

Table 3. Potential applications, advantages, and disadvantages of silver nanoparticles.

Application Area	Specific Use	Description	Advantages	Disadvantages	Refs.
Antimicrobials	- Coatings for medical devices (catheters, implants)-Wound dressings-Textiles-Food storage containers-Air and water purification	Silver nanoparticles inactivate a broad spectrum of bacteria, viruses, and fungi through various mechanisms.	- Effective against multi-drug resistant pathogens-Long-lasting antimicrobial activity-Can be incorporated into various materials	- Potential for silver nanoparticle release into the environment-May contribute to antimicrobial resistance development-Cytotoxic effects at high concentrations	[8]

Table 3. *Cont.*

Application Area	Specific Use	Description	Advantages	Disadvantages	Refs.
Wound Healing	- Wound dressings-Burn dressings-Ointments	Silver nanoparticles promote wound healing by reducing inflammation, stimulating cell proliferation, and fighting infection.	- Accelerates wound closure-Reduces scarring-Minimises infection risk	- Potential for cytotoxicity at high concentrations-Costlier than traditional wound dressings	[18,54]
Diagnostics	- Biosensors for disease detection-Imaging contrast agents	Silver nanoparticles can be conjugated with biomolecules for specific target detection or used to enhance signal intensity in imaging techniques.	- High sensitivity and specificity-Improved detection limits-Real-time monitoring capabilities	- Complex development and manufacturing processes-Potential for non-specific binding	[8,23]
Drug Delivery	- Drug carriers-Targeted drug delivery-Controlled drug release	Silver nanoparticles can encapsulate drugs and deliver them to specific sites in the body, improving efficacy and reducing side effects.	- Enhanced drug delivery efficiency-Reduced systemic exposure-Controlled release profiles	- Potential for nanoparticle aggregation-Difficulty in achieving sustained release	[22,55]
Electronics	- Conductive inks for printed electronics-Antimicrobial coatings for electronic devices	Silver nanoparticles offer high conductivity and antimicrobial properties, making them valuable for various electronic applications.	- Improved conductivity-Enhanced device functionality-Reduced risk of device contamination	- Potential for nanoparticle migration-Higher cost compared to traditional materials	[1,56]
Textiles	- Antibacterial clothing-Sportswear-Socks	Silver nanoparticles embedded in textiles provide long-lasting odour control and inhibit bacterial growth.	- Freshness and odour control-Reduced risk of skin infections-Long-lasting antimicrobial effect	- Potential for nanoparticle release during washing-May irritate sensitive skin	[40]
Cosmetics	- Acne creams-Anti-aging creams	Silver nanoparticles are used in some cosmetics for their claimed antimicrobial and anti-inflammatory properties.	- Potential for reducing acne breakouts-May have soothing effects on irritated skin	- Limited scientific evidence for some claims-Potential for skin irritation-Regulatory concerns regarding safety	[57]

Furthermore, additional investigations [16,57,58] were conducted on synthetic nanoparticles to evaluate their efficacy in combating cancer, providing antioxidant benefits, and exhibiting antibacterial properties. The impact of silver nanoparticles on bacterial signal transmission is attributed to their ability to interfere with tyrosine phosphorylation and protein substrate phosphorylation processes, ultimately leading to cellular apoptosis and the inhibition of proliferation. A study by Radzig et al. [59] revealed that hydrolysed casein peptides could effectively stabilise silver nanoparticles, significantly reducing the population of Gram-negative bacteria. One hypothesis suggests that nano-silver toxicity may be attributed to the generating of reactive oxygen species (ROS), mainly free radicals, which arise from oxidative damage (Figure 4). Multiple pathways are implicated in the ROS generation induced by nanoparticles.

A well-designed delivery system can enhance the antimicrobial, antiretroviral, and antitumour properties of silver nanoparticles [60,61]. Earlier studies [30,62] have demonstrated the potent synergistic effects of combining doxorubicin (DOX) with silver nanoparticles (AgNPs) in inhibiting tumour cell growth and metastasis. The concurrent use of DOX and AgNPs exhibits a significantly stronger synergistic effect than when each is used alone. Moreover, the attachment of silver nanoparticles results in the release of a substantial quantity of silver ions onto the bacterial surface, leading to chemical interactions that ultimately destroy the bacterial membrane [60].

2.1.2. Gold Nanoparticles

Colloidal gold solutions have been used for centuries to treat various infections. Gold is highly biocompatible and possesses numerous advantageous properties, making it increasingly sought after for precisely engineering gold nanoparticles (AuNPs). These nanoparticles have unique attributes, including their small size, varied shapes, strong oxidation resistance, and remarkable biocompatibility [63]. Figure 5 and Table 4 present the wide-ranging applications of gold nanoparticles (AuNPs) in enhancing human welfare across diverse domains.

Table 4. Overview of the applications of gold nanoparticles and key challenges in their use. This table summarises the diverse applications of gold nanoparticles in various fields, such as medicine, diagnostics, and nanotechnology, while highlighting the significant challenges associated with their use.

Application Area	Specific Use	Advantages of Using Gold Nanoparticles	Challenges and Considerations	Refs.
Biomedicine	Targeted drug delivery, Biosensing, photothermal therapy, cancer theranostics, gene therapy	High biocompatibility, easy surface functionalisation, efficient drug loading and controlled release, localised heating capabilities (photothermal therapy), multifunctional potential (diagnosis and treatment), contrast enhancement in imaging techniques	Potential for non-specific interactions, difficulty in controlling in vivo behaviour, high production costs, potential clearance by immune system	[15]
Drug Delivery	Delivery of chemotherapeutic drugs, delivery of gene therapy vectors, delivery of antibiotics, delivery of proteins and peptides	Enhanced drug efficacy and reduced side effects, targeted delivery to specific cells and tissues, controlled drug release, improved cellular uptake	Optimisation of surface properties for specific drug targeting, ensuring biocompatibility and minimising toxicity, overcoming biological barriers, maintaining drug stability during delivery	[37,54]
Biosensing	Detection of biomolecules (e.g., proteins, DNA), detection of pathogens, early disease diagnosis, environmental monitoring	High sensitivity and specificity, label-free detection, real-time monitoring, multiple detection capabilities	Development of precise and reliable assays, optimisation of surface chemistry for target biomolecule binding, integration with detection systems	[50]
Photothermal Therapy (PTT)	Ablation of cancer cells, catalysis, tumour destruction, localised hyperthermia for treatment	Minimally invasive therapy, precise targeting of diseased tissue, synergistic effect with other therapies (e.g., chemotherapy)	Optimisation of the light source and irradiation parameters, controlling heat generation and preventing damage to healthy tissue, ensuring efficient delivery of gold nanoparticles to the target site	[64,65]
Cancer Theranostics and anticoagulant therapy	Combining diagnosis and treatment, early cancer detection and monitoring, image-guided therapy, personalised medicine approach	Multifunctional gold nanoparticles for imaging and therapy, improved diagnostic accuracy, tailoring treatment based on specific cancer characteristics	Development of integrated theranostic platforms, maintaining biocompatibility of multifunctional nanoparticles, addressing potential toxicity concerns.	[66–68]

Scientists use different techniques to create gold nanoparticles, and one popular method involves reducing gold (III) derivatives. Daniel and Astruc [64] successfully employed the reduction of HAuCl4 with citrate in water to produce gold nanoparticles.

The formation of AuNPs is facilitated by fruit extracts that contain water-soluble organic constituents, which act as both reducing and capping agents in this process [69]. This finding takes advantage of the organic components found in fruit extracts. The AuNPs demonstrate antimicrobial properties, highlighting their potential importance in biomedical applications. Using plant extracts to synthesise gold nanoparticles (AuNPs) by reducing gold salt presents a vast range of potential applications in biomedicine (Figure 3). This approach has led to the advancement of various associated technologies.

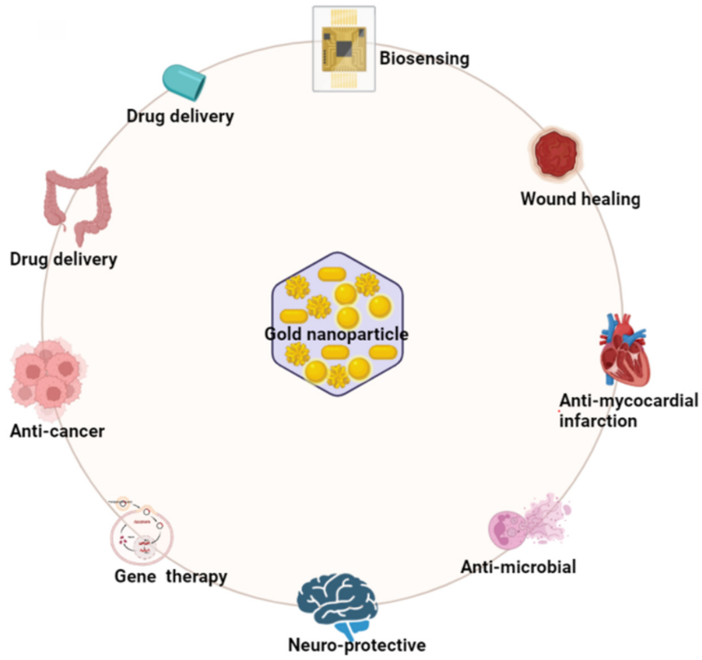

Figure 5. Application of gold nanoparticles in various areas for human welfare. From biomedical fields such as diagnostics, therapeutics, and drug delivery to environmental remediation and catalysis, AuNPs showcase remarkable versatility. Their unique physicochemical properties enable precise imaging in medical diagnostics, targeted drug delivery for enhanced therapeutic efficacy, and efficient pollutant removal from water and air. As a result, AuNPs stand as critical players in advancing technologies to improve human health and environmental sustainability.

2.1.3. Copper Nanoparticles

Copper-based substances have extensive applications in guarding crops against diverse microorganisms and moulds, including those that cause bacterial and fungal diseases. This approach is favoured due to its cost-effectiveness, strong protective capabilities, and the low risk of developing microbial resistance associated with copper compounds [70]. The antibacterial efficaciousness of copper originates from its ability to generate hydroperoxide free radicals, deactivate vital enzymes, and alter membrane integrity. In addition, copper can replace necessary ions and impede the functioning of protein groups [34]. The activation of the antioxidant system is facilitated by CuNPs, which possess characteristics similar to those of antioxidant molecules. This enables them to effectively absorb, neutralise, or quench singlet and triplet oxygen. The production of copper nanoparticles involves the use of copper acetate tetrahydrate, which is combined with an aqueous plant extract and stirred until it dissolves [24]. After boiling, a paste with a greenish hue is obtained, which is then heated in a furnace, resulting in dark black powdered copper. The surface of CuNPs contains numerous bioreductive groups, particularly phytochemicals, which contribute to their potent antioxidant activity.

2.1.4. Platinum Nanoparticles (PtNPs)

Platinum nanoparticles (PtNPs) and their alloys exhibit remarkable catalytic properties due to their large surface areas. These materials are effective in reducing pollutants and support chemical processes that are beneficial for producing different chemicals. In addition, PtNPs have shown great promise in medicine [46]. PtNPs can enhance the effectiveness of anti-cancer drugs and shrink tumours when combined with low doses. Additional research methods are required to investigate this potential thoroughly. The first step in making platinum nanoparticles is extracting the plant material by grinding its parts. Subsequently, the extract is introduced into H2PtCl5 while being continuously stirred magnetically [71]. The solution is then centrifugated to separate and collect the platinum nanoparticles. The research conducted by Kim et al. [72] provides insights into the anti-ageing effects of platinum nanoparticles in *Caenorhabditis elegans*. The study also highlights their antioxidant properties, ability to mimic superoxide dismutase (SOD), and similarities to platinum nanoparticles [72]. Furthermore, PtNPs have shown promise as therapeutic agents for disorders related to oxidative stress. This is supported by their ability to inhibit the growth of tongue cancer cells when dissolved in hydrogen-infused water. The National Center for Biotechnology Information conducted this investigation focusing on HSC-4 cells.

2.2. Metal Oxide Nanoparticles (MO-NPs)

Metallic oxides are helpful in many areas due to their unique physiochemical characteristics; these include electronics, research, and more. In recent decades, metal oxide nanoparticles (MO-NPs) have been widely used in various biological contexts. There are various types of oxides present in MO-NPs (ZnO), including iron oxide (Fe_3O_4), zinc oxide (ZnO), copper oxide (CuO), and titanium dioxide (TiO_2) [73,74].

The applications of these MO-NPs are diverse, encompassing both the medicinal and environmental domains. They serve as catalysts capable of mitigating or eradicating harmful impurities and hazardous substances in their surroundings. MO-NPs are generally regarded as resistant to human and environmental influences. In bacteria, the presence of MO-NPs can cause damage to proteins and DNA due to the generation of oxidative stress, which produces reactive oxygen species (ROS) [12]. Figure 6 and Table 5 portray the widespread utility of metal oxide nanoparticles across diverse sectors, underscoring their versatility and profound impact. From catalysis to environmental remediation, these nanoparticles play pivotal roles in advancing technology and addressing global challenges. Their electronics, sensing, and medicine applications highlight their adaptability and potential for transformative innovations. This illustration serves as a visual testament to the multifaceted contributions of metal oxide nanoparticles across scientific disciplines.

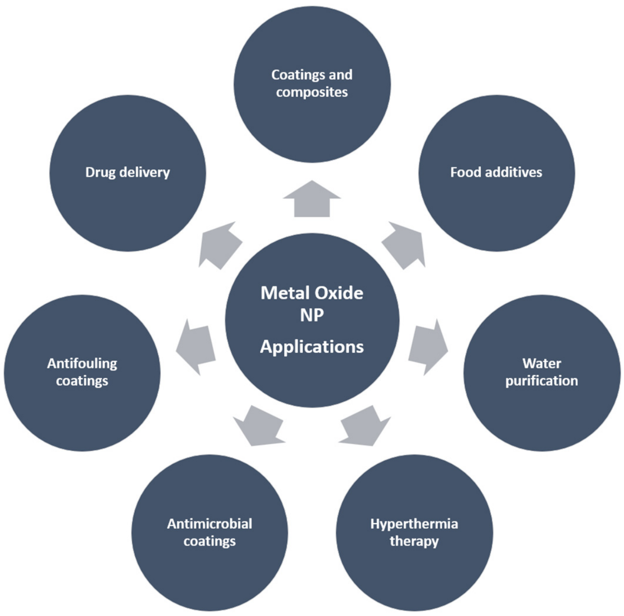

Figure 6. Illustration depicting common applications of metal oxide nanoparticles in various fields, showcasing their versatility and impact.

Table 5. A comprehensive overview of various metal oxide nanoparticles, their diverse applications, and the advantages and disadvantages associated with their use.

Metal Oxide Nanoparticle	Application	Advantages	Disadvantages	Refs.
Titanium Dioxide (TiO_2)	Sunscreens, photocatalysis	- Excellent UV absorption properties	- Potential toxicity concerns	[48]
	Water purification	- Photocatalytic activity for pollutant degradation	- Limited photocatalytic efficiency under visible light	[48]
	Antimicrobial coatings	- High stability and durability		[48]
Zinc Oxide (ZnO)	Sunscreens, photocatalysis	- Broad-spectrum UV protection	- Concerns regarding nanoparticle penetration into skin	[57,75]
	Antibacterial applications	- Effective antimicrobial properties	- Possible cytotoxicity	[25,76]
Iron Oxide (Fe_2O_3, Fe_3O_4)	Drug delivery	- Biocompatibility for in vivo applications	- Limited drug-loading capacity	[37,77]
	Hyperthermia and antifungal therapy	- Ability to generate heat under alternating fields - kill pathogenic fungi	- Potential long-term toxicity concerns	[33,78]
Copper Oxide (CuO)	Antimicrobial	- Efficiently kill bacteria and fungal pathogens	- Potential toxicity, especially in high concentrations	[24]
	Oxidative stress management	- Effective inhibition of ROS	- Limited stability under harsh environmental conditions	[34]
Silicon Dioxide (SiO_2)	Drug delivery	- Biocompatible and inert	- Limited drug-loading capacity	[23]
	Biosensor	- Safe and non-toxic	- Potential silica dust inhalation risks in manufacturing	[23]
	Coatings and composites	- Excellent mechanical properties in supercapacitors	- Susceptibility to hydrolysis and dissolution	[23]

2.2.1. Zinc Oxide Nanoparticles (ZnO-NPs)

Zinc oxide nanoparticles (ZnO-NPs) have been widely acknowledged and classified as a "safe material" due to their small size, large surface area to volume ratio, and unique biological characteristics [47]. A recent study [44] has demonstrated the remarkable effectiveness of ZnO-NPs in combating HepG2, a liver cancer cell line. The observed effectiveness was associated with a significant increase in genotoxicity and cytotoxicity, resulting in cellular death through apoptosis or cell death. The ZnO nanoparticles, ranging from 96 to 115 nm, exhibit substantial anti-inflammatory properties, as indicated by their IC50 value of 66.78 g/mL [79]. Zinc oxide nanoparticles (ZnO-NPs) have practical applications in bioimaging. They exhibit blue and near-UV emission spectra, and their luminescence can change to yellow or green depending on the presence or absence of oxygen vacancy. A study conducted by Hameed et al. [80] found that a combination of nanoparticles (Ag-ZnO-NPs) demonstrated significantly stronger antibacterial effects when compared to ZnO-NPs.

Zinc oxide is widely used in various industries, including plastics, glass, ceramics, cement, rubber, and dietary supplements. The positive aspects of this material arise from its ability to work well with non-flammable substances, as well as its convenient availability and cost efficiency [81]. Zinc nanoparticles have UV-blocking properties and exhibit antimicrobial efficacy, making them suitable for textile integration. This integration offers multiple benefits, such as protection against visible and ultraviolet light and antibacterial and deodorising functions. Additionally, different forms, such as ZinS and ZinSe, display fluorescent properties when combined with quantum dots like CdSe/ZnS [82]. Research has shown that zinc oxide nanoparticles exhibit the most substantial antimicrobial effects compared to other metal oxide nanoparticles when tested in a controlled environment against *Salmonella typhi* and *Staphylococcus aureus* [83,84]. Furthermore, zinc oxide nanoparticles are gaining considerable attention due to their affordability and minimal toxicity as a nanomaterial. They show potential applications in various fields, including cancer therapy, antibacterial effectiveness, anti-inflammatory properties, anti-diabetic capabilities, and drug delivery. Zinc oxide nanoparticles are synthesised using zinc chloride and plant leaf extract as starting materials [85]. The procedure entails dissolving zinc acetate dihydrate in distilled water while maintaining constant agitation. Afterwards, the solution of zinc acetate dihydrate is combined with an aqueous leaf extract. Following a thorough stirring, a pale yellow precipitate is gathered and undergoes several rinses with distilled water. After rinsing with distilled water, a further rinse with ethanol removes any impurities. Finally, the precipitate is dried under vacuum to produce zinc oxide nanoparticles [86,87].

2.2.2. Copper Oxide Nanoparticles (CuO-NPs)

Copper oxide nanoparticles (CuO-NPs) have gained considerable attention as potential nanomaterials due to their distinct chemical, physical, electrical, thermal, and biological properties [88]. Copper nanoparticles are synthesised using $Cu(CH_2COO)_2H_2O$ as a catalyst. The $Cu(CH_2COO)_2H_2O$ is dissolved in distilled water while being stirred continuously. Afterwards, the solution is mixed with plant leaf extract and agitated for several hours [89]. After the synthesis process, the nanoparticles undergo centrifugation, are dried in an oven, and subsequently collected. The durability of CuO nanoparticles is remarkable, surpassing that of both organic and inorganic materials. They boast an impressive shelf life. They significantly impact various applications, such as solar energy cells, catalytic processes, batteries made from lithium-ion, and antimicrobial substances [70,90]. Furthermore, CuO-NPs have demonstrated heightened sensitivity to bacterial strains compared to plant extracts, rendering them highly effective in antibacterial treatments. Their mechanism of action involves interactions with DNA molecules, resulting in structural disruption through cross-linking between nucleic acids.

2.2.3. Iron Oxide Nanoparticles (Fe_3O_4-NPs)

Nanoparticles of iron oxide exhibit magnetic properties which are very useful in the treatment of different ailments, including bacterial infections. These nanoparticles are much praised for their biocompatibility and biological activity. Research undertaken by Chauhan and Upadhyay [77] dealt with iron oxide nanoparticle functionalisation via the L-tyrosine coating of the nanoparticles. Their study demonstrated that modified iron oxide nanoparticles had a profound efficacy on pathogenic bacterial strains such as *Staphylococcus typhimurium* and *Staphylococcus aureus*. To synthesise iron oxide nanoparticles, henna powder was first immersed in a sulfuric solution of ferrous salt. The henna powder served as a reducing agent, lowering the concentration of the ferrous salt aqueous solution. The henna was then removed by rinsing with the clean salt solution under stirring, after which, this reduced solution was transferred into the container. The development of iron oxide nanoparticles was signalled by the transition of the medium to a deep hue. The nanoparticles were separated by cooling the suspension and then centrifuging it to form pellets. These pellets were soaked in water and methanol to help eliminate the leftover henna deposits and then dried for 12 h to obtain the pure iron oxide nanoparticles.

Peer-reviewed articles have expanded upon iron oxide nanoparticles' safety and therapeutic applicability for treating hyperthermia mediated by magnetic nanoparticles [33,91]. Such nanoparticles are widely used in cancer treatment, since they can elevate the temperature in the vicinity of tumours to provoke—or kill—cancer cells [28]. Furthermore, Fe_3O_4 nanoparticles (derived from Euphorbia plant extract) exhibit strong antibacterial activity against *Aspergillus fumigatus*, *Aspergillus niger*, and *Arthogrophis cuboidal* [48,92,93].

2.2.4. Titanium Oxide Nanoparticles (TiO_2-NPs)

Titanium dioxide nanoparticles (TiO_2-NPs) have unique properties, making them incredibly versatile in various biomedical and environmental applications [94]. These properties include their form, surface chemistry, optics, and biocompatibility. As a result, TiO_2-NPs are highly valuable in multiple fields, such as disease identification, surgical instrument development, biological imaging, tissue engineering, and drug delivery. In addition, TiO_2-NPs are widely used in various industries, including textiles, cosmetics, polymers, and food production. Their effectiveness extends to fighting a wide range of pathogens, such as bacteria, protozoa, algae, viruses, prions, and microbial toxins. Studies [94,95] have been dedicated to the development of environmentally friendly TiO_2-NPs, which have shown remarkable effectiveness in combating larval parasites such as *Catharanthus roseus, Calotropis gigantea, Solanum trilobatum*, and *Aspergillus niger*. This approach utilises a professional and environmentally conscious method by incubating TiO_2 with plant extracts at room temperature. The result is the production of green-coloured TiO_2-NPs that can be used in various applications.

3. Exploring the Therapeutic Potential of Plant-Derived Nanoparticles in Biomedicine

Refining particle sizes using nanotechnology can significantly improve the oral bioavailability of drugs [60,75]. Therefore, nanotechnology can be viewed as a resourceful approach to many oral formulations that are ineffective due to their low bioavailability. Considering environmental concerns, nanoparticles (NPs) are viewed as an alternative to chemically synthesised fungicides [78]. They have such benefits as the enhanced transport of the medicinal product, the partitioning of active substances, and lower amounts of the active component being needed (Table 6). Enhanced safety and comfort for patients and better PK characteristics of drug delivery systems concerned with labile, short-lived peptides and proteins are offered. This also alleviates the toxicological burden imposed by pharmaceutical agents.

Recent findings have indicated that the oral administration of grape exosome-like nanoparticles to mice stimulates epithelial cell growth in the intestine and encourages intestinal stem cell growth [96]. Hence, the use of nanoparticles for drug delivery in the form of plant products, which are safer and more natural, appears promising [97,98]. Such products are also rich in dietary fibres, which help retain the colonic tissue and can aid in treating conditions related to the intestinal tract, such as inflammatory bowel conditions (IBD), since they also have anti-inflammatory effects [25,98]. Furthermore, research on the interaction of leukocytes with nanoparticles has shown their ability to block Cyclin D1, which is important in regulating the cell cycle [99]. This research offers valuable insights into the involvement of nanoparticles in gut inflammation. Other studies [76,100] found that metal oxide nanoparticles have strong antibacterial properties, even at low concentrations, and are safe for humans to use. This is quite different from their larger forms. This finding highlights their importance in the field of healthcare.

Table 6. Overview of plant-based nanoparticles (NPs), their biomedical applications, key properties, advantages, and disadvantages, including plant sources and nanoparticle types [97,99–102].

Plant Source	Nanoparticle Type	Biomedical Application	Key Properties	Advantages	Disadvantages	Refs.
Aloe vera	Curcumin NPs	Wound healing, anti-inflammatory	Antioxidant, antimicrobial, biocompatible	Promotes tissue regeneration, reduces inflammation	Limited in vivo studies, potential for allergic reactions	[101]
Green tea	Epigallocatechin gallate (EGCG) NPs	Cancer therapy, neurodegenerative diseases	Antioxidant, anti-inflammatory, blood–brain barrier penetration	Potential for targeted drug delivery, protects against oxidative stress	Limited bioavailability, requires further research on long-term safety	[24,102]

Table 6. *Cont.*

Plant Source	Nanoparticle Type	Biomedical Application	Key Properties	Advantages	Disadvantages	Refs.
Ginger	Gingerol NPs	Anti-inflammatory, pain relief	Anti-inflammatory, analgesic	Potential for treating chronic inflammatory diseases, improved bioavailability	Limited aqueous solubility, requires optimisation for controlled release.	[68]
Neem	Azadirachtin NPs	Antibacterial, antifungal, antiparasitic	Antibacterial, antifungal, antiparasitic	Broad-spectrum antimicrobial activity, potential for treating drug-resistant infections	Limited data on in vivo efficacy, requires careful control of particle size for safety.	[103]
Turmeric	Curcumin NPs	Anti-cancer, anti-inflammatory	Anti-inflammatory, anti-cancer, poor water solubility	Improved bioavailability of curcumin, the potential for cancer treatment and prevention	Rapid degradation in the body, requires the development of effective delivery systems	[104]
Grape seed	Procyanidin NPs	Cardiovascular health, antioxidant	Antioxidant, vasoprotective	Potential for improving blood vessel health, reducing oxidative stress	Limited human studies, requires further research on the optimal dosage	[105]
Holy basil (tulsi)	Eugenol NPs	Antibacterial, antiviral	Antibacterial, antiviral	Potential for treating infections, immune system modulation	Limited data on in vivo efficacy, requires optimisation for controlled release	[106]
Citrus fruits	Limonin NPs	Anti-cancer, anti-inflammatory	Anti-cancer, anti-inflammatory	Potential for cancer treatment and prevention, reduces inflammation	Limited data on bioavailability, requires further research on optimal dosage	[24]
Wheatgrass	Chlorophyll NPs	Wound healing, anti-inflammatory	Anti-inflammatory, promotes wound healing	Potential for accelerating wound closure, reduces inflammation	Limited data on in vivo efficacy, requires further research on optimal formulation	[107]
Gotu kola	Centella asiatica extract NPs	Wound healing, skin regeneration	Promotes collagen synthesis, improves skin healing	Potential for treating scars and wrinkles, enhanced bioavailability	Limited data on long-term safety, requires further research on optimal dosage	[108]
Bael fruit	Aegle marmelos extract NPs	Antibacterial, anti-diarrheal	Antibacterial, anti-diarrheal	Potential for treating gastrointestinal infections, reduces diarrhoea	Limited human studies, requires further research on optimal dosage	[109]

The increasing focus on green chemistry and nanotechnology has led to a higher demand for sustainable synthesis techniques in the production of nanomaterials. These methods utilise botanical origins, microorganisms, and additional natural reservoirs, demonstrating a collaborative effort to address the changing demands of expanding sectors. Plant-derived nanoparticles have a wide range of uses in environmentally friendly industries, including catalytic processes, healthcare, beauty products, the agricultural sector, food packaging, wastewater treatment, dye degradation, fabric technology, biological engineering disciplines, devices such as sensors, image processing, biotechnology, electronic devices, optical technology, and various biological fields (Table 6) [110–114].

3.1. Exploring Plant-Based Biopolymer Nanofibers for Advanced Wound Care

Recent advancements in nanofiber technology have shown an impressive adhesion to skin wounds, offering an exciting potential for reducing scars [115]. Their unique porous structure and the complex interconnectivity between pores make them extremely sought-after for wound-healing applications (Figure 7). In addition, they offer several benefits such as retaining moisture, allowing oxygen to pass through, and preventing the growth of microbes, all of which promote wound healing [116]. The exploration of natural biopolymers is a fascinating area of research in biomedicine. Cellulose, silk fibroin, zein, fibrin, keratin, gelatin, chitosan, chitin, and starch are among the intriguing substances being studied [117].

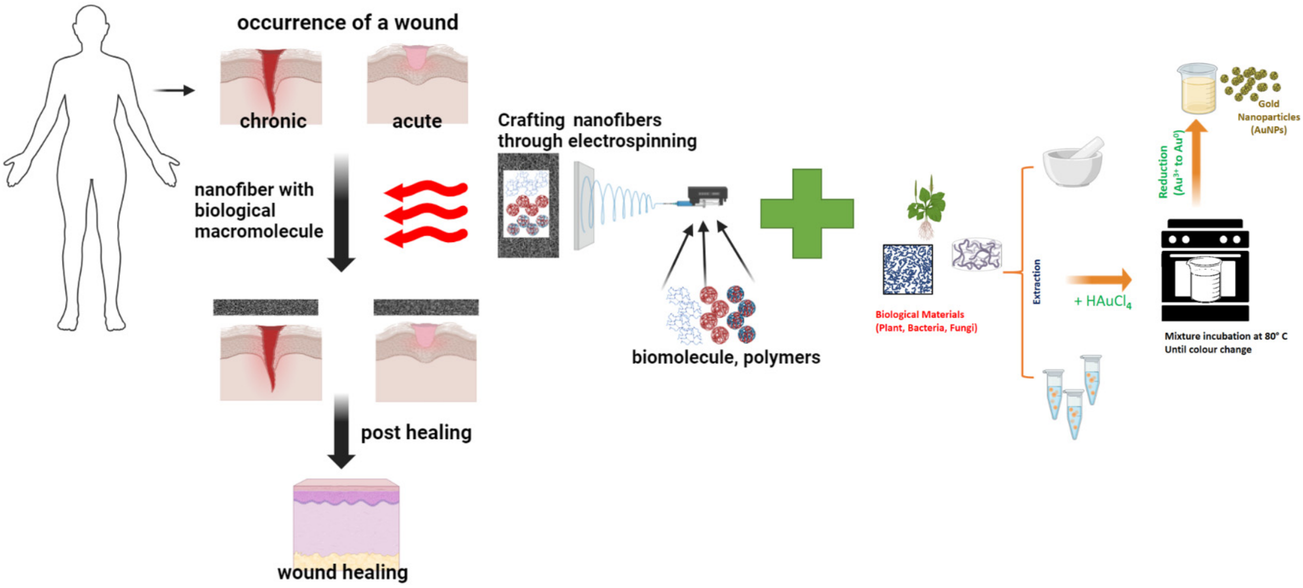

Figure 7. Revitalising wounds with eco-friendly nanoparticles: A sustainable approach to accelerated healing using green-derived nanoparticles. This figure illustrates the application of biologically synthesised nanoparticles, emphasising their biocompatibility, enhanced wound repair properties, and reduced environmental footprint.

Furthermore, various substances such as bioactive compounds, plant gums, algal and bacterial polysaccharides, and proteoglycans derived from plants have attracted significant interest due to their potential in biomedical applications [116–118]. These naturally derived biopolymers have been successfully used to create nanofibers via electrospinning, which is particularly important for wound dressing. They are ideal for wound care because they are compatible with human macromolecules, can degrade naturally, stop bleeding, and lack toxicity. However, the use of synthetic antibiotics and nanoparticles in electrospun nano-fibrous wound dressings raises concerns regarding health and environmental implications [119].

On the other hand, nanoparticles containing phytochemicals provide a range of benefits. They tend to have fewer negative effects, are easily accessible, and are cost-effective compared to traditional pharmaceuticals. When synthesising nanoparticles, a wide variety of natural biomolecules and chemicals are carefully chosen and then converted into nanofibers, which can be used for highly effective wound dressing [118]. A notable example is the application of electrospinning to produce nanofibers infused with *Curcuma longa* L. plant extract, representing a groundbreaking use of ultra-fine cellulose acetate fibre mats [120]. Curcumin, the active compound found in *Curcuma longa* L., demonstrates various biological activities, such as antibacterial, anti-inflammatory, antimicrobial, antioxidant, angiogenic, and anti-cancer effects.

3.2. Plant Polyphenols and Nanostructured Scaffolds for Enhanced Bone Tissue Regeneration

A small bone fracture triggers the activation of many types of cells, such as mesenchymal cells, osteogenic cells, and immune system cells, which commence the bone regeneration process [121]. These self-repair mechanisms lead to the development of distinct physiochemical and mechanical properties during the replacement of bone tissue.

Plant polyphenols have shown promise in promoting tissue regeneration, namely in the complex process of bone tissue regeneration [61]. Polyphenols are considered promising medicinal agents in modern biomedicine because of their natural antibacterial and antioxidant capabilities. In addition, polyphenols consist of a wide range of bioactive chemicals and micronutrients crucial for enhancing bone health.

Electrospinning technology is commonly utilised and shows promise in creating nano-sized pores and fibres from plant-derived polyphenols during the production of nanofibrous scaffolds [121]. Nanofibers created using electrospinning demonstrate similar levels of porosity, mechanical properties, and surface area to volume ratio (Figure 8). These qualities enhance cell adhesion, division, development, and propagation, resembling the extracellular matrix (ECM). Almost 60% of bone's dry weight comes from its nanostructured composite, which includes minerals like calcium phosphate (CaP) [20].

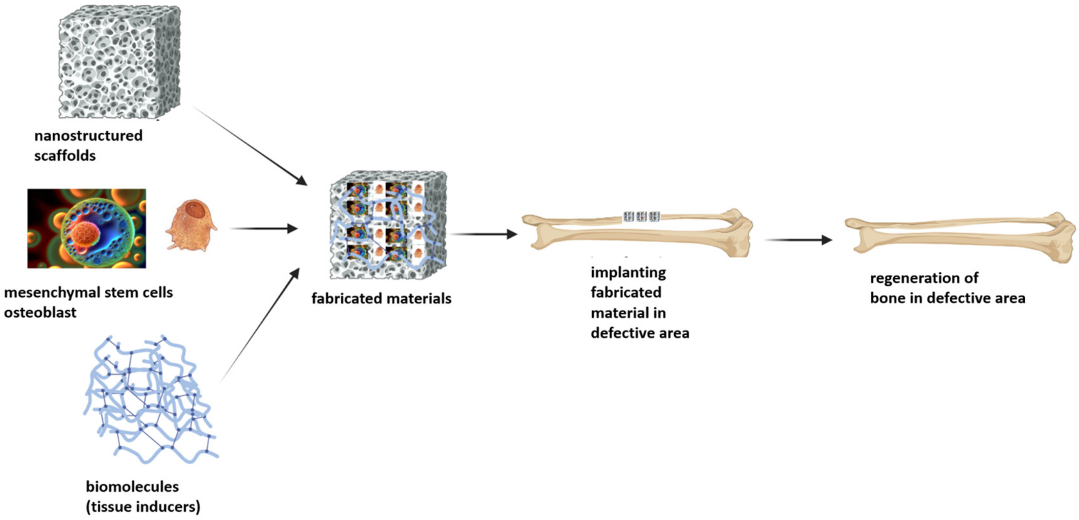

Figure 8. Treatment of defective bone using green nanomaterial: a schematic representation showcasing the application of nanostructured scaffolds in bone repair. These greener nanomaterials are designed to enhance biocompatibility, promote cellular regeneration, and provide structural support, paving the way for sustainable and efficient bone tissue engineering solutions.

4. Practical Applications of Plant-Derived Nanoparticles (PDNPs) in Drug Delivery, Cancer Therapies, Regenerative Medicine, and Antimicrobial Treatments

Plant-derived nanoparticles (PDNPs) have gained significant attention due to their biocompatibility, non-toxicity, and potential for versatile medical applications [38]. Their unique physicochemical properties, such as size, surface charge, and the presence of bioactive molecules, make them suitable candidates for various therapeutic interventions.

4.1. Drug Delivery

Plant-derived nanoparticles (PDNPs) are increasingly utilised in drug delivery systems due to their capacity to encapsulate and deliver bioactive compounds, improving their bioavailability, solubility, and targeted action [10,44]. The natural surface chemistry of PDNPs allows them to interact favourably with biological systems, facilitating the efficient release of drugs at specific sites. Key advantages of PDNPs in drug delivery include their biocompatibility and biodegradability, which ensure they are well tolerated by the body and do not elicit significant immune responses. Additionally, PDNPs can be functionalised to target specific cells or tissues, enhancing therapeutic outcomes while reducing side effects [23]. For example, green tea (*Camellia sinensis*)-derived nanoparticles have been employed to deliver poorly soluble drugs, such as curcumin [122]. This study demonstrated that these nanoparticles significantly improved curcumin's bioavailability and therapeutic efficacy, even crossing the blood–brain barrier, making them ideal for treating neurological conditions like brain tumours. The enhanced anti-cancer activity was attributed to the nanoparticles' ability to protect the drug from degradation and facilitate a targeted release at tumour sites [10,15]. Similarly, neem (*Azadirachta indica*)-derived silver nanoparticles have been explored for their potential to enhance antibiotic delivery, specifically ciprofloxacin, for combating multidrug-resistant bacteria [123]. These nanoparticles improved the drug's efficacy by targeting bacterial biofilms, enhancing drug penetration and retention at infection sites. Clinical evidence further supports the utility of PDNPs in drug delivery, as demonstrated by a Phase I clinical trial (NCT01713640) involving curcumin-loaded PDNPs for treating inflammatory diseases [124]. The trial showed promising results, with the formulation enhancing bioavailability, reducing systemic toxicity, and providing better therapeutic effects in patients with chronic inflammation.

4.2. Cancer Therapy

Plant-derived nanoparticles (PDNPs) offer several significant advantages in cancer therapy, particularly in targeted drug delivery, gene therapy, and photothermal therapy. These nanoparticles can be engineered to deliver chemotherapeutic agents, therapeutic genes, or proteins directly to cancer cells, thereby minimising damage to surrounding healthy tissues [16,30]. One of the primary benefits of PDNPs is their ability to target tumour cells effectively. By functionalising PDNPs with specific ligands, they can selectively bind to receptors on cancer cells, enhancing the accumulation of drugs at the tumour site. Additionally, PDNPs enable combination therapies, where chemotherapeutic agents can be co-delivered with other treatment modalities, such as gene therapy or photodynamic therapy (PDT). For example, *Moringa oleifera*-derived nanoparticles loaded with doxorubicin have been shown to selectively target and deliver the drug to breast cancer cells in rats [27], significantly reducing side effects like cardiotoxicity while enhancing anti-cancer efficacy. Similarly, turmeric-derived nanoparticles loaded with curcumin have demonstrated a high drug encapsulation efficiency and stability, improving ovarian cancer therapeutic effects [125]. In vitro studies indicated that these nanoparticles induce apoptosis in cancer cells while sparing healthy cells, offering promising potential for clinical applications. A clinical trial involving doxorubicin-loaded PDNPs (NCT03122715) further demonstrated their potential, showing that patients with metastatic cancer experienced fewer side effects, such as hair loss and nausea, while it achieved a comparable or improved efficacy compared to conventional doxorubicin treatments [126].

4.3. Regenerative Medicine

Regenerative medicine focuses on repairing or replacing damaged tissues and organs, and plant-derived nanoparticles (PDNPs) are being explored for their potential role in tissue regeneration. PDNPs can deliver bioactive molecules such as growth factors, cytokines, and genes that promote cell proliferation, differentiation, and tissue healing, making them highly beneficial for various regenerative applications [127]. These include promoting tissue regeneration by delivering molecules that stimulate repair, enhancing stem cell therapy by facilitating stem cell delivery to damaged tissues or promoting their differentiation, and aiding wound healing by providing drugs or peptides that accelerate tissue regeneration. For instance, aloe vera-derived nanoparticles, known for their healing properties, have enhanced wound healing. These nanoparticles, loaded with growth factors like epidermal growth factor (EGF), were demonstrated to promote cell migration, proliferation, and angiogenesis, significantly accelerating the healing of chronic wounds in rats [128]. Similarly, ginseng-derived nanoparticles loaded with vascular endothelial growth factor have been studied for their potential in tissue regeneration [129]. Preclinical studies revealed that these nanoparticles promoted angiogenesis and accelerated tissue repair in animal myocardial infarction and bone fracture models. Clinical studies have also support the regenerative potential of PDNPs, such as a clinical trial that investigated ginseng-derived nanoparticles for bone regeneration in osteoarthritis patients [130,131].

The trial found that these nanoparticles enhanced osteoblast differentiation and accelerated bone healing, offering a promising alternative to traditional bone-grafting techniques.

4.4. Antimicrobial Treatments

Due to their potent antimicrobial properties, plant-derived nanoparticles (PDNPs) have demonstrated significant promise in combating microbial infections. These nanoparticles can act both as antimicrobial agents and as carriers for antimicrobial drugs, enhancing the efficacy of the drugs while reducing the risk of resistance [7]. The mechanisms through which PDNPs exert their antimicrobial effects include disrupting microbial cell membranes, inhibiting biofilm formation, and interfering with microbial metabolism. Key advantages of PDNPs in antimicrobial treatments include their broad-spectrum activity against various pathogens, including bacteria, fungi, and viruses, as well as their ability to reduce antibiotic resistance by improving the targeted delivery of antibiotics [9]. For example, neem-derived silver nanoparticles have been shown to exhibit strong antimicrobial activity against a broad spectrum of pathogens such as *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans*, with their antimicrobial effect attributed to oxidative damage to microbial cells and the inhibition of cell wall synthesis [103,123]. Similarly, garlic-derived nanoparticles have demonstrated enhanced antimicrobial properties against *Pseudomonas aeruginosa*, a common pathogen in hospital-acquired infections, and have shown promise in improving wound healing and infection control [132]. Clinical trials have further validated the potential of PDNPs, such as a study involving neem-derived silver nanoparticles for wound infections, where patients treated with the nanoparticles experienced faster healing and a reduced microbial load compared to conventional antibiotic therapies [133].

Plant-derived nanoparticles (PDNPs) have demonstrated significant potential across various therapeutic fields, including drug delivery, cancer therapies, regenerative medicine, and antimicrobial treatments. Their advantages, such as biocompatibility, efficient cellular uptake, low toxicity, and cost-effective production, make them an attractive alternative to synthetic nanoparticles and mammalian cell-derived therapies. Clinical trials and case studies further validate the efficacy of PDNPs, offering promising therapeutic avenues with reduced side effects and enhanced therapeutic outcomes. As the field of nanomedicine continues to evolve, PDNPs are poised to play a pivotal role in advancing treatments for a wide range of diseases and conditions

5. Advantages of Plant-Derived Nanoparticles (PDNPs) over Artificial Nanoparticles and Mammalian Cell-Secreted Exosomes

Plant-derived nanoparticles (PDNPs) are gaining increasing attention due to their remarkable properties and potential applications in various fields, including medicine, agriculture, and environmental sciences. They offer several advantages compared to traditional synthetic (artificial) nanoparticles and mammalian cell-secreted exosomes [134]. These advantages include non-toxicity, efficient cellular uptake, and cost-effective production methods. Below is a detailed elaboration of these benefits.

5.1. Non-Toxicity

One of the key advantages of plant-derived nanoparticles (PDNPs) is their relatively low toxicity compared to synthetic nanoparticles. Nanoparticle toxicity is influenced by size, shape, surface charge, and the materials used in their synthesis. Synthetic nanoparticles, particularly metal-based ones like silver, gold, and copper, are known to induce toxicity due to the release of metal ions, which can cause oxidative stress, inflammation, and cellular damage [135]. In contrast, PDNPs are often stabilised by biocompatible plant-derived compounds such as polyphenols, alkaloids, and flavonoids, which help to mitigate toxicity. These plant metabolites stabilise the nanoparticles and possess antioxidant and anti-inflammatory properties, further reducing the potential adverse effects. For example, neem (*Azadirachta indica*)-derived silver nanoparticles have been shown to exhibit a minimal toxicity to human cells, making them suitable for drug delivery applications [133]. Green tea (*Camellia sinensis*)-derived copper and gold nanoparticles are recognised for their low toxicity and excellent biocompatibility, with studies demonstrating their safe use in cancer therapy [24,136].

In comparison, while mammalian cell-secreted exosomes offer some biocompatibility advantages, their production is more complex and often carries the risk of immunogenic responses. For instance, exosomes derived from cancer cells may carry tumour antigens, potentially provoking immune reactions in therapeutic contexts [137]. Furthermore, isolating exosomes from mammalian cells is costly and time-consuming, with the risk of contamination or batch-to-batch variability, which is not a concern with PDNPs [138].

5.2. Efficient Cellular Uptake

One of the key advantages of plant-derived nanoparticles (PDNPs) in biomedical applications is their ability to be efficiently taken up by various cell types, including cancer cells, macrophages, and endothelial cells [139]. The unique surface properties of PDNPs, such as phytochemicals and their surface charge, facilitate their interaction with cellular membranes, promoting endocytosis. Biomolecules like polyphenols, flavonoids, and proteins on the surface of PDNPs play a crucial role in enhancing cellular uptake by mimicking natural ligands that interact with cell receptors [50,135]. This enhanced cellular internalisation is vital for the effectiveness of drug delivery, gene therapy, and other therapeutic applications. For example, basil (*Ocimum basilicum*)-derived silver nanoparticles have shown an efficient uptake by cancer cells, promoting apoptosis while minimising the side effects typically associated with conventional chemotherapy [140].

Coconut (*Cocos nucifera*)-derived nanoparticles have also been found to enhance drug delivery to targeted cells with minimal toxicity, demonstrating their therapeutic potential [141]. In comparison, mammalian cell-derived exosomes exhibit an efficient cellular uptake through their lipid bilayer. However, their uptake efficiency can be influenced by the cell type they are derived from and may require more sophisticated targeting methods to optimise cellular internalisation. Despite their promise, exosome uptake may not be as universally efficient as PDNPs, particularly in non-targeted delivery scenarios.

5.3. Economic Production

Plant-derived nanoparticles (PDNPs) offer significant economic advantages over synthetic ones and exosomes, primarily due to their low-cost and sustainable production methods. The synthesis of PDNPs typically employs green synthesis techniques that utilise plant extracts as reducing agents for metal nanoparticles, eliminating the need for expensive chemicals and energy-intensive processes [142]. This reduces production costs while being environmentally friendly. Additionally, plants can be cultivated in large quantities at a relatively low cost, making PDNPs a scalable and sustainable solution for industrial applications. In contrast, synthetic nanoparticles require costly raw materials, chemicals, and high-energy processes, such as high temperatures or pressures, which increase production costs.

Furthermore, the environmental impact of chemical waste and energy consumption makes the large-scale production of synthetic nanoparticles less efficient and sustainable. Exosome production, which involves labour-intensive and expensive mammalian cell cultures, also presents significant cost challenges. Specialised equipment, such as ultracentrifuges or chromatography columns, is needed to isolate exosomes, further increasing costs. Additionally, the scalability of exosome production is limited by the availability of cells for culture, making it less feasible for large-scale applications. For example, producing exosomes from stem cells or tumour cells for therapeutic purposes involves significant expense, and the variability in production from batch to batch further complicates their use on a large scale [143]. In contrast, examples such as *Neem (Azadirachta indica)*-derived nanoparticles, which are synthesised through simple, water-based extraction methods, demonstrate the cost-effective potential of PDNPs [123]. Similarly, green tea (*Camellia sinensis*)-derived nanoparticles and *Moringa (Moringa oleifera)*-derived nanoparticles are produced using environmentally sustainable and cost-effective water-based extraction techniques, making them more economically viable than synthetic nanoparticles or exosomes for many applications [144].

5.4. Environmental Impact

The eco-friendly synthesis of plant-derived nanoparticles (PDNPs) offers a cost-effective and environmentally sustainable alternative to conventional nanoparticle production methods. By utilising plant extracts as natural reducing and stabilising agents, PDNPs minimise the generation of harmful by-products, contributing to a greener and more sustainable process. Plants, being renewable resources, are an ideal source for the synthesis of nanoparticles, eliminating the need for the toxic chemicals commonly used in traditional synthetic nanoparticle production [51]. In contrast, synthetic nanoparticle production often involves hazardous chemicals and solvents, which, if not disposed of properly, can have severe environmental consequences. Additionally, these processes are energy-intensive, raising concerns about their carbon footprint. Exosome production, while a promising area in nanomedicine, also contributes to environmental impacts due to its reliance on energy-intensive cell culture systems and animal-derived components, increasing its overall ecological burden [48]. Examples of eco-friendly PDNP synthesis include the production of nanoparticles using *Azadirachta indica* (neem) and *Camellia sinensis* (green tea) through simple, water-based extraction methods, which are low-impact and sustainable [24,102,123].

Similarly, nanoparticles derived from *Moringa oleifera* are produced using water-based solutions, significantly reducing the environmental toxicity associated with chemical synthesis [27]. PDNPs provide several advantages over synthetic nanoparticles and mammalian cell-secreted exosomes, including non-toxicity, improved efficiency in cellular uptake, and more economical, eco-friendly production methods. Produced through green chemistry techniques, PDNPs are scalable, biocompatible, and suitable for various medical, agriculture, and environmental applications. In comparison, synthetic nanoparticles and exosomes often involve higher production costs, complex synthesis protocols, and potential toxicity issues, making PDNPs a promising and sustainable alternative in the growing field of nanotechnology.

6. Potential and Challenges of Plant-Based Nanoparticles: Towards Sustainable Applications

Plant-based nanoparticles (NPs) have garnered considerable interest recently because of their potential benefits in diverse fields, including medicine, agriculture, and environmental cleanup. These nanoparticles, derived from plant extracts or by-products, have many advantages as well as certain intrinsic restrictions that influence their applicability in different areas [145]. An important benefit of nanoparticles created from plants is their environmentally friendly nature. Using plant extracts for nanoparticle production avoids the requirement for strong chemicals and minimises the environmental consequences linked to conventional synthesis methods. Using plant-derived nanoparticles (NPs) aligns with the increasing global focus on sustainability and green technologies, making them an attractive choice for industries aiming to reduce their environmental impact.

Moreover, nanoparticles generated from plants frequently demonstrate compatibility with living organisms and the ability to break down naturally, rendering them appropriate for use in medicinal applications [146]. Generally, plant-derived nanoparticles are considered safer for medical treatments and drug delivery systems than synthetic nanoparticles, which can potentially cause toxicity or immunological responses. Their compatibility with biological systems decreases the probability of negative reactions and improves patient safety, a crucial element in healthcare applications [147]. Additionally, plant-derived nanoparticles are abundant and easy to obtain. As a renewable resource, plants can be cultivated in large quantities, providing a sustainable source of raw materials for nanoparticle production. The large amount of plant-derived nanoparticles guarantees a reliable and continuous supply, which makes them economically feasible for extensive utilisation in diverse industries [148].

Moreover, nanoparticles generated from plants frequently feature intrinsic therapeutic qualities that are linked to the bioactive chemicals found in plant extracts. These nanoparticles can maintain the beneficial characteristics of their source plants, such as their antioxidant, antibacterial, or anti-inflammatory activities [67]. Utilising these inherent healing substances in nanoparticle format presents fresh opportunities for pharmaceutical advancement, medical intervention, and nutritional enhancement. Nevertheless, plant-derived nanoparticles have significant drawbacks and obstacles that must be considered. An important limitation is the inconsistency in nanoparticle properties due to variations in plant species, growth circumstances, and extraction techniques [113]. The variability in nanoparticle synthesis can impact the consistency and repeatability of the process, which creates difficulties in achieving standardisation and ensuring quality control.

In addition, the intricate nature of plant extracts can hinder the isolation and purification of nanoparticles, often leading to contaminants or unwanted by-products in the end product. Attaining the purity and consistency of nanoparticles obtained from plants necessitates a careful refinement of extraction and synthesis methods, which increases the intricacy and expense of nanoparticle manufacturing. Moreover, the capacity to scale up the production of nanoparticles produced from plants is still a challenge, particularly for industrial uses on a big scale. Although plants provide a renewable supply of raw materials, the capacity to increase the size of nanoparticle synthesis processes may be restricted by factors such as the effectiveness of extraction, the time required for processing, and the expenses involved in manufacturing [149]. It is essential to tackle these scalability difficulties to fully exploit plant-derived nanoparticles' potential in commercial applications. Nanoparticles derived from plants have several benefits, such as being environmentally friendly and compatible with living organisms, possessing medicinal characteristics, and being easily obtainable. These nanoparticles show potential for various uses, including healthcare and environmental remediation, due to their natural origin and advantageous properties.

Nevertheless, to fully exploit the promise of plant-derived nanoparticles and promote their extensive use in industrial and medicinal applications, it is crucial to tackle the difficulties related to variability, purity, and scalability [112,150]. Plant-based nanoparticles (PNPs) also face several regulatory challenges in clinical applications due to variations in composition, extraction methods, and biological activities. These inconsistencies complicate establishing universal safety standards and quality controls. We propose a multilayered regulatory framework that standardises synthesis methods to ensure consistency in nanoparticle properties. Additionally, guidelines should be formulated for in-depth toxicity evaluations, comprehensive risk assessments, and clinical testing to validate the safety and efficacy of PNPs. Collaboration between regulatory agencies, researchers, and industry stakeholders will be vital in developing such frameworks to provide clear pathways for approval and commercialisation.

7. Challenges in Plant-Derived Nanoparticle Research

Plant-derived nanoparticles (PDNPs) have emerged as a promising alternative to conventional synthetic nanoparticles, owing to their eco-friendly synthesis, cost-effectiveness, and biocompatibility. PDNPs are primarily synthesised using plant extracts containing bioactive compounds that act as reducing, stabilising, and capping agents [35]. These nanoparticles have significant applications in biomedicine, agriculture, and environmental sciences. However, the field is fraught with technical, economic, and regulatory challenges that limit its progress and industrial scalability [151].

7.1. Variability in Phytochemical Composition

The synthesis of plant-derived nanoparticles (PDNPs) is highly influenced by the phytochemical composition of the plant extract used, with variations in bioactive compounds such as flavonoids, terpenoids, alkaloids, and phenolics playing a significant role. These compounds, which serve as reducing agents or stabilisers, vary considerably across plant species, geographic regions, and environmental conditions, including soil type, climate, and seasonal changes [151,152]. For instance, a study on silver nanoparticles (AgNPs) synthesised from *Azadirachta indica* (neem) extracts revealed nanoparticle size and morphology variations when leaves from different geographic regions were used. This variability was attributed to fluctuations in the levels of bioactive compounds such as Nimbin and azadirachtin, which influence the reducing potential and, consequently, the size and shape of the nanoparticles [133]. Similarly, silver nanoparticle synthesis from *Camellia sinensis* (green tea) exhibited altered morphologies due to seasonal fluctuations in catechin and polyphenol levels, which play a role in nanoparticle formation [102]. Additionally, the synthesis of iron oxide nanoparticles using *Curcuma longa* (turmeric) rhizome extract showed inconsistent magnetic properties, attributed to variations in curcuminoid concentrations that resulted from different drying methods [104]. These examples underscore the critical impact of plant species and environmental conditions on the consistency and properties of plant-derived nanoparticles.

Impact of Extraction Methods: The choice of extraction methods, such as aqueous, ethanolic, or supercritical fluid extraction, significantly influences the yield and bioavailability of phytochemicals, which in turn affects the efficiency of nanoparticle synthesis. Aqueous extractions, though environmentally friendly, typically yield lower concentrations of hydrophobic compounds, which can impact the reducing and capping efficiency of the extract, leading to variations in nanoparticle properties [153]. These variations hinder reproducibility and scalability, as inconsistent phytochemical profiles can result in discrepancies in nanoparticle size distribution, stability, and functional properties. In contrast, ethanol extracts from *Eucalyptus globulus* produced nanoparticles with smaller size distributions, owing to the better solubilisation of hydrophobic compounds. Microwave-assisted extraction in *Allium cepa* (onion) facilitated the formation of gold nanoparticles with a faster synthesis and higher uniformity, attributed to the enhanced availability of sulphur-containing phytochemicals. Additionally, silver nanoparticles synthesised from Soxhlet-extracted turmeric extracts demonstrated superior antimicrobial properties, emphasising the critical role of extraction methods in determining the bioactivity of nanoparticles [154–156].

7.2. Challenges in Nanoparticle Synthesis

Optimisation of Reaction Parameters: The synthesis of nanoparticles using plant extracts requires the precise optimisation of various parameters, including the concentration of metal precursors, extract volume, temperature, pH, and reaction time. Even small variations in these parameters can significantly impact the resulting nanoparticles' morphology, surface characteristics, and stability.

Scalability Concerns, While the laboratory-scale synthesis of plant-derived nanoparticles (PDNPs) can be tightly controlled, scaling up to industrial production presents significant challenges. Large-scale reactions often encounter issues such as uneven heating, inconsistent mixing, and increased impurity levels, which can lead to the formation of heterogeneous nanoparticles [151]. The absence of robust standardisation protocols makes it difficult to maintain a consistent quality in large-scale production. For instance, the industrial-scale production of nanoparticles using *Eucalyptus globulus* extracts struggled with regulating the reaction kinetics, leading to difficulties in achieving a uniform particle size and shape. Similarly, the production of nanoparticles from *Trigonella foenum-graecum* (fenugreek) at an industrial scale faced challenges in maintaining consistent pH levels across large batches, which is crucial for controlling particle formation [157,158].

7.3. Characterisation and Analytical Limitations

Advanced Instrumentation Requirements: The accurate characterisation of plant-derived nanoparticles (PDNPs) necessitates the use of advanced techniques such as transmission electron microscopy (TEM), dynamic light scattering (DLS), X-ray diffraction (XRD), and Fourier-transform infrared spectroscopy (FTIR), which collectively provide detailed insights into the size, shape, crystalline structure, and surface functionalisation of the nanoparticles. For instance, in the case of gold nanoparticles (AuNPs) synthesised from *Allium cepa* (onion) extracts, challenges arose in determining surface functional groups using FTIR due to interference from residual phytochemicals, requiring additional purification steps. However, these steps introduced the risk of nanoparticle aggregation. In the case of *Ocimum basilicum* (basil)-derived zinc oxide nanoparticles, XRD analysis successfully identified crystalline phases, but discrepancies between facilities resulted in uncertainties in the interpretation of the data [140]. Furthermore, the FTIR analysis of nanoparticles from *Cocos nucifera* (coconut) faced challenges in peak resolution due to the overlapping vibrational modes of polyphenols present in the coconut extract, further complicating the identification of nanoparticle characteristics [159]. These examples underscore the complexities in accurately characterising PDNPs, highlighting the need for standardisation in methods and instrument calibration to ensure reproducibility and reliability across studies.

7.4. Biocompatibility and Toxicity Concerns

Incomplete Understanding of Toxicity Profiles: While plant-derived nanoparticles (PDNPs) are generally considered biocompatible, their safety profile is not universally guaranteed. The phytochemicals used to cap the nanoparticles can impart diverse biological activities, some of which may induce cytotoxic or immunogenic effects in certain cell types or organisms [63]. For instance, silver nanoparticles synthesised from *Eclipta prostrata* extracts exhibited potent antimicrobial activity but also triggered cytotoxicity in mammalian fibroblast cell lines. This toxicity was attributed to the combined effects of residual phytochemicals and the release of silver ions from the nanoparticles [34,51]. Similarly, zinc oxide nanoparticles derived from *Ocimum sanctum* induced oxidative stress in zebrafish embryos, underscoring their potential ecological risks [160]. This highlights the importance of comprehensive safety evaluations in developing PDNP-based therapeutics, as their nanoparticulate nature does not solely define their biological activity, which is also influenced by interactions between the nanoparticle core and its phytochemical coatings.

Lack of Standardised Toxicity Testing: The lack of standardised methodologies for evaluating the biocompatibility and toxicity of plant-derived nanoparticles (PDNPs) presents a significant challenge in their risk assessment, hindering their translation from research to real-world applications. Current evaluation models often fail to adequately address long-term effects, bioaccumulation, and environmental impact, leading to an incomplete understanding of the potential risks associated with PDNPs.

7.5. Regulatory and Ethical Challenges

Ambiguity in Regulatory Guidelines: The regulatory landscape for plant-derived nanoparticles (PDNPs) remains in flux. Key governing bodies such as the FDA and EMA lack specific regulatory frameworks for nanoparticles synthesised through green methods. This regulatory gap introduces significant uncertainty for researchers and manufacturers striving to commercialise PDNPs, especially in highly regulated fields such as food, agriculture, and biomedical applications [161]. For example, a biotechnology company developing PDNP-based antimicrobial coatings faced substantial delays in obtaining market approval due to the absence of clear guidelines for eco-friendly nanomaterials [162]. Similarly, a startup focused on *Curcuma longa*-derived silver nanoparticles encountered market entry delays because of regulatory ambiguity surrounding eco-friendly nanomaterials. *Azadirachta indica*-based silver nanoparticle formulations lacked comprehensive environmental safety guidelines in the agrochemical sector, further delaying their commercialisation. Similarly, regulatory uncertainties also hindered the approval of *Zingiber officinale*-mediated zinc nanoparticles in food applications and *Ocimum basilicum*-derived nanoparticles for biomedical use, with both applications stalled due to the lack of harmonised international standards [163]. These examples highlight the critical need for regulatory bodies to establish clear, standardised frameworks to address the growing demand for plant-derived nanomaterials in diverse industries.

Sustainability and Biodiversity Concerns: The large-scale use of specific plants for nanoparticle synthesis presents significant concerns related to overharvesting and the potential loss of biodiversity. Ethical sourcing practices are essential to ensure the sustainability of plant resources [62,164,165]. For instance, the growing demand for *Withania somnifera* (ashwagandha) in nanoparticle synthesis has raised alarms about its overexploitation, especially given its high demand in traditional medicine. Similarly, the large-scale extraction of various plants for nanoparticle production has led to the depletion of its natural populations, disrupting local ecosystems [165]. The excessive use of *Eucalyptus globulus* for industrial-scale silver nanoparticle synthesis has also led to concerns over monoculture plantations, which may adversely affect soil health and local biodiversity. Additionally, producing nanoparticles from *Camellia sinensis* (green tea) extract requires large volumes of raw material, contributing to sustainability issues in cultivation practices, as the high demand may strain natural resources and threaten long-term availability. These examples highlight the need for responsible harvesting and sustainable sourcing practices to mitigate the environmental impact of plant-derived nanoparticle production [164,166].

7.6. Environmental Considerations

The improper disposal of nanoparticles and residual plant materials from their synthesis presents a risk of environmental contamination. Despite plant-derived nanoparticles (PDNPs) being greener alternatives to chemically synthesised nanoparticles, their long-term ecological impact remains largely underexplored [4,6].

7.7. Economic Barriers

The synthesis of plant-derived nanoparticles (PDNPs) presents significant challenges, particularly concerning the high cost of raw materials and technology transfer. The production of PDNPs often requires large quantities of plant material, which can be expensive and resource-intensive, especially for rare or medicinal plants in high demand [142]. For instance, the use of *Terminalia arjuna* bark extracts for synthesising gold nanoparticles encountered economic constraints, as this plant is crucial for nanoparticle production and holds a substantial value in traditional medicine. Furthermore, adopting green synthesis methods for PDNPs at an industrial scale presents another hurdle. The transition from laboratory-scale processes to large-scale production requires considerable investments in infrastructure, equipment, and specialised expertise [144]. Many industries face difficulties in integrating these environmentally friendly technologies into their existing workflows, as it often involves re-engineering production processes and ensuring consistency in nanoparticle synthesis. These challenges hinder the widespread commercialisation and scalability of PDNPs in various industries [151].

8. Need for More In Vivo Studies to Translate Plant-Derived Nanoparticles into Clinical Settings

Plant-derived nanoparticles (PDNPs) have emerged as a promising avenue in nanotechnology, particularly in drug delivery, diagnostics, and therapeutic interventions. These nanoparticles are synthesised using plant extracts, which act as reducing and stabilising agents and offer a biocompatible, eco-friendly, and cost-effective alternative to chemically synthesised nanoparticles. Despite their potential, the translation of PDNPs into clinical settings remains limited (as mentioned below), primarily due to insufficient in vivo studies.

8.1. Lack of Comprehensive Pharmacokinetics and Pharmacodynamics Data

In vitro studies provide insights into the interaction of PDNPs with target cells, but they fail to replicate the complexity of living organisms. In vivo studies are essential to evaluate the absorption, distribution, metabolism, and excretion (ADME) profiles of PDNPs. For instance, nanoparticles synthesised using *Azadirachta indica* (neem) extract have shown anti-cancer activity in vitro. However, their biodistribution and long-term organ retention need in vivo verification to ensure safety and efficacy [167].

8.2. Complex Immune System Interactions

The immune response to nanoparticles varies significantly in a living system. While PDNPs are generally considered biocompatible, in vivo studies are crucial to assess the potential for immunogenicity or adverse inflammatory responses. A study using silver nanoparticles synthesised with *Camellia sinensis* (green tea) extract demonstrated antibacterial properties in vitro. However, their systemic toxicity and immunomodulatory effects require further investigation in animal models [102].

8.3. Evaluation of Biodegradability and Long-Term Toxicity

The biodegradability of PDNPs in vivo is influenced by enzymatic activities and physiological conditions that cannot be simulated in vitro. For instance, zinc oxide nanoparticles derived from *Ocimum sanctum* (holy basil) have shown promise in wound healing. However, their potential accumulation in tissues and long-term toxicity need in vivo assessment [160].

8.4. Challenges in Targeted Delivery

Targeted drug delivery systems based on PDNPs require in vivo studies to determine their efficacy in navigating biological barriers, such as the blood–brain barrier or tumour microenvironments. Curcumin-loaded PDNPs from *Curcuma longa* have shown potential for treating neurodegenerative diseases. However, in vivo validation is critical to confirm their ability to cross the blood–brain barrier and achieve therapeutic concentrations [168].

8.5. Scale-Up and Dosage Optimisation

In vivo studies help determine the optimal dosage and scaling up for clinical applications. Factors such as nanoparticle size, surface charge, and coating must be tailored to minimise toxicity and enhance therapeutic outcomes. Iron oxide nanoparticles synthesised using *Moringa oleifera* have demonstrated promise in magnetic hyperthermia for cancer treatment, but their effective dosage and heating efficiency need validation in animal models [27].

8.6. Regulatory Approvals and Clinical Trials

Regulatory agencies demand robust in vivo data to approve nanomedicine formulations [163]. To progress to human trials, PDNPs must demonstrate safety and efficacy across multiple preclinical models. For example, chitosan nanoparticles derived from *Aloe vera* extracts have shown potential in delivering anti-diabetic drugs, but the regulatory pathways necessitate thorough in vivo testing for approval [161,163].

Gold nanoparticles derived from *Terminalia arjuna* bark extract exhibit strong anticancer properties in vitro. However, animal models must evaluate their tumour-targeting ability, therapeutic index, and off-target effects [169]. Similarly, PDNPs synthesised from *Eucalyptus globulus* have shown broad-spectrum antibacterial activity against multidrug-resistant pathogens [157]. In vivo studies are essential to confirm their efficacy in treating systemic infections without disrupting the host microbiota. It was also found that silver nanoparticles derived from *Catharanthus roseus* have shown accelerated wound healing in vitro. In vivo studies on their interaction with fibroblasts, keratinocytes, and immune cells are necessary to optimise formulations for clinical use [85,170].

8.7. Challenges in Conducting In Vivo Studies

Using animal models in research involving plant-derived nanoparticles (PDNPs) raises several ethical concerns, necessitating strict adherence to animal welfare guidelines to ensure humane treatment. Additionally, in vivo studies are often more costly and time-consuming than in vitro experiments, which can limit their widespread adoption in nanoparticle research. Variability in results is another challenge, as physiological differences between animal models and humans can lead to discrepancies, requiring further refinement of the experimental protocols. Despite these challenges, in vivo studies remain indispensable for bridging the gap between bench and bedside in developing PDNPs. They provide crucial insights into these innovative materials' safety, efficacy, and therapeutic potential, facilitating their successful translation into clinical applications. By addressing the ethical, cost-related, and experimental challenges and prioritising comprehensive in vivo research, PDNPs have the potential to usher in a new era of sustainable and effective nanomedicine.

9. Conclusions and Future Perspectives

In conclusion, integrating nanotechnology into the fabrication of materials with diverse compositions holds immense promise, particularly in medicine. Nanotechnology allows for the meticulous manipulation of materials at the nanoscale, enabling the creation of tailored, multi-dimensional materials for specific therapeutic applications. This capability opens new avenues in cancer treatment, wound healing, bone regeneration, and diagnostics. Nanoparticles, with their unique size and characteristics, offer precision in drug delivery, which can potentially minimise side effects and enhance therapeutic efficacy. However, further research is needed to optimise the targeting techniques and fully unlock the potential of nanoparticles in cancer treatment. Using plant-derived nanoparticles (PNPs) with inherent antibacterial properties presents an innovative approach to treating microbial infections. Leveraging secondary metabolites from plants in nanoparticle synthesis improves antimicrobial efficacy and enhances the biocompatibility of metal and metal-oxide nanoparticles. While these developments show promise, it is essential to conduct extensive toxicity and biocompatibility testing to ensure the safety of these nanoparticles for medical applications. Given the growing interest in eco-friendly and sustainable practices, plant-based synthesis methods offer a safer alternative for developing nanoparticles with versatile applications, particularly in nanomedicine.

Future developments in nanotechnology should focus on the establishment of standardised protocols for synthesising PNPs. It is essential to design scalable production methods that can meet the growing demand for medical applications and conducting thorough toxicity and biocompatibility evaluations. Long-term safety assessments, including in vitro and in vivo studies, are critical for understanding the potential risks of PNPs, such as cytotoxicity, genotoxicity, and immunogenicity. Advanced techniques like proteomics, metabolomics, and histopathological analysis will play a significant role in studying the interactions between PNPs and biological systems.

Additionally, it is crucial to develop regulatory frameworks and standardised protocols to safely and effectively use nanoparticles in clinical settings. This will ensure that PNPs meet rigorous safety and efficacy standards before widespread application. By addressing these challenges and continuing to explore innovative solutions, nanotechnology in medicine will undoubtedly reshape healthcare and provide effective treatments for a wide range of diseases, offering transformative solutions to global health challenges.

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