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Green Synthesis of Plant-Based Nanoparticles: Recent Advances, Biomedical Applications and Future Perspectives

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Abstract
Green synthesis of nanoparticles using plant extracts has emerged as a sustainable and eco-friendly alternative to conventional chemical and physical nanoparticle fabrication. In this approach, phytochemicals present in various plant parts (e.g., leaves, fruits, roots) act as natural reducing and stabilizing agents, enabling the formation of diverse metal and metal oxide nanoparticles under mild conditions. This review highlights recent advances in plant-based green synthesis of nanoparticles, with a focus on their biomedical applications and future prospects. Notably, plant-mediated synthesis produces nanoparticles that are biocompatible and less toxic, making them attractive for nanomedicine and therapeutic use. In the past five years, research in this field has intensified, with silver nanoparticles being the most extensively studied, followed by gold, zinc oxide, copper oxide, and others. We discuss how these green-synthesized nanoparticles have demonstrated potent antimicrobial (antibacterial, antifungal, antiparasitic) properties, anti-cancer effects (e.g., inducing apoptosis in tumor cells), and capabilities in drug delivery and bioimaging. Key examples include silver nanoparticles showing broad-spectrum antimicrobial and antiparasitic activity, gold nanoparticles for anti-biofilm and cancer therapy, and metal oxide nanoparticles (ZnO, CuO, etc.) for their therapeutic and diagnostic potential. While significant progress has been made in understanding and applying plant-based nanoparticles, challenges such as scalability, reproducibility, and thorough toxicity evaluation remain. Future research directions are proposed to address these challenges, improve green synthesis methods (including leveraging machine learning and bioprocess optimization), and fully realize the biomedical potential of plant-derived nanoparticles in a safe and sustainable manner.
Keywords: *Green synthesis; plant extracts; nanoparticles; nanomedicine; antimicrobial; anticancer; sustainable nanotechnology; phytochemistry*

INTRODUCTION

Nanotechnology has revolutionized multiple fields, including medicine, by enabling the manipulation of materials at the nanometer scale. Nanoparticles (NPs) – typically 1–100 nm in size – exhibit unique physicochemical properties (high surface area, tunable optical/magnetic behaviors, etc.) that can be exploited for biomedical applications in diagnostics, therapy, and drug delivery. Conventional NP synthesis methods (chemical reduction, physical milling, etc.), however, often involve toxic reagents, high energy consumption, and environmental hazards. In response, **green synthesis** approaches have gained prominence as a sustainable, eco-friendly alternative. Green synthesis utilizes biological entities – such as microorganisms or plant extracts – to produce NPs in an environmentally benign manner. Among these methods, plant-based green synthesis has emerged as a particularly attractive "gold standard" due to the abundance and diversity of plant phytochemicals that can reduce metal ions and stabilize the resulting nanoparticles.

In plant-mediated NP synthesis, natural compounds in the plant extract (e.g., polyphenols, flavonoids, terpenoids, sugars, amino acids) serve as reducing agents that convert metal ions (like Ag^+, Au^3+, Zn^2+, etc.) into zero-valent nanoparticles, while simultaneously capping and stabilizing the NP surface. This one-pot biogenic process typically occurs in aqueous medium under mild conditions, aligning with green chemistry principles (use of non-toxic solvents and reagents). Plant-based synthesis is simple, cost-effective, and easily scalable, and it avoids hazardous chemicals, thus minimizing adverse environmental impact. Moreover, the resulting nanoparticles often exhibit better biocompatibility and are **less likely to cause harmful side effects** compared to chemically synthesized counterparts. Indeed, plant-derived NPs tend to be more acceptable for medical and pharmaceutical uses due to their lower inherent toxicity and

the biological coating from phytochemicals, which can improve their stability and functionality in biological systems (e.g., preventing aggregation and conferring specific bioactivity).
Over the last five years, there has been a surge in research on plant-based NP synthesis and applications.

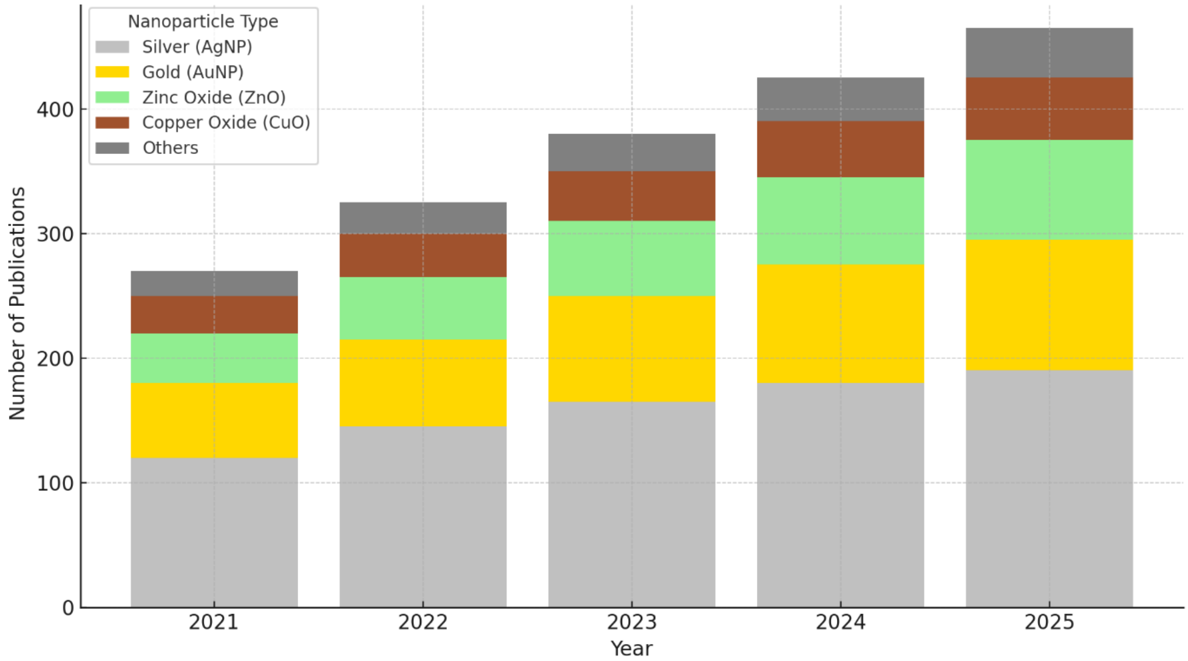

Figure 1 illustrates the distribution of publications on green synthesis of various nanoparticles from 2021 to 2025, underscoring that silver nanoparticles (AgNPs) have dominated the literature in this domain. AgNPs alone account for roughly 42% of recent green nanotechnology publications, about double the number of studies on gold nanoparticles (AuNPs). Other metal/metal oxide NPs synthesized via plant extracts include zinc oxide (ZnO), copper/copper oxide (Cu/CuO), iron oxide, titanium dioxide, and more, each contributing a share of the research output. The prominence of AgNPs is attributed to their broad-spectrum antimicrobial efficacy and the ease with which nearly any plant species can generate silver nanoparticles in solution. Nonetheless, interest in AuNPs is high due to their biomedical potential (e.g. in cancer therapy and drug delivery), and plant-synthesized AuNPs benefit from low toxicity and facile surface functionalization. Likewise, green-synthesized ZnO and CuO nanoparticles have drawn attention for their biomedical uses (antimicrobial, anticancer, antioxidant properties) and are valued for being inexpensive and abundant.

Figure 1: Five-year distribution of research publications on green synthesis of nanoparticles by type (2021–2025). Silver nanoparticles (AgNPs) constitute the largest segment of publications (~42%), followed by gold (AuNPs), zinc oxide (ZnO NPs), copper/copper oxide (Cu/CuO NPs), and others. This reflects the considerable focus on AgNPs in recent green nanotechnology research, although a wide variety of plant-based NPs have been explored.
In the following sections, we discuss the mechanisms of plant-based NP synthesis and highlight recent advances in improving and characterizing these green-synthesized nanoparticles. We then examine the diverse biomedical applications of plant-derived NPs, including their roles as antimicrobials, anticancer agents, drug delivery vehicles, and more. Finally, we address the current challenges facing this field and outline future perspectives for translating green nanotechnology into clinical and industrial practice.

Green Synthesis Approaches Using Plant Extracts

Mechanism of NP Formation: In plant-mediated NP synthesis, a typical procedure involves mixing a plant extract with a solution of a suitable metal salt (such as $AgNO_3$ for silver NPs, $HAuCl_4$ for gold NPs, or metal chloride salts for metal oxides). The phytochemicals in the extract (e.g., phenolic acids, flavonoids, tannins, alkaloids, proteins, sugars) rapidly reduce the metal ions to form elementary metal atoms, which nucleate into small clusters. These nascent clusters further aggregate and grow into nanoparticles, while concurrent adsorption of plant molecules on their surface prevents uncontrolled agglomeration. The plant biomolecules thus act as both **reducing agents** (initiating NP formation) and

capping agents (stabilizing NP surfaces), yielding nanoparticles often coated with a layer of organic compounds from the extract. This green capping imparts stability (e.g., via electrostatic and steric hindrance) and can also enhance biocompatibility and biological activity of the nanoparticles. Key factors influencing this synthesis include the concentration of plant extract, pH, temperature, reaction time, and metal salt concentration, all of which can be tuned to control NP size and shape. For instance, higher reaction temperatures generally accelerate NP formation and can produce smaller particles up to an optimal point, while pH affects the ionization of phytochemicals and thus the reduction kinetics and capping efficiency (moderate pH often yields more stable NPs). By optimizing these parameters, researchers have achieved various nanoparticle morphologies – including spherical, cubic, rod-shaped, and others – using plant extracts as facile one-pot synthesis platforms.

Advantages of Plant-Based Synthesis: Green synthesis via plants offers several compelling advantages. It eliminates the need for hazardous chemicals (e.g., sodium borohydride, hydrazine) as reductants and surfactants, thereby reducing environmental and health risks. The process is typically conducted in water or other benign solvents at ambient or mild heating conditions, aligning with sustainable chemistry principles. Importantly, plant-based methods are generally **simple and cost-effective**, often requiring nothing more than mixing the extract with metal salt and waiting for NP formation (which may be evident by a color change due to surface plasmon resonance in metallic NPs). This simplicity lends itself to easy scale-up and potentially low-cost mass production of nanoparticles. Another advantage is the rich diversity of phytochemicals across different plant species, which means a vast range of organisms can be exploited to synthesize NPs with potentially distinct sizes and functionalities. In fact, almost any plant (from herbs and crops to algae and agricultural wastes) contains suitable metabolites to produce nanoparticles, giving researchers tremendous flexibility in raw material choice. Moreover, the biological coating from plant molecules often renders the NPs more biocompatible and sometimes primes them with inherent bioactivity (such as antioxidant or antimicrobial properties from the capping compounds). This can be beneficial for medical applications, as **plant-capped NPs tend to interact favorably with cells and tissues and exhibit lower cytotoxicity to normal cells**. For example, green-synthesized gold and silver nanoparticles have been reported to cause fewer side effects in vitro and in vivo compared to chemically synthesized equivalents, while still exerting desired therapeutic actions. Plant-based NPs are thus regarded as **economical, sustainable, and biocompatible** materials that align well with the goals of green nanotechnology and nanomedicine.

Common Nanoparticles Produced: A wide array of nanoparticle types have been successfully synthesized using plant extracts. **Silver nanoparticles (AgNPs)** are the most frequently reported, owing to silver's potent antimicrobial properties and the ease of its reduction; many studies note that AgNP formation is rapid with plant extracts, and virtually any plant can yield AgNPs under the right conditions. **Gold nanoparticles (AuNPs)** are also extensively studied, especially for biomedical uses – gold's relatively low toxicity and unique optical properties (surface plasmon resonance) make AuNPs ideal for imaging and photothermal therapy, and plants like Turmeric, Neem, Green tea, and others have been used to produce AuNPs. **Zinc oxide nanoparticles (ZnO NPs)** have gained traction more recently; green-synthesized ZnO NPs (using flowers, leaves, etc.) have shown promise in antibacterial and anticancer applications, and they benefit from ZnO's intrinsic semiconductor and photocatalytic properties. **Copper and copper oxide nanoparticles (Cu/CuO NPs)** represent another category of interest – copper is inexpensive and widely available, and plant-mediated Cu/CuO NPs have demonstrated antimicrobial and anticancer activities, though concerns remain regarding their stability and potential toxicity if not properly capped. Other metal nanoparticles produced via plants include **iron oxide (Fe_3O_4 or Fe_2O_3) NPs** for magnetic and imaging applications (e.g., using Camellia sinensis or Moringa oleifera extracts), **palladium (Pd) and platinum (Pt) NPs** for catalytic and anticancer uses (plants have been used to reduce Pd^{2+} and Pt^{4+} to their nanoscale form), and **metal sulfide NPs** (like CdS, PbS) in a few reports. The versatility of plant extract chemistry allows not only single-metal NPs but even **bimetallic nanoparticles** (such as Ag–Au core-shell structures) to be synthesized by a one-step green process, as demonstrated in some recent studies (using two metal precursors with a plant extract).

Overall, plant-based green synthesis has opened a convenient route to fabricate a broad spectrum of nanomaterials. As research in this area expands, efforts continue to optimize reaction conditions and understand the mechanistic role of specific phytochemicals in nanoparticle formation. Advanced characterization techniques (TEM, SEM, XRD, FTIR, DLS, etc.) are routinely employed to confirm nanoparticle morphology, size distribution, crystalline structure, and surface chemistry. These studies collectively lay the groundwork for deploying green-synthesized nanoparticles in various biomedical applications, which are discussed in the next section.

Recent Advances in Green Nanoparticle Synthesis

The past few years have seen significant advancements in the green synthesis of plant-based nanoparticles. Researchers have explored numerous plant species – from medicinal herbs and fruit peels to agricultural wastes – to improve yield and tailor the properties of the nanoparticles. One notable trend is the **strategic use of plant combinations or additives** to enhance synthesis. For example, some studies use blended extracts from multiple plants or add benign substances (like vitamins or sugars) to the extract to achieve better control over NP size and stability. Microwave-assisted green synthesis is another innovation: by applying microwave irradiation, reaction kinetics are accelerated, often yielding smaller and more uniform NPs in a shorter time. **Figure 1 (above)** already highlighted the surge in publications, particularly for silver NPs. Recent bibliometric analyses confirm exponential growth in this field and a diversification of nanoparticle types and plant sources investigated.

One advance has been in **understanding and leveraging specific phytochemicals**: researchers have identified which components in an extract are primarily responsible for NP formation. For instance, polyphenolic compounds (like epigallocatechin gallate in green tea or curcumin in turmeric) are potent reducing agents, and their high concentration can produce nanoparticles rapidly. In some cases, isolated phytochemicals or purified fractions of plant extracts have been used to synthesize NPs, which helps in producing more consistent particle characteristics. However, the use of whole extracts is still prevalent since the mix of biomolecules can synergistically improve reduction and capping.

Another area of progress is **scaling up green synthesis**. Initial experiments often produced nanoparticles in small volumes (a few milliliters), but recent studies report successful scale-up to liter-scale reactions without loss of NP quality. This involves controlling parameters like mixing rate and extract-to-metal ratio in larger reactors. The development of continuous-flow green synthesis systems, where plant extract and metal ion solution are continuously fed into a reactor, has also been reported as a means to produce larger quantities of NPs efficiently.

Characterization techniques have grown more sophisticated as well. Beyond basic UV-Vis and TEM analyses, researchers now employ X-ray photoelectron spectroscopy (XPS) to confirm the oxidation state of green-synthesized metal NPs, zeta potential measurements to assess colloidal stability, and various spectroscopic methods to identify the functional groups from plants attached on NP surfaces. These insights are crucial for reproducibility – a known challenge in biogenic synthesis. Indeed, ensuring consistency in NP size and properties between batches (given natural variability in plant extract composition) is an active area of research. Standardizing extract preparation (e.g., drying plant material, controlled solvent extraction) and using analytical profiling (like HPLC or mass spectrometry) to quantify key phytochemicals are being adopted to improve reproducibility of green synthesis.

Crucially, recent advances also involve **expanding the scope of plant-based NPs to new applications and composite materials**. For example, green-synthesized metal NPs have been integrated into polymer matrices, hydrogels, or coating materials to create nanocomposites for wound dressings and antimicrobial surfaces. There are reports of plant-made AgNPs embedded in bandages or ointments that show enhanced healing of infected wounds, combining the antimicrobial power of AgNPs with the biocompatibility of natural product-based dressings. In another vein, plant-mediated synthesis of metallic **nanoparticles on supporting substrates** (like green-synthesized metal NP on graphene or clay) has been explored for catalytic and environmental applications, though those are beyond the biomedical focus of this review.

Table 1 provides representative examples of nanoparticles synthesized via plant extracts and their demonstrated biomedical applications, highlighting the variety of plant sources and particle types achieved through green synthesis.

Table 1. Examples of plant-mediated nanoparticles and their reported biomedical applications.

Plant Source (Extract)	Nanoparticle Type	Approx. Size & Shape	Biomedical Application	Reference
Corn cob xylan (agricultural waste)	Silver (AgNP)	~102 nm, spherical	Antileishmanial (against Leishmania parasites);	Silva Viana et al., 2020 (Biomolecules)

			antifungal (active against Candida spp.)	
Trachyspermumammi (Ajwain seed)	Gold (AuNP)	~16–17 nm, spherical	Inhibits drug-resistant bacterial biofilms (Listeria monocytogenes, Serratia marcescens) by ~73–81%; induces cytotoxicity in HepG2 liver cancer cells via ROS-mediated apoptosis	Perveen et al., 2021 (Biomolecules)
Cassia auriculata (leaf)	Zinc Oxide (ZnO NP)	~20 nm, hexagonal	Selectively cytotoxic to MCF-7 breast cancer cells (with minimal effect on normal breast cells); antibacterial activity through disruption of bacterial cell walls	Prasad et al., 2020 (Biomolecules)

Note: All nanoparticles above were synthesized at room temperature using aqueous plant extracts without additional chemical reducers or surfactants. The cited studies confirm nanoparticle morphology via electron microscopy and report significant biomedical efficacy, demonstrating the potential of green-synthesized NPs in nanomedicine.

Biomedical Applications of Plant-Based Nanoparticles

One of the most compelling aspects of green-synthesized nanoparticles is their broad range of **biomedical applications**. The biogenic capping from plant metabolites can endow these NPs with enhanced interaction with biological systems, and their inherent properties (high surface reactivity, nanoscale size) enable novel therapeutic mechanisms. Below, we detail key application areas in medicine where plant-based nanoparticles have shown promising results.

Antimicrobial and Antiparasitic Applications

Antibacterial and Antifungal Agents: Green-synthesized nanoparticles, especially silver and zinc oxide, are well-established as potent antimicrobials. Silver nanoparticles produced using plant extracts have demonstrated broad-spectrum antibacterial activity against both Gram-negative and Gram-positive bacteria, including multi-drug-resistant strains. The mechanism generally involves AgNPs attaching to bacterial cell membranes and penetrating inside, where they release Ag^+ ions and generate reactive oxygen species (ROS) that damage cellular components, leading to cell death. For instance, AgNPs synthesized with Ocimum or Solanum plant extracts showed strong inhibition zones against pathogens like Staphylococcus aureus and Escherichia coli, even outperforming some conventional antibiotics. The green synthesis route often enhances the antimicrobial effect because phytochemicals on the NP surface (e.g., flavonoids, terpenes) may themselves have antibacterial properties or synergize with the metal's action. Similarly, plant-derived ZnO NPs exhibit significant antibacterial effects; ZnO NPs can disrupt bacterial membranes and interfere with microbial enzyme function, and they are being explored for use in surface coatings to prevent hospital-acquired infections.

In addition to bacteria, green NPs are effective against fungi. For example, the **nanoxylan silver nanoparticles** from corn cob shown in **Table 1** had potent antifungal activity, completely inhibiting pathogenic yeasts (Candida albicans, C. parapsilosis, and Cryptococcus neoformans) at low micromolar concentrations. This suggests applications in treating fungal infections or incorporating into antifungal coatings for medical devices. Another study reported **green-synthesized AgNPs using Azadirachta indica (neem)** that suppressed the growth of opportunistic fungi and mold, highlighting their potential in managing skin and systemic mycoses (fungal infections).

Biofilm Inhibition: A significant challenge in infectious disease management is the formation of biofilms – communities of microbes encased in a protective matrix that are highly resistant to antibiotics. Green nanoparticles have shown the ability to prevent biofilm formation and even disrupt established biofilms. As noted in Table 1, AuNPs synthesized using Trachyspermumammi seeds exhibited ~73% and 81% inhibition of biofilm development by L. monocytogenes and S. marcescens, respectively. They could also

eradicate mature biofilms by about 60% by penetrating the biofilm matrix and killing the embedded bacteria. The mode of action involved induced oxidative stress (ROS generation) in the microbial cells, as evidenced by decreased glutathione levels in treated bacteria and morphological damage observed under microscopy. Such findings are encouraging for using plant-based NPs as **anti-biofilm agents**, possibly as coatings on implants or in dental applications to prevent biofilm-related infections. Green AgNPs have similarly been reported to inhibit biofilms of Pseudomonas aeruginosa and Staphylococcus epidermidis on catheter materials, indicating broad utility in combating biofilm-associated bacteria.
Antiparasitic Activity: Plant-derived nanoparticles have also made strides in antiparasitic medicine. Silver and gold NPs have been tested against parasites like Leishmania, Plasmodium (malaria parasite), and helminths. The nanoxylanAgNPs (Table 1) demonstrated an IC_{50} of ~25 µg/mL against Leishmania amazonensis promastigotes, effectively killing the parasite in vitro while the plant xylan alone had no effect. This suggests that green NPs could be developed into treatments for leishmaniasis, which is a significant tropical disease. The advantage of using plant-based NPs here is their potential lower toxicity to host cells; indeed, many studies have found that such NPs can kill parasites at concentrations that are relatively non-toxic to mammalian cells. Beyond protozoa, green ZnO and Ag NPs have shown larvicidal activity against mosquito larvae (e.g., Anopheles and Aedes species), opening the door to eco-friendly vector control strategies to combat malaria and dengue. Even in veterinary and agricultural contexts, plant-synthesized NPs are being explored to treat parasitic infections in animals or to protect crops by targeting nematodes and other pests.
Overall, **antimicrobial and antiparasitic applications** are among the most advanced uses of green nanoparticles. Numerous studies have confirmed that these biogenic NPs possess strong activity against pathogens, sometimes rivaling or exceeding traditional antimicrobials. Given the global rise of antibiotic resistance, green NPs are being investigated as novel nano-antibiotics or as adjuncts to existing antibiotics (some AgNPs have been shown to re-sensitize drug-resistant bacteria to antibiotics). Comprehensive reviews in 2022 have emphasized that plant-based nanoparticles represent a “safer” and potent approach to combating resistant microbes, with research showing their efficacy against a broad spectrum of bacteria and viruses (including influenza and herpes viruses). While further in vivo studies and toxicity assessments are needed, the current evidence supports the incorporation of green-synthesized NPs into next-generation antimicrobial therapies and materials.

Anticancer and Drug Delivery Applications
Cytotoxic and Anticancer Effects: The application of nanoparticles in cancer therapy is a major focus of nanomedicine. Green-synthesized nanoparticles have demonstrated the ability to selectively kill cancer cells through various mechanisms. For example, **ZnO nanoparticles from Cassia auriculata** (Table 1) significantly enhanced the tumoricidal effect on human breast cancer (MCF-7) cells while having minimal toxicity on normal breast cells (MCF-12A). The mechanism in that study was linked to the generation of oxidative stress by the ZnO NPs, leading to apoptosis in cancer cells. Similarly, green-synthesized gold nanoparticles have been widely studied for anticancer activity. AuNPs made using Terminalia arjuna bark extract (to cite another example) were shown to induce apoptosis in lung carcinoma cells via mitochondrial pathway activation, all while exhibiting negligible toxicity in normal fibroblasts. Many plant-based NPs appear to exploit oxidative stress and mitochondrial damage to preferentially trigger cancer cell death – cancer cells often have higher baseline ROS and weakened antioxidant defenses, making them more susceptible to nanoparticle-induced oxidative damage. Additionally, some phytochemicals on the NP surface may have intrinsic anticancer properties (e.g., epigallocatechin from green tea or curcumin from turmeric-coated NPs can contribute to anti-proliferative effects).
Green silver nanoparticles have also shown cytotoxic effects against a variety of cancer cell lines, including breast, liver, cervical, and colon cancers. AgNPs can attach to cell membranes and modulate signaling pathways or directly enter cells and cause DNA damage and apoptosis. A notable example involved **green AgNPs using Dalbergia spinosa** leaf extract that exhibited dose-dependent killing of human cervical cancer cells, attributed to DNA fragmentation and caspase activation, while causing significantly less harm to normal cells at equivalent doses (due to the protective effect of the phytochemical corona). Plant-mediated **copper oxide nanoparticles** have likewise been explored; for instance, CuO NPs synthesized via Tamarindus indica leaves showed higher cytotoxicity against breast and lung carcinoma cells than chemically made CuO, presumably due to the smaller size and plant-based capping, although their use will require careful toxicity evaluation to ensure safety for normal tissue.

In **in vivo** contexts, some green NPs have progressed to animal model testing. There are reports of plant-synthesized AuNPs that, when functionalized with targeting ligands, accumulated in tumors and enhanced the efficacy of photothermal therapy – converting laser light into heat to ablate cancer cells. Another intriguing application is using green NPs as **nano-antioxidants** to mitigate oxidative stress-related diseases, including cancer: for example, biogenic cerium oxide (CeO_2) NPs can scavenge ROS in normal cells (protecting them) while still exerting oxidative stress in the acidic tumor microenvironment, thus acting as smart anti-cancer agents. This area is still emerging, but it highlights the potential sophistication of plant-based nanomedicine strategies.

Drug Delivery and Therapeutic Nanocarriers: Beyond directly killing pathogens or tumor cells, plant-based nanoparticles can serve as carriers for drugs, genes, or therapeutic molecules. Their biocompatible coatings and functional surfaces make them suitable for **drug delivery systems**. For instance, green-synthesized AuNPs have been loaded with chemotherapeutic drugs (like doxorubicin) or photosensitizers for combined drug/nanoparticle therapy, showing improved drug targeting and reduced side effects. The phytochemical cap can sometimes facilitate a degree of targeting; for example, folate-presenting compounds in a plant extract could lead to folate-coated NPs that specifically bind to cancer cells overexpressing folate receptors. Researchers have also experimented with attaching plant-based NPs to antibodies or peptides post-synthesis to create targeted nanoconjugates for delivering drugs to specific cell types.

Another promising avenue is using **magnetic iron oxide NPs** synthesized by plant methods for combined diagnostic and therapeutic ("theranostic") purposes. Green iron oxide NPs can be used as MRI contrast agents and simultaneously as carriers for delivering anti-cancer drugs or for hyperthermia treatment (where an alternating magnetic field heats the NPs to kill cancer cells). For instance, iron oxide NPs made with Azadirachta indica (neem) leaf extract have been studied for magnetic hyperthermia therapy, demonstrating effective tumor temperature elevation in lab models along with MRI traceability, all with a plant-based benign synthesis route.

Plant-derived NPs are also being applied in **gene delivery**. Chitosan-coated gold NPs (where gold was green-synthesized and then coated) have delivered small interfering RNA (siRNA) into cancer cells, achieving gene silencing with minimal toxicity. The mild synthesis conditions help preserve sensitive cargo molecules that might be loaded during NP formation (e.g., some protocols mix plant extract and metal salt in the presence of a drug or gene, encapsulating it as the NP forms).

Finally, it's worth noting the use of plant-based **nanoparticles in imaging and diagnostics**. Fluorescent or plasmonic NPs (like green-made AuNPs) have been used for bioimaging; for instance, gold and silver NPs have unique optical signatures that can enhance contrast in techniques like optical coherence tomography or as probes in lateral flow diagnostic kits. The phytochemical layer can aid in bioconjugation of targeting molecules for imaging specific tissues or pathogens. While these applications are still under development, they illustrate the versatility of green NPs in the biomedical arena.

Other Biomedical Applications

Beyond the major categories above, plant-synthesized nanoparticles find several niche yet important biomedical applications:

- **Anti-Inflammatory and Healing**: Many phytochemicals are anti-inflammatory; when they cap NPs, they can direct the NPs to modulate inflammatory responses. Green AgNPs have shown anti-inflammatory effects in models of skin irritation and wound healing. For example, a green silver NP ointment using Calendula flower extract not only prevented infection in wounds but also reduced inflammation and promoted faster wound closure compared to controls, attributed to the combined antimicrobial and anti-inflammatory action of the NP preparation. Similarly, ZnO NPs capped with plant polyphenols have been reported to decrease inflammatory cytokine production in activated immune cells, indicating potential use in treating inflammatory diseases (with careful dosing).
- **Vaccines and Immunomodulation**: Nanoparticles can serve as adjuvants or carriers in vaccines. Some studies have used plant-based NPs to present antigens to the immune system, improving vaccine efficacy. A recent study formulated a nanovaccine using green-synthesized gold NPs linked with a viral antigen; the AuNP acted as both carrier and adjuvant, resulting in a stronger immune response in mice than the antigen alone. The advantage of green NPs here is their lower toxicity and ease of functionalization. While this application is in early stages, it could be impactful for developing safer nanovaccines.

- **Environmental and Food Safety in Healthcare Context**: In hospital environments, plant-based NPs are being tested for coating surfaces, masks, or fabrics to render them antimicrobial (important for infection control). A notable example during the COVID-19 pandemic was the integration of green-synthesized AgNPs into face mask filters to inactivate viruses and bacteria on contact. Likewise, plant-based NPs (like Ag or ZnO) are being explored for food packaging materials to prevent microbial growth, thereby protecting food safety – an intersection of biomedical and environmental application.
- **Cosmetics and Dermatology**: The cosmeceutical industry has interest in green NPs for skincare, given their antimicrobial and anti-aging properties. For instance, plant-derived gold NPs are incorporated in some topical formulations for their purported skin benefits (anti-wrinkle, antioxidant), and silver NPs for acne treatment. The natural origin of these NPs is a marketing and safety advantage in this space.

It is clear that plant-based nanoparticles have permeated various facets of biomedicine, from fighting infections and cancer to aiding in drug delivery and diagnostics. The examples discussed underscore the principal benefits of green NPs: multi-functionality, biocompatibility, and efficacy. However, translating these promising lab results into clinical or commercial products requires addressing certain challenges and knowledge gaps, as discussed in the next section.

Future Perspectives and Challenges

Plant-based green synthesis of nanoparticles, while highly promising, faces several **challenges** that must be overcome to fully realize its potential in practical biomedical applications. A primary concern is **scalability and reproducibility**. Biological synthesis methods can suffer from batch-to-batch variability due to changes in plant metabolite composition (influenced by season, geography, extraction method, etc.). Ensuring consistent nanoparticle characteristics at large-scale production is non-trivial. Efforts are needed to standardize plant extract preparation and perhaps to identify specific key phytochemicals that can be quantified as markers for reproducibility. The implementation of good manufacturing practices (GMP) for botanically derived nanomaterials will be crucial. As Parab et al. (2024) note, current green synthesis technologies have "limitations in terms of scalability, reproducibility and standardization", which must be addressed through engineering solutions and rigorous process control.

Another challenge is the **comprehensive evaluation of toxicity and biocompatibility**. While plant-capped NPs are generally less toxic than their chemically synthesized counterparts, they are not automatically safe. Detailed in vivo studies are required to assess the biodistribution, pharmacokinetics, and long-term fate of these nanoparticles in the body. For instance, a green CuO NP might show potent anti-cancer effects but could also accumulate in the liver or kidneys; determining the safe dosage window is important. Letchumanan et al. (2021) highlighted that although plant-based Cu/CuO NPs have therapeutic benefits, their toxicity to normal cells and organs at higher doses is a concern, and careful toxicological profiling is needed. Similar cautions apply to other NPs: even silver NPs, if over-accumulated, can cause argyria or oxidative stress in healthy tissues. **Regulatory approval** for medical use will hinge on thorough toxicology data. One future direction is to develop **in situ coatings or 'stealth' strategies** (using biocompatible polymers like PEG or natural proteins) on green NPs to further reduce any off-target effects and immune clearance, without negating their green synthesis advantages.

Improving the **targeting and specificity** of plant-based nanoparticles is another area for future work. Currently, many studies simply apply NPs to cells or animals and observe effects. In a clinical scenario, delivering NPs to the right site (e.g., a tumor or an infection site) while minimizing systemic exposure is key. This could be achieved by conjugating targeting ligands (antibodies, peptides) to the phytochemical coat of NPs or by designing stimuli-responsive green NPs that release drugs only in specific conditions (like the acidic tumor microenvironment). The combination of green synthesis with advanced nanotechnological design (such as core-shell structures, magnetic guidance, or photoactivatable systems) is a fertile ground for innovation. For example, one could envision a plant-synthesized iron oxide core coated with gold and plant polyphenols, which could be guided by a magnet to a tumor and then used for photothermal ablation – a multi-modal therapy platform.

From a technological standpoint, integrating **machine learning and automation** in green synthesis could markedly accelerate progress. Machine learning algorithms can help in optimizing the synthesis parameters by predicting outcomes based on experimental datasets, thereby reducing trial-and-error in discovering optimal conditions. They can also assist in elucidating the relationships between extract composition and NP properties, guiding the selection of plant sources for specific nanoparticle needs. In the next few years, we might see automated microreactor systems that produce plant-based NPs with feedback control, ensuring each batch meets certain size and concentration specifications – an essential step for industrial viability.

Future perspectives for applications are equally exciting. In antimicrobial therapy, green NPs could be used in synergy with antibiotics to revive old antibiotics' effectiveness against resistant strains (acting as nano-antibiotic boosters). In cancer, the marriage of immunotherapy and green nanotechnology might yield **nano-immunomodulators** that both kill tumor cells and stimulate an anti-tumor immune response. With the growing emphasis on sustainability, even the pharmaceutical and biotech industries are interested in "green" nanomaterials that align with eco-friendly production; plant-based NPs could find niche markets in environmentally conscious healthcare products.

However, to translate these perspectives into reality, researchers must address the current **limitations** head-on. Green synthesis techniques need to be refined and standardized so that they can produce medical-grade nanoparticles under controlled conditions (meeting purity, sterility, and consistency requirements of regulatory bodies). Collaboration between nanotechnologists, botanists, pharmacologists, and chemical engineers will be vital to overcome these interdisciplinary challenges. It will also be important to establish clear regulatory guidelines for plant-based nanomaterials – currently, the regulatory framework for nanomedicines is still evolving, and introducing complex biological synthesis adds another layer of complexity that regulators will consider.

In summary, the future of plant-based nanoparticle synthesis is bright, with immense potential to contribute to sustainable and effective healthcare solutions. As one review aptly stated, green synthesis is not just a bench-top curiosity but "represents a promising direction for sustainable nanotechnology". By surmounting the hurdles of scalability, standardization, and comprehensive safety profiling, plant-derived nanoparticles could move from laboratory research to mainstream clinical and commercial use, embodying the principles of green chemistry while addressing critical needs in medicine. The continued advancement of this field will require careful balancing of innovation with validation, but its trajectory suggests that greener nanomedicine is on the horizon.

CONCLUSION

Plant-based green synthesis of nanoparticles has transitioned from a novel concept to a robust field of study producing a wide variety of functional nanomaterials. This review outlined how plant extracts can serve as bio-factories for nanoparticles, leveraging nature's diversity to create NPs that are effective in antimicrobial, anticancer, and other biomedical applications. Recent advances have expanded our toolkit for synthesizing and tuning these nanoparticles, while numerous studies have validated their potent biological activities – from killing drug-resistant microbes to selectively targeting cancer cells. Equally important, green-synthesized NPs offer an approach that is aligned with sustainability and reduced toxicity, key considerations for future medical technologies.

Despite the demonstrable successes, the journey towards fully integrating plant-based nanoparticles into medicine continues. Challenges like ensuring reproducible large-scale production, thoroughly understanding in vivo behavior, and meeting regulatory standards must be addressed. Ongoing research is actively targeting these issues, and interdisciplinary efforts are paving the way to clinical translation. In looking ahead, the convergence of green nanotechnology with advanced biomedical engineering and computational optimization holds great promise.

In conclusion, **plant-based nanoparticles exemplify the synergy between traditional botanical knowledge and cutting-edge nanoscience**. They offer a pathway to create next-generation therapeutics and diagnostics that are both effective and environmentally conscious. With sustained research and development, what is now an innovative "green" alternative could soon become a mainstream method for producing nanomedicines, fulfilling the dual goals of improving human health and maintaining ecological responsibility.

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