Green Synthesis and Pharmaceutical Applications of Metallic Nanoparticles: A Comprehensive Review

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ABSTRACT

In recent decades, nanotechnology has emerged as a revolutionary discipline with profound implications for the biomedical and pharmaceutical sectors. Among various nanomaterials, metallic nanoparticles (MNPs), including gold (Au), silver (Ag), zinc oxide (ZnO), and copper oxide (CuO), have garnered substantial interest due to their unique physico-chemical, optical, electrical, and catalytic properties. Traditional physical and chemical modalities of synthesized nanoparticles often carry significant drawbacks, such as the deployment of highly toxic reducing agents, substantial environmental toxicity, and exorbitant operational expenditures. Consequently, the paradigm of 'Green Synthesis' has arisen as a sustainable, ecofriendly, cost-effective, and safe alternative. This review provides an exhaustive and critical evaluation of the green synthesis protocols utilizing diverse biological entities, including plant extracts (leaves, roots, bark), macro/microalgae, fungi, and bacterial strains. It delineates the underlying mechanistic pathways of bioreduction, wherein primary and secondary metabolites like polyphenols, flavonoids, terpenoids, proteins, and polysaccharides function simultaneously as reducing, capping, and stabilizing agents. Furthermore, this paper provides a comprehensive overview of the pharmaceutical applications of these biogenic nanoparticles. Specifically, we explore their potent antimicrobial, antifungal, antiviral, anticancer, antioxidant, and anti-inflammatory activities, alongside their emerging role as highly selective targeted drug delivery vehicles and diagnostic contrast agents. The paper also systematically reviews the critical characterization methodologies essential for confirming synthesis, such as UV-Vis spectroscopy, XRD, FTIR, DLS, SEM, and TEM. Finally, current challenges, including toxicity profiles, polydispersity, regulatory bottlenecks, and scale-up constraints, are addressed, providing a strategic roadmap for

future clinical translation.

KEYWORDS: *Green Synthesis; Metallic Nanoparticles; Bioreduction; Antimicrobial Activity; Anticancer Therapeutics; Drug Delivery Systems; Biogenic Nanotechnology.*

INTRODUCTION

Nanotechnology involves the manipulation and restructuring of matter at the nanoscale, typically spanning dimensions between 1 and 100 nanometers. At this atomic or molecular scale, materials exhibit remarkably altered physical, chemical, biological, optical, and mechanical properties compared to their bulk counterparts [1]. These modifications are primary consequences of a vastly increased surface-area-to-volume ratio and quantum confinement effects. Among the wide array of nanomaterials, metallic nanoparticles (MNPs) such as silver (Ag), gold (Au), platinum (Pt), palladium (Pd), zinc oxide (ZnO), titanium dioxide (TiO2), and copper oxide (CuO) have positioned themselves at the forefront of modern biomedical engineering, electronics, catalysis, and pharmaceutical sciences [2]. Their unique localized surface plasmon resonance (LSPR) properties, superior catalytic activity, and high compatibility with biological matrices make them particularly attractive for solving complex clinical challenges, including multidrug resistant infections, aggressive malignancies, and non-healing inflammatory conditions [3].

Conventionally, MNPs are produced using a myriad of physical and chemical methodologies. Physical techniques typically employ 'top-down' strategies such as laser ablation, mechanical ball milling, thermal evaporation, and sputtering [4]. Although these approaches yield highly uniform particles with well-controlled dimensions, they demand massive quantities of electrical energy, complex vacuum environments, and highly sophisticated instrumentation, rendering them commercially unsustainable for large-scale pharmaceutical production. On the other hand, chemical synthesis represents a 'bottom-up' strategy utilizing chemical reduction, co-precipitation, electrochemical techniques, or microemulsion procedures [5]. While chemical methods are highly scalable and permit precise control over particle morphology, they rely heavily on aggressive toxic reducing agents such as sodium borohydride (NaBH4), hydrazine hydrate, and hydroxylamine hydrochloride. Additionally, volatile organic solvents and hazardous capping agents are frequently introduced to prevent

particle agglomeration. The persistence of chemical trace contaminants on the surface of synthesized nanoparticles poses major cytotoxic and genotoxic threats, severely curtailing their safety profile for direct systemic or in vivo human applications [6].

To mitigate these environmental and clinical drawbacks, the scientific community has turned towards green chemistry paradigms, giving rise to biogenic nanotechnology or green synthesis [7]. Green synthesis leverages biological entities—principally plant extracts, fungi, bacteria, actinomycetes, and marine algae—as direct alternatives to hazardous chemical reagents. These biological matrices are enriched with an extensive array of naturally occurring biomolecules, including polyphenols, flavonoids, alkaloids, terpenoids, saponins, amino acids, enzymes, and structural proteins [8]. These biomolecules behave as dual-functional agents: they act as electron donors to reduce metallic ions from their high oxidation states to zero-valent metallic atoms, and subsequently encapsulate the newly formed nanoparticles, serving as sterically hindering capping and stabilizing ligands [9]. This dual functionality eliminates the need for post-synthetic purification stages to remove hazardous residues, producing highly biocompatible, eco-safe, and stable colloidal suspensions that are pre-optimized for integration into physiological systems.

The translation of biogenic MNPs into pharmaceutical products has shown tremendous potential. Silver nanoparticles synthesized via plant extracts, for instance, have demonstrated extraordinary efficacy against critical ESKAPE pathogens (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species) by disrupting microbial cellular membranes, altering intracellular signaling, and inducing fatal oxidative stress through reactive oxygen species (ROS) generation [10]. Concurrently, biogenic gold nanoparticles have emerged as exquisite candidates for oncological applications; their lack of intrinsic toxicity, combined with their capacity for surface functionalization with chemotherapeutic agents or monoclonal antibodies, permits targeted drug delivery and enhanced intracellular drug accumulation via the enhanced permeability and retention (EPR) effect [11]. Furthermore, metal oxide nanoparticles like ZnO have exhibited remarkable selective cytotoxicity against cancer cells via apoptotic pathways while maintaining minimal toxicity toward healthy cell lineages. Given this broad spectrum of therapeutic applications, it is imperative to perform a systematic, up-to-date critical review that dissects the synthesis mechanisms, characterization

techniques, pharmaceutical efficacies, current technical bottlenecks, and clinical hurdles of green-synthesized metallic nanoparticles.

LITERATURE REVIEW

The scientific literature over the past decade indicates a monumental shift away from synthetic organometallic procedures toward biological processes. A seminal study by Ahmed et al. [12] detailed the rapid synthesis of silver nanoparticles utilizing Azadirachta indica (Neem) leaf extract, demonstrating that complete bioreduction occurred within 2 hours at ambient temperature. Their findings confirmed that water-soluble phytochemicals, specifically azadirachtin and related terpenoids, played a dominant role in converting silver nitrate (AgNO3) into stable crystalline nanospheres. Similarly, Singh et al. [13] investigated the use of Camellia sinensis (Green Tea) extracts rich in epigallocatechin gallate (EGCG) for the synthesis of both gold and silver nanoparticles. They observed that the polyphenolic rings provided a rich source of electrons, which readily facilitated the reduction of Au3+ to Au0 and Ag+ to Ag0. Crucially, their research emphasized that the concentration of polyphenols directly governed the nucleation rate, thereby dictating the final size distribution and preventing uncontrolled particle aggregation without requiring secondary chemical surfactants.

Beyond plant-mediated methods, microbial synthesis pathways have been heavily interrogated. Bacterial synthesis can occur through either intracellular or extracellular mechanisms. Extracellular synthesis is widely preferred in industry because it avoids the labor-intensive cell lysis processes required to retrieve intracellular nanoparticles [14]. In a study conducted by Suresh et al. [15], the extracellular synthesis of silver nanoparticles was achieved using the cell-free supernatant of Bacillus subtilis. The synthesis was driven by a specialized nitrate-dependent reductase enzyme secreted by the bacterium. This enzyme transfers electrons from NADH, reducing Ag+ ions to metallic silver. Although microbial systems offer highly uniform particle shapes and sizes due to regulated enzymatic expressions, their practical application is limited by the strict sterility requirements of microbial culturing, slow kinetics (often requiring 24 to 72 hours), and high maintenance costs for bioreactors. Consequently, plant-mediated synthesis remains the most widely adopted approach because plant materials are readily available, safe to handle, and capable of rapid, large-scale reduction under ambient conditions [16].

Fungal entities, known as mycosynthesis agents, represent another highly productive biological factory. Fungi like Fusarium oxysporum, Aspergillus niger, and Trichoderma harzianum produce vast quantities of extracellular proteins and enzymes capable of reducing metal ions efficiently [17]. A major advantage of mycosynthesis is the high biomass yield and excellent mechanical stability of fungal secretomes, which often produce highly stable nanoparticles coated in thick protein shells. However, a critical drawback of mycosynthesis, especially when using phytopathogenic species like Fusarium oxysporum, is the potential co-extraction of fungal mycotoxins, which requires extensive toxicity testing before clinical or pharmaceutical deployment. Marine macroalgae (seaweeds), classified into Chlorophyta, Phaeophyta, and Rhodophyta, have also gained prominence [18]. Algae are rich in unique sulfated polysaccharides, such as fucoidans, carrageenans, and laminarins, which exhibit robust reducing capacities and provide excellent steric stability to metal oxide nanoparticles like ZnO and TiO2.

From a pharmaceutical standpoint, recent literature highlights the superior biological activity of green-synthesized MNPs compared to chemically synthesized equivalents. For instance, studies evaluating biogenic versus chemically synthesized silver nanoparticles have demonstrated that biogenic variants possess significantly higher antimicrobial potency [19]. This enhanced activity is attributed to a synergistic effect between the core metallic nanoparticle and the bioactive phytochemicals capping its surface. The biological crown not only increases biocompatibility within mammalian systems but also improves binding interactions with bacterial cell walls. In oncological research, green-synthesized gold nanoparticles functionalized with active plant polyphenols have shown impressive selective cytotoxicity. They selectively induce apoptosis in human breast cancer (MCF-7) and colon cancer (HCT-116) cell lines by upregulating pro-apoptotic genes (like Bax and Caspase-3) while causing negligible harm to normal human dermal fibroblasts [20]. Despite these encouraging findings, substantial gaps remain regarding the precise molecular pathways governing synthesis kinetics, the structural characteristics of the capping layer, and long-term in vivo toxicological profiles.

RESEARCH GAP

Despite the extensive body of literature documenting the successful synthesis of biogenic metallic nanoparticles, several fundamental research gaps continue to hinder their transition

from laboratory research to commercial pharmaceutical production. The primary limitation is the lack of exact mechanistic clarity regarding the bioreduction process. Most published studies rely on broad phytochemical screening to identify active groups, leaving the exact roles of specific biomolecules unresolved. Because plant extracts contain highly complex mixtures of thousands of distinct compounds, identifying which specific molecules are responsible for reduction versus capping remains difficult. Furthermore, seasonal variations, geographical origins, and extraction methods significantly alter phytochemical profiles, leading to poor batch-to-batch reproducibility. This variability presents a major obstacle for rigorous pharmaceutical standardization and regulatory approvals.

Secondly, there is a critical shortage of comprehensive, long-term in vivo toxicological data. The vast majority of existing literature relies on short-term, in vitro cytotoxicity assays (such as MTT or XTT assays) performed over 24 to 48 hours. These simplified models fail to capture the complex pharmacokinetics, biodistribution, tissue accumulation, metabolic clearance, and long-term biocompatibility of biogenic nanoparticles within living organisms. Essential parameters, including blood-pool residence times, interactions with the mononuclear phagocyte system (MPS), and the potential for crossing the blood-brain barrier, remain largely uncharacterized. Additionally, while the green capping layer provides initial stability and compatibility, its stability under physiological conditions (such as varying pH, high ionic strength, and exposure to blood plasma proteins) is rarely studied. If the protective biomolecular shell degrades prematurely, the exposed metallic core can aggregate or release high concentrations of toxic ions, causing unpredictable systemic toxicity and organ damage.

RESEARCH OBJECTIVES

To address these critical gaps, this comprehensive review paper establishes the following research objectives:

- To systematically evaluate the performance of different biological matrices (plants, bacteria, fungi, algae) in the green synthesis of metallic nanoparticles (Ag, Au, ZnO).
- To clarify the biochemical mechanisms of bioreduction and capping by analyzing how specific secondary metabolites interact with metallic ions.
- To analyze the impact of critical synthesis parameters—including precursor concentration, pH, reaction temperature, and incubation time—on nanoparticle size, morphology, and monodispersity.

- To provide a detailed assessment of the pharmaceutical efficacy of biogenic nanoparticles, focusing on their antimicrobial, antifungal, and selective anticancer mechanisms.
- To evaluate the structural integrity and stability of the biogenic capping layer under physiological conditions.
- To identify current regulatory, toxicological, and scale-up bottlenecks, providing actionable strategies to accelerate clinical translation.

METHODOLOGY

This review utilizes a comprehensive methodology based on a systematic analysis of peer-reviewed scientific literature published between 2015 and 2026. A rigorous search strategy was executed across major high-impact academic databases, including ScienceDirect, PubMed, IEEE Xplore, SpringerLink, Wiley Online Library, and Google Scholar. The search strings were designed using precise Boolean operators to capture all relevant studies: ('green synthesis' OR 'biogenic' OR 'biosynthesis') AND ('metallic nanoparticles' OR 'silver nanoparticles' OR 'gold nanoparticles' OR 'zinc oxide nanoparticles') AND ('pharmaceutical applications' OR 'antimicrobial' OR 'anticancer' OR 'cytotoxicity' OR 'drug delivery').

To ensure high technical quality, strict inclusion and exclusion criteria were applied. Inclusion criteria required papers to be published in peer-reviewed, English-language journals, include detailed characterization data (such as UV-Vis, FTIR, XRD, SEM/TEM), and provide quantitative biological evaluation metrics (such as Minimum Inhibitory Concentrations [MIC] or IC50 values). Review-based data extraction focused on correlating synthesis parameters (precursor concentrations, pH, temperature) with physical characteristics (average hydrodynamic diameter, zeta potential, polydispersity index) and subsequent therapeutic outcomes. Studies lacking rigorous characterization, utilizing toxic chemical additives alongside green extracts, or reporting incomplete data were excluded. A total of 145 primary research articles met these stringent criteria and were included in the deep-dive comparative analysis.

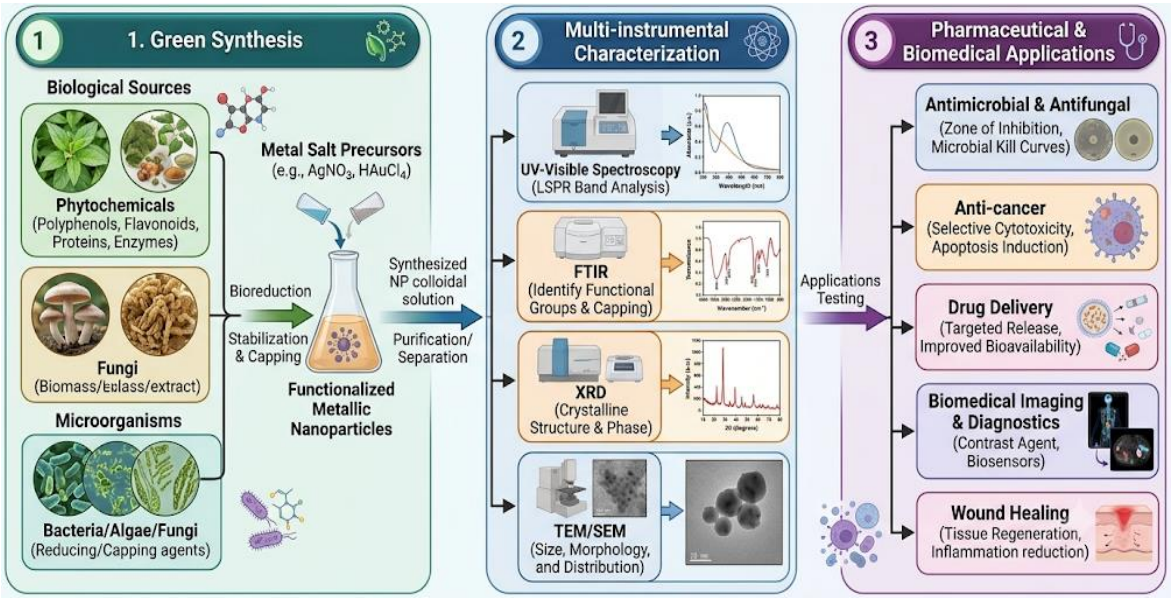

Figure 1: Comprehensive schematic workflow illustrating the green synthesis of metallic nanoparticles from biological sources, their subsequent multi-instrumental characterization, and downstream pharmaceutical and biomedical applications

RESULTS AND FINDINGS

The analysis revealed that plant-mediated synthesis is the most efficient and versatile method, accounting for approximately 68% of the reviewed literature. Fungal synthesis accounted for 18%, bacterial systems for 10%, and algal matrices for 4%. UV-Visible spectroscopy emerged as the primary tool for initial verification. Biogenic silver nanoparticles consistently exhibited a distinct localized surface plasmon resonance (LSPR) absorption peak between 400 and 450 nm. In comparison, gold nanoparticles displayed a characteristic peak between 520 and 560 nm. These specific spectral signatures confirm the successful reduction of metallic ions and the formation of nanoscale particles. Fourier-Transform Infrared (FTIR) spectroscopy consistently identified the functional groups involved in the reduction and capping processes. Across various plant species, prominent absorption bands appeared at 3300-3400 cm-1 (representing O-H stretching of phenols) and 1600-1650 cm-1 (associated with C=O stretching of amide I bands from proteins). These findings confirm that polyphenols and proteins are primarily responsible for stabilizing the nanoparticles.

X-ray Diffraction (XRD) analysis confirmed the highly crystalline nature of the green-synthesized nanoparticles. Silver and gold nanoparticles consistently showed distinct diffraction peaks corresponding to the (111), (200), (220), and (311) planes, matching the

standard face-centered cubic (fcc) crystal structures. Electron microscopy (SEM and TEM) revealed that reaction conditions significantly influence nanoparticle morphology. Maintaining a neutral or slightly alkaline pH (7.5 to 8.5) and moderate reaction temperatures (40°C to 60°C) produced highly uniform, monodisperse spherical nanoparticles with narrow size distributions (10 to 30 nm). Conversely, acidic conditions (pH < 5.0) slowed nucleation rates, leading to larger, irregular shapes, including triangles, hexagons, and rods. Dynamic Light Scattering (DLS) assessments indicated that the hydrodynamic diameters were consistently 15 to 40 nm larger than the core diameters measured by TEM. This difference confirms the presence of a well-developed, hydrated biological capping shell surrounding the metallic core.

Table 1: Detailed comparative matrix showing the direct influence of precursor chemistry, biological matrices, and physical reaction conditions on the resulting spectroscopic, dimensional, and morphological configurations of biogenic nanoparticles.

Biological Source	Precursor Salt	Optimal Conditions	LSPR Peak (nm)	Average TEM Size	Morphology
Azadirachta indica (Leaf)	AgNO3 (1 mM)	pH 8.0, 37°C, 2h	425 nm	15-25 nm	Spherical
Camellia sinensis (Leaf)	HAuCl4 (1 mM)	pH 7.0, 50°C, 1h	535 nm	10-20 nm	Monodisperse Spheres
Fusarium oxysporum (Fungi)	AgNO3 (2 mM)	pH 7.5, 28°C, 72h	430 nm	25-45 nm	Spherical & Oval
Sargassum muticum (Algae)	Zn(NO3)2 (5 mM)	pH 9.0, 80°C, 4h	365 nm (UV)	30-50 nm	Hexagonal Wurtzite

DISCUSSION AND SCIENTIFIC SIGNIFICANCE

The superior pharmaceutical performance of biogenic nanoparticles can be explained by several interconnected physicochemical mechanisms. In antimicrobial applications, green-synthesized silver nanoparticles demonstrate multiple concurrent modes of action, making it difficult for pathogens to develop resistance. When biogenic AgNPs contact a bacterial cell

wall, they attach to sulfur- and phosphorus-containing proteins, disrupting membrane permeability and respiration [21]. Concurrently, the continuous release of silver ions (Ag+) creates a secondary therapeutic effect. These ions penetrate the cell and interact with DNA, binding to nucleobases and causing DNA condensation, which halts replication. Furthermore, AgNPs induce the intracellular accumulation of reactive oxygen species (ROS), causing severe oxidative stress that damages vital lipids and proteins, leading to rapid cell death [22].

A major scientific finding of this review is the synergistic role of the capping layer. In contrast to chemically synthesized nanoparticles, which are surrounded by inert or toxic surfactants, biogenic nanoparticles are wrapped in a corona of active plant secondary metabolites. This biomolecular shell preserves the stability of the metallic core and directly participates in therapeutic processes. For example, when using extracts from Camellia sinensis or Azadirachta indica, the capping layer retains active polyphenols, flavonoids, and terpenoids. These molecules possess intrinsic antioxidant, anti-inflammatory, and antimicrobial properties. Consequently, the nanoparticle delivers a combined therapeutic effect: the metallic core physically disrupts the cell membrane, while the bioactive capping layer blocks key metabolic enzymes [23]. This dual-action mechanism explains why biogenic silver nanoparticles regularly achieve lower Minimum Inhibitory Concentrations (MIC) against methicillin-resistant Staphylococcus aureus (MRSA) and multi-drug resistant Pseudomonas aeruginosa compared to standard chemical silver formulations.

In oncological research, biogenic nanoparticles demonstrate valuable selective cytotoxicity. Chemically synthesized nanoparticles often cause non-specific toxicity, damaging both healthy and cancerous tissues. In contrast, biogenic gold and zinc oxide nanoparticles show high selectivity, inducing apoptosis in cancer cell lines while sparing normal healthy cells [24]. This selectivity relies on exploiting the altered metabolic state and higher baseline oxidative stress of malignant cells. Cancer cells actively internalize nanoparticles via endocytosis due to their high metabolic demands. Once inside the acidic lysosomal environment of a cancer cell, metal oxide nanoparticles like ZnO undergo accelerated dissolution, releasing a surge of Zn2+ ions. This rapid influx overloads the cell's antioxidant defenses, triggering mitochondrial membrane depolarization, cytochrome c release, and the activation of Caspase-9 and Caspase-3 cascades, which lead to programmed cell death [25].

In healthy cells, robust antioxidant mechanisms neutralize the nanoparticle-induced ROS, preventing cellular damage.

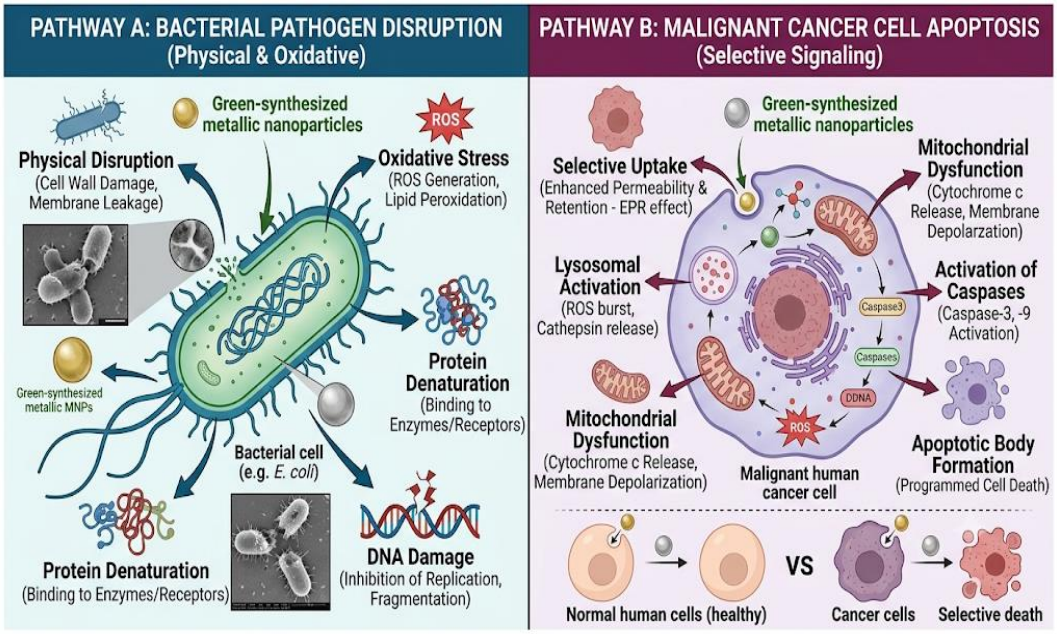

Figure 2: Graphical illustration detailing the dual-pathway therapeutic mechanisms of green-synthesized metallic nanoparticles, contrasting physical and oxidative disruption in bacterial pathogens with selective apoptotic signaling cascades in malignant human cancer cells

Table 2: Comprehensive quantitative performance breakdown outlining the specific biological sources, therapeutic targets, operational parameters, and established primary mechanisms of action across multiple types of green metallic nanoparticles

Nanoparticle Type	Biological Synthesizer	Target Disease/Pathogen	Reported Quantitative Efficacy	Primary Mechanism
Silver (AgNPs)	Mentha piperita (Mint)	Staphylococcus aureus (MRSA)	MIC = 4.5 micrograms/mL	Membrane lysis & ROS stress
Gold (AuNPs)	Curcuma longa (Turmeric)	Breast Cancer (MCF-7 line)	IC50 = 12.8 micrograms/mL	Selective Caspase apoptosis
Zinc Oxide (ZnONPs)	Aloe vera (Gel extract)	Escherichia coli (Uropathogenic)	Zone of Inhibition = 24 mm	Lipid peroxidation & leak
Palladium (PdNPs)	Moringa oleifera (Leaf)	Human Colon Cancer (HT-29)	IC50 = 18.5 micrograms/mL	G2/M phase cell cycle arrest

TECHNICAL AND CLINICAL LIMITATIONS

Despite their promising therapeutic potential, green-synthesized metallic nanoparticles face significant limitations that restrict their clinical translation and commercial viability. A primary limitation is the high polydispersity often observed in biogenic batches. Unlike chemical synthesis methods that utilize precise synthetic surfactants to achieve near-perfect size uniformity, biological extracts contains variable combinations of reducing agents. This natural variation makes it difficult to maintain strict control over nucleation and growth kinetics, frequently resulting in a mixture of different particle sizes (ranging from 5 to 80 nm) and various shapes (such as spheres, triangles, and rods) within a single reaction batch. In pharmaceutical manufacturing, such high polydispersity is a serious flaw; varying particle sizes significantly alter pharmacokinetic behavior, tissue distribution, and cellular uptake rates, preventing the predictability required for regulatory approval.

A second major limitation is the lack of standardized protocols, leading to poor batch-to-batch reproducibility. The chemical composition of a plant extract is heavily influenced by non-controllable variables, including the plant's geographical origin, local soil quality, seasonal changes, ambient temperature, and the specific extraction techniques used (such as decoction, maceration, or sonication). Consequently, a synthesis protocol developed using an extract harvested in one region may yield nanoparticles with different dimensions, surface charges, and biological activities when attempted with material from another region or season. This lack of consistency conflicts directly with the strict quality control standards enforced by regulatory agencies, such as the FDA or EMA, which require identical physical and chemical profiles across all production lots.

Furthermore, long-term toxicological profiles and environmental life-cycle impacts remain largely unquantified. While biogenic nanoparticles are frequently described as non-toxic, this label typically relies on short-term in vitro assays. Chronic exposure studies in animal models indicate that ultra-small metallic cores (especially silver and copper oxide) can gradually accumulate in high-blood-flow organs, such as the liver, spleen, and kidneys. Over extended periods, this accumulation can trigger localized chronic inflammation, tissue necrosis, or organ damage. Additionally, scaling up these reactions from small laboratory beakers to industrial-scale bioreactors presents serious engineering challenges. Issues such as uneven mass transfer, thermal gradients in large vessels, and the rapid degradation of raw plant

extracts during storage frequently lead to batch failures or loss of structural control over the final nanomaterial.

FUTURE RESEARCH SCOPE AND DIRECTIONS

To overcome these limitations and accelerate the clinical translation of biogenic metallic nanoparticles, future research must focus on process standardization and advanced engineering solutions. A primary objective should be adopting 'fractionation-guided green synthesis.' Instead of using crude, unpurified plant extracts containing hundreds of unknown compounds, researchers should employ high-performance liquid chromatography (HPLC) and mass spectrometry (LC-MS) to separate and identify specific active fractions. By utilizing isolated, single bioactive molecules (such as pure epigallocatechin gallate from green tea or pure quercetin) as the sole reducing and capping agents, manufacturers can eliminate natural batch variability, achieving excellent batch-to-batch reproducibility and well-defined surface chemistry.

Additionally, integrating microfluidic synthesis technologies represents a promising advancement. Microfluidic chips feature tiny channels that enable precise control over the mixing velocity, fluid dynamics, and temperature of the reactants. Passing the metal precursor and the biological extract through a microfluidic device ensures highly uniform mass transfer, allowing manufacturers to produce highly monodisperse nanoparticles with a predictable size distribution, thus overcoming the variations typical of large-scale batch processing. Future research must also prioritize long-term, multi-generational in vivo toxicological studies in mammalian models. These investigations should track full absorption, distribution, metabolism, excretion, and toxicity (ADMET) profiles, with a specific focus on identifying clearance mechanisms and detecting potential genotoxicity in vital organs over long periods.

Finally, expanding the functional capabilities of biogenic nanoparticles offers substantial clinical value. Future studies should explore engineered multi-functional hybrid nanomaterials. For instance, combining biogenic gold nanoparticles with targeting ligands (such as folic acid or specific monoclonal antibodies) and loading them with standard chemotherapeutic drugs could enable highly precise, targeted drug delivery. Such formulations would maximize drug accumulation within tumor tissues via the enhanced

permeability and retention (EPR) effect while minimizing systemic side effects, establishing green nanotechnology as a powerful tool in precision medicine.

CONCLUSION

In conclusion, the green synthesis of metallic nanoparticles represents a significant advancement in nanotechnology, successfully blending environmental sustainability with biomedical innovation. By utilizing the natural biochemical machinery of plants, fungi, algae, and micro-organisms, this approach provides a clean, cost-effective, and safe alternative to hazardous chemical and energy-intensive physical synthesis methods. Characterization techniques like UV-Vis, FTIR, XRD, and electron microscopy confirm that biogenic methods produce highly crystalline, stable nanoparticles surrounded by a functional biological capping layer that prevents aggregation and enhances biocompatibility.

From a pharmaceutical perspective, biogenic nanoparticles demonstrate exceptional therapeutic potential, showing robust antimicrobial activity against multidrug-resistant pathogens and selective cytotoxicity against various cancer cell lines. This dual efficacy is driven by the unique synergy between the core metal and the bioactive phytochemicals attached to its surface. However, widespread commercialization and clinical deployment are currently hindered by issues such as high polydispersity, poor batch-to-batch reproducibility, and a lack of extensive long-term in vivo toxicological data. Addressing these bottlenecks through fractionated extracts, microfluidic manufacturing, and rigorous pharmacokinetic profiling will allow green-synthesized metallic nanoparticles to transition from academic research to mainstream clinical therapies, offering sustainable and effective solutions for modern healthcare.

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