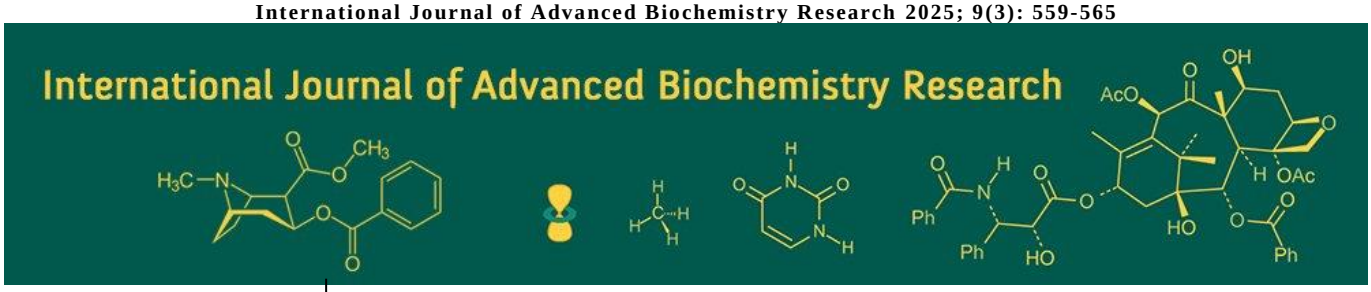

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Green synthesis of silver nanoparticles from medicinal plant extracts: Applications in antibacterial, antifungal, and biomedical fields

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Abstract
In recent years, the development of sustainable and efficient green chemistry methodologies for the synthesis of metal nanoparticles has become a significant area of research. A major objective in this field is to establish eco-friendly approaches for the controlled production of well-characterized nanoparticles. Among various biosynthetic strategies, the utilization of biological organisms has garnered substantial attention, with plants being recognized as highly suitable candidates for large-scale nanoparticle biosynthesis. Nanoparticles synthesized via plant-mediated processes exhibit enhanced stability and a higher synthesis rate compared to those produced by microorganisms. Furthermore, plant-derived nanoparticles display a broader range of morphological variations in terms of shape and size, offering greater versatility for diverse applications. The inherent advantages of plant-based nanoparticle synthesis have prompted extensive investigations into the underlying biochemical and molecular mechanisms governing metal ion uptake, bioreduction, and nanoparticle formation within plant systems.

Keywords: Green chemistry, metal nanoparticles, biosynthesis, plant-mediated synthesis

Introduction

Synthesis of Nanoparticles: Chemical vs. Biosynthetic Approaches

Nanoparticle synthesis has been extensively explored through various methodologies, primarily classified into chemical and biosynthetic approaches. Although chemical synthesis methods yield effective results, they are often associated with high production costs due to the requirement of expensive reagents. Furthermore, these methods frequently involve toxic chemicals, leading to significant environmental hazards and potential biological risks (Nath & Banerjee, 2013) [29]. To overcome these limitations, biosynthetic methods have emerged as sustainable and environmentally friendly alternatives, particularly for biomedical applications. These green synthesis approaches leverage the biological activity of various plant-associated microorganisms, including fungi, algae, and bacteria, to facilitate nanoparticle formation (Ahmed *et al.*, 2016) [1]. The biosynthesis of nanoparticles is governed by three essential factors: the selection of an eco-friendly solvent, the use of a biocompatible reducing agent, and the incorporation of a non-toxic stabilizing agent. In this context, various plant components—such as leaves, fruits, roots, stems, and seeds—have been widely utilized due to their inherent stabilizing and reducing properties (Narayanan & Sakthivel, 2011) [28]. Plants are rich sources of bioactive phytochemicals, which play a pivotal role in nanoparticle biosynthesis (Iravani, 2011) [19]. The process typically involves the careful selection and thorough cleansing of specific plant parts to eliminate impurities. These plant materials are then subjected to thermal treatment, usually boiling in distilled water, to extract the desired phytochemicals. The resulting extract is filtered to remove residual contaminants before being mixed with metal precursor solutions to initiate the reduction reaction, leading to nanoparticle formation. A key indicator of successful nanoparticle biosynthesis is the observable color change in the reaction mixture, signifying the reduction of metal ions and subsequent nanoparticle formation. Once synthesized, nanoparticles can be efficiently separated and purified using techniques such as centrifugation or filtration (Mittal *et al.*, 2013) [26].

The utilization of plant-based materials for nanoparticle synthesis offers a promising and sustainable approach with extensive applications in nanomedicine, catalysis, and environmental remediation (Alagarasi, 2011) [2].

Green Synthesis of Metal Nanoparticles

Green synthesis of metal nanoparticles involves the utilization of plant extracts as multifunctional agents that act as reducing, capping, and stabilizing agents. This approach is highly advantageous due to its biocompatibility, environmental sustainability, cost-effectiveness, and absence of toxic byproducts (Rai *et al*., 2015) [33]. The preparation of plant extracts follows a standardized procedure to ensure the integrity of bioactive compounds. Selected plant parts—such as leaves, stems, fruits, and roots—are meticulously washed with distilled water to remove contaminants. These plant materials are then dried to preserve their biochemical composition before being finely pulverized into powder. The powdered material is subsequently mixed with a suitable solvent or Milli-Q water and subjected to controlled thermal treatment, facilitating the extraction of bioactive compounds. If solvent extraction is employed, the final extract undergoes filtration to eliminate residual solid particles, yielding a purified solution rich in phytochemicals (Kalpana *et al*., 2018) [22]. Through this systematic process, green synthesis enables the production of metal nanoparticles with superior physicochemical properties. These nanoparticles have demonstrated significant potential in a wide range of applications, including nanomedicine, antimicrobial agents, biosensors, and environmental pollution control (Mittal *et al*., 2013) [26].

Biosynthesis of Different Metal Nanoparticles

Plant-derived extracts possess intrinsic reducing, capping, and stabilizing properties, which are crucial for the synthesis of biocompatible, eco-friendly, and economically feasible nanoparticles. These extracts are obtained from various plant parts—including leaves, stems, fruits, and roots—through a controlled process that involves collection, washing, drying, and pulverization. The powdered material is subsequently treated with a solvent or Milli-Q water and subjected to thermal processing to enhance its bioactivity. Following solvent-based extraction, the solution is carefully filtered to obtain a purified extract, which is then utilized in the biosynthesis of various metal nanoparticles (Ahmed *et al*., 2016) [1]. This green approach to nanoparticle synthesis serves as a promising and sustainable alternative to conventional chemical methods, offering high efficiency, minimal environmental impact, and extensive applications in medicine, biotechnology, and materials science (Rai *et al*., 2015) [33].

Gold (AuNPs) and Silver (AgNPs) Nanoparticles: Synthesis and Applications

Gold (AuNPs) and silver (AgNPs) nanoparticles are among the most widely studied nanomaterials due to their exceptional physicochemical properties and extensive applications across various scientific disciplines. The synthesis of AgNPs involves the reduction of silver ions (Ag^{+}), whereas AuNPs are synthesized through the reduction of gold ions (Au^{3+}). Green synthesis, which employs plant-derived biomolecules as reducing and stabilizing agents, has emerged as a cost-effective and environmentally sustainable approach to producing these nanoparticles (Tolaymat *et al*., 2010) [39]. The green synthesis of AgNPs typically involves biomolecules such as polysaccharides, proteins, vitamins, amino acids, alkaloids, saponins, terpenes, and phenolic compounds, which facilitate the reduction and stabilization of silver ions. Several medicinal plants have been reported to effectively mediate AgNP biosynthesis, including *Saccharum officinarum* (Chaudhari *et al*., 2012) [7], *Helianthus annuus* (Dubchak *et al*., 2010) [11], *Cinnamomum camphora* (Huang *et al*., 2008) [17], *Oryza sativa* (Dar *et al*., 2016) [9], *Aloe vera* (Chandran *et al*., 2006) [6], *Capsicum annuum* (Li *et al*., 2007) [24], *Medicago sativa* (Lukman *et al*., 2011) [25], *Zea mays* (Rajkumar *et al*., 2019) [34], and *Magnolia kobus* (Lee *et al*., 2014) [23]. AgNPs have demonstrated significant antimicrobial, antioxidant, and anticancer properties, making them highly valuable in the pharmaceutical and biomedical sectors.

Among metallic nanoparticles, AuNPs have garnered substantial interest due to their unique optical, electronic, and catalytic properties, which make them suitable for biomedical and technological applications (Jain *et al*., 2006) [20]. AuNPs exhibit superior biocompatibility (Sperling *et al*., 2008) [37], tunable surface plasmon resonance (Huang & El-Sayed, 2010) [17], low toxicity (Jeong *et al*., 2011) [21], and strong absorption and scattering properties (El-Sayed *et al*., 2006) [20]. Furthermore, their synthesis and surface functionalization can be readily customized to suit specific applications (Ghosh *et al*., 2008) [14]. The biosynthesis of AuNPs primarily involves plant-derived biomolecules, such as flavonoids, phenolics, and proteins, which act as reducing agents in the conversion of Au^{3+} ions into gold nanoparticles. These biomolecules not only facilitate nanoparticle formation but also contribute to their stability and functionality. The ability to fine-tune the surface properties of AuNPs enhances their applicability in drug delivery, bioimaging, cancer therapy, and biosensing (Dreaden *et al*., 2012) [10]. Overall, the green synthesis of AgNPs and AuNPs using plant extracts presents a promising, sustainable, and cost-effective alternative to conventional chemical methods. The biocompatibility, functional versatility, and diverse applications of these nanoparticles make them highly valuable in nanomedicine, diagnostics, catalysis, and environmental remediation.

Palladium (PdNPs) and Platinum (PtNPs) Nanoparticles: Synthesis and Applications

Palladium (Pd) and platinum (Pt) are precious metals with a silvery-white appearance, high density, and remarkable catalytic and electronic properties. These metals have found extensive applications in biomedical diagnostics, catalysis, and environmental remediation. In recent years, significant attention has been directed toward the green synthesis of Pd and Pt nanoparticles due to their potential advantages in sustainable nanotechnology. Various plant species, including *Anogeissus latifolia*, *Cinnamomum zeylanicum*, *Cinnamomum camphora*, *Curcuma longa*, *Diospyros kaki*, *Gardenia jasminoides*, *Glycine max*, *Musa paradisiaca*, *Ocimum sanctum*, *Pinus resinosa*, and *Pulicaria glutinosa*, have been successfully employed in the biosynthesis of PdNPs and PtNPs. A major advantage of PdNPs and PtNPs synthesized via plant-mediated green synthesis is their biocompatibility and non-toxic nature, particularly in medical applications. These nanoparticles have been found

to exhibit minimal genotoxicity and do not induce DNA damage, making them highly suitable for use in biomedical diagnostics and therapeutic applications (Gopinath *et al*., 2016) [15].

Additionally, PdNPs and PtNPs have demonstrated remarkable catalytic efficiency, particularly in heterogeneous catalysis. One of their most notable applications is in the Suzuki-Miyaura coupling reaction, a widely used chemical reaction for forming carbon-carbon bonds in pharmaceutical and material sciences (Suresh *et al*., 2018) [38]. Unlike traditional catalysts that require additional ligands, PdNPs enable ligand-free catalytic reactions in aqueous media, enhancing their efficiency and environmental sustainability. Remarkably, even at a catalyst loading of just 1 mol%, PdNPs exhibit high reaction yields, demonstrating their significant potential in industrial catalysis (Astruc, 2018) [4].

Furthermore, biosynthesized PdNPs have exhibited excellent selectivity and catalytic performance, making them ideal nanocatalysts for hydrogenation, oxidation, and cross-coupling reactions. The superior catalytic properties of PdNPs and PtNPs open new avenues in sustainable chemistry, energy storage, and environmental applications. Overall, the green synthesis of PdNPs and PtNPs using plant-based methods represents an environmentally friendly and efficient alternative to conventional synthesis techniques. Their diverse applications in catalysis, medicine, and nanotechnology underscore the importance of further research to fully explore their potential and optimize their large-scale production.

Antibacterial and Antimicrobial Properties

Recent research has highlighted the antibacterial properties of nanoparticles synthesized through green synthesis using medicinal plant extracts. For instance, silver nanoparticles (AgNPs) synthesized from medicinal plants have demonstrated significant antibacterial activity. The active biomolecules present in these plant extracts facilitate the reduction of silver ions to AgNPs, thereby enhancing their antibacterial properties (Vanaja *et al*., 2014) [41]. Furthermore, AgNPs synthesized from plants such as *Artemisia vulgaris* and *Callistemon citrinus* have exhibited potent antibacterial activity against a wide spectrum of bacterial strains. Additionally, titanium dioxide (TiO_2) nanoparticles have also shown remarkable antibacterial and antimicrobial properties.

Green-synthesized antibacterial nanoparticles hold immense potential in medical applications, particularly in the treatment of bacterial infections such as diabetic foot ulcers. These nanoparticles disrupt bacterial energy metabolism pathways, inhibit bacterial growth, and facilitate bacterial cell membrane destruction (Aldosary, 2019) [3]. Studies have demonstrated that silver nanoparticles synthesized from *Lawsonia inermis*, *Rhamnus frangula*, *Camellia sinensis*, and *Thymus vulgaris* exhibit potent antibacterial effects. Similarly, *Azadirachta indica* gum-derived zinc oxide (ZnO) nanoparticles have shown strong antibacterial properties (Geetha, 2016) [13]. The significant antibacterial and antibiofilm effects of Ag/Au nanoparticles synthesized from willow bark have been further supported by Sandulovici *et al*. (2022) [35]. Silver nanoparticles synthesized using *Skimmia laureola* leaf extracts exhibited maximum bacterial growth inhibition against *Staphylococcus aureus*, followed by *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Escherichia coli*. Additionally, AgNPs prepared from *Origanum vulgare* extracts have displayed antimicrobial activity against *Escherichia coli*, *Aeromonas hydrophila*, *Salmonella spp.*, *Shigella dysenteriae*, *Salmonella paratyphi*, and *Shigella sonnei*. Gold and silver nanoparticles have also been widely investigated for their antimicrobial potential against bacterial and fungal plant pathogens (Castillo-Henríquez, 2020) [5]. Their ultra-small size and shape, approximately 250 times smaller than bacteria, enable them to interact electrostatically with microbial cell walls. This interaction distorts essential membrane functions such as permeability, osmoregulation, electron transport, and respiration, ultimately leading to cell death. Smaller nanoparticles exhibit greater bactericidal effects due to their increased surface availability and higher binding affinity to bacterial membranes. Moreover, AgNPs and AuNPs have shown greater efficacy against Gram-negative bacteria compared to Gram-positive bacteria. Green-synthesized AgNPs, when tested at concentrations of 2 and 4 ppm, demonstrated significant antibacterial activity against both Gram-positive and Gram-negative bacteria. The AgNPs synthesized from *Aloe tingtinkie*, *Actaea racemosa*, *Sansevieria trifasciata*, and *Impatiens scapiflora* leaf extracts exhibited potent antibacterial properties, suggesting their potential application in developing novel antibacterial agents.

Antiviral Properties

In recent years, there has been a growing interest in utilizing plant-based compounds for synthesizing nanoparticles with antiviral properties. Numerous studies have demonstrated the efficacy of plant-derived nanoparticles in combating viral infections. For example, Umoren *et al*. (2017) [40] successfully synthesized AgNPs using plant extracts and reported their antiviral activity against various viruses, including influenza viruses, HIV, and herpes simplex viruses. The antiviral mechanism of AgNPs can be classified into two modes: intracellular and extracellular. Intracellularly, AgNPs inhibit viral replication by interfering with critical viral processes, while extracellularly, they interact with viral proteins such as gp120, preventing viral entry into host cells. These mechanisms vary depending on the viral strain, highlighting the versatility of AgNPs. Notably, AgNPs have demonstrated potent antiviral activity against *Feline coronavirus* (FCoV), *Influenza virus*, *HIV*, *Adenovirus*, *Herpes simplex virus*, *Dengue virus*, *Chikungunya virus*, *Norovirus*, *Bovine herpesvirus*, and *Human parainfluenza virus type 3*.

Several studies have investigated the antiviral potential of green-synthesized nanoparticles. Naikoo (2021) [27] and Sharma (2018) [36] have underscored their effectiveness in combating viral infections. Sharma (2018) [36] reported that AgNPs synthesized from *Andrographis paniculata*, *Phyllanthus niruri*, and *Tinospora cordifolia* exhibited significant antiviral activity against the chikungunya virus. Haggag (2019) [16] demonstrated that AgNPs derived from *Lampranthus coccineus* and *Malephora lutea* effectively inhibited *HSV-1*, *HAV-10*, and *CoxB4 virus*. Additionally, Pradhan (2013) [31] highlighted the antimicrobial activity of AgNPs synthesized from *Hibiscus rosa sinensis*, *Moringa oleifera*, *Acorus calamus*, *Cucurbita maxima*, and *Azadirachta indica*. These findings collectively support the potential of plant-derived nanoparticles for antiviral applications.

Antifungal Properties

Green-synthesized nanoparticles have also shown significant antifungal activity, making them a promising alternative to conventional fungicides. These nanoparticles have demonstrated efficacy against multiple fungal strains, offering a sustainable and eco-friendly approach to fungal infection management. Several studies have highlighted the antifungal potential of green-synthesized nanoparticles. Copper nanoparticles (CuNPs) synthesized in aqueous media induced morphological changes and membrane damage in plant pathogenic fungi (Pariona, 2019) [30]. Similarly, silver nanoparticles derived from red seaweed extract effectively inhibited *Fusarium solani* (Ciambelli, 2023) [8]. Starch-stabilized AgNPs exhibited potent antifungal activity by disrupting fungal cell membranes (Prasher, 2018) [32]. One critical aspect of green-synthesized AgNPs is their size and dispersibility. Studies have shown that these nanoparticles range from 6 to 40 nm and exhibit high dispersibility in water (Pariona, 2019) [30]. This characteristic enhances their efficacy in antifungal applications. Furthermore, a comparative analysis of AgNPs synthesized from different plant parts revealed that leaf extracts produced significantly higher antifungal activity than stem and root extracts (Pariona, 2019) [30].

Green synthesis of nanoparticles using plant extracts has demonstrated immense potential in combating bacterial, viral, and fungal infections. These nanoparticles exhibit strong antimicrobial properties, making them promising candidates for medical applications. Silver and gold nanoparticles have shown potent antibacterial, antiviral, and antifungal activity due to their small size, electrostatic interactions, and ability to disrupt microbial membranes. The eco-friendly nature of green synthesis provides a sustainable approach to nanoparticle production, eliminating the use of hazardous chemicals. Additionally, the choice of plant extracts plays a crucial role in enhancing the effectiveness of synthesized nanoparticles. Future research should focus on optimizing nanoparticle synthesis conditions, exploring novel plant sources, and investigating their mechanisms of action to fully unlock their potential in biomedical and pharmaceutical applications.

Medical Properties and Applications of Nanoparticles Prepared from Plants via Green Synthesis

The application of plant-derived nanoparticles (NPs), synthesized through green chemistry principles, has garnered significant attention in biomedical research due to their unique physicochemical properties and bioactive constituents. These NPs, typically ranging from 1 to 100 nanometers in size, are produced using plant extracts as reducing and stabilizing agents, minimizing the reliance on hazardous chemicals. This eco-friendly approach aligns with the tenets of green synthesis, offering a sustainable platform for developing nanomaterials with diverse medical applications, including drug delivery, diagnostics, tissue engineering, antimicrobial therapies, and environmental remediation.

Biomedical Properties of Plant-Derived Nanoparticles

Plant-mediated NPs exhibit a suite of therapeutic properties that enhance their suitability for clinical use. Their capacity for targeted drug delivery stems from their ability to encapsulate pharmaceutical agents, protect them from degradation, and facilitate controlled release at specific physiological sites. This enhances bioavailability and reduces systemic toxicity, making them promising candidates for precision medicine. Additionally, these NPs demonstrate potent antibacterial and antifungal activities, attributed to their ability to disrupt microbial cell membranes and inhibit enzymatic functions. For example, silver nanoparticles (AgNPs) synthesized from Tephrosia tinctoria stem extracts have shown efficacy in regulating blood glucose levels by scavenging free radicals, inhibiting carbohydrate-hydrolyzing enzymes (e.g., α-glucosidase and α-amylase), and enhancing glucose uptake.

Moreover, plant-derived NPs possess anti-inflammatory and antioxidant properties, which are critical for mitigating oxidative stress and inflammation-related pathologies. Gold nanoparticles (AuNPs) synthesized from medicinal plants, for instance, exhibit anti-inflammatory, anticancer, and anti-angiogenic effects, positioning them as potential therapeutic agents for conditions such as cancer and rheumatoid arthritis. Similarly, AgNPs from Indigofera aspalathoides have demonstrated wound-healing capabilities in animal models, promoting tissue regeneration without scar formation. AgNPs incorporated into ultrasound gels, such as those synthesized with Chrysanthemum morifolium extracts, exhibit bactericidal activity, enhancing the sterility of medical instruments.

Applications in Drug Delivery and Diagnostics

In drug delivery systems, plant-derived NPs serve as versatile nanocarriers, capable of encapsulating hydrophobic and hydrophilic drugs. Their biocompatibility and tunable surface properties enable precise targeting, improving therapeutic outcomes. For gene therapy, these NPs facilitate the efficient delivery of nucleic acids to target cells, offering potential treatments for genetic disorders. In diagnostics, their optical and electrochemical properties make them ideal for biosensing and imaging applications. For instance, AuNPs have been employed in early disease detection due to their plasmonic properties, which enhance signal amplification in diagnostic assays.

Parasitological and Environmental Applications

Beyond clinical uses, plant-derived NPs exhibit larvicidal activity against disease vectors. AgNPs synthesized from Euphorbia prostrata extracts have shown efficacy against Anopheles subpictus and Culex tritaeniorhynchus, key mosquito vectors of malaria and filariasis, respectively. This highlights their potential in public health and environmental management.

Biosensors: Principles and Applications

Biosensors are sophisticated analytical devices that integrate biological recognition elements with transducers to convert biomolecular interactions into quantifiable electrical signals. These tools have revolutionized fields such as healthcare, environmental monitoring, food safety, agriculture, and bioprocess control by offering rapid, sensitive, and cost-effective analysis. Unlike traditional methods, biosensors provide advantages such as portability, non-invasiveness, and real-time monitoring, making them integral to wearable diagnostics and point-of-care testing.

Mechanism and Properties

A biosensor comprises three core components: (1) a biological recognition element (e.g., enzymes, antibodies, or

nucleic acids) that selectively binds to a target analyte; (2) a transducer that converts this interaction into a measurable signal (e.g., electrical, optical, or thermal); and (3) a signal processor that amplifies and interprets the output. The efficacy of biosensors hinges on their sensitivity, selectivity, stability, and miniaturization potential. Advances in nanotechnology, such as the integration of plant-derived NPs, have further enhanced their detection limits and specificity.

Applications of Biosensors

Biosensors are widely employed across diverse domains

- **Healthcare:** Monitoring biomarkers such as glucose and cholesterol levels in blood, or detecting pregnancy hormones.
- **Food Industry:** Ensuring safety by detecting pathogens, allergens, and contaminants.
- **Environmental Monitoring:** Quantifying pollutants and toxins in air, water, and soil.
- **Agriculture:** Assessing soil health and diagnosing plant diseases to optimize crop yields.
- **Bioprocess Control:** Regulating fermentation parameters in biopharmaceutical production.

Production Methods

Biosensor fabrication involves techniques such as microfabrication (e.g., photolithography), immobilization of biorecognition elements (via adsorption, covalent bonding, or crosslinking), and nanotechnology integration. Plant-derived NPs, such as AgNPs and AuNPs, enhance biosensor performance by improving signal transduction and enabling miniaturization.

Conclusion

The green synthesis of nanoparticles using plant-based extracts presents a sustainable and eco-friendly alternative to conventional chemical methods. Plant-derived nanoparticles, particularly silver (AgNPs) and gold (AuNPs), have demonstrated significant potential across various fields, including nanomedicine, catalysis, and environmental remediation. Their biocompatibility, minimal toxicity, and functional versatility make them promising candidates for drug delivery, antimicrobial therapies, and diagnostics. Additionally, the ability to fine-tune their surface properties enhances their applications in biomedical technologies. As research progresses, optimizing synthesis techniques and exploring novel plant sources will further expand their potential in both clinical and industrial applications.

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