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Review Article

Green Pathways to Silver Nanoparticles: A Comparative Review of Plant, Microbial, and Biopolymer-Mediated Synthesis

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ABSTRACT

Silver nanoparticles (AgNPs) have emerged as one of the most extensively investigated nanomaterials due to their distinctive physicochemical properties, including nanoscale dimensions, large surface area-to-volume ratio, surface plasmon resonance, and broad-spectrum antimicrobial activity. These attributes have enabled their application in pharmaceuticals, biomedical devices, wound management, diagnostics, food packaging, and environmental remediation. Conventional physical and chemical synthesis methods frequently employ toxic reagents, hazardous solvents, and energy-intensive processes, raising serious concerns regarding environmental sustainability and biocompatibility. Consequently, green synthesis strategies have gained prominence as eco-friendly alternatives aligned with the principles of green chemistry. This review presents a comprehensive and critical comparison of plant-mediated, microbe-mediated, and biopolymer-assisted synthesis of silver nanoparticles. Mechanistic pathways, influencing parameters, advantages, limitations, and recent advancements associated with each approach are systematically discussed. Particular emphasis is placed on nanoparticle characterization, biological and pharmacological activities, biocompatibility, toxicity, scalability, and regulatory considerations. Comparative evaluation reveals that while plant- and microbial-mediated routes offer simplicity and biological functionality, biopolymer-assisted synthesis provides superior reproducibility, stability, and pharmaceutical suitability. The review highlights existing challenges and future perspectives for the clinical and industrial translation of green-synthesized silver nanoparticles.

INTRODUCTION

Nanotechnology has profoundly transformed modern pharmaceutical and biomedical research by enabling the manipulation of materials at the

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nanoscale to achieve enhanced functionality and therapeutic performance. Among various metallic nanoparticles, silver nanoparticles (AgNPs) have attracted exceptional attention owing to their potent antimicrobial activity, optical properties, catalytic efficiency, and relative ease of synthesis [1]. AgNPs have demonstrated efficacy against a wide range of pathogenic microorganisms, including multidrug-resistant bacteria, fungi, and viruses, positioning them as promising candidates for addressing global antimicrobial resistance [2].

Traditionally, AgNPs are synthesized using physical methods such as evaporation–condensation and laser ablation, or chemical methods involving reducing agents such as sodium borohydride, hydrazine, and citrate [3]. Despite their effectiveness, these methods suffer from critical drawbacks, including high energy consumption, generation of toxic by-products, limited biocompatibility, and environmental hazards. Such limitations restrict their applicability, particularly in biomedical and pharmaceutical formulations where safety and sustainability are paramount.

Green synthesis has emerged as a sustainable alternative that minimizes environmental impact while enhancing biological compatibility [4]. Green routes utilize biological entities or naturally derived materials as reducing and stabilizing agents, eliminating the need for harsh chemicals and extreme reaction conditions. Plant extracts, microorganisms, and biopolymers have been extensively explored for this purpose due to their intrinsic reducing capability and stabilizing potential [5]. However, variations in synthesis mechanisms, reproducibility, scalability, and regulatory acceptance necessitate a systematic comparative evaluation.

This review critically examines plant-mediated, microbe-mediated, and biopolymer-assisted synthesis of AgNPs, focusing on their mechanistic aspects, pharmaceutical relevance, biological performance, and translational potential.

2. Concept of Green Synthesis of Silver Nanoparticles

Green synthesis of silver nanoparticles is founded on the principles of green chemistry, which emphasize waste minimization, use of renewable resources, energy efficiency, and reduction of toxic substances [6]. In green routes, biological molecules act simultaneously as reducing agents, converting Ag^+ ions into metallic Ag^0, and as capping agents, stabilizing the nanoparticles and preventing aggregation.

Biological systems offer unique advantages due to their inherent chemical diversity and functional groups capable of interacting with metal ions. Polyphenols, flavonoids, proteins, enzymes, polysaccharides, and organic acids play crucial roles in nucleation, growth, and stabilization processes [7]. Unlike conventional methods, green synthesis typically occurs under ambient temperature and pressure, further enhancing its sustainability.

Despite these advantages, challenges such as limited mechanistic understanding, batch-to-batch variability, and scale-up constraints persist. Therefore, understanding the comparative strengths and limitations of different green synthesis pathways is essential for rational selection in pharmaceutical and industrial applications.

3. Plant-Mediated Synthesis of Silver Nanoparticles

Plant-mediated synthesis is the most extensively investigated green approach for the fabrication of silver nanoparticles due to its operational simplicity, rapid reaction kinetics, cost-effectiveness, and minimal environmental impact. This method utilizes aqueous or hydro-alcoholic extracts derived from different parts of plants, including leaves, stems, roots, flowers, fruits, peels, bark, and seeds. These extracts are rich in a diverse range of phytochemicals that play a dual role as reducing as well as stabilizing agents during nanoparticle formation [21].

3.1 Phytochemical Composition and Reducing Mechanism

Plant extracts contain bioactive constituents such as polyphenols, flavonoids, tannins, alkaloids, terpenoids, saponins, sugars, amino acids, and proteins. These compounds possess hydroxyl, carbonyl, and amine functional groups capable of donating electrons to silver ions (Ag^{+}), resulting in their reduction to metallic silver (Ag^{0}) [22]. Simultaneously, these phytochemicals adsorb onto the nanoparticle surface, forming a capping layer that prevents aggregation and enhances colloidal stability.

Polyphenols and flavonoids are considered the primary contributors to the reduction process due to their strong antioxidant properties. FTIR and XPS studies have confirmed the involvement of hydroxyl and carbonyl groups in the stabilization of plant-derived AgNPs [23]. The presence of such biofunctional moieties not only stabilizes the nanoparticles but also imparts additional biological activity.

3.2 Synthesis Parameters Influencing Nanoparticle Characteristics

The physicochemical properties of plant-mediated AgNPs are highly dependent on synthesis parameters. Plant species and extract composition play a decisive role in determining reduction rate, particle size, shape, and dispersity. Reaction pH significantly influences nanoparticle morphology; alkaline conditions generally favor the formation of smaller, uniformly distributed nanoparticles, whereas acidic conditions may lead to aggregation [24].

Temperature and reaction time directly affect nucleation and growth kinetics. Elevated temperatures accelerate reduction, producing smaller nanoparticles, while prolonged reaction times may result in particle growth and agglomeration. Silver precursor concentration and extract-to-metal ion ratio further modulate nanoparticle size and yield [25].

3.3 Advantages of Plant-Mediated Synthesis

Plant-mediated synthesis offers several advantages over microbial and chemical methods. The process is rapid, often completed within minutes to hours, and does not require stringent aseptic conditions or complex instrumentation. The use of renewable plant resources and water as solvent enhances sustainability and scalability [26].

Additionally, plant-derived AgNPs exhibit excellent biocompatibility and enhanced biological activity due to the presence of surface-bound phytochemicals. Numerous studies have demonstrated superior antimicrobial, antioxidant, anti-inflammatory, and wound-healing properties of plant-synthesized AgNPs compared to chemically synthesized counterparts [27].

3.4 Limitations and Reproducibility Challenges

Despite its advantages, plant-mediated synthesis suffers from significant limitations related to reproducibility and standardization. Variability in plant age, geographical origin, harvesting season, extraction method, and phytochemical composition leads to batch-to-batch inconsistency in nanoparticle characteristics [28]. Furthermore, the precise mechanistic role of individual phytochemicals remains inadequately understood, complicating process optimization.

From a pharmaceutical perspective, these inconsistencies pose challenges in meeting regulatory requirements for quality control, uniformity, and scalability. Therefore, extensive standardization of plant sources and extraction protocols is required before clinical translation.

3.5 Pharmaceutical and Biomedical Relevance

Plant-mediated AgNPs have shown remarkable potential in pharmaceutical applications, particularly as antimicrobial agents, wound dressings, topical formulations, and anticancer therapeutics. The synergistic interaction between silver nanoparticles and plant-derived bioactive compounds enhances therapeutic efficacy while reducing cytotoxicity toward normal cells [29]. This dual functionality positions plant-mediated AgNPs as promising candidates for next-generation phytopharmaceutical-nanomedicine hybrids.

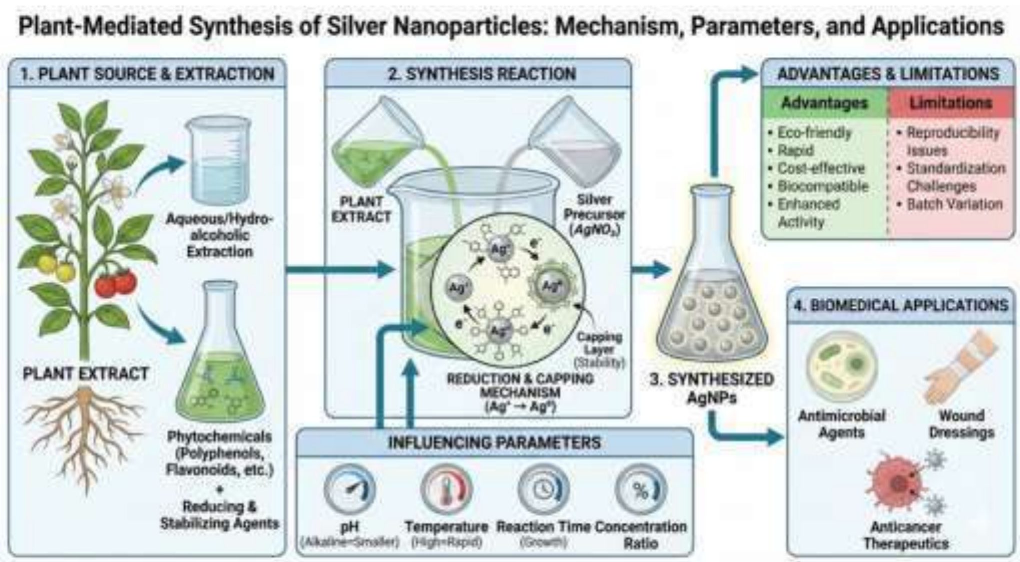

Fig. 1 Plant-Mediated Synthesis of Silver Nanoparticles

4. Microbe-Mediated Synthesis of Silver Nanoparticles

Microbe-mediated synthesis of silver nanoparticles represents a biologically sophisticated green approach that exploits the inherent metabolic and enzymatic capabilities of microorganisms such as bacteria, fungi, yeast, and algae. Unlike plant-mediated synthesis, which relies on complex phytochemical mixtures, microbial synthesis is primarily governed by enzymatic reduction processes and cellular biomolecules, offering comparatively better control over nanoparticle formation [30].

4.1 Mechanistic Pathways of Microbial Synthesis

Microbial synthesis of AgNPs occurs via two principal mechanisms: intracellular and extracellular synthesis. In intracellular synthesis, silver ions penetrate the microbial cell wall and are reduced within the cytoplasm by enzymes such as nitrate reductase and other electron shuttle proteins. The nanoparticles formed are subsequently accumulated inside the cell, often bound to proteins or cellular organelles [31]. In contrast, extracellular synthesis involves the secretion of enzymes, proteins, and metabolites into the surrounding medium, where silver ions are reduced outside the cell. Extracellular synthesis is generally preferred due to easier recovery and purification of nanoparticles.

4.2 Role of Different Microorganisms

Bacteria such as *Pseudomonas*, *Bacillus*, and *Escherichia coli* have been extensively explored due to their rapid growth rates and genetic manipulability [32]. Fungi, including *Fusarium*, *Aspergillus*, and *Penicillium* species, offer significant advantages such as higher metal tolerance, secretion of large quantities of reductive enzymes, and superior nanoparticle yield [33]. Algae and yeast provide additional benefits, including eco-sustainability and unique surface functionalization.

4.3 Advantages and Limitations

Microbe-mediated synthesis enables relatively uniform particle size, enhanced stability, and well-defined morphology under controlled culture conditions. However, the process is time-consuming, requires strict aseptic handling, and faces scale-up challenges. Intracellular synthesis further complicates nanoparticle recovery and purification, limiting its industrial feasibility [34].

4.4 Pharmaceutical Relevance

Microbially synthesized AgNPs exhibit excellent antimicrobial, antibiofilm, anticancer, and catalytic properties. The presence of proteinaceous capping agents enhances biocompatibility and cellular interaction, making them promising candidates for biomedical applications such as antimicrobial coatings, cancer therapy, and environmental remediation [35].

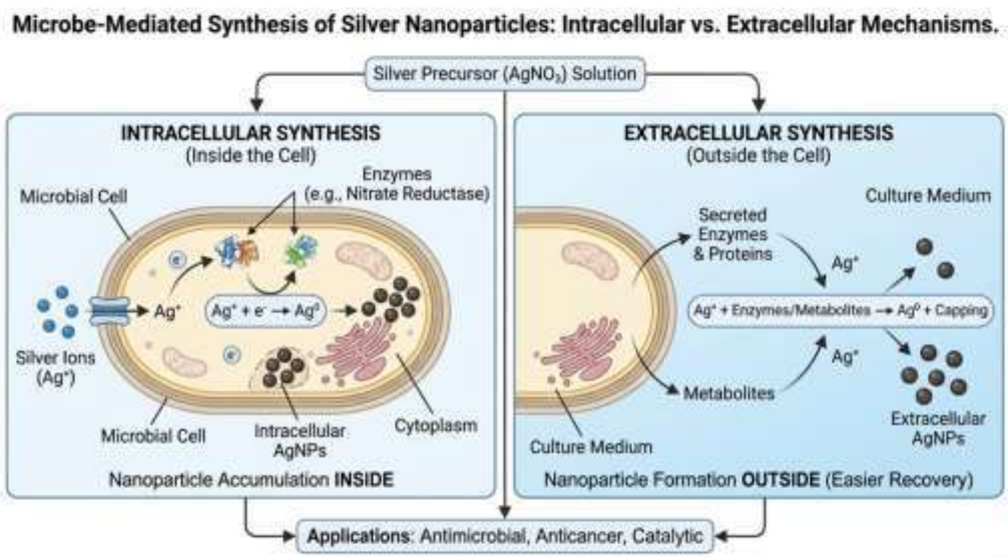

Fig. 2 Microbe-Mediated Synthesis of Silver Nanoparticles

5. Biopolymer-Assisted Synthesis of Silver Nanoparticles

Biopolymer-assisted synthesis is considered one of the most promising green routes for the pharmaceutical-grade production of silver nanoparticles. This approach utilizes naturally derived polymers such as chitosan, cellulose, alginate, starch, gelatin, dextran, and pectin as reducing, stabilizing, or supporting matrices [36].

5.1 Mechanism and Role of Functional Groups

Biopolymers contain abundant functional groups including hydroxyl, amino, and carboxyl moieties, which facilitate silver ion reduction and nanoparticle stabilization through electrostatic and steric interactions. For instance, chitosan's amino groups effectively bind Ag^{+} ions, enabling controlled nucleation and preventing aggregation [37].

5.2 Advantages Over Biological Extracts

Compared to plant and microbial systems, biopolymers offer superior reproducibility, enhanced colloidal stability, and better control over nanoparticle size and surface charge. Their chemical uniformity and ease of modification make them highly attractive for pharmaceutical formulation and regulatory approval [38].

5.3 Pharmaceutical Applications

Biopolymer-assisted AgNPs are extensively used in wound dressings, drug delivery systems, antimicrobial coatings, and tissue engineering scaffolds. The polymer matrix allows sustained release, surface functionalization, and improved therapeutic performance [39].

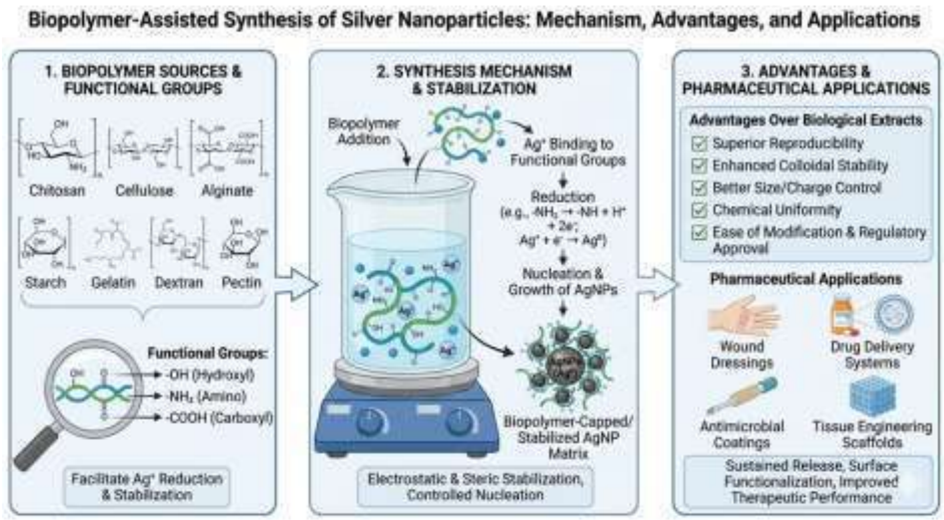

Fig. 3 Biopolymer-Assisted Synthesis of Silver Nanoparticles

6. Characterization of Green-Synthesized Silver Nanoparticles

Comprehensive characterization is essential to establish the quality, safety, and performance of green-synthesized AgNPs. Standard pharmaceutical characterization techniques include transmission electron microscopy (TEM), scanning electron microscopy (SEM), and dynamic light scattering (DLS) to determine particle size, morphology, and dispersity [40].

X-ray diffraction (XRD) confirms crystalline structure, while Fourier-transform infrared spectroscopy (FTIR) identifies functional groups responsible for reduction and stabilization. Zeta potential analysis provides insight into surface charge and colloidal stability, which are critical for biological applications [41].

7. Biological and Pharmacological Applications

Green-synthesized silver nanoparticles exhibit broad-spectrum antimicrobial activity against Gram-positive and Gram-negative bacteria, fungi, and drug-resistant pathogens. The enhanced bioactivity is attributed to small particle size, high surface reactivity, and biofunctional surface capping [42].

In wound healing, AgNPs promote faster epithelialization, reduced inflammation, and prevention of secondary infections. In anticancer applications, green-synthesized AgNPs induce apoptosis, oxidative stress, and cell cycle arrest in various cancer cell lines while showing reduced toxicity toward normal cells [43].

8. Biocompatibility and Toxicity Considerations

Although silver nanoparticles are inherently cytotoxic at high concentrations, green synthesis significantly mitigates adverse effects by replacing toxic chemical capping agents with biologically compatible molecules [44]. In vitro studies using MTT, LDH, and hemolysis assays demonstrate improved cell viability for green-synthesized AgNPs.

Nevertheless, toxicity remains dose-, size-, and surface-dependent. Long-term in vivo studies and standardized toxicological evaluation are essential to ensure clinical safety [45].

9. Comparative Pharmaceutical Evaluation

From a pharmaceutical perspective, plant-mediated synthesis excels in simplicity and cost-effectiveness, microbial synthesis offers controlled enzymatic production, while biopolymer-assisted synthesis provides superior reproducibility, scalability, and regulatory compatibility [46]. Among these, biopolymer-assisted systems are most suitable for drug delivery, controlled release, and biomedical formulations.

10. Regulatory and Translational Challenges

Despite extensive laboratory research, clinical translation of green-synthesized AgNPs remains limited due to lack of standardized synthesis protocols, variability in biological models, and insufficient long-term safety data [47]. Regulatory agencies require detailed characterization, toxicological profiling, and reproducibility to approve nanomaterial-based therapeutics.

11. Future Perspectives

Future research should focus on integrating green synthesis with advanced nanofabrication techniques, surface engineering, and computational modeling to achieve precise control over nanoparticle properties. Development of standardized guidelines, scalable manufacturing processes, and comprehensive regulatory frameworks will be critical for successful commercialization and clinical adoption of green-synthesized silver nanoparticles [48].

CONCLUSION

Green synthesis of silver nanoparticles provides an eco-friendly and sustainable alternative to conventional methods. Plant-, microbe-, and biopolymer-mediated approaches each offer unique advantages, but also present challenges in reproducibility and scalability. Continued optimization and standardization of these green routes are essential for their successful pharmaceutical, biomedical, and industrial applications.

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