A Comprehensive Review on Chemically and Green Synthesized Silver Nanoparticles: Mechanisms, Toxicological Insights, and Biomedical Applications

Harshad J. Salunkhe
Sunrise University, Alwar, Rajasthan
harshadsalunkhe1998@gmail.com

Abstract: *Silver nanoparticles (Ag NPs) are among the most widely studied metallic nanomaterials because of their exceptional chemical, physical, and biological properties. Recent advances in nanotechnology have enabled multiple synthesis routes that significantly influence the characteristics and behaviour of Ag NPs. Chemical reduction methods historically dominated the field but often involve hazardous reagents and generate toxic by-products. In contrast, green synthesis using biological systems offers an environmentally sustainable and cost-effective alternative. This review consolidates current knowledge on both chemical and green synthetic strategies, discusses their comparative advantages, and explores the toxicological implications and biomedical applications of Ag NPs. It also highlights future directions toward safer nanomaterial design and sustainable industrial use.*

Keywords: Silver nanoparticle, Chemically and Green Synthesis route, environmentally sustainable Comprehensive study

I. INTRODUCTION

Nanotechnology has revolutionized material science, biology, and medicine by allowing manipulation of matter at dimensions between 1 and 100 nm. Within this nanoscale regime, materials exhibit novel physicochemical and biological properties distinct from their bulk counterparts. Among metallic nanostructures, silver nanoparticles (Ag NPs) have drawn enormous attention because of their high surface area, optical tunability, antimicrobial activity, and catalytic potential (Zahoor et al., 2021).

Silver's antimicrobial capacity has been recognized since the nineteenth century; however, nanosizing dramatically amplifies its reactivity and spectrum of applications. The ability to engineer particle size, morphology, and surface chemistry determines their performance in biomedical coatings, drug delivery, diagnostics, and water. Despite these advantages, the production route chemical or biological—plays a crucial role in defining environmental impact and biological safety. Hence, understanding both chemical and green synthesis mechanisms and their consequences on toxicity and efficacy is essential for advancing sustainable nanotechnology.

II. OVERVIEW OF SILVER NANOPARTICLE SYNTHESIS

Two fundamental approaches exist for nanoparticle fabrication: the top-down and bottom-up methods. Top-down approaches, such as laser ablation and evaporation–condensation, fragment bulk metals into nanoparticles but often produce irregular shapes and require high energy (Rafique et al., 2017). Bottom-up approaches, on the other hand, rely on atomic or molecular self-assembly to form nanostructures through reduction or precipitation reactions. Chemical and biological syntheses fall under this category and are preferred for their ability to control particle morphology and dispersity.

The chemical synthesis of Ag NPs typically involves three components: a metal precursor (commonly silver nitrate, $AgNO_3$), a reducing agent, and a stabilizer or capping agent. The reducing agent converts Ag^+ to Ag^0, while the stabilizer prevents aggregation and controls size distribution (Zahoor et al., 2021). In green synthesis, biological extracts from plants, fungi, or bacteria serve dual functions as reducing and stabilizing agents. Biomolecules such as flavonoids, terpenoids, phenolic acids, and proteins replace toxic chemicals, making the process more biocompatible and eco-friendlier (Rafique et al., 2017).

The following sections discuss both synthetic routes in detail.

III. CHEMICAL SYNTHESIS OF SILVER NANOPARTICLES

3.1. Mechanisms and Common Reducing Agents

Chemical reduction remains the most established and reproducible route for Ag NP fabrication. Common reducing agents include sodium borohydride ($NaBH_4$), hydrazine, ascorbic acid, trisodium citrate, ethylene glycol, and N,N-dimethylformamide (Zahoor et al., 2021). During the process, Ag^+ ions from silver nitrate gain electrons supplied by these reagents, forming metallic nuclei that grow into nanoparticles through nucleation and aggregation stages. Capping agents such as polyvinylpyrrolidone (PVP), citrate, or surfactants stabilize the particles and modulate size from 2 nm to several hundred nanometers.

For instance, hydrazine and $NaBH_4$ produce smaller particles (< 10 nm) due to rapid nucleation, whereas citrate yields larger but more stable colloids. Ethylene glycol, in the well-known polyol process, simultaneously acts as solvent and reducing medium, providing good control over monodispersity.

3.2. Advantages and Limitations

Chemically synthesized Ag NPs exhibit high uniformity, reproducibility, and scalability. The reactions are fast, and particle characteristics can be tuned by adjusting reagent concentration, temperature, or pH. However, these methods often involve hazardous chemicals that leave residues on particle surfaces, leading to environmental and cytotoxic concerns. Sodium borohydride and hydrazine, for example, are highly reactive and produce toxic by-products that complicate biomedical applications (Rafique et al., 2017).

Additionally, solvent contamination and the need for inert atmospheres make chemical synthesis energy-intensive. Despite these drawbacks, chemical methods remain essential for industrial production where precise control over particle morphology is required.

IV. GREEN SYNTHESIS OF SILVER NANOPARTICLES

4.1. Concept and Biological Routes

The emergence of green nanotechnology addresses the ecological and health limitations of chemical synthesis. Green synthesis utilizes biological entities—plants, microorganisms, and biomolecules—to mediate nanoparticle formation in aqueous systems without toxic reagents. In these reactions, phytochemicals act as natural reducing and capping agents, while reaction conditions such as pH, temperature, and extract concentration determine the nanoparticle morphology (Rafique et al., 2017).

Plant extracts from species such as *Acalypha indica*, *Moringa oleifera*, *Carica papaya*, and *Cymbopogon citratus* have demonstrated effective reduction of Ag^+ to Ag^0 through polyphenolic and flavonoid constituents. Bacteria like *Pseudomonas stutzeri* and fungi such as *Fusarium oxysporum* also biosynthesize Ag NPs via enzymatic pathways (Rafique et al., 2017).

4.2. Mechanistic Insights

In plant-mediated synthesis, bioactive compounds donate electrons to silver ions, leading to nucleation of nanocrystals. Enzymes, polysaccharides, and proteins stabilize the formed nanoparticles through surface adsorption. The presence of hydroxyl, carbonyl, and amine groups enhances binding affinity, conferring long-term colloidal stability. Microbial synthesis involves either intracellular or extracellular reduction, where enzymes such as nitrate reductase play a pivotal role.

4.3. Advantages and Challenges

Green synthesis is environmentally benign, inexpensive, and easily scalable. It avoids hazardous reagents, thus reducing cytotoxic residues. Moreover, the biological corona formed around nanoparticles can enhance biocompatibility and therapeutic potential. However, achieving precise control over particle size, crystallinity, and yield remains challenging because biological extracts vary in composition depending on growth conditions and extraction methods. Standardization is therefore essential for reproducibility and clinical translation.

V. CHARACTERIZATION OF SILVER NANOPARTICLES

Accurate characterization is critical to link synthesis methods with functional properties. Techniques such as UV-Visible spectroscopy, Transmission Electron Microscopy (TEM), and Scanning Electron Microscopy (SEM), X-ray Diffraction (XRD), Dynamic Light Scattering (DLS), and Fourier-Transform Infrared Spectroscopy (FTIR) are routinely employed.

UV-Vis spectroscopy identifies surface plasmon resonance bands between 400 – 450 nm, confirming nanoparticle formation.

TEM and **SEM** provide morphology and size distribution.

XRD verifies crystalline structure, typically face-centered cubic silver.

FTIR helps identify biomolecules responsible for capping in green synthesis.

These analyses collectively determine the stability, purity, and potential applications of the produced Ag NPs.

VI. TOXICOLOGICAL CONSIDERATIONS OF AG NPS

Despite their promising applications, the toxicity of Ag NPs remains a major concern. Nanoparticles can cross biological barriers and accumulate in organs, eliciting oxidative stress, inflammation, and genotoxicity (Zahoor et al., 2021).

6.1. Mechanisms of Toxicity

Ag NP toxicity primarily arises from:

Release of Ag^{+} ions, which interact with thiol groups in proteins, disrupting cellular respiration.

Generation of reactive oxygen species (ROS), leading to oxidative stress and mitochondrial dysfunction.

DNA damage and apoptosis, resulting from direct nanoparticle-nucleus interaction.

In vitro studies have shown that exposure of human lung epithelial cells to Ag NPs increases ROS production and causes lipid peroxidation and cytotoxicity. The extent of toxicity depends on particle size, coating, concentration, and exposure duration. Smaller particles (< 20 nm) generally exhibit higher toxicity because of greater surface reactivity.

6.2. Comparative Toxicity of Chemical and Green Synthesized Ag NPs

Chemically synthesized Ag NPs often retain residual reagents that exacerbate cytotoxic effects, whereas biologically synthesized nanoparticles display improved compatibility due to natural capping layers. Several reports have demonstrated reduced haemolytic activity and enhanced antimicrobial efficacy of green-synthesized Ag NPs compared to their chemically produced counterparts (Rafique et al., 2017). Nevertheless, long-term in vivo studies are still needed to determine safe dosage ranges and metabolic fates.

6.3. Environmental Impact

Ag NPs released into wastewater and soil can affect microbial communities and aquatic organisms. Green synthesis can mitigate this risk by minimizing chemical waste, but responsible disposal and recycling strategies remain necessary to prevent ecological accumulation.

VII. BIOMEDICAL APPLICATIONS

7.1. Antimicrobial and Antifungal Activity

Ag NPs possess broad-spectrum antimicrobial activity against bacteria, fungi, and viruses. They disrupt microbial membranes, interfere with DNA replication, and denature essential enzymes (Zahoor et al., 2021). This property has been exploited in wound dressings, surgical textiles, and coatings for medical devices such as catheters and implants. Green-synthesized Ag NPs exhibit similar or superior antibacterial performance due to biomolecule-assisted stability and controlled ion release. Their effectiveness against *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans* has been well documented.

7.2. Anticancer and Antiviral Properties

Ag NPs induce cytotoxicity in cancer cells through ROS generation and apoptosis signalling. Studies have shown significant inhibitory effects on human breast and lung cancer cell lines. Moreover, Ag NPs have been reported to block viral replication, including HIV-1 inhibition via interference with gp120–CD4 binding.

The advantage of green-synthesized nanoparticles lies in their reduced collateral toxicity to healthy cells, offering potential for targeted therapy.

7.3. Drug Delivery and Diagnostics

Due to their surface modifiability, Ag NPs can be conjugated with drugs, antibodies, or nucleic acids for controlled release and targeted delivery. Their plasmonic properties also make them excellent candidates for biosensing and imaging. Surface-Enhanced Raman Scattering (SERS) using Ag NPs enables highly sensitive detection of biomolecules (Rafique et al., 2017).

7.4. Water Treatment and Environmental Remediation

Silver nanoparticles demonstrate potent antimicrobial activity in water filtration systems, effectively eliminating pathogens. Composite membranes embedded with Ag NPs enhance disinfection efficiency and prevent biofouling. Green synthesis provides an attractive route for producing these materials with minimal environmental burden (Zahoor et al., 2021).

VIII. COMPARATIVE ANALYSIS: CHEMICAL VS. GREEN SYNTHESIS

Aspect	Chemical Synthesis	Green Synthesis
Reducing agent	$NaBH_4$, hydrazine, citrate	Plant phytochemicals, enzymes
Cost and safety	Expensive, toxic reagents	Low-cost, non-toxic
Control over size	High precision	Moderate, dependent on extract composition
Reaction time	Rapid (minutes)	Slower (hours)
Environmental impact	Generates hazardous waste	Eco-friendly, sustainable
Biocompatibility	Requires post-purification	Naturally biocompatible

Both approaches have distinct advantages: chemical methods ensure reproducibility and industrial scalability, while green synthesis aligns with the principles of sustainable chemistry. A hybrid approach integrating green reducing agents with controlled chemical parameters may yield the most optimized results for biomedical use.

IX. FUTURE PROSPECTS

The future of Ag NP research lies in developing standardized, reproducible, and safe synthesis protocols that balance performance with environmental responsibility. Efforts are underway to integrate machine learning for predictive control of particle characteristics and to use biopolymer-based stabilizers that degrade harmlessly after use. Furthermore, toxicological profiling using advanced in-vitro and in-silico models will be essential to establish safety thresholds for consumer and medical products.

Regulatory frameworks must also evolve to ensure the responsible translation of nanomaterials into commercial applications. Emphasis on life-cycle assessment and green chemistry metrics will support sustainable nanomanufacturing.

X. CONCLUSION

Silver nanoparticles stand at the intersection of innovation and responsibility. Their unique physicochemical and biological properties underpin diverse applications from medicine to environmental engineering. While chemical synthesis offers precision and scalability, its ecological and toxicological burdens necessitate cleaner alternatives. Green synthesis, leveraging nature's reducing power, presents a viable and sustainable pathway for nanoparticle production. A comprehensive understanding of synthesis mechanisms, characterization, and biological interactions enables the design of safer nanomaterials. The integration of green principles into chemical nanotechnology can harmonize human advancement with environmental stewardship ensuring that the next generation of silver nanoparticles contributes positively to both science and society.

REFERENCES

[1]. Remya, V. R., Abitha, V. K., Rajput, P. S., Rane, A. V., & Dutta, A. (2017). Silver nanoparticles green synthesis: A mini review. *Chemistry International, 3*(2), 165–171.

[2]. Ahmed, S., Ahmad, M., Swami, B. L., & Ikram, S. (2016). Green synthesis of silver nanoparticles: A review. *Artificial Cells, Nanomedicine, and Biotechnology, 45*(7), 1272–1291.

[3]. Zahoor, M., Nazir, N., Iftikhar, M., Naz, S., Zekker, I., Burlakovs, J., Uddin, F., Kamran, A. W., Kallistova, A., Pimenov, N., & Khan, F. A. (2021). A review on silver nanoparticles: Classification, various methods of synthesis, and their potential roles in biomedical applications and water treatment. *Water, 13*, 2216.

[4]. Rafique, M., Sadaf, I., Shahid Rafique, M., & Tahir, M. B. (2017). A review on green synthesis of silver nanoparticles and their applications. *Artificial Cells, Nanomedicine, and Biotechnology, 45*(7), 1272–1291.

[5]. Zahoor, M., Nazir, N., Iftikhar, M., Naz, S., Zekker, I., Burlakovs, J., Khan, F. A. (2021). A review on silver nanoparticles: Classification, various methods of synthesis, and their potential roles in biomedical applications and water treatment. *Water, 13*, 2216.

[6]. Geetha, N., Geetha, T., Manonmani, P., & Thiyagarajan, M. (2014). Green synthesis of silver nanoparticles using *Cymbopogon citratus* (DC) Stapf. extract and its antibacterial activity. *Australian Journal of Basic and Applied Sciences, 8*, 324–331.

[7]. Ghanbari, H., Viatge, H., Kidane, A. G., Burriesci, G., Tavakoli, M., & Seifalian, A. M. (2009). Polymeric heart valves: New materials, emerging hopes. *Trends in Biotechnology, 27*(6), 359–367.

[8]. Remya, V. R., Abitha, V. K., Rajput, P. S., Rane, A. V., & Dutta, A. (2017). Silver nanoparticles green synthesis: A mini review. *Chemistry International, 3*(2), 165–171.