DOI: https://doi.org/10.46811/jngm/2.1.1

Review Article

Green synthesis of silver nanoparticles using plant extracts: A Sustainable Approach to Nanotechnology

Harshit Saklani[1], Jhuma Samanta[2*], Praveen Kumar Ashok[2], Abhishek Bhardwaj[3], Amandeep Singh[4]

[1]Student, School of Pharmaceutical Sciences, Jigyasa University, Dehradun,Uttarakhand,India
[2]Professor, School of Pharmaceutical Sciences, Jigyasa University, Dehradun,Uttarakhand,India
[3]Assistant Professor, School of Pharmaceutical Sciences, Jigyasa University, Dehradun,Uttarakhand,India
[4]Principal & Professor, School of Pharmaceutical Sciences, Jigyasa University, Dehradun, Uttarakhand,India.

Abstract

Nanotechnology has emerged as a promising field in pharmaceutical sciences, offering innovative approaches for drug delivery, diagnosis, and therapy. Among various nanomaterials, silver nanoparticles (AgNPs) have gained significant attention due to their potent antibacterial, anti-inflammatory, and anticancer properties. This review focuses on the environmentally friendly synthesis of silver nanoparticles using natural plant extracts, highlighting their therapeutic applications, safety aspects, and characterization techniques. Emphasis is placed on green synthesis as a sustainable and eco-friendly alternative to conventional chemical and physical methods, addressing concerns related to environmental impact and human health. The study compiles and analyzes recent research findings on plant-mediated AgNP synthesis, covering reaction mechanisms, phytochemical involvement, and advanced analytical techniques employed for nanoparticle characterization. Overall, this review underscores the potential of green-synthesized AgNPs in biomedical and pharmaceutical applications while promoting sustainable nanotechnology practices.

Keywords: Silver nanoparticles, green synthesis, plant extracts, phytochemicals, pharmaceutical applications, nanomedicine

Introduction

A. Overview of Nanotechnology in Pharmaceutical Sciences

Nanotechnology is the design, manufacturing, and use of systems, devices, and structures by manipulating size and form at the nanoscale (1–100 nm). Nanotechnology is employed in pharmaceutical sciences for imaging, targeted therapy, medication delivery, and diagnostic instruments.[1] Many nanomedicines licensed for clinical use and numerous others undergoing clinical trials, nanocarriers (liposomes, polymeric nanoparticles, metallic nanoparticles, nanocrystals) are increasingly essential to innovative formulations and precision medicine methods. These advancements put nanotechnology at the nexus of pharmacokinetics, regulatory science, and formulation science. [2]

B. Importance of silver Nanoparticles AgNPs) in Pharmacy

Silver nanoparticles are a desirable choice for use in pharmaceutical applications like topical ointments, wound dressings and drug delivery system . AgNPs are being investigated for their anticancer, anti-inflammatory, and antioxidant qualities in addition to their broad-spectrum efficacy against bacteria, viruses, and fungus.[3] Because of their broad-spectrum antibacterial action, comparatively simple production, and adaptable surface chemistry, silver nanoparticles (AgNPs) are one of the most extensively researched metallic nanomaterials in pharmaceutics. Compared to single target antibiotics, AgNPs lessen the possibility of resistance through a variety of processes, including membrane disruption, the production of reactive species (ROS), and interactions between proteins and DNA.[4] AgNPs are being research for antiviral applications, anticancer adjuvant, biosensors, and as functional excipients to provide antimicrobial qualities to dosage forms and medical devices, In addition to topical antimicrobials and wound dressings. Their tiny size enables them to interact with intracellular targets and microbial membranes, and surface functionalization modifies pharmacokinetics and biocompatibility.[5]

C. Chemical Synthesis Restrictions

Toxic chemicals like sodium borohydride, which are hazardous to the environment and human health, are frequently used in the conventional chemical production of AgNPs. Concerns regarding the safety and environmental sustainability of such processes are raised by the possibility of producing hazardous byproducts from the creation of these nanoparticles under harsh chemical conditions.[6] Surfactants, solvent traces, or residual reducing agents can affect biocompatibility, make regulatory clearance more difficult, and raise environmental disposal issues. Furthermore, strict purification procedures may be necessary for the scale-up of some chemical processes in order to satisfy pharmaceutical impurity requirements.[7] The developments of synthesis pathways that lessen the impact on the environment, streamline downstream purification, and produce nanoparticles with intrinsically safer surface chemistries is therefore highly motivated.[8]

D. Concept of Green Synthesis with Plant Extracts

Using plant extracts as reducing and capping agents, green synthesis of AgNPs is an ecofriendly substitute. Cost-effectiveness, biocompatibility, and a smaller environmental impact like few benefits of plant-based synthesis. Plant phytochemicals, including polyphenols, flavonoids, and alkaloids, are essential for stabilizing AgNPs.[9]

A typical plant-mediated synthesis involves mixing an aqueous plant extract with a silver salt (usually $AgNO_3$) in ambient or

*Correspondence
Dr.Jhuma Samanta
Professor, School of Pharmaceutical Sciences, Jigyasa University, Dehradun,Uttarakhand,India
E-Mail: jhuma.samanta@jigyasauniversity.edu.in

slightly elevated conditions. Phytochemicals adsorb onto the surfaces of nanoparticles to prevent aggregation and provide biological functionality while donating electrons to reduce Ag^+ to Ag_4. This onepot method can produce biocompatible AgNPs whose surface corona contains plant-derived compounds that may improve therapeutic synergy (e.g., antibacterial or antioxidant properties), minimizes the requirement for dangerous chemicals, and frequently takes place at room temperature.[10] The variety of plant species employed, operational factors (pH, extract concentration, temperature), and the ways in which phytochemical profiles affect particle stability and shape are all documented in systematic reviews.[11]

E. Scope and Importance for Pharmaceutical Applications

Plant-mediated (green) AgNPs offer pharmacists and formulation scientists three compelling advantages: (1) lower synthetic toxicity and possibly easier purification; (2) a biologically active surface layer that may enhance therapeutic effects and (3) compatibility with topical and biomedical device applications where antimicrobial performance and safety are critical. However, strict characterisation (size, shape, surface chemistry, crystallinity), repeatable production, and compliance with regulatory requirements for nanomaterials (risk assessment, biodistribution, impurity control) are necessary for conversion into regulated pharmaceutical products.[12] Green synthesized AgNPs must be evaluated not only for biological activity but also for batch-to-batch consistency, stability, and well-designed toxicokinetic studies, as regulatory agencies (FDA, EMA) have emphasized the importance of taking nanoscale properties into account when assessing product safety and efficacy.The current challenges and possible future advancements of plant-mediated AgNP synthesis for pharmaceutical applications are discussed in this review. Since it also looks at the characterization of these nanoparticles and their pharmacological effects, it is relevant to pharmaceutical research and drug development.[13]

MECHANISM OF GREEN SYNTHESIS OF SILVER NANOPARTICLES

Plant extracts simultaneously function as reducing, stabilizing (capping), and occasionally shape-directing agents for the conversion of soluble Ag^+ salts (typically $AgNO_3$) into colloidal Ag^0 nanoparticles in the one-pot, biologically driven process known as plant-mediated (green) synthesis of silver nanoparticles (AgNPs).[14] Plant-based methods are less expensive, operate in mild conditions, avoid toxic reagents, and often produce nanoparticles whose surfaces are coated with natural biomolecules that can enhance biocompatibility and add extra bioactivity when compared to classical chemical reduction (e.g., sodium borohydride, hydrazine).[15] The redox chemistry of several phytochemicals (polyphenols, flavonoids, terpenoids, alkaloids, proteins, and polysaccharides), their binding interactions with nucleating silver atoms, and subsequent colloidal stability through steric and electrostatic effects provide the mechanistic justification.[16]

A. Phytochemicals as Reducing and Capping agent

Silver ions (Ag^+) are reduced to silver nanoparticles (Ag_2) by plant-derived chemicals in the green production of AgNPs. Alkaloids, phenolic acids, terpenoids, and flavonoids are examples of phytochemicals that act as reducing agents. These substances also serve as capping or stabilizing agents, which keeps nanoparticles from clumping together and maintains their stability.Phenolic -OH groups that may reduce Ag^+ to Ag_2 while oxidizing and giving electrons to quinone-like molecules.[17] Additionally, their aromatic structures enable surface adsorption and π-interaction, which results in steric capping.[Terpenoids and essential oil components (e.g., limonene, eugenol) provide electron density and hydrophobic interactions that can assist in nucleation and influence particle shape.Polysaccharides frequently result in highly stable colloids that can be used in biomedicine.[18]

B. **Proposed Chemical Pathways**

Two phases are usually included in the synthesis are reduction and stabilization. Plant extracts reduce silver ions to silver atoms in the reduction stage by giving them electrons. Phytochemicals create a shield over the nanoparticles during the stabilization stage to keep them scattered throughout the fluid.[19]

C. Pharmacognostic Relevance of Plant Metabolites

Given that many of these substances have established biological functions, plant metabolites have substantial pharmacognostic significance. For instance, flavonoids, anti-inflammatory and antioxidant qualities can boost AgNPs' therapeutic potential. The characteristics of the produced nanoparticles can also be influenced by the type of plant used and the parts employed (such as leaves, roots, and flowers).[20]

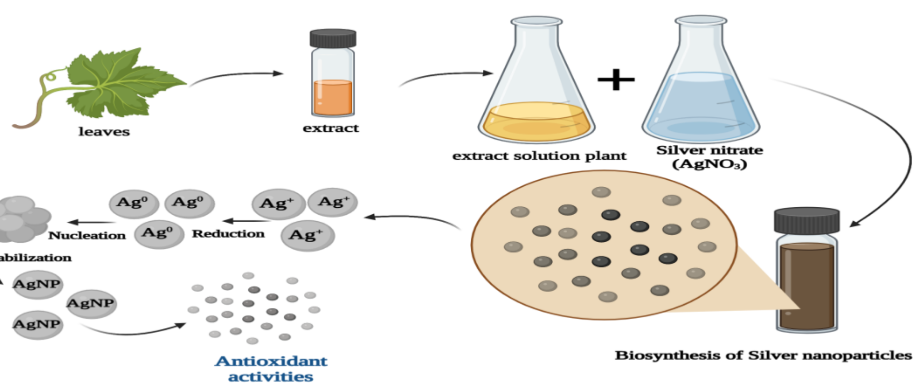

Fig 1:Synthesis of nanoparticles[21]

COMMONLY USED MEICINAL PLANTS IN AgNP SYNTHESIS

The ability of certain plants to synthesize silver nanoparticles (AgNPs) has been extensively investigated, and several plant species are frequently employed for this purpose.

Table 1:Medicinal plants used in nanoparticle synthesis

S. No.	PLANT SPECIES	PART USED	KEY PHYTOCHEMICALS	SIZE AND SHAPE OF AgNPs	Ref.no
1.	*Azadirachta indica*	Leaves	Flavonoids, alkaloids	10-15nm, spherical	[22]
2.	*Curcuma longa*	Rhizomes	Curcumin, polyphenols	20-40nm, spherical	[23]
3.	*Rosmarinus officinalis*	Leaves	Rosmarinic acid, flavonoids	15-30nm, spherical	[24]
4.	*Cinnamomum verum*	Bark	Cinnamaldehyde, tannins	20-50nm, spherical	[25]
5.	*Mentha piperita*	Leaves	Menthol, Flavonoids	15-30nm, spherical	[26]

CHARACTERISATION OF SILVER NANOPARTICLES

It is essential to characterize AgNP's characteristics for ensure their medicinal application. The following methods are frequently employed:

A. UV–Vis Spectroscopy

Used to identify the surface plasmon resonance peak (usually at 400–450 nm) in order to verify the production of AgNPs. The production of nanoparticles is indicated by the appearance of the distinctive surface plasmon resonance (SPR). The peak position and width provide information about size and polydispersity.[27]

B. FTIR (Fourier Transform Infrared Spectroscopy)

Its helps to identify the functional groups in plant extracts that decrease and stabilize the nanoparticles. • FTIR spectroscopy shows that the oxidation of phenolics and the binding of carbonyl/phenolate groups to Ag surfaces are indicated by the loss or shift of O–H, C=O, and C–O stretching bands following synthesis new bands or shifts are indicative of capping.[28]

C. XRD (X-ray Diffraction)

It verifies the crystallinity and metallic condition of silver. The chemical states of capping elements (N1s, S2p from proteins/thiols) can be identified by XPS.[29]

D. SEM/TEM (Scanning Electron Microscopy/Transmission Electron Microscopy)

It provides information about the nanoparticles size ,shape and morphology.[30]

E. DLS (Dynamic Light Scattering) and **Zeta Potential**

used to gauge the AgNPs' surface charge and size distribution, both of which are critical to their stability.[31]

F. Influence of Plant Type on NP Size, Shape, and Stability

The plant species utilized, the extraction technique, and environmental variables can all affect the size and stability of AgNPs. For example, compared to plants with lower amounts of phenolic chemicals, plants high in flavonoids may create smaller and more stable nanoparticles.[32]

PHARMACOLOGICAL APPLICATIONS OF GREEN-SYNTHESIZED AgNPs

A. Antimicrobial and Antiviral Properties

1. Antimicrobial Activity

AgNPs are well known for their broad-spectrum antibacterial qualities, which enable them to effectively combat a wide range of harmful microorganisms, such as viruses, fungus, and bacteria. AgNPs' antibacterial activity is mainly ascribed to.

- **Silver Ion Release (Ag^+):** Silver ions are release into the environment by AgNPs. It has been demonstrated that these silver ions damage bacterial cell walls and membranes, causing cellular contents to seep out and cell death.
- **DNA interaction:** When silver ions attach to bacterial DNA, they can stop transcription and DNA replication, which stops cells from dividing.
- **Production of Reactive Oxygen Species (ROS):** AgNPs produce ROS, which exacerbate their antimicrobial activity by harming cellular constituents such lipids, proteins, and nucleic acids.[33]

2. Antiviral Activity

AgNPs have demonstrated potential in antiviral applications in addition to their antibacterial qualities, especially against enveloped viruses such as influenza, herpes simplex, and HIV. Its consider that the antiviral mechanism includes

- **Binding to Viral Particles:** AgNPs can engage with viruses' surface proteins to stop them from attaching themselves to host cells.
- **Inhibition of Viral Replication:** By harming the viral genome or preventing the functioning of viral enzymes, the silver ions produced by AgNPs can prevent viruses from replicating. [34]

B. Antioxidant and Anti-inflammatory properties

1. Antioxidant Activity: AgNPs produced by green synthesis have strong antioxidant qualities that aid in scavenging free radicals and lowering oxidative stress. Because of this, they are useful in treating oxidative damage-related disorders like Cardiovascular Diseases, Neurodegenerative Disorders (e.g., Alzheimer's disease, Parkinson's disease), Diabetes and Metabolic Syndromes [35].

2. Anti-inflammatory Activity: Additionally, AgNPs have strong anti-inflammatory properties that help cure ailments like chronic inflammatory diseases, inflammatory bowel disease, and arthritis. AgNPs have the following anti-inflammatory mechanisms.

- **Inhibition of Pro-inflammatory Cytokines:** It has been demonstrated that green-synthesized AgNPs influence the release of pro-inflammatory cytokines (like TNF-α, IL-6, and IL-1β) and inflammatory response-related enzymes (like cyclooxygenase-2 or COX-2).
- **Decrease in Inflammatory Markers:** AgNPs have the ability to lower pro-inflammatory mediators and reactive oxygen species (ROS), which are raised during inflammation.[36]

C. Anticancer Properties

Silver nanoparticles are promising possibilities for cancer treatment since they have shown strong anticancer activity. Their several anticancer mechanisms consist of the following:

- **Induction of Apoptosis:** By triggering important apoptotic pathways, AgNPs have been demonstrated to cause apoptosis, or programmed cell death, in a variety of cancer cell lines. The process entails the production of reactive oxygen species (ROS), which causes mitochondrial malfunction and caspase activation, ultimately resulting in cell death.
- **Cell Cycle Arrest:** By interfering with the cell cycle, AgNPs can stop cancer cells from multiplying and dividing. They could inhibit cell proliferation by delaying the S-phase or G2/M phase.
- **Inhibition of Tumor Growth:** In vivo research has been shown that AgNPs, either by themselves or in conjunction with chemotherapeutic medications, can stop tumor growth in animal models. The biocompatibility and less adverse effects of plant-mediated AgNPs frequently increase the anti-cancer activity.
- **Targeting Cancer Cells:** By designing green-synthesised AgNPs to target certain cancer cell markers, their selectivity for tumor cells can be increased while their effects on healthy cells are reduced.[37]

D. In Drug delivery system

Drug delivery is one of the most promising uses of AgNPs in pharmacy. They are perfect for targeted drug delivery due to their high surface-to-volume ratio, biocompatibility, and ease of functionalization.[38]

There are various benefits of using green-synthesised AgNPs in medication delivery such as

- **Controlled Release:** Drugs can be encapsulated in AgNPs and released gradually. This can enhance patient compliance and lessen the frequency of medication delivery.[39]
- **Targeted Drug Delivery**: AgNPs can be functionalized to target particular cells or tissues by using targeting ligands, such as peptides, antibodies, or other biomolecules. AgNPs can carry chemotherapeutic medicines directly to tumor cells, reducing adverse effects on healthy cells, which is especially helpful in cancer therapy.[40]
- **Increased Bioavailability**: AgNPs' tiny size facilitates their passage across biological barriers, such as the blood-brain barrier, which is a major barrier to the delivery of drugs to the brain. As a result, they can be used in Neuro pharmaceutical applications. Compared to chemically produced AgNPs , green synthesized AgNPs have a number of advantages. Among them some principal distinctions are
- **Stability**: Because green synthesised AgNPs have natural capping agents that stop aggregation and extend their shelf life, they are frequently more stable.[41]
- **Environmental Sustainability**: Compared to chemical synthesis, which frequently uses dangerous chemicals and has toxic byproducts, green synthesis is more environment friendly and sustainable . [42]

SAFETY, TOXICOLOGY and BIOCOMPATIBILITY

Plant derived capping layers might enhance colloidal stability and perhaps lessen acute cytotoxicity, green produced silver nanoparticles (AgNPs) show promise for application in pharmaceuticals. However, prior to clinical translation, a thorough, evidence-based evaluation of safety, toxicity, pharmacokinetics (PK), biodistribution, and practical pharmacy issues is crucial. The available in vitro and in vivo data, our understanding of PK and organ distribution.[43]

The particular issues pharmacists and formulation scientists need to take into account all are summarized here.

A. Overview of In Vitro and In Vivo Studies

1. In Vitro Research

To ascertain the cytotoxicity, genotoxicity, and interaction of AgNPs with different cell lines, in vitro research mainly uses cell culture models. These investigations evaluate the effects of AgNPs on oxidative stress, inflammation, apoptosis, and cell viability. MTT (for cell viability), comet assays (for genotoxicity), and ROS detection techniques (for oxidative stress) are often employed assays.[44]

2. In Vivo Research

Usually carried out in animal models (mice, rats, rabbits), in vivo research evaluates the pharmacokinetics, biodistribution, and toxicity of AgNPs when given via various routes (oral, intravenous, topical). These investigations have shown that, depending on the size, charge, and surface properties of the nanoparticles, AgNPs can build up in a variety of organs, including the liver, spleen, kidneys, and lungs. [45]

B. Pharmacokinetics and Biodistribution

For the therapeutic use of AgNPs, pharmacokinetics,the movement of nanoparticles inside the body and biodistribution ,the distribution of nanoparticles across tissues are important factors to take into account.

1. Absorption: Oral, cutaneous, and respiratory channels are among the ways that AgNPs can be absorbed. Particle size, surface charge, and the presence of capping agents from plant extracts are some of the variables that affect the absorption effectiveness

2. Distribution: After being absorbed, AgNPs frequently build up in organs such the kidneys, liver, spleen, and lungs. AgNPs have a strong attraction for the liver and spleen, according to studies, most likely because of the organs' function in filtering and detoxifying foreign particles. AgNPs' size has a significant impact on their biodistribution , smaller nanoparticles are more widely distributed than bigger ones.

3. Elimination: The body can remove nanoparticles via the hepatobiliary (fecal) or renal (urinary) systems. Particle size, surface charge, and AgNP functionalization all affect the clearance rate. Biocompatible capping compounds can improve the excretion of smaller particles, which are usually eliminated more quickly than bigger ones, lowering the chance of accumulating in critical organs. [46]

C. Issues Particular to Pharmacy Practice

The use of green-synthesised AgNPs in pharmaceutical formulations gives a number of difficulties for pharmacy practice such as

1. Dosing: Determining the optimal dosage is necessary to ensure the safety and efficacy of AgNPs. The ideal dosage is determined by the patient's condition and the therapeutic use. Clear criteria are necessary to determine safe and effective dosages for clinical use.[47]

2. Formulations and Excipients: To guarantee stability, bioavailability, and safety when incorporating AgNPs into pharmaceutical products like oral tablets, topical creams, or injectable solutions, excipients must be carefully chosen. For example, in order to improve their therapeutic efficacy and avoid aggregation during storage, AgNPs must be appropriately stabilized. To preserve the intended nanoparticle properties (such as size, charge, and surface area), the selection of excipients (such as stabilizers, dispersants, and preservatives) is crucial.[48]

3. **Long-term Stability**: Because of phytochemicals form a protective layer, green-synthesised AgNPs are typically more stable than chemically synthesised particles. To make sure they don't aggregate or degrade over time, their long-term stability in pharmaceutical products especially in suspension or gel formulations needs to be closely watched.

4. Biocompatibility: By using natural plant extracts, green synthesis increases the biocompatibility of the nanoparticles and lowers their potential for toxicity. On the other hand, chemically produced AgNPs might need hazardous reagents and might contain leftover compounds that could be dangerous in biological applications.[49-56]

CHALLENGES AND FUTURE OUTLOOK

1. Standardization of Synthesis protocol: The absence of defined synthesis techniques is one of the main obstacles in the field of green synthesized AgNPs. Variations in the size, shape, and surface characteristics of nanoparticles can result from differences in plant species, extraction techniques, and environmental factors. In order to guarantee their reproducibility and quality control in both research and industrial production, standardizing these methods is essential.[57-59]

2. Reproducibility and Plant Variability: The reproducibility of the synthesis process may be impacted by the intrinsic variability of plant metabolites, which are essential for the synthesis and stabilization of AgNPs. Variability in the phytochemical content can occur from variations in the geographic location, time of harvest, and processing conditions of plants, which in turn influences the characteristics of the final nanoparticles. To address these obstacles, research into the standardization and optimization of plant-based synthesis techniques is required.[60]

3. Opportunities for Pharmacists in Nano pharmaceutical Research: Pharmacists can contribute in a special way for advancement of nanopharmaceutical research. They are excellent contributors to the creation of pharmaceutical products which are based on AgNP because of their knowledge of medication formulation, safety, and regulatory compliance. [61] Pharmacists have the following opportunities

4. Formulation Design: Creating stable and efficient drug delivery system based on nanoparticles.[62]

5. Regulatory Affairs: Handling the intricate regulatory environment surrounding nanomedicines.[63]

6. Clinical Studies: To assess the safety and effectiveness of green synthesis, for which clinical trials are being conducted. [64]

CONCLUSION

The green synthesis of Silver nanoparticles (AgNPs) using natural plant extracts represents a significant advancement in sustainable nanotechnology, offering a safe, eco-friendly, and economically viable alternative to conventional chemical synthesis. For the pharmaceutical field, these green-synthesized AgNPs provide a powerful platform for developing innovative therapeutic and diagnostic products. Key insights from current research include:

- **Improved Biocompatibility and Decreased Toxicity:** Natural phytochemical capping of plant-mediated AgNPs lessens the toxic effects often linked to chemically manufactured nanoparticles. Their usefulness for pharmaceutical applications, including topical gels, wound dressings, antibacterial agents, and drug delivery systems, is improved by this property.
- **Versatility in Pharmacological Applications**: Green-synthesized AgNPs show a wide range biological activities including antiviral, antibacterial, antioxidant, and anti-inflammatory properties. These action create opportunity for their integration into both traditional and cutting-edge therapeutic formulations.
- **Improved Stability and Functionalization:** Plant extract contain phytochemicals that work as stabilizing, functionalizing, and reducing agents. Long-term stability, improved biological interactions, and effective drug loading and targeting in nanomedicine applications are all made possible by this natural functionalization.

References

1. Sim S, Wong NK. Nanotechnology and its use in imaging and drug delivery. Biomed Rep. 2021;14(5):42.
2. Shan X, Gong X, Li J, Wen J, Li Y, Zhang Z. Current approaches of nanomedicines in the market and various stages of clinical translation. Acta Pharmaceutica Sinica B. 2022;12(7):3028–3048.
3. Feng QL, Wu J, Chen GQ, Cui FZ, Kim TN, Kim JO. A mechanistic study of the antibacterial effect of silver ions on Escherichia coli and Staphylococcus aureus. J Biomed Mater Res. 2000;52(4):662-68.
4. Kumar A, Yadav S, Yadav SC. Silver nanoparticles: mechanism of antimicrobial action, synthesis, medical applications, and challenges. Int J Nanomedicine. 2021;16:1509-1529.
5. Gomes D, Baptista PV. Silver Nanoparticles in Therapeutics and Beyond: A Review of Mechanism Insights and Applications. Nanomaterials. 2024;14(20):1618
6. Mandal S, Phadtare S, Sastry M. Interfacing biology with nanoparticles: green synthesis and its advantages. Biotechnol Appl Biochem. 2005;41(1):1–7.
7. Snodin DJ, McCrossen EM. Critical assessment of purification processes for the robust production of polymeric nanomedicine. J Control Release. 2024;384:127-140.
8. Sharma V, Yngard RA, Lin Y. Silver nanoparticles: Green synthesis and their antimicrobial efficacy. Adv Colloid Interface Sci. 2009;145(1-2):83–96.
9. Rónavári A, Kovács D, Darvas F, Papp C, Kovács T, Vágvölgyi C, Kónya Z, Pfeiffer I. Green synthesis of silver nanoparticles mediated by plant extracts: A critical review. Nanomaterials. 2021;11(10):2824.
10. Chhangte V, Lallianrawna S, Biswas A, Selvaraj M, Changmai B, Rokhum SL. Green synthesis of silver nanoparticles using plant extracts and their antimicrobial activities: a review of recent literature. RSC Adv. 2021;11(6):2804-2837.
11. Khatami M, Zare M, Khezri M, Akhavan-Karbassi A. A review of factors affecting the biosynthesis of silver nanoparticles using plant extracts: pH, temperature, plant species, extract concentration and phytochemical profile. Green Chem Lett Rev. 2022;15(4):658–674.
12. Zulfiqar Z, Khan RRM, Khan M, Saeed Z, Pervaiz M, Rasheed S. Plant-mediated green synthesis of silver nanoparticles: synthesis, characterization, biomedical applications, and regulatory challenges. Int J Mol Sci. 2025; 26(13):6222.
13. Uboldi C, Canaparo R, Capasso Palmiero U, Bellomo G, Bogni A, Donadon M, et al. Regulating nanomedicines: challenges, opportunities, and the path forward. Wiley J Nanomed Nanobiotechnol. 2023;15:150-166.
14. Khan I, Saeed K, Khan I. Green synthesis of silver nanoparticles using plant extracts and their mechanism of action: A review. J Chem Rev. 2019;1(3):77–99.
15. Chhangte V, Lallianrawna S, Biswas A, Selvaraj M, Changmai B, Rokhum SL. Green synthesis of silver nanoparticles using plant extracts and their antimicrobial activities: a review of recent literature. RSC Adv. 2021;11(6):2804–2837.
16. Singh P, Kim YJ, Zhang D, Yang DC. Biological synthesis of nanoparticles from plants and microorganisms. Trends Biotechnol. 2016;34(7):588–599.
17. Medicinal plants mediated the green synthesis of silver nanoparticles and their biomedical applications. Int J Nanomedicine. 2022;17:585–607.
18. Singh P, Kim YJ, Zhang D, Yang DC. Biological synthesis of nanoparticles from plants and microorganisms. Trends Biotechnol. 2016;34(7):588–599.
19. Vidyasagar A, Patel RR, Singh SK, Singh M. Green synthesis of silver nanoparticles: methods, biological applications, delivery and toxicity. Mater Adv. 2023;4(6):1831–1849.
20. Vanlalveni C, Lallianrawna S, Biswas A, Selvaraj M, Changmai B, Rokhum SL. Green synthesis of silver nanoparticles using plant extracts and their antimicrobial activities: a review of recent literature. RSC Adv. 2022;12(25):16093–16117.
21. Mittal AK, Chisti Y, Banerjee UC. Synthesis of metallic nanoparticles using plant extracts. Biotechnol Adv. 2013;31(2):346–356.
22. Noruzi M. Biosynthesis of silver nanoparticles by Azadirachta indica (Neem) leaf extract. World Appl Sci J. 2011;12(11):1821–1824.
23. Sheikh E, Bhatt MLB, Tripathi M. Bio-based synthesised and characterized monodispersed Curcuma longa silver nanoparticles induce targeted anticancer activity in breast cancer cells. Pharmacogn Mag. 2018;14(58):40–47.
24. Farghaly F, Nafady N. Green synthesis of silver nanoparticles using leaf extract of Rosmarinus officinalis and its effect on tomato and wheat plants. J Agric Sci. 2015;7(11):277–285.
25. Almalah HI, Alzahrani HA, Abdelkader HS. Green synthesis of silver nanoparticles using Cinnamomum zeylanicum bark extracts and their synergistic effect against multidrug-resistant bacteria. J Nanotechnol Res. 2019;1(3):95-107.
26. Deshmukh S, Patil S, Ingle A, Gade A, Rai M. Silver nanoparticles from Mentha piperita leaves: Eco-friendly synthesis, characterization, and acetylcholinesterase inhibitory activity. Int J Nanomedicine. 2018;13:3447–3454.
27. Gajendiran R, Kavitha R, Phanindranath Reddy HR, Manuel A, Meena KS. Silver nanoparticle biosynthesis and characterization using UV-visible spectroscopy, TEM, and XRD. Appl Nanoscience. 2019;9(6):1127–1139.
28. Frontiers. Green synthesized silver nanoparticles: Optimization, characterization, antimicrobial activity, and cytotoxicity study by hemolysis assay [Internet]. Front Chem. 2022;10:952006.
29. Khan M, Siddiqui MN, Akhtar MJ, Ahmad I. Silver nanoparticles: A review on synthesis, characterization, and novel applications. J Nanostruct Chem. 2019;9(3):195–210.
30. Ansari MA, Khan HM, Khan AA, Ali SM, Ahmed I, Iqbal J, et al. Green synthesis of silver nanoparticles using Moringa oleifera leaf extract and in vitro evaluation of their

cytotoxicity and antibacterial potential. J Saudi Chem Soc. 2018;22(8):817–825.
31. Gajendiran R, Kavitha R, Meena KS, Phanindranath Reddy HR, Viswanathan K. Green synthesis of silver nanoparticles using flaxseed extract: DLS, zeta potential and biological evaluations. Appl Sci. 2021;11(2):2182.
32. Kaur S, Mishra M, Sharma A, Mittal V, Duklan N, Sashank SS, et al. Eco-Friendly Synthesis of Silver Nanoparticles: A Sustainable Route for Multifunctional Applications. Green Chem. 2022; 1
33. Rai M, Yadav A, Gade A. Silver nanoparticles as a new generation of antimicrobials. Biotechnol Adv. 2009;27(1):76-83.
34. Galdiero S, Falanga A, Vitiello M, Cantisani M, Marra V, Galdiero M. Silver nanoparticles as potential antiviral agents. Molecules. 2011;16(10):8894–8918.
35. Vijayaraghavan K, Priyadharshini S, Sellamuthu P. Green synthesis, characterization, and evaluation of antioxidant potential of Plantago major mediated silver nanoparticles. J Mol Struct. 2023;1295:134167.
36. Green Synthesis and Characterization of Silver Nanoparticles from Tinospora cordifolia Leaf Extract: Evaluation of Their … Nanomaterials. 2025;15(5):381.
37. Galdiero S, Falanga A, Vitiello M, Cantisani M, Marra V, Galdiero M. Silver nanoparticles as potential anticancer agents: a review. Int J Mol Sci. 2020;21(15):5335.
38. Panwar MS, Pal P, Joshi D. Advances in green synthesis of silver nanoparticles: sustainable approaches and applications. J Drug Deliv Ther. 2024;14(11):177-184.
39. Saruchi, Kaur M, Kumar V, Ghfar AA, Pandey S. A green approach for the synthesis of silver nanoparticle-embedded chitosan bionanocomposite as a potential device for the sustained release of itraconazole drug and its antibacterial characteristics. Polymers. 2022;14(9):1911.
40. Vidyasagar A, Patel RR, Singh SK, Singh M. Green synthesis of silver nanoparticles: methods, biological applications, delivery and toxicity. Mater Adv. 2023;4(6):1831–1849.
41. Aliev G, Ahmad I, Ali M, Ahmad A, Alam M, Ullah S. Green synthesis of silver nanoparticles and their application in brain-targeted drug delivery: Addressing the blood–brain barrier issue. Int J Nanomedicine. 2024;19:123-140.
42. Kaabipour S, Hemmati S. A review on the green and sustainable synthesis of silver nanoparticles and one-dimensional silver nanostructures. Beilstein J Nanotechnol. 2021;12:102–136.
43. Desai AS, Singh A, Edis Z, Bloukh SH, Shah P, Pandey B, Agrawal N, Bhagat N. An in vitro and in vivo study of the efficacy and toxicity of plant-extract-derived silver nanoparticles. J Funct Biomater. 2022;13(2):54.
44. Awasthi KK, Awasthi A, Verma R, Kumar N, Roy P, Awasthi K, et al. Cytotoxicity, genotoxicity and alteration of cellular antioxidant enzymes in silver nanoparticles exposed CHO cells. RSC Advances. 2015;5(44):34927–35.
45. Jiménez-Lamana J, Laborda F, Bolea E, Abad-Álvaro I, Castillo JR, Bianga J, et al. An insight into silver nanoparticles bioavailability in rats. Metallomics. 2014;6(12):2242–2249.
46. Virkutyte J, García-García D, Monzón M, et al. Health impact of silver nanoparticles: a review of the biodistribution and toxicity following various routes of exposure. Int J Mol Sci. 2020;21(7):2375.
47. Hussain S, Al-Nawaz M, Ansari SA, et al. Molecular mechanisms of silver nanoparticle-induced cytotoxicity: role of physicochemical properties. Nanotoxicology. 2019;13(1):1–25.
48. Rai M, Yadav A, Gade A. Silver nanoparticles as a new generation of antimicrobials. Biotechnol Adv. 2009;27(1):76–83.
49. Iravani M. Green synthesis of metal nanoparticles using plants. Green Chem. 2011;13(10):2638–2650.
50. Mitragotri S, Anderson DG, Langer R. Nanoparticles in drug delivery: regulatory considerations and future perspectives. Nat Rev Drug Discov. 2015;14(7):485–512.
51. Suk JS, Xu Q, Kim N, Hanes J, Ensign LM. PEGylation as a strategy for improving nanoparticle-based drug and gene delivery. Adv Drug Deliv Rev. 2016;99(Pt A):28–51.
52. SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks). Nanosilver: safety, health and environmental effects and role in antimicrobial resistance. Final Opinion, 11 June 2014. European Commission. Available from: https://health.ec.europa.eu/publications/nanosilver-safety-health-and-environmental-effects-and-role-antimicrobial-resistance_en
53. Hosny S, Gaber GA, Ragab MS, et al. A Comprehensive Review of Silver Nanoparticles (AgNPs): Synthesis Strategies, Toxicity Concerns, Biomedical Applications, AI-Driven Advancements, Challenges, and Future Perspectives. Arab J Sci Eng. 2025; (published online 13 Sep 2025). doi:10.1007/s13369-025-10612-0.
54. Tarannum N, Divya, Gautam YK. Facile green synthesis and applications of silver nanoparticles: a state-of-the-art review. RSC Advances. 2019;9:34926–34948.
55. Shahzadi S, Fatima S, Qurat ul ain, Shafiq Z, Janjua MRS-A. A review on green synthesis of silver nanoparticles (SNPs) using plant extracts: a multifaceted approach in photocatalysis, environmental remediation, and biomedicine. RSC Adv. 2025;15:3858-3903.
56. Kaya M, Akdaşçi E, Eker F, Bechelany M, Karav S. Recent advances of silver nanoparticles in wound healing: evaluation of in vitro and in vivo studies. Int J Mol Sci. 2025;26(20):9889.
57. Raj S, Krishna S, Naseem S, Rosilda S. Review on Synthesis, Characterization and Medical Applications of Silver Nanoparticles. Nanomedicine & Nanotechnology Open Access. 2025;10(1):1
58. Nidhi Chaudhary, Praveen K. Ashok, Deepak Nanda, Esha Vatsa "Comprehensive Macroscopic and Microscopic profiling of *Cassia auriculata* L. in relationship to its Medicinal use" Journal of Hospital Pharmacy, 2025; 20(3): 1-11.
59. Eker F, Akdaşçi E, Duman H, Bechelany M, Karav S. Green Synthesis of Silver Nanoparticles Using Plant Extracts: A Comprehensive Review of Physicochemical Properties and Multifunctional Applications. Int J Mol Sci. 2025;26(13):6222.
60. Chhangte V, Lallianrawna S, Biswas A, Selvaraj M, Changmai B, Rokhum SL. Green synthesis of silver nanoparticles using plant extracts and their antimicrobial activities: a review of recent literature. RSC Adv. 2021;11:2804–2837.
61. Bhawana Rani,,Esha Vatsa, Arti Rauthan "Awareness and Health Impacts of Improper Biomedical Waste Management: A Preventive Approach" International Journal of Environmental Sciences, 2025; 11 (16s): 929-934.
62. Nanocarrier Drug Delivery Systems: Characterization, Limitations, Future Perspectives and Implementation of Artificial Intelligence. Pharmaceutics. 2022;14(4):883
63. Biliaieva A, Hofmann H, Stark GF, et al. Regulatory safety evaluation of nanomedical products: key issues to refine. Drug Delivery and Translational Research. 2022;12(8):2042–2047.
64. Boroumand Z, Golmakani N, Boroumand S. Clinical trials on silver nanoparticles for wound healing (review). Nanomedicine Journal. 2018;5(4):186–191.

Conflict of Interest:Nil
Source of support:None