Investigational
Medicinal Chemistry & Pharmacology

Review Article Open Access

Nanodrugs therapy for combating antimicrobial resistance: a review on green silver nanoparticles

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Abstract

Background: A nanotechnology-based approach offers researchers an opportunity to address the challenges of antimicrobial resistance. In this review, we summarize the antimicrobial properties, mechanisms, current synthesis trends, and limitations of green silver nanoparticles.

Methods: The review examines a wide range of scientific databases, such as ScienceDirect, Scopus, PubMed, Google Scholar, and Web of Science, to assess the effectiveness, mechanisms of action, and synthesis of silver nanoparticles in overcoming the challenges of antimicrobial resistance. It accentuates the complexity concerns of using crude extracts and compound isolates in the synthesis of silver nanoparticles.

Results: The use of crude extracts as reducing, capping, and stabilizing agents has been widely explored in the synthesis of silver nanoparticles because it is eco-friendly, non-hazardous, and economical. However, diversity and complexity present in the composition of crude extracts, with resultant effects on the size, shape, crystal structure, purity, reproducibility, surface chemistry, and toxicity of the silver nanoparticles, are a common challenge. The use of pure compound isolates has been suggested for the synthesis of silver nanoparticles to develop novel antimicrobial drugs for combating multidrug resistance.

Conclusion: The use of pure compound isolates for synthesizing silver nanoparticles offers better control compared to crude extracts. However, it is crucial to consider factors such as the cost of isolation and purification, limited availability, reduced synergistic effects, and toxicity concerns at high concentrations of pure compounds, which potentially restrict their use as antimicrobial drugs.

Keywords: Antimicrobial resistance; crude extracts, green synthesis; isolates; silver nanoparticles.

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Citation on this article: David IO, Alayande SO, Dare EO, Oladoyinbo FO, Adedeji GA, Babatunde AA. Nanodrugs therapy for combating antimicrobial resistance: a review on green silver nanoparticles. Investigational Medicinal Chemistry and Pharmacology (2026) 9(1):128; Doi: https://dx.doi.org/10.31183/imcp.2026.00128

Background

Nanotechnology is fast becoming an important tool in research and medical industries, with the potential to help overcome the crisis of antimicrobial resistance (AR). In the past decades, nanomaterials (NMs) have been employed to combat pathogenic microorganisms due to their unique physical and chemical properties that make them highly reactive; their large surface area relative to volume enables intimate interactions with microbial membranes, as well as surface functionalization, which helps in developing alternative and more effective antibacterial agents [1-2]. The discovery of penicillin successfully controlled pathogens, making it a remarkable milestone in medical history and helping humanity escape the disastrous grip of infectious diseases [3]. However, penicillin resistance was documented in 1942, which led to the discovery of several classes of antibiotics with various targeting mechanisms, as shown in Figure 1. The introduction of these antibiotics in modern medical practice revolutionized healthcare. Unfortunately, microbes have developed resistance against most of these antibiotics, significantly limiting their potency and leading to treatment failure due to excessive and uncontrolled use, which has caused a significant rise in drug-resistant pathogens [4-5]. NMs of varying classes (metal-based, smart, nanoemulsions, liposomes, nanocomposites, polymers, and carbon-based) have been employed to combat and identify lasting solutions to the problems posed by AR. This phenomenon is because NMs can employ multiple bactericidal mechanisms, making it difficult for bacteria to survive and develop resistance. Among these classes, metal-based nanomaterials (MBNMs) have been extensively studied for many biomedical applications due to their reduced size and selectivity for bacteria. The World Health Organization has said that MBNMs work against pathogens that are high on its list of priorities [6]. Silver nanoparticles (AgNPs) are now one of the most well-known and well-studied MBNMs in the world. They are also the most widely exploited MBNMs against various pathogenic microorganisms because of their strong toxicity to bacterial cells and relatively simple synthesis methods. Many researchers have reported the antimicrobial activities of AgNPs against both Gram-positive and Gram-negative bacteria [7]. This is attributed to their multiple mechanisms of antimicrobial action, although the exact mechanism is not yet fully understood. This review provides an overview of recent literature on the mechanisms of action and green synthesis of silver nanoparticles for overcoming the challenges of antimicrobial resistance.

Methods

In this review, we searched for research papers using keywords such as antimicrobial resistance, mechanisms of microbial resistance, silver nanoparticles, and green synthesis. The researchers then critically examined the research papers that met these word criteria and reported their conclusions.

Results and discussion

Mechanism of microbial resistance

Several mechanisms have been reported to describe bacterial resistance to antimicrobial drugs. Naturally, some bacteria are resistant to antimicrobial drugs, while others acquire resistance through excessive and indiscriminate use of these drugs, which has led to the emergence of new resistant strains [8]. The antibiotic resistance mechanism is therefore divided into two sorts:

Natural

Cell wall or outer membrane thickening prevents antimicrobial entry, activates efflux pumps (lipophilic and hydrophilic) on the cell membrane, and inactivates the drug (beta-lactamases hydrolyze the beta-lactam ring in penicillin and cephalosporins) [9].

Acquired

Comprises genetic material alterations (mutations, transformation, transposition, and conjugation) and biochemical mechanisms (secretion of alternative enzymes to degrade the concerned antibiotics; enzymatic modification, such as methylation, adenylation, acetylation, etc., of target molecules; use of alternative pathways and quorum sensing; antibiotic sequestration) [10]. Some of the most important mechanisms by which bacteria obtain a survival advantage range from efflux pump mutations to destruction of antibacterial agents, as shown in Figure 2. To understand the mechanisms of antibacterial resistance, it is important to know how antimicrobial agents work. In general, the mechanism of antibacterial resistance ranges from accelerating antibiotics efflux through bacterial efflux pumps to decreasing the time required for medication to diffuse inside bacteria [11-12], to alteration of binding sites for antibiotics [13], alteration of bacterial porins' structure, which decreases bacterial permeability to antibiotic influx [14], and destruction of antibacterial agents by hydrolytic enzymes [11]. Usually, bacteria may develop resistance using one mechanism or combining more than one to fight antimicrobial drugs. Understanding the resistance mechanism is essential to identify the possible target for effective medication and new antibiotic development in the future.

Nanotechnology-based perspectives on overcoming Antimicrobial Resistance

Nanotechnology is rapidly becoming an essential tool that offers a transformative solution to combat the escalating menace of AR. To develop innovative strategies for targeted drug delivery, biofilm disruption, and overcoming bacterial resistance mechanisms, researchers are harnessing the unique properties of NMs. The admiration of nanotechnology results from the possibility of obtaining materials that have better chemical, electrical, thermal, mechanical, or optical properties. Materials with dimensions of 1–100 nm are commonly referred to as NMs. Their unique small size provides novel properties, such as greater interaction with cells due to a larger surface area and controllable application [15]. NMs penetrate bacterial envelopes through Van der Waals forces, receptor-ligand interactions, and hydrophobic interactions, damaging the structural integrity of the bacterial membrane. As a result, they interfere with the proton motive force across the cell membrane, limiting the bacteria's ability to store or produce energy [16]. These novel properties have caught the attention of researchers because they can help overcome bacterial resistance patterns. By encapsulating various antibiotics within the same NMs, researchers can prevent resistance development, reduce higher drug efflux and lower uptake, target intracellular bacteria, and inhibit biofilm formation. This approach also aids systemic drug circulation time and reduces side effects on healthy cells and tissues, ensuring that a larger amount of the dose reaches the disease site [17-18]. By exploring the interaction between NMs and bacteria, researchers may use nanotherapeutics as an alternative

to conventional antibiotics to treat bacterial infections. Many different classes of NMs have been reported to control and combat microbial resistance [19]. During this review, we shall focus on green AgNPs. This is because silver has a strong and independent action over pathogens, and its antimicrobial properties may be applied to various research, medical, and industrial uses and offer solutions to the crisis of AR compared to conventional approaches.

Green synthesis of AgNPs

The shift from conventional to green nano-formulations indicates a noteworthy change in antimicrobial research and therapy. The unlimited pharmacological possibilities in nature's resources provide optimism for novel therapies and improve healthcare. Green synthesis explores naturally sourced starting materials and low-energy processes as a sustainable alternative to conventional synthesis approaches, as shown in Figure 3. This approach relies on a cleaner, safer, and more eco-friendly nanomaterial manufacturing process [18]. Synthesis of green AgNPs is of considerable interest in the struggle against AR because of their unique mechanism of action. Although NPs are prepared by a series of chemical and physical methods, as shown in Figure 3, these methods are avoided due to their tendency to result in undesired toxicity, which is due to the use of perilous chemicals as reducing and capping agents. However, the development of biologically inspired experimental processes, such as using plant extracts, bacterial extracts, yeast extracts, microbial extracts, and algal extracts as reducing, capping, and stabilizing agents, offers significant advantages [20]. Generally, two major approaches are in practice in the synthesis of AgNPs, which are the "top to bottom" and "bottom to top" approaches. A bottom-to-top approach involves using chemical or biological processes to synthesize NPs by self-assembly of atoms into new nuclei, which grow into nanosized particles. In the top-to-bottom approach, bulk material is broken down into fine particles by size reduction with various lithographic techniques, e.g., grinding, milling, sputtering, and thermal/laser ablation. Generally, phytochemicals (including terpenoids, alkaloids, phenolics, sugars, etc.) present in biological extracts can reduce metal salts from a positive oxidation state to a zero-oxidation state when mixed in solution. Silver, gold, iron, and copper are the most used metals, with silver being the most widely studied because of its unique antimicrobial properties, which can be incorporated into composite fibers, cryogenic superconducting materials, cosmetic products, the food industry, and electronic components [21]. It is important to state that till present, plant extract has become the preferred choice over microbes and chemicals in the synthesis of AgNPs due to its fast development, giving a single-step strategy, affordable convention, and nonpathogenic and eco-friendly nature for NPs amalgamation, as shown in Table 1. It has been widely proven that the presence of secondary metabolites like terpenoids, alkaloids, phenolic compounds, reducing sugars, proteins, etc. are grossly responsible for the reduction, capping, and stabilization of AgNPs, as shown in Figure 4. In the process of AgNPs synthesis using plant extract, secondary metabolites present not only reduce the silver salts (Ag^+) to metallic silver (Ag^0) but also cover the formed AgNPs or act as in situ reducing, stabilizing, and capping agents [23-24]. Usually, the synthesis of plant extract-mediated AgNPs can be divided into three stages: activation phase, growth phase, and termination phase [24]. This type of green synthesis is advantageous because it acts in a multifunctional way: it (i) prevents the agglomeration of the NPs, (ii) reduces the toxicity, and (iii) improves antimicrobial action, especially with plants that have high antimicrobial properties [25]. Synthesis of AgNPs using plant extract finds its possible application in the biomedical field, especially in antimicrobial development. The first approach of the green synthesis of AgNPs from alfalfa sprout species was reported by Gardea-Torresdey [26].

$$AgNO_3 \longrightarrow Ag^+ + NO^{3-}$$
$$Ag^+ + Phytochemicals \longrightarrow Ag^0,\ E^0 = +0.08\ V$$

Antimicrobial mechanism of AgNPs

AgNPs are now well-established as a promising alternative to antibiotic therapy because they possess remarkable potential for solving the problem associated with the development of multidrug resistance in pathogenic microorganisms, hence regarded as next-generation antibiotics [37]. Although antimicrobial activities of AgNPs alone or together with conventional antibiotics have been reported against several Gram-negative and Gram-positive bacteria, there is no comprehensive knowledge about the exact mechanism of their mode of antimicrobial action and toxicity [38]. Nevertheless, more research has focused on the antimicrobial mechanism of AgNPs to reveal their mode of action. Up to date, three well-defined mechanisms of AgNPs have been proposed so far: (i) cell wall and membrane damage, (ii) intracellular penetration and damage, and (iii) oxidative stress [39]. Two major ways exist by which AgNPs act against microbial resistance. (i) Ag^+ ions, which are released, can react with the phosphorus and sulfur groups containing proteins of the microbial cell wall, thereby causing AgNPs to attach onto cell membranes and making a hole and shrinkage of the cytoplasm and membrane detachment, finally leading to cell wall destruction as shown in Figure 5. The leakages created during cell wall destruction allow inward passage of Ag^+, which destroys ribonucleic acid (RNA) and deoxyribonucleic acid (DNA), hinders DNA duplication, and generates reactive oxygen species (ROS), which cause both intra- and extracellular damage [40]. (ii) AgNPs in combination with other drugs are used as carriers to bypass microbial efflux pumps, intracellular hydrolysis, and biofilm formation. Also, AgNPs have been used to ensure that the highest concentration of antimicrobial drugs was delivered to the target or infected sites and, in that way, overcome AR [41].

Toxicity of green AgNPs

The toxicity of green AgNPs is a major issue that needs to be carefully studied because the conversion of metal to its nanoform brings the risk of toxicity. The toxicity concern of AgNPs is suitably reduced with the green synthesis approach, i.e., reduction, stabilization, and coating of the AgNPs are achieved by the biocompatible material, and hence the toxicity concern is reduced in most of the cases. Generally, the main essence of coating the AgNPs is to provide stability and thus prevent agglomeration or accumulation, but the biocompatibility feature of the coating makes the green-synthesised AgNPs employable for antimicrobial applications [62]. The severity of the toxicity of the AgNPs is also a factor in the mode of administration and exposure duration. Small AgNPs demonstrate a higher degree of toxicity in comparison to large AgNPs with the same chemical composition, crystalline and lattice structure, because their removal from the environment is not as easy or efficient. They can also penetrate the cellular membrane with ease, leading to nucleic acid and free radical production [63]. Toxicological investigations have demonstrated that small AgNPs (less than 100 nm) cause more severe respiratory health impacts and inflammation in comparison to bigger AgNPs (greater than 100

nm). Higher concentrations of AgNPs can promote NP accumulation, thus reduce their toxicity when compare with smaller concentrations [64].

Limitations of green AgNPs

Over the past decades, NMs have been developed using classical chemical methods. The disadvantages of classical methods were the use of hazardous chemicals, which resulted in serious toxicity. Presently, the global research community has noticed the importance of green synthetic methods as a simpler process that provides a way out of the use of toxic compounds and unstable precursors. Developing NMs through green nanotechnology proves to be a far better method, as it not only removes the use of toxic and expensive chemicals but also is energy efficient and produces eco-friendly products and by-products [65]. Although the rapid and green synthetic methods using biological extracts have shown great potential in AgNPs, there are drawbacks associated with this method because the current trend of research is mainly focused on using the crude extracts as reducing and capping agents. There is no comprehensive knowledge about the mechanism by which isolated pure phytochemicals are involved in the synthesis, purity, stability, and mode of antimicrobial inhibition [62]. In addition, significant variation exists in the chemical compositions of crude extracts of the same species when collected from different parts of the world, and this may lead to different results in different laboratories [30]. This is the major drawback of the synthesis of AgNPs using extracts as reducing and stabilizing agents.

Overcoming the limitations of green AgNPs

In providing solutions to the complexity and diversity associated with using crude extracts as reducing, capping, and stabilizing agents, researchers have tilted towards isolating pure compounds and using them to carry out green synthesis of AgNPs. Although this is an innovation, people have not done much in this regard. Only a few works have reported the use of pure compound isolates in the preparation of MBNPs. Very recently, Omolaja and others used two pure chalcones, helichrysetin and helichrysin, isolated from Helichrysum foetidum, for the successful synthesis of quasi-monodispersed gold nanoparticles in the size range of 2–12 nm. These MBNPs are biostable with no cytotoxicity when tested against the HaCaT keratinocytes and provide a therapeutic appraisal of the AuNPs/chalcones conjugate towards the development of antidiabetic drugs [66]. The first report of the phytomediated synthesis of gold and silver nanoparticles using Aspalathin (ASP) as a reducing and capping agent in the formation of crystalline structures with different shapes and dispersity of ASP-AgNPs and ASP-AuNPs in the ranges of 1.6–6.7 nm for AgNPs and 7.5–12.5 nm for the AuNPs. Although they are stabilized with polyethene glycol, they are less stable in selected biogenic media. However, they have remarkable potential for cancer cell treatment soon [35].

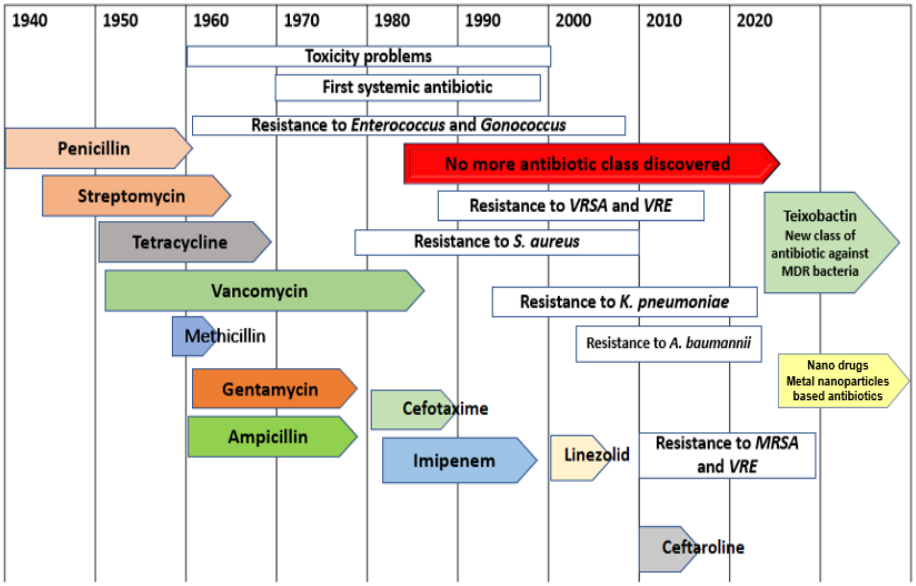

Figure 1. Antibiotic discovery and its associated resistance development [4].

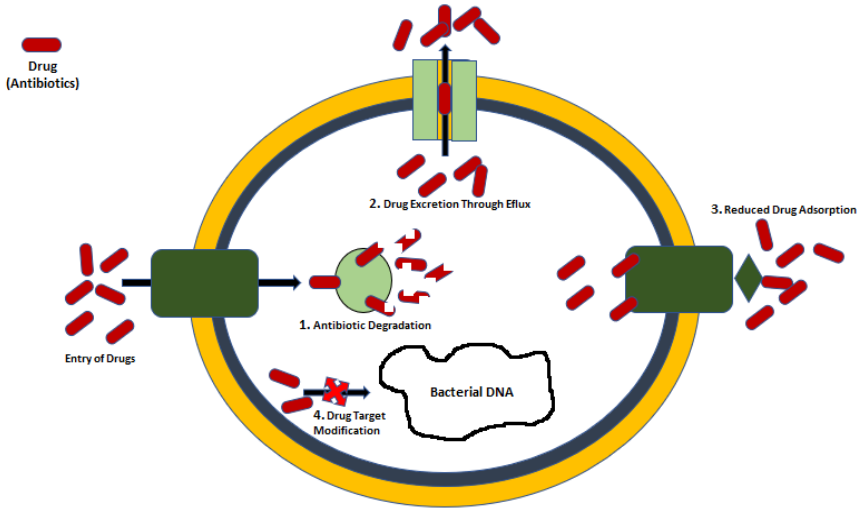

Figure 2. Mechanism of antimicrobial resistance [6].

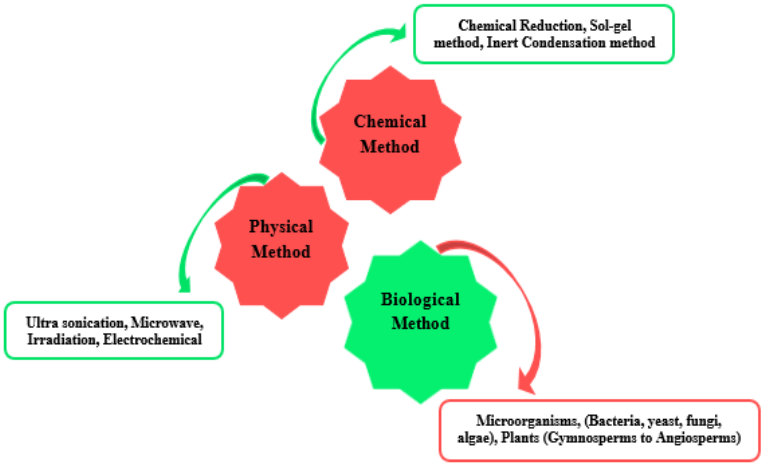

Figure 3. Different approaches to synthesising NPs [18].

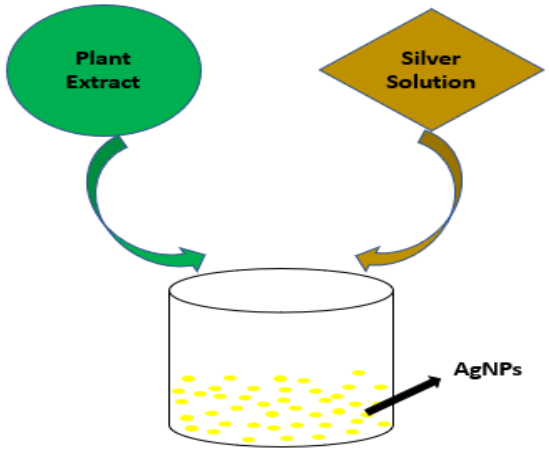

Figure 4. One pot green synthesis of AgNPs [27].

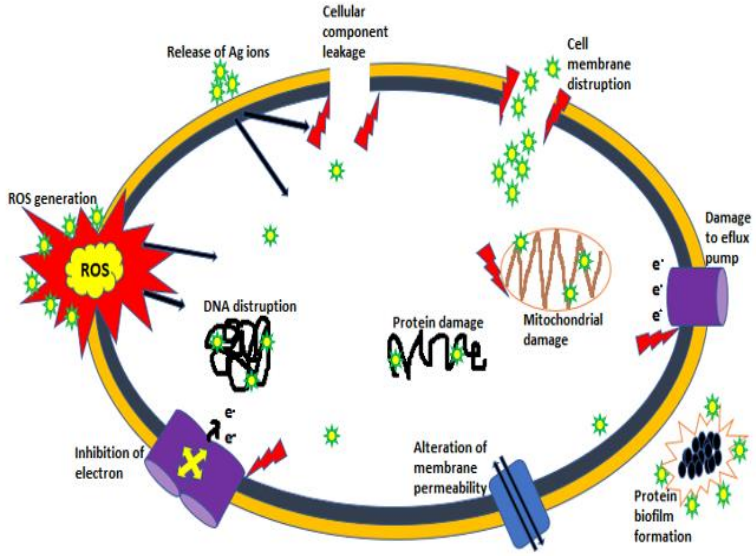

Figure 5. Antimicrobial mechanism of AgNPs [42].

Table 1. Examples of phytochemicals involved in green synthesis of AgNPs as capping, stabilizing, and reducing agents.

Plants	Capping, stabilizing and reducing agents	References
Aegel marmelos	Tannin	[28]
Trianthema decandra	Saponin	[29]
Acalypha indica	Quecetin	[31]
Hibiscus rosa-sinensis	Carboxylate ion groups	[32]
Solanum xanthocarpum	Alkaloids, phenolics, sugars	[33]
Syzygium cumini	Polyphenols	[34]
Azadirachta indica	Flavonoids, terpenoids	[35]
Achyranthes aspera	Polyols	[36]

Table 2. Examples of green AgNPs with antibacterial and antifungal activity.

Plant	Shape and size (nm)	Antimicrobial property against	References
Malva parviflora	Spherical, 50	*Fusarium solani, fusarium oxysporum, helminthosporium rostratum and alternaria alternate*	[43]
Brassica oleracea	Spherical, 20	*Streptococcus pneumonia ATCC 10015, Staphylococcus aureus ATCC 6538*	[44]
Fragaria ananassa	Spherical, 7-65	*Pseudomonas aeruginosa and bacillus licheniformis*	[45]
Nyctanthes arbortristis	Spherical and oval, 5-20	*Escherichia coli*	[46]
Carica papaya	Spherical, 5-40	*Staphylococcus aureus, bacillus substills*	[47]
Mangifera indica	Quasi spherical, 30.51 ± 5.3	*Pseudomonas aeruginosa*	[48]
Cestrum nocturnum	Spherical, 20	*Vibrio cholera and enterococcus faccalis*	[49]

Table 3. Examples of green AgNPs with antibiofilm activity.

Plant	Shape and size (nm)	Anti-biofilm properties against	References
Hyptis suoveolens	Spherical, 40-55	*Candida sp.*	[50]
Dononaea viscosa	Spherical, 40-55	*Candida sp.*	[50]
Camellia sinensis	Spherical, 11.3	*Pseudomonas aeruginosa, Staphylococcus aureus, klebsiella pneumoniae and enterococcus faecalis*	[51]
Anethum graveolens	Spherical, 9.67	*Pseudomonas aeruginosa, Staphylococcus aureus, klebsiella pneumoniae and enterococcus faecalis*	[51]
Glochidion lanceolarium	Spherical, 92.3	*Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli*	[52]
Semecarpus anacardium	Spherical, 62.72	*Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli*	[52]
Bridelia retusa	Spherical, 74.56	*Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli*	[52]

Table 4. Examples of green AgNPs having cytotoxic activity.

Plant	Shape and size (nm)	Cytotoxic activity	References
Juglans regia	Spherical, 31.4	Breast cancer cell line (MCF-7)	[53]
Phoenix dactylifera	Spherical, 67	Colon cancer cell line (LoVo)	[54]
Ferula asafoctida	Spherical, 105.7	Colon cancer cell line (LoVo)	[54]
Acacia nilotica	Spherical, 100.4	Colon cancer cell line (LoVo)	[54]
Piper longum	Spherical, 15-40	Breast cancer cell line (MCF-7)	[55]
Azadirachta indica	Spherical, 34	HepG2, LoVo and MDA-MB231	[56]
Calligonum comosum	Spherical, 90.8	Hepatoma G2 (HepG2), Colon cancer cell line (LoVo) and Breast cancer cell line (MDA-MB231)	[56]
Cyperus conglomeratus	Spherical, 70-100	Breast cancer cell line (MCF-7)	[57]
Tinospora cordifolia	Spherical, 25-50	Human lung adenocarcinoma cell line (A549)	[58]

Table 5. Examples of green AgNPs with wound healing properties.

Plant	Shape and size (nm)	Form used	Studied using	References
Curcuma longa	Spherical, 15-40	AgNPs loaded cell lines	*In vitro* wound scratch assay using l.929 fibroblast cell lines	[59]
Catharanthus roseus	Spherical, 80-250	Nano-formulation	Mice excision wound model	[59]
Azadirachta indica	Spherical, 40-80	Nano-formulation	*In vitro* mice excision wound model	[59]
Scutellaria barbata	Spherical, 20-40	Coated cotton wound dressing	*In vitro* wound scratch assay	[60]
Boletus pinnata	87.77	Different concentration of AgNPs	*In vitro* wound scratch assay using l.929 fibroblast cell lines	[61]

Conclusion

Antibiotic resistance has obviously become a global crisis, which necessitated the urgent search for alternative antimicrobial agents. In the last decade, researchers have channeled many efforts into developing safer methods for synthesizing AgNPs. Green synthesis is one of the methods that has gained massive attention from researchers due to numerous advantages mentioned earlier. However, limitations have been reported in recent works carried out using this method. These limitations are due to the complex nature of crude extracts. Also, significant variation exists in the chemical compositions of crude extracts of the same species when collected from different parts of the world. At present, pure compound isolates are better alternatives to crude extracts for the synthesis of AgNPs. However, more work is needed to understand factors like the cost of isolation and purification, limited availability, reduced synergistic effects, and toxicity concerns at high concentrations of pure compounds, which could restrict their use as antimicrobial drugs.

Abbreviations

AR: antimicrobial resistance
NMs: nanomaterials
MBNMs: metal-based nanomaterials
AgNPs: silver nanoparticles
RNA: ribonucleic acid
DNA: deoxyribonucleic acid
ROS: reactive oxygen species
ASP: aspalathin

Authors' Contribution

SOA, EOD and IOD came up with the idea and participated in writing of the manuscript. IOD, GAA and AAB performed all literature surveys. FOO and IOD analyzed the interpretation of literature. All authors read and approved the final manuscript.

Acknowledgments

None

Conflict of interest

The authors declare no conflict of interest

Article history:

Received: 27 February 2026
Received in revised form: 9 April 2026
Accepted: 9 April 2026
Available online: 9 April 2026

References

1. Mubeen B, Ansar AN, Rasool R, Ullah I, Imam SS, Alshehri S, Ghoneim MM, Alzarea SI, Nadeem MS, Kazmi I. 2021. Nanotechnology as a novel approach in combating microbes providing an alternative to antibiotics. *Antibiotics*. 10: 1473.
2. Thapa M, Choudhury SR. 2021. Green synthesized nanoparticles: Physicochemical properties and mode of antimicrobial activities. *Compr Anal. Chem*. 94: 49–79.
3. Butler MS, Capon RJ. 2026. Natural product inspired antibiotics approved for human use – 1943 to 2025. *Nat Prod Rep*. Advance Article.
4. Sagar S, Kaistha S, Das AJ, Kumar R. 2019. *'Era of Antibiotic Discovery', in Antibiotic resistant bacteria: A challenge to modern medicine*. Springer: Singapore; pp. 1–13. 1: 1–13.
5. Hashem I, Van Impe JF. 2022. A game theoretic analysis of the dual function of antibiotics. *Front Microbiol*. 12: 812788.
6. Makabenta JMV, Nabawy A, Li CH, Schmidt-Malan S, Patel R, Rotello VM. 2021. Nanomaterial-based therapeutics for antibiotic-resistant bacterial infections. *Nat Rev Microbiol*. 19: 23–37.
7. Shahzadi S, Fatima S, ul Ain Q, Shafiq Z, Janjua MRSA. 2025. A review on green synthesis of silver nanoparticles (SNPs) using plant extracts: a multifaceted approach in photocatalysis, environmental remediation, and biomedicine. *RSC Adv*. 15: 3858–3903.

8. Jubair N, Rajagopal M, Chinnappan S, Abdullah NB, Fatima A. 2021. Review on the antibacterial mechanism of plant-derived compounds against multidrug-resistant bacteria (MDR). *Evid Based Complement Altern Med*. 2021: 3663315.
9. Nikolic P, Mudgil P. 2023. The cell wall, cell membrane and virulence factors of *Staphylococcus aureus* and their role in antibiotic resistance. *Microorganisms*. 11: 259.
10. Kapoor G, Saigal S, Elongavan A. 2021. Action and resistance mechanisms of antibiotics: a guide for clinicians. *J. Anaesthesiol. Clin Pharmacol*. 37(1): 53–58.
11. Khameneh B, Iranshahy M, Soheili V, Bazzaz BSF. 2019. Review on plant antimicrobials: a mechanistic viewpoint. *Antimicrob. Resist Infect. Control*. 8: 117.
12. Silva KPT, Sundar G, Khare A. 2023. Efflux pump gene amplifications bypass necessity of multiple target mutations for resistance against dual-targeting antibiotic. *Nat Commun*. 14: 38507.
13. Sun S, Li X, Zhang Y. 2025. Emerging antibiotic resistance mechanisms mediated by novel proteins and translational regulation. *Eur. J. Clin. Microbiol Infect Dis*. 44: 1125–1139.
14. Vergalli J, Bodrenko IV, Masi M, Moynié L, Acosta-Gutiérrez S, Naismith JH, Pagès JM. 2024. Porins and small-molecule translocation across the outer membrane of Gram-negative bacteria. *Nat Rev Microbiol*. 22: 164–179.
15. Al-Awsi GRL, Alameri AA, Al-Dhalimy AMB, Gabr GA, Kianfar E. 2023. Application of nano-antibiotics in the diagnosis and treatment of infectious diseases. *Braz J Biol*. 84: e264946.
16. López C, de Dicastillo M, Correa G, Martínez FB, Streitt C, Galotto MJ. 2020. In *Antimicrobial Effect of Titanium Dioxide Nanoparticles*, López C (ed). *IntechOpen*: London; Chapter 7: 1–20.
17. Mondal SK, Chakraborty S, Manna S, Mandal SM. 2024. Antimicrobial nanoparticles: current landscape and future challenges. *RSC Pharm*. 1(3): 388–402.
18. Sharma D, Gautam S, Singh S, Srivastava N, Khan AM, Bisht D. 2025. Unveiling the nanoworld of antimicrobial resistance: integrating nature and nanotechnology. *Front Microbiol*. 15: 1391345.
19. Ullah S, Khan MN. 2022. Classification, synthetic, and characterization approaches to nanoparticles, and their applications in various fields of nanotechnology: a review. *Catalysts*. 12: 1386.
20. Khan T, Ullah N, Nadhman A, Wahab A, Khan AU. 2024. Plant-mediated green synthesis of silver nanoparticles and their antimicrobial applications. *J Adv Res*. 48: 1–18.
21. Haque S, Patra CR. 2021. Biosynthesized nanoparticles (gold, silver and platinum): therapeutic role in angiogenesis. *Compr Anal Chem*. 94: 25–48.
22. Altammar KA. 2023. A review on nanoparticles: characteristics, synthesis, applications, and challenges. *Fron. Microbiol*. 14: 1155622.
23. Alqahtani O, Mirajkar KK, Kumar KRA, Mahnashi MH, Shaikh IA, Mitra S, Nagaraj H, More SS, Muddapur UM, Khan AA. 2022. In vitro antibacterial activity of green synthesized silver nanoparticles using *Azadirachta indica* aqueous leaf extract against MDR pathogens. *Molecules*. 27(21): 7244.
24. Sathishkumar M, Geethalakshmi S, Saroja M, Venkatachalam M, Gowthaman P. 2021. Antimicrobial activities of biosynthesized nanomaterials. *Compr Anal Chem*. 94: 81–102.
25. Saed M, Ayivi DR, Wei J, Obare SO. 2024. Gold nanoparticles antibacterial activity: does the surface matter? *Colloid Interface Sci Commun*. 62: 100804.
26. Gardea-Torresdey JL, Gomez E, Peralta-Videa JR, Parsons JG, Troiani H, Jose-Yacaman M. 2003. Alfalfa sprouts: a natural source for the synthesis of silver nanoparticles. *Langmuir*. 19: 1357–1361.
27. Sur UK, Ankamwar B, Karmakar S, Halder A, Das P. 2018. Green synthesis of silver nanoparticles using the plant extract of Shikakai and Reetha. *Mater Today Proc*. 5: 21467–21472.
28. Dhir R, Chauhan S, Subham P, Kumar S, Sharma P, Shidiki A, Kumar G. 2024. Plant-mediated synthesis of silver nanoparticles: unlocking their pharmacological potential–a comprehensive review. *Front Bioeng Biotechnol*. 12: 1324805.
29. El-Shabasy RM, Yosri N, El-Gendy AO, El-Shabasy AM. 2024. Green synthesis of silver nanoparticles using plant extracts: synthesis, characterization and antimicrobial applications. *Environ. Nanotechnol. Monit Manag*. 21: 100923.
30. Fahim M, Shahzaib A, Nishat N, Jahan A. 2024. Green synthesis of silver nanoparticles: methods, influencing factors, and applications. *JCIS Open*. 16: 100125.
31. Krishnaraj C, Jagan EG, Rajasekar S, Selvakumar P, Kalaichelvan PT, Mohan NJCSB. 2010. Synthesis of silver nanoparticles using *Acalypha indica* leaf extracts and its antibacterial activity against water borne pathogens. *Colloids Surf B Biointerfaces*. 76: 50–56.
32. Nayak D, Ashe S, Rauta PR, Nayak B. 2015. Biosynthesis, characterisation and antimicrobial activity of silver nanoparticles using *Hibiscus rosa-sinensis* petals extracts. *IET Nanobiotechnol*. 9: 201–206.
33. Sengottaiyan A, Mythili R, Selvankumar T, Aravinthan A, Kamala-Kannan S, Manoharan K. 2016. Green synthesis of silver nanoparticles using *Solanum indicum* L. and their antibacterial, splenocyte cytotoxic potentials. *Res Chem Intermed*. 42: 8773–8787.
34. Kumar V, Yadav SC, Yadav SK. 2010. *Syzygium cumini* leaf and seed extract mediated biosynthesis of silver nanoparticles and their characterization. *J Chem Technol Biotechnol*. 85: 597–603.
35. Akinfenwa AO, Abdul NS, Docrat FT, Marnewick JL, Luckay RC, Hussein AA. 2020. Cytotoxic effects of phytomediated silver and gold nanoparticles synthesised from Rooibos (*Aspalathus linearis*) and aspalathin. *Plants*. 10: 2460.
36. Elumalai D, Ashok K, Suresh A, Hemavathi M. 2016. Green synthesis of silver nanoparticle using *Achyranthes aspera* and its larvicidal activity against three major mosquito vectors. *Eng Agric Environ. Food*. 9: 1–7.
37. Liao C, Li Y, Tjong SC. 2024. Bactericidal and cytotoxic properties of silver nanoparticles: mechanisms, applications and future perspectives. *Int J Mol Sci*. 25(2): 1123.
38. Velidandi A, Dahariya S, Pabbathi NPP, Kalivarathan D, Baadhe RR. 2020. A review on synthesis, applications, toxicity, risk assessment and limitations of plant extracts synthesized silver nanoparticles. *NanoWorld J*. 6: 79.
39. Zhang Y, Chen Y, Westerhoff P, Hristovski K. 2024. Mechanisms of antimicrobial activity of metal and metal oxide nanoparticles: a review. *Chem Eng J*. 475: 145924.
40. Rodrigues AS, Batista JGS, Rodrigues MAV, Thipe VC, Minarini LAR, Lopes PS, Lugão AB. 2024. Advances in silver nanoparticles: a comprehensive review on their potential as antimicrobial agents and their mechanisms of action elucidated by proteomics. *Front Microbiol*. 15: 1440065.
41. Eker F, Akdasci E, Duman H, Bechelany M, Karav S. 2025. Microbial-based green synthesis of silver nanoparticles: a comparative review of bacteria- and fungi-mediated approaches. *Int J Mol Sci*. 26: 10163.
42. Zhu C, Diao Z, Yang Y, Liao J, Wang C, Li Y, Liang Z, Xu P, Liu X, Zhang Q, Gong L, Ma Q, Liang L, Lin Z. 2025. Recent advances and challenges in metal-based antimicrobial materials: a review of strategies to combat antibiotic resistance. *J Nanobiotechnol*. 23: 193.
43. Al-Otibi F, Perveen K, Al-Saif NA, Alharbi RI, Bokhari NA, Albasher G. 2021. Biosynthesis of silver nanoparticles using *Malva parviflora* and their antifungal activity. *Saudi J Biol Sci*. 28: 5320–5328.
44. Ansar S, Tabassum H, Aladwan NS, Naiman Ali M, Almaarik B, AlMahrouqi S. 2021. Eco-friendly silver nanoparticles synthesis by *Brassica oleracea* and its antibacterial, anticancer, and antioxidant properties. *Sci Rep*. 11: 14789.
45. Umoren SA, Nzila AM, Sankaran S, Solomon MM, Umoren PS. 2017. Green synthesis, characterization and antibacterial activities of silver nanoparticles from strawberry fruit extract. *Pol J Chem Technol*. 19: 61–68.
46. Gogoi N, Babu PJ, Mahanta C, Bora U. 2015. Green synthesis and characterization of silver nanoparticles using alcoholic flower extract of *Nyctanthes arbortristis* and in vitro investigation of their antibacterial and cytotoxic activities. *Mater Sci Eng C*. 50: 8–15.
47. Banala RR, Nagati VB, Karnati PR. 2015. Green synthesis and characterization of *Carica papaya* leaf extract coated silver nanoparticles through X-ray diffraction, electron microscopy and evaluation of bactericidal properties. *Saudi J Biol Sci*. 22: 262–267.
48. Hai ND, Dat NM, Thinh DB, Nam NTH, Dat NT, Phong MT. 2022. Phytosynthesis of silver nanoparticles using *Mangifera indica* leaves extract at room temperature: formation mechanism, catalytic reduction, colorimetric sensing, and antimicrobial activity. *Colloids Surf B Biointerfaces*. 218: 112974.
49. Keshari AK, Srivastava R, Singh P, Yadav VB, Nath G. 2020. Antioxidant and antibacterial activity of silver nanoparticles synthesized by *Cestrum nocturnum*. *J Ayur Integr Med*. 11: 7–13.
50. Muthamil S, Devi VA, Balasubramaniam B, Balamurugan K, Pandian SK. 2018. Green synthesized silver nanoparticles demonstrating enhanced in vitro and in vivo antibiofilm activity against *Candida* spp. *J Basic Microbiol*. 58: 443–452.
51. Rolim WR, Lamilla C, Pieretti JC, Díaz M, Tortella GR, Cristina Diez M. 2019. Comparison of antibacterial and antibiofilm activities of biologically synthesized silver nanoparticles against several bacterial strains of medical interest. *Energy Ecol Environ*. 4: 149–157.
52. Mohanta YK, Biswas K, Jena SK, Hashem A, Abd_Allah EF, Mohanta TK. 2020. Anti-biofilm and antibacterial activities of silver nanoparticles synthesized by the reducing activity of phytoconstituents present in the Indian medicinal plants. *Front Microbiol*. 11: 1143.
53. Khorrami S, Zarrabi A, Khaleghi M, Danaei M, Mozafari MR. 2018. Selective cytotoxicity of green synthesized silver nanoparticles against the MCF-7 tumor cell line and their enhanced antioxidant and antimicrobial properties. *Int J Nanomedicine*. 13: 8019–8033.
54. Mohammed AE, Al-Qahtani A, Al-Mutairi A, Al-Shamri B, Aabed K. 2018. Antibacterial and cytotoxic potential of biosynthesized silver nanoparticles by some plant extracts. *Nanomaterials*. 8: 382.
55. Jayapriya M, Dharumadurai D, Arulmozhi M, Eswaramoorthy N, Senthil NC, Sureshkumar K. 2019. Green synthesis of silver nanoparticles using *Piper longum* catkin extract irradiated by sunlight: antibacterial and catalytic activity. *Res Chem Intermed*. 45: 5861–5875.
56. Algebaly AS, Mohammed AE, Abutaha N, Elobeid MM. 2020. Biogenic synthesis of silver nanoparticles: antibacterial and cytotoxic potential. *Saudi J Biol Sci*. 27: 2419–2428.
57. Al-Nuairi AG, Mosa KA, Mohammad MG, El-Keblawy A, Soliman S, Alawadhi H. 2020. Biosynthesis, characterization, and evaluation of the cytotoxic effects of biologically synthesized silver nanoparticles from *Cyperus conglomeratus* root extracts on breast cancer cell line MCF-7. *Biol Trace Elem Res*. 196: 381–391.
58. Mittal J, Pal U, Sharma L, Verma AK, Ghosh M, Sharma MM. 2020. Unveiling the cytotoxicity of phytosynthesized silver nanoparticles using *Tinospora*

cordifolia leaves against human lung adenocarcinoma A549 cell line. *IET Nanobiotechnol*. 14: 606–614.

59. Lakkim V, Reddy MC, Pallavali RR, Reddy KR, Reddy CV, Bilgrami AL. 2020. Green synthesis of silver nanoparticles and evaluation of their antibacterial activity against multidrug-resistant bacteria and wound healing efficacy using a murine model. *Antibiotics*. 9: 902.
60. Veeraraghavan VP, Periadurai ND, Karunakaran T, Hussain S, Surapaneni KM, Jiao X. 2021. Green synthesis of silver nanoparticles from aqueous extract of *Scutellaria barbata* and coating on the cotton fabric for antimicrobial applications and wound healing activity in fibroblast cells (L929). *Saudi J Biol Sci*. 28: 4205–4213.
61. Kaplan Ö, Tosun NG, Özgür A, Tayhan SE, Bilgin S, Türkekul İ. 2021. Microwave-assisted green synthesis of silver nanoparticles using crude extracts of *Boletus edulis* and *Coriolus versicolor*: characterization, anticancer, antimicrobial and wound healing activities. *J Drug Deliv Sci Technol*. 66: 102641.
62. Bamal D, Singh A, Chaudhary G, Kumar M, Singh M, Rani N, Sehrawat AR. 2021. Silver nanoparticles biosynthesis, characterization, antimicrobial activities, applications, cytotoxicity and safety issues: An updated review. *Nanomaterials*. 11: 2086.
63. Singh R, Lillard JW, Singh S. 2024. Nanoparticle toxicity: mechanisms, evaluation and regulatory perspectives. *Nanotoxicology*. 18(2): 145–170.
64. Wang H, Li X, Zhang Y, Chen J, Liu Q. 2024. Oxidative stress and DNA damage: mechanisms, biomarkers and implications for human diseases. *Redox Biol*. 71: 103118.
65. Mehnath S, Das AK, Verma SK, Jeyaraj M. 2021. Biosynthesized/green-synthesized nanomaterials as potential vehicles for delivery of antibiotics/drugs. *Compr Anal Chem*. 94: 179–204.
66. Omolaja AA, Pearce B, Omoruyi SI, Badmus JA, Ismail E, Marnewick J, Hussein AA. 2021. The potential of chalcone-capped gold nanoparticles for the management of diabetes mellitus. *Surf Interfaces*. 25: 101251.