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Review Article

Plant-Derived Silver Nanoparticles as Promising Therapeutic Agents in Overcoming the Global Challenge of Antimicrobial Resistance

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ABSTRACT

Antimicrobial resistance has reached a critical inflection point, with drug-resistant infections directly responsible for over one million deaths annually and projected to cause 1.91 million deaths per year by 2050. The failure of the antibiotic pipeline leaves a therapeutic need for new, non-resistance approaches, especially against ESKAPE pathogens that have evolved multiple mechanisms of resistance, including the ability to produce enzymes that degrade antimicrobials, express increased amounts of efflux pumps that pump the antimicrobials out of the cell, modify target molecules, and thrive in biofilms, which rapidly neutralise any single-mechanism antibiotic. Plants-derived silver nanoparticles hold another approach to this crisis, one that comes in combination with several different fields: ethnomedicine-based phytochemistry and nanotechnology. Phytochemicals such as flavonoids, polyphenols and tannins, play multifunctional roles, such as reducing and capping agents, regulating the size, shape and composition of the organic corona that imparts biocompatibility to the nanoparticles. This combination of modes of action, namely disruption of the membrane, formation of ROS, inhibition of the respiration and arrest of the DNA replication, shows the nanomaterials the multi-target profile, which makes the development of resistance highly improbable. This critical review discusses the phytochemical-based determinants for biofabrication, details the antimicrobial spectrum that is resistant bacteria and fungal pathogens and investigates approaches to surface engineering such as polymer coating and synergistic antibiotic conjugation. Toxicology and regulatory hurdles remain to be overcome before this can be realised in the clinic, while anticancer and wound healing applications are also evaluated.

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INTRODUCTION

Penicillin was first discovered in 1928 and totally changed the course of modern medicine by making bacterial infections that once had near 100% mortality rates treatable [1]. These times are teeing up and in trouble. AAMR is the ability of microorganisms to continue to grow and multiply despite treatment with a given antimicrobial agent, and has become an actual global health crisis. Led by the Global Research on Antimicrobial Resistance project, a September 2024 paper in The Lancet magazine using 520 million individual health records from 204 countries and territories revealed more than one million people had died annually from drug resistant infections between 1990 and 2021, and more than 1.14 million of them only in 2021 were directly attributed to resistance [2]. If left unchecked, direct deaths caused by AMR are expected to rise to 1.91 million deaths per year by 2050 (67.5% increase) and resistant infections may cause up to 8.2 million deaths per year [3]. In cumulative terms, more than 39 million lives could be lost to antimicrobial-resistant infections from 2025 to 2050 where the highest geographic impact is estimated to be in South Asia with around 11.8 million lives lost in that time period.

This grand level of projection is a parallel to a somewhat discouraging fact, and one that is even more concerning: the near stagnation of the antibiotic development pipeline [4]. The financial upside of developing antibiotics is increasingly falling behind the financial upside of developing drugs against chronic non-communicable diseases and has led to a progressive de-investment by major pharma companies in antibiotic research, with the clinical community now tasked with coping with an increasing problem with antibiotic resistant organisms using a pharmaceutical toolbox that hasn't really changed in decades. Empirical design of structurally related compounds to the known classes of antibiotics has been defeated again and again in the battle against the mutational and horizontal gene transfer abilities of bacteria, especially in a nosocomial environment where repeated antibiotic exposure increases the speed at which bacteria can acquire resistance [5]. In fact, the global scientific and regulatory framework has failed to deliver a sustainable solution to the issue on scale, which is why the World Health Organization has officially declared antimicrobial resistance as one of the top global public health and development threats [6]. In this context, plant-based production of silver nanoparticles has appeared a scientifically fascinating solution, in which two well-established knowledge systems are combined. Silver has long been recognized to be an antimicrobial agent, and its antimicrobial action has been used for centuries as an antiseptic to treat wounds, to clean water, and to preserve food, when any understanding of the physiology of bacteria existed [7].

The parallel tradition of plant-based medicine has been formally validated in many national pharmacopoeia and supported by an extensive literature of phytochemicals hundreds of biologically active secondary metabolites polyphenols, flavonoids, alkaloids, tannins and terpenoids each of which has a meaningful pharmacological activity [8]. The reducing and capping role of phytochemicals in the medium leads to the formation of zerovalent metallic nanoparticles having specific morphology and also forms a corona of biologically active molecules on the surface of the silver nanoparticles, which brings these two traditions together: the reducing and capping role of phytochemicals in the medium, transforming ionic silver into the zerovalent form of the metal, and the association of biologically active molecules in the corona on the surface of the nanoparticles. The antimicrobial activity of the resulting nanomaterial is more of a combination of mechanism of action (MoA) via the release of silver ions and via phytochemicals, which different from the mechanism of action of a single targeted antibiotic [9,10].

This review focuses on the scientific findings and therapeutic significance of plant-derived silver nanoparticles: with emphasis on antimicrobial resistance. It moves from outlining the molecular mechanisms giving rise to resistance, and the organisms that they target, to the phytochemical control of nanoparticle synthesis, then the multi-target modes in which they differ from traditional antibiotics, and their proven array of activities Then it discusses engineering approaches that facilitate clinical use, areas of non-antimicrobial activity and toxicologic and regulatory challenges for the translational pathway for this class of emerging nanomaterials.

2. The Antimicrobial Resistance Landscape: Burden, Drivers, and Unmet Clinical Need

These bacteria, known as the ESKAPE group *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter* species cause the highest clinical and epidemiological damages under antimicrobial pressure [11]. According to the World Health Organization's new 2024 Bacterial Priority Pathogens List, carbapenem-resistant *A. baumannii*, carbapenem-resistant *P. aeruginosa* and carbapenem-resistant Enterobacteriaceae are all in the World Health Organization's critical tier, which represents the top priority for bacteria. In healthcare facilities the global carbapenem resistance rates for *A. baumannii* are higher than 70%, with mortality rates of 67% in intensive care units (ICUs) [12]. The increase in deaths attributed to methicillin-resistant *Staphylococcus aureus*, highlighted as a high-priority, rose from 57,200 in 1990 to 130,000 in 2021 and is not expected to stop any time soon with current treatment patterns [13].

The resistance mechanism (s) used and maintained by these pathogens are very varied, and importantly many of the mechanisms are also used within the same pathogen, providing a multi-mechanism defence response which makes single mechanism antibiotic therapy inherently weak [14]. Notably, *A. baumannii* is capable of inactivating the antibiotic by means of carbapenemase activity, such as OXA-type (OXA-23, OXA-24/40 and OXA-58), and Enterobacteriaceae are capable of inactivating the antibiotic by means of KPC and NDM carbapenemase activity. Target site modification, such as the alternative penicillin binding protein (PBP2a) encoded by mecA in MRSA which has a low affinity for β-lactam antibiotics, is sufficient to make an entire class of drug useless, but not to degrade the drug itself [15]. Bacteria with efflux pump overexpression, in particular those from the resistance-nodulation-division (RND) family found in *P. aeruginosa* and *A. baumannii*, actively pump structurally diverse antibiotics out of the cytoplasm and provide a single-step cross-class resistance. Outer membrane porin proteins are lost or reduced, which contributes to the decrease in accumulation of drugs in the cell, and horizontal gene transfer of these resistance determinants occurs across species lines with alarming effectiveness via mobile genetic elements.

Biofilm formation is another facet of this resistance and a very serious one at that [16]. In a mature biofilm, extracellular polymeric matrix surrounds the bacteria, which are in a metabolically arrested state, and greatly diminish the effectiveness of antibiotics against actively metabolizing cells. The matrix slows antibiotic uptake to the cell surface and quorum-sensing dependent regulatory circuits activate collective defensive response over the entire population [17]. Antibiotic minimum inhibitory concentrations for biofilm-associated infections are 100–1000-fold greater than concentrations needed to kill planktonic cells, a threshold which is clinically inaccessible with the current arsenal of drugs without unacceptable systemic effects. These resistance mechanisms are increasingly pushing and pushing the pharmacist towards the very latest drugs with incredibly narrow therapeutic index, and of course, with no new, novel drug being on the horizon in the pipeline, it just keeps going [18]. The resistance patterns of ESKAPE members, WHO priority classifications and clinical consequences of treatment failure summarized for each member are shown in Table 1.

Table 1: Classification of Who Priority Resistant Pathogens, Predominant Resistance Mechanisms, and Current Treatment Limitations [19,20]

Pathogen	WHO Priority Tier (2024)	Key Resistance Mechanisms	Clinically Critical Phenotype	Consequence of Treatment Failure
Carbapenem-resistant *A. baumannii*	Critical	OXA-23, OXA-24/40, OXA-58 carbapenemases; RND efflux pumps; porin loss; biofilm	CRAB; pan-drug-resistant strains increasingly reported	ICU mortality up to 67%; limited salvage options

Pathogen	WHO Priority Tier (2024)	Key Resistance Mechanisms	Clinically Critical Phenotype	Consequence of Treatment Failure
Carbapenem-resistant *K. pneumoniae*	Critical	KPC, NDM, OXA-48 carbapenemases; ESBL production	CRKP; NDM-producing strains resist most β-lactams	Neonatal sepsis; bloodstream infections with >50% mortality
Carbapenem-resistant *P. aeruginosa*	Critical	VIM/IMP metallo-β-lactamases; OprD porin loss; RND efflux	XDR strains resistant to carbapenems, aminoglycosides, fluoroquinolones	Ventilator-associated pneumonia; colistin as last resort
Methicillin-resistant *S. aureus* (MRSA)	High	*mecA*-encoded PBP2a; biofilm formation; toxin production	VRSA (rare); VISA strains with reduced vancomycin susceptibility	Bacteraemia, endocarditis; 130,000 deaths annually (2021)
Vancomycin-resistant *E. faecium* (VRE)	High	*vanA/vanB* gene clusters; intrinsic ampicillin resistance	VRE phenotype; linezolid/ daptomycin as remaining options	Bloodstream and urinary tract infections in immunocompromised patients
Carbapenem-resistant *Enterobacter* spp.	High	AmpC β-lactamases; KPC; porin modification; efflux	CRE phenotype spreading via mobile plasmids	Post-surgical infections; hospital-acquired neonatal sepsis

3. Phytochemical Governance of Silver Nanoparticle Biofabrication

Although the synthesis of metallic nanoparticles from plant extracts, as described in popular literature, is often described as a simple replacement of one solvent with another, it is not [21]. Each important physical property of the resulting nanoparticle, its size, shape, surface charge, colloidal stability and the nature of colloidal organic corona, is determined, with high degree of specificity, by the phytochemical composition of the plant extract [22]. This relationship is not only of academic curiosity but also a prerequisite for designing artificial silver nanoparticles with predictable and reproducible therapeutic performance which are derived from plants. The chemical process for biosynthesis starts with the reaction between aqueous silver nitrate ($AgNO_3$) as the usual precursor that provides Ag^+ and the functional groups which are electron-donating components of the plant secondary metabolites. Polyphenols, flavonoids and tannins possess several hydroxyl (–OH) and carbonyl (>C=O) groups, which donate an electron to Ag^+ to generate zerovalent metallic silver (Ag^0) under mild conditions, that is, near-ambient temperature and pressure [23]. The flavonoids, very abundantly found in several genera of medicinal plants, especially in those of the Fabaceae and Caesalpiniaceae families, are especially active as reducing agents, thanks to the presence of catechol B-ring structures that allow step-by-step oxidation to induce an efficient electron transfer to reduce Ag^+ to Ag. These less potent reductants merely serve as a critical role in the stabilisation by adsorption to the nascent surface of the NP during growth and reducing the coalescence of the particles and prevent uncontrolled aggregation [24]. It is this polyfunctional nature of the plant extracts, which reduce, cap and stabilise it at the same time, that makes them different from the chemical synthesis methods where all three of these functions are performed by different reagents, that are often toxic.

The nucleation and growth process after reduction takes place in two steps [25]. In primary nucleation, the initial Ag^0 atoms created by the reduction process cluster together and become covered by the molecules of the phytochemicals, which provide the necessary stabilization. Such seeds then grow via additional Ag+ reduction at the surface and controlled growth of smaller particles in which the capping layer of phytochemicals plays a critical role in determining the ultimate growth morphology [26]. The extracts containing flavonoids and phenolic compounds usually give the majority of spherical nanoparticles with a diameter range between 10 and 25 nm which is related mainly with strong antimicrobial activity [27]. A tannin-rich extract is expected to give smaller and more monodisperse spherical particles because the tannins are capable of cross-linking a particle's surface very densely, whereas a high terpenoid extract is expected to give the triangular prismatic (or polyhedral) shapes. They're not

just random and rather predictable ones that the researchers have started exploiting by choosing their plants judiciously, based on their chemistry.

The interaction between phytochemicals and nanoparticles can be modulated by the processing parameters and such modulation is not underestimable in the formulation development process [28]. Solution pH is likely to be the most significant parameter, alkaline conditions will promote the ionisation of the hydroxyl groups in the phenol, and will increase the ability of phenol to donate electrons, leading to the formation of smaller and more uniform particles; acidic conditions will inhibit deprotonation and will result in larger and less uniform particles. Raise the temperature to increase collision frequency of phytochemical reductants with the Ag^+ ions, which decrease the synthesis time and generally result in smaller nanoparticles; be careful that the temperature does not get too high, because the protein-based capping agents found in some extracts may be denatured [29]. The molar ratio of silver nitrate to extract dictates the number of available reducing equivalents and the number of metal ions, a low molar ratio of extract to metal causes a number of the particles to remain incompletely capped leading to aggregation, and a high molar ratio of extract to metal reduces the surface coverage of the particles, but can lead to the ingression of other chromophores that may make it difficult to characterize the next step in the process. A systematic study of these parametric effects over a wide range of plant systems confirms biofabrication as an optimisable process whose results are not only dependent on the choice of botanicals but also on formulation science [30]. The organic corona, the phytochemical shell around the silver core, isn't pharmacologically inactive. FTIR spectroscopic studies of plant-derived AgNPs regularly reveal the presence bound polyphenols, flavonoids, and terpenoids on the surface of AgNPs, each of which possesses its intrinsic biological activity, which the composite nanomaterial inherits. This introduces a unique situation in normal pharmaceutical production: The excipient used to synthesize under the same time, also provides a therapeutic activity, making the distinction between the active pharmaceutical ingredient and the excipient somewhat indistinct [31]. The schematic of such a transformation, from phytochemical to nanoparticle, from Ag^+ reduction to nucleation, Growth, and surface capping is shown in Figure 1.

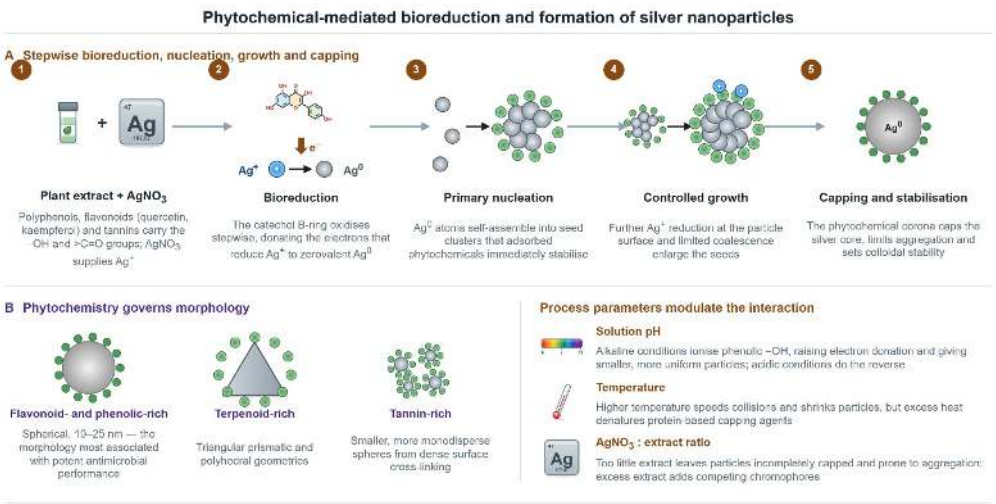

Figure 1: Schematic Representation of Phytochemical-Mediated Bioreduction and Nanoparticle Formation. the Figure Illustrates the Stepwise Process by Which Hydroxyl and Carbonyl Groups on Flavonoids and Polyphenols Donate Electrons to Ag^+ Ions (from $AgNO_3$), Driving Nucleation and Controlled Growth of Zerovalent Silver Nanoparticles, with the Phytochemical Corona Adsorbed on the Nanoparticle Surface Serving as the Capping and Stabilising Layer.

4. Multi-Target Antimicrobial Mechanisms: Why Plant-Derived AgNPs Outmanoeuvre Resistance

The key pharmacodynamic benefit of plant-based nanoparticles of silver over traditional antibiotics is that they do not attack just one target from one bacterium but may attack multiple targets of multiple bacteria [32]. Most antibiotics can be classified as suppressing a single molecular pathway, such as beta-lactams binding the penicillin-binding proteins, fluoroquinolones binding the DNA gyrase and macrolides binding the 50S ribosomal subunit. Mechanism is beautiful but at the same time, this monopharmacological precision has its own vulnerabilities: If a mutation occurs in the gene that encodes that target, or if a gene encoding an enzyme that neutralises the drug is acquired, the whole category of drugs is useless [33]. The antimicrobial activity of AgNPs targeting multiple structurally different physiological pathways of bacteria is fourfold and at the same time; this is a multi-step, unlikely event when compared with acquisition of single-step resistance [34]. In the first bactericidal action, silver nanoparticles come in contact with the surface of the bacterial cells, which bears a negative charge. This interaction occurs to both Gram-negative and Gram-positive bacteria due to their surface electronegativities, having the Gram-negative bacteria with their outer membrane and rich LPS content and the Gram-positive bacteria with their thick peptidoglycan wall and teichoic acid residues [35]. Physically, binding of the AgNPs onto the bacterial surface disrupts the membrane integrity by inducing membrane denaturation caused by accumulation of AgNPs in the pits of the cell wall, which leads to leakage of cytoplasmic contents such as potassium ions, proteins and nucleic acids through the increase in the permeability of the cell wall. It is a physical disruption which is not a receptor mediated event, meaning that bacteria cannot simply mutate into avoiding the receptor.

The Ag+ ions released from the surface of the nanoparticle can disrupt the membrane and trigger a chain of reactions within the cell that ultimately lead to the destruction of the cell, leading to the main bactericidal mechanism [36]. Silver ions react with thiol (–SH) groups of enzymes of the bacterial electron transport system that are part of the bacterial inner membrane, inhibiting the electron transport chain and thus interrupting the production of adenosine triphosphate [37]. The resulting collapse of cellular bioenergetics leads to high levels of reactive oxygen species (ROS) such as superoxide radicals ($O_2^{\cdot -}$), hydroxyl radicals ($^{\cdot}OH$) and hydrogen peroxide (H_2O_2) beyond the antioxidant capacities of bacteria. In multidrug-resistant bacteria, the accumulation of ROS has been shown to be a specific attack on bacterial antioxidant proteins: the enzymes glutathione reductase and alkyl hydroperoxide reductase were found to be significantly downregulated in AgNP treated bacteria in studies using iTRAQ-based quantitative proteomics [38]. In total, the combined effects of the ROS present as three types of cellular damage: lipid peroxidation of membrane phospholipids, protein oxidation and double stranded DNA breaks, which together exceed the capacity of the bacteria to survive [39].

On a molecular level, proteomic studies have shown some penicillin binding proteins involved in the synthesis of peptidoglycan in the cell wall were downregulated upon AgNP exposure, and the cell division protein FtsZ and the chromosomal replication initiating protein DnaA were found to be inhibited; these findings indicate that silver-mediated DNA interaction is not a general effect of toxicity but a mechanistically specific event. A silver ion attaches to the purine and pyrimidine bases, disrupting hydrogen bonding between complementary strands, and preventing the polymerase from moving along the DNA during replication [40]. This results not just in mutagenic damage but in cessation of cell division, as is seen in apoptosis-like bacterial response, with phosphatidylserine externalisation on the outer membrane leaflet and activation of a bacterial caspase-like protease in *E. coli* treated with silver nanoparticles. One extra area of activity where plant-derived AgNPs are potentially useful is the architecture that allows bacterial communities to form their most clinically undesirable infections known as Biofilm [41]. The two pivotal events that are essential for initiation and maturation of biofilms were found to be disruption of the quorum sensing signalling system and the impairment of bacterial cell adhesion to abiotic surfaces by AgNPs at 25 μg/mL in multidrug resistant *Streptococcus suis*. Figure 2 represents a schematic

model of the effects of TMG on membrane integrity, cellular bioenergetics (ATP production), DNA replication, protein synthesis, and quorum sensing, a pharmacodynamic profile unmatched in the traditional antibiotic armamentarium.

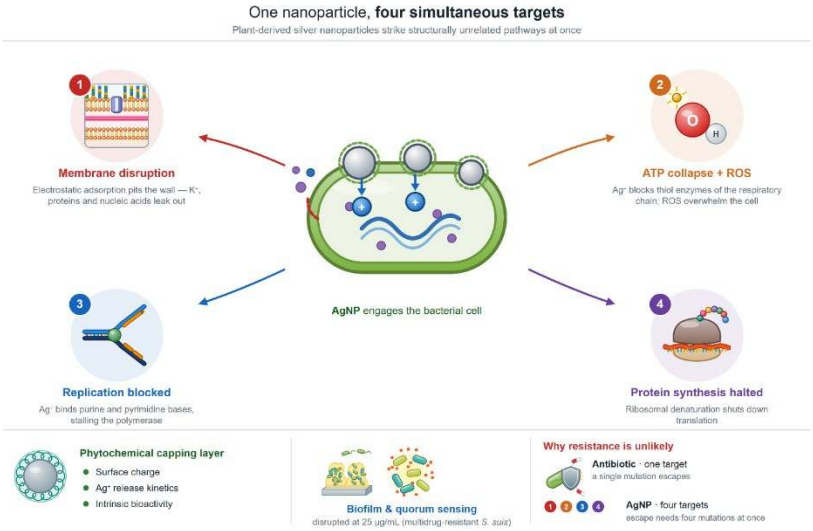

Figure 2. Integrated multi-target mechanism map of plant-derived silver nanoparticle antimicrobial action. The figure illustrates, as an original schematic, the four simultaneous mechanisms by which a single AgNP engages the bacterial cell: outer membrane disruption via electrostatic adsorption; Ag^+ ion-mediated respiratory chain inhibition and ROS generation; silver-DNA intercalation preventing replication; and ribosomal denaturation inhibiting protein synthesis with the phytochemical capping layer annotated as contributing to surface charge, Ag^+ release kinetics, and intrinsic bioactivity.

5. Spectrum of Activity: Resistant Bacteria, Fungal Pathogens, and Emerging Antiviral Potential

The anti-microbial potential of the plant derived silver nanoparticles is wider than that of almost all of the antibiotics around us and this is not merely because of the non-specificity in its physicochemical properties, but because of multi-target pharmacodynamics that interact with conserved bacterial structures without the need for a specific molecular receptor [42]. Not only are Gram-positive and Gram-negative bacteria susceptible, along with certain viruses, fungi as well; and Gram-positive and Gram-negative bacteria are very different in their cell envelopes.Gram-positive and Gram-negative bacteria, fungal species and certain viruses are vulnerable these nanomaterials are truly cross-kingdom antimicrobial.

Presents a good amount of evidence for activity against bacteria that are resistant to drugs [43]. Cascabela thevetia aqueous leaves extract was used for the synthesis of plant derived AgNPs which led to the formation of spherical shaped nanoparticles with the size range of 20–30 nm and shown to possess high antibacterial potential against MRSA, *Staphylococcus aureus*, *Enterococcus faecalis* and *Escherichia coli* with the minimum inhibitory concentration as low as 8 µg/mL against *S. aureus*, *E. faecalis* and *E. coli* among all the organisms tested. Significant antibacterial activity against MRSA in both in vitro and in vivo experimental models were reported for both Foeniculum vulgare and Alysicarpus monilifer leaf extracts using AgNPs [44]. The difference here is that the synthesized nanomaterials used in the in vivo models need to be stable and have to be bioavailable in the physiological environment, which in vitro cannot be reproduced [45]. The activity against ESKAPE Gram-negative pathogens has also been confirmed: AgNPs derived from Spirostachys africana extracts exhibited inhibition zone diameters up to 22 mm against the pathogen *Pseudomonas aeruginosa*, and minimum inhibitory concentrations as low as 0.08 mg/mL against *Acinetobacter baumannii*, an organism that has become

resistant to most available antibiotics due to carbapenem resistance.

In addition to the antibacterial aspect of the plant-derived activity of AgNP's, the antifungal activity is an aspect of the activity that should always be recognized; fungal pathogens identified on the WHO priority list cause about 3.8 million deaths every year, and because there is a limited armamentarium available for antifungal treatment, many fungal pathogens have been found to show signs of resistance [46]. The clinical isolate *Candida albicans* was tested with biogenic AgNPs synthesised using Pyracantha koidzumii and Schinus molle aqueous extracts and showed activity beyond MIC suppresses—AgNPs induced disruption in the cell wall, and inhibited hyphal growth, the morphological change that occurs during invasive candidal infection, and their inhibitory activity of secreted aspartyl proteinases, which are virulence factors involved in the penetration of tissues [47]. Silver nanoparticles prepared by the plant extract of Trillium govanianum exhibited antifungal activities against both *Candida auris* and *Candida glabrata*, which are two new fungi of clinical interest, with their inherent low level of susceptibility to azole treatment and their ability to form biofilms. These results confirm that the antifungal mechanism of plant-derived AgNPs is not similar to azoles targeting a single enzyme in ergosterol biosynthesis pathway, thus the cross-resistance issue observed with azole treatment might not be applicable to the antifungal therapy using AgNPs [48].

Although the antiviral evidence for plant derived AgNPs is less systematically characterised than the antibacterial data, published data suggest that binding to viral envelope proteins and surface glycoproteins which prevent host-cell binding and fusion events essential for viral infection can occur. Phytochemical capping could enhance antiviral effect by separate antiviral effect of the organic corona polyphenols and flavonoids [49]. This places plant-derived AgNPs as likely platforms for the antiviral activity against enveloped viruses, but the in vitro observations of antiviral activity would need significant more investment in their in vivo mechanistic and pharmacokinetic characterisation for translating into clinically effective antiviral therapy. A detailed comparative (preclinical) evidence from published studies is presented across different bacterial, fungal and viral targets as given in Table 2 [50].

Table 2: Comparative Antimicrobial Efficacy of Plant-Derived Silver Nanoparticles Against Key Resistant Pathogens: Summary of Preclinical Evidence [51,52]

Botanical Source	Phytochemical Class (Dominant)	Target Organism	Particle Size (nm)	MIC / Zone of Inhibition	Study Model	Key Outcome
Cascabela thevetia (aqueous leaf)	Flavonoids, phenolics	MRSA, *S. aureus*, *E. faecalis*, *E. coli*	20–30	Lowest MIC recorded for *S. aureus* and *E. coli*	In vitro	Broad antibacterial + antioxidant activity confirmed
Foeniculum vulgare (leaf extract)	Polyphenols, terpenoids	MRSA	Not specified	Significant antibacterial effect	In vitro & in vivo	In vivo efficacy validated in infection model
Alysicarpus monilifer (leaf extract)	Flavonoids	MRSA	Not specified	Active against MRSA clinical strains	In vitro & in vivo	Comparable to reference antibiotic in vivo
Spirostachys africana (acetone bark)	Tannins, phenolics	*P. aeruginosa*, *A. baumannii*	Not specified	Inhibition zone 22 mm (*P. aeruginosa*); MIC 0.08 mg/mL (*A. baumannii*)	In vitro	Activity against two WHO critical-priority pathogens
Pyracantha koidzumii (aqueous)	Polyphenols	*Candida albicans* (clinical isolates)	Not specified	Active at and beyond MIC	In vitro	Inhibited hyphal growth and proteolytic virulence factors

Botanical Source	Phytochemical Class (Dominant)	Target Organism	Particle Size (nm)	MIC / Zone of Inhibition	Study Model	Key Outcome
Trillium govanianum (plant extract)	Saponins, alkaloids	*C. auris*, *C. glabrata*, *K. pneumoniae*, *P. aeruginosa*	Not specified	Broad-spectrum antifungal and antibacterial	In vitro	First report of AgNP activity against *C. auris* from this source

6. Surface Engineering, Nanoplatform Integration, and Synergistic Antibiotic Combinations

While the in vitro antimicrobial properties of plant-based AgNPs are established, the use of plant-derived AgNPs to develop effective plant-based therapeutics needs to overcome the challenges of maintaining the antimicrobial activity in physiologically complex systems, which are far more complex than microbroth dilution assays [53]. Unmodified nanoparticles will be coated with blood plasma proteins within seconds of systemic administration, creating a protein corona that influences the coloid stability, cellular uptake behaviour and can significantly impair the antibacterial efficacy by hiding the surface charges that mediate electrostatic interaction with bacterial plasma membranes. Designed to meet these specific needs, surface engineering approaches that have been developed span from biopolymer coating to liposomal encapsulation to antibiotic conjugation to become a unique and new growing field in research on AgNPs derived from plants [54].

Beyond its ease of biocompatibility, chitosan, which is a cationic polysaccharide obtained when chitin is deacetylated, is one of the most widely studied coating materials for AgNPs for antibacterial uses [55]. The positively charged chitosan at physiological pH complements and reinforces the electrostatic effect of AgNPs binding to negative surfaces of bacteria, increasing the efficiency of targeting membranes. The functionalisation of plant-derived AgNPs with chitosan and subsequent conjugation with amoxicillin, cefixime and levofloxacin resulted in chitosan-based silver nanocomposites with synergistic antibacterial properties when tested against the same bacteria demonstrated in an animal system with minimal toxicity (direct translational significance) that was validated in the histopathological evaluation and biodistribution of the target tissues. A synergistic antibacterial activity between chitosan and AgNPs was seen in most of the combination combinations, resulting in a 37% to 97% reduction in the minimum inhibitory concentration of the assayed antibiotics when compared to the respective antibiotic alone [56]. This understanding of the underlying mechanism of this synergism is that the silver ions disrupt the membrane structure, and at the same time inhibit the function of efflux pumps, so that an intracellular accumulation of the co-administered antibiotic occurs, to a level that is too high for the bacteria's defence mechanism to eradicate [57].

The PEG coating deals with other clinical translation issues. PEGylation by steric repulsion prevents non-specific binding of proteins, provides longer half-life of circulation of nanoparticles by decreasing recognition by the mononuclear phagocyte system, and increases the colloid stability in ionic physiological media. A study with clinical isolates of *Escherichia coli* (*E. coli*) revealed improved inhibitory concentration values for PEG-coated AgNPs than those of conventional antibiotics, with the small particle size obtained during PEG stabilisation as the main factor responsible for the greater antimicrobial activity [58]. Similarly, polyvinylpyrrolidone (PVP) is utilized as a steric stabiliser in particular in the formulations applicable for topical application, with the expected surface contact time and local concentration maintenance as the dominating pharmacokinetic parameters [59]. In other formulations, poly combinations of chitosan, PEG, polyvinyl alcohol and PVP have been utilized to manufacture AgNPs with desirable size dispersities and to maintain their anti-bacterial activity to *S. aureus*, *P. aeruginosa* and *S. enterica* simultaneously [60]. For the AgNP, the structurally more complex approach of liposomal encapsulation protects the AgNP within a phospholipid bilayer compartment, preventing premature release of ionic silver during circulation and allowing the release of the AgNP at infection sites via pH-triggered and/or enzymatic destabilisation of the compartment, mechanisms well documented in the

liposomal antibiotic literature and readily applicable to silver nanoparticles [61].

This is further amplified in stimuli responsive platforms that feature pH-sensitive polymers, thermoresponsive coatings, or enzyme-cleavable linkers that allow for the controlled release of small molecules in the microenvironments that are unique to bacterial infection, such as the endogenous release triggers generated by tissue acidification and the production of bacterial proteases and lipases. While simpler polymer coating strategies offer some prospects for achieving targeting in translation, antibody-conjugated AgNPs offer the promise of species-specific targeting, with drawbacks of complexity and cost that are unique to antibody-based targeting agents [62]. The features of these nanoplatform strategies with respect to excipient type, the rationale for the pharmacokinetic considerations and increased antibacterial effect are summarized in Table 3.

Table 3: Nanoplatform Engineering Approaches for Plant-Derived AgNPs: Excipient Systems, Functionalization Rationale, and Enhanced Pharmacological Outcomes [63,64]

Nanoplatform Type	Excipient / Strategy	Pharmacokinetic/Pharmacodynamic Rationale	Demonstrated Benefit	Limitation
Chitosan-coated AgNPs	Chitosan (cationic polysaccharide)	Reinforces electrostatic engagement with bacterial membrane; mucoadhesive for topical use	Synergistic MIC reduction 37–97% with co-conjugated antibiotics; low in vivo toxicity validated	Activity pH-dependent; solubility decreases at alkaline pH
PEGylated AgNPs	Polyethylene glycol (PEG)	Steric protein repulsion; prolongs systemic circulation; reduces opsonisation	Enhanced antibacterial effect against MDR *E. coli*; improved colloidal stability in physiological media	Reduced surface reactivity; may lower Ag^+ release rate
PVP-stabilised AgNPs	Polyvinylpyrrolidone (PVP)	Steric stabiliser; suitable for topical sustained-contact applications	Controlled particle size; maintained antibacterial activity against multispecies panels	No targeted delivery capacity; rapid clearance systemically
Polymer-blend composites (CS+PEG+PVA+PVP)	Multi-polymer blend	Combines membrane-targeting, steric stability, and film-forming properties	Broad-spectrum activity against *S. aureus*, *P. aeruginosa*, *Salmonella enterica* simultaneously	Complex formulation optimisation required; interaction between polymers poorly characterised
Liposomal AgNPs	Phospholipid bilayer encapsulation	Shields Ag^+ from premature release; enables pH/enzyme-triggered release at infection sites	Anticipated improved bioavailability; reduced off-target silver toxicity	Liposomal stability with ionic AgNPs remains a formulation challenge
Stimuli-responsive platforms	pH/thermoresponsive or enzyme-cleavable polymers	Localised release in acidic or protease-rich infection microenvironments	Targeted infection-site delivery with reduced systemic exposure	Most evidence at proof-of-concept stage; in vivo validation limited

7. Therapeutic Applications Beyond Antibacterials: Wound Healing, Anticancer Activity, and Biosensing

While antibacterial properties have driven the commercial and research momentum behind AgNPs, the same properties that make AgNPs microbicidal also render them as "nanoscale surface reactivity" (NSR), "sustained ion release," and "biologically active phytochemical corona" that also qualify them as genuine multidomain therapeutic agents whose full potential as pharmaceuticals cannot be adequately assessed by antibacterial endpoints [65]. The anticancer activity is best cited of these secondary therapeutic uses. Synthesis of AgNPs using plant extract from Heliotropium bacciferum resulted in an intracellular ROS level increase of 150–250% in MCF-7 breast cancer and HCT-116 colorectal cancer cell lines at 5.44 µg/mL and 9.54 µg/mL respectively which is well below the

concentration typically used in cytotoxic reactions against normal non-cancer cells. The differential expression of pro- and anti-apoptotic proteins in the cells after treatment was verified by RT-PCR analysis, which allowed us to confirm that the devastating effect is not just due to the necrosis of the cytoplasm but also due to the regulated mitochondrial apoptosis pathway [66]. Such a mechanistic difference is pharmacologically relevant because mitochondria-induced apoptosis does not destroy neighbouring tissue architecture as a result of necrosis, an important factor to consider for any therapeutic agent to be used clinically in oncology. AgNPs prepared from Catharanthus roseus showed anticancer activity against HeLa cervical cancer cells with evident induction of apoptosis and arrest of the cell cycle, whereas AgNPs prepared from Polianthes tuberosa flower extract damaged the DNA to a remarkable extent (39.9%) in A431 melanoma cells and effectively induced ROS-driven apoptosis by COMET and fluorescence staining measurements [67]. An exhaustive review of the plant-mediated AgNP anticancer studies published during the years 2010–2024, analyzing their cytotoxic effects in colorectal cancer cell lines HCT-116, HT-29, Caco-2 and SW480, revealed that anticancer efficacy was tightly linked to AgNP size, surface charge and the type of phytochemical used to surround the particles, thus supporting the topic introduced in previous sections of this review that biological efficacy is governed by the plant from which AgNPs are derived. One application area where this dual functional profile, both antimicrobial and reparative for the wound microenvironment, is clinically relevant and could be achieved by plant-based agents like AgNPs, is wound healing. The silver nanoparticles synthesized by Rhizophora apiculata aqueous leaf extract were seen to close wounds at a rate of 82.79% in scratch assay model, which is significantly higher than that of plant extract, which closed wounds at 75.23% thereby indicating that silver nanoparticle was making a significant contribution to wound healing other than that of the plant extract [68]. AgNPs derived from Ageratina adenophora exhibited wound closure activity of 57.97% and exhibited antimicrobial and antioxidant properties. Overall, the 57.97% wound closure activity along with the antimicrobial and antioxidant properties of AgNPs derived from Ageratina adenophora showed the multiphasic nature of impaired wound healing, comprising of infection, oxidative damage and reduced cellular migration [69]. The most new and promising application area is biosensing. Considering how the localised surface plasmon resonance wavelength of silver nanoparticles is sensitive to changes in the dielectric environment caused by the binding of analytes, the inherent property of silver nanoparticles renders them extremely attractive as transducer candidates for electrochemical and colorimetric biosensors for detection of clinically relevant concentrations of bacterial pathogens, toxins and biomarkers. The collective scope of the face value of these applications is shown in Figure 3.

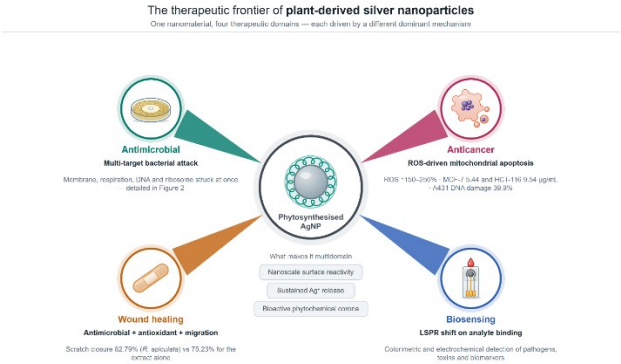

Figure 3: Graphical Summary of the Therapeutic Frontier of Plant-Derived Silver Nanoparticles. an Original Radial Diagram Centred on a Phytosynthesised AgNP, with Four Labelled Arms Indicating Antimicrobial Activity (Not Elaborated Here), Anticancer Therapy, Wound Healing, and Biosensing, Each Annotated with the Dominant Mechanism Operative in That Domain.

8. Toxicity, Biocompatibility, and the Regulatory Landscape

The clinical translation of plant-derived silver nanoparticles is not a simple scientific problem but rather a safety issue and without a scientific approach to this problem, in a manner that avoids any element of optimism, the responsible development of this class of agents cannot be expected to materialize [70]. Silver ions are the main components which mediate the antibacterial effect of AgNP, and have the natural ability to induce cytotoxicity, genotoxicity and immunological responses in mammalian cells at high levels. Under the condition of uncontrolled silver ion release, the same type of oxidative mechanisms which disrupt bacterial membranes and denature bacterial enzymes can, under similar conditions, disrupt mitochondrial function leading to ROS-mediated apoptosis in host cells [71]. The middle challenge for the biocompatibility of AgNP therapeutics is the selective toxicity towards the pathogen and acceptable host cell viability. Data collected in a variety of in vitro systems indicates that the most important factor in the mammalian toxicity of AgNP-based systems is the capping layer [72]. The character of the surface capping and the toxicity of structurally different capping agents were shown to be significantly different in both cell lines and experimental conditions when the toxicity of AgNPs was compared in 2024 in a Comparative Study published in Environmental Science: Nano. For plant derived AgNPs, polyphenolic, flavonoid rich and polysaccharide based capping layers of medicinal plants extracts have been consistently demonstrated to exhibit less mammalian cytotoxicity than their chemically synthesised counterparts using citrate or PVP capping [73]. The AgNPs capped with the synthesis of carboxymethyl tamarind as both the reductant and capping agent displayed strong antibacterial effects at clinically relevant concentrations with minimal or no cytotoxicity to mammalian cells, a selectivity window that is very few for chemically synthesized AgNPs [74]. According to studies conducted with the AgNPs extracted from turmeric, their biocompatibility was found to be greater than that of commercially available AgNPs as well as other biogenic AgNPs, and their cytotoxic and wound-healing activity was highly dependent on particle size, shape and colloidal stability, both in cell viability and in the in vivo Drosophila model. A new dimension of regulatory worry is added with environmental nanotoxicology. As AgNPs become more widely used in consumer and medical products, ambient levels of silver ions are likely to rise over time in aquatic and terrestrial ecosystems, a situation that may lead to further increases in ambient levels of silver at nanomolar concentrations, with silver ions known to be toxic to microalgae, invertebrates and fish [75]. Various scientific guidelines have been developed by regulatory authorities such as the US Food and Drug Administration and the European Medicines Agency to facilitate assessment of medical products containing AgNPs, and these guidelines require characterisation of size distribution, surface properties, dissolution behaviour and biopersistence of AgNPs which many preclinical studies do not yet satisfy [76]. The lack of standardised synthesis procedures that guarantee batch-to-batch reproducibility further hinders compliance due to inter-botanical harvest variability in phytochemical content which generates batch-specific preparations with different pharmacology and thus cannot be considered as the same preparation under current regulatory requirements [77].

9. Limitations and Future Perspectives

While significant preclinical evidence has been gathered throughout this review, numerous structural drawbacks still restrict the potential clinical applications of plant-derived AgNPs and need to be confessed candidly. The lack of standardised synthesis protocols is the most prevalent, physicochemical properties of plant-derived AgNPs can vary significantly by botanical species, extraction solvents, plant parts used and seasonal differences in phytochemical content that lead to variation from one synthesis batch to another and make direct inter-study comparisons and regulatory approval operationally challenging. Much of the antimicrobial information that has been published comes from in vitro broth dilution assays that do not attempt to mimic the physiological context of an in vivo infectious focus, such as the protein-rich environment that alters the surface charge of nanoparticles, the activity of immune cells that can regulate the activity of silver nanostructures, or the challenge of making these nanoparticles deliver therapeutic levels of silver ions to

target tissues while avoiding systemic deposition of silver ions [78]. Data regarding long-term in vivo safety in mammalian models is still limited for plant-based systems and human clinical trials data are virtually nonexistent to confirm regulatory-grade efficacy and safety levels [79]. These gaps are not fundamental barriers, however, but thoughtfully identified areas of research that can be systematically researched, and thus directly expedite translation. In the future, machine learning tools to distinguish phytochemical profile similarities between different botanicals, while linking the size and electrical charge of nanoparticles into biological activity, offer significant potential for rationally selecting botanicals through data to eliminate empirical optimisation [80]. Stimuli-responsive combinatorial nanoplatforms that are capable of delivering an antibiotic payload when needed, or a dispersing enzyme to break down biofilm, would overcome the clinical complexity of polymicrobial infections which can't be solved by single-agent approaches. In vitro-to-in vivo correlations like those developed for lipid nanoparticles would serve as the immediate link between these modeling approaches and regulatory requirements, whereas clinical adoption would be the most likely pathway in the short term when in vitro-to-in vivo correlation models are developed for AgNP pharmacokinetics and the NPs are integrated into such systems as wound dressings, implant coatings, and biosensing platforms.

CONCLUSION

Silver Nanoparticles from plant origin have a truly unique role in the field of nanomedicine. They are also resultants of an old pharmacological tradition, medicinal plants and modern nanotechnological science, when combined in them, they create a therapeutic entity, whose antibacterial activity combined with its mechanical complexity and translatability in terms of accessibility to the endemic population makes it quite different from conventional antibiotics and chemically synthesized metallic nanoparticles. The evidence discussed here indicates that the architecture of nanoparticles depends on their content of phytochemicals, that they possess multi-target bactericidal activity, and that the resulting nanoparticles exhibit some clinical relevance against the most critical ESKAPE pathogens. The antibacterial properties documented are only one aspect of the therapeutic significance of this class; other indications include anticancer and wound healing. The challenges are very real and should not be underestimated: Standardization, long-term safety validation and regulatory compliance all require continued and coordinated investment. The scientific study evidence reviewed here does not, however, show that this investment would be channeled into a pharmacologic strategy with a mechanistically robust rationale, an expanding body of experimental evidence, and a clear potential to provide to the global response to antimicrobial resistance.

REFERENCES

1. Gerberi D. Alexander Fleming: a second look. J Med Libr Assoc 2024;112:55–9. https://doi.org/10.5195/jmla.2024.1780.
2. Ajulo S, Awosile B. Global antimicrobial resistance and use surveillance system (GLASS 2022): Investigating the relationship between antimicrobial resistance and antimicrobial consumption data across the participating countries. PLOS ONE 2024;19:e0297921. https://doi.org/10.1371/journal.pone.0297921.
3. Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050. Lancet Lond Engl 2024;404:1199–226. https://doi.org/10.1016/S0140-6736 (24)01867-1.
4. Piddock LJV, Alimi Y, Anderson J, de Felice D, Moore CE, Røttingen J-A, et al. Advancing global antibiotic research, development and access. Nat Med 2024;30:2432–43. https://doi.org/10.1038/s41591-024-03218-w.
5. Nasrollahian S, Graham JP, Halaji M. A review of the mechanisms that confer antibiotic resistance in pathotypes of E. coli. Front Cell Infect Microbiol 2024;14:1387497. https://doi.org/10.3389/fcimb.2024.1387497.
6. Sati H, Carrara E, Savoldi A, Hansen P, Garlasco J, Campagnaro E, et al. The WHO Bacterial Priority Pathogens List 2024: a prioritisation study to guide research, development, and public health strategies against antimicrobial resistance. Lancet

Infect Dis 2025;25:1033–43. https://doi.org/10.1016/s1473-3099 (25)00118-5.

7. Phatanodom K, Angthong C. Silver Nanoparticle-Based Dressings for Various Wounds: Benefits and Adverse Effects. Pol J Surg 2022;96:46–52. https://doi.org/10.5604/01.3001.0016.1101.
8. Pathak M, dwivedi A, Kumar S, Verma G, Pal V. Plant-Based Therapeutics Against Communicable Diseases: A Review of Ethnopharmacology and Medicinal Chemistry Approaches. Chem Biodivers 2026;23:e71535. https://doi.org/10.1002/cbdv.71535.
9. Jiang X, Khan S, Dykes A, Stulz E, Zhang X. Biogenic Synthesis of Silver Nanoparticles and Their Diverse Biomedical Applications. Molecules 2025;30:3104. https://doi.org/10.3390/molecules30153104.
10. Gwada CA, Ndivhuwo PS, Matshetshe K, Aradi E, Mdluli P, Moloto N, et al. Phytochemical-assisted synthesis, optimization, and characterization of silver nanoparticles for antimicrobial activity. RSC Adv 2025;15:14170–81. https://doi.org/10.1039/d4ra08900f.
11. Miller WR, Arias CA. ESKAPE pathogens: antimicrobial resistance, epidemiology, clinical impact and therapeutics. Nat Rev Microbiol 2024;22:598–616. https://doi.org/10.1038/s41579-024-01054-w.
12. Bujor CG, Dinuti M, Sfrijan F. Carbapenem-Resistant Acinetobacter baumannii Isolation and In-Hospital Mortality in Adults Hospitalized with COVID-19 in Romania: A Retrospective Single-Center Cohort Study. J Clin Med 2026;15:8093. https://doi.org/10.3390/jcm15208093.
13. Wei K, Liu Q. Global burden of antimicrobial-resistant Staphylococcus aureus lower respiratory tract infections in older adults: a secondary analysis of the MICROBE database (1990–2021). BMC Infect Dis 2026;26:1350. https://doi.org/10.1186/s12879-026-13649-0.
14. Rajput P, Nahar KS, Rahman KM. Evaluation of Antibiotic Resistance Mechanisms in Gram-Positive Bacteria. Antibiotics 2024;13:1197. https://doi.org/10.3390/antibiotics13121197.
15. Lade H, Kim J-S. Molecular Determinants of β-Lactam Resistance in Methicillin-Resistant Staphylococcus aureus (MRSA): An Updated Review. Antibiotics 2023;12:1362. https://doi.org/10.3390/antibiotics12091362.
16. Hanot M, Lohou E, Sonnet P. Anti-Biofilm Agents to Overcome Pseudomonas aeruginosa Antibiotic Resistance. Pharmaceuticals 2025;18:92. https://doi.org/10.3390/ph18010092.
17. Ferreres G, Ivanova K, Ivanov I, Tzanov T. Nanomaterials and Coatings for Managing Antibiotic-Resistant Biofilms. Antibiotics 2023;12:310. https://doi.org/10.3390/antibiotics12020310.
18. Lewandowska W, Swiecicka I. Perspectives on Colistin—An Old Antibiotic with Renewed Relevance in Modern Medicine. Int J Mol Sci 2026;27:3115. https://doi.org/10.3390/ijms27073115.
19. Hansen MK, Østergaard L. Non-Traditional Antibacterial Agents Relevant to the WHO 2024 Priority Pathogens: A Structured Update of the Clinical Pipeline. Antibiotics 2026;15:899. https://doi.org/10.3390/antibiotics15090899.
20. Nisa TT, Nakatani D, Kaneko F, Takeda T, Nakata K. Antimicrobial resistance patterns of WHO priority pathogens isolated in hospitalized patients in Japan: A tertiary center observational study. PLOS ONE 2024;19:e0294229. https://doi.org/10.1371/journal.pone.0294229.
21. Mokhtar MM, Soliman RW, Salim J, Mohamed SK, Abdelsalam L, Abdelmonem R. Biologically Mediated Nanoparticle Synthesis as a Potential Green Strategy: Principles, Methods, and Pharmaceutical Applications. Pharmaceutics 2026;18:1151. https://doi.org/10.3390/pharmaceutics18091151.
22. Soares AR, Pavoski G, Espinosa DCR, Yin W, dos Passos Galluzzi Baltazar M. Current challenges and future directions in the green synthesis of nanoparticles using fungi. Bioprocess Biosyst Eng 2026;49:3059–84. https://doi.org/10.1007/s00449-026-03430-7.

23. Bundi AA, Jahan I, Lodhi V, Tripathi HM, Fatima A, Yamini, et al. Mechanistic understanding and comprehensive insights into green-synthesized cerium oxide nanoparticles and its applications. Discov Nano 2026;21:451. https://doi.org/10.1186/s11671-026-04919-6.
24. Bahari N, Hashim N, Abdan K, Md Akim A, Maringgal B, Al-Shdifat L. Role of Honey as a Bifunctional Reducing and Capping/Stabilizing Agent: Application for Silver and Zinc Oxide Nanoparticles. Nanomaterials 2023;13:1244. https://doi.org/10.3390/nano13071244.
25. Vorkapić M, Filipović N, Stanković A, Amić A. Who Reduces Silver? A Critical Review of the Biomolecular Drivers of Fungal-Mediated Silver Nanoparticle Biosynthesis. Int J Mol Sci 2026;27:6029. https://doi.org/10.3390/ijms27136029.
26. Nadaf AH, Mohammed AA, Mahmoud HQ, Aherkar VishwajeetV, Bhairungi SiddhalingB, Ovhal RekhaM, et al. Solvent dependent synthesis of silver nanoparticles using *Morus rubra* : correlating physicochemical properties with antimicrobial and anticancer activity. RSC Adv 2026;16:53564–79. https://doi.org/10.1039/d6ra04849h.
27. Al-Dbass AM, Daihan SA, Al-Nasser AA, Al-Suhaibani LS, Almusallam J, Alnwisser BI, et al. Biogenic Silver Nanoparticles from Two Varieties of Agaricus bisporus and Their Antibacterial Activity. Molecules 2022;27:7656. https://doi.org/10.3390/molecules27217656.
28. Mehmood A, Zahir S, Rauf Khan MA, Ahmad KS, Abasi F, Raffi M, et al. Optimization and biofabrication of phyto-mediated silver nanoparticles (Ag-NPs) for antibacterial potential. J Biomol Struct Dyn 2023;42:8063–72. https://doi.org/10.1080/07391102.2023.2242960.
29. Rajawat S, Malik MM. Study of the Effect of Temperature on the Size of Silver Nanoparticles Synthesized Using the Green Tollens Method. Curr Org Synth 2026;23. https://doi.org/10.2174/0115701794491228260914063348.
30. Chutrakulwong F, Thamaphat K, Intarasawang M. Investigating UV-Irradiation Parameters in the Green Synthesis of Silver Nanoparticles from Water Hyacinth Leaf Extract: Optimization for Future Sensor Applications. Nanomaterials 2024;14:1018. https://doi.org/10.3390/nano14121018.
31. Jan S, Rabbani G, Jan AT, Ahmad K. Nanocarrier Systems for Plant-Derived Bioactives: Design, Biosafety, and Translational Challenges. Pharmaceutics 2026;18:1148. https://doi.org/10.3390/pharmaceutics18091148.
32. Hao Z, Wang M, Cheng L, Si M, Feng Z, Feng Z. Synergistic antibacterial mechanism of silver-copper bimetallic nanoparticles. Front Bioeng Biotechnol 2024;11:1337543. https://doi.org/10.3389/fbioe.2023.1337543.
33. Hervin V, Roy V, Agrofoglio LA. Antibiotics and Antibiotic Resistance—Mur Ligases as an Antibacterial Target. Molecules 2023;28:8076. https://doi.org/10.3390/molecules28248076.
34. More PR, Pandit S, Filippis AD, Franci G, Mijakovic I, Galdiero M. Silver Nanoparticles: Bactericidal and Mechanistic Approach against Drug Resistant Pathogens. Microorganisms 2023;11:369. https://doi.org/10.3390/microorganisms11020369.
35. Hassan Afandy H, Sabir DK, Aziz SB. Antibacterial Activity of the Green Synthesized Plasmonic Silver Nanoparticles with Crystalline Structure against Gram-Positive and Gram-Negative Bacteria. Nanomaterials 2023;13:1327. https://doi.org/10.3390/nano13081327.
36. Wang X, Liu Z, Lin C. Metal ions-induced programmed cell death: how does oxidative stress regulate cell death? Life Sci 2025;374:123688. https://doi.org/10.1016/j.lfs.2025.123688.
37. Zou W, Liu Z, Chen J, Zhang X, Jin C, Zhang G, et al. Impact of sulfhydryl ligands on the transformation of silver ions by molybdenum disulfide and their combined toxicity to freshwater algae. J Hazard Mater 2022;435:128953. https://doi.org/10.1016/j.jhazmat.2022.128953.

38. Ameh T, Gibb M, Stevens D, Pradhan SH, Braswell E, Sayes CM. Silver and Copper Nanoparticles Induce Oxidative Stress in Bacteria and Mammalian Cells. Nanomaterials 2022;12:2402. https://doi.org/10.3390/nano12142402.

39. Ali HM, Karam K, Khan T, Wahab S, Ullah S, Sadiq M. Reactive oxygen species induced oxidative damage to DNA, lipids, and proteins of antibiotic-resistant bacteria by plant-based silver nanoparticles. 3 Biotech 2023;13:414. https://doi.org/10.1007/s13205-023-03835-1.

40. Krishnamoorthy R, Athinarayanan J, Periyasamy VS, Alshuniaber MA, Alshammari G, Hakeem MJ, et al. Antibacterial Mechanisms of Zinc Oxide Nanoparticle against Bacterial Food Pathogens Resistant to Beta-Lactam Antibiotics. Molecules 2022;27:2489. https://doi.org/10.3390/molecules27082489.

41. Tunç AK, Gecer EN, Erenler R, Marzi M. Biofilm inhibition by silver nanoparticles produced from Stachys spectabilis. BMC Complement Med Ther 2026;26:253. https://doi.org/10.1186/s12906-026-05438-8.

42. Campo-Beleño C, Villamizar-Gallardo RA, López-Jácome LE, González EE, Muñoz-Carranza S, Franco B, et al. Biologically synthesized silver nanoparticles as potent antibacterial effective against multidrug-resistant Pseudomonas aeruginosa. Lett Appl Microbiol 2022;75:680–8. https://doi.org/10.1111/lam.13759.

43. Singh RP, Hiteshi P, Sharma A, Kumar D, Kaur T. Interaction of Nanoparticles with Multidrug-Resistant Bacteria. ACS Omega 2025;10:53138–50. https://doi.org/10.1021/acsomega.5c07739.

44. Aljaafrih M, Choukaife H, Alfatama M. Polymyxin B and silver nanoparticles: a nanotechnology-driven approach to overcome antibiotic resistance. Drug Dev Ind Pharm 2025;51:1417–29. https://doi.org/10.1080/03639045.2025.2541790.

45. Kumar L, Singla S, Yadav J, Sharma J, Mehta SK, Singh S. In vivo evaluation of the antibacterial efficacy of polyethyleneimine nanoparticle-modified glass ionomer cement versus conventional glass ionomer cement. J Indian Prosthodont Soc 2026;26:389–96. https://doi.org/10.4103/jips.jips_481_25.

46. Eltahir AOE, Omoruyi BE, Lilly M, Luckay RC, Hussein AA. Biosynthesis of Silver Nanoparticles Using Ocimum basilicum Extract and Evaluation of Their Antifungal Efficacy Against Selected Fusarium Plant Pathogens. Molecules 2026;31:2985. https://doi.org/10.3390/molecules31172985.

47. Ahamad I, Bano F, Anwer R, Srivastava P, Kumar R, Fatma T. Antibiofilm Activities of Biogenic Silver Nanoparticles Against Candida albicans. Front Microbiol 2022;12:741493. https://doi.org/10.3389/fmicb.2021.741493.

48. Naumenko K, Zahorodnia S, Pop CV, Rizun N. Antiviral activity of silver nanoparticles against the influenza A virus. J Virus Erad 2023;9:100330. https://doi.org/10.1016/j.jve.2023.100330.

49. Luceri A, Francese R, Lembo D, Ferraris M, Balagna C. Silver Nanoparticles: Review of Antiviral Properties, Mechanism of Action and Applications. Microorganisms 2023;11:629. https://doi.org/10.3390/microorganisms11030629.

50. Sati A, Ranade TN, Mali SN, Yasin HKA, Samdani N, Satpute NN, et al. Silver Nanoparticles (AgNPs) as Potential Antiviral Agents: Synthesis, Biophysical Properties, Safety, Challenges and Future Directions─Update Review. Molecules 2025;30:2004. https://doi.org/10.3390/molecules30092004.

51. Garg M, Parashar S, Sharma MK, Garg C. Green Synthesized Silver Nanoparticles as Silver Lining in Antimicrobial Resistance: A Review. Curr Drug Deliv 2022;19:170–81. https://doi.org/10.2174/1567201818666210331123022.

52. Eker F, Duman H, Akdaşçi E, Witkowska AM, Bechelany M, Karav S. Silver Nanoparticles in Therapeutics and Beyond: A Review of Mechanism Insights and Applications. Nanomaterials 2024;14:1618. https://doi.org/10.3390/nano14201618.

53. Menichetti A, Mavridi-Printezi A, Mordini D, Montalti M. Effect of Size, Shape and Surface Functionalization on the Antibacterial Activity of Silver Nanoparticles. J Funct Biomater 2023;14:244. https://doi.org/10.3390/jfb14050244.

54. Muteeb G, Siraj RA. Nanotechnology-Enabled Strategies to Overcome Antibiotic Resistance in Respiratory Infections: Mechanisms, Platforms, and Translational Challenges. Biomedicines 2026;14:1693. https://doi.org/10.3390/biomedicines14081693.

55. Haji SH, Ali FA, Aka STH. Synergistic antibacterial activity of silver nanoparticles biosynthesized by carbapenem-resistant Gram-negative bacilli. Sci Rep 2022;12:15254. https://doi.org/10.1038/s41598-022-19698-0.

56. Gao F, Mi Y, Wu X, Yao J, Qi Q, Chen W, et al. Preparation of quaternized chitosan/Ag composite nanogels in inverse miniemulsions for durable and antimicrobial cotton fabrics. Carbohydr Polym 2022;278:118935. https://doi.org/10.1016/j.carbpol.2021.118935.

57. Shabatina TI, Vernaya OI, Melnikov MY. Hybrid Nanosystems of Antibiotics with Metal Nanoparticles—Novel Antibacterial Agents. Molecules 2023;28:1603. https://doi.org/10.3390/molecules28041603.

58. Muenraya P, Sawatdee S, Srichana T, Atipairin A. Silver Nanoparticles Conjugated with Colistin Enhanced the Antimicrobial Activity against Gram-Negative Bacteria. Molecules 2022;27:5780. https://doi.org/10.3390/molecules27185780.

59. Chirizzi D, Pellegrino R, Paladini F, D'Urso F, Pollini M, Broccolo F. Silver Nanoparticle-Functionalized Medical Devices for Primary Prevention of Healthcare-Associated Infections: In Vitro Efficacy Against Multidrug-Resistant Clinical Isolates. Microorganisms 2026;14:1534. https://doi.org/10.3390/microorganisms14071534.

60. Maqsood S, Taj Y, Satti L, Bakhat S. Synergistic effects of silver nanoparticles in combination with ineffective antibiotics against multidrug resistant Salmonella typhi. Pak J Med Sci 2024;40. https://doi.org/10.12669/pjms.40.6.7900.

61. Rofeal M, Abdelmalek F, Steinbüchel A. Naturally-Sourced Antibacterial Polymeric Nanomaterials with Special Reference to Modified Polymer Variants. Int J Mol Sci 2022;23:4101. https://doi.org/10.3390/ijms23084101.

62. Terzioğlu E, Arslan M, Balaban BG, Çakar ZP. Microbial silver resistance mechanisms: recent developments. World J Microbiol Biotechnol 2022;38:158. https://doi.org/10.1007/s11274-022-03341-1.

63. Abullais SS, Dhadse P, Kumar P M. Comparative antimicrobial potential of silver and zinc oxide nanoparticles versus chlorhexidine and tetracycline-based local drug delivery agents against periodontal pathogens: a systematic review. Discov Nano 2026;21:589. https://doi.org/10.1186/s11671-026-05027-1.

64. Wang X, Shan J, Zhang J, Yang D, Tian G, Dang Y, et al. Synergistic thermoresponsive and photothermal antimicrobial dressing based on bacterial cellulose with surface-grafted PNIPAM and PDA-coated silver nanoparticles for chronic wound treatment. Colloids Surf Physicochem Eng Asp 2025;727:138357. https://doi.org/10.1016/j.colsurfa.2025.138357.

65. Kumar A, Kumar D, Agrawal M, Kaur J, Kumar M, Kumar D, et al. Wound Healing Potential of Multifunctional Nanomaterials: Mechanism, Future Prospects, and Challenges. Pharmaceutics 2026;18:1054. https://doi.org/10.3390/pharmaceutics18091054.

66. Algotiml R, Gab-Alla A, Seoudi R, Abulreesh HH, El-Readi MZ, Elbanna K. Anticancer and antimicrobial activity of biosynthesized Red Sea marine algal silver nanoparticles. Sci Rep 2022;12:2421. https://doi.org/10.1038/s41598-022-06412-3.

67. Zhou B, Khan IM, Ding X, Niazi S, Zhang Y, Wang Z. Fluorescent DNA-Silver nanoclusters in food safety detection: From synthesis to application. Talanta 2024;273:125834. https://doi.org/10.1016/j.talanta.2024.125834.

68. Eze ED, Afodun AM, Ninsiima HI, Swase Terkimbi D. The role of nanoparticles in the treatment of diabetic foot ulcers: mechanisms, delivery platforms, translational challenges, and future directions. Discov Nano 2026;21:485. https://doi.org/10.1186/s11671-026-04953-4.

69. Hosseini K, Alizadeh M, Jalilian A, Hoseini S, Bahrami S, Shamosi A, et al. Silver nanoparticles combine with Nigella sativa oil to potentiate apoptosis in cervical cancer. Sci Rep 2026;16:11446. https://doi.org/10.1038/s41598-026-36082-4.

70. Auclair J, Gagné F. Shape-Dependent Toxicity of Silver Nanoparticles on Freshwater Cnidarians. Nanomaterials 2022;12:3107. https://doi.org/10.3390/nano12183107.

71. Reijnders L. Are Silver and Gold Nanoparticles Obtained by 'Green' Synthesis Biocompatible? Nanomaterials 2026;16:993. https://doi.org/10.3390/nano16160993.

72. Gao X, Johnson WE, Yourick MR, Campasino K, Sprando RL, Yourick JJ. Hepatotoxicity of silver nanoparticles: Benchmark concentration modeling of an in vitro transcriptomics study in human iPSC-derived hepatocytes. Regul Toxicol Pharmacol 2024;151:105653. https://doi.org/10.1016/j.yrtph.2024.105653.

73. Oćwieja M, Barbasz A, Wasilewska M, Smoleń P, Duraczyńska D, Napruszewska BD, et al. Surface Charge-Modulated Toxicity of Cysteine-Stabilized Silver Nanoparticles. Molecules 2024;29:3629. https://doi.org/10.3390/molecules29153629.

74. Ren Q, Ma J, Li X, Meng Q, Wu S, Xie Y, et al. Intestinal Toxicity of Metal Nanoparticles: Silver Nanoparticles Disorder the Intestinal Immune Microenvironment. ACS Appl Mater Interfaces 2023;15:27774–88. https://doi.org/10.1021/acsami.3c05692.

75. Jadaun P, Sharma D, Banerjee J, Mishra N. Gold and silver nanoparticles for safe and effective biomedical applications. Discov Nano 2026;21:468. https://doi.org/10.1186/s11671-026-04917-8.

76. Niu S, Guo M, Yang H, Chang X, Shang M, Wu L, et al. Ferroptosis effects and behavioral changes associated with high accumulation and low elimination percentage of silver in brain following a 28-day nasal instillation of silver nanoparticles in mice. Food Chem Toxicol 2025;202:115567. https://doi.org/10.1016/j.fct.2025.115567.

77. Al-Shaeri MA. Cytotoxicity and genotoxicity effects of green silver nanoparticles in mosquito Aedes aegypti and Culex pipiens larvae. Sci Rep 2026;16:34362. https://doi.org/10.1038/s41598-026-65320-y.

78. Frippiat T, Art T, Delguste C. Silver Nanoparticles as Antimicrobial Agents in Veterinary Medicine: Current Applications and Future Perspectives. Nanomaterials 2025;15:202. https://doi.org/10.3390/nano15030202.

79. Kalantari H, Turner RJ. Biogenic nanoparticles: overview of challenges in production, characterization and use. Front Chem 2026;14:1930144. https://doi.org/10.3389/fchem.2026.1930144.

80. Zawidlak-Węgrzyńska B, Rydz J. Polymer Nanoparticles in Medical Applications—Future Directions. Nanomaterials 2026;16:630. https://doi.org/10.3390/nano16100630.

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