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Silver nanoparticles: From green synthesis to antibacterial mechanisms, healthcare applications and toxicological considerations

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Abstract

With the alarming rise in multidrug-resistant bacterial strains, the search for new antimicrobial agents has become critical. Silver nanoparticles (AgNPs) have emerged as a highly promising contender, owing to their unique physiochemical properties, particularly their high surface-to-volume ratio and distinctive crystalline structure. This article delves into the comprehensive landscape of AgNPs, highlighting advancements from their environmentally conscious synthesis to their multifaceted mechanisms of action and diverse healthcare applications. A significant shift in AgNP production favors green synthesis methods, utilizing biological resources like plant and microbial extracts, notably Actinomycetes. This sustainable approach addresses the environmental concerns associated with traditional chemical and physical synthesis, paving the way for safer and more economically viable production routes. The antibacterial prowess of AgNPs stems from several key mechanisms: they physically disrupt bacterial cell membranes, leading to permeability changes and leakage; they interact intracellularly with sulfur and phosphorus-containing biomolecules like DNA and proteins, disrupting vital cellular processes; and they generate reactive oxygen species (ROS), inducing oxidative stress. Crucially, the release of silver ions from the nanoparticles further amplifies these cytotoxic effects, with optimal bactericidal activity observed in nanoparticles typically ranging from 1-10 nm. Beyond their direct antimicrobial capabilities, AgNPs find varied applications in healthcare. They are being integrated into existing restorative materials to enhance antibacterial properties, and are explored for use in medical devices such as surgical masks and catheters, offering sustained antimicrobial protection. However, the article also thoughtfully addresses the critical aspect of toxicology. While AgNPs demonstrate dose-dependent cytotoxicity to mammalian cells in vitro, their impact is significantly influenced by factors like particle size, surface chemistry, and the capping agents used during synthesis. Future research must continue to refine synthesis parameters and explore in vivo models more extensively to fully understand their long-term safety profile and ensure their responsible and effective deployment in clinical settings. Ultimately, AgNPs represent a vital component in our collective strategy to overcome the challenges posed by antimicrobial resistance.

Keywords: Silver Nanoparticles; Green Synthesis; Toxicological Considerations; Healthcare Applications; Antimicrobial Resistance

1. Introduction

The advent of nanotechnology holds immense promise for revolutionizing disease control and prevention, leveraging materials meticulously engineered at the atomic level. Among the most compelling nanomaterials noted for their antibacterial properties are metallic nanoparticles, whose heightened chemical activity stems from their expansive surface-to-volume ratio and distinctive crystalline surface structure [1,2]. Given the escalating emergence of bacterial strains resistant to even the most potent antibiotics, the investigation into bactericidal nanomaterials has become exceptionally pertinent and urgent. Building upon the established activity of silver ions and various silver-based compounds, this particular study delves deeper into the efficacy of silver nanoparticles. Specifically, this current work

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meticulously examines the effects of silver nanoparticles, ranging from 1 to 100 nm in size, on Gram-negative bacteria, employing high-angle annular dark field (HAADF) scanning transmission electron microscopy for detailed observation [3,4,5]. Our findings compellingly suggest that the bactericidal efficacy of these nanoparticles is notably size-dependent; indeed, only those typically measuring approximately 1-10 nm in diameter appear to engage in direct interaction with bacterial cells [6].

Silver nanoparticles (AgNPs) are precisely characterized as nanomaterials, meaning their dimensions consistently fall within the 1–100 nanometer range. What truly sets them apart is their significantly enhanced capacity and a remarkably higher surface-to-volume ratio compared to conventional bulk silver [7, 8]. Operating at this minuscule scale, silver unveils unique electrical, optical, and catalytic properties. These attributes have, in turn, driven widespread research and the creation of specialized products for applications spanning targeted drug delivery, sophisticated diagnostics, innovative detection methods, and advanced imaging technologies [9, 10]. Nevertheless, it's primarily the extraordinary antibacterial prowess of AgNPs that has captured the intense interest of both the scientific community and various industries. Consistently, these nanoparticles have exhibited powerful antimicrobial effects across a broad spectrum of infectious and harmful microorganisms, critically including those infamous multidrug-resistant bacterial strains. [11,12,]. The heightened antibacterial efficacy of nanoscale silver has proven exceptionally valuable within the medical and broader healthcare sectors. Consequently, the integration of AgNPs into a vast number of products, such as surgical instruments, food handling tools, various forms of clothing, cosmetics, dental products, catheters, and medical dressings, has been a subject of widespread study [13,14]. The inherent potential of AgNPs to serve as effective antibiotic alternatives is closely linked to their multifaceted mechanisms of action. Unlike many conventional treatments, these nanoparticles are capable of simultaneously targeting microorganisms across multiple structural components, thereby conferring upon them the ability to neutralize a wide range of bacterial types [15].

Currently, the pursuit of developing novel antibiotics is a notoriously arduous endeavor. Such investigations typically demand years of meticulous study concerning agent efficacy and safety, thereby consuming considerable time and financial resources. Concurrently, infections stemming from multi-resistant microorganisms continue their relentless proliferation, tragically contributing to global mortality rates [16]. In this context, often termed the 'post-antibiotic era,' AgNPs, along with other advanced nanomaterials, have become crucial subjects of research. The aim is to identify new agents capable of effectively combating pathogenic microorganisms without inadvertently fostering the emergence of further resistance [17,18]. Given that infections caused by antibiotic-resistant microbes represent a pressing global health concern, AgNPs stand out as a compelling alternative. Their versatility allows for applications in preventing such infections, decontaminating medical supplies, and even actively treating ongoing infections [19]. As a viable substitute for conventional antibiotics, this particular application has undergone extensive examination in recent years. The overarching objective has been to innovate new bactericidal products for decontamination or therapeutic intervention, leveraging the well-established knowledge of their effectiveness, even against highly challenging multidrug-resistant organisms [20].

2. Spectroscopic diagnosis of silver nanoparticles

The successful synthesis of silver nanoparticles was unequivocally confirmed through UV-Vis spectroscopic analysis, which revealed a prominent surface plasmon resonance (SPR) band precisely centered at 434 nm—a hallmark characteristic of these nanomaterials. Subsequent structural elucidation, performed using both transmission electron microscopy (TEM) and scanning electron microscopy (SEM), further validated the formation of spherical silver nanoparticles. These particles displayed a size distribution primarily ranging from 21.7 nm to 42.6 nm [21]. This specific spherical morphology, coupled with the observed size range, is deemed particularly advantageous. Such characteristics are recognized for promoting efficient cellular uptake while concurrently minimizing the likelihood of triggering an immune response, largely due to the nanoparticles' proportionally extensive surface area [22].

Consistent with previous findings [24], the Energy Dispersive X-ray (EDX) spectrum obtained from the biosynthesized silver nanoparticles presented characteristic absorption peaks indicative of metallic silver. While minor, weaker signals attributable to impurities were detected, the robust signal prominently observed at 3.5 keV within the silver region conclusively validated the successful formation of silver nanoparticles. Crucially, X-ray diffraction (XRD) analysis offered conclusive evidence regarding the crystalline structure of the silver nanoparticles. The resulting pattern showcased clear diffraction peaks appearing across the 2θ range of 35° to 90°. More precisely, distinct Bragg angle values at 2θ, measured at 37.77°, 43.92°, and 64.04°, were found to correspond directly to the characteristic reflections of metallic silver nanoparticles. Significantly, these observations align strongly with similar findings previously documented in the scientific literature [25,26,27].

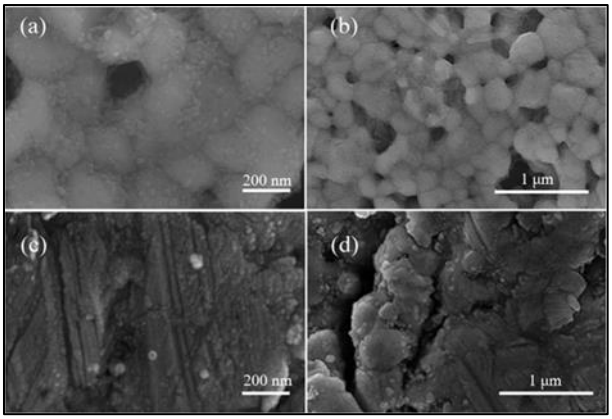

Figure 1 The Scanning Electron Microscopy (SEM) images membranes. [23]

Fourier Transform Infrared (FTIR) spectroscopic analysis performed on the extract revealed a broad and intense absorption peak centered at 3338 cm^{-1}, primarily ascribed to the stretching vibrations of both hydroxyl (-O-H) and N-H groups. Notably, the aliphatic (-C-H) stretching band was found to overlap with this broader peak. Additionally, the extract displayed a distinct amide peak (NH_2-C=O) at 1637 cm^{-1}, accompanied by a minor peak at 1100 cm^{-1}, characteristic of C-N amine-like functionalities [28].

Following the introduction of silver nanoparticles, the FTIR spectrum underwent notable transformations: the aliphatic C-H band, previously overlapped, emerged distinctly at 2979 cm^{-1} with increased amplitude. Furthermore, two discrete peaks materialized at 1552 cm^{-1} and 1388 cm^{-1}, signifying the presence of C=O and N-H- functionalities, respectively. The detection of N-H stretching vibrations strongly suggests the involvement of amide bonds within proteins in the bioreduction of $AgNO_3$ [48, 49]. This observation supports the hypothesis that the presence of reactive N-H and O-H groups enhances the susceptibility of Ag(I) ions to reduction, thereby facilitating the formation of elemental silver, Ag(29,30).

3. In Vitro Toxicity Assessments for Silver Nanoparticle Exposure

With the burgeoning development of novel products and technologies incorporating silver nanoparticles, a substantial body of research has emerged, specifically aimed at deciphering the potential cytotoxic consequences associated with exposure to high concentrations of these nanomaterials [31]. This section aims to shed light on the intricate mechanisms behind the observed effects by exploring the in vitro responses of mammalian cells to silver nanoparticles, considering diverse doses and sizes. We recognize that the use of medical products containing AgNPs presents various potential exposure routes, including ingestion, inhalation, or direct dermal contact [32,33].

4. Impact on Skin Cell Lines

Cancer remains a leading global cause of mortality [43], a clear dose-dependent reduction in cell viability was consistently observed with Ag-NPs. This cytotoxicity, effective even at low concentrations, aligns with similar findings reported by [34] and is often attributed to the inherently small size of the nanoparticles. Reinforcing these observations, comparable research published by [35] further indicates an inverse proportionality between Ag-NP concentration and the viability of the Caco-2 cell line. Specifically for Caco-2 cells, as Ag-NP doses escalated from 12.5 to 200 µg/mL, cell viability progressively decreased to 98.0%, 68.8%, 46.5%, 28.6%, and 4.8% respectively. At the highest tested concentration of 200 µg/mL, the cell viability plummeted to 4.8%. In this particular study, Ag-NPs demonstrated an IC50 value of 0.049 mg/mL[36].

Silver nanoparticles exhibit clear cytotoxic effects on skin cell lines in vitro, primarily via oxidative stress and mitochondrial dysfunction. The severity of toxicity is greater in 2D cultures than in 3D skin models, which better mimic in vivo barrier properties and reduce nanoparticle penetration and inflammatory responses. Surface chemistry and nanoparticle size further modulate toxicity, with smaller and certain surface-capped AgNPs showing higher cytotoxicity, especially toward cancerous skin cell [37,38].

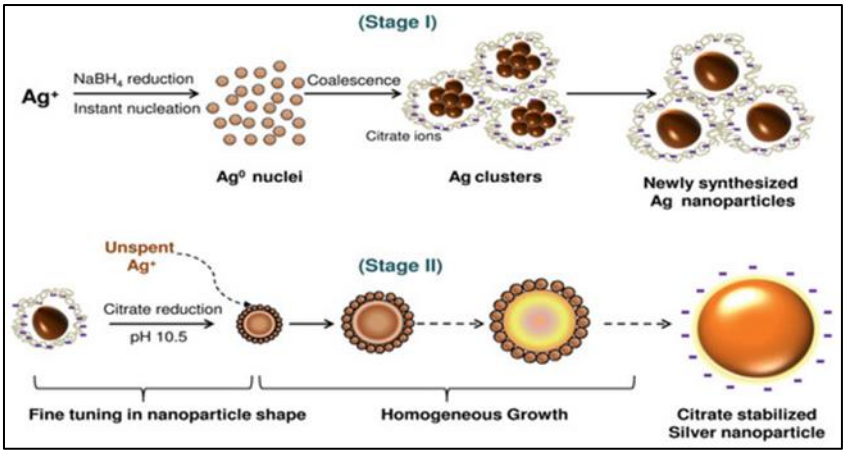

Figure 2 Offers a clear schematic representation illustrating the synthesis of silver nanoparticles (AgNPs) with controlled sizes, specifically detailing the co-reduction strategy. It is reproduced with permission from courtesy of the Royal Society of Chemistry[39]

Investigations into the potential effects of silver nanoparticles on the skin, particularly their permeability, have predominantly utilized keratinocyte cell lines and dermal fibroblasts. For instance, Sapkota et al. [40] meticulously assessed the impact of exposing CRL-2310 cells (human keratinocytes) to 20-nm silver nanoparticles, which were derived from a natural extract. Their MTT assay results conclusively demonstrated that the nanoparticles' influence on cell proliferation was distinctly dose-dependent: after 48 hours of exposure to 10 µg/ml of AgNPs, cell viability subtly declined to 98.76%, whereas a more pronounced reduction to 74.5% was observed following 48 hours of exposure to a higher concentration of 100 µg/ml. A similar dose-dependent correlation was also identified in a study involving HaCaT cells (another human keratinocyte lineage). In this particular study, the researchers meticulously utilized silver nanoparticles featuring a range of diameters—specifically 10, 30, and 60 nanometers—and experimented with diverse surface coatings, including sodium citrate (CIT), polyethylene glycol (PEG), and bovine serum albumin (BSA). Their investigation then precisely evaluated both cell viability and any metabolic alterations occurring subsequent to the AgNP exposure [41].

Kaur and Tikoo [42] conducted a study involving the synthesis of silver nanoparticles (AgNPs) using two distinct methods: one employing tannic acid (resulting in TSNPs) and another utilizing sodium borohydride (yielding BSNPs). These synthesis routes produced AgNPs with differing characteristics; TSNPs were measured at 30 nm with a zeta potential of −34 mV, while BSNPs were larger at 50 nm, exhibiting a less negative potential of −22 mV.

Upon exposing the A431 skin epithelial cell line to a 100 µg/mL concentration of TSNPs, we observed clear cytotoxic effects. These included significant disruption to the cell membranes, a noticeable decrease in cell count, and the induction of oxidative stress. Notably, these findings align well with observations from other studies previously discussed, this impact was also found to be dose-dependent. Further examination of these cells using Transmission Electron Microscopy (TEM) revealed a key difference: TSNPs successfully entered the cells, accumulating within both the cytoplasm and nuclei, The cytotoxicity of AgNPs is influenced by their capping agents. For example, alginate-capped AgNPs are selectively toxic to melanoma cells but not to normal fibroblasts, while PSSMA-capped AgNPs are toxic to both cell types. Cancer cell lines are generally more sensitive to AgNP-induced apoptosis than normal skin cell [43,44]. Conversely, BSNPs demonstrated limited efficiency in cellular uptake, a phenomenon likely attributed to their aggregation, possibly due to their lower zeta potential. This critical observation underscores the significant influence of nanoparticle size and their stability within the biological medium (in addition to the applied dosage) on the final cytotoxic outcomes. These findings also align with supporting literature that indicates a tendency for smaller nanoparticles to induce higher cytotoxic effects [45,46].

5. Antibacterial Applications of Silver Nanoparticles in Healthcare

The healthcare and medical sectors stand out as areas experiencing significant advancements in technologies that harness the potent antimicrobial capabilities of nanoparticles [47]. Given their inherent biocompatibility and ease of integration, (AgNPs) can can be successfully integrated into a wide array of products, endowing them with bacteria-killing properties. This section will delve into pertinent research concerning these applications and highlight some currently available topical commercial products [48,49].

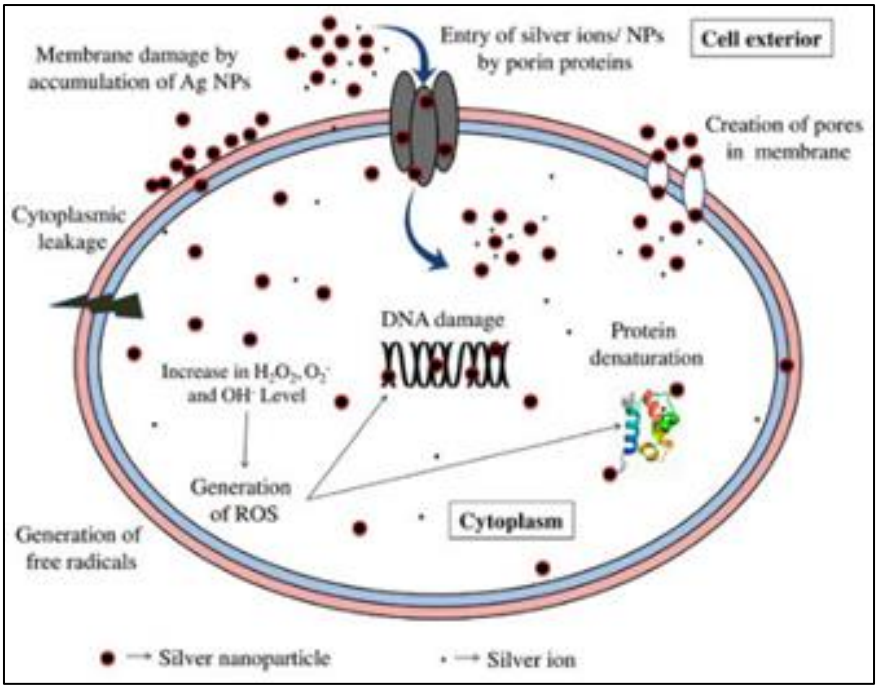

Figure 3 Bactericidal mechanisms of AgNPs due to their direct contact with the bacterial cell wall and the release of silver ions [50]

A primary application of silver nanoparticles lies in their use for enhancing the protective capacity of face masks for instance, The research's [51] developed a face mask featuring a coating of nanoparticles composed of silver nitrate and titanium dioxide. An innovative mask showcased an impressive capacity to diminish E. coli and Staphylococcus aureus colony-forming units by a complete 100% within just 24 hours. Similarly, another study involved a commercially available mask that, once impregnated with silver nanoparticle solutions at either 50 or 100 ppm, proved highly effective in curbing the growth of both E. coli and Staphylococcus aureus [52]. These AgNP-enhanced face masks, therefore, hold considerable promise for infection prevention, especially in vulnerable settings such as hospitals where pathogenic microorganisms commonly thrive. Furthermore, separate research investigated the utility of a disinfectant containing silver nanoparticles as an active sterilizing agent specifically for surgical masks [53]. The resulting formulation exhibited robust antibacterial activity, and masks impregnated with this formulation successfully inhibited the growth of *E. coli*, *Staphylococcus*, and *Pseudomonas.*

Moving beyond face masks, catheters enhanced with silver nanoparticle coatings have also drawn considerable research attention for their significant role in preventing infections and improving overall sterility [6]. Indeed, one compelling study provided strong evidence that catheters with embedded nanoparticle coatings effectively suppressed the growth and biofilm development of challenging organisms like *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans* for a minimum of 72 hours [7]. Moreover, these specially coated catheters markedly reduced the proliferation of *Enterobacteriaceae* and *Pseudomonas aeruginosa* strains. Crucially, this same research also extended its scope to investigate the potential toxic effects associated with these coated catheters within animal models [54,55]. Reassuringly, the use of these coated catheters for periods up to 10 days did not induce any discernible toxic effects or inflammation at the application site. The experiment further confirmed that up to 84% of the nanoparticle coating remained stably encapsulated throughout the study period, thereby lending strong support to the adoption of this technology for enhancing both the antimicrobial efficacy and safety of AgNP-coated catheters [56].

Firstly, Evidence suggests that silver nanoparticles primarily exert their effects at the membrane level. They possess the ability to penetrate the outer membrane of bacterial cells and subsequently accumulate within the inner membrane. Adherence of nanoparticles to the cell membrane destabilizes and damages it, increasing its permeability and triggering the leakage of its vital contents, ultimately leading to cell death [57,58]. Moreover, findings indicate that silver nanoparticles can interact with sulfur-containing proteins found within the bacterial cell wall. This interaction is believed to induce structural damage, ultimately leading to the rupture of the cell wall itself. A second hypothesized mechanism posits that these nanoparticles do more than just penetrate the cell membrane; they also significantly alter its fundamental structure and permeability; They can also penetrate the cell interior. Once inside, and due to their intrinsic properties, silver nanoparticles (AgNPs) are believed to exhibit a strong affinity for sulfur or phosphorus

groups. These groups are ubiquitous in intracellular components such as DNA and proteins, and their interaction with them can radically alter their structure and essential functions. Additionally, these nanoparticles may disrupt the respiratory chain Once situated within the inner membrane, they interact with the thiol groups found in various enzymes, stimulating the production of reactive oxygen species (ROS) and free radicals. This chain of events damages the intracellular machinery and may activate the apoptotic pathway (programmed cell death) [59,60]. A third mechanism, hypothesized to occur simultaneously with the two previously mentioned, involves Owing to their minute size and specific charge, silver ions are gradually released from these nanoparticles, these liberated silver ions can easily interact with many cellular components, leading to changes in critical metabolic pathways, compromising membrane integrity, and even damaging genetic material [61,62].

In a distinct investigation, silver nanoparticles of various dimensions were synthesized using the same foundational reagents and general methodology, albeit with carefully modulated pH conditions and differing ratios of reducing and stabilizing agents within the reaction mixtures. The bactericidal and antibacterial efficacy of these nanoparticles, ranging in length from 5 to 100 nm, was subsequently assessed against both Gram-negative and Gram-positive bacterial strains [63]. The resulting minimum inhibitory concentrations (MICs) demonstrated considerable variability across the tested strains: values from 20 to 110 µg/ml were observed for two *Escherichia coli* strains, 60 to 160 µg/ml for *Bacillus subtilis*, and 30 to 120 µg/ml for *Staphylococcus aureus*, with an overall observed range extending up to 200 µg/ml. Crucially, a consistent trend emerged wherein the smaller 5 nm nanoparticles generally correlated with the lower end of these inhibitory concentration ranges, while the larger 100 nm nanoparticles were associated with the higher concentrations required for inhibition[64,65].

Furthermore, bactericidal concentrations (BCs) for all strains under study spanned a range of 30 to 140 µg/ml. It was also specifically noted that the minimum bactericidal concentration (MBC) required for *Staphylococcus aureus* exceeded 200 µg/ml. As clearly evidenced by the MIC outcomes, the antibacterial activity of these nanoparticles is profoundly size-dependent, this effect is attributed to the considerably larger surface area that smaller nanoparticles present, thereby facilitating more comprehensive direct engagement with the bacterial cell surface [66,67,68]. The synergistic antimicrobial activity of silver nanoparticles (AgNPs) when combined with conventional antibiotics has been consistently highlighted across a multitude of investigations.[1] For instance, a recent notable study explored the effects of AgNPs alongside antibiotics such as chloramphenicol, kanamycin, and ampicillin. It was reported that the combination of silver nanoparticles with chloramphenicol achieved up to a 50% inhibition The synergistic application of silver nanoparticles and kanamycin demonstrated a remarkable effect, leading to nearly 95% higher growth inhibition *against Escherichia coli, S. typhimurium,* and *S. aureus*. This stands in stark contrast to individual treatments, showcasing a significantly elevated efficacy for these identical bacterial strains [69].

These compelling findings suggest that the enhanced efficacy of such combined treatments stems from AgNPs' capacity to compromise the bacterial membrane's integrity and potential. This disruption effectively heightens membrane permeability, thereby facilitating a more efficient uptake of antibiotics into the bacterial cell. It is crucial to highlight that these particular experiments employed sublethal concentrations of silver nanoparticles in conjunction with half the minimum inhibitory concentration of the respective antibiotics [70].

Silver nanoparticles (AgNPs) have traditionally been fabricated through a diverse array of physical and chemical approaches. These methods encompass techniques such as the chemical reduction of silver ions (Ag^{2+}) using agents like sodium citrate (Na3C6H5O7), polyol synthesis, various electrochemical and photochemical methods, photoablation [72], ultrasonic chemical approaches, and surfactant-assisted synthesis. However, the inherent toxicity and lethal nature of the chemicals frequently employed in these conventional physical and chemical processes present significant environmental concerns [73]. Consequently, there is an escalating imperative to explore and develop safer, less toxic, environmentally benign, and biocompatible methods for producing AgNPs with precise dimensions and morphologies [74]. In this context, biological synthesis routes are gaining prominence, as they are largely considered safe, economically viable, feasible, and ecologically sound, despite potential drawbacks like increased synthesis time and a somewhat lesser degree of control over the resulting crystal size, shape, and overall structure [75].

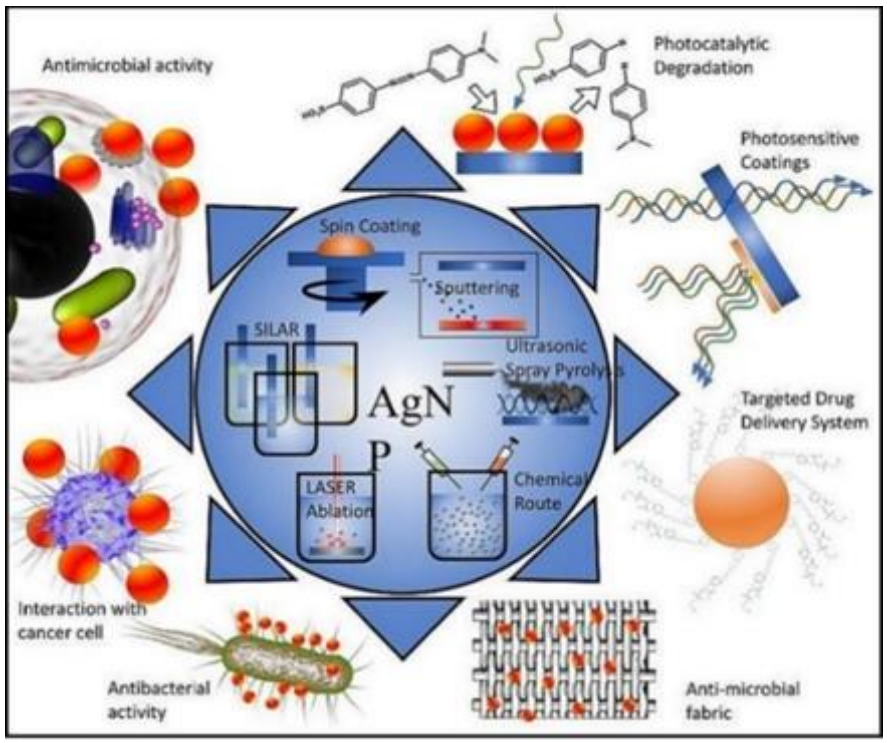

Figure 4 Biological effects of silver nanoparticles [71]

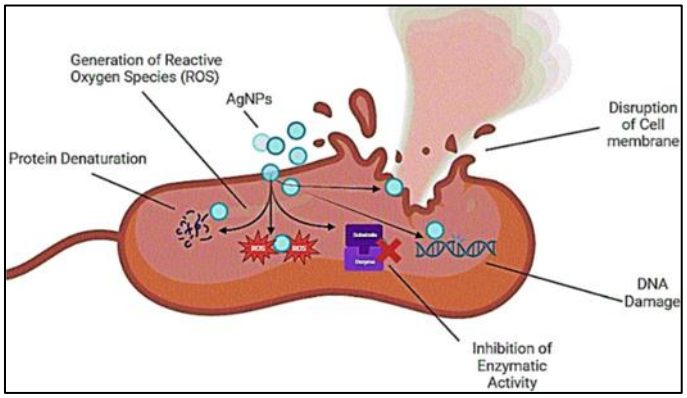

Figure 5 Offers a hypothetical illustration, outlining the various potential mechanisms through which silver nanoparticles exert their antibacterial effects against bacterial cells [76]

It is well-established that various experimental parameters profoundly influence the ultimate size and morphological characteristics of nanoparticles [77]. These critical factors include the sample's pH, prevailing temperature conditions, the overall reaction duration, the specific nature of the extract employed, the precise mixing rate of the extract with the metal salt, and the way the metal salt associates with the chosen reducing agent. While silver nanoparticles are often not perfectly monodispersed and can be produced at a relatively slower pace [78], naturally occurring unicellular and multicellular components from plants and microbes offer promising avenues. These biological entities serve as excellent bioreductants for developing AgNPs, often facilitating high proliferation rates and the formation of well-defined cellular or extracellular nanostructures [79]. The green synthesis of silver nanoparticles, in essence, involves three foundational steps: the careful selection of a suitable solution medium, the utilization of an environmentally friendly reducing agent, and the incorporation of a non-harmful substance to stabilize the nascent AgNPs, typically, this eco-conscious synthesis is performed using plant and microbial extracts at mild temperatures, a condition conducive to maintaining controlled reaction velocities and optimizing Ag^{2+} ion conversion levels [80]. In essence, bio-based synthesis methods present distinct advantages, primarily owing to their amenability to large-scale development, simplified environmental control during production, and straightforward post-processing requirements [81]. Globally, researchers have extensively

focused on silver nanoparticles, recognizing them as superior antimicrobial agents due to their predominant antibacterial functionality and high specific surface area (SSA). A crucial added benefit is the diminished likelihood of bacteria developing resistance, attributed to the complex and multifaceted antibacterial mechanisms inherent to these nanomaterials [82].

As compelling candidates for antibacterial agents, metal nanoparticles (MNPs) have been widely investigated, celebrated for their exceptional electromagnetic, photothermal, and physicochemical attributes, emerging research indicates that MNPs possess the capability not only to identify and treat bacterial infections but also to serve as effective vehicles for targeted antimicrobial drug delivery [83]. Fundamentally, the antibacterial efficacy of metal nanoparticles is intricately dependent on their specific size, structural configuration, and elemental composition. To this end, a variety of sophisticated methods have been developed to engineer metal nanoframes into diverse geometric forms, including rod-like structures, nanoclusters, cubic shapes, spherical particles, and even caged configurations [84].

The notable efficacy of *Streptomyces enissocaesilis* BS1 cell filtrate in serving as both a reducing and capping agent for nanoparticle synthesis is a significant finding. Subsequent bioactivity assessments unequivocally confirmed that the silver nanoparticles produced through this method displayed outstanding antibacterial potency against a diverse range of pathogenic bacterial strains [85]. Pre-established biofilms displayed a significant reduction in biomass—from 10.7% for Pseudomonas aeruginosa up to 39.08% for Staphylococcus aureus—after just 24 hours of exposure to 50 mg/mL silver nanoparticles. Beyond this, these AgNPs also exhibited notable in vitro anticancer sensitivity. Further highlighting their versatility, Actinomycetes emerge as promising agents for nanoparticle biosynthesis, capable of producing these structures both inside (intracellularly) and outside (extracellularly) their cells [86]. This remarkable ability stems from enzymes generated during their metabolic processes, which efficiently capture and reduce environmental metal ions. Within actinomycetes, intracellular reduction pathways typically involve either direct interaction on the fungal mycelium's surface or active transport of metal ions into the cell, mediated by intracellular enzymes [86]. Conversely, extracellular synthesis relies specifically on reductase enzymes [87].

Actinomycetes possess unique attributes that notably foster the biosynthesis of silver nanoparticles. Specifically, their cell wall bears a negative charge, allowing it to efficiently bind with positively charged silver ions (Ag^+) found in silver nitrate solutions. Once bound, a range of active molecules and secondary metabolites—including various intracellular proteins, cofactors, specific enzymes like nitrate reductase, extracellular enzymes, and exopolysaccharides—collectively work to reduce these silver ions to AgO [88]. Beyond that, exopolysaccharides serve a dual purpose: they act as both reducing agents and highly effective stabilizing agents, significantly aiding the uniform dispersion of the newly formed metal nanoparticles [89,90].

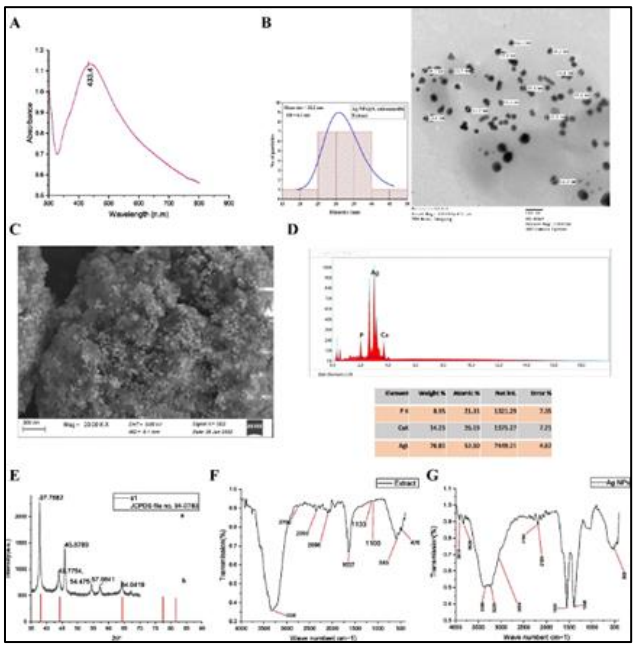

Figure 6 Spectral characterization of the synthesized silver nanoparticles; (a): UV-vis, (b): TEM (transmission electron micrograph), (c): SEM (scanning electron micrograph), (d): EDAX spectrum, (e): X-ray diffraction pattern (JCPDS file), (f): FTIR spectra, (g): FTIR spectra [91]

6. Conclusion

In the ongoing battle against increasingly resistant pathogens, silver nanoparticles (AgNPs) are truly emerging as a pivotal and versatile solution for antimicrobial intervention. Our review distinctly highlighted their potent bactericidal efficacy, a strength closely tied to their size; indeed, smaller nanoparticles, particularly those between 1-10 nm, proved most effective at interacting with and disrupting microbial membranes. Beyond direct damage, AgNPs operate within cells, instigating protein denaturation, DNA impairment, and the generation of reactive oxygen species, all while gradually releasing active silver ions that further compromise cellular integrity. Crucially, their synergistic potential when combined with conventional antibiotics offers a compelling strategy to enhance therapeutic outcomes and potentially overcome existing resistance mechanisms. The practical implications of AgNPs for healthcare are vast, ranging from enhancing the protective capabilities of surgical masks and catheters to improving restorative dental materials. While their therapeutic promise is undeniable, we must not overlook the critical need for meticulous toxicological assessment. Factors such as dose, particle size, and surface chemistry profoundly influence their impact on mammalian cells. It is particularly encouraging to witness the burgeoning shift towards green synthesis methods, leveraging biological entities like Actinomycetes. This sustainable approach for producing these essential nanomaterials significantly curtails hazardous byproducts. Ultimately, continued dedication to refining synthesis techniques and deeply elucidating their long-term biological interactions will cement AgNPs' indispensable role in our collective fight against microbial threats, thus paving the way for safer and more impactful nanomedicine.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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