# **REVIEW ON ANTIBACTERIAL ACTIVITY OF SILVER NANOPARTICLE: RECENT ADVANCES AND FUTURE SCOPE**

#### Abstract

Silver nanoparticles (AgNPs) have been promoted as a superior antibacterial agent capable of combating bacteria that cause infections both in vitro and in vivo. Multidrug-resistant strains including of Gram-negative and Gram-positive bacteria are all covered by AgNPs' antibacterial wide range of ability. Α antiviral. antifungal, and antibacterial activities can be found in silver nanoparticles. The bacterial cell membrane and DNA can be destroyed due to the presence of Ag+ ions and reactive oxygen species (ROS) generated by Ag nanoparticles. Silver nanoparticles can penetrate bacterial cell walls, altering the shape of cell membranes and even causing cell death. Their effectiveness is attributable not only to their nanoscale size, but also to their enormous surface area to volume ratio. The current work comprises the development and use of silver nanoparticles in both the physical, and chemical methods and green approaches and their bacterial efficiency. This review paper also emphasizes the current works based on the antibacterial activity of Ag nanoparticles their applications and in drug administration. Furthermore, the limitations opportunities and future for silver nanoparticle antibacterial applications are evaluated and discussed.

Keywords:	Antibacterial,	Silver
Nanoparticle,	Drug	Delivery,
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## I. INTRODUCTION

Nanotechnology or nanoscience is an emerging field of research, which has various applications moving forward in different fields of science and technology. It can be widely used in the characterization, design, and application of devices just by controlling shape and size. [1] Nanoparticles have unique properties which makes them a perfect candidate for an immense field of applications [2]. In recent years, most bacteria have become immune to the majority of the antibiotics resulting in high levels of dosage which leads to high levels of microbial resistance and the appearance of multi-resistant bacteria which puts the patient's life at risk [3].

In recent studies, silver (Ag) nanoparticles have been one of the most desirable for the development of nanosystems having potential applications in drug delivery. As a silver nanoparticle having a particle size of less than 100 nm, because of this silver nanoparticles portray excellent antimicrobial activity due to large surface-to-volume ratio, tiny size and generation of silver ions that can attack bacterial cells with high penetrability [4]. Additionally, Silver nanoparticles have low cytotoxicity to normal human cells. Due to these properties, silver nanoparticles are a great candidate for biomedical applications such as targeted anti-cancer drug delivery, molecular diagnostics, and medical imaging. In addition to biomedical applications, they can also be employed in being used as therapeutics such as wound dressing, medicament for wound healing, surgical mesh, and fabrication joint replacement. Silver nanoparticles can restrain bacterial growth and have very less side effects on the human body by its exposure in lower concentrations [5].

## **II. SYNTHESIS OF Ag NANOPARTICLES**

Silver nanoparticles can be synthesized in various methods such as using different types of chemicals and reagents. Additionally, green methods can be employed to synthesize Ag nanoparticles using fruit, plant, and leaf extracts and lastly physical methods are also being used to develop silver nanoparticles. In-depth explanations of each process are given in this review.

1. Top Down & Bottom-Up Approach: Due to an extensive field of application of silver nanoparticles, the synthesis method plays an important role in obtaining the required efficacy of the nanoparticles in the given applications. The challenges faced are to control its physical properties such as identical shape, uniform particle size, morphology, stabilizing agent, crystal structure, and chemical composition. Thus, these can be classified into different methods of approaches: Top-Down and Bottom-Up Approach, conventional and non-conventional, and green and non-green.

The synthesis approach of nanoparticles employing chemical, physical, and biological is known as the Top-down and bottom-up approach. Firstly, the top-down approach involves the mechanical grinding of bulk materials and converting them into tiny particles. Secondly, the bottom-down approach takes the miniaturization of materials components to the atomic level with additional processes. Some examples of bottom-down approaches are electrochemical methods, reduction of metals, and decomposition respectively.[6]

- 2. Physical Methods: Recently, silver nanoparticles are conveniently synthesized using physical methods such as laser ablation, gamma irradiation, evaporation condensation, lithography, and electrical irradiation. An experiment was conducted by Kimura and Bandow [7], which examined the optical spectra of various metal colloidal solutions and showcased new procedures to prepare metal colloids inorganic solvents without the means of using any chemicals such as polymers, electrolytes, glue, and redox reagents. There are various preparation procedures such as the gas flow-cold trap method, gas flow-solution method, and matrix isolation method are used to inspect the synthesis of silver nanoparticles.[6]
  - Laser Ablation Method: The laser ablation technique is beneficial and efficient to obtain and prepare metal colloids in the absence of chemical reagents and hence by changing the laser pulses, one can control the size of the colloids.

An experiment conducted by Pyatenko et al. [8] showed that the production of silver nanoparticles can be achieved by irradiating a silver target with a laser beam of 532 nm in pure water. This technique is hence applied to successfully create small silver nanoparticles with narrow size distribution without any means of chemical reagent but by just using a powerful laser and small laser beams. Additionally, Sadrolhesseini et al. [9] came up with a new synthesis method to fabricate silver nanoparticles by spreading it in graphene oxide using thermal effusivity and laser ablation of the nanocomposite. It does not require any external chemical reagents, surfactants, or polymerics but simply works on the principle of releasing the nanoparticles in a solution and therefore is completely environmentally friendly.

- Lithography: This method is a physical approach to synthesizing nanoparticles in an inexpensive and simple way to fabricate a large variety of well-ordered 2-dimensional nanoparticle arrays and nanoparticle structures. A study given by Jensen et al. [10] investigated different samples having different nanoparticle arrays, from which three samples had nanoparticles that were in tetrahedral shape but differed in out-of-plane height and the other sample had nanoparticles that were in oblate ellipsoidal shape. It was also shown that the nanoparticles can be continuously tuned through near-infrared, visible, and mid-infrared regions of the spectrum using localized surface plasmon resonance extinction.
- Mechanical Milling: A solid-state powder processing method called mechanical milling is used to create fine-grained nanocrystalline materials and alloys from the top down. In a high-energy ball mill, metallic or nonmetallic particles are repeatedly cold-welded, broken up, and re-welded [11]. The output of the milling process is controlled by variables that can be controlled, such as the ball-to-powder ratio, milling speed, and milling time [12]. The milling process is conducted in a cylindrical vessel holding grinding balls and a powdered sample. Balls and powder colliding during milling create concentrated areas of high temperature, which causes melting, solidification, and the production of new phases and alloys [13]. Atom diffusion and element mixing are made possible by powder mechanical deformation and fracture, allowing the creation of homogenous structures.

- **3.** Chemical Methods: Nanoparticles can be synthesized using various chemical methods such as microemulsion, photo-induced reduction, chemical reduction, initiated photo reduction, irradiation methods, electrochemical synthetic approaches, and microwave-assisted synthesis. In this section, we will delve into the details of several chemical methods employed for the synthesis of silver nanoparticles.
  - Chemical Reduction: The method of chemical reduction stands as one of the most popular techniques for nanoparticle synthesis, utilizing both organic and inorganic reducing agents. This method is crucial as the resulting shape, size, and surface morphology significantly influence the optical, physical, electronic, and chemical properties of the nanoparticles. Among the array of reducing agents available, examples include ammonium formate, Tollens reagent, and elemental hydrogen. These agents are employed to effectively reduce silver (Ag) ions in both aqueous and nonaqueous solutions.
  - **Microemulsion Technique:** The microemulsion technique involves the use of surfactants, creating a mixture of water and oil phases. A diverse range of surfactants finds application in the preparation of silver nanoparticles through this method, which relies on the formation of microemulsions. [2] Various surfactant types, including anionic, non-ionic, and cationic, can be employed to create microemulsions. Examples of each type are provided below:

Anionic surfactants such as bis(2-ethylhexyl) sulfosuccinate, lauryl sodium sulfate, and sodium dodecyl benzene sulfonate; non-anionic surfactants such as Triton X-100; and cationic surfactants such as polyvinylpyrrolidone and cetyltrimethylammonium bromide.

In this method, water molecules surrounded by their respective surfactants serve as micro-reactors, creating a distinct microenvironment conducive to the formation of nanoparticles. [14-19]

• **Microwave-Assisted Synthesis Technique:** The microwave-assisted synthesis method facilitates the reduction of silver nanoparticles by utilizing variable microwave radiation, which is often compared to conventional heating techniques. This approach is particularly advantageous for expediting chemical reactions that would typically require days or hours using traditional methods, thus delivering rapid results. Furthermore, microwave-assisted synthesis ensures uniform heating during nanoparticle formation and aids in preventing aggregation. This technique accelerates the maturation of nanoparticles, contributing to their controlled growth without the risk of undesired particle clustering.

While chemical methods offer several advantages for nanoparticle synthesis, they also come with significant drawbacks. For instance, a majority of chemically synthesized nanoparticles exhibit inherent toxicity [20-23]. Additionally, these methods often require higher energy input during production, leading to environmental concerns due to their limited eco-friendliness. Furthermore, the

substantial quantity of chemicals needed in these processes contributes to elevated synthesis costs, posing economic challenges.

4. Green Methods: Biological processes offer a streamlined approach to nanoparticle synthesis, enabling their creation in a single step. Organisms such as molds, bacteria, plants, and algae play a pivotal role in this method. Through reduction processes facilitated by molecules like enzymes and proteins inherent in microorganisms and plants, nanoparticles can be conveniently synthesized. The notable advantage lies in the absence of chemical reagents, rendering this approach environmentally friendly and cost-effective compared to traditional chemical methods. The utilization of green synthesis methods not only yields metallic nanoparticles but also provides a source of bioactive molecules. Consequently, these methods contribute to reduced nanoparticle toxicity and minimize their environmental impact. [24]

The utilization of plants for nanoparticle synthesis offers a multitude of advantages. Plants are readily accessible and possess an extensive array of active functional groups that facilitate the reduction of silver ions. In nanoparticle synthesis, various parts of the plant can be harnessed, including leaves, stems, bark, latex, roots, and seeds. Key compounds employed for nanoparticle reduction encompass tannins, phenolics, saponins, proteins, vitamins, flavones, and amino acids. These components collectively contribute to the efficient reduction of nanoparticles, highlighting the versatility and potential of plants in this innovative approach.

The procedural steps for synthesizing nanoparticles using these green methods involve a systematic process. It commences with a thorough washing of the collected plants using both distilled and tap water to eliminate any impurities. Subsequently, sterile distilled water is employed to eliminate any residual contaminants. Once distillation and purification are completed, the plants are air-dried for a minimum of 15 days before being blended using a suitable apparatus. Furthermore, a plant broth is prepared by mixing the previously blended powder with deionized distilled water and boiling the mixture. The resulting concoction is then rigorously extracted and filtered until all insoluble materials are removed. Next, a few millilitres of this plant extract are added to a silver nitrate solution with a concentration of 1mM. The reduction process is confirmed by observing a distinct colour change in the solution. To provide further verification of nanoparticle formation, techniques such as UV-Visible spectroscopy or Scanning Electron Microscopy (SEM) can be employed. [25]

While green methods offer distinct advantages in nanoparticle synthesis, they also present challenges, particularly in controlling the size and shape of nanoparticles. Temperature emerges as a critical factor influencing nanoparticle characteristics, as various materials exhibit unique temperature thresholds. Literature has revealed that nanoparticles may not form at lower temperatures; however, at approximately 80°C, nanoparticle synthesis becomes evident. Furthermore, elevating the temperature to around 100°C accelerates the reaction rate while impeding excessive particle growth.

As previously mentioned, temperature profoundly impacts nanoparticle morphology. Lower temperatures tend to yield small spherical particles, whereas higher temperatures favor the formation of nanorods and platelets. Another essential variable to consider is the reaction time. According to Nishanthi et al., silver nanoparticles typically form within a mere 10 minutes, while the introduction of rind extract triggers the appearance of gold nanoparticles. [26]

## **III. ANTIBACTERIAL ACTIVITY OF Ag NANOPARTICLES**

In the last 3 decades, a lot of research has been done for developing new forms of antibiotics that have better efficacy against protein synthesis, bacterial cell wall synthesis, and DNA replication. However, with each iteration of advancement, there is still a high fatality rate due to the resistance increment of antimicrobials in bacterial infections. This is a major concern for the healthcare industry as this has a huge impact on the world. [27]

As nanotechnology and nanoscience are steadily becoming the frontier in biomedical applications, thus the development of such technology has become an evident importance in our lives. Numerous studies and research are conducted to find non-toxic and cost-effective materials that can be conveniently used in various applications of pharmaceutical, medical, and other domains. One of the important applications of this technology is drug-resistant bacteria and disease control. Metals like Gold (Au), Silver (Ag), and Platinum (Pt) can be used to fabricate nanosystems that can be used as delivery agents to successfully deliver drugs to the targeted area in the human body. These particles are highly effective against bacteria as they have excellent antimicrobial properties due to their large surface area. [28-29]

Various nanoparticles have been synthesized for being used in the application of antibacterial treatments. One of the most common and widely used materials for this application ought to be Silver (Ag) nanoparticles due to their broad antimicrobial properties and strong effectiveness against bacteria, fungi, and viruses. Today, drugs that contain silver, for example, silver nitrate and sulfadiazine are used to treat wounds and dental burns.

It has been agreed upon that silver nanoparticles interact with bacterial cell envelope, but still, the primary cellular target is unknown. These nanoparticles are capable of being used against diseases of 650 types. In recent studies, there is evidence of silver nanoparticles having antibacterial properties when combined with antibiotics which conveniently worked against bacteria like Escherichia coli and Staphylococcus aureus. [30]

The antibacterial effect of the silver nanoparticle can be subsequently increased when combined with antibiotics specifically against drug-resistant bacteria, this method can be a potential solution to overcome drug resistance. A higher antimicrobial activity can be achieved by binding these nanoparticles with various antibacterial agents. Some studies have shown that Ag nanoparticles have better antibacterial results against both Gram-positive and Gram-negative bacteria. [31] When compared to other materials like zinc, platinum, and gold, silver nanoparticles have proven to show increased antimicrobial properties and significantly low cytotoxicity levels.

**Recent Works on Antibacterial Activity:** As discussed above, in recent years silver nanoparticles have become a point of interest in the field of biomedical research. Silver nanoparticles possess excellent antibacterial properties that certainly improve the overall

treatment. In this section, we are going to discuss different applications of silver nanoparticles in various fields.

- 1. AgNP Used in Face Masks: Silver nanoparticles application in face masks is to increase the ability of face masks to be protective from foreign bacteria. Y. Li et al. [32] synthesized a face mask using silver nitrate and titanium dioxide coated with silver nanoparticles. The results showed that the developed face mask could reduce the bacteria concentration of S. aureus and E. coli. Similarly, another commercially available face mask was coated with silver nanoparticles at a given concentration of 50 and 100 ppm, which resulted in to decrease in the growth of S. aureus and E. coli [33]. This successful result shows that AgNPs can be used as a great candidate to prevent infections in highborne areas such as hospitals which could significantly reduce the risk of contamination due to these bacteria. Since then, various studies have been conducted to vastly incorporate silver nanoparticles into a variety of medical apparatus such as surgical masks [34], etc.
- 2. AgNP Used in Catheters: Like face masks, silver nanoparticles are also actively used in catheters to control bacterial infections and improve sterility. Results showed that catheters that were coated with silver nanoparticles have less bacterial growth like P. aeruginosa and Enterococcus after 72 hours. A study was given by Wu et al. where a catheter was developed by coating silver nanoparticles uniformly around the catheter [35-36]. The developed catheter showed excellent antibacterial activity against S. aureus, with variable doses [37-38]. It also resulted in good biocompatibility. This gives evident proof of using silver nanoparticles in medical apparatuses to subsequently decrease the risk of transmission of bacterial or infectious diseases.
- **3. AgNP Used as Healing Agent:** Silver nanoparticles are great candidates for healing because of their antibacterial effect. Developments have been made in this area as given by Tian et al. [39], where a silver nanoparticle solution was used to treat superficial wounds, which resulted in shorter healing time and improved skin regeneration. As stated, this is the modulating action of silver nanoparticles on pro-inflammatory cytokines. It is considered that by reducing the inflammatory period, silver nanoparticles speed up the regeneration process. In the context of the same property silver nanoparticles formation can be modified to be used in dermal wounds as well.

In recent years, silver is used in many industries such as pharmaceutical and cosmetics respectively which aims at increasing the rate and healing efficiency. Thus, silver nanoparticles can be employed in various branching industries such as catheters, wounds, hydrogel, and medical textiles due to their excellent antibacterial property and non-toxic nature.

## IV. APPLICATION OF Ag NANOPARTICLES IN DRUG DELIVERY

The burgeoning field of nanotechnology has catalyzed a paradigm shift in drug delivery strategies, and among the various nanomaterials explored, silver nanoparticles (Ag NPs) have emerged as compelling candidates with diverse applications. Their remarkable physicochemical properties have spurred extensive research into their potential as carriers for therapeutic agents. Ag NPs possess an inherent ability to encapsulate a wide range of drugs,

from small molecules to biomacromolecules, owing to their large surface area, which can be precisely tuned based on synthesis parameters.

This attribute not only enhances drug loading capacity but also offers a platform for multi-drug encapsulation, enabling synergistic therapeutic effects. Moreover, the controlled release of drugs from Ag NPs can be tailored to suit specific therapeutic requirements. Surface modifications through functionalization with polymers, ligands, or biomolecules facilitate controlled release profiles, extending the therapeutic window and minimizing side effects. This flexibility in drug release kinetics is crucial for optimizing treatment outcomes, particularly for conditions demanding sustained or pulsatile drug delivery [40]. Beyond their role as drug carriers, Ag NPs exhibit inherent biological activity that amplifies their potential in drug delivery systems.

Their antimicrobial properties have been leveraged to develop infection-responsive drug carriers, where the release of therapeutic agents is triggered in response to pathogenic cues. This innovation holds promise for combatting localized infections, reducing the risk of antibiotic resistance. The synthesis and design of Ag NPs for drug delivery necessitate a balance between therapeutic efficacy and biocompatibility. Rigorous investigation into their toxicity profiles and interactions with biological systems is imperative for clinical translation. Preclinical studies evaluating the biodistribution, pharmacokinetics, and long-term effects of Ag NPs provide crucial insights into their safety and potential challenges.

### V. CONCLUSION

Silver nanoparticles can be used as an excellent antibacterial agent and a very good drug delivery agent. Silver nanoparticles (AgNPs) have antibacterial properties that include: (a) Silver ions (Ag+) released by silver nanoparticles penetrate the bacteria cell wall and cytoplasmic membrane, causing disruption. (b) Ribosomes are denatured and protein synthesis is inhibited by silver ions.

This comprehensive review article navigates through the myriad facets of Ag NPs in drug delivery, encompassing their synthesis methods, antimicrobial activity of silver nanoparticles, different applications, and applications of silver nanoparticles in drug delivery. By collating the latest advancements and addressing potential hurdles, this article not only underscores the transformative impact of Ag NPs on drug delivery but also offers a roadmap for future research directions. Ultimately, the amalgamation of nanotechnology with therapeutic delivery holds the promise of revolutionizing medical treatment modalities, paving the way for personalized and targeted therapies with enhanced efficacy and reduced side effects.

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