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Silver Nanoparticle: A Review on Method and Application

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A B S T R A C T

In recent years, nanoparticles have gained significant attention in research and development due to their promising applications across various fields. Among them, silver nanoparticles have emerged as a major focus, particularly in the medical field, owing to their remarkable biological properties. Extensive research has demonstrated that silver nanoparticles exhibit antibacterial, antifungal, anti-inflammatory, antiviral and anti-platelet activities, making them valuable in numerous medical and technological applications. This paper aims to review the different synthesis methods of silver nanoparticles and their applications. Two fundamental approaches for silver nanoparticle synthesis are the top-downandbottom-up methods. Physical synthesis techniques typically involve mechanical, thermal or radiation-based processes. Chemical reduction methods utilize organic and inorganic reducing agents to produce nanoparticles, whereas biological synthesis offers an eco-friendly, biocompatible alternative using natural sources such as plants, bacteria and fungi. Various techniques are used to characterize silver nanoparticles, including UV-visible spectroscopy, X-ray diffraction (XRD), Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM). The antibacterial activity of silver nanoparticle is primarily attributed to cell wall and membrane disruption, intracellular penetration leading to cellular damage and induction of oxidative stress, which collectively hinder microbial growth. The focus remains on developing efficient and sustainable synthesis techniques to maximize silver nanoparticle potential across various industries.

Keywords: Silver nanoparticle, Top-down, Bottom-up, UV-visible spectroscopy, Transmission Electron microscopy, Scanning Electron microscopy

1. Introduction

In the term “Nanotechnology”, the prefix 'nano' is derived from the Greek word *nanos*, meaning 'small' or 'dwarf.' It refers to a scale of one-billionth of a meter (10^{-9} m). Nanotechnology involves the design, synthesis and application of materials at the nanoscale. In this rapidly advancing field, researchers and engineers are actively developing and manipulating nanomaterials to harness their unique properties for diverse applications. Nanotechnology plays a vital role in cutting-edge research, particularly in the design and synthesis of particle structures ranging from approximately 1 to 100 nanometers. It has become an increasingly important aspect of modern pharmaceutical research.[1]. Nanotechnology-based drug delivery systems can prolong the drug's presence in the bloodstream, reducing fluctuations in plasma levels and minimizing side effects. These nanoparticles or structures can efficiently penetrate tissues and are readily absorbed by cells[2]. Nanoparticles are currently being widely employed for the delivery of antibiotics, anticancer drugs, vaccines, proteins, polypeptides, antibodies, genes, and various other therapeutic agents[3].Metal nanoparticles (MNPs) are tiny particles, typically ranging from 1 to 100 nm in size, composed of metals such as silver, gold, copper and platinum[4]. They are widely studied due to their unique physicochemical properties, including high surface area, optical, electrical and catalytic activity. Their small size allows for enhanced reactivity and improved interactions with biological and chemical systems. Additionally, MNPs exhibit stable behavior, making them valuable in various applications, including medicine, electronics and environmental science[5]. Recent advancements in technology have introduced silver nanoparticles into the medical field. As research on silver nanoparticles has progressed, various medical applications have been developed to prevent infections and promote faster wound healing.

1.1 Silver Nanoparticle

Silver nanoparticles play a crucial role in biology and medicine due to their unique physicochemical properties. Silver-based products have long been recognized for their strong antibacterial and bactericidal effects, as well as their broad-spectrum antimicrobial activity[6,7,8]. Studies have shown that silver nanoparticles possess antiviral, antifungal, anti-inflammatory and antiplatelet properties[9].Silver nanoparticles have many applications in medical devices, textile, pharmaceuticals and cosmetic[10].

Silver nanoparticles demonstrate excellent conductivity because of the easy movement of electrons within the conduction band that facilitates proximity between the conduction and valence bands in silver. Additionally, silver nanoparticle improves the effectiveness of electrochemical sensors, particularly in point-of-care testing devices, where they enable fast and sensitive detection[11].Silver nanoparticles are now widely utilized as antibacterial and antifungal agents in a variety of consumer products, including air sanitizer sprays, socks, pillows, slippers, refrigerator coatings and mobile phones[12].

The reduced size of silver nanoparticle allows them to easily penetrate cell membranes, enabling the precise delivery of therapeutic agents to specific cells or tissues. This highlights their advantages in targeting diseased cells for drug delivery. It demonstrates excellent biocompatibility and minimal toxicity, making them ideal for various biological applications, including drug delivery and imaging. Their size-dependent properties enhance their interactions with biological systems, allowing for easy cell penetration and effective intracellular activity[13]. The optical, magnetic, electrical and catalytic properties of NPs are influenced by their size, shape, and chemical environment[14].Since the advent of nanotechnology, multiple methods have been developed for synthesizingsilver nanoparticle. These techniques can be broadly classified into two fundamental approaches: top-down and bottom-up[15].

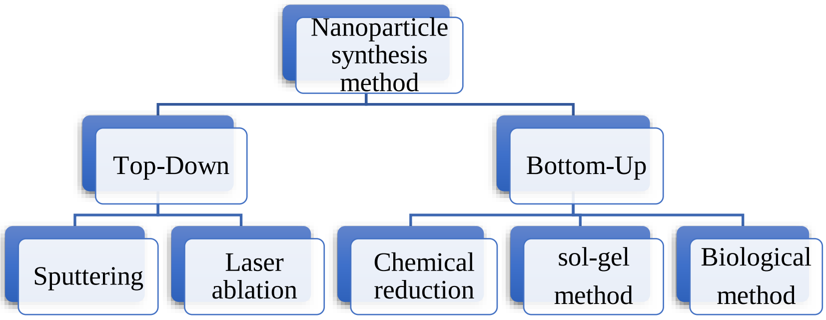

Fig 1. Classification of Nanoparticle synthesis technique

- **Top-down approach**

Physical methods for synthesizing silver nanoparticles generally involve mechanical, thermal, or radiation-based techniques to produce nanoparticles without the need for harmful chemical reagents. These methods often provide better control over particle size and shape while minimizing toxic by-products. This method of synthesizing silver nanoparticle enables the production of large quantities with high purity without the use of chemicals. It involves two main processes: Sputtering and the laser ablation technique[16].

1. Sputtering:

Sputtering is a phenomenon in which microparticles of a solid material are ejected from its surface when it is bombarded by high-energy plasma or gas particles. In the sputtering deposition process, energetic gaseous ions physically dislodge small clusters of atoms from the target surface, depending on the energy of the incident ions[17].The sputtering method is notable for being more cost-effective than electron-beam lithography while also producing nanomaterials with a composition closely resembling the target material and minimal contamination[18]. Silver nanoparticle and thin films were synthesized through sputtering by applying discharge voltage onto canola and castor substrates[19].

2. Laser ablation:

Laser ablation in a liquid enables the rapid synthesis of nanoparticles from simple precursor materials by directing a high-intensity laser beam onto a liquid or a solid-liquid interface. This process facilitates the formation of various nanostructures, including alloys, metals, carbides, oxides and hydroxides, with diverse morphologies such as nanoparticles, nanorods, nanocomposites and nano cubes. Compared to conventional wet-chemical methods for producing colloidal nanoparticles and nanocomposites, laser ablation in liquid offers several advantages. It allows for the generation of significant nanoparticle quantities within minutes, requiring minimal or no post-synthetic processing, whereas traditional approaches often take hours or even days to achieve similar results[20].

- **Bottom-up approach**

Unlike the "top-down" approach, the "bottom-up" method builds nanoparticles by carefully assembling smaller building blocks. This approach is divided into two main categories: chemical and biological methods. Chemical methods primarily involve the reduction of precursor compounds using reducing agents, surfactants, and stabilizers. Common techniques in this category include sol-gel synthesis, coprecipitation, and hydrothermal methods. In contrast, biological synthesis provides an eco-friendly and sustainable alternative by utilizing plant extracts, microbes and other natural resources as reducing agents and stabilizers, thereby reducing reliance on potentially harmful chemicals[21].

1. Chemical reduction method:

Chemical reduction is one of the most common approaches for synthesizing silver nanoparticle, utilizing both organic and inorganic reducing agents. This process typically involves a single step, resulting in the formation of a coloured silver solution. The colour change occurs because the metal surface contains free electrons in the conduction band and positively charged nuclei. As the reaction progresses, long-lived silver clusters are formed, confirming the successful synthesis of AgNPs[22]. The chemical synthesis process typically requires four main components:

a) Reducing agent

b) Capping/stabilizing agents

c) Precursor

d) Solvent

Chemical reduction is the most commonly used method for synthesizing AgNPs as stable colloidaldispersions in water or organic solvents[23]. For synthesizing silver nanoparticles (AgNPs) it involves various reducing agents, such as sodium citrate, ascorbate, sodium borohydride ($NaBH_4$)[24,25], elemental hydrogen, the polyol process, N, N-dimethylformamide (DMF), ascorbic acid, poly (ethylene glycol) block copolymers, hydrazine and ammonium formate. These reducing agents are used to reduce silver ions (Ag^+) in both aqueous and non-aqueous solutions.

2. Sol-Gel method:

The sol–gel process is a highly effective chemical method for creating advanced materials across various research domains. By integrating techniques like phase separation, hybridization and templating induction, this approach allows for enhanced control over size and shape, offering innovative possibilities for a wide range of applications[26]. AgNPs with a pristine surface were produced using the sol–gel method at room temperature. During this process, sodium acetate (CH_3COONa) was employed to inhibit the aggregation of AgNPs, while hydrazine acted as the reducing agent.

3. Biological method:

Biological methods are often regarded as more effective, cost-efficient, sustainable and environmentally friendly than chemical andphysical approaches, as biological materials are readily available and typically require little to no prior processing[27].In general, silver nanoparticles (AgNPs) synthesized by plants or microorganisms can be produced through either extracellular or intracellular processes[28]. Furthermore, algae, fungi and beneficial bacteria capable of withstanding toxic substancessuch as heavy metals and organic pollutantswhile still producing organic and inorganic reducing agents, present a promising biological approach for silver nanoparticle synthesis. A general mechanism for the formation and growth of silver nanoparticles (AgNPs) can be proposed. Biomolecules such as polyphenols contain functional groups that release electrons into the reaction medium. These electrons interact with silver ions (Ag^+), typically derived from a silver salt like silver nitrate, leading to the reduction of Ag^+ and the initiation of nanoparticle formation. As reduction progresses, silver atoms begin to form and surface plasmon resonance (SPR) increases, often indicated by a noticeable darkening of the solution.

Mechanism of antibacterial activity of silver nanoparticle

The bio-reduction of Ag^+ ions to Ag^0 atoms in plant extract-mediated synthesis involves electron transfer from the biomolecules in the extract. Compounds such as polyphenols, saponins, flavonoids, terpenes, sugars and alkaloids act as effective reducing agents. These biomolecules donate electrons from functional groups like hydroxyl (-OH) and carboxyl (-COOH) to Ag^+ ions, facilitating their reduction to elemental silver (Ag^0).

1) Interaction between biomolecules and Ag^+ ions:

Functional groups like hydroxyl (-OH) and carboxyl (-COOH) in these biomolecules play a crucial role in the reduction process. Upon dissolution in water, $AgNO_3$ dissociates into Ag^+ cations and NO_3^- anions. The negatively charged O^- in phenols or COO^- in organic acids establishes electrostatic interactions with the positively charged Ag^+ions. This interaction enables the donation of electrons, reducing Ag^+ to Ag^0 and forming silver nanoparticles.

2) Antibacterial Mechanism:

Studies on the antibacterial properties of silver nanoparticle are typically conducted in vitro using either solid media or aqueous cultures. The antibacterial action of silver nanoparticle operates through three primary mechanisms:

a) Disruption of the cell wall and membrane

b) Intracellular penetration and subsequent damage

c) Induction of oxidative stress[29].

a) Disruption of the cell wall and membrane:

The cell wall and membrane protect microbes from external threats and maintain cellular stability while allowing the uptake of nutrients. Silver nanoparticles exhibits greater bactericidal efficiency against Gram-negative bacteria compared to Gram-positive bacteria. This difference arises because the thick peptidoglycan layer in the cell walls of Gram-positive bacteria acts as a natural barrier, limiting nanoparticle diffusion. The interaction between AgNPs and microbial cell walls occurs due to the electrostatic attraction between the positively charged nanoparticles and the negatively charged microbial membrane. This adhesion disrupts the structural integrity of the cell membrane, leading to depolarization and impairment of cellular respiration, ultimately causing the membrane to rupture and initiating cell death[30].

b) Intracellular Penetration and Damage:

Upon penetrating the cell, silver nanoparticle interferes with critical biological processes, including DNA and protein synthesis. The release of Ag^+ from the nanoparticles disrupts microbial activity, transforming bacterial DNA from a relaxed state to a compact form and inhibiting its ability to replicate. Additionally, Ag^+ ions react with the thiol groups of proteins, disrupting enzymatic functions[31].Ag^+ ions also interact with the nucleosides in DNA, altering base-pairing by disrupting hydrogen bonds between DNA strands.

c) Oxidative Stress:

ROS (reactive oxygen species) are oxygen-based molecules with high redox potential, playing a crucial role in cellular oxidative stress. Under normal conditions, cells regulate ROS production through enzymatic and non-enzymatic defence mechanisms. However, when silver nanoparticle is introduced, the balance between ROS generation and the cells antioxidant capacity is disturbed, leading to oxidative stress[32]. This imbalance damages essential bio-molecules, including proteins, lipids and DNA, as well as the bacterial electron transport chain and proton gradient, ultimately inhibiting cellular functions. The oxidative stress induced by silver nanoparticle promotes the release of proteins from the cell membrane, contributing to increased membrane permeability and further degradation of cellular components. Apoptosis ensues as silver nanoparticle interacts with these released proteins. Studies have also indicated that oxidative stress alters gene expression, with specific proteins being overexpressed in response to silver nanoparticle treatment[33].

Table 1- Advantages and Disadvantages of different methods used in synthesis of silver nanoparticle

METHODS	**ADVANTAGE**	**DISADVANTAGE**
Chemical Method	High Yield– Produces large amounts of AgNPs efficiently. Simple and Scalable – Easier to perform and scale up for industrial applications. Controlled Size and Shape – By adjusting reaction conditions, nanoparticle properties can be fine-tuned. Cost-effective – Uses relatively inexpensive reagents and does not require specialized equipment.	Chemical Contaminants – Residual reducing/stabilizing agents can affect nanoparticle purity. Toxicity Issues – Some chemical reagents (e.g., $NaBH_4$) are hazardous and environmentally harmful. Agglomeration Risks – Without proper stabilizers, nanoparticles may clump together. Waste Generation – Some synthesis routes produce toxic by-products, leading to disposal concerns.
Physical Method	Purity – No chemical contaminants since reducing or stabilizing agents are not required. Eco-friendly – No toxic chemicals involved, making it safer for the environment. Controlled Size – Precise control over nanoparticle size and shape using tuneable parameters. Fast Process – Some techniques, like laser ablation, can produce nanoparticles rapidly.	High Energy Consumption – Requires lasers, vacuum systems, or mechanical force, making it expensive. Low Yield – Often produces a smaller quantity of nanoparticles compared to chemical methods. Complex Equipment – Requires specialized and costly equipment, limiting accessibility. Agglomeration Issues – Nanoparticles tend to cluster together without stabilizing agents.
Biological Method	Eco-Friendly & Non-Toxic – Avoids harmful chemicals, making it safe for humans and the environment. Biocompatible – More suitable for medical and pharmaceutical applications. Cost-Effective – Uses readily available plant extracts or microorganisms. EnhancedStability – Biomolecules from biological sources act as natural stabilizers, reducing agglomeration.	SlowProcess – Can take longer than chemical methods to produce nanoparticles. DifficulttoControlSize&Shape – Requires optimization, as biological reactions vary. ImpurityIssues – Presence of biological residues may affect nanoparticle purity. ScalabilityChallenges – Mass production is complex due to variability in biological sources.

Characterization of silver nanoparticles

Various techniques are employed to characterize nanoparticle, each providing essential insights into their properties. UV-Visible spectroscopy is a widely used analytical technique for both qualitative and quantitative analysis. It is simple, cost-effective and rapid, based on the electronic transitions of atoms or molecules from lower to higher energy levels[34].UV-visible spectrophotometry is a key spectroscopic method used for the preliminary confirmation of nanoparticle formation. X-ray diffraction (XRD) helps determine the metallic nature of the particles, distinguishing between crystalline and amorphous structures. Fourier transform infrared (FTIR) spectroscopy analyses the infrared intensity as a function of wavelength, offering valuable chemical insights. FTIR analysis is used to check the functional groups of that compound responsible for the reduction of silver nanoparticles or its stabilization[35].

Atomic Force Microscopy (AFM) is particularly useful for examining the surface morphology of nanoparticles and can operate in diverse environments, including ambient air, controlled conditions, and liquid dispersions. Transmission Electron Microscopy (TEM) is widely used in nanotechnology to assess the morphology and shape of nanoparticles. Similarly, Scanning Electron Microscopy (SEM) provides high-resolution imaging by scanning a sample with a high-energy electron beam, enabling detailed structural analysis.

Application

a. Anti-bacterial activity:

Silver nanoparticles (AgNPs) have the potential to overcome bacterial resistance to antibiotics, making them a promising alternative antibacterial agent. Their high surface-to-volume ratio and unique crystallographic surface structure contribute to their strong antibacterial properties[36]. Silver nanoparticles (AgNPs) are the most widely utilized antibacterial nanomaterials, known for their broad-spectrum antimicrobial activity against various bacterial strains. AgNPs can continuously release silver atoms (Ag^0), which play a crucial role in microbial elimination. Silver ions adhere to the bacterial cell wall and cytoplasmic membrane due to their electrostatic affinity for sulphur proteins, increasing membrane permeability and disrupting the bacterial envelope. Once inside the cell, Ag^0 deactivates respiratory enzymes, generates reactive oxygen species (ROS) and inhibits ATP production. ROS further contribute to DNA damage and membrane disruption, while Ag^0 interacts with sulphur and phosphorus in DNA, leading to modifications. Additionally, Ag^0 denatures ribosomes, hindering protein synthesis[37].

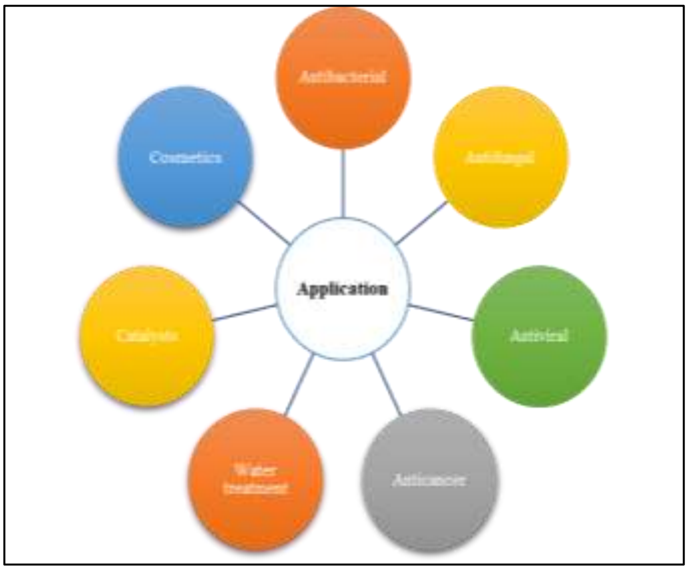

Fig 2. Application of silver nanoparticles

b. Anti-fungal activity:

The limited availability of antifungal drugs makes treating fungal infections challenging, especially in immunocompromised individuals. This highlights the urgent need for biocompatible, non-toxic and eco-friendly antifungal treatments. AgNPs play a vital role in antifungal therapy, though their exact mechanism remains unclear. They interact with ergosterol in the fungal cell wall, creating pores that lead to organelle leakage. AgNPs also generate reactive oxygen species (ROS), triggering apoptosis, disrupt DNA and RNA to inhibit cell division, and attack sulfhydryl groups in proteins, preventing synthesis. Additionally, they interfere with the G1/M phase, halting cell division and create pores in fungal membranes, leading to cell death. Their small size allows them to penetrate fungal cells and bind to functional groups, while the release of silver ions further enhances their antifungal effects.

c. Targeted drug delivery:

Silver nanoparticles (AgNPs) have gained significant attention in targeted drug delivery due to their unique properties, such as antimicrobial activity, high surface area, and ease of functionalization. Targeted drug delivery is a specialized drug delivery system that ensures the medication is directed specifically to the site of action, minimizing exposure to non-targeted organs, tissues, or cells[38]. Their small size and large surface area enhance cellular uptake and drug loading capacity, while surface functionalization allows modification with ligands, polymers, or biomolecules for targeted delivery.

d. Anti-cancer activity:

In cancer cells, apoptosis is often suppressed despite being triggered by DNA damage or severe cellular stress. Green-synthesized AgNPs using a bioactive fraction of *Pinus roxburghii* have shown cytotoxic effects against lung and prostate cancer cells. These AgNPs induce apoptosis via the intrinsic pathway by causing mitochondrial depolarization and DNA damage. Additionally, increased ROS production,cell cycle arrest, and caspase-3 activation contribute to cancer cell apoptosis[39].

e. Anti-viral activity:

Recent outbreaks of infectious diseases have been linked to newly emerging pathogenic viruses. Viruses can infect both eukaryotic and prokaryotic cells, relying on living hosts for replication, often causing cell damage or destruction. Viral infections can lead to systemic illnesses and severe complications in both acute and chronic conditions. Viruses are commonly found in air, water, and especially soil. The emergence of drug-resistant viral strains has driven researchers to explore new antiviral therapies. As a result, silver nanoparticles (AgNPs) have gained attention as a potential antiviral agent in the biomedical field. AgNPs interact with pathogenic viruses in two ways: (1) They bind to the viral outer coat, preventing attachment to cell receptors (2) They bind to the viral DNA or RNA, inhibiting replication and propagation[40].

f. Water treatment:

Metallic AgNPs possess excellent properties that make them useful across various industries beyond wastewater treatment, including biology, coatings, DNA sequencing, food products, drug therapy, cosmetics, and biomedicine. However, a significant portion of silver nanoparticle research focuses on their antimicrobial activity against various microorganisms, particularly in water purification, dye removal, and wastewater treatment. The synthesis of AgNPs is designed to be reproducible and cost-effective, with methods varying based on differences in reactants and reaction conditions[41]. The use of bactericidal paper infused with silver nanoparticles for point-of-use water treatment[42].

g. Cosmetics:

Silver nanoparticles (AgNPs) are widely used in cosmetics due to their antimicrobial and skin-healing properties. They are incorporated into skin care products such as creams, lotions, and serums for their antibacterial and anti-aging benefits. In deodorants, AgNPs help inhibit bacterial growth, effectively reducing odour. Sunscreens also utilize silver nanoparticles as UV filters and antimicrobial agents to enhance product efficacy. Additionally, they are found in wound healing creams, promoting skin regeneration and preventing infections. In makeup products like foundations and powders, AgNPs contribute to preservation by preventing microbial contamination, thereby extending product shelf life.

h. Nano emulsions:

Nano emulsions are novel drug delivery system includes an emulsified oil and water systems having mean droplet size which ranges from 50 to 1000 nm[43]. Silver nanoparticles incorporated into nano emulsions have gained interest in biomedical, pharmaceutical and cosmetic applications due to their enhanced stability, bioavailability and antimicrobial properties. It offers several advantages for silver nanoparticles by enhancing their stability, bioavailability, and therapeutic effectiveness. Nano emulsions provide a stable dispersion medium that prevents clumping and maintains their functionality. They also facilitate controlled and targeted release of silver ions, reducing toxicity and minimizing side effects.

Conclusion

It is concluded that silver-based products have long been recognized for their potent antibacterial and antimicrobial properties, exhibiting strong bactericidal effects. Silver nanoparticles, in particular, possess antifungal, anti-inflammatory, antiviral and anti-platelet properties. Their synthesis methods are broadly categorized into top-down and bottom-up approaches. Various analytical techniques, such as UV-Visible spectroscopy, X-ray diffraction (XRD), Fourier Transform Infrared (FTIR) spectroscopy, Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM), are used to characterize these nanoparticles. Silver nanoparticles exert their antimicrobial effects by disrupting the cell wall and membrane, infiltrating cells, causing DNA damage and inducing oxidative stress. Due to their versatile properties, they find applications in cosmetics as well as in targeted drug delivery.

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