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# Synthesis of silver nanoparticles: A comprehensive review

Islom Turdikulov[1,2,] *, Abdumutolib Atakhanov[1], Doniyor Ergashev[1], Saidmukhamedova Mukhlisa[1], Shoxruh A'zamkulov[1], Obloberdiyev Sardor[2], Majidova Maftuna[3], Fazilova Surayyo[4], Ramazonova Gavharshod[5], Sabu Thomas[6], Pietro Calandra[7]

[1]*Institute of Polymer Chemistry and Physics, Academy of Sciences Republic of Uzbekistan, Tashkent, Uzbekistan.*
[2]*Yangiyer Branch of the Tashkent Chemical Technology Institute, Tashkent, Uzbekistan.*
[3]*University of Business and Science, Tashkent, Uzbekistan.*
[4]*Gulistan State Pedagogical Institute, Tashkent, Uzbekistan.*
[5]*Tashkent University of Architecture and Construction Tashkent, Uzbekistan*
[6]*Trivandrum Engineering Science & Technology Research Park, Mahatma Gandhi University, Kottayam, Kerala, India.*
[7]*Institute for the Study of Nanostructured Materials, National Research Council, Montelibretti (RM), Italy.*

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ABSTRACT

This review article examines the synthesis of silver nanoparticles (AgNPs), highlighting modern methods in their production. The discussion encompasses chemical, physical, and biological synthesis techniques, detailing the advantages and limitations of each approach. Chemical synthesis often involves reducing agents like sodium borohydride and ascorbic acid, producing nanoparticles with controlled size and shape but posing environmental risks. Physical methods, such as laser ablation and ball milling, offer high-purity nanoparticles but require significant energy and specialized equipment. Biological synthesis, using plant extracts, bacteria, and fungi, provides a green alternative, producing biocompatible nanoparticles though with variable results. Recent advancements emphasize green synthesis methods, particularly the use of gallic acid, a natural antioxidant, which offers a consistent, eco-friendly, and efficient approach to nanoparticle production. After comparing the advantages and disadvantages using the latest literature, the study finds that the biological synthesis method, especially with gallic acid, is the most preferable due to its biocompatibility and ability to produce stable, uniform nanoparticles. The review explores the potential applications of AgNPs in medicine, electronics, and environmental science, concluding that gallic acid-mediated synthesis is particularly suited for biomedical applications. This comprehensive review aims to provide a detailed understanding of AgNP synthesis methods, contributing to the advancement of this crucial field in nanotechnology.

## 1. Introduction

Nanoparticles exhibit size-dependent physicochemical behaviors that diverge markedly from bulk matter, enabling broad functional utility across science and technology [1, 2].

Among them the synthesis of silver nanoparticles (AgNPs) has garnered significant attention due to their unique properties and wide range of applications in fields such as medicine, electronics, and environmental science. These nanoparticles exhibit remarkable antimicrobial, optical, and electrical properties, making them suitable for diverse applications. In addition, both AgNPs and $Ag_2O$ nanoparticles have emerged as efficient heterogeneous catalysts in organic transformations, particularly in the synthesis of heterocyclic frameworks, owing to their ability to enhance yield, selectivity, and reaction efficiency under mild conditions [3, 4].

Recent advancements in nanotechnology have enabled the development of various synthesis methods for AgNPs, each offering distinct advantages and addressing specific challenges. This review aims to provide a comprehensive overview of the methods used to synthesize AgNPs, with a focus on recent advancements and future prospects. Previous studies have highlighted the importance of optimizing synthesis methods to achieve desired particle sizes and shapes,

* Corresponding author E-mail: i.turdiqulov@mail.ru
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which are crucial for their application-specific properties [5]. The drive towards greener and more sustainable synthesis methods has also been a significant focus, with researchers exploring eco-friendly alternatives to traditional chemical and physical methods. Recent literature has reported innovative approaches and modifications to existing techniques to enhance the efficiency, yield, and biocompatibility of AgNPs [6]. For instance, biosynthesis methods using plant extracts and microorganisms have shown promising results, offering a green alternative to conventional methods. Additionally, the development of hybrid methods combining chemical and biological approaches has been explored to improve nanoparticle stability and functionality [7]. This review consolidates these findings, providing a detailed examination of current trends and future directions in the synthesis of AgNPs.

## 2. Importance and Applications of Silver Nanoparticles

Silver nanoparticles (AgNPs) have attracted considerable interest due to their unique properties, which stem from their high surface area-to-volume ratio and the presence of quantum size effects. These properties confer upon AgNPs a wide range of functionalities, making them suitable for diverse applications in various fields such as medicine, electronics, and environmental science (Figure 1).

### 2.1. Medical Applications

In the medical field, AgNPs are extensively utilized due to their potent antimicrobial properties. They are commonly incorporated into wound dressings, catheters, and surgical instruments to prevent infections. The antimicrobial activity of AgNPs is largely attributed to their ability to release silver ions, which disrupt the cellular processes of a broad spectrum of pathogenic microorganisms, including bacteria, viruses, and fungi [8].

This makes AgNPs invaluable in healthcare settings where infection control is critical, particularly in the prevention of hospital-acquired infections.

One of the most promising areas of research involves the use of AgNPs in the development of advanced wound dressings. These dressings not only prevent infection but also promote healing by maintaining a moist environment, which is essential for tissue regeneration. AgNPs are often integrated into hydrogels, foams, or bandages, providing a sustained release of silver ions that ensures prolonged antimicrobial activity.

In addition to wound care, AgNPs have been explored for their potential in cancer treatment. Research has demonstrated that AgNPs can induce apoptosis (programmed cell death) in cancer cells, which may offer a pathway for targeted cancer therapies [9]. AgNPs have shown the ability to enhance the effects of traditional chemotherapy agents, potentially allowing for lower doses of toxic drugs while maintaining or even improving therapeutic efficacy. This synergy between AgNPs and chemotherapy agents is an area of significant interest, particularly for treating drug-resistant cancers.

Moreover, AgNPs are being utilized in diagnostic applications. They are employed in the creation of biosensors designed to detect biomolecules, pathogens, and even specific DNA sequences with high sensitivity.

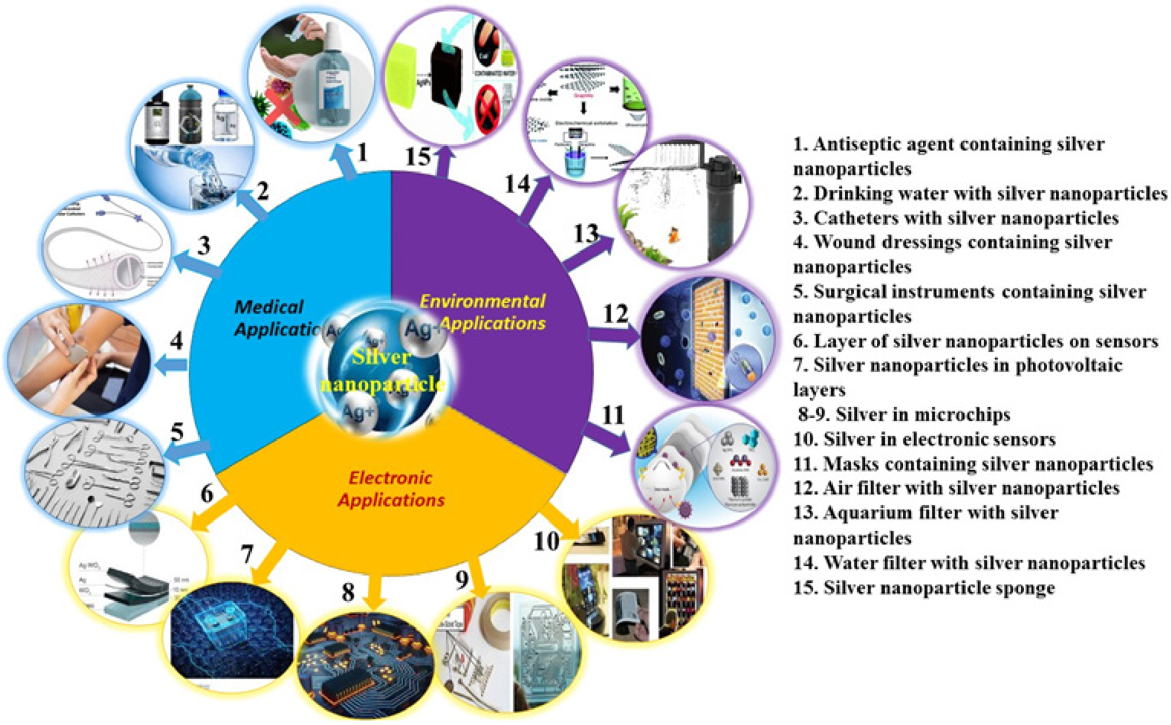



**Fig. 1.** Modern applications of silver nanoparticles

The plasmonic properties of AgNPs enhance the signal output in various sensor designs, making them particularly useful in point-of-care diagnostics and early detection of diseases [10]. This is critical in the management of infectious diseases, where rapid and accurate detection can significantly improve patient outcomes.

The biocidal properties of AgNPs also extend to coatings on medical devices, such as implants and prosthetics, which are prone to biofilm formation. Biofilms are communities of microorganisms that adhere to surfaces and are notoriously difficult to eradicate with standard antimicrobial treatments. AgNP coatings can prevent the initial adhesion of bacteria and disrupt biofilm formation, thereby reducing the risk of infection associated with implanted medical devices [11]. This application is particularly relevant in the context of orthopedic and cardiovascular implants, where infections can lead to severe complications and require complex revision surgeries.

### 2.2. Electronic Applications

In the field of electronics, AgNPs are valued for their excellent electrical conductivity. They are key components in the development of conductive inks and pastes used in flexible electronics, printed circuits, and touch screens. The small size and high surface area of AgNPs enable the production of highly conductive films and coatings, which are essential for the advancement of flexible and wearable electronic devices [12]. Furthermore, AgNPs are used in the fabrication of sensors and photovoltaic devices. Their unique optical properties, such as localized surface plasmon resonance (LSPR), enhance the sensitivity and performance of sensors, making them capable of detecting low concentrations of analytes [13]. In solar cells, AgNPs are employed to improve light absorption and enhance the efficiency of energy conversion, contributing to the development of more efficient and cost-effective photovoltaic systems [14].

### 2.3. Environmental Applications

Silver nanoparticles also play a significant role in environmental science, particularly in water treatment and air purification. AgNPs are incorporated into filtration systems to remove contaminants and pathogens from water, providing a more effective means of water purification compared to traditional methods [15]. The antimicrobial properties of AgNPs ensure that the treated water is free from harmful microorganisms, making it safe for consumption [16]. In air purification, AgNPs are used in coatings and filters to eliminate airborne pathogens and pollutants. They are effective in degrading volatile organic compounds (VOCs) and other harmful substances, improving air quality in indoor and outdoor environments [17]. Additionally, AgNPs are being explored for their potential in soil remediation, where they can help break down toxic substances and promote the growth of beneficial microorganisms [18].

## 3. History of Silver Nanoparticles

The use of silver for its antimicrobial properties dates back thousands of years, with evidence of its use in ancient civilizations such as the Egyptians, Greeks, and Romans. These early cultures utilized silver in various forms, including vessels, coins, and powders, to preserve food, purify water, and treat wounds. Silver's ability to prevent spoilage and infection was well recognized, even if the mechanisms behind these effects were not fully understood at the time [19]. The Phoenicians, for instance, stored water, wine, and vinegar in silver vessels to prevent contamination, and Hippocrates, the father of medicine, wrote about the use of silver for wound care and disease treatment [20].

The scientific exploration of silver's antimicrobial properties began in earnest during the 19th century. In 1884, the German obstetrician Carl Crede introduced the use of silver nitrate eye drops to prevent neonatal conjunctivitis, a practice that significantly reduced the incidence of blindness in newborns [21]. This application of silver nitrate marked one of the earliest documented uses of silver in a medical context, leading to further exploration of silver compounds in various therapeutic applications.

The advent of antibiotics in the mid-20th century led to a decline in the use of silver in medicine, as penicillin and other antibiotics became the preferred treatment for bacterial infections. However, the rise of antibiotic-resistant bacteria in the latter part of the 20th century reignited interest in silver as an alternative antimicrobial agent. Researchers began to explore the potential of silver nanoparticles (AgNPs) as a more effective and versatile form of silver due to their enhanced surface area and reactivity [22].

The scientific exploration of silver nanoparticles began in the late 20th century, with pioneering work focusing on their synthesis and antimicrobial properties. In 1959, Richard Feynman, in his famous lecture "There's Plenty of Room at the Bottom," alluded to the possibilities of manipulating matter on an atomic scale, which later inspired research in nanotechnology. However, it wasn't until the 1970s that practical research into metal nanoparticles, including silver, gained traction. During this period, researchers developed methods for producing metal colloids, including silver, using chemical reduction techniques. These early studies laid the groundwork for understanding the unique properties of nanoparticles and their potential applications [23].

One of the key milestones in the field of silver nanoparticles was the development of the Turkevich method in 1951, which originally applied to gold but later adapted for silver nanoparticles. This method involves the reduction of silver nitrate using citrate as a reducing agent and stabilizer, producing colloidal silver with controlled size and shape. The Turkevich method remains a fundamental technique in nanoparticle synthesis, and its principles continue to inform modern synthesis methods [24].

In the 1990s, advancements in microscopy and spectroscopy allowed for the precise characterization of nanoparticles, leading to a deeper understanding of their size-dependent properties. This period saw significant progress in the controlled synthesis of silver nanoparticles, with researchers exploring various chemical, physical, and biological methods to produce nanoparticles with specific sizes, shapes, and functionalities. These advancements expanded the range of applications for silver nanoparticles, particularly in the fields of medicine, electronics, and environmental science [25].

The last decade has witnessed exponential growth in nanoparticle research, with silver nanoparticles (AgNPs) gaining particular interest due to their broad-spectrum applications in fields like medicine, electronics, and environmental science. According to recent bibliometric data, the study of nanoparticles, especially AgNPs, has gained momentum with over 66,838 published documents in the the last between 2021 and 2024. Of these 7,682 publications are specifically related to silver nanoparticles, comprising 11,5% of the total literature on nanomaterials. This rise in publications underscores the substantial research interest in AgNPs [26].

One of the dominant trends in AgNP research has been the focus on the green synthesis of nanoparticles, addressing the growing concerns about the environmental and toxicological implications of chemically synthesized AgNPs [27]. Researchers have prioritized methods that use biological extracts (from plants, bacteria, and fungi) to synthesize AgNPs in a more sustainable and biocompatible manner. This has led to advancements in the production of nanoparticles that are safer for biomedical applications, including drug delivery systems and antimicrobial coatings [28].

Moreover, analysis of patent filings over the last five years reveals an interesting shift. Approximately 38% of the patents related to AgNPs are focused on new synthesis techniques, while 18.1% explore properties associated with their physical and chemical characteristics [29]. The higher ratio of method-based patents suggests that green synthesis is not just a scientific curiosity but a commercially viable field with the potential for large-scale industrial applications.

As industries recognize the importance of sustainable production methods, there has been a noticeable decline in patents based on traditional chemical synthesis approaches. This trend suggests that researchers and industry professionals are exploring novel, environmentally benign techniques for producing AgNPs, especially methods involving plant-based reducing agents like galli c acid, as previously mentioned. These advancements in green chemistry aim to minimize the harmful environmental effects typically associated with nanoparticle production [30].

## 4. Methods for synthesizing silver nanoparticles

Silver nanoparticles (AgNPs) can be synthesized using three primary approaches***: physical, chemical, and biological*** methods [31]. Each method offers unique advantages and limitations, making them suitable for different applications. Physical methods, such as laser ablation and evaporation-condensation, are known for producing high-purity nanoparticles without the use of stabilizing agents. Chemical methods often involve the reduction of silver salts using reducing agents, offering precise control over particle size and shape. Biological methods utilize natural extracts or microorganisms for eco-friendly nanoparticle synthesis, though challenges in scalability remain. The choice of synthesis method depends on factors like desired particle characteristics, cost, and environmental considerations [32].

### 4.1. Physical Methods for Synthesizing Silver Nanoparticles

Physical methods for synthesizing silver nanoparticles (AgNPs) typically rely on the use of physical forces or conditions to induce the production of nanoparticles. These methods are known for their ability to produce particles with controlled size and shape while avoiding the use of chemical reagents, thus reducing potential impurities in the final product. Common physical methods include evaporation-condensation, laser ablation, and physical vapor deposition (PVD), among others [33]. This section provides an overview of these methods along with notable studies conducted by researchers in the field.

#### 4.1.1. Evaporation-Condensation Method

This technique involves the generation of nanoparticles by heating a bulk silver source under reduced pressure until it vaporizes, followed by condensation of the vapor to form nanoparticles. The size and morphology of the particles can be influenced by factors such as temperature, pressure, and carrier gas flow rate [34].

In one study, Sakono et al. demonstrated the effectiveness of the evaporation-condensation method for producing nanoparticles with a narrow size distribution. The researchers used a silver target and optimized the process conditions to produce monodisperse nanoparticles suitable for various applications [35]. Another significant contribution was made by Rahman and colleagues, who investigated the role of cooling rates during condensation. They reported that rapid cooling resulted in smaller nanoparticles with high stability, which is essential for optical and electronic applications [36]. One significant limitation of the evaporation-condensation method for synthesizing silver nanoparticles (AgNPs) is the high energy consumption required for the process. This method involves heating a bulk silver source to high temperatures, leading to substantial energy costs, especially for large-scale production. Additionally, maintaining a controlled environment, such as vacuum or inert gas conditions, further increases operational expenses [37].

### 4.1.2. Laser Ablation Method

Laser ablation is a physical process in which a high-energy laser beam is directed onto a silver target submerged in a liquid medium or kept in an inert gas atmosphere. This process creates plasma, which leads to the ejection of silver atoms and their subsequent aggregation into nanoparticles [38].

Ganash et al. were among the first to study laser ablation for synthesizing AgNPs in water. They highlighted that the method does not require stabilizing agents, making it an environmentally friendly alternative. Their work also demonstrated that laser wavelength and pulse duration significantly influence particle size and distribution [39] (Figure 2).

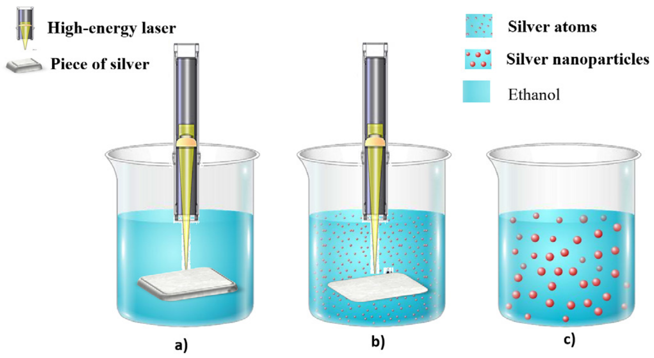



**Fig. 2.** Mechanism of Synthesis of Silver Nanoparticles via Laser Ablation Method

Another notable study by Ali et al. explored laser ablation in various liquids, including ethanol and acetone. The researchers observed that the choice of liquid medium greatly affects the stability and size of the nanoparticles, with ethanol providing better size control due to its stabilizing properties [40]. The synthesis of silver nanoparticles through laser ablation is costly, primarily due to the expensive laser systems and the necessity for precise adjustments of parameters like pulse duration and energy fluence. Moreover, this technique generally yields a low production rate, with inconsistencies in particle size and a tendency for nanoparticle aggregation, often requiring additional treatments to improve stability and usability [41].

### 4.1.3. hysical Vapor Deposition (PVD)

PVD involves the vaporization of a silver source in a vacuum chamber, followed by the deposition of nanoparticles onto a substrate. This method is particularly suitable for producing uniform nanoparticle films for optical and electronic devices [42].

Durmanov et al. investigated the use of PVD for fabricating thin films of silver nanoparticles on silicon substrates. Their study revealed that the deposition rate and substrate temperature play critical roles in determining the particle size and coverage density [43].

Another study by Yang et al. focused on optimizing PVD parameters for large-scale production. They demonstrated that by controlling the chamber pressure and deposition angle, it is possible to achieve consistent nanoparticle characteristics, making this method viable for industrial applications.

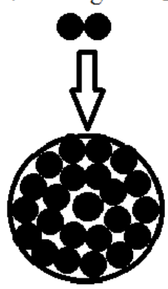
### 4.2. Chemical Synthesizing Silver Nanoparticles

Chemical methods are versatile and commonly used approaches for synthesizing silver nanoparticles (AgNPs), allowing precise control over their size, shape, and properties [44]. These methods typically involve chemical reduction, microemulsion, or photochemical techniques, each with its unique advantages and applications. Here, we detail the mechanisms, reagents, and influencing factors involved in these processes.

### 4.2.1. Reduction Using Sodium Borohydride ($NaBH_4$)

The chemical reduction method transforms silver ions ($Ag^+$) into elemental silver ($Ag^0$) using reducing agents. One of the most commonly used reducing agents for the synthesis of silver nanoparticles by chemical reduction is sodium borohydride ($NaBH_4$), which reacts with the following mechanism and reduces silver to silver atoms. Several of the resulting silver atoms combine to form a silver nanoparticle [45].

$$2AgNO_3 + 2NaBH_4 \rightarrow 2Ag^o + H_2 + B_2H_6 + 2NaNO_3$$



Iqbal et al. (2024) synthesized sodium alginate-coated silver nanoparticles using sodium borohydride ($NaBH_4$) as a reducing agent and investigated their potential as mitochondria-targeted drug delivery systems for breast cancer therapy. Their study demonstrated that resveratrol-loaded sodium alginate-coated silver nanoparticles exhibited enhanced antioxidant activity and significant anticancer effects against MCF-7 breast cancer cells. This approach highlights the potential of nanocarriers in targeted cancer treatment [46]. Liu et al. (2023) synthesized silver nanoparticles using sodium borohydride ($NaBH_4$) as a reducing agent, two-step enhanced Raman technique, where the $NaBH_4$ synergistic chemical and physical enhancement of highly sensitive and non-invasive platform for food safety, pharmaceuticals, and medical diagnostics [47].

Silver nanoparticle synthesis is highly dependent on the choice of reducing agents, as demonstrated by Velgosova et al. (2022). Their research systematically examined the effects of sodium borohydride ($NaBH_4$), trisodium citrate (TSC), polyvinylpyrrolidone (PVP), and hydrogen peroxide ($H_2O_2$) on nanoparticle formation, revealing that $NaBH_4$ plays a crucial role in rapidly reducing $Ag^+$ ions to $Ag^0$. Interestingly, while $NaBH_4$ contributed to fast nucleation and the formation of small spherical nanoparticles, TSC was found to be a key determinant in shaping the final morphology of the particles. The study also illustrated how different reagent combinations influenced solution color, particle size, and structural variation, with UV-Vis spectroscopy and TEM analysis confirming the presence of various shapes, including spherical, triangular, hexagonal, and irregular structures. These findings emphasize the importance of reagent selection in tailoring nanoparticle properties for specific applications [48].

The stability and transformation of ultrasmall silver nanoparticles in aqueous environments remain a crucial topic in nanomaterials research. Wolff et al. (2024) synthesized ultrasmall glutathione-coated silver nanoparticles (2 nm) using sodium borohydride ($NaBH_4$) as a reducing agent, highlighting its essential role in the rapid reduction of $Ag^+$ ions. Their study revealed a gradual conversion of these silver nanoparticles into silver sulfide nanoparticles due to ligand-induced hydrogen sulfide ($H_2S$) release, which reacted with the silver core over four weeks. Notably, this transformation significantly altered the nanoparticles' chemical, physical, and biological properties, with freshly synthesized particles exhibiting higher cytotoxicity against cells and bacteria due to the presence of silver nanoclusters. These findings emphasize the importance of nanoparticle aging and environmental interactions in determining their long-term functionality and biocompatibility [49].

The sodium borohydride method is hindered by its toxicity and environmental impact, along with challenges in preventing nanoparticle aggregation without stabilizers [50].

### 4.2.2. Reduction Using Ascorbic Acid ($C_6H_8O_6$)

Ascorbic acid, a naturally occurring reducing agent, has been extensively studied for synthesizing silver nanoparticles (AgNPs) due to its biocompatibility and antioxidant properties. Reaction equation:

$$2AgNO_3+C_6H_8O_6 \rightarrow 2Ag^o+C_6H_6O_6+2HNO_3$$

The hydroxyl groups in ascorbic acid donate electrons to silver ions, converting them into metallic silver. During this process, ascorbic acid is oxidized to dehydroascorbic acid ($C_6H_6O_6$) [51].

Mughal et al. (2024) developed a facile, room-temperature synthesis approach for cetyltrimethylammonium bromide (CTAB)-coated silver nanoparticles (AgNPs) using ascorbic acid as a reducing agent in a basic reaction medium. Their findings revealed that by adjusting CTAB concentration and pH levels, it is possible to optimize nanoparticle yield, size uniformity, and stability, making the synthesized AgNPs highly effective for long-term storage in both light and dark conditions [52]. Biosynthesized silver nanoparticles (AgNPs) using L-ascorbic acid as a reducing agent, demonstrating their potential application in skin lesion treatments due to their antimicrobial activity and biocompatibility. Their study revealed that the AgNPs exhibited strong inhibitory effects against both Gram-positive and Gram-negative bacteria, maintained low cytotoxicity on VERO cells, and only affected seed growth at higher concentrations, highlighting their safety profile and promising role in biomedical applications [53].

Qin et al. (2010) demonstrated the synthesis of spherical AgNPs with a size range of 10–30 nm using ascorbic acid at room temperature. The study highlighted that the pH of the reaction medium significantly influenced the size and distribution of nanoparticles, with alkaline conditions favoring smaller, more uniform particles. The biocompatible nature of the nanoparticles made them suitable for applications in drug delivery and biosensing [54].

The ascorbic acid method for synthesizing silver nanoparticles has limitations, including its mild reducing power leading to slower reactions and larger particles, as well as challenges with nanoparticle stability and sensitivity to reaction conditions. [55]

### 4.2.3. Reduction Using Hydrazine ($N_2H_4$)

The reduction of silver ions ($Ag^+$) to form silver nanoparticles (AgNPs) using hydrazine ($N_2H_4$) is a common method in nanoparticle synthesis [56]. Below is the reaction equation for this process:

$$2Ag^{+}+N_2H_4 \rightarrow 2Ag^o+N_2+2H_2O$$

In this method, like the above, the reduced silver atoms combine to form nanoparticles [57].

The study explored the effect of hydrazine concentration, revealing that higher concentrations of hydrazine resulted in smaller nanoparticles, suggesting that hydrazine concentration directly influenced nucleation and growth rates. The synthesized AgNPs exhibited excellent catalytic properties for the reduction of organic pollutants, making them promising candidates for environmental remediation applications. Dugandžić et al. highlighted the simplicity of the method and the high yield of nanoparticles, though they noted that careful control of hydrazine concentration is crucial to prevent particle aggregation [58]. Charistoudi and colleagues focused on synthesizing silver nanoparticles using hydrazine hydrate and investigated the influence of pH on the particle size and stability. They found that an alkaline pH favored the reduction reaction, resulting in more uniform and smaller nanoparticles (~5 nm), while a neutral or acidic pH led to the formation of larger particles with more varied sizes. These AgNPs exhibited strong antibacterial activity against both Gram-positive and Gram-negative bacteria, with the authors concluding that hydrazine-reduced AgNPs could serve as a viable alternative for antibiotic treatments [59]. Ghosh et al. explored the synthesis of silver nanoparticles using hydrazine as a reducing agent, with an emphasis on the effect of reaction temperature and time on particle morphology. The study demonstrated that increasing the temperature accelerated the reduction process and led to the formation of smaller nanoparticles (~7 nm) with narrower size distributions. In contrast, prolonged reaction times resulted in larger particles and less uniform dispersions. The researchers also investigated the stability of the AgNPs in various solvents and found that the nanoparticles were stable for several weeks in water, but showed aggregation in organic solvents without stabilizing agents [60]. Obtaining silver nanoparticles with hydrazine can be disadvantageous due to hydrazine's toxicity, potential environmental hazards, and the need for careful handling to avoid harmful exposure. [61]

### 4.2.4. Reduction Using Glucose ($C_6H_{12}O_6$)

Silver nanoparticles can be synthesized by reducing silver ions ($Ag^+$) with glucose ($C_6H_{12}O_6$) as a reducing agent, where glucose is oxidized to gluconic acid, resulting in the formation of metallic silver nanoparticles. Reaction equation:

$$2AgNO_3+C_6H_{12}O_6 \rightarrow 2Ag^o+C_6H_{12}O_7$$

Multiple studies have investigated glucose-based synthesis methods and have shown that factors like temperature and pH significantly influence the reaction efficiency [62]. Research findings suggest that an alkaline environment accelerates reduction, leading to well-dispersed AgNPs with controlled morphology.

Another study explored how the addition of sodium hydroxide enhances the role of glucose in nanoparticle synthesis [63, 64]. It was observed that NaOH improves reaction efficiency and particle stability while affecting nanoparticle shape and size, depending on glucose concentration and reaction time.

In a different approach, researchers examined the stabilizing effect of modified forms of starch and cellulose derivatives when combined with glucose, reporting that this mixture yields uniformly sized spherical AgNPs. [65, 66]. The presence of starch plays a key role in preventing nanoparticle aggregation, ensuring long-term stability of the colloid. Moreover, glucose-mediated AgNP synthesis has also been performed at room temperature using silver nitrate as the precursor [67]. Furthermore, reaction parameters must be carefully optimized to prevent nanoparticle aggregation, which can compromise their uniformity and stability. Silver nanoparticles synthesized using β-D-glucose as a reducing agent (AgNPs-G) have dantitumor efficacy in a breast cancer mouse model, neoadjuvant therapy toAgNPs-G treatment significantly suppressed tumor growth and reduced metastatic lung nodules, while also influencing expression, a key marker of cell proliferation. These findings highlight the potential of glucose-reduced silver nanoparticles as an alternative therapeutic strategy, though further investigations are required to fully understand their mechanisms and optimize their clinical application [68]. The results confirmed that glucose is capable of producing nanoparticles with desirable optical and structural properties, making them suitable for diverse applications. Despite these advantages, glucose does have some limitations as a reducing agent. Studies indicate that due to its mild reducing nature, glucose-mediated reduction proceeds more slowly than stronger agents like sodium borohydride, often resulting in larger particle sizes [69].

### 4.2.5. Photochemical Synthesis of Silver Nanoparticles

Photochemical synthesis is an emerging method for producing silver nanoparticles (AgNPs) that utilizes light energy to drive the reduction of silver ions ($Ag^+$) to metallic silver ($Ag^0$). This method is advantageous due to its simplicity, cost-effectiveness, and ability to produce nanoparticles with controlled size and morphology without the need for harsh reducing agents. The process typically involves irradiating a solution containing a silver precursor, such as silver nitrate ($AgNO_3$), and a stabilizing agent with ultraviolet (UV) or visible light. The light energy excites the silver ions, leading to their reduction and subsequent nucleation into nanoparticles [70].

Recent studies have demonstrated the effectiveness of photochemical synthesis in producing AgNPs with high purity and uniformity. For instance, Yunusov et al. (2025) reported the synthesis of spherical AgNPs with an average size of 15 nm using UV light irradiation in the presence of polyvinyl alcohol, carboxymethylcellulose as a stabilizing agent. The researchers highlighted that the wavelength and intensity of the light significantly influenced the particle size distribution, with shorter wavelengths yielding smaller nanoparticles [71-72] (Figure 3).

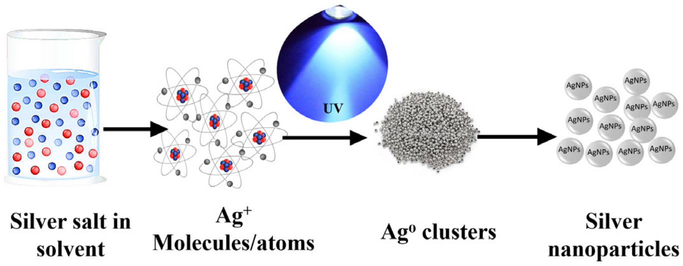



**Fig. 3.** Mechanism of Photochemical Synthesis of Silver Nanoparticles

One of the key advantages of photochemical synthesis is its ability to produce nanoparticles under ambient conditions, making it an environmentally friendly alternative to traditional chemical methods. Additionally, the method allows for precise control over the reaction kinetics by adjusting parameters such as light intensity, irradiation time, and the concentration of the silver precursor [73].

However, challenges remain in scaling up the process for industrial applications, as the efficiency of light absorption and the uniformity of nanoparticle formation can vary depending on the reaction setup [74].

Recent advancements in photochemical synthesis have also explored the use of plasmonic effects to enhance the reduction process. For example, Li et al. (2024) demonstrated that the incorporation of gold nanoparticles as plasmonic enhancers could significantly accelerate the reduction of silver ions, leading to the formation of AgNPs with narrow size distributions and improved stability [75].

These innovations highlight the potential of photochemical synthesis as a versatile and sustainable approach for producing AgNPs with tailored properties for various applications.

### 4.3. Biological Synthesis of Silver Nanoparticles

The biological synthesis of silver nanoparticles (AgNPs) has gained significant attention in recent years due to its eco-friendly nature and ability to produce biocompatible nanoparticles. Unlike traditional chemical and physical methods, biological synthesis utilizes natural sources such as plants, microorganisms, and biomolecules to reduce silver ions ($Ag^+$) into metallic silver nanoparticles ($Ag^0$) [76, 77].

This approach not only minimizes the use of toxic chemicals but also offers a sustainable and cost-effective alternative for nanoparticle production. Researchers have explored various biological systems, each with unique mechanisms and advantages, to synthesize AgNPs with controlled size, shape, and functionality.

Below, we discuss the three main categories of biological synthesis: plant-mediated, microorganism-mediated, and biomolecule-mediated synthesis.

#### 4.3.1. Microorganism-Mediated Synthesis

Microorganisms, including bacteria, fungi, and algae, have shown remarkable potential in synthesizing AgNPs. These organisms utilize their unique metabolic pathways and enzymes to reduce silver ions and stabilize the resulting nanoparticles.

Bacteria, such as Bacillus subtilis and Pseudomonas aeruginosa, are among the most studied microorganisms for AgNP synthesis. Extracellular enzymes produced by these bacteria play a critical role in reducing silver ions and stabilizing the nanoparticles. For instance, Bacillus subtilis has been shown to produce AgNPs with potent antimicrobial activity, effective against both Gram-positive and Gram-negative bacteria [78]. Similarly, Muddassir et al. (2022) reported that Pseudomonas aeruginosa synthesizes AgNPs with applications in medical devices and wound healing [79].

Fungi, such as Aspergillus niger and Fusarium oxysporum, have also been widely explored for AgNP synthesis. These fungi produce extracellular enzymes and proteins that act as reducing and stabilizing agents. For example, Nasr et al. (2024) used Aspergillus niger to produce AgNPs with strong antifungal activity, making them suitable for agricultural applications [80]. Meanwhile, *Fusarium oxysporum* has been employed to synthesize AgNPs with potential applications in cancer therapy, as they induce apoptosis in cancer cells [81].

Algae, such as *Chlorella vulgaris* and *Spirulina platensis*, have also gained attention for their ability to synthesize AgNPs. *Chlorella vulgaris* has been used to produce nanoparticles with high photocatalytic activity, effective in degrading organic pollutants [82]. Similarly, Gul et al. (2024) showed that Spirulina platensis synthesizes AgNPs with antioxidant and antimicrobial properties, making them suitable for biomedical applications [83].

Despite its advantages, microorganism-mediated synthesis faces challenges such as slow reaction rates and the need for sterile conditions. Recent studies have addressed these challenges by optimizing growth conditions and nutrient availability, significantly improving nanoparticle yield and stability [84].

#### 4.3.2. Biomolecule-Mediated Synthesis

Biomolecule-mediated synthesis involves the use of isolated biomolecules, such as enzymes, proteins, and polysaccharides, to produce AgNPs. This approach offers high specificity and control over nanoparticle properties, making it suitable for various applications.

Enzymes, such as nitrate reductase and laccase, have been widely studied for their ability to synthesize AgNPs.

For example, Kazeem et al. (2021) used nitrate reductase to produce nanoparticles with high catalytic activity, making them suitable for environmental applications [85]. Similarly, Barabadi et al. (2024) employed laccase to synthesize AgNPs with potential applications in biosensing, as they enhance the sensitivity of biosensors [86].

Proteins, such as bovine serum albumin (BSA) and casein, have also been explored for AgNP synthesis. Zhang et al. (2023) demonstrated that BSA can produce nanoparticles with high biocompatibility, making them suitable for drug delivery applications [87]. Casein, on the other hand, has been shown to produce AgNPs with enhanced stability and antimicrobial activity, effective against a wide range of pathogens [88].

Polysaccharides, such as chitosan and alginate, have gained attention for their ability to act as both reducing and stabilizing agents. Aranaz et al. (2023) used chitosan to synthesize AgNPs with potential applications in wound healing, as they promote tissue regeneration [89]. Similarly, alginate has been employed to produce nanoparticles with high antioxidant activity, making them suitable for treating oxidative stress-related diseases [90]. Along with these advantages, biomolecule-mediated synthesis faces challenges such as the high cost of biomolecules and the need for precise reaction conditions [91].

### 4.3.3. Plant-Based Synthesis of Silver Nanoparticles

Plant-mediated synthesis of silver nanoparticles (AgNPs) has emerged as a widely accepted green synthesis approach due to its simplicity, cost-effectiveness, and sustainability. Various plant extracts, containing diverse phytochemicals such as flavonoids, phenolic acids, and alkaloids, serve as natural reducing and stabilizing agents, facilitating the conversion of $Ag^+$ ions into stable AgNPs [92].

Recent research highlights several plant species that have demonstrated high efficiency in AgNP synthesis. In 2024, Prathibha et al. extensively used Azadirachta indica (neem) leaf extract, which produced uniformly distributed nanoparticles with potent antimicrobial activity [93]. Similarly, in 2024, Pathak et al. employed Ocimum sanctum (holy basil) extract for AgNP formation, yielding highly stable nanoparticles with strong antioxidant properties [94].

Additionally, in 2024, Haris et al. reported the synthesis of nanoparticles with enhanced biocompatibility using Moringa oleifera extract, making them ideal for medical applications [95].

Phytochemicals in plant extracts influence nanoparticle size, shape, and stability. It has been observed that adjusting the extract concentration and reaction parameters, such as pH and temperature, can optimize nanoparticle characteristics [96]. In a study conducted by Soundharajan et al. (2025), Camellia sinensis (green tea) extract was found to produce smaller AgNPs with high surface-area-to-volume ratios, increasing their effectiveness in biomedical and catalytic applications [97].

Despite these advantages, the variability in plant composition due to geographical and seasonal factors poses challenges in achieving reproducibility. However, recent advances, including microwave-assisted and ultrasound-assisted synthesis, have improved process consistency and nanoparticle uniformity [98]. In 2024, Thai et al. developed hybrid methods by combining plant extracts with other reducing agents, further enhancing the stability and functional properties of AgNPs [99].

Researchers have actively explored various plant extracts to improve nanoparticle synthesis. In 2025, Kurra et al. successfully demonstrated that Cymbopogon citratus (lemongrass) extract enables rapid AgNP synthesis with notable antibacterial properties [100], whereas Curcuma longa (turmeric) extract was used to generate nanoparticles with remarkable anti-inflammatory effects [101]. Similarly, in 2021, Nallal et al. discovered that Allium sativum (garlic) extract synthesizes AgNPs with potent antifungal activity, further broadening their biomedical applications [102].

## 4.4. Gallic Acid-Mediated Synthesis of Silver Nanoparticles

The synthesis of nanoparticles using gallic acid (GA), a naturally occurring polyphenol found in various plants, has also gained prominence as a promising plant-based method [103-105]. Gallic acid has shown great promise in biomedicine due to its potent antioxidant, anti-inflammatory, and antimicrobial properties [106]. Recent studies highlight its potential in cancer therapy, where gallic acid-derived nanoparticles exhibit selective cytotoxicity against tumor cells while minimizing damage to healthy tissues. Additionally, its ability to enhance drug delivery efficiency makes it a valuable stabilizing agent in nanoparticle-based therapeutic systems [107]. Gallic acid also plays a crucial role in wound healing, as its antimicrobial and regenerative properties accelerate tissue repair [108]. With ongoing research, its integration into nanomedicine could lead to innovative treatments for infections, oxidative stress-related diseases, and drug-resistant pathogens. Gallic acid not only acts as a reducing agent, facilitating the transformation of $Ag^+$ to $Ag^0$, but also plays a critical role as a stabilizer, preventing nanoparticle aggregation and ensuring high dispersion [109]. The presence of hydroxyl and carboxyl functional groups in GA enhances its reducing capability, leading to the formation of nanoparticles with controlled size and shape. Studies have reported that varying the GA concentration, reaction time, and pH can significantly influence AgNP morphology and stability [110, 111]. In 2022, Williams et al. found that increasing GA concentration results in smaller nanoparticles with a uniform distribution, which is beneficial for biomedical applications [112]. Additionally, in 2015, Kim et al. demonstrated that GA-based AgNPs exhibit strong antimicrobial activity against drug-resistant bacteria, making them an attractive option for medical treatments [113]. Beyond silver nanoparticles, gallic acid has been explored for the synthesis of other metallic nanoparticles, including gold, copper, and zinc oxide nanoparticles, due to its excellent reducing properties [114, 115].

Scientists have actively investigated the multifunctional properties of GA-functionalized nanoparticles. In 2021, Aldawsari et al. demonstrated that GA-coated nanoparticles improve cellular uptake efficiency in drug delivery systems, enhancing their therapeutic potential [116]. Furthermore, in 2023, Zhao et al. highlighted GA's role in hybrid nanoparticle synthesis, where it ensures prolonged stability in biological environments [117].

## 5. Conclusions

Among the various methods for AgNP synthesis, the biological approach remains the most preferable due to its eco-friendliness and biocompatibility. Within green synthesis methods, plant-based synthesis has proven to be the most efficient and sustainable, offering a wide range of bioactive compounds for controlled nanoparticle formation. Furthermore, among plant-based methods, gallic acid stands out as an optimal reducing and stabilizing agent, providing nanoparticles with superior stability, antimicrobial properties, and biomedical applicability. As research advances, further optimization of gallic acid-mediated synthesis will play a crucial role in enhancing the large-scale production and industrial applications of biogenic silver nanoparticles.

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