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SILVER NANOPARTICLES AS ANTIMICROBIAL AGENTS: SYNTHESIS, APPLICATIONS AND CURRENT STUDIES

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Abstract: Silver nanoparticles (AgNPs) have garnered significant scientific attention due to their potent antibacterial properties and versatile applications in medicine, environmental remediation, and industry. This review presents an in–depth analysis of the antibacterial activity of AgNPs, focusing on their mechanisms of action against Gram–positive and Gram–negative bacteria. Various synthesis methods are critically examined, including chemical reduction techniques, physical methods such as light–mediated synthesis, and green approaches utilizing plant extracts, microbial agents, and natural polymers. Each method's advantages and limitations are discussed, highlighting their influence on nanoparticle size, shape, stability, and antibacterial performance. The potential of combining synthetic methods to enhance nanoparticle properties is briefly explored. Particular attention is given to green synthesis, emphasized as a sustainable, biocompatible alternative for large–scale production. The study underscores the importance of strategic selection of synthesis routes to achieve optimal safety, efficiency, and scalability of AgNPs for biomedical and technological applications. Overall, this work supports the ongoing efforts toward the responsible and innovative use of silver nanoparticles as advanced antibacterial agents in future applications.
Keywords: silver nanoparticles, antibacterial properties, synthesis methods, green synthesis, biomedical applications

1. INTRODUCTION

The modernization of technologies has become essential for the advancement of science, with precious metals being frequently employed in various manufacturing processes. Among them, silver stands out due to its unique properties, finding constantly diversifying applications both as a precious metal and in industrial contexts, where it is used in numerous technological operations. The development of nanotechnologies, combined with the high purity, versatility, and increasingly precise control over the shape and morphology of silver nanoparticles, led to the emergence of new applications fields of application. These nanoparticles have evolved into high–potential products used in environmental protection, the pharmaceutical industry, as antibacterial agents, in cancer therapies, and medical imaging. The discovery and the development of silver nanoparticle synthesis methods have advanced in parallel with a deeper understanding of their properties. A pivotal moment in nanotechnology was the identification of the unique behavior of materials at extremely small dimensions, particularly the distinctive physical and chemical effects that arise at the nanoscale—such as optical, magnetic, and electrical properties that differ significantly from those of conventional materials. These unique traits stem from the high surface–to–volume ratio, which enhances their reactivity. Researchers in materials science and chemistry have demonstrated that silver nanoparticles possess significantly greater antimicrobial activity than silver in bulk forms such as powder or foil, due to their extremely small size and large specific surface area. Therefore, future research must focus on the development of simple, efficient, and environmentally friendly methods to facilitate the recovery of nanoparticles while minimizing the risks associated with unsafe synthesis techniques.

It is essential to continuously improve the synthesis processes of silver nanoparticles to prevent the formation of hazardous by–products if not properly managed. The synthesis of silver nanoparticles can be achieved through various methods, including chemical reduction (using organic and inorganic reducing agents), electrochemical techniques, physicochemical reduction, radiolysis, laser ablation, microwave irradiation, as well as sonoelectrochemical and sonochemical reduction [17,32].

2. STUDY OF THE PROBLEM

Silver nanoparticles are increasingly used in the pharmaceutical industry, with their shape and size being largely dependent on the synthesis technology employed. However, the absence of a clear correlation between reaction parameters and particle morphology remains a significant challenge. An integrated strategy is essential for the efficient use of resources. The broad applicability of silver nanoparticles stems directly from their unique physicochemical properties, particularly their nanoscale behavior and surface plasmon resonance phenomena. Due to their small dimensions, high specific surface area, and interaction with light, they hold great promise for applications in medicine, the food industry, sensing, water purification, textiles, electronics, and catalysis. Their optical, electrical, catalytic, and antimicrobial properties are strongly influenced by the synthesis method, which determines their shape, size, and surface morphology.

Based on these considerations, the present article aims to provide a review–style analysis of the antibacterial properties of silver nanoparticles, highlighting the most relevant international research, alongside a description of synthesis methods tailored to achieve specific nanoparticle characteristics—such as size, shape, stability, and biological or catalytic activity. To achieve these specific characteristics, the synthesis of silver nanoparticles is primarily based on two main approaches: the top–down and bottom–up strategies.

- The top–down approach involves the fragmentation of a bulk material or substance into smaller particles.
- In contrast, the bottom–up approach relies on the assembly of organic and inorganic structures atom by atom, molecule by molecule, or cluster by cluster [34].

The growth of a cluster requires a specific amount of energy at a well–defined size, enabling atoms to diffuse within the solution and be captured on its surface. Typical anisotropic shapes are formed in the presence of a stabilizing polymer, which preferentially binds to one of the crystal facets more rapidly than to the others [44].

In chemical processes, a strong reducing agent is initially employed to obtain small particles, followed by the use of a weaker reducing agent (or the same one) to promote particle growth. The synthesis of metallic nanoparticles, which are among the most relevant, involves the reduction of the corresponding metal cation. Reducing agents such as glucose, ethylene glycol, hydrazine hydrate, and sodium citrate [27] can be used, along with more eco–friendly approaches like ultrasonic irradiation [45], sodium borohydride in the presence of sodium citrate (Na_3Cit) at room temperature [51], or hydroxylamine.

Typically, the second selectively added reducing agent accounts for approximately one mole ±5% per mole of silver to be reduced; however, when sodium formate is used as the second reducing agent, at least two moles are required. In general, controlled particle size can be achieved by adjusting reaction parameters. Indeed, the chemical synthesis of metallic nanocrystals is influenced by a range of thermodynamic and kinetic factors, and a major challenge lies in capturing the distinct stages of nucleation and crystal growth. Moreover, it is difficult to define a precise quantitative function that accurately describes the relationship between synthesis conditions and final particle size. Thus, achieving both qualitative and quantitative control over the synthesis of silver nanoparticles remains a significant challenge. The synthesis process has been widely studied to gain control over its kinetics. Ensuring optimal conditions for each synthesis method has a significant impact on the composition, structure, and size of the nanoparticles, directly affecting their properties. A comparison between the homogeneous matrix of nanoparticles and that of metal ions reveals substantial differences in their physical, chemical, and biological characteristics [28, 29].

Silver nanoparticles are smaller than the wavelength of light, and their color is determined by their interaction with light, a phenomenon known as Surface Plasmon Resonance (SPR). The free electrons on the surface of metals such as silver or gold oscillate collectively and are referred to as plasmons. These electrons oscillate (similar to the vibration of a solid body under the action of an external force) in synchrony with light, both as a wave and as particles, transferring energy to the electrons on the surface of the metal particles. When the energy of the photon matches the energy required to excite the electrons to their natural frequency of oscillation (i.e., the plasmon resonance frequency), the electrons become excited and begin to oscillate collectively, generating the phenomenon known as surface plasmon resonance.

As the frequency of the incident light coincides with the natural frequency of the electron oscillations on the surface of the nanoparticles, the absorption and scattering of light reach a maximum. At this point, the light is absorbed more efficiently by the nanoparticle at a specific frequency, which depends on the size and shape of the nanoparticles. Therefore, spherical, cubic nanoparticles, or nanorods exhibit different optical effects. The concentration and aggregation of nanoparticles can modify the plasmonic resonance effect and influence the intensity of the color. Variations in the distance between silver nanoparticles lead to changes in color. [47]

Optical properties are determined by plasmon resonances, with plasmons being collective excitations of free electrons in a conductive material, manifesting as quantized oscillations of the electron plasma. At optical frequencies, plasmons can interact with photons to form a mixed state known as a plasmon polariton, exhibiting properties of both entities. Plasmonics is associated with the localization, guiding, and manipulation of electromagnetic waves at the nanoscale, surpassing the diffraction limit and opening up new possibilities for manipulating electromagnetic waves in the field of nanotechnology.

In Figure 1.a, it is observed that the nanostructure is smaller than the wavelength of light, and free electrons can be displaced from the network of positive ions (which consist of nuclei and core electrons) and oscillate collectively in resonance with the light, generating localized surface plasmon resonance (LSPR).

In Figure 1.b, the nanostructure is much larger than the wavelength of light. In this case, light coupled to the nanostructure excites the free electrons, creating a propagating surface plasmon (PSP), which can move along the surface of the metallic nanostructure [47].

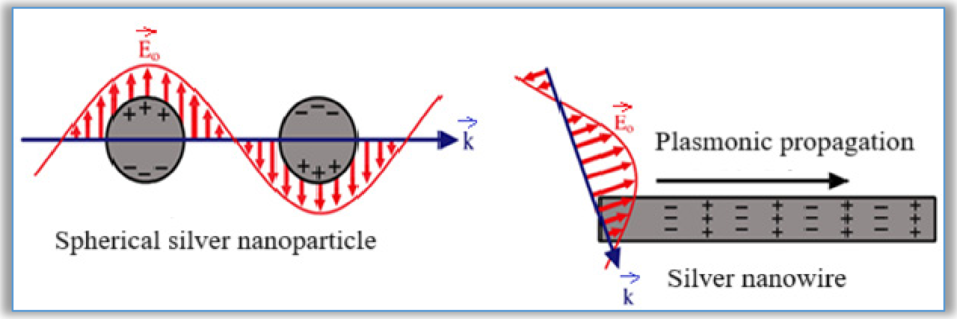

Figure 1. Schematic illustration of two types of plasmonic nanostructures excited by the electric field vector (E_0) of the incident light, with the wave vector (k)

Surface plasmon resonance is used in a wide range of fields, including biomedicine (e.g., for molecular imaging or biological marker testing), sensor technology (for detecting chemical or biological substances), as well as in the electronics industry and catalysis technologies. Silver nanoparticles have been extensively studied due to the surface plasmon resonance phenomenon and their optical and electronic properties, thus opening new opportunities for the development of new technologies.

3. MEDICAL APPLICATIONS, METHODS OF SYNTHESIZING AND THE NECESSARY PROPERTIES OF THE SILVER NANOPARTICLES

The remarkable antimicrobial, antifungal, and anti–inflammatory properties of silver nanoparticles have made them a central focus in biomedical research in recent decades. Their nanometric size enables them to interact effectively with cellular and bacterial structures, significantly enhancing their therapeutic efficacy compared to traditional forms of silver. In this context, silver nanoparticles are successfully used in a variety of medical applications: from wound care products, antibacterial coatings for implantable medical devices, to therapies against antibiotic–resistant infections, controlled drug delivery systems, and advanced medical imaging. In addition to these applications, the physicochemical characteristics of NpAg, such as biocompatibility, high specific surface area, and cellular penetration ability, make them versatile therapeutic agents. To effectively fulfill their antibacterial role, nanoparticles must possess a set of essential structural and functional properties that determine their biological activity and interaction with microorganisms. The formation of silver nanoparticles involves complex physical phenomena occurring at the micrometric or nanometric scale. These phenomena are influenced by chemical and electrochemical processes, as well as by physical interactions between ions, molecules, and surfaces. The physical properties of nanomaterials (NM) depend on the size, shape, color, and morphology of the particles, which in turn affect the size, crystal structure, lattice parameters, and morphology. [4,38,46]

In the context of biomedical applications, the choice of synthesis method for silver nanoparticles is crucial. The method must ensure controllable sizes, colloidal stability, biocompatibility, and a high degree of purity, avoiding toxic contaminants or harmful by–products. Some methods generate silver nanoparticles that meet the requirements for use in various fields, including medical applications. The synthesis of silver nanoparticles (AgNP) with antibacterial activity is carried out through various methods, generally classified into three main categories: chemical methods (involving the reduction of silver compounds using chemical agents, allowing control over the size and shape of the nanoparticles), physical methods (providing an alternative without the use of chemicals), and biological methods (using living organisms or natural extracts to produce AgNP in an eco–friendly manner). Each of these approaches presents advantages and disadvantages in terms of cost, control over size and shape, product purity, and environmental impact. [37]

— CHEMICAL METHODS: are the most commonly used for the large–scale synthesis of AgNPs. They involve the reduction of silver ions (Ag^+) to silver atoms (Ag^0) in a chemical solution, followed by nucleation and growth of the nanoparticles. A stabilizing agent is often used to prevent agglomeration and control the particle size.
— PHYSICAL METHODS: do not involve chemical reactions and, generally, do not use chemical reducing agents.
— BIOLOGICAL METHODS: utilize living organisms (bacteria, fungi, algae, plants) or their extracts to reduce silver ions and stabilize the nanoparticles. They are considered eco–friendly, non–toxic, and potentially less costly. For example, one study investigates the activity of AgNPs against Pseudomonas aeruginosa, a pathogen known for its resistance to multiple drugs, highlighting the relevance of AgNPs as alternative antimicrobial agents that act through interconnected mechanisms. The mechanisms by which silver nanoparticles act include adhesion to the bacterial cell surface, membrane disruption, penetration into the cell, and interference with vital components. Additionally, AgNPs induce oxidative stress by generating ROS and interfere with essential bacterial enzymatic functions. Ongoing research focuses on understanding the precise mechanisms and optimizing the safe and effective use of these nanoparticles. [7,31]

Each method has its own advantages and disadvantages in terms of controlling the size and shape of nanoparticles, cost, yield, and environmental impact. The choice of method depends on the specific application of the antibacterial silver nanoparticles.

In medical applications, it is essential that nanoparticles are compatible with human cells without generating toxic effects on healthy tissues. The surface properties and degree of functionalization of AgNPs influence the cellular uptake rate, local immunity, and bioavailability, which are critical factors for clinical applications.

The properties of AgNPs influence their antimicrobial efficiency and medical applicability. The ideal size (1–100nm, optimal under 20nm) provides a large surface area for interaction and cellular penetration. The shape (spherical, triangular, etc.) affects adherence to bacterial cells. Colloidal stability, ensured by stabilizing agents, prevents aggregation. Controlled release of silver ions (Ag^+) is crucial for antimicrobial action. Optical properties (color) indicate stability. Biocompatibility and controlled toxicity are essential for medical applications. [1,37]

CHEMICAL METHODS

— Chemical Reduction

In this type of process, reactions occur in solution, and the result is a product with colloidal properties, such as heterogeneous nature (dispersed phase and dispersion medium) or stability (the particles are in motion and do not settle at the bottom of the container). Some of the chemical reduction methods for silver, aimed at nanoparticle formation, are described below.

≡ Polyol Synthesis

The polyol synthesis process can provide better control over the size and morphology of silver nanoparticles, as the temperature and concentration of precursors can directly influence their characteristics. This method is relatively simple and efficient in obtaining silver nanoparticles, with a high production yield. Polyols such as ethylene glycol can stabilize silver nanoparticles, preventing agglomeration and loss of efficiency in various applications.

From one method results in silver nanoparticles with varying shapes and sizes. Polyol synthesis involves reducing a metal salt precursor with a polyol, typically ethylene glycol, 1,2–propylene glycol, or 1,5–pentanediol, at high temperatures (110–160°C). The most common protective, capturing, and coating agents are polymeric compounds such as poly(vinyl alcohol, PVA), poly(vinylpyrrolidone, PVP), and poly(ethylene glycol).

Temperature is a particularly important factor for reducing agents, influencing nucleation and growth processes. For example, ethylene glycol can serve both as a solvent and as a reducing agent. However, it is assumed that if the reducing agent and the coating agent are different, better control over the particle size distribution and geometric arrangement can be achieved. Using the typical synthesis with ethylene glycol results in single and aggregated crystals. Certain conditions that favor rapid nucleation and growth (a concentration of 0.125–0.25M $AgNO_3$) and the PVP/Ag+ ratio (=1.5) lead to the formation of nanocubes. When the concentration of 0.085M $AgNO_3$ is reduced with the same PVP/Ag+ ratio, the resulting particles are nanorods [36].

In the polyol method with ethylene glycol, the primary reducing agent is, in the first phase, actually glycolaldehyde, a stronger reducing agent formed in the presence of oxygen when ethylene glycol is heated, and which is immediately consumed. However, it has a decisive influence on the nucleation and growth kinetics, as well as on the shape and distribution of the particles [47] – a process synthetically outlined in reaction (1).

$$2HOCH_2CH_2OH + O_2 \rightarrow 2HOCH_2CHO + 2H_2O \quad (1)$$

There are two methods for the synthesis of silver nanoparticles, depending on the precursor temperature. The difference between the two methods lies in the way the silver nanoparticles are reduced and nucleated: gradual (when the precursor was heated in solution) or rapid (when the precursor was injected into a hot solution). In the second case, the nanoparticle sizes are smaller [19].

In the Polyol process, temperature is very important. A temperature difference of a few degrees can influence the reaction, the explanation coming with the discovery of the presence of glycolaldehyde in the reaction. Initially, small groups of silver atoms with a fluctuating structure are formed, and their stability increases as the cluster grows, tending towards a unique predominant shape, usually pentagonal wires, straight bipyramids, and cubes, although nanoparticles with other geometric shapes can also form – Figure 2. To induce rapid nucleation over a short period and achieve a smaller size distribution, injecting the precursor solution into a hot solution is an effective means.

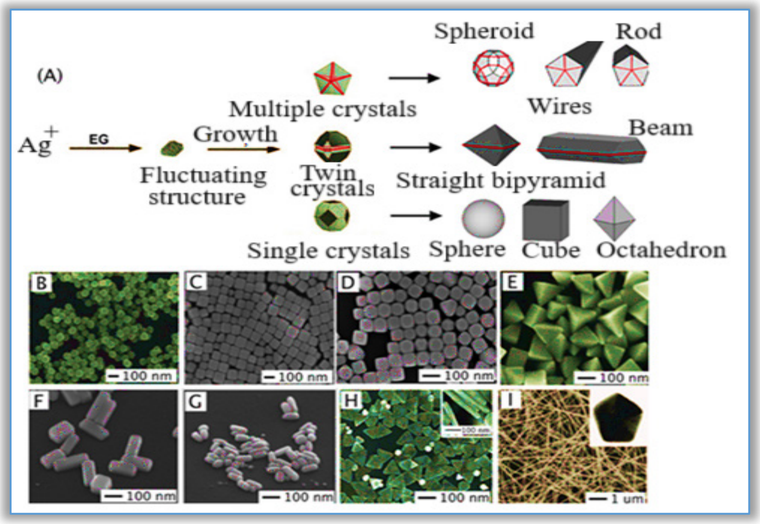

Figure 2. Clusters of Ag atoms are typically referred to as seeds, which will eventually grow into nanostructures with different shapes, such as: (B) spheres, (C) cubes, (D) truncated cubes, (E) regular bipyramids, (F) rods, (G) spheroids, (H) triangular plates, and (I) wires [27] .

The Polyol method is effective in the controlled synthesis of silver nanoparticles, offering precision in adjusting their size, shape, and distribution. Polyols, such as ethylene glycol, act both as reducing agents and stabilizers, resulting in colloidally stable nanoparticles with well–defined morphology, ideal for biomedical applications. The versatility of the method is due to the influence of reaction parameters, especially temperature and the type of reducing agent, making it suitable for syntheses with high antibacterial functionality.

≡ Reduction with Saccharides

In the chemical synthesis of nanoparticles, growth inhibitors are used to prevent metallic agglomeration, and studies analyze the influence of silver precursor concentrations, the reducing agent, and stabilizing/coating agents, as well as the choice of environmentally friendly solvents. In the context of environmental regulations, less harmful methods are promoted, and the chemical reduction of silver with polysaccharides (glucose, fructose, maltose, dextrose, sugar) is considered a viable approach in green synthesis, as polysaccharides act as both reducing and stabilizing agents.
An ecological method for synthesizing nanoparticles involves reduction with glucose and gelatin (a protein from collagen, with a triple–chain helical structure where individual helical chains are centered in a super–helix around the common molecular axis) [15], which induces surface stabilization by modifying interface properties and creating a steric barrier, functioning as a stabilizing agent in suspensions and emulsions [30].
To obtain the suspension, $AgNO_3$ at a concentration of 0.001mol/dm³ and gelatin in a 2:1 ratio were continuously mixed in a water bath, respectively under magnetic stirring. For 50dm³ of $AgNO_3$ and 25ml of gelatin, 25cm³ of aqueous glucose solution were used. Sodium carbonate, 0.1M, was used to adjust the pH, playing an important role in the process. The working temperature was 70–80°C; an increase within this range led to the formation of smaller particles due to the intensification of chemical reduction, increased glucose activity and ion mobility, as well as better suspension stability, reflected in the increase of the electrokinetic potential [42].
In a similar process, using glucose reduction and gelatin as a stabilizer, NaOH served as a reaction accelerator. The silver nanoparticles obtained had a cubic shape with dimensions smaller than 20nm [8].

Another method for obtaining silver nanoparticles involves the reduction of silver nitrate in the presence of two reducing agents: ethylene glycol and glucose, with the use of PVP as a stabilizer. The study showed that the obtained nanoparticles had a spherical shape and a smooth morphology, exhibiting a more efficient antibacterial effect compared to synthesis carried out exclusively with ethylene glycol [25].

Silver nanoparticles were also synthesized with $AgNO_3$ as a precursor and monosaccharides such as ribose, fructose, sorbose, glucose, xylose, and galactose in a household microwave oven. The reaction took place within a very short time frame of a few seconds. These nanoparticles demonstrated an inhibitory effect on Gram–positive bacteria [22,41].

An entirely ecological method is the synthesis of silver nanoparticles with dextrose and maltose, using gelatin as a stabilizer. Dextrose proved to be a better reducing agent than maltose. The reactions pertaining to the processes are presented below [33]:

–Formation of the gelatin–silver complex ion:

$$Ag^{+}_{(aq)} + gelatin_{(aq)} \rightarrow [Ag(gelatin)]^{+}_{(aq)} \quad (2)$$

$$C_{12}H_{22}O_{11(aq)} + gelatin \rightarrow C_6H_{12}O_{6(aq)} \equiv 2C_6H_{11}O_5\text{–}CHO_{(aq)} \quad (3)$$

The reaction takes place in the presence of water:

$$2[Ag(gelatin)]^{+}_{aq} + 2C_5H_{11}O_{5(aq)} - CHO_{(aq)} \rightarrow Ag - NP(s)\text{covered by gelatin} + 2C_5H_{11}O_5 - COOH_{(aq)} \quad (4)$$

–Reduction relations and standard reduction potentials of Ag^{+} with glucose under standard conditions:

$$2Ag^{+} + 2e^{-} \rightarrow 2Ag^{0} \qquad E^{0}_{reduction} = 0{,}800V... \quad (5)$$

$$C_6H_{12}O_6 + H_2O \rightarrow C_6H_{12}O_7 + 2H^{+} + 2e^{-} \qquad E^{0}_{oxidare} = -0{,}050V... \quad (6)$$

$$2Ag^{+} + C_6H_{12}O_6 + H_2O \rightarrow 2Ag^{0} + C_6H_{12}O_7 + 2H^{+} + 2e^{-} \qquad E^{0} = 0{,}750V... \quad (7)$$

where, E_0 represents the sum of the reduction potential, $E^{0}_{reduction}$ and oxidation $E^{0}_{oxidation}$

–Reduction relations and standard reduction potentials of Ag^{+} with glucose in the presence of ammonia:

$$2Ag(NH_3)_2^{+} + 2e^{-} \rightarrow 2Ag^{0} + 2NH_3 \qquad E^{0}_{reduction} = 0{,}373V... \quad (8)$$

$$C_6H_{12}O_6 + H_2O \rightarrow C_6H_{12}O_7 + 2H^{+} + 2e^{-} \qquad E^{0}_{oxidation} = -0{,}600V... \quad (9)$$

$$2Ag(NH_3)_2^{+} + C_6H_{12}O_6 + H_2O \rightarrow 2Ag^{0} + C_6H_{12}O_7 + 2NH_4 \quad E^{0} = 0{,}973V \quad (10)$$

where E_0 represents the sum of the reduction potential, $E^{0}_{reduction}$ and oxidation $E^{0}_{oxidation}$

In the case of using white sugar, a simple and inexpensive method, without high energy consumption, has been developed that can be used on an industrial scale in the presence of NaOH and light [33].

Starch, a polysaccharide composed of amylose and amylopectin, treated with NaOH (20g/l) at a pH ≈12, can function as both a reducing and a stabilizing agent for the synthesis of silver nanoparticles. The process takes place in two stages: the formation of silver atoms and their polymerization. In the absence of polymerization, the particles would continue to grow, and their aggregation would not be prevented. In this case, the nanoparticles have a spherical shape, with dimensions between 2–30nm [12].

The synthesis methods for silver nanoparticles using natural reducing agents such as saccharides and starch offer ecological and efficient solutions for obtaining nanoparticles with applications in various fields, including medical ones. The use of these agents allows for the control of particle size and shape, representing a promising alternative to traditional methods involving toxic chemicals. However, to maximize the potential of these processes, rigorous control of the reaction conditions and the stabilizers used is necessary. [39]

≡ Tollens' reagent

Tollens' reagent, $[Ag(NH_3)_2]OH$, is a mild oxidizing agent used for the identification of aldehydes, which are oxidized to carboxylic acids, with the silver being reduced to its metallic form (silver

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mirror). In aqueous solutions of glucose and starch with $AgNO_3$ as a precursor, Tollens' reagent reduces $Ag(NH_3)_2^+$ to silver nanoparticles (50–200nm), generating colloidal hydrosols with particles of 20–50nm in various shapes.

Reduction with HTAB (n–hexadecyltrimethylammonium bromide) produces nanoparticles in the shape of cubes, triangles, or aligned wires. Their size is influenced by the ammonia concentration and the nature of the reducing agent, due to the stability of the $Ag(NH_3)_2^+$ complex. The smallest particles were obtained at low ammonia concentrations ($\log\beta_1 = 3.367$, $\log\beta_2 = 7.251$) [40,48].

For the preparation of Tollens' reagent under ordinary laboratory conditions, a solution of $AgNO_3$, NaOH şi NH_3:

$$AgNO_3 + NaOH = AgOH + NaNO_3 \tag{11}$$

$$AgOH + NH_3 = [Ag(NH_3)_2]OH \tag{12}$$

For the separation of Ag, the classic preparation conditions of Tollens' reagent must be followed, the reactions considered being those with an aldehyde (13, 14) and respectively with glucose, for its oxidation to gluconic acid (4.14).

Generally for aldehydes:

$$RCHO + 2[Ag(NH_3)_2]^+ + 2OH^- \rightarrow RCOOH + 2Ag + 4NH_3 + H_2O \tag{13}$$

For formaldehyde, the reaction is:

$$CH_3CHO + [Ag(NH_3)_2]OH = CH_3COOH + 2Ag + 4NH_3 + H_2O \tag{14}$$

In the case of glucose:

$$C_6H_{12}O_6 + 2[Ag(NH_3)_2]OH = C_6H_{12}O_7 + 2Ag + 4NH_3 + H_2O \tag{15}$$

With the increasingly wide applications of silver in industry, obtaining very fine and uniformly distributed particles is desirable. The reducing potential of formaldehyde depends on pH. The stoichiometric reaction between the silver ion and formaldehyde is given by the relations:

$$2Ag^+ + HCOO + 3OH^- \rightarrow 2Ag + HCOOH^- + 2H_2O \tag{16}$$

$$2Ag^+ + HCHO + OH^- \rightarrow Ag + HCOOH + 1/2H_2 \tag{17}$$

A relative ratio of 4:1 is sufficient for all Ag ions from a 0.01M $AgNO_3$ solution to be reduced in the solution. At a pH<5, with a $[NaOH]/[AgNO_3]$ ratio of 1, the reducing agent capacity of formaldehyde is very weak, but upon the addition of an additional amount of Na_2CO_3 in the same ratio as $AgNO_3$, the pH was greater than 7. The increased degree of conversion showed the importance of alkalinity in this type of process, but the particle sizes increased, while simultaneously decreasing the yield of the coating agents PVA and PVP [5].

A characteristic of this synthesis of metallic particles is that a change in absorption or wavelength provides a measure of the particle size, geometric distribution, and the interaction between particles. Silver nanoparticles obtained by the reduction of Tollens' reagent have significant importance in the antibacterial field, due to their ability to effectively destroy bacteria through direct interaction with cell membranes, thus preventing their proliferation.

≡ The Citrate Anion

Silver citrate has a white color and is sparingly soluble in water, but dissolution can occur in citric acid solutions due to the formation of the silver citrate complex with the formula $[Ag_3(C_6H_5O_7)_{n+1}]^{3n-}$

From the beginning of studies related to the citrate anion, it has been known that it acts both as a reducing agent, by reducing metal ions and as a complexing agent, and as a stabilizer by attaching to the surface of metal particles, and the reactants play a special role in the size and geometric distribution of the particles, forming a barrier around them, thus avoiding agglomeration.

The reducing agent capacity of citrate is low compared to that of borohydride and/or L–ascorbic acid used in the same system, concurrently with a reduction in particle stability compared to other coating agents, such as bis(2–ethylhexyl)sulfosuccinate (AOT) and thiols. The processes take place at fairly high temperatures (100°C) to maximize the monodispersity of the particles. Kinetic analysis shows that the molar ratio between citric acid or sodium citrate and silver ions influences the reaction rate, respectively the growth of particle sizes. In the interaction between the silver surface and the citrate ion, a slow cluster growth occurs, making this process unique compared to other chemical and radiolytic synthesis methods [20,36].

Under normal physicochemical conditions for the production of silver citrate, the following methods can be used:

— Sodium Citrate Method

$$(Na_3C_6H_5O_7): AgNO_3 + Na_3C_6H_5O_7 \rightarrow Ag_3C_6H_5O_7\downarrow + NaNO_3 \quad (18)$$

The method using sodium hydroxide (NaOH), when very pure silver citrate can be obtained under specific filtration and washing conditions:

$$2AgNO_3 + 2NaOH \rightarrow Ag_2O\downarrow + 2NaNO_3 + H_2O \quad (19)$$

$$3Ag_2O\downarrow + 3H_3C_6H_5O_7 \rightarrow b\ 2Ag_3C_6H_5O_7\downarrow + 3H_2O \quad (20)$$

— Ammonium Hydroxide Method (NH_4OH):

$$AgNO_3 + 3NH_4OH \rightarrow [Ag(NH_3)_2]OH + NH_4NO_3 + 2H_2O \quad (21)$$

$$[Ag(NH_3)_2]OH + 2H_3C_6H_5O_7 \rightarrow Ag_3C_6H_5O_7\downarrow + (NH_4)_3C_6H_5H_5O_7 + 3NH_4OH \quad (22)$$

In the latter method, filtrations and washings are also necessary due to the high water solubility of the by–products. To increase the amount of silver citrate, it is necessary to raise the concentration of citric acid. The maximum concentration of Ag(I) in solution is estimated at 23–25g/L for a citric acid concentration of at least 4mol/L. The dissolution of silver citrate in citric acid solutions is attributed to the formation of silver citrate complexes with the general formula $[Ag_3C_6H_5O_7]_n \cdot nH_2O$, which exhibit good stability [9].

It has been observed that pH plays a significant role in determining the shape, size, and crystallinity of the particles through its effect on the distribution of citrate species. Experimental conditions consider a pH range between 1.6 and 5.17, with the latter yielding particles with the most favorable properties [23].

The reduction of the anion involves reducing a silver source particle, typically $AgNO_3$ sau $AgClO_4$, to colloidal silver using trisodium citrate, $Na_3C_6H_5O_7$ with the traditional citrate ion acting as a complexing agent, reducing agent, and capping ligand. The process of producing silver nanoparticles is, in this case, relatively simple, with a short reaction time, sometimes only 20 minutes. Other methods for the chemical reduction of silver include sodium borohydride ($NaBH_4$), hydroquinone, gallic acid, or seed–mediated growth, with combined methods being increasingly used recently.

In conclusion, the utilization of silver citrate as a reducing and complexing agent presents multiple advantages, including a simple and relatively rapid synthesis process for silver nanoparticles, with good control over particle size and shape depending on the reaction conditions, such as pH and citric acid concentration. Although citrate has a lower reducing capacity compared to other agents like sodium borohydride or L–ascorbic acid, it contributes to the stabilization of the particles, preventing agglomeration. Furthermore, the method is environmentally friendly and safe, suitable for applications in the medical field due to its biocompatibility and efficiency. However, rigorous control of the experimental conditions is necessary to ensure the stability and uniformity of the obtained nanoparticles.

— Electrochemical Methods

Electrochemical methods involve the dissolution of a silver metal anode in an aprotic solvent, without dissociable hydrogen, to produce spherical silver nanoparticles. The traditional synthesis of silver nanoparticles using wet chemical and biochemical methods involves high costs, the use of flammable and environmentally toxic substances, as well as adverse reactions in medical applications. Electrochemical techniques are more economically viable and easier to implement, with better process control.

In classical electrochemical methods, the salt of a metal is reduced at the cathode, and the metal ions are transformed into nanoparticles through a "bottom–up" particle growth mechanism, with their stability ensured by stabilizing and coating agents. In a "top–down" particle growth approach, Ag+ ions were obtained from a pure metal anode, as Ag was anodically dissolved, resulting in intermediate Ag+ ions that were reduced by the negative cathode made of the same metal. This yielded a colloidal solution of silver nanoparticles stable by a negative Zeta (ζ) potential—the potential difference between the dispersion medium and the stationary layer of fluid attached to the dispersed particle, a key indicator of the stability of colloidal dispersions. This potential ensures the appearance of mutual repulsive forces between similar charges, thus stabilizing the colloidal sol by separating the particles and preventing agglomeration. A Zeta potential that ensures ideal stability is ±61mV, but a value of at least ±40mV indicates good stability.

The main advantage of this method is the particularly high purity of the particles, as no other substances are used in the synthesis except pure metallic silver and deionized water. For the refinement of the method, more in–depth studies are needed, taking into account parameters such as [14]: current density, responsible for the electrochemical process and control over particle sizes; temperature; purity, size, and shape of the electrodes.

Using electrochemical methods, which are based on the dissolution of a metallic anode in an aprotic solvent (one that does not contain dissociable hydrogen), spherical silver nanoparticles with sizes between 2–20nm were obtained, stable without any stabilizing agent, having a long lifespan in aqueous solution suspensions and as silver powders. The influence of various electrochemical parameters on the size of the nanoparticles was studied by using different types of counter–electrodes, as well as the effect of the presence of oxygen in the reaction medium [24].

In Romania, the study of nanoparticle synthesis from colloidal silver solutions using electrochemical methods was carried out using the "sacrificial anode" technique, employing a mixture of biocompatible ionic and non–ionic surfactant stabilizing and co–stabilizing agents, PVP (non–ionic), and sodium lauryl sulfate, a synthetic organic compound with the formula $CH_3(CH_2)_{11}SO_4Na$ (Na–LS, anionic). The dimensions of the obtained particles were 10–20nm. The value of the negative Zeta potential, ranging from (–17mV, –30mV), indicates the existence of a stable colloidal system with particles coated in PVP. The research utilized a pulsed current generator with alternating polarity and a stirrer, and the silver electrodes, with dimensions of 105×30mm and a purity of almost 100%, were immersed in deionized water as the dispersion medium (electrical conductivity less than $1\mu Scm^{-1}$). The applied current was 5–10mA for 3–7 hours [10].

Considering the stability and controllable dimensions obtained by the electrochemical method, the nanoparticles find applications in a wide range of fields such as inkjet printing, surface–enhanced Raman scattering, photography, catalysis, imaging, photonics, or optoelectronics.

PHYSICAL METHODS

A direct method for obtaining silver nanostructures is the controlled laser irradiation (single or dual beam excitation) of colloidal silver in the presence of appropriate chemical species, resulting in nanoparticles with a clear and predictable shape and structure.

Controlled laser irradiation refers to the use of a laser beam to excite colloidal silver particles in a solution, under the influence of precise control of parameters such as the wavelength and intensity of the excitation source. In laser irradiation, the wavelength of the excitation source and the type of capping agent play an important role in controlling the shape. When the pulsed laser focuses on the surface of a solid, nanostructuring of the substance occurs, accompanied by a series of effects: heating, melting, and laser ablation, which involves the removal of material from a solid (less often, liquid) surface by irradiation with a laser beam. Cluster growth depends on several factors, including the energy and angular distribution of photons, the initial density of the material, and their interaction with the medium in which the laser irradiation process takes place. The energy of the

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photons is capable of producing nucleation centers, in order to modify the growth dynamics of the nuclei and alter the diffusion of species in the vapor phase.

The properties of the formed nanostructures are unique and irreproducible by any other route and do not have the residual toxicity of chemical synthesis methods. For obtaining nanoparticles in aqueous solutions, chemical reducing agents that would condition the unique surface chemistry and purity of the nanomaterials produced are not necessary [13].

Using the light–mediated growth method in aqueous solution, silver nanoparticles with tetrahedral shapes were synthesized under the effect of tartrate and citrate as structural directing reagents in the corresponding stages of the reaction. In addition, nanocrystals can be assembled by electrostatic interaction to generate strong localized electromagnetic fields for surface–enhanced Raman scattering (SERS) studies. This new type of nanocrystals can find applications in surface–enhanced spectroscopy and plasmonic field enhancement [52]

The realization of anisotropic nanostructures by photochemical conversion, transforming silver nanospheres into triangular prisms, is an eloquent example of control over the shape of the synthesized particles [21].

The stability of nanoparticles is essential, and in the case of silver nanoparticles synthesized by ultraviolet irradiation in an aqueous solution of $[Ag(NH_3)_2]^+$, stability was confirmed by the presence of plasmon absorption at 420nm, having a durability of 6 months at a temperature of 25°C [52].

Light–assisted methods for obtaining silver nanoparticles are innovative, rapid, and environmentally friendly technologies that allow the controlled synthesis of nanoparticles with excellent antibacterial properties. In addition, the absence of toxic reagents and the possibility of obtaining specific shapes make them ideal for biomedical and optoelectronic applications.

BIOLOGICAL METHODS

Biological methods, also known as “green” methods, represent a significant ecological alternative to conventional chemical and physical procedures for obtaining silver nanoparticles (AgNPs). These innovative approaches harness the capabilities of living organisms, such as bacteria and fungi, or utilize extracts from various plant sources to achieve the reduction of silver ions (Ag^+) to their metallic state (Ag^0) and to ensure the stabilization of the resulting nanoparticles. By their nature, these methods are distinguished by a reduced impact on the environment, aligning with the principles of sustainability in nanotechnology.

It is important to emphasize that the fundamental properties of silver nanoparticles are intrinsically linked to the specific conditions of the synthesis process. Factors such as the type of method used, the reaction temperature, the pH value, the concentration of the silver precursor, the nature of the reducing agents, and the stabilizing agents play a crucial role in determining the final characteristics of the nanoparticles. In this context, green synthesis has gained considerable attention in the scientific community, being recognized as an effective alternative strategy for obtaining silver nanoparticles with diverse morphologies, thus meeting the specific requirements of different antibacterial applications. Green synthesis methods, such as viral–bio–template synthesis using TMV (Tobacco mosaic virus), have attracted particular attention, being used in the synthesis of 1D silver nanometric structures. [35,49,50]

— Synthesis with Plant Extracts

The use of plants for the synthesis of silver nanoparticles is one of the most popular green synthesis methods. This involves utilizing plant extracts that contain organic compounds such as flavonoids, alkaloids, and terpenoids, which act as reducing and stabilizing agents for silver ions. Plants are easily accessible and have a low cost, thus being an excellent source of raw materials for nanoparticle production. Furthermore, plant extracts are often rich in antioxidants that can help maintain the stability of the nanoparticles and prevent their agglomeration. The method is also considered environmentally safe, not involving toxic chemical substances. In many cases,

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nanoparticles obtained through green synthesis using plant extracts have demonstrated significant antibacterial effects and have been used in various medical and environmental protection applications. [6]

— Synthesis with Bacteria

Bacteria have been identified as efficient reducing agents in the synthesis of silver nanoparticles due to their natural ability to reduce metal salts. In this process, bacteria act as microorganisms that transform silver ions into metallic silver through biochemical reduction processes. This method has the advantage of potentially producing nanoparticles with well–controlled sizes and uniform distribution. Bacteria can produce silver nanoparticles with dimensions below 20nm, which gives them a larger surface area and, consequently, increased antibacterial activity. However, the biological process can be more complex and harder to manage than that of plants or other methods, and controlling reaction parameters (such as pH and temperature) is essential for obtaining nanoparticles with the desired characteristics. [2,16].

— Synthesis with Yeasts

Yeasts, like bacteria, are living organisms that can reduce silver salts through biological processes. The use of yeasts for the synthesis of silver nanoparticles has been actively studied due to their ability to reduce silver ions and stabilize the nanoparticles by forming a protective layer on their surface. Yeasts also have the advantage of being obtainable quickly and easily, with a low cost. They can be used in a variety of conditions, and the nanoparticles obtained can be used in biomedical applications, especially in combating bacterial and fungal infections. Research has shown that nanoparticles obtained with the help of yeasts have significant antibacterial activity, being effective against pathogenic bacteria such as *Escherichia coli* and *Staphylococcus aureus* [43].

In conclusion, biological methods are considered more environmentally friendly because they avoid the use of toxic chemical substances and reduce hazardous waste, aligning with the principles of "green chemistry." Silver nanoparticles obtained through these methods can have diverse applications, including in the medical field due to the biocompatibility of the biological materials used.

The green synthesis of silver nanoparticles represents a promising and ecological approach for their production, utilizing natural, easily accessible, and safe agents. Methods based on plant extracts, bacteria, and yeasts have demonstrated significant potential in obtaining nanoparticles with desired characteristics, such as controlled dimensions, high stability, and strong antibacterial effects. These nanoparticles have wide applications in biomedicine and environmental protection, and future research should focus on improving these techniques, optimizing synthesis parameters, and increasing the efficiency of industrial–scale production methods.

4. CONCLUSIONS

As a general conclusion, this article has provided a detailed overview of the various synthesis methodologies for silver nanoparticles (AgNPs), highlighting their essential role as next–generation antibacterial agents. From conventional chemical approaches, through innovative physical methods, to biological (green) syntheses that promise sustainability and biocompatibility, each strategy presents specific advantages and limitations regarding the control of size, morphology, and stability of AgNPs, critical factors that influence their antimicrobial efficacy.

The importance of choosing an appropriate synthesis method, or even the synergistic combination thereof, becomes evident in optimizing the performance of AgNPs for biomedical and technological applications. While chemical and physical methods offer precise control over nanoparticle characteristics, green synthesis stands out for its ecological potential and inherent biocompatibility, addressing concerns related to environmental impact and safety of use.

Ultimately, ongoing research in this field is crucial to overcome current challenges related to scalability, production costs, and long–term stability, thus paving the way for a widespread and responsible use of silver nanoparticles as effective and safe antibacterial agents in diverse applications.

Silver nanoparticles (AgNPs) represent an extremely effective antibacterial agent in combating bacterial infections, including antibiotic–resistant strains, and are being integrated into medical products, textiles, coatings, and biomedical devices. Future research regarding the use of silver nanoparticles as antibacterial agents aims to optimize ecological synthesis methods, precisely control size and shape, functionalize the surface with bioactive molecules, and understand the molecular mechanisms of action. Furthermore, the development of controlled release systems, the evaluation of long–term toxicological risks, and the prevention of bacterial resistance are essential to ensure safe and effective applicability in the medical field. [3,11,18].

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