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An Updated Overview of Nanostructured Silver as a Novel Class of Biomedical Agent

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Abstract: In vitro and in vivo antibacterial activity of silver nanoparticles (AgNPs) against pathogenic bacteria has been demonstrated. Gram (+) and Gram (-) bacteria, including multidrug-resistant species, are susceptible to AgNPs' antibacterial effects. AgNPs have several concurrent mechanisms of action, and they work effectively with other antibacterial agents, such as antibiotics or chemical compounds, against infections like *Esecheria coli* and *Staphylococcus aureus*. Due to their unique characteristics, silver nanoparticles are perfect for use in healthcare and biomedical products where they can successfully treat or prevent infections. AgNPs′ demonstrated genuine properties and significant potential for the development and improvement of novel antimicrobial agents, drug-delivery formulations, identification, detection, and diagnosis platforms, biomaterial and medical device coverings, tissue restoration and regeneration materials, complex healthcare condition schemes and strategies, and performance-enhanced therapeutic alternatives. The purpose of this review was to give a comprehensive discussion of the present state of the art in using the most relevant types of silver nanoparticles as antibacterial agents. This review aims to identify factors influencing the antibacterial impacts of silver nanoparticles and to highlight the benefits of using AgNPs as new antibacterial agents in addition to antibiotics, which will decrease the dosage necessary and avoid secondary effects combined with both. This is due to the need for new, effective, and efficient antibacterial agents.

Keywords: silver nanoparticles; synthesis; antibacterial activity; biomedical application.

1. Introduction

Due to their distinct and genuine physical, chemical, and biological properties, metallic nanoparticles made of noble metals, such as gold and silver, have received much interest and significant research efforts in recent years [1]. Special focus was given to the biological assessment of AgNPs, which sought attention when first developed as potential antibacterial agents. AgNPs have long been employed as antibacterial agents in medical equipment, cosmetics, food storage, and fabric coatings, and some ecological uses have been discovered regarding their toxicology and in vivo biological activity [2]. AgNPs are from a class of zero-dimensional substances with distinctive morphology patterns and dimensions between 1 and 100 nm. These have been indicated to have a higher surface (area-to-volume ratio) and capacity than silver in bulk form. Due to the material's exceptional nanoscale electrical, optical, and catalytic properties, systems for targeted administration of drugs, diagnostics, identification, and imaging have been investigated and developed [3]. Scientists and businesses are most interested in AgNPs because of their exceptional antibacterial activity. AgNPs have been shown to have antibacterial efficacy against a variety of contagious and pathogenic diseases, including bacteria that are multidrug resistant[4].

The following events are believed to contribute to the antimicrobial attributes of nanosilver-based systems, even though the precise anti-pathogenic mechanisms of silver nanoparticles are unknown: (a)damage of microbial membrane or outer covering, which is caused by AgNPs' physicochemically influenced adherence to the cell surface and subsequent functional and structural modifications (such as membrane destabilization, gap formation, cytoplasm spillage, and membrane piercing); and (b) miRNA production. AgNP-based antimicrobial activity's most important mechanistic mechanisms include adherence to microbial cells, the formation of ROS and free radicals, microbial wall penetration and invasion inside the cell membrane, and the control and modification that leads to improving microbial signal-transduction pathways [5,6]. Metallic silver ions are effective antimicrobials on their own, but it is simple to isolate them thanks to proteins, phosphate, chloride actions, and additional biological components [7]. The inherent bactericidal or biostatic activity of AgNPs is significantly influenced by various physicochemical properties, such as shape, size, surface coating, surface charge, and oxidation and dissolution states [8].

To determine how effective biomaterials based on nanosilver are used as antimicrobial agents, research has been conducted on various bacteria, viruses, fungi, yeasts, and other medically important planktonic and sessile pathogenic microorganisms. When developing innovative, performance-improving nanosilver-influenced biomedical goods such as orthopedic materials and gadgets, anticancer drugs, bandages, catheters, antiseptic sprays, and drug delivery systems. AgNPs' exceptional antibacterial activity is a fantastic place to start [13]. AgNPs have exceptional potential in nanotechnology, medical care, and ecological sustainability [14], necessitating improved economical procedures for their synthesis. A rough understanding of the proper physicochemical specificities, in vivo and in vitro impacts, biodistribution, safety monitoring mechanisms, pharmaceutical kinetics, and pharmacodynamics of AgNPs is necessary for advancing nanotechnology based on silver to applications in medicine [15]. These objectives must also be satisfied by creating simple, safe, eco-friendly, and affordable processes for creating silver nanoparticles.

2. Synthesis of Silver Nanoparticles

Silver nanoparticles are not a novel or recent discovery. Some bacteria's biological production of metal-based nanoparticles has been described as a heavy metal detoxification mechanism. Metal-based nanoparticles are often used in the formation of cosmetics and textiles, although the technique's applicability has only been explored lately [16]. Their versatility intrigued The scientific community, which led to a constant search for novel compositions, applications, and synthesis techniques. Numerous synthesis techniques have been developed, including physical, chemical, and, more recently, novel biological strategies [17]. Physical methods are top-down in nature (Figure 1), starting with bulk metal and separating it into successively smaller fragments through mechanical action. Despite being straightforward, this method produces nanoparticles with a relatively uniform size distribution, rendering it undesirable to create metal-based nanoparticles, where size can be a factor in activity [18]. On the contrary, bottom-up methods are used in biological processes that concentrate on green synthesis processes using a variety of microbes, as well as chemical processes that use organic solvents [19].

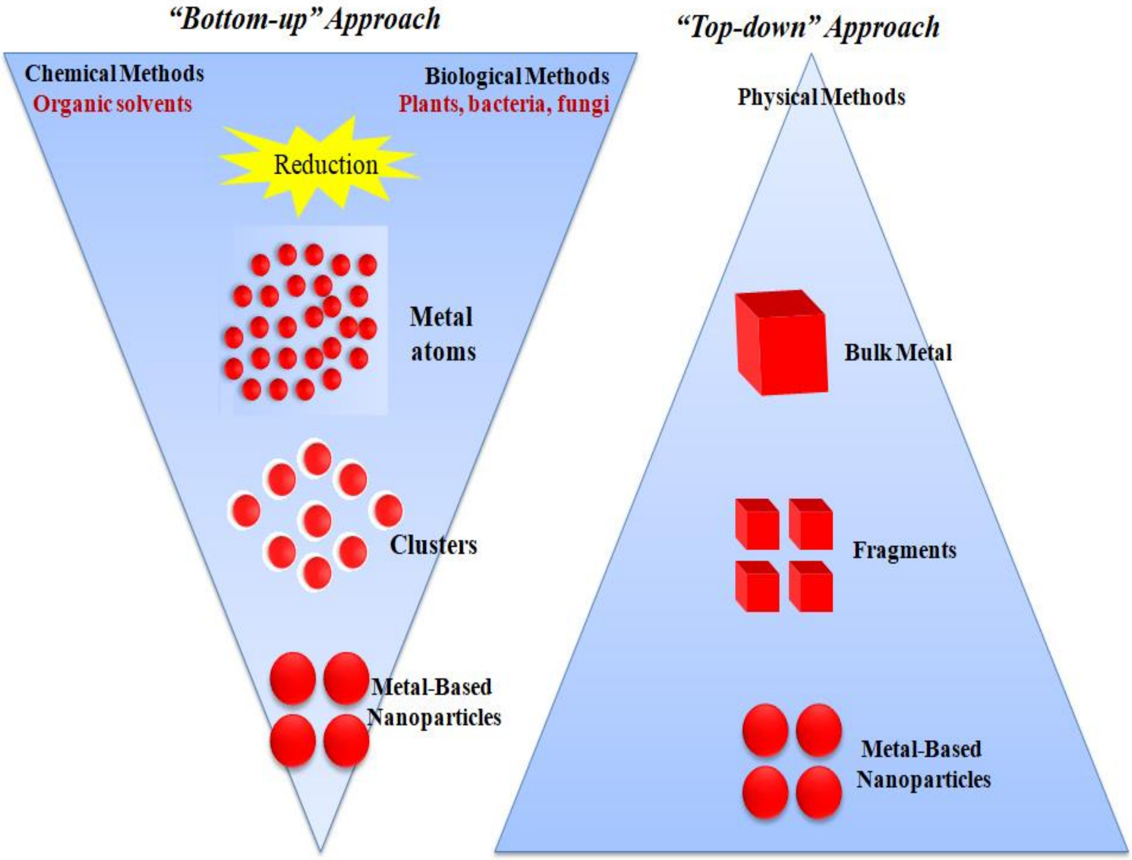

Figure 1. Different methods used for the synthesis of silver nanoparticles.

2.1. Thermolysis methods.

This given procedure completely relies on the disintegration of organ metallic precursors in organic solvents at temperatures typically greater than 100°C under inert gas to prevent surface oxidation of the nanoparticles [20]. Using these reactions for large-scale synthesis is challenging due to their exothermic settings and much-diluted nature. The regulated thermolysis of silver alkyl carboxylates is one method for making silver nanoparticles (AgNPs) even without using organic solvents. The major benefit of the controlled thermolysis technique is that it is very economical for commercial large-scale production [21].

2.2. Chemical reduction methods.

In these processes, a metal precursor dispersed in a solvent is combined with an appropriate reducing agent, a surfactant, and an inert gas in a batch reactor that is constantly stirring. When two or more metal cationic species are present in the solvent, a nanosized phase with varying compositions is produced. This technique of making stabilized metal nanoparticles shows promise. There are numerous alternatives for the reducing agent. However, it could also depend on the particular redox thermodynamics. In most instances, the mixture's pH significantly impacts the action of reducing agents [22]. For instance, the precursor copper acetate will dissolve in stirred deionized water to produce copper nanoparticles (CuNPs) [23].

2.3. Biochemical methods.

In recent years, these processes have also included the utilization of plants, algae, fungi, yeasts, bacteria, and even viruses [24]. Growth can take either intracellularly or extracellularly, and it depends on reducing mechanisms that are either enzymatic or non-enzymatic. Depending on the host cells and process variables, bacteria or fungi may create gold and silver nanoparticles in various shapes (cubes, spheres, triangles, wires, or plates). Biosynthesis process optimization is still a problem despite these methods being documented in numerous patents [25].

2.4. Electrochemical methods.

Electrochemical procedures have explained several important benefits over chemical techniques in the creation of size-shape-selective or shape-controlled extremely pure metal nanoparticles. Metal particles stabilized by ammonium salts are formed when a metal sheet is anodically dissolved, and the intermediate metal salt that is produced decreases at the cathode [26]. According to some researchers [27], bimetallic Cd-Ag nanoalloys can be created by sequentially arranging two different cations on a carbon electrode. Templated-assisted electro-accumulation from electrolytes holding salts of the required cation precursor was also used to produce palladium metallic nanostructures [28]. Other scientists have described the immediate electro-reduction of gold ions in mass to produce AuNPs, employing polyvinylpyrrolidone (PVP) to promote the synthesis of gold nanoparticles while preventing metal accumulation on the cathode.

2.5. Biological methods.

The quest to develop new, more ecologically friendly procedures that are not dependent on harmful chemicals or organic solvents gave rise to biological approaches. They have also proven to be affordable and secure substitutes. By modifying the strain, incubation time and temperature, metal precursor concentration, and required optimal pH conditions, for example, it is possible to overcome crucial aspects of metal-based nanoparticle production, such as distribution of size and crystalline [29].

By utilizing the mechanisms of defense found in particular organisms (against high metal ions concentrations), biological techniques produce nanoparticles based on metals. These methods include extracellular (such as bioabsorption, biomineralization, complexation, or precipitation) as well as intracellular (like bioaccumulation) mechanisms [30]. Fungi have a higher resilience to flow pressure and bioreactor agitation than bacteria, making them a better choice for creating metal-based nanoparticles on an industrial scale [31]. However, the bulk of research has reported using plant extracts recently since, in addition to the pros mentioned above, it makes sample treatment, scale-up manufacture, and product gathering easier.

3. Silver Nanoparticles (AgNPs)

Silver is frequently used as an antibacterial agent to speed up healing. $AgNO_3$-impregnated dressings are readily accessible, both in their solid form and in combination with salt solutions to treat wounds [32]. Silver has fascinating characteristics due to its good conductivity, chemical stability, catalytic activity, and antimicrobial activity. One of the nanoparticles currently being studied the most is silver nanoparticles (AgNPs) [33]. Textiles, clothing, cosmetics, the food industry, biomedicine, and other industries have used AgNPs. Due to their utilization as antibacterial agents, medical equipment coatings, and chemotherapeutic drug transporters, they are becoming more and more prominent in the biomedical field [34]. Despite substantial research, more bio-sustainable synthesis techniques and the disclosure of the procedures involved in the toxicological consequences of AgNPs are still needed.

3.1. Synthesis.

3.1.1. Conventional chemistry.

AgNPs can be produced chemically at a low cost and with ease on a larger scale while maintaining the size distribution that should be monodispersive. Out of the the different chemical techniques available, chemical reduction is the way that produces this type of nanosystems the most frequently. The three main elements of this process are reducing agents, metal precursors, and stabilizing agents. Nucleation and development occur in two stages (Figure 2). The stabilizing agent in this synthesis can also act as a reducing agent in the identical reaction [35]. The nucleation stage can be controlled by monitoring experimental parameters such as the reaction's precursor, reducing agents, reagents concentration, pH, and temperature to produce AgNPs with the right average size, polydispersity, and shape [36].

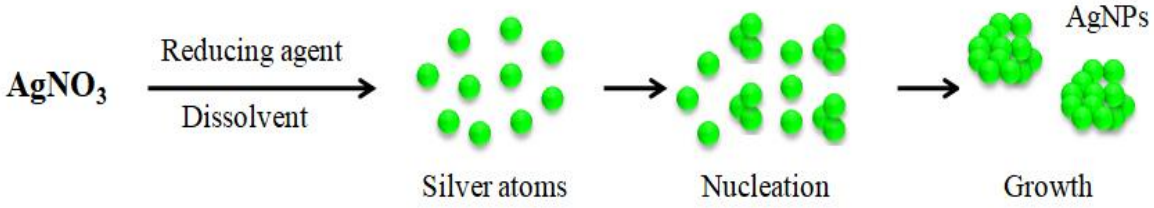

Figure 2. Process for the synthesis of AgNPs.

AgNP stabilization is a crucial stage in their manufacturing, especially in stopping the processes of agglomeration and oxidation. As a result, the most popular method is the use of stabilizing agents that can shield AgNPs. Amine derivatives, gluconic acid, thiols, or chitosan may be used to stabilize the product. Additionally, it has been shown to be advantageous to use polymeric materials as polyacrylates, polyvinylpyrrolidone (PVP), polyvinyl alcohol (PVA), polyacrylonitrile, polyethylene glycol (PEG) or polyacrylamide. Adding a negative charge to the surface of these NPs, typically through citrate groups, can stabilize them by electrostatic repulsion [37]. The Creighton approach, which yields monodispersed and small (approximately 10 nm) nanoparticles, is the chemical process that is most frequently employed to make AgNPs [38]. In this method, $AgNO_3$ serves as the precursor, and $NaBH_4$ acts as the reducing agent. The following is the reaction that is carried out:

$$2\ AgNO_3 + 2\ NaBH_4 \rightarrow 2\ Ag(s) + B_2H_6 + H_2 + 2\ NaNO_3$$

3.1.2. Green chemistry.

Despite the lower cost and higher chemical synthesis performance, reducing agents can be dangerous. Eco-friendly reagents and techniques have been created as a result. It is particularly interesting to study the chemical reduction of $AgNO_3$ salt using β-D-glucose as a reducing agent. This method employs starch as a stabilizing component (Figure 3). These environmentally friendly synthesis techniques can create AgNPs with mean diameters under 10 nm. [39].

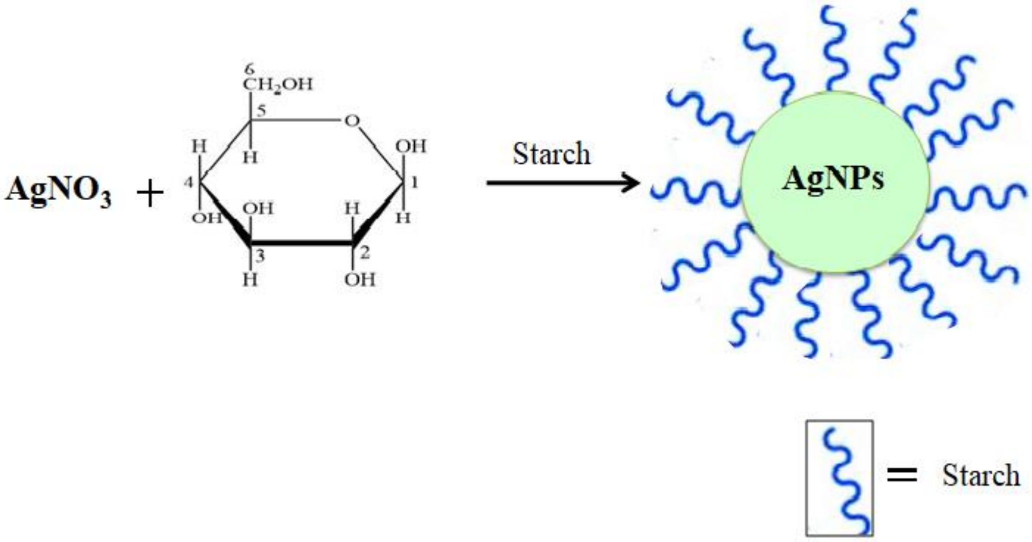

Figure 3. Chemical reduction of $AgNO_3$ salt from β-D-glucose.

Ascorbic acid was used as a reducing agent in the process that Ho *et al.* reported for reducing $AgNO_3$. They were successful in producing hybrid AgNPs inside polylysine shells that had changed from various fatty acids. AgNPs with mean diameters that range from 2 to 5 nm were created using this green synthesis technique [40]. As indicated by a rise in publications on the topic in recent years, modern eco-friendly biosynthesis methods are gradually replacing conventional chemical synthesis. The biosynthesis of AgNPs uses the same building blocks as chemical synthesis, but rather than a chemical entity, it uses the reductive characteristics of biological entities. Bacteria that can produce reductase enzymes can produce AgNPs either intracellularly or extracellularly [41]. Intracellular biosynthesis uses a simpler passage of Ag+ ions inside the bacteria cells. By transforming ionic Ag+ to neutral Ag^0, bacteria can also produce AgNPs. In this case, AgNP recovery requires an additional step (like cell lysis). Extracellular biosynthesis is carried out outside the bacterial cell using bacterial biomass, bacterial culture supernatant, or cell-free extracts. An organic base is used in the supernatant to encourage the correct recovery of AgNPs by centrifugation followed by resuspension [42]. Because extracellular biosynthesis does not require downstream processing, it is preferred to intracellular biosynthesis. One of the first bacteria used for the manufacture of AgNPs by cultivation in high concentrations of $AgNO_3$ was *Pseudomonas stutzeri*, a silver-resistant bacterium obtained from a silver mine that transforms Ag^+ to Ag^0 with accumulation inside the cell [43]. $AgNO_3$ is typically combined with the organic base and incubated under ideal conditions. According to Jang *et al.*, alkaline pH in the pH range from 8 to 10 results in smaller-sized particles while increasing reaction yield.

On the contrary hand, Ag^+ ions precipitation takes place, and AgNP formation is uncommon at acidic pH [44]. Extracellular enzymes produced by fungi are secreted outside the cell and break down extracellular macromolecules, followed by nutrient absorption. Due to their distinctive property, they play a crucial role in the extracellular production of AgNPs. After incubation and colony formation, fungi are normally taken out of the aqueous media carrying extracellular enzymes. The first is taken out, and the medium is then infused with $AgNO_3$. Then, this mixture is incubated, often at close to room temperature. The formulae mentioned above control the creation of AgNPs. The media's color changes to verify the synthesis reaction [45]. Important considerations include medium characteristics, incubation period, temperature, $AgNO_3$ and biomass quantities, and activity. Zhao *et al.* discovered that pH 7, 25°C, 1 mM $AgNO_3$, and 15-20 g of wet cell filtrates are the best conditions for fungus to produce AgNPs extracellularly. The generated nanoparticles had an average size of 25 to 30 nm and were spherical in shape [46]. Based on their comparatively high concentrations of steroids, sapogenins, carbohydrates, and flavonoids, which serve as reducing agents, as well as bio-capping compounds, which lessen nanoparticle aggregation and enable better size control, plant extracts are used to synthesize AgNPs [47]. In general, the process of making AgNPs from extracts of plants is simple. Freshly collected plant parts are washed in sterile water, allowed to dry in the shade, and then ground. To create the plant extract, dry powder is boiled in deionized water. The resulting infusion is filtered to get rid of any insoluble particles. The 1 mM $AgNO_3$ solution is then enhanced with a specific amount of plant extract. By changing the color of the medium (usually dark brown) and verifying it with the ultraviolet-visible (UV-Vis) spectra, the synthesis of AgNPs can be checked once more. Produced AgNPs can be easily collected by centrifuging repeatedly for 15 minutes at 12,000 rpm [48].

4. Characterization of AgNPs

AgNPs have been characterized and controlled using a variety of methods. The most often reported techniques include UV-Vis spectrophotometry, X-ray diffraction (XRD), transmission electron microscopy (TEM), and infrared spectroscopy (IR). Typically performed at various points throughout the reaction, UV-Vis spectrophotometry provides significant insight into the success of AgNP generation [49]. AgNPs are extremely effective at both absorbing and dispersing light. When certain wavelengths of light activate the metal surface's electrons, generating a collective oscillation, this interaction with light takes place. These oscillations are described by the surface plasmon resonance. In the case of AgNPs, this emerges at a wavelength of about 400 nm; its precise location relies on the diameter, shape, and dispersion of the nanoparticles [50]. AgNPs' crystalline nature is assessed by XRD, which records data in the range of 30-80 and validates their morphology. Face-centered cubic (FCC) metallic silver structures are frequently produced in AgNPs, as seen in their XRD pattern. TEM image can be used to see the morphology of biosynthesized AgNPs. AgNPs are generally spherical and have a large average size dispersion [51]. Using free amine groups, cysteine residues, or carboxyl electrostatic interaction, IR is frequently used to detect important functional groups and characterize biomolecules attached, notably on synthetic AgNPs. The pellet of biologically produced AgNPs is mixed with potassium bromide and put in the sample container. According to the study, these substances and proteins are believed to be crucial for capping stabilization. The IR spectra are impacted by the characteristics of the species or organism utilized to synthesize AgNPs [52]. Two other techniques for determining size and size distribution are scanning electron microscopy (SEM) and atomic force microscopy (AFM). Additionally, the nanoparticles' zeta potential (an indirect measurement of the surface electrical charge) is evaluated using electrophoresis laser Doppler, and the size and polydispersity index of the nanoparticles is determined using dynamic light scattering (DLS).

Furthermore, energy-dispersive X-ray (EDX) is used for elemental analysis or chemical characterization, and field emission scanning electron microscopy (FESEM) provides information on surface morphology. A useful technique for figuring out the stability of AgNPs and the surface electrical charge of aqueous colloidal suspensions is zeta potential measurement. Balakrishnan *et al.* incorporated zeta potential measurement in their thorough analysis of AgNPs, and it was found to be approximately 9.56 mV, indicating a mild repulsion of AgNPs [53]. On the other side, Farhadi *et al*. measured about 35 mV. The colloidal AgNP suspension is stable since this latter value is greater than |30| mV, illustrating the attraction between generated nanoparticles that prevents agglomeration [54]. Zeta potential readings can be positive or negative, although they are usually negative. This is most likely because the bio-organic components in the extract have been capped. Lower antibacterial activity is often correlated with AgNPs having a negative zeta potential [55].

5. Antimicrobial Activity

Despite several attempts made over the years, AgNPs' precise mode of action is still unknown. The four primary mechanisms by which AgNPs exert their antimicrobial activity are as follows: (i)attraction to the bacterial surface; (ii) destabilization of the bacterial cell wall and membrane with alterations in permeability; (iii) induction of toxicity and oxidative stress via the generation of ROS and free radicals; and (iv)modulation of signal transduction pathways [56]. Many authors refer to the adherence of AgNP to bacterial surfaces as the beginning of a sophisticated mechanism of bacterial suppression. AgNP zeta potential, in addition to their size, has a significant impact on how well they adhere. Depending on the production method, AgNPs may possess a positive, neutral, or negative surface charge. According to research by Abbaszadegan *et al*., changing the surface charge of nanoparticles results in a noticeable change in their antibacterial activity. Positively charged AgNPs strongly attract the slightly negatively charged bacterial surface, increasing the antibacterial effect. On the other hand, neutral or negatively charged nanoparticles have significantly less of an antibacterial effect. However, utilizing a bacterial surface saturation approach, raising the concentration of AgNPs allows the reduction of electrostatic repulsion. [57].

After sticking to the bacterial surface, AgNPs may communicate with cells via two different strategies. While larger nanoparticles stay outside the bacteria, smaller AgNPs directly penetrate the cell. AgNPs continuously release Ag^+ ions in both scenarios. These ions attach to the cell membrane components, breaking the membrane potential and proton leakage. Cell wall instability significantly increases bacterial permeability, allowing larger AgNPs to penetrate the cell [58].

Invading AgNPs and Ag^+ ions interact with a range of cellular components, including proteins, lipids, and DNA, leading to cellular dysfunction. It is widely known that AgNPs have a significant capacity to produce free radicals and reactive oxygen species (ROS), including hydrogen peroxide (H_2O_2), superoxide anion (O_2), and hydroxyl radical (OH). As a consequence of cellular respiration, ROS are produced naturally in bacteria. However, under normal circumstances, bacteria have defense mechanisms that act as antioxidant enzymes and eliminate these dangerous species, such as glutathione (GSH), superoxide dismutase, and catalase. High levels of Ag^+ generated by AgNPs lead to excessive oxidative stress (Figure 4). Antioxidant enzymes can only partially neutralize the amount of released ions, even if they remove some [59]. These species communicate with respiratory chain proteins on the outer layer and render enzymes inactive because of their attraction for phosphates, thiols, and carboxyl groups [60]. Their interaction with phosphate groups restricts protein phosphorylation, which is frequently involved in enzymatic activation, hence preventing the development of bacteria. Dephosphorylation of protein tyrosine residues has also been associated with disruption of exopolysaccharide and capsular polysaccharide synthesis and transport to the membrane, leading to cell cycle disruption [61]. Additionally, Ag^+ has the ability to intercalate DNA strands, breaking H-bonds and forming complexes with nucleic acids within the purine and pyrimidine base pairs [62].

It's also crucial to remember that exposing human cell cultures to AgNP can cause cytotoxicity [63], cell-type-dependent inflammatory responses, and genotoxicity. Due to their innate capacity to produce stimuli-dependent reactions by precisely adjusting their optical characteristics, chemical surroundings, high molar absorptive, and the numerous sorption sites located on their vast surface, AgNPs are also used for numerous analytical applications [64]. The biocide effects of silver are specifically covered in a large number of research studies. State-of-the-art focuses on the favorable pairing of antimicrobial silver nanoparticles with synthetic or natural polymers in the current endeavor to minimize or even abolish microbial contamination and colonization processes [65]. The main advantage of nanosilver-based biomaterials created for innovative antibacterial applications is related to their innate anti-pathogenic capabilities shown against both planktonic and biofilm-organized pathogens. AgNP bactericidal impact is believed to be caused by silver cations' ability to selectively attach to thiol groups in bacterial proteins, inhibiting their physiological activity and leading to cell death [66].

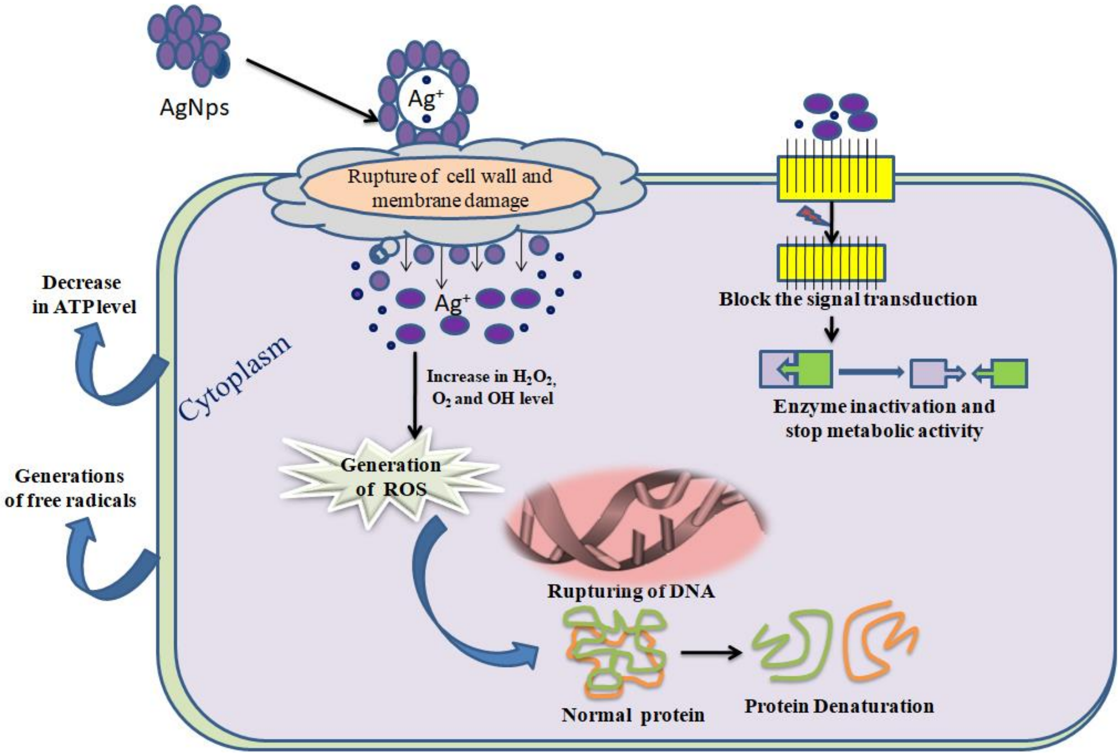

Figure 4. Schematic representation of AgNPs mechanism of antimicrobial activity.

6. Applications of Silver Nanoparticles in Healthcare

The industries that have invested the most in the development and research of technologies that take advantage of nanoparticle antibacterial activity are health and medicine. AgNPs can be used in a wide range of products to enhance bactericidal capabilities due to their biocompatibility and simplicity of functionalization. In the healthcare industry, there are many different kinds of applications:

6.1. Silver nanoparticles for drug-delivery systems.

The pharmacodynamics and pharmacokinetics of a drug are equally important in medicine as their inherent therapeutic benefits. The particular and selective administration and effects of therapeutic agents became one of the most investigated topics for improving current human healthcare practice, which attracted a lot of attention to nanoparticles in developing and designing new and improved drug-delivery systems [67]. Anti-inflammatory [68], antioxidant [69], antibacterial [70], and anticancer [71] biosubstances are only a few of the therapeutic chemicals that have been looked into as potential therapeutic molecules for AgNP-based nanosystems. To offer a specific therapeutic impact onhuman or animal species, the procedure or method utilized during the administration of the selected pharmaceutical chemical must be taken into account. Because of their exceptional biocompatibility and practical features for nanoscale-derived therapeutic settings, hybrid molecular units made of AgNPs were chosen successfully for the development of new and performance-enhanced drug-delivery systems adaptable to thermal, optical, or pH variations to target inflammatory, infectious, and malignant illnesses [72]. Due to difficulties in AgNP synthesis and concerns regarding nanosilver-based systems' toxicity and poor stability whenever functionalized using conventional salt-aging procedures, silver is not widely employed in nanoparticle-based drug delivery applications [73]. It is substituted with gold or other nanomaterials. For drug delivery applications, a great trigger-able and tunable nanosystem should be easy to build from widely available components, have the best adaptability, and function with various triggers. [74].

6.2. Silver nanoparticles for catheter modification.

Central venous catheters (CVCs) have evolved since Niederhuber first described them in 1982 into essential therapeutic tools for a range of clinical conditions requiring starvation and substitute treatment (such as cancer and renal disease) [75]. CVCs frequently provide accessibility for intravenous fluid administration, hemodynamics tracking, pharmaceutical delivery methods, and nutritional support in critically ill patients. These medical devices are an important risk factor for microbial contamination and colonization phenomenon in addition to being a significant contributor to hospital-acquired illnesses [76, 77]. Several Staphylococcus aureus strains cause infections associated with catheter usage, 82% of that are methicillin-resistant strains with several genes expressed during bacterial dispersion and biofilm formation procedures [78]. In order to produce antibacterial effects in clinically relevant materials and devices, AgNPs have been extensively studied for the alteration of one-dimensional and two-dimensional surfaces, like cotton fabrics [80], natural and synthetic fibers [81], thin polymer films [82], and wound pads [83]. The exceptional surface-to-volume atomic ratio of AgNPs justifies the continual local supply of Ag^+ ions at the coating/tissue interface because silver, a semi-noble metal, is rapidly oxidized [84]. Recent studies have demonstrated the value of AgNP-modified catheters as non-toxic instruments that deliver antibacterial silver continuously and reduce infection-related complications. A thorough investigation was conducted into how AgNPs and AgNP-coated catheters affected coagulase-negative *staphylococci* (CoNS), among the major microorganism groups responsible for device-related infections. Gram-positive and Gram-negative bacteria biofilms are significantly inhibited by CVCs coated with AgNPs [85, 86].

6.3. Silver nanoparticles for dental applications.

Dental caries, one of the most prevalent oral disease-related diseases worldwide, is also expensive. By accelerating remineralization and controlling biofilm formation, dental-related nanotechnology-based solutions seek to lessen or eliminate caries' clinical effects [87]. In addition to their inherent highly biocompatible behavior, the materials for dental barrier membranes (DBM), which are widely used for efficient alveolar bone healing, must carry out several extra and particular features and functions. Studies have been done on the efficiency of different metal-coated implants against the microbes that result in dental-related biofilm formation and eventual implant failure [88]. To avoid the bacterial contamination of dental implants, it is specifically advised that you brush your teeth properly, take preventive antibiotics, and use antimicrobial mouthwash. Dentistry's main goal is to protect the mouth cavity, which acts as a disease entrance point into the body [89]. The possibility that biofilms on dental implant surfaces will potentially cause inflammatory lesions on the peri-implant mucosa raises the risk of implant failure. Silver has been used in oral care for millennia due to its crucial function in dental amalgams that are employed to replace teeth. In the 19th century, silver rose to international prominence [90]. Few dental disciplines have employed AgNPs, including implantology, restorative and endodontic dentistry, and dental prosthetics. Due to their unique properties, silver nanoparticles play a vital role in restorative, regenerative, and multifunctional biomedicine. This is because they can be used in various real-world applications in modern society [91].

6.4. Silver nanoparticles for wound healing.

Wound infections are a serious clinical issue because they substantially impact patient morbidity and mortality in addition to a significant financial impact. Preventing dehiscence of wounds and infection at the surgical site is a challenging and important aspect of contemporary therapeutic practice. Despite being the largest and one of the most intricate organs in the body, the skin is prone to harm from various external factors [92]. Physically or chemically induced cutaneous wounds may substantially compromise the epidermis' functional and structural integrity at different stages, leading to permanent damage or even death, depending on the degree of the injury. The significance of wound infections caused by opportunistic pathogenic microbes has lately increased in contemporary medical practice [93]. The best way to treat infected wounds is to promote rapid tissue recovery processes, maximum functionality restoration, and minimal scar tissue development. The wound-healing process has numerous stages, including coagulation, inflammation, the proliferation of cells, and matrix and tissue remodeling, just like any complex pathophysiological mechanism [94].

Acticoat^{TM} and Bactigras^{TM} (Smith & Nephew), Aquacel^{TM} (ConvaTec), PolyMem Silver^{TM} (Aspen), and Tegaderm^{TM} (3M) are a few examples of biocomposites enriched with ionic silver that have been approved by the US Food and Drug Administration (FDA) for use in wound-dressing applications. In addition to these commercial goods, including AgNPs inside innovative, naturally occurring biomaterials for enhanced wound-healing management, such as (but not limited to) modified cotton textiles, bacterial cellulose, chitosan, and sodium alginate, have shown promising results. The combination of AgNPs and Ag^+ carriers also offers a beneficial strategy for delayed diabetic wound-healing processes since diabetic wounds can cause various secondary infections. AgNPs can help diabetic individuals in the initial phases of wound healing and cause only mild scarring [95, 96].

6.5. Silver nanoparticles for bone healing.

Each year, millions of people around the world are affected by a wide range of diverse and complex bone-related diseases, including infectious diseases, degenerative and genetic diseases, cancers, and fractures [97]. Unfortunately, opportunistic contamination and colonization of orthopedic implants pose important issues in osseous-tissue replacement schemes due to the high morbidity associated with infections [98]. Regeneration and restorative processes are made possible by the inherent and complex bone-remodeling mechanism in bone [99]. Most of the time, serious osseous tissue deficiencies caused by trauma, cancer, or hereditary malformations are repaired or replaced using bone grafts. High levels of inflammation, implant loss, and bone-destroying events are frequently present alongside orthopedic and bone-implant-related illnesses [100].

The crystallized calcium-phosphate salt hydroxyapatite is the main component of human bone, dentin, and dental enamel. Given that synthetic and biosynthesized hydroxyapatite have special biocompatibility, these substances and their derivatives are being carefully studied for the advancement of novel osseous-related healing and regeneration strategies, either as material coatings for metallic implants or as synthetic bone grafts [101]. Regarding the superficial alteration of various metallic implant surfaces, biocompatible hydroxyapatite combined with silver (either metallic or ionic) is an excellent choice for producing bioactive and antibacterial bone implants. Gram-positive [102] and Gram-negative [103] nanosilver-coated hydroxyapatite-based coatings successfully inhibited strains of bacteria. In bone-replacement procedures, AgNPs are frequently used as doping components for synthetic and bio-inspired bone scaffolds, and relevant results have recently been published [104]. Several experimental techniques, such as beam-assisted deposition, electrochemical deposition, magnetron sputtering, ion-beam-assisted deposition, sol-gel technology, and micro-arc oxidation, to introduce antibacterial properties into hydroxyapatite coatings, proved effective [105].

7. Conclusions

These days, AgNPs are a potent antimicrobial agent with strong antibacterial properties. Nanoparticles can also be altered to achieve specificity and delivery to particular targets. These requirements are considered, including antibacterial effectiveness, prompt action, and low cytotoxicity. Drug delivery, wound dressing, tissue scaffolding, and protective coating are some applications for AgNP-based nanosystems and nanomaterials. It was discovered that many physicochemical elements, such as size, shape, concentration, surface charge, and colloidal state, had an impact on the innate antibacterial capabilities of AgNPs. The incredible surface area of nanosilver also enables the interaction of several ligands, providing a myriad of options for the surface functionalization of AgNPs.

Much research evidence supports the beneficial effects of AgNPs in emerging biocompatible and nanostructured substances and devices developed for modern therapeutic approaches. AgNPs are a good option for designing, acquiring, testing, and clinically evaluating performance-enhanced biomaterials and medical devices because they provide additional mechanical, optical, chemical, and biological characteristics in addition to their appealing and versatile antibacterial potential. However, further research is required on their short- and long-term toxicity and the mechanisms underlying hazardous effects. Silver nanoparticles have great potential for use in biomedical applications, highlighted by the limitations on conventional medical practice already in place and the most recent challenges imposed by nanosilver-based technologies. Whether we consider changing previously current biomaterials and devices or constructing entirely novel nanostructured ones, AgNPs are good options for achieving the aim of approaching modern biomedicine.

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Conflicts of Interest

No conflict of interest was declared.

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