Review Article

Biosynthesis of Silver Nanoparticles and Their Roles in the Biomedical Field: A Review

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Abstract

Developing novel antibiotics, traditional pharmaceuticals, and chemically altered drugs addresses medical concerns and underscores the need for sustained and productive implementation of metallic nanotechnology across various domains. Nanoparticles (NPs) present a range of advantages over bulk particles due to their targeting capabilities, wound repair characteristics, capacity for biocomposite preparation, and potential as a gene and drug delivery system. Silver nanoparticles (AgNPs) have garnered significant interest among researchers as a result of their exceptional conductivity, chemical stability, catalytic behavior, and antimicrobial properties compared with other metal NPs. This study aims to provide a basic understanding of AgNPs and their functions in biomedical research.

Keywords: AgNPs, biomedical applications, silver nanoparticles

Introduction

Nanotechnology is a rapidly developing science with wide-ranging potential applications. Particles with a size of 1–100 nm are called nanoparticles (NPs).[1] Silver nanoparticles (AgNPs) are presently extensively used across multiple fields, including agriculture, commerce, medicine, and industry.[2] The unique characteristics of AgNPs with smaller dimensions make them suitable for diverse applications. The application of nanomaterials in biomedicine has become more prevalent, resulting in the emergence of nanobiotechnology.[3] AgNPs and compounds containing silver are widely recognized in this area for their ability to eliminate microorganisms.[4] At present, AgNPs are mainly used in unconventional and advanced biomedical uses, including wound care, drug delivery systems, tissue scaffolds, and protective coatings. Consequently, the utilization of AgNPs has expanded in the fields of nanotechnologies, biomedical science, and ecological sustainability.[5] Therefore, there is a necessity to devise a cost-efficient approach for the bioproduction of AgNPs.

Bioproduction (Synthesis) of AgNPs

Numerous techniques are currently under investigation for the production of AgNPs, intending to address various contemporary issues faced by humanity.[6,7] Previously, the controlled size and shape of AgNPs were concerned with their synthesis, whereas other specific methods, including biological, chemical, and physical approaches, have been established for synthesizing AgNPs[8] [Figure 1].

The use of hazardous chemicals and the significant consumption of energy can make chemical and physical processes expensive.[9,10]

Two techniques are mainly used in the physical realm: the destructive approach (top-down) and the self-assembly method (bottom-up) [Figure 1]. The main idea of the destruction approach is based on the use of physical power pressure on bulk material for metal NPs formation of size 10–100 nm, such as mechanical energy used in ball milling, crushing, and grinding; electrical energy used in the electrical arc-discharge method and laser ablation method; and thermal energy used in the vapor condensation method.[11]

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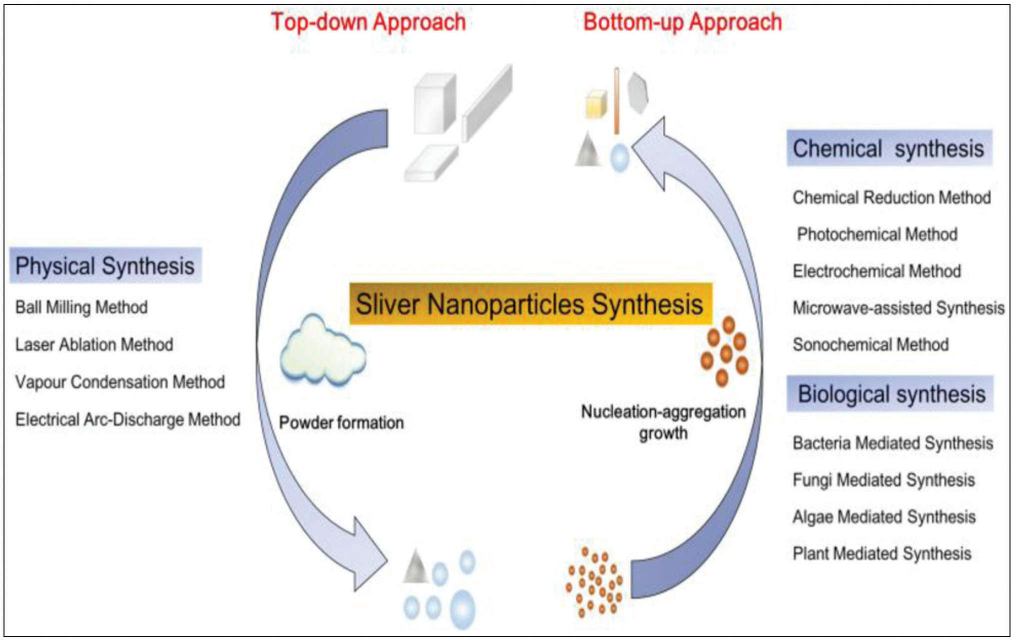

Figure 1: The synthesis of AgNPs can be achieved through various methods, such as physical, chemical, and biological approaches. Physical synthesis methods involve a top-down approach, which entails the formation of NPs from bulk materials, whereas chemical and biological synthesis methods follow a bottom-up approach that involves the growth of complex clusters and molecular components to obtain NPs

Biological Method

New research recommends different types of bacteria and plants for AgNP biosynthesis. The byproducts of microorganisms, such as metallic ions, have a tolerance capacity to counteract the toxic effects of heavy environmental silver, resulting in AgNP formation as an end byproduct of free Ag^+.[12,13]

Varieties of plant parts are used in AgNP biosynthesis; the most common ones are leaves, peel, callus, bark, flower, seed, fruit, and rhizome. From these extracts, dextran, starch, chitin, and cellulose are obtained, whereas microorganism components include nitrate reductase, polysaccharides, peptides, and c-type cytochromes.[14] Compared with physical or chemical approaches, the bioproduction of AgNPs through plant extracts or microorganisms can be performed under typical temperature and pressure conditions. Additionally, it offers a more regulated dimension and form of the NPs without necessitating the use of hazardous and deleterious materials.[10] At this point, we will discuss the different techniques employed in the bioproduction of AgNPs by microorganisms and plants, as well as the chemical and biological processes that occur during these syntheses [Table 1].

The production of singular AgNPs with specific compositions was documented previously at the beginning by Klaus *et al.*[12] via *Pseudomonas stutzeri* bacteria, commonly referred to as silver mine bacteria. Al-Rajhi *et al.*[27] have recently documented the biogenesis of AgNPs that exhibit fewer harmful effects on healthy cells, a higher degree of stability, and generate fewer toxic byproducts. The production of AgNPs by microorganisms can be broken down into two distinct types: intracellular and extracellular. Various bacterial strains, including *Pseudoduganella eburnea*, *Pseudomonas* sp., *Escherichia coli*, *Bacillus licheniformis*, *Serratia nematodiphila*, *Bacillus flexus*, and *Shewanella oneidensis*, have been found to facilitate the extracellular synthesis of AgNPs, as reported in several studies.[28] The *Shewanella* genus is recognized for its ability to reduce metals and engage in biomineralization processes. Additionally, it has been documented for its involvement in the biofabrication of AgNPs.[29]

Jabbar and Hussein[30] conducted a study in which they utilized *Lactobacillus gasseri*, a Gram-positive bacterium that is, catalase-negative and facultatively anaerobic, to biosynthesize AgNPs. The resulting AgNPs exhibit promising potential for utilization in the realm of biomedical applications as effective antibacterial agents.[30] Another investigation has exhibited the bacterial production of AgNPs using two prevalent Gram-negative bacterial strains, *E. coli* K12 MG1655, and *Pseudomonas putida* KT2440. As mentioned earlier, the observation can optimize and expedite the utilization of green NPs for enhanced antibacterial efficacy.[31] AgNPs have recently been produced from an extract of *Cuminum cyminum* seeds. Cumin seeds, with their intense aromas, were thought to play a key role in reducing silver ions.[32]

Medical Application of AgNPs

A combination of their widely acknowledged application in biological and medical domains and their extensive range of commercial uses, AgNPs have captured the scientific community and industrialists' interest.[34] Silver possesses various functions in antimicrobial, catalytic, and biological environments [Figure 2]. The distinctive chemical and physical characteristics of AgNPs enhance the effectiveness of silver.[35]

Silver NPs as antibacterial

Since oligodynamic metals encapsulate ions that damage living cells, silver has been linked to both bacteriostatic (growth suppression) and bactericidal (eradication)

Table 1: Bacteria-, fungi-, and algae-mediated synthesis of silver NPs

Bacteria/fungi/algae	Responsible organic components/functional groups	Size (nm)	Precursor	Operating conditions	Position	Shape	References
Streptomyces violaceus	Exopolysaccharide	10–60	$AgNO_3$	37°C; shaking; pH 7.0;	Extracellular	Cubic; crystalline; spherical	Sivasankar *et al.*[15]
Penicillium polonicum	Proteins	10–15	$AgNO_3$	Room temperature; shaking; light	Extracellular	Spherical; near spherical	Neethu *et al.*[16]
Falcaria vulgaris	Hydroxyl group	10–30	$AgNO_3$	50°C	Extracellular	Spherical	Kohsari *et al.*[17]
Pseudomonas	Aromatic and aliphatic amines	10–40	$AgNO_3$	28°C; shaking	Extracellular	Irregular	Singh *et al.*[18]
Pantoea ananatis	Proteins or amino acids	7–30	$AgNO_3$	37°C; shaking	Extracellular	Spherical	Monowar *et al.*[19]
Fusarium oxysporum	Proteins	21.3–37.3	$AgNO_3$	28°C; shaking	Extracellular	Spherical; oval	Ahmed *et al.*[20]
Botryosphaeria rhodina	NADH-dependent nitrate reductase	Below 20	$AgNO_3$	Room temperature; dark	Extracellular	Spherical	Akther *et al.*[21]
Monascus	Lactone ring	10–30; 15–40	$AgNO_3$	28°C–30°C; shaking	Extracellular	Spherical	Koli *et al.*[22]
Aspergillus tamarii	NADH-dependent nitrate reductase	3.5 ± 3	$AgNO_3$	25 ± 2°C; shaking	Extracellular	Spherical	Devi and Joshi[23]
Nostoc linckia	Phycocyanin	9.39–25.89	$AgNO_3$	Room temperature; pH 10.0	Extracellular	Spherical	El-Naggar *et al.*[24]
Caulerpa serrulata	Caulerpenyne; caulerpin	10 ± 2	$AgNO_3$	27°C–95°C; pH 4.1–9.5	Extracellular	Crystalline; spherical	Aboelfetoh *et al.*[25]
Laurencia aldingensis	Proteins	5–10	$AgNO_3$	Dark, shaking	Extracellular	Spherical	Vieira *et al.*[26]

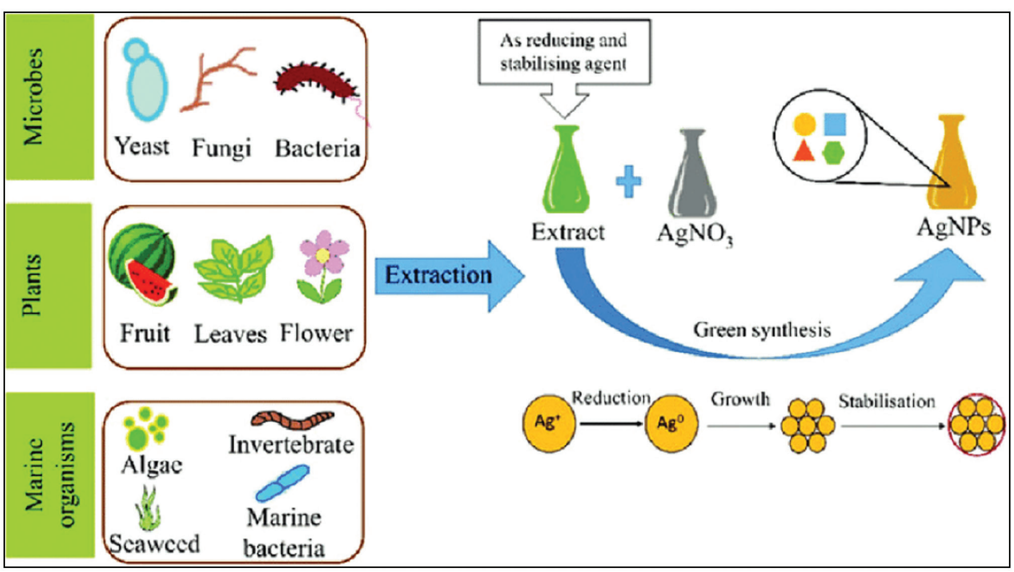

Figure 2: Biosynthetic pathway for AgNPs[33]

effects.[36] Ionic silver exhibits a robust interaction due to the existence of thiol groups in crucial bacterial enzymes; the presence of AgNPs can result in the inactivation of these enzymes and consequent loss of DNA replication ability.[37] Considering that AgNPs are effective against a wide variety of harmful microbes and have antibacterial properties despite their low concentrations, they have been employed to combat the spread of antibiotic-resistant pathogens.[38] The application of AgNPs has been observed to induce destabilization of membrane potential and reduction of intracellular ATP levels via targeted mechanisms, ultimately leading to bacterial mortality [Figure 3].[39] AgNPs exhibit greater efficacy against Gram-negative bacteria. Gram-negative bacterial cells possess a comparatively more restricted cellular wall in comparison to their gram-positive counterparts. The dense cellular wall can potentially impede the entry of NPs into the cellular structures.[40] Articles have shown that certain strains of bacteria become extremely susceptible to AgNPs after repeated and prolonged contact. In laboratory research, sublethal exposure of *E. coli* and *Staphylococcus aureus* to AgNPs demonstrates this Balasubramaniam *et al.*[41] Acrylic resin is a frequently utilized material in the production of removable dental prostheses. Incorporating AgNPs into acrylic resin has been found to possess inhibitory effects against bacterial cultures such as *Streptococcus* mutants, *E. coli*, and *S. aureus*.[36] In another study using *T. kotschyanus* extract as a reducing agent, Abdulazeem *et al.*[32] synthesized AgNPs and characterized them with various analytical methods. Synthesized AgNPs were discovered to possess efficacy against pathogenic bacteria isolated from chicken droppings when used as an alternative to conventional treatments.

Silver NPs as antiviral

The exact mechanism by which AgNPs induce viral death is currently unknown.[27,42] AgNPs can potentially prevent viral infections through two mechanisms: hindering virus infection in cells and directly deactivating viruses.[43] Examples of viruses that can be inactivated by AgNPs include herpes simplex virus, respiratory syncytial virus, and adenovirus serotype 3. The significant surface area of AgNPs enables enhanced interaction with viral particles, resulting in heightened antiviral efficacy.[44] Using bacteriophage X174, murine norovirus, and adenovirus, Haggag *et al.*[45] assessed the antivirus efficacy of these AgNPs in various settings without observing any major ecological hazards. In a separate investigation, AgNPs with mean sizes of 10 nm (Ag10Ns) and 50 nm (Ag50Ns) were used to inhibit the viral replication of the hepatitis B virus genome.[42] According to previous research, poliovirus-infected human rhabdomyosarcoma cells were found to be susceptible to being killed by AgNPs that were electrochemically synthesized. The particles utilized in combining AgNPs and poliovirus exhibited quasi-spherical morphology, with an average diameter of approximately 7.1 nm.[46]

Silver NPs as antiparasitic

Over the past 10 years, researchers in parasitology have documented promising outcomes in managing parasites by employing AgNPs that have been synthesized through

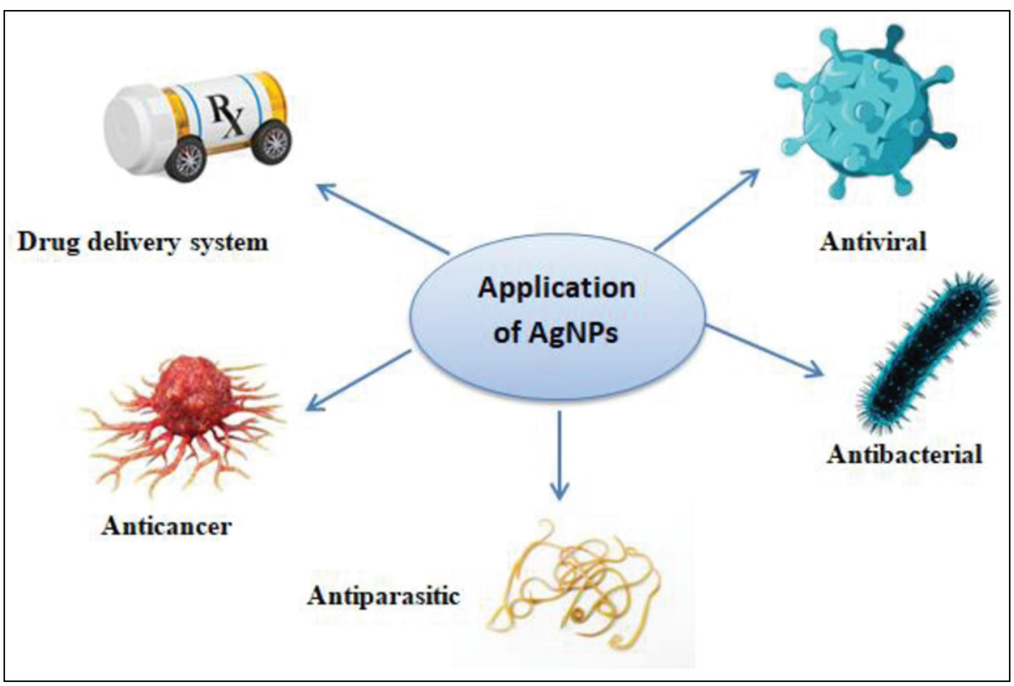

Figure 3: The main application of AgNPs

environmentally friendly means.[47] It was discovered that these AgNPs have potent anti-plasmodial efficacy against several types of parasites, for instance, *Plasmodium falciparum*. The *in vitro* investigations conducted on the effectiveness of AgNP treatment against *Leishmania tropica* have revealed the generation of reactive oxygen species (ROS), which are recognized to elicit a heightened sensitivity response in *Leishmania*.[48] Furthermore, applying AgNPs against *Toxoplasma gondii* caused impairment of the parasite's mitochondrial and cytoplasmic membrane and a 90% reduction in infection.[49] Moreover, AgNPs were synthesized using the plants *Artemisia abrotanum* and *Artemisia arborescens* because of their effectiveness toward the *P. falciparum* parasite and the many benefits of "green" AgNPs in the medical field.[50]

AgNPs as anticancer

Several studies have revealed that the addition of AgNPs to standard chemotherapeutics improves their effectiveness against cancer cells that have developed resistance to multiple drugs.[51] Coating NPs with receptor-specific binders allows them to selectively target malignant or otherwise abnormal cells. Although research into various metal NPs for use as anticancer treatments continues, interest in silver has recently increased due to its beneficial antibacterial action.[52] Several different types of cancer cells, including HepG2 (tumor cells from the liver), HCT (intestinal cancer cells), HeLa (cancer cells from the cervix), MCF 7 (cancerous cells from the breast), and others, were used to test how harmful AgNPs are to cells.[53]

AgNPs as drug delivery systems

AgNPs, with their short carbon chain and insufficiently binding oxygen atom, may provide powerful synergistic antibacterial effects when released with medication via a ligand-dependent silver release.[54] Empirical studies have shown that modifying AgNPs can be utilized for pharmaceutical transport and to mitigate the harmful effects of drugs.[55] It was also found that the cytotoxic activities of the AgNP conjugates were not significantly reduced with increasing concentration related to the cytotoxicity of the cells.[56] Other research has shown that AgNP catalytic activity is enhanced when bound to β-cyclodextrin. Conversely, there has been extensive study into using oligonucleotide conjugation to coat AgNPs for targeted genetic therapy and bio-diagnostics.[54] In addition to expressing synergism with synthetic antibiotics in terms of antibacterial activities, it has been hypothesized that AgNPs can transport drug molecules to target areas, hence improving therapeutic performance.[57] The previously mentioned assumptions have been subjected to empirical scrutiny by numerous researchers in the relevant discipline, who have documented the efficacious conjugation of tetracycline (which possesses multiple hydroxyl, phenol, and amide groups) and the immunosuppressant azathioprine (which contains S-atom and basic N-atoms in heterocycle).[58]

Conclusion

This brief study explores the wide range of biomedical uses for AgNPs and their more specific applications. AgNPs are well-suited for targeting pathogenic to diseased mammalian cells due to their structure, size, and adhesion. Moreover to their ability to combat pathogenic bacteria, AgNPs have also shown promise as an anticancer agent and a vehicle for medication delivery. The examined literature indicates that AgNPs may exhibit a synergistic impact with both anticancer agents and drug delivery systems, thereby enabling the administration of reduced dosages. Hence, these nanocarriers offer reduced toxicity in non-cancerous cells, thereby potentially mitigating the adverse effects associated with anticancer agents.

Ethical approval

Not applicable.

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Conflicts of interest

There are no conflicts of interest.

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