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REVIEW PAPER OPEN ACCESS

Silver nanoparticles in the biomedical field

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Abstract

Silver nanoparticles are gaining popularity due to their potential uses in bioengineering and medical diagnosis. Nanoparticles possess specific characteristics, including an enhanced surface-to-volume ratio and improved magnetic properties, making them suitable for various biological applications. They feature several functionalities, a high surface plasmon resonance, a huge surface area, a stable nature, and are simple to produce. Silver nanoparticles have promising uses in biomedical fields such as biomaterials, detection and diagnostics, formulations, medication transport, and medical device coatings. This review covers current research on silver nanoparticles in biomedical applications, including their creation methods, antimicrobial properties, and potential biological uses.

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INTRODUCTION

Nanotechnology is fast-growing subject that works on the materials at the nanoscale with the dimensions 1-100nm (Vinayagam *et al.,* 2024). The term nano is a Greek word derived from word nano which means dwarf and the unit represents a part of a billion (Jafar and Athbi, 2024). It has gained enormous potential and diverse use in nanomedicine, electronic gadgets, biosensors and in agriculture. Nanomaterial, is opposed to the bulk materials and have a superior physicochemical characteristic, distinctive properties. Nanotechnology to cover the area to design and manipulate various well-known attribute of nanoparticles (NPs) like stability, high surface area to volume ratio, charge and shape. NPs are divided into different categories such as organic, inorganic, metal, metal oxide and carbon based etc. NPs is produced by Ag, Au, and Platinum. Metal NPs are widely used in healthcare or medical industry, electronic gadgets, biosensors, and in agriculture(Vinayagam *et al.,* 2024).

Silver is relatively soft, tiny metal. The surface of black silver sulphide negatively impacts progressively in air due to the reaction of sulphur compounds with it. Silver is a transition metal. It is used to make mirror, as it is best reflector of visible light, used in dental alloys, electrical contacts and batteries, and to make printed circuits. Silver lacks a biological function; yet, prolonged consumption or inhalation of silver compounds may induce a disorder termed argyria, characterised by a greyish pigmentation of the skin and mucous membranes. It has antibacterial properties and kill lower organisms quite effectively. Silver nanoparticles are incorporated into textiles to inhibit bacterial degradation of sweating, hence mitigating unpleasant odours. Silver fibres are integrated into the fingertips of gloves to enable their usage with touchscreen devices.

The field of biology and therapeutics places special emphasis on AgNPs. It is well-established that AgNPs have an antibacterial impact against several pathogens, including bacteria, fungi, and viruses. Physical, chemical, biological, and environmentally friendly approaches can all be used to synthesise NPs (Soliman *et al.,* 2023). Simply the biosynthesized NPs have recently been identified as significant nanomedicines for a wide range of biomedical uses(Balaraman *et al.,* 2020; Choudhary *et al.,* 2024).Green synthesis is an alternative technique to physical and chemical methods that use toxic chemicals, surfactants, and unfavourable circumstances such as high temperatures or excessive energy. The green is relatively energy efficient, sustainable, affordable, simple and scalable for industrial production (Nindawat and Agrawal, 2019).There are three preconditions such as- (i) opting for environmentally favourable systems of solvents, (ii) sustainable reducing agent, and (iii) an appropriate capping agent for stabilizing NPs (Choudhary *et al.,* 2024).

Varieties of algae are utilized for green synthesis. When it comes to bioactive chemicals, seaweeds are head and shoulders above the competition. Not only that, but they have medical, culinary, and wastewater treatment applications. Nanoparticles (NPs) mediated by seaweeds are rich in bioactive chemicals and secondary components with several specific biological functions. The many types of seaweed (green, brown, red, and blue green) have a wide range of biological activities. Some of these activities include fighting microbes, preventing cancer, reducing inflammation, delivering drugs, preventing blood clots, and even killing sperm (Balaraman *et al.,* 2020; Choudhary *et al.,* 2024).

Because algae have such a remarkable ability to absorb metals and decrease metal ions, the production of AgNPs by algae is quite intriguing. Because they can withstand a broad variety of extreme environmental conditions, they can be employed as efficient bioagents to eliminate heavy metal contamination (Hamida *et al.* 2022). Algae are a plentiful and widely dispersed organism; their ability to thrive in a lab setting is an additional benefit. These organisms offer low cost in large production.

One of the main components that helps algae synthesise AgNPs is the cellular reductase, which leads to reduction during the process. The ability of algae to create silver nanoparticles both within and outside of their cells was recently discovered (Khanna *et al.,* 2019). The bioactive chemicals contained in green algae, which include proteins, lipids, carbs, carotenoids, vitamins, and secondary metabolites, stabilise the produced nanoparticles by acting as both a cap and an anchor, and reductant(Mahajan *et al.,* 2019; Nindawat and Agrawal, 2019).

Bioimaging, biosensors, gene transfer, photocatalysis, antimicrobial, antioxidant, and anti-cancer medicines are just a few of the many biological uses for silver nanoparticles (Rahmani *et al.,* 2018; Nindawat and Agrawal, 2019). Interactions between Ag+ and bacterial cell walls, inactivation of enzymes linked to membranes, bacterial cell assembly, impairment of vital biomolecules, breakdown of the cell envelope, and generation of reactive oxygen species (ROS) all contribute to the enhanced antimicrobial activity of AgNPs (Aref and Salem 2020). Pharmaceutical companies utilise AgNPs due of their wide temperature stability and low toxicity to human cells (Chugh *et al.,* 2021).The bioactive substances found in algae like polysaccharides, phenolic compound, proteins and alkaloids are allow to the creation of NPs (Patel *et al.,* 2024).

Synthesis of silver nanoparticles

Biological methods involve the use of plant extracts and microorganisms. Due to their detoxifying, reducing, and accumulation-inducing capabilities, plants are the sole ingredients in the water-based Ag+ ion solution used in green synthesis. Research conducted by Logeswari *et al.* (2015), Nadaroglu *et al.* (2017), Ansari and Alzohairy (2018), and Chugh *et al.* (2021) has shown that plant extracts include a variety of chemicals, including polysaccharides, flavonoids, alkaloids, enzymes, polymers, and proteins, which can both reduce and cap substances (Logeswari *et al.,* 2015; Nadaroglu *et al.,* 2017; Ansari and Alzohairy, 2018; Chugh *et al.,* 2021) (Fig. 1).

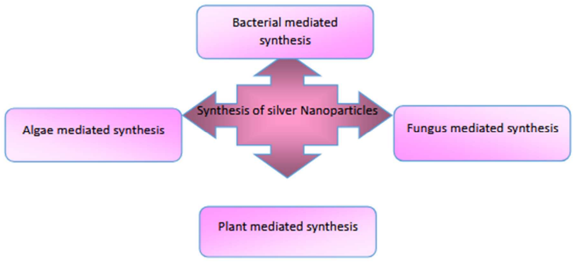

Fig. 1. Different organisms mediated synthesis of silver nanoparticles

Algae-mediated synthesis

Algae are a kind of autotrophic organisms of significant economic and ecological value. They are unicellular or multicellular creatures that inhabit many environments, including freshwater, marine ecosystems, or moist rock surfaces. The two distinct groups of algae are microalgae (microscopic) and macroalgae (macroscopic). They serve a crucial role in applications such as medicine, pharmacology, forestry, aquaculture, and cosmetics. They are a significant source of several commercial items, including natural dyes and biofuels (LewisOscar *et al.,* 2016). The field of nanoscience that focusses on the creation of nanoparticles utilising algae is referred to as "Phyco-nanotechnology." This is a very recent field of nanoscience. Algae are utilised for the synthesis of nanoparticles due to their significant capacity to absorb metals, ease of handling and cultivation, ability to thrive at low temperatures, and less environmental toxicity (Negi and Singh, 2018). Chlorophyceae, Phaeophyceae, Cyanophyceae, and Rhodophyceae are the predominant algal groups utilised for the production of silver nanoparticles (LewisOscar *et al.,* 2016). AgNPs synthesised by several algal species, including the dimensions and morphology of the synthesised nanoparticles. Various parameters influence the physical and chemical properties of nanoparticles, including shape, size, and stability. The factors encompass temperature, pH, starting concentration and type of metals, length of exposure, type and concentration of reducing agents in the aqueous phase, among others (Sharma *et al.,* 2016; Chugh *et al.,* 2021).

Fungus mediated synthesis

Fungi are useful for the production of metallic nanoparticles because of their high binding capacity, ability to bioaccumulate metals, and high intracellular uptake (Ahmad *et al.,* 2003). The advantage of synthesizing nanoparticles with fungus is that it grows faster, is easier to handle, can be quickly manufactured in a laboratory, and can survive harsh climatic conditions. Metallic nanoparticles function by reducing their ions using enzymes released by them (Mandal *et al.,* 2006), and reduction is reported to be assisted by extracellular enzymes such as naphthoquinones and anthraquinones. In the first effort for fungi-mediated manufacture of metallic nanoparticles in the early twentieth century, the fungus *Verticillium* was employed to produce AgNPs (Mukherjee *et al.,* 2001). The extract from the saprophytic straw mushroom fungus *Volvariella volvacea* was used to create gold, silver, and silver-gold nanoparticles in fungus-mediated nanoparticle synthesis (Philip, 2009). Using *Penicillium fellutanum,* which was isolated from coastal mangrove silt, and $AgNO_3$ as a substrate, Kathiresan *et al.* reported producing silver nanoparticles in vitro (Kathiresan *et al.,* 2009). In fungus, nanoparticles are produced by forming them on the surface of the mycelia rather than in solution. First, the electrostatic interaction of positively charged Ag ions and negatively charged carboxylate groups in enzymes deposits Ag+ particles on the surface of fungal cells. The fungus's cell wall enzymes subsequently degrade the Ag particles, resulting in the formation of Ag nuclei.

Bacteria mediated synthesis

Bacteria are single-celled creatures that produce diverse inorganic compounds both intracellularly and extracellularly. In the intracellular type of synthesis, silver deposited in the cell commences the process, which continues owing to microbial proliferation. After optimal bacterial growth, the cells and nanoparticles are collected. The cell then undergoes a specific mechanism to release the nanoparticle. In contrast, the extracellular type of synthesis uses bacteria's extracellular secretion and does not require any special treatment. They are an attractive source for manufacturing nanoparticles such as gold and silver; nevertheless, some of them are resistant to silver and can accumulate a dry mass of silver on their cell wall (Paulkumar *et al.,* 2013). Isolating the *Pseudomonas stutzeri* AG259 strain from a silver mine provided the first evidence of bacteria producing silver nanoparticles. In the presence of alpha-nicotinamide adenine dinucleotide phosphate reduced by NADPH-dependent nitrate reductase, AgNPs were produced in vitro, converting nitrate to nitrite. There have been several hypotheses on how bacteria produce silver nanoparticles, but the most probable one is that AgNPs are synthesized in the presence of the enzyme nitrate reductase. Rathod *et al.* investigated the manufacture of AgNPs from the alkaliphilic actinobacterium *Nocardiopsis valliformis* and discovered that they have antibacterial and cytotoxic characteristics (Rathod *et al.,* 2016). Lateef *et al.* proposed using crude extracellular keratinase to synthesize AgNPs from *Bacillus safensis*, a keratin-degrading bacterial strain (Lateef *et al.,* 2015). Patrycja *et al.* found that conjugating antibiotics with AgNPs produced by *Pilimelia columellifers* subsp. Pallida, an acidophilic actinomycete, improved their activity (Golińska *et al.,* 2016). The main disadvantage of using bacteria to make nanoparticles is their sluggish rate of synthesis and limited size range when compared to other approaches (Rafique *et al.,* 2017).

Plant mediated synthesis

Plant-mediated nanoparticle synthesis has grown in favor in recent years because to its speed, environmental friendliness, simplicity, and lack of pathogenicity. Plants have a wide range of metabolites that aid in the formation of AgNPs. Plant extracts create nanoparticles with greater kinetics than other biological or chemical agents. Alfalfa sprouts were employed by (Gardea-Torresdey *et al.* 2003) to offer the first evidence of plant-mediated synthesis of metallic nanoparticles. Alfalfa roots may extract silver from an agar media and transfer it to the plant's shoots in the same oxidation state, where the silver atoms are rearranged to form AgNPs. Various crops, including *Oryza sativa, Helianthus annus, Saccharum officinarum, Sorghum bicolor, Aloevera, Zeamays, Basella alba,* and *Capsicum annuum*, have been employed to synthesize AgNPs

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with medicinal and biological applications (Kasthuri *et al.,* 2009). AgNPs produced from *Justicia glauca* leaf extracts were shown to have antibacterial and antifungal activities (Emmanuel *et al.,* 2015).

Latha *et al.* (2015) found that using *Hemidesmus indicus* leaf extract resulted in faster production of AgNPs and improved antibacterial activity against *Shigella sonnei* bacteria at 40µg/mL. According to dynamic light scattering, banana peel extract is most effective when employed as a reducing agent to produce AgNPs from silver nitrate solution. When coupled with levofloxacin antibiotics, AgNPs showed strong antibacterial activity against several yeast and bacterial pathogens (Ibrahim, 2015). Spherical AgNPs varying in diameter from 20 to 118nm were produced from *Erythrina indica* root extract. They demonstrated a cytotoxic effect on breast and lung cancer cell lines and strong antibacterial activity against both gram-positive and gram-negative bacteria (Sre *et al.,* 2015). Palaniyandi *et al.* produced silver nanoparticles from *Azadirachta indica* gum extract, which when combined with silver nitrate solution, shown antibacterial action against Salmonella enteritidis and Bacillus cereus (Velusamy *et al.,* 2015).

Biomedical applications of silver nanoparticles

A variety of planktonic and sessile pathogenic microorganisms, including bacteria, were evaluated to determine the effectiveness of biomaterials derived from nanosilver as potential antibacterial agents (Alshareef *et al.,* 2017; Adur *et al.,* 2018), viruses (Etemadzade *et al.,* 2016; Tamilselvan *et al.,* 2017), fungi, and yeasts (Dojčilović *et al.,* 2017; Kalaivani *et al.,* 2018) (Fig. 2).

Nanosilver-based biomedical goods including anticancer agents, drug delivery platforms, orthopaedic materials and devices, and more may be designed, developed, and implemented thanks to AgNPs' remarkable antibacterial activity (Zhang *et al.,* 2016), bandages, antiseptic sprays, and catheters (Wei *et al.,* 2015). Because of its outstanding relevance in nanotechnology, biology and the environment, there is an ongoing demand for the development of cost-effective AgNP synthesis techniques (Singh *et al.,* 2015). The translation of silver-based nanotechnology to clinical applications necessitates not only the development of safe, simple, environmentally friendly, and cost-effective methods for silver nanoparticle synthesis, but also a thorough understanding of the related physicochemical properties, in vitro and in vivo effects, biodistribution, safety control mechanisms, pharmacokinetics, and pharmacodynamics of AgNPs (Wei *et al.,* 2015; Burdușel *et al.,* 2018). There are some biomedical applications of silver nanoparticles are given below.

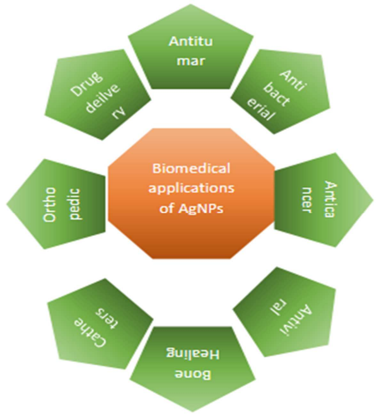

Fig. 2. Biomedical applications of silver nanoparticles

Anticancer activity

Researchers are investigating the potential of many medicinal chemicals found in Chaetomorpha sp. as chemo-protective agents, anticancer agents, and drug-delivery systems for the treatment of cancer (Jiang and Shi 2018; Rocha *et al.* 2018). The secondary metabolites found in *Chaetomorpha* sp. include phenols, sulfated polysaccharides, and halogenated chemicals, in addition to proteins, carbs, fatty acids, pigments, and more (Salehi *et al.,* 2019). GC-MS analysis of *C. ligustica* extracts revealed the presence of anticancer chemicals. Investigating *C. ligustica* and its biogenic nanoparticles for anticancer chemicals seems to be a promising endeavour. *C. ligustica* and the AgNPs it biosynthesises have tremendous promise as medicinal agents, particularly in the treatment of cancer. Nanoparticles were determined to be more harmful than the algal extract, while the cytotoxicity of AgNPs against cancer cell types was dose-dependent. Our results are well supported by Gurunathan *et al.* (Gurunathan *et al.,* 2018) reporting plant-based nanoparticles are more effective against HCT116 as compared to HT29 (Al-Zahrani *et al.* 2021).

Antimicrobial activity

Nanoparticle antimicrobials have several benefits over traditional antibiotics, including less acute toxicity, resistance prevention, and cost savings (Pal *et al.,* 2007; Weir *et al.,* 2008). Antibiotics in the NPs form may sustain for long run than in tiny molecules (Nisizawa and Mchaugh, 1988; Kathiraven *et al.,* 2015). Metal nanoparticles produced via green synthesis can serve as antioxidants, biosensors, and for the detection of heavy metals (Teodoro *et al.,* 2019; Akjouj and Mir, 2020; Chavan *et al.,* 2020). Their unique physicochemical properties make them ideal antimicrobial agents for use against plant disease pathogens and other organisms that can cause foodborne diseases. These agents have a large surface area to volume ratio, high surface reactivity, are easy to synthesise and characterise, have reduced cytotoxicity, and can enhance gene expression for redox processes (Bhattacharya and Mukherjee, 2008; Murphy *et al.,* 2008; Giljohann *et al.,* 2020; Pardhi *et al.,* 2020). A wide range of plant extracts have been studied for their potential antibacterial efficacy against bacterial and fungal plant diseases, and these nanoparticles have been synthesised from a number of plants (Ali *et al.,* 2019; Nishanthi *et al.,* 2019).

Bone healing

Silver nanoparticles have antibacterial capabilities, rendering them well-suited for the prevention of infections throughout the bone- mending process. Moreover, their diminutive size facilitates enhanced tissue penetration, hence accelerating and optimizing the healing process. Silver nanoparticles have been discovered to decrease inflammation and enhance cell proliferation, hence expediting the bone repair process. In general, their distinctive characteristics make them a potential choice for enhancing results in orthopaedic procedures.

Table 1. Antiviral activity of silver nanoparticles in different viruses and their family

Virus and family	AgNPs synthesis methods	Mechanism of Action	Main Features of and factors influencing the antiviral Activity	references
Respiratorysyncytial virus(RSV) (Paramyxoviridae family)	Curcumin-modified silvernanoparticles (cAgNPs)	Directvirus inactivation	Shape:/Size: 20nm Concentration: range 1.23–900 g/mL. C. A.e. Modification/functionalization:/ Exposuretime:90min	(Khandelwal *et al.,* 2014)
Vacciniavirus (VACV) (Poxvirus family)	AgNPs	Inhibition of viral entry through a micropinocytosis dependent mechanism	Shape:/Size:25nm 10nm Concentration:32 g/mL Modification/functionalization:/ Exposuretime:1h	(Trefry and Wooley, 2013)
Felinecalicivirus(FCV) (Calicidiviridae family)	AgNPs	Alteration of the viral capsid protein	Shape:spherical Size:10,75,110nm. Strongereffectwithsmallerdimension Concentration:25,50,100 g/mL. C. A.e. Modification/functionalization:/ Exposuretime:15min,30min,1h,2h,4h	(Bekele *et al.,* 2016)

Moreover, studies have shown that silver nanoparticles may improve the mechanical robustness of the repaired bone, resulting in enhanced bone quality as a whole. Due to their biocompatibility and capacity to enhance osteoblast activity, they are very beneficial in facilitating effective bone regeneration. Crystallized hydroxyapatite is the mineral that makes up human bones. Hydroxyapatite is a combination of calcium and phosphate. It is a commonly acknowledged and utilized sub stance for use in body implants. Biocompatible hydroxyapatite that has been combined with either metallic or ionic forms of silver is employed as a superficial implant material because it is an excellent choice for the creation of antibacterial and bioactive bone implants. These hydroxy apatite coatings coated with silver nanoparticles were discovered to be efficient inhibitors of both Gram-negative and Gram-positive bacteria (Bharti *et al.,* 2016; Meher *et al.,* 2024).

Antiviral activity

AgNPs have gained attention for their exceptional antibacterial properties. Despite their well-documented antibacterial efficiency, the interaction of AgNPs with viruses was overlooked until recent scientific research revealed their intriguing antiviral activity (Ghosh *et al.,* 2022).

These expanding investigations have demonstrated AgNPs' potential as powerful antiviral medicines, particularly against enveloped viruses (Galdiero *et al.,* 2011). The ease with which enveloped viruses are spread, their high rates of reproduction and mutation, and the current absence of comprehensive broad-spectrum antiviral medicines all contribute to the necessity for research into AgNP-virus interactions (Ghosh *et al.,* 2022). The rising threat of enveloped viruses contributing to imminent pandemics and biosafety concerns heightens the significance of this work (Mosidze *et al.,* 2025).

Catheters

Artificial catheters implanted in patients are highly inclined to contamination which leads to complications. Catheters made up of polyurethane are coated with silver nanoparticles for preventing biofilm formation. The silver nanoparticle-coated catheter is nontoxic and reduces bacterial growth and helps avoid Catheter-Associated Ventriculitis (Ahuja *et al.,* 2024).

Orthopaedic implants

The greatest challenge in orthopaedic surgery has always been bacterial contamination, so to reduce bacterial resistance, silver nanoparticles (AgNPs) were used to make the prosthesis. Silver nanoparticles also began to be used in orthodontic adhesive for increasing the shear bond strength and expanding resistance to bacteria(Ahuja *et al.,* 2024).

CONCLUSION

The review covers many synthetic approaches, including physical, chemical, and environmentally friendly biological processes. The biological synthesis is the simplest, quickest, and most cost-effective, commercial, ecologically friendly, and energy-efficient method for synthesizing silver nanoparticles. Chemical methods of producing silver nanoparticles offer advantages, but they are also dangerous and environmentally unfriendly.

This review examines the possibilities for mass-producing silver nanoparticles by a biological technique. Nanoparticles are believed to have several biomedical applications. It has a wide range of medicinal uses, including anti-cancer, antiviral, antibacterial, and antifungal properties, wound healing, and anticancer activity. Researchers are now developing green production methods for silver nanoparticles, which will be useful for biological applications. The limitations of standard medical therapy, as well as the challenges associated with nano-silver-based technologies, underscore the potential of silver nanoparticles in biology. Nanostructured biomaterials and technologies used in modern biomedicine may come into close contact with AgNPs.

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