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Review Article

Green Synthesis of Silver Nanoparticles for Potential Therapeutical Applications

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ABSTRACT

The advancement of nanotechnology has revolutionized the pharmaceutical sciences and enhanced the identification and management of numerous life-threatening illnesses. Many metallic nanoparticles have found broad application as nanomedicines due to their potential therapeutic applications. Among them, silver nanoparticles are unique due to their unique physical and chemical properties. The term "silver nanoparticles" (AgNPs) has gained a lot of attention recently. Their accessibility, chemical stability, conductivity, catalytic activity, biocompatibility, antibacterial activity, and inherent medicinal qualities are mostly to blame. AgNPs synthesis can be carried out by following three main methods: chemical, physical, and biological. Due to the use of dangerous chemicals or their exorbitant cost, several chemical and physical processes are less common nowadays. An appropriate replacement synthesis strategy for the conventional physical and chemical methodologies has been introduced by the biological method. Plant extracts have been found to be an eco-friendly and very efficient method for reducing, stabilizing, and coating AgNPs. The different types of nanoparticles, their reduction mechanisms, and environmentally friendly production methods employing commercially viable reducing materials including flowers, algae, and seaweeds are all covered in this paper. Apart from the eco-friendly methods, several biological activities such as wound healing, antiviral, antibacterial, antifungal qualities and anticancer activities are in detail. Therefore, we have focused on how silver nanoparticles enhance the toxic effects, drug release mechanism, and targeted medication administration. Therefore, we have focused on how silver nanoparticles enhance the toxic effects, drug release mechanism, and targeted medication administration. One of the easiest, most useful, most economical, and least harmful ways to utilize less dangerous chemicals is to make metal nanoparticles using plant extracts.

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Therefore, many environmentally acceptable ways for the rapid production of silver nanoparticles have been found recently using aqueous extracts of plant components such as leaves, bark, roots, etc. The most recent research on the ecologically friendly synthesis of silver nanoparticles (AgNPs) using various plant extracts and their possible uses as antibacterial agents is compiled in this review

INTRODUCTION

Rapid growth has made nanobiotechnology a crucial component of contemporary illness diagnosis and treatment. A class of environmentally benign, economically viable, and biocompatible substances known as biosynthesized silver nanoparticles (AgNPs) has garnered interest due to its potential uses in biomedicine and bioengineering. AgNPs have been extensively researched as parts of cutting-edge anticancer drugs to improve cancer treatment in the clinic, much like many other inorganic and organic nanoparticles, including AuNPs, iron oxide, and quantum dots. Usually, reducing agents react with silver ions to form AgNPs. Living things and natural products can be a superior and efficient source for the synthesis of AgNPs precursors, in addition to the many laboratory-based techniques for reducing silver ions. At the moment, biogenic AgNPs precursors are available to bacteria, fungi, and plants. ⁽¹⁾ A new age of opportunities in the medical field has been brought about by these special nanoparticles. Silver's remarkable antibacterial qualities make it essential for tissue regeneration, cancer treatment, infection prevention, and wound healing. AgNPs also have a lot of potential as contrast agents for cutting-edge medical imaging procedures and as adaptable drug carriers for targeted therapy. The green synthesis of AgNPs transforms medical procedures and satisfies the requirement of sustainability in a time marked by growing environmental concerns and the need for creative healthcare solutions, highlighting its crucial position at the intersection of nanotechnology and medicine. ⁽²⁾

Biological techniques, also referred to as "green synthesis," which are mostly carried out using medicinal plants, have advantages over physical and chemical methods due to their affordability, environmental friendliness, and accessibility. The implications of various parameters on green synthesis are covered in this publication, which also examines recent advancements in green synthesis, optimization conditions, processes, and characterisation methodologies for AgNPs, with an emphasis on the application of extracts from medicinal plants. UV-visible (UV-Vis) spectrophotometry, Fourier transform infrared (FTIR) spectroscopy, transmission electron microscopy (TEM), scanning electron microscopy (SEM), dynamic light scattering (DLS), X-ray diffraction (XRD), and zeta potential analysis are examples of standard characterization methods. Also covered are various uses for biosynthesized AgNPs derived from herbal plants. ⁽³⁾

Materials with special qualities are reduced to the size of individual atoms and molecules, which are referred to as nanoparticles. Usually, these particles are between 1 and 100 nm in size. Business, industrial, agricultural, and therapeutic applications are among the possible uses for these particles. Despite having the same chemical makeup as the parent material, nanoparticles can differ greatly in their strength, colour, magnetic and thermodynamic characteristics, and other physical attributes. The majority of nanomaterial uses in medicine are currently in the research and development phase, making this a relatively new field.

Human health is at risk worldwide due to the spread of multidrug-resistant (MDR) bacteria ^(4,5). By 2050, an illness will kill one person every three seconds, according to the Centres for Disease Control (CDC) ⁽⁶⁾. A staggering 722,000 cases of healthcare-associated infections were reported annually during the previous five years, and around 10% of those individuals passed away as a



result of their severe infections, according to a 2016 CDC report ⁽⁷⁾. The misuse of antibiotics and the formation of biofilm by a microbial population are two of the most important resistance mechanisms (8,9). A bacterial biofilm is a group of bacteria adhered to a surface and immersed in a matrix of extracellular protein, polysaccharides, and nucleic acids that the bacteria manufacture on their own ⁽¹⁰⁾. One common type of silver with antibacterial qualities is silver nitrate (NO₃⁻). Furthermore, because of their larger surface area, which exposes more microorganisms, silver nanoparticles are more advantageous than free silver. Additionally, because of their exceptional ability to combat a wide variety of bacteria and their resistance to widely used antibiotics, silver nanoparticles have become a highly sought-after area of study for scientists ⁽¹¹⁾. Food processing, agriculture and agro-based industries, biomedical and medical remediation, healthcare products, consumer goods, various industries, pharmaceuticals, diagnostics, orthopaedics, drug delivery, imaging, filters as antitumor agents, and as an enhancer of the tumour-killing effects of anticancer drugs are just a few of the fields where applications have been documented to date.

Numerous techniques are used to create the wide range of silver nanoparticles. Toxic substances in synthesis protocols must be avoided in environmental sustenance in order to prevent negative effects in medicinal applications. This requires the development of environmentally friendly processes.

Recent findings have motivated scientists to use biological systems to create safe nanoparticles utilizing yeast, bacteria, and plants or plant extracts—a process known as "green chemistry approaches"⁽¹¹⁾.

A team of scientists creates silver nanoparticles that are widely produced utilizing extracts from different plant leaves.

AgNPs can be created using both top-down and bottom-up methods. The top-down method uses methods like pattering and laser ablation to reduce a bulk material to nanoscales. The bottom-up strategy, on the other hand, refers to creating nanoparticles through smaller entities, like chemical and biological processes (Varadan et al., 2010).

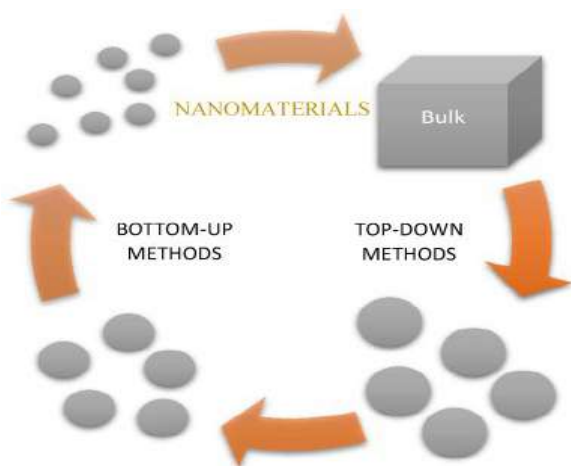
New and improved nano-methodologies have been introduced by the ongoing development of nanoscience and technology, making earlier strategies outdated. Because of the special qualities that nanoscale materials exhibit, nanotechnology has attracted a lot of attention and offers a wide range of potential uses in scientific study. It is impossible to overestimate the importance of using a green chemical approach when creating nanomaterials. This strategy appears to have the potential to produce environmentally friendly, sustainable nanomaterials that are ready for broad use in the field of nanobiotechnology. It is important to stress that the choice of reducing agents and solvents used in the synthesis of nanoparticles has a significant impact on the final particle morphology, including size, physicochemical characteristics, and shape. ⁽¹²⁾

Silver nanoparticles: synthesis, characterisation and biomedical applications.

1) Methods of synthesis of AgNPs

The two most popular approaches for producing nanoparticles are top-down and bottom-up. Top-down methods are physical processes that use tools to shape, cut, and mill materials. On the other hand, bottom-up processes—chemical or biological—are thought to be the most effective ways to create nanoparticles, as Fig. 1 illustrates. In these approaches, atoms or molecules self-assemble to produce larger particles. A number of recent research that have produced AgNPs utilizing various techniques are shown in Table 1.





2) Physical method

The two physical methods that are most commonly employed to produce nanoparticles are laser ablation and evaporation-condensation. These physical techniques allow AgNPs to be produced using a small ceramic heater⁽¹³⁾. For example, one study created AgNPs by laser-ablating large metallic particles in solution⁽¹⁴⁾. Physical approaches provide the advantages of fast synthesis and the lack of radiation or other dangerous reagents as reducing agents. However, these techniques have a number of disadvantages, such as low yield, high energy consumption, non-uniform dispersion, and solvent contamination⁽¹⁵⁾.

3) Chemical method

Trisodium citrate and sodium borohydride were used as stabilizing agents and AgNO₃ as a precursor to create AgNPs. Trisodium citrate and sodium borohydride, which have diameters of 60–100 nm and 5–20 nm, respectively, are efficient reducing agents for the synthesis of AgNPs. Polyvinyl alcohol and hydrazine hydrate have also been used as stabilizing and reducing agents in the synthesis of AgNPs. The biotechnology and biomedical areas can make use of the spherical nanoparticles⁽¹⁶⁾

One major benefit of chemical techniques over their physical equivalents is their ability to produce high yields of nanoparticles. Nevertheless, chemical processes are expensive,

and the chemicals that are utilized to make AgNPs—like citrate—are frequently hazardous and poisonous. Furthermore, it is extremely challenging to create AgNPs with a precise size, and extra precautions must be taken to prevent particle aggregation.⁽¹⁷⁾

4) Biological method

Since the beginning of life on Earth, biological beings and inorganic materials have been in close contact with one another. Life might exist on this planet with a well-organized mineral deposit because of this regular interaction. The relationship between biological species and inorganic molecules has recently piqued the curiosity of scientists. Numerous bacteria can generate inorganic nanoparticles via extracellular or intracellular pathways, according to studies. The synthesis of silver nanoparticles by biological processes is covered in this section.

5) Green synthesis

Green synthesis refers to the biological production of the nanoparticle, while Phyto-synthesis refers to the synthesis of nanoparticles using any plant species. Bioactive chemicals are known to be abundant in plants. Most plant species contain flavonoids, terpenoids, and phenols. These biological substances are essential to the bio-reduction process that creates AgNPs. Over the past ten years, interest in Phyto-nanotechnology has grown significantly. The photo-nano synthesis method is essential for the control size and unique shape. The chemical synthesis method has been replaced by the biosynthesis of AgNPs by plant species because the production of nano-silver from plants is less harmful and more advantageous than chemical synthesis. Numerous investigations toward the production of nano-silver have been documented⁽¹⁸⁾. Any part of the plant can be used for the green synthesis.

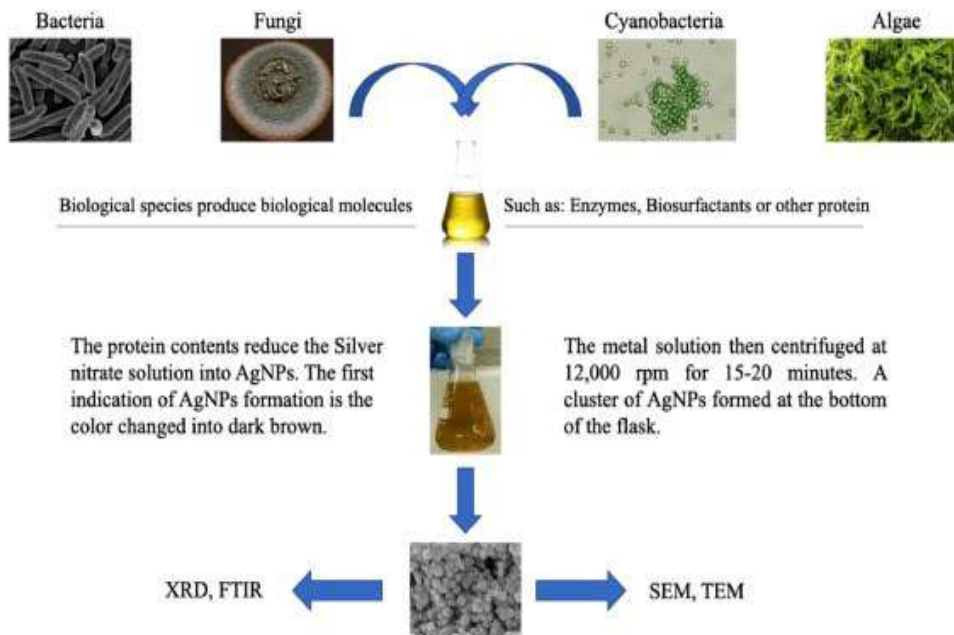


6) Microbial synthesis of silver nanoparticles

Microbial strains provide a highly easy, affordable, and environmentally friendly way to synthesize AgNPs. Microorganisms biosynthesize nanoparticles by capturing target ions from their surroundings and using enzymes produced by cell activity to convert the metal ions into element metal. The manufacture of AgNPs on the cell

surface and the creation of AgNPs by microorganisms within cells are two distinct processes.

Silver particles that are nanoscale have a high surface area to volume ratio. The silver salt can be readily reduced into AgNPs using microorganisms like fungi, bacteria, archaea, etc.; these methods are inexpensive and environmentally friendly.



Characterization of silver nanoparticles

The behaviour, biodistribution, safety, and effectiveness of nanoparticles are all influenced by their physicochemical characteristics. Consequently, it is crucial to characterize AgNPs in order to assess the functional characteristics of

the produced particles. Numerous analytical methods are used for characterization, such as atomic force microscopy (AFM), scanning electron microscopy (SEM), transmission electron microscopy (TEM), X-ray diffractometry (XRD), Fourier transform infrared spectroscopy (FTIR),

X-ray photoelectron spectroscopy (XPS), dynamic light scattering (DLS), and UV-vis spectroscopy. Although the ideas and use of many analytical techniques for the characterisation of AgNPs have been covered in a number of certified books and reviews, the fundamentals of the key approaches used for AgNP characterization are explained below for ease of understanding.

Green synthesis refers to environmentally friendly methods of producing chemicals, materials, or nanoparticles using natural compounds or biological processes. In the field of biomedicine, green synthesis has several promising applications, including:

1.Nanoparticle Synthesis: Green synthesis methods are often used to produce biocompatible nanoparticles for drug delivery, imaging, or diagnosing diseases. For example, plant extracts can reduce metal salts to form nanoparticles like silver, gold, or zinc oxide, which can have antimicrobial properties or enhance drug delivery mechanisms.

2.Drug Development: Natural compounds obtained through green synthesis can serve as lead compounds for drug development. Phytochemicals from plants can be extracted and modified to create new pharmaceuticals, reducing the environmental impact compared to conventional chemical synthesis.

3.Antimicrobial Agents: Compounds synthesized using green methods can exhibit resistance to antibiotic activity, addressing the growing issue of multidrug-resistant pathogens. Plant-based antimicrobials produced via green synthesis offer potential alternatives to synthetic antibiotics.

4.Vaccines and Biologics: Green synthesis techniques can be used to produce safer adjuvants (substances that enhance the immune response) and antigens (substances recognized by the immune system) derived from natural sources.

This can improve the efficacy and safety of vaccines.

5.Biomedical Imaging: Biocompatible nanoparticles, synthesized from bio-based materials, can be functionalized for targeted imaging in biomedical applications, allowing for improved diagnostics and monitoring of diseases.

6.Tissue Engineering: Green synthetic methods can create scaffolds or matrices using natural polymers like chitosan or cellulose for tissue engineering applications. These materials can promote cell adhesion, proliferation, and differentiation.

7.Biosensors: Green synthesized nanomaterials can be utilized in biosensors for the detection of pathogens, toxins, or biomarkers. These biosensors can be designed to provide rapid and accurate diagnostics with minimal environmental impact.

8.Regenerative Medicine: Plant-derived compounds and materials created through green synthesis can be used in regenerative medicine applications, promoting healing and tissue repair while minimizing adverse effects.

9.Natural Pigments for Imaging: Natural pigments extracted and processed using green synthesis methods can serve as contrast agents in various imaging modalities, providing a lower toxicity alternative to synthetic dyes.

By focusing on sustainability, green synthesis not only acknowledges the importance of eco-friendliness but also paves the way for innovations that align with the principles of biocompatibility and safety in biomedical applications.

CONCLUSION

Recent advances in nanoscience and nanotechnology have profoundly changed how we diagnose, treat, and prevent various diseases in every aspect of human life. AgNPs are one of the most studied nanostructures produced by nanotechnology in recent years due to their special properties and their size and shape-dependent



biomedical applications. Researchers from all around the world have been very interested in the many uses of green produced AgNPs and their enhanced antibacterial qualities. Among the different types of natural extract from biocomponents such as plants, yeast, fungi, etc., that are utilized to synthesize AgNPs, the plant extract has been shown to be extremely effective. By using this technique, less dangerous compounds are now used to create AgNPs. Since AgNPs have shown enormous and dynamic functions in the medical area, exhibiting anti-fungal, anti-bacterial, anti-diabetic, anti-cancer effects, etc., their applications are more extensive than those of other NPs. AgNPs derived from plants have shown great biological activity, significant toxicity to cancer cells, and low toxicity to healthy cells.

Furthermore, AgNP-based targeted drug delivery systems could be a future cancer therapeutic option. Their physicochemical properties have been investigated in order to create biosensors, especially for biomedical applications that will help with the diagnosis of various illnesses. In conclusion, expanding laboratory-based research to an industrial scale should be the main goal of future studies and development of the possible green synthesis of nanoparticles.

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