

Review Paper on the Analysis of Silver Nanoparticles (Ag-NPs) in Pharmaceutical and Biomedical Products

Type of paper: Review

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Abstract

Silver nanoparticles (Ag-NPs) are particles measuring between 1 and 100 nm in size. In the realm of green chemistry, Ag-NPs are synthesized by biological methods. This has thus augmented the likelihood of interactions between Ag-NPs and both terrestrial and aquatic ecosystems, along with possible exposure and damage to human health. The primary modes of entry for nanoparticles (NPs) are ingestion, inhalation, skin contact, and direct entry into systemic circulation. AgNPs accumulated in the duodenum as the initial contact site were subsequently transported to additional target organs. Developing innovative antibacterial agents, restoring tissue and regenerating materials, coatings for biomaterials and medical devices, and drug delivery formulations mainly based on applying AgNPs in biomedicine. Reports indicate that AgNPs can provoke cellular apoptosis, DNA damage, and oxidative stress in cells. This review concentrates on the most recent data concerning the biosynthesis methods, medicinal applications, and toxicity mechanisms of silver-based nanostructures. The toxicological effects of AgNPs vary according to their dimensions, morphology, surface charge, and coating. The molecular mechanisms responsible for the toxicity of silver nanoparticles encompass producing reactive oxygen species, disrupting cellular membranes, and activating proinflammatory cytokines.

Keywords: bio-administration, biosynthesis, nanotechnology, silver nanoparticles, toxic effects.

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1. Introduction

Nanotechnology has been a recognized study domain since the nineteenth century [1] and has been used in various industrial applications, experiencing exponential growth over the past five decades [2]. Nanotechnology is the science and engineering focused on the design, synthesis, characterization, and use of materials and devices with at least one dimension measuring on the nanoscale scale, or one billionth of a meter [3]. Nanoparticles (NPs) constitute the essential element of nanotechnology. They may consist of carbon, metals, metal oxides, or organic substances [4].

Furthermore, NPs can be synthesized utilizing two primary methods: the top-down method and the bottom-up one. The synthesis of NPs can occur through physical, chemical, and biological means. Notwithstanding the advantageous effects of chemical and physical procedures, there are notable disadvantages, including the elevated costs of synthesis, energy demands, the use of hazardous compounds, and environmentally detrimental processes [5, 6].

Nanotechnology is a rapidly advancing interdisciplinary field encompassing research and development in biology, chemistry, physics, food science, medicine, electronics, and aerospace.

Metallic nanoparticles, a novel term, have emerged in the domain of nanoparticles in recent years. Noble metals such as gold, silver, and platinum, which confer health benefits, are employed in the synthesis of NPs and referred to as metallic nanoparticles [6].

In little, controlled doses, silver nanoparticles could be applied in biomedical industry due to their physical, chemical and antibacterial properties. While, an acute doses or long term exposure could be toxic to vital cells [7]. AgNPs provide extensive applications in global scientific and technological domains. The principal aim of creating AgNPs methods is to exploit their distinctive qualities, including visual, electrical, high surface-to-volume ratio, and antibacterial attributes [8]. Recently, AgNPs have garnered significant interest due to their therapeutic uses in oncology such as anticancer medicines, in diagnostics, and in probing. However, there are certain detrimental effects associated with silver nanoparticles. Some studies indicate that the liver and lungs are primary sites affected by chronic exposure to AgNPs [9].

This review article examines recent advancements in synthesis, characterization, properties, and bio-applications, taking literature into account. It also highlights the mechanism underlying the toxicity of silver nanoparticles. The review ends with a conclusion and outlook on AgNPs.

2. Methodology and Literature Search Strategy

This study adopts a narrative review methodology to comprehensively synthesize and evaluate current literature regarding the synthesis, biomedical applications, and toxicological mechanisms of silver nanoparticles (Ag-NPs). A systematic search of electronic databases—including Web of Science, Scopus, PubMed, and Google Scholar—was conducted for peer-reviewed literature published up to 2024, utilizing keywords such as silver, nanotechnology, nanomaterials, biosynthesis, biomedical applications, and toxic effects. Articles focusing on physico-chemical properties, biological synthesis routes, therapeutic applications in drug delivery and tissue engineering. Cellular toxicity pathways (such as oxidative stress and apoptosis) were also described. This non-systematic approach provides a broad, critical overview of recent advancements and safety considerations concerning Ag-NPs in pharmaceutical and biomedical domains.

3. Synthesis Methods, Structure, and Properties

The morphology of AgNPs is contingent upon the synthesis conditions, preparation methodology, and the specific attributes of the reducing agents and stabilizers employed. Key characteristics of AgNPs include aspect ratio, crystal size, crystal density, surface chemistry, composition, coating, agglomeration, and overall morphology.

These properties encompass elevated electrical and thermal conductivity, antimicrobial efficacy, and optical characteristics (figure 1) [10].

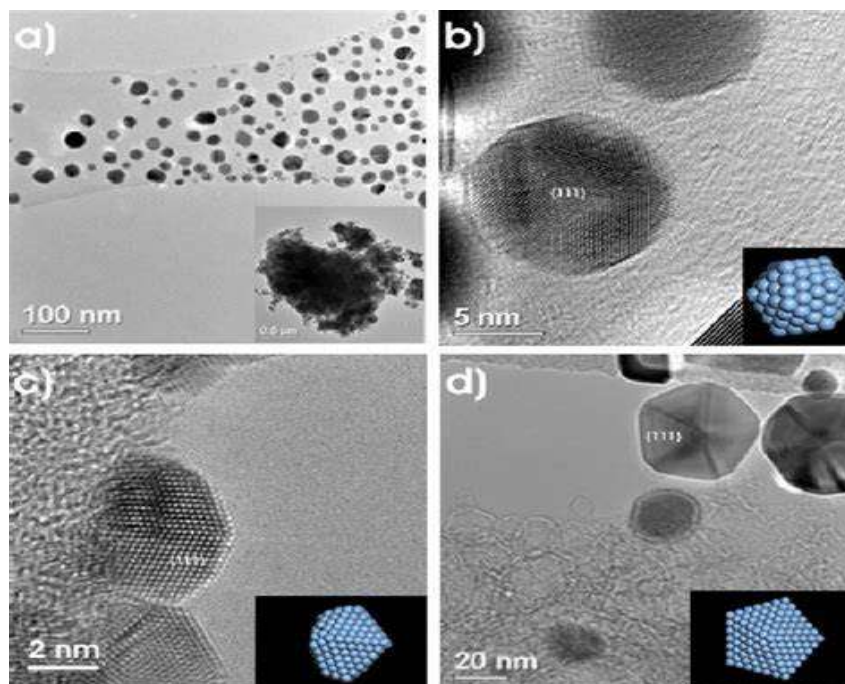


Figure 1. AgNPs. (a) TEM image depicting the AgNPs liberated from the carbon matrix; the inset highlights the agglomerated particles within the carbon matrix. (b)-(d) Predominant morphologies of the used particles. The {111} facets are designated, and their corresponding models are illustrated as insets: (b) Icosahedral particle, (c) twinned particle, and (d) decahedral particle seen in the [100] orientation [11].

The two primary methods employed for nanoparticle synthesis are top-down and bottom-up strategies. These methods include three synthesis techniques: physical, biological, and chemical (figure 2). The physical technique employs a top-down method, while biological and chemical techniques often adopt a bottom-up method [10].

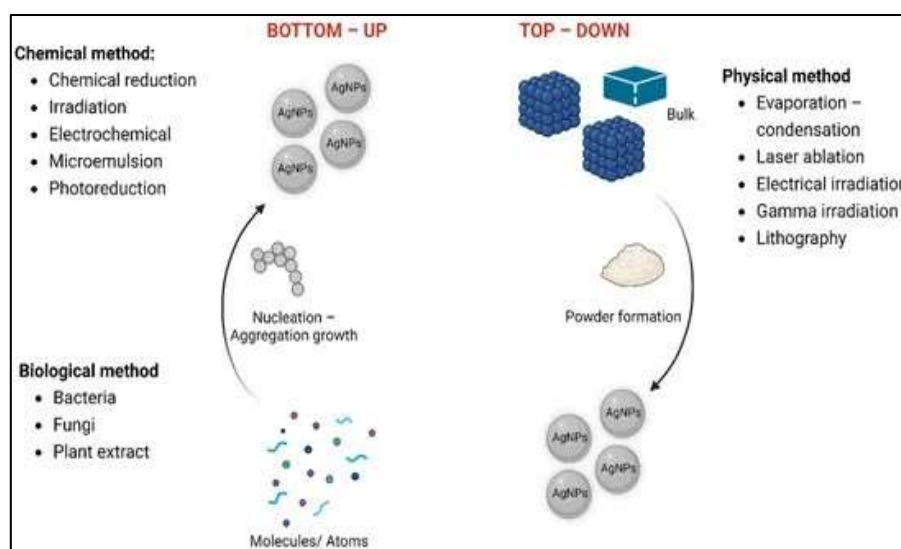


Figure 2. Synthesis of AgNP via top-down and bottom-up methods. The top-down method involves the formation of NPs from bulk materials, whereas the bottom-up method entails the assembly of NPs from molecular components [12].

Evaporation-condensation and laser ablation are the principal physical techniques. The lack of solvent contamination in the fabricated thin films and the uniform distribution of NPs are the benefits of physical synthesis techniques. The physical production of AgNPs using a tube furnace at atmospheric pressure presents certain drawbacks [13].

The synthesis of metal nanoparticles in solution involves three components: i) metal precursor; ii) reducing agent; and iii) stabilizing agent. The creation method of colloidal solutions from silver (I) ion reactions comprise two stages: nucleation and growth [14, 15].

The biological method, or green synthesis, seeks to minimize waste, mitigate environmental effects, and utilize sustainable, renewable resources. This approach employs microbes, algae, and plants. The improved antibacterial effectiveness of the biosynthesized AgNP was ascribed to their advantageous surface-to-volume ratio and crystalline configuration. These NPs displayed strong antibacterial activity against Gram-positive and Gram-negative bacterial strains and exhibited notable antioxidant characteristics. Nonetheless, the microbial technique presents drawbacks due to its time-consuming nature and the complexities involved in culture maintenance. Currently, NPs are synthesized utilizing various components of plant sources. The primary benefits of plant-based extracts for the synthesis of AgNPs are their availability, safety, and non-toxicity under harsh conditions [16].

4. Biological Applications

The biological application of AgNPs has been pivotal in the advancement of sophisticated antibacterial agents, tissue repair and regeneration materials, coatings for biomaterials and medical devices, drug delivery systems, diagnostic platforms, and improved therapeutic alternatives. Silver nanoparticles have prospective applications in antioxidative, anti-inflammatory, antibacterial, antiviral, and anticancer therapy. In addition, silver nanoparticles have the potential to serve as additives in a wide range of medical devices and materials. These include bone cement, membranes, dental implants, denture bases, fractured bones, catheters, and hydrogels. These additives have the ability to prevent or reduce the growth of biofilms or other medical pathogens, while also promoting and accelerating the healing process for bone growth, wounds, and gums (figure 3) [6,17].

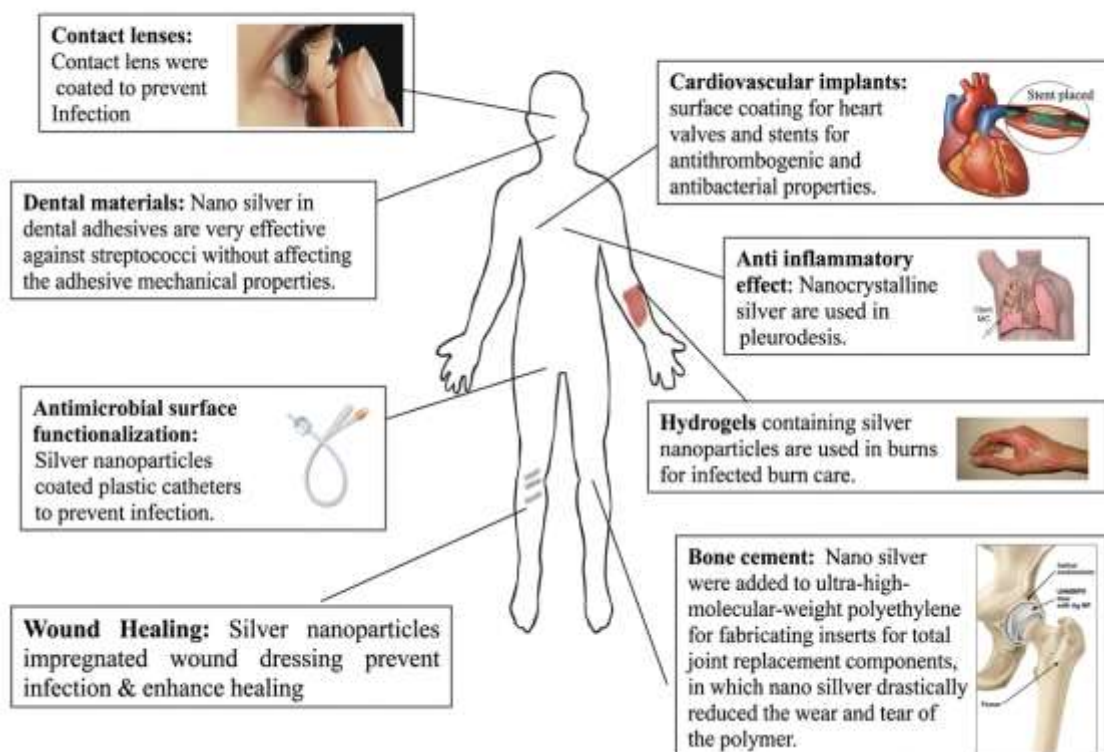


Figure 3. Biomedical applications of AgNPs [18].

5. Pharmacokinetics and Toxicity

The absorption mechanism of NPs is more intricate than that of small molecules. Orally administered nanoparticles can be absorbed via paracellular transport, transcytosis, and M cell uptake in the gastrointestinal system, whereas macrophages and lymphatic uptake absorb intramuscular or inhaled NPs subcutaneously.

The in vivo distribution of NPs relies on several transport mechanisms. Silver has been observed to accumulate as particles in tissues, including the skin epidermis, glomeruli, and intestines, after oral exposure to both ionic and nanoparticulate silver solutions. Certain studies indicated diminished silver excretion in urine, although elevated levels in feces [19, 20].

Upon entering the biological system, NPs may instigate biochemical transformations, resulting in secondary particles that can have prolonged detrimental effects on human health. Numerous studies have documented the absorption and pharmacotoxicity of orally administered AgNPs in different organs. For instance, AgNPs induced developmental and structural deformities in model organisms, along with histopathological abnormalities in the spleen, liver, skin, and other organs, as well as immune-toxic and genotoxic effects, including alterations to the glomerular basement membrane [20]. Concerning cerebral absorption, silver delivered via drinking water was concentrated in the glial cells and neurons of the hippocampus, where its impact was not associated with oxidative stress [21]. Conversely, multiple studies have demonstrated that low-level exposure induces oxidative stress and impairs mitochondrial function (figure 4) [19].

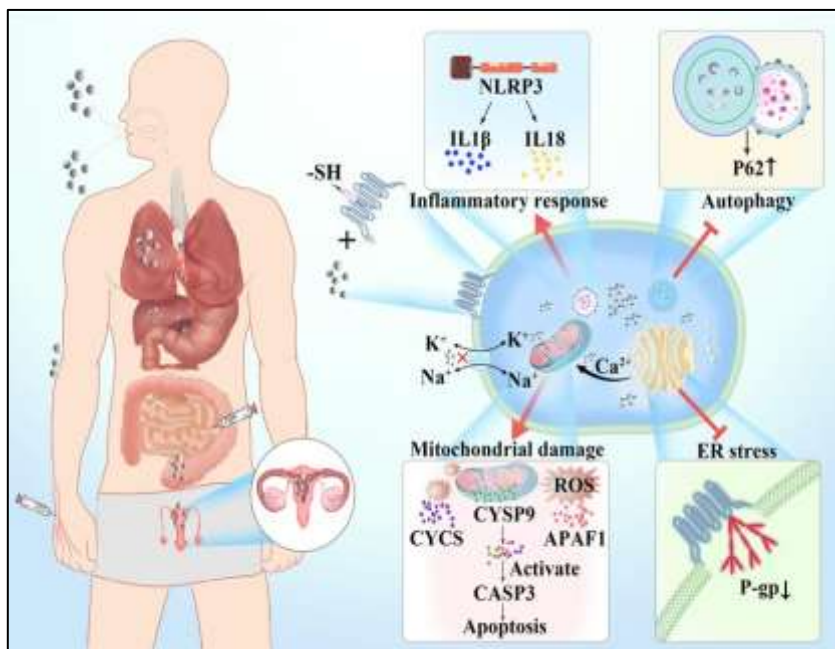


Figure 4. Mechanisms of cellular ingress and cytotoxicity pathways associated with nanosilver. [21].

6. Conclusion

Silver nanoparticles present promising therapeutic approaches for managing dental infections, metabolic disorders, and neurodegenerative conditions, alongside expanding utility in biochemical engineering. To optimize efficacy and minimize biosafety risks, strategies such as green synthesis optimization, precise morphological control, surface functionalization, and targeted drug-loading systems should be implemented. Rigorous biocompatibility assessments and low-dose administration protocols remain essential to prevent adverse effects on non-target biological tissues.

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8. Conflict of interest statement

The authors certify that there is no conflict of interest with any financial organization regarding the subject matter or materials discussed in this manuscript.

9. Authors' biography

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