Illuminating the Expanding Frontiers of Silver Nanoparticles: A Comprehensive Review of Synthesis, Mechanisms, and Applications

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Abstract

Silver nanoparticles (AgNPs) continue to play a pivotal role in nanotechnology, finding wide applications across healthcare, environmental remediation, food packaging, and agriculture. Their unparalleled antimicrobial, antifungal, antiviral, and anticancer properties stem from a unique combination of large surface area, shape-dependent electronic configurations, and the ability to release bioactive silver ions. This review offers a comprehensive examination of AgNPs, starting with a discussion of different synthesis pathways—chemical reduction, green synthesis, and physical methods such as laser ablation and ball milling. It then explores the diverse mechanisms underlying their broad-spectrum antimicrobial and antiviral activities, emphasizing the significance of reactive oxygen species (ROS) production, membrane disruption, and intracellular interference with proteins and DNA. The paper also highlights the importance of characterization techniques, including electron microscopy, X-ray diffraction, dynamic light scattering, and zeta potential measurement, for confirming particle morphology and stability. In addition to antibacterial and antifungal applications, recent findings on the antiviral potential of AgNPs against influenza, HIV, and emerging coronaviruses are discussed, alongside novel anticancer strategies leveraging ROS-mediated cytotoxicity and drug delivery enhancements. The review concludes by addressing key safety and toxicity concerns, underscoring the role of green synthesis and targeted design strategies in ensuring responsible use. Emerging research areas—ranging from Ångström-scale silver clusters to multifunctional theranostic systems—point to an evolving landscape where AgNPs can continue to address critical challenges in science and technology.

Keywords: *Silver nanoparticles, Nanotechnology, Green synthesis, Antimicrobial mechanisms, Antiviral applications, Anticancer strategies, Characterization techniques, Toxicity, Reactive oxygen species, Drug delivery*.

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1. INTRODUCTION

Metal-based nanomaterials continue to reshape modern science and technology by enabling innovative solutions to longstanding challenges. Among them, silver nanoparticles (AgNPs) have garnered immense attention as multifunctional platforms suitable for diverse applications—ranging from biomedicine and food preservation to environmental remediation (Bruna, Maldonado-Bravo, Jara, & Caro, 2021). Their potent antimicrobial, antiviral, antifungal, and anticancer activities, coupled with their unique optical, electrical, and catalytic properties, have established silver nanoparticles at the forefront of nanotechnology research (Menichetti, Mavridi-Printezi, Mordini, & Montalti, 2023).

Over the years, the field has advanced significantly, shedding light on the core mechanisms responsible for AgNP efficacy. These mechanisms include reactive oxygen species (ROS) generation (Park et al., 2009), membrane disruption (Li et al., 2016), and direct interactions with nucleic acids and protein complexes (Yin et al., 2020). Moreover, studies examining the size-, shape-, and surface-functionalization dependence of AgNP effects have become pivotal to understanding how best to optimize these nanomaterials for specific tasks (More et al., 2023). While silver nanoparticles offer numerous advantages, pressing concerns about toxicity, safe design, and environmental impact have also spurred extensive research to elucidate and mitigate risks (Nie, Zhao, & Xu, 2023).

This review aims to provide a detailed exploration of the current state of silver nanoparticle research, focusing on their synthesis routes, mechanistic insights, and broad-spectrum applications. We also highlight the key considerations necessary for achieving safe and effective use in various domains. By drawing on the latest findings—ranging from antibacterial and antifungal activities to antiviral and anticancer potentials—this comprehensive synthesis aims to support continued innovation in AgNP-related technologies.

2. Classification and Overview of Silver Nanoparticles

2.1 Historical Evolution

Silver has been employed as an antimicrobial agent for centuries, from ancient water vessels to modern wound dressings (Bruna et al., 2021). As nanotechnology emerged, a pivotal shift occurred: scientists discovered that silver's beneficial properties become dramatically enhanced at the nanoscale. The large surface area of nanosilver allows more efficient ion release and interactions with microbial membranes, leading to stronger biocidal activity (Yin et al., 2020).

2.2 General Attributes

Silver nanoparticles typically range in size from 1 to 100 nm and can assume various morphologies, including spherical, rod-shaped, triangular, plate-like, and multi-branched structures (Menichetti et al., 2023). This morphological diversity allows researchers to fine-tune physical and chemical properties—such as surface area, catalytic potential, optical absorption (via localized surface plasmon resonance, LSPR), and biological interactions (Li et al., 2016).

2.2.1 Size-Dependent Properties

- **Surface Area**: Smaller AgNPs exhibit higher surface area-to-volume ratios, thus increasing active sites for antimicrobial or catalytic reactions (Park et al., 2009).
- **Ion Release**: Smaller nanoparticles can release silver ions more readily, potentiating their bactericidal effects (Nie et al., 2023).
- **Cellular Uptake**: Nano-scale dimensions facilitate internalization by microbial and mammalian cells, influencing toxicity and therapeutic efficacy (Yin et al., 2020).

2.2.2 Shape-Dependent Properties

- **Nanorods**: Often exhibit multiple LSPR peaks, making them ideal for certain sensing and photothermal applications (Menichetti et al., 2023).
- **Nano-plates**: Larger surface area on planar facets can enhance interactions with bacterial membranes (Li et al., 2016).
- **Spherical Particles**: Typically yield more uniform properties but may exhibit reduced surface contact compared to anisotropic shapes (Bruna et al., 2021).

2.3 Relevance Across Disciplines

Silver nanoparticles are at the interface of materials science, life sciences, and environmental engineering. They appear in:

- **Medical Devices**: Wound dressings, surgical instruments, and catheters (Bruna et al., 2021).
- **Dentistry**: Dental fillings, sealants, and disinfecting solutions (Yin et al., 2020).
- **Food Packaging**: Active packaging films to extend shelf life by preventing microbial contamination (Istiqola & Syafiuddin, 2020).
- **Water Treatment**: Nanofiltration and disinfection to inhibit microbial growth in water systems (Rangaraju et al., 2024).

- **Agriculture**: Controlling pathogenic bacteria and fungi on crops (Urnukhsaikhan, Bold, Gunbileg, Sukhbaatar, & Mishig-Ochir, 2021).

By mapping silver nanoparticle features—size, shape, surface chemistry—to their target application, researchers can more precisely engineer next-generation nanotechnologies (Menichetti et al., 2023).

3. Synthesis of Silver Nanoparticles

3.1 Chemical Reduction Methods

Traditional bottom-up synthesis involves chemically reducing silver salts (e.g., silver nitrate) in the presence of reducing agents such as sodium borohydride, ascorbic acid, or hydrazine (Keshari, Srivastava, Singh, Yadav, & Nath, 2020). Stabilizers or surfactants, like polyvinylpyrrolidone (PVP) or citrate, are often added to prevent agglomeration:

1. **One-Pot Chemical Reduction**: Commonly produces spherical AgNPs with relatively narrow size distributions (Nie et al., 2023).
2. **Polyol Process**: Ethylene glycol or other polyols act as both solvent and reducing agent, yielding nanoparticles with specialized morphologies (Li et al., 2016).

Advantages: Straightforward, scalable, and consistent.

Limitations: Potential use of toxic chemicals; leftover reaction byproducts may impact biological applications (Van Dong, Ha, Binh, & Kasbohm, 2012).

3.2 Green Synthesis

Green or biological synthesis leverages plant extracts (Keshari et al., 2020), microbial cultures (Ghodake et al., 2020), or other biogenic materials (Urnukhsaikhan et al., 2021) as reducing and capping agents. This approach aligns with eco-friendly principles, reducing the reliance on harsh chemicals and generating biocompatible nanoparticles:

1. **Plant Extracts**: Rich in phenolics, flavonoids, and carbohydrates that facilitate the reduction of silver ions to metallic silver (Khan et al., 2018).
2. **Microbial Synthesis**: Bacteria or fungi such as *Stenotrophomonas maltophilia* can produce AgNPs extracellularly (Oves et al., 2013).
3. **Algal or Lichen Synthesis**: Less commonly explored but promising for large-scale production with minimal environmental footprint (Urnukhsaikhan et al., 2021).

Advantages: Low toxicity, fewer byproducts, and generally safer handling.

Limitations: Sometimes challenging to control particle size and shape; potential batch-to-batch variability (Singh et al., 2015).

3.3 Physical Methods (Top-Down Synthesis)

3.3.1 Laser Ablation

In laser ablation, a high-energy laser pulse strikes a silver target submerged in a liquid medium, resulting in the ejection of silver atoms that subsequently condense into nanoparticles (Sadrolhosseini, Mahdi, Alizadeh, & Rashid, 2018). Adjusting the laser wavelength, fluence, and pulse duration can fine-tune particle size:

- **Advantages**: Free of chemical reducing agents, minimal contamination risk.
- **Limitations**: Low yields, high equipment costs, and sometimes broad size distributions (Boutinguiza et al., 2015).

3.3.2 Arc Discharge

Arc discharge forms a plasma between electrodes composed of silver, causing molten droplets to condense into nanoscale particles (Tien et al., 2008). Modulating the arc current and electrode gap helps control particle formation:

- **Advantages**: Produces highly pure nanoparticles.
- **Limitations**: Demanding operational conditions, specialized equipment.

3.3.3 High-Energy Ball Milling

Ball milling involves mechanical attrition: silver powders are repeatedly fractured and welded by grinding media, gradually reducing particle size (Khayati & Janghorban, 2012). Process control agents and milling parameters (rotation speed, milling duration) influence the resultant nanoparticle characteristics:

- **Advantages**: Suitable for bulk production, relatively simple.
- **Limitations**: Potential contamination from milling media, polydisperse size distributions (Xing et al., 2013).

3.4 Emerging Hybrid Approaches

Recent advances integrate chemical or biological routes with mechanical or physical processes to optimize yield, reduce toxicity, and achieve better morphological control (Stagon & Huang, 2013). For instance, laser ablation in reactive media can help form specialized capping layers in situ, while mechanochemical methods combine ball milling with subsequent chemical reduction steps (Jayaramudu et al., 2016).

4. Mechanisms of Action: Antibacterial, Antifungal, Antiviral, and Beyond

Silver nanoparticles exert broad-spectrum antimicrobial effects through multiple, often interlinked, mechanisms (Bruna et al., 2021; Yin et al., 2020). Understanding these pathways is vital for designing effective nanosilver-based therapeutics and materials.

4.1 Antibacterial Action

4.1.1 Ion Release and ROS Generation

One prevailing theory is that AgNPs dissolve partially to release silver ions (Ag^+), which bind to bacterial cell components, inactivating enzymes and disrupting membrane permeability (Li et al., 2016; Park et al., 2009). Additionally, AgNPs can induce the production of reactive oxygen species (ROS), such as hydroxyl radicals and superoxide anions, which damage proteins, lipids, and nucleic acids (Dakal, Kumar, Majumdar, & Yadav, 2016).

4.1.2 Membrane Disruption

Direct contact between AgNPs and bacterial cell walls can cause mechanical disruption. Positively charged nanoparticles can also interact more favorably with negatively charged bacterial surfaces, leading to enhanced uptake and cell damage (Romero-Urbina et al., 2015). Changes in membrane potential, loss of integrity, and leakage of intracellular contents eventually lead to cell death (Yin et al., 2020).

4.1.3 Protein and DNA Interference

Silver ions and nanoparticles can form complexes with thiol groups in proteins, inhibiting key metabolic enzymes (Li et al., 2016). Additionally, nanosilver may intercalate with DNA bases, inhibiting replication and transcription (Park et al., 2009).

4.1.4 Influence of Size, Shape, and Surface Functionalization

- **Size**: Smaller AgNPs possess enhanced antibacterial activity due to greater surface area contact and faster ion release (Khan et al., 2021).
- **Shape**: Studies reveal that rod-shaped, triangular, and flower-like morphologies may demonstrate superior activity compared to spheres, although results can vary by strain (Van Dong et al., 2012).
- **Surface Coatings**: PEGylation or chitosan coatings can modulate nanoparticle interactions with bacterial cell walls, altering antibacterial efficacy (Mumtaz et al., 2023).

4.2 Antifungal Activity

Fungal pathogens present additional challenges for healthcare and agriculture. Silver nanoparticles have shown efficacy against various fungal species, including *Candida*, *Aspergillus*, and *Fusarium* (Żarowska et al., 2019; Li et al., 2022). Mechanisms largely parallel antibacterial pathways:

1. **Membrane Permeabilization**: AgNPs interact with ergosterol and phospholipids in fungal cell

membranes, causing morphological changes and leakage of cytoplasmic content (Xue et al., 2016).

2. **ROS-Induced Damage**: Nanosilver-mediated ROS production disrupts fungal intracellular components (Panáček et al., 2009).
3. **Surface Charge Interactions**: Cationic AgNPs bind strongly to the negatively charged fungal cell wall, enhancing internalization (Matras et al., 2022).

Silver nanoparticles also see application in antifungal textiles and coatings designed to inhibit mold growth on surfaces (Ratnasari & Endarko, 2020). In agriculture, antifungal AgNPs provide an alternative to chemical fungicides for controlling post-harvest rot in fruits (Vieira, de Matos Fonseca, Menezes, Monteiro, & Valencia, 2020).

4.3 Antiviral Activity

Recent studies highlight the potential of AgNPs to combat a range of viruses, including influenza, HIV, and coronaviruses (Naumenko, Zahorodnia, Pop, & Rizun, 2023; Ratan et al., 2021; Jeremiah, Miyakawa, Morita, Yamaoka, & Ryo, 2020). Proposed mechanisms include:

1. **Viral Inactivation**: AgNPs bind to viral envelope proteins or spike proteins, preventing viral attachment and entry into host cells (Luceri, Francese, Lembo, Ferraris, & Balagna, 2023).
2. **Disruption of Viral Genomic Material**: Intracellularly, AgNPs may hinder viral replication by interacting with viral RNA or DNA (Elechiguerra et al., 2005).
3. **Particle Size and Coating Effects**: Smaller particles (e.g., 2–15 nm) demonstrate higher antiviral efficacy, particularly when coated with biocompatible agents that facilitate target-specific delivery (He et al., 2022).

Studies on SARS-CoV-2 suggest that specially engineered silver nanoparticles can reduce viral infectivity (Almanza-Reyes et al., 2021). This has prompted investigations into embedding AgNPs in personal protective equipment (Abulikemu et al., 2022), coatings, and air filtration systems (Srikhao et al., 2023; Noppradit et al., 2023).

4.4 Anticancer and Cytotoxic Mechanisms

Silver nanoparticles also exhibit selective cytotoxicity against cancer cells (Abass Sofi, Sunitha, Ashaq Sofi, Khadheer Pasha, & Choi, 2022). Key mechanisms include:

1. **ROS Generation and Oxidative Stress**: Elevated ROS levels induce apoptosis, autophagy, or necrosis in

tumor cells (Farah et al., 2016; Piao et al., 2011).
2. **DNA Damage**: AgNPs can disrupt the DNA double helix in rapidly dividing cancer cells (Takáč et al., 2023).
3. **Mitochondrial Dysfunction**: Mitochondrial membrane potential loss triggers cell death pathways (Mao, Tsai, Chen, Yan, & Wang, 2016).
4. **Drug Carrier Potential**: Researchers are exploring silver–drug conjugates for synergistic anti-tumor action (Kim et al., 2021; Namulinda et al., 2024).

Although promising, the therapeutic use of AgNPs in oncology demands rigorous evaluation of toxicity, dosage, and clearance pathways (Al-Khedhairy & Wahab, 2022; Pavan, Venkatesan, & Prabhu, 2022).

4.5 Wound Healing and Anti-Inflammatory Effects

In wound care, AgNPs accelerate healing by preventing infection and modulating inflammation (Kong et al., 2022). Their bioactivity can promote keratinocyte and fibroblast proliferation while minimizing chronic inflammation (Craciunescu, Seciu, & Zarnescu, 2021):

1. **Reduced Bacterial Load**: Preventing infection helps maintain an optimal healing environment (Sabarathinam, 2021).
2. **Regulation of Pro-Inflammatory Cytokines**: AgNPs can reduce cytokine overproduction, thereby facilitating tissue repair (Adeleye et al., 2020).
3. **Green Synthesis Approaches**: Biosynthesized AgNPs often exhibit potent anti-inflammatory effects, especially when derived from medicinal plants (Khashan & Dawood, 2023).

5. Characterization Techniques

Accurate characterization underpins the successful development and application of AgNPs (Ivanov et al., 2023). Each method serves a distinct purpose, from confirming nanoparticle formation to ascertaining stability, size, shape, and surface chemistry.

5.1 Optical Characterization

5.1.1 UV–Vis Spectroscopy

A standard, quick method to detect the surface plasmon resonance (SPR) peak of silver nanoparticles, typically ranging from 380 to 460 nm depending on size and shape (Li et al., 2016). Shifts in peak intensity and wavelength can indicate changes in particle aggregation or morphology (Menichetti et al., 2023).

5.1.2 Photoluminescence and Fluorescence Spectroscopy

Useful for examining electronic transitions and functional group interactions, although silver nanoparticles generally exhibit weak intrinsic fluorescence (Ivanov et al., 2023). Conjugation with fluorescent tags can facilitate imaging and biosensing.

5.2 Electron Microscopy

5.2.1 Transmission Electron Microscopy (TEM)

TEM provides high-resolution images, revealing particle size distributions, morphologies, and crystallographic features (Amendola & Meneghetti, 2009). For silver nanoparticles, lattice fringes corresponding to the face-centered cubic (fcc) structure are common.

5.2.2 Scanning Electron Microscopy (SEM)

SEM images the surface topology of nanoparticles or nanoparticle-coated surfaces at high magnification, though resolution is generally lower than TEM. Coupled with energy-dispersive X-ray spectroscopy (EDS), SEM can confirm elemental composition (Ivanov et al., 2023).

5.3 X-Ray Diffraction (XRD)

XRD is crucial for identifying the crystalline phases of silver (Stagon & Huang, 2013). Characteristic Bragg reflections at 2θ angles of about 38°, 44°, 64°, and 77° correspond to the (111), (200), (220), and (311) planes, confirming an fcc structure (Khayati & Janghorban, 2012).

5.4 Dynamic Light Scattering (DLS) and Zeta Potential

- **DLS**: Measures hydrodynamic diameter in colloidal suspensions, providing a mean particle size and polydispersity index (Nie et al., 2023).
- **Zeta Potential**: Evaluates surface charge and colloidal stability. Highly positive or negative zeta potential values generally confer better dispersion (Li et al., 2016).

5.5 Spectroscopic Techniques for Surface Chemistry

- **Fourier Transform Infrared (FTIR)**: Identifies functional groups from capping agents or ligands (Li et al., 2016).
- **X-ray Photoelectron Spectroscopy (XPS)**: Explores surface elements and oxidation states, critical for verifying silver’s metallic or ionic forms (Amendola & Meneghetti, 2009).

5.6 Other Methods

- **Thermogravimetric Analysis (TGA)**: Assesses thermal stability and capping agent content (Khayati & Janghorban, 2012).
- **Inductively Coupled Plasma Mass Spectrometry (ICP-MS)**: Quantifies silver ion release, relevant for toxicity studies (Bruna et al., 2021).

Taken together, these techniques form a robust toolkit for characterizing AgNPs, guiding rational design for specific applications. Researchers often employ multiple methods to build a comprehensive profile of the nanoparticle system under study.

6. Antibacterial Applications

6.1 Medical Devices and Coatings

The potent antibacterial properties of AgNPs are leveraged in implants, catheters, and wound dressings to reduce infection rates (Sabarathinam, 2021). In dentistry, silver nanoparticle-containing mouthwashes and fillings demonstrate broad-spectrum antibacterial activity to combat oral pathogens (Yin et al., 2020):

- **Wound Healing Dressings**: Accelerated tissue regeneration and infection control (Kong et al., 2022).
- **Dental Sealants and Fillings**: Inhibit biofilm formation, reducing the risk of secondary caries (Yin et al., 2020).
- **Suture Materials**: Coated sutures reduce surgical site infections and post-operative complications (Sabarathinam, 2021).

6.2 Food Preservation and Packaging

Active packaging materials incorporating silver nanoparticles can inhibit bacterial growth on food surfaces, extending shelf life (Istiqola & Syafiuddin, 2020). Nanocomposite films with embedded AgNPs have been tested on fruits and meat products, effectively reducing microbial contamination (Vieira et al., 2020).

6.3 Water Disinfection

Nanosilver-based filtration systems target pathogenic bacteria, offering a non-chlorine alternative for water treatment (Rangaraju et al., 2024). Coating membranes or resins with AgNPs can also reduce biofilm accumulation (Bruna et al., 2021). Despite their efficacy, concerns persist about nanoparticle leaching and environmental impact, underscoring the need for responsible design (Nie et al., 2023).

6.4 Antibiotic-Resistant Pathogens

The rise in multidrug-resistant bacteria drives demand for novel antimicrobial strategies (More et al., 2023). Silver nanoparticles, sometimes combined with conventional antibiotics, show synergistic effects, revitalizing the efficacy of older drugs (Menichetti et al., 2023). By disrupting cell membranes and metabolic pathways, AgNPs can reduce the frequency of resistance mutations (Dakal et al., 2016).

7. Antifungal and Antiviral Applications

7.1 Combatting Fungal Infections

7.1.1 Medical Mycology

Fungal infections, particularly in immunocompromised patients, pose significant clinical challenges. AgNP-based formulations have demonstrated success against *Candida albicans* and other species by disrupting cell membranes and metabolic pathways (Panáček et al., 2009). New research also explores synergy with antifungal medications, potentially lowering drug dosage and reducing side effects (Żarowska et al., 2019).

7.1.2 Agricultural Impact

Fungal pathogens are a major source of post-harvest losses worldwide. Silver nanoparticle treatments on produce such as kiwifruit and papaya have shown efficacy in reducing decay caused by *Fusarium*, *Botrytis cinerea*, and other common fungi (Li et al., 2022; Vieira et al., 2020). Field trials and large-scale implementations underscore the promise of nanosilver-based fungicides with lower environmental persistence compared to conventional chemicals (Xue et al., 2016).

7.2 Antiviral Prospects

7.2.1 Targeting Influenza and Respiratory Viruses

Silver nanoparticles effectively disrupt viral surface glycoproteins, such as hemagglutinin and neuraminidase, hampering viral attachment and replication in host cells (Naumenko et al., 2023). They can also reduce cytokine storms, a severe complication in viral infections (Ratan et al., 2021).

7.2.2 HIV and Other Retroviruses

Early work showed nanosilver binding to HIV-1 gp120, blocking virus-to-cell fusion (Elechiguerra et al., 2005). The effect depends on size and surface functionalization; smaller nanoparticles (~10 nm) appear more potent than larger ones. Ongoing research focuses on designing nano-formulations that minimize systemic toxicity while maintaining antiviral efficacy (Luceri et al., 2023).

7.2.3 SARS-CoV-2

The COVID-19 pandemic accelerated research on AgNP antiviral applications. In vitro studies report significantly reduced infectivity of SARS-CoV-2 upon exposure to silver nanoparticles (Jeremiah et al., 2020). Coatings on masks, protective garments, and high-touch surfaces are explored as additional layers of defense (Abulikemu et al., 2022; Srikhao et al., 2023). Some researchers also investigate the synergy of nanosilver with other antiviral agents to curb viral replication more effectively (He et al., 2022; Noppradit et al., 2023).

8. Anticancer Applications

8.1 Cytotoxic Mechanisms Against Tumor Cells

Silver nanoparticles exhibit selective toxicity to cancer cells through multiple mechanisms, including the generation of reactive oxygen species (ROS), perturbation of mitochondrial function, and DNA damage (Farah et al., 2016; Piao et al., 2011). Cells with high proliferation rates are more susceptible to these disruptions, allowing targeted killing in some tumor models (Mao et al., 2016).

8.2 Photothermal and Photodynamic Therapies

1. **Photothermal Therapy**: AgNPs can absorb near-infrared radiation and convert it to heat, destroying tumor cells via hyperthermia (Kim et al., 2021).
2. **Photodynamic Therapy (PDT)**: When coupled with photosensitizers, AgNPs can boost the generation of cytotoxic singlet oxygen, enhancing PDT efficacy (Namulinda et al., 2024).

8.3 Synergistic Drug Delivery

Functionalizing silver nanoparticles with chemotherapeutic drugs or gene therapies offers the potential for a combined assault on tumor cells. The ability to customize size and surface chemistry allows for improved targeting, reduced off-target toxicity, and possible synergy between AgNPs and conventional therapies (Al-Khedhairy & Wahab, 2022; Pavan et al., 2022).

8.4 Clinical Translational Hurdles

Despite promising in vitro and in vivo findings, concerns about systemic toxicity, accumulation in non-target organs, and incomplete clearance hamper the clinical transition of AgNP-based cancer treatments (Takáč et al., 2023). Ongoing research focuses on refining nanoparticle design, optimizing dosage, and understanding pharmacokinetics to ensure safe implementation (Mao et al., 2016).

9. Anti-Inflammatory and Wound-Healing Applications

9.1 Mechanisms of Anti-Inflammation

Silver nanoparticles can modulate inflammatory pathways by inhibiting key cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) (Kong et al., 2022). By reducing excessive inflammation, AgNPs create a more favorable environment for tissue repair and regeneration (Adeleye et al., 2020).

9.2 Dermal Applications

- **Burn Treatment**: In burn wounds, AgNP dressings lower bacterial loads and inflammation, accelerating healing (Khashan & Dawood, 2023).
- **Oral Lesions**: Biomimetic scaffolds embedded with AgNPs have shown promise in treating oral ulcers by reducing local inflammation and preventing secondary infections (Craciunescu et al., 2021).
- **Topical Formulations**: Creams containing green-synthesized silver

nanoparticles can ease inflammatory skin conditions (Adeleye et al., 2020).

9.3 Surgical and Traumatic Wounds

From suture coatings to large-area wound dressings, nanosilver-based strategies target infection prevention while promoting rapid tissue granulation (Sabarathinam, 2021). Combining silver nanoparticles with bioactive compounds (e.g., curcumin, aloe vera) can further enhance anti-inflammatory and antibacterial efficacy (Khashan & Dawood, 2023).

10. Environmental Remediation and Catalysis

10.1 Pollutant Degradation

Silver nanoparticles exhibit catalytic potentials for decomposing hazardous organic dyes and pollutants (Barman, Chowdhury, & Baruah, 2020). They can break down aromatic compounds via oxidative or reductive pathways, leveraging active surface sites to accelerate reactions (Rasheed et al., 2018). This approach has garnered interest in textile effluent treatment, where dyes constitute a significant environmental concern.

10.2 Water and Wastewater Treatment

In addition to disinfecting water from pathogens, AgNPs can facilitate redox reactions that degrade organic contaminants (Rasheed et al., 2018). Their integration into membranes or porous supports addresses multiple contaminants simultaneously—microbes and chemical pollutants—though the potential release of silver ions into water systems warrants careful risk assessment (Nie et al., 2023).

10.3 Advanced Catalyst Systems

Hybrid materials combining silver nanoparticles with other metals or carbon-based supports—graphene, carbon nanotubes—enhance catalytic activity by tuning electron transfer properties (Ivanov et al., 2023). Such advanced catalysts find application in fuel cells, sensors, and hydrogen production.

11. Toxicity, Safety, and Regulatory Considerations

11.1 In Vitro and In Vivo Toxicity

The toxicity profile of silver nanoparticles depends on multiple factors:

1. **Particle Size**: Smaller nanoparticles (<10 nm) often exhibit higher cytotoxicity due to increased cellular uptake (Onodera et al., 2015).
2. **Surface Charge and Coatings**: Positive charges can enhance membrane interactions but may also provoke higher toxicity (Khan et al., 2021).
3. **Shape**: Rod-shaped and triangular nanoparticles sometimes show distinct cytotoxic profiles compared to

spherical forms (Menichetti et al., 2023).

4. **Dose and Duration**: Chronic low-level exposure can lead to bioaccumulation, whereas acute high doses can cause immediate cell damage (Nie et al., 2023).

Studies in liver (Piao et al., 2011), kidney, and neuronal cells highlight oxidative stress and mitochondrial dysfunction as key injury pathways (Farah et al., 2016). Autophagy and apoptosis are frequently triggered, revealing multiple nodes of potential therapeutic and toxic intersection (Mao et al., 2016).

11.2 Ecotoxicity and Environmental Impact

Once released into the environment, AgNPs can interact with soil microbes, aquatic organisms, and plants (Istiqola & Syafiuddin, 2020). Concerns over nanoparticle persistence and ion release have prompted calls for comprehensive life-cycle assessments. Studies indicate that silver nanoparticles may alter microbial community structures, affecting nutrient cycling (Nie et al., 2023). Transformations to silver sulfide or other less soluble forms in wastewater can mitigate some risks, but detailed fate and transport models remain necessary (Rasheed et al., 2018).

11.3 Human Exposure and Safety

Human exposure occurs primarily through inhalation (during manufacturing or usage), dermal contact (medical devices, personal care products), or ingestion (food packaging, water) (Istiqola & Syafiuddin, 2020). Regulatory bodies have begun to set exposure limits, but comprehensive guidelines for nanosilver remain incomplete (Nie et al., 2023).

11.4 Regulatory Landscape

- **FDA Approvals**: Some silver-based wound dressings and coatings have received clearance, but regulation specific to nanosilver is evolving.
- **REACH (EU)**: Requires manufacturers to provide safety data on nanomaterials, although silver nanoparticles are still under active review.
- **ISO Standards**: Developments in international standards for nanotechnology testing and risk assessment.

Ongoing research aims to harmonize testing protocols—evaluating parameters like dissolution rate, aggregation, and bioaccumulation—to produce reliable risk assessments (Bruna et al., 2021).

12. Strategies for Safe and Sustainable Use

12.1 Green and Biocompatible Synthesis

Encouraging eco-friendly reduction agents and stabilizers can help mitigate potential hazards (Khan et al., 2018). Plant-based and microbial syntheses reduce toxic residuals, making resulting nanoparticles more suitable for biomedical and environmental applications (Urnukhsaikhan et al., 2021).

12.2 Intelligent Formulation and Dosage

Designing formulations with controlled ion release or triggered dissolution allows for antibacterial action without oversaturating the environment with silver ions (Ivanov et al., 2023). Researchers explore stimuli-responsive coatings that release AgNPs only under certain conditions, such as changes in pH or temperature (He et al., 2022).

12.3 Lifecycle Analysis and Circular Approaches

Recovering silver from spent nanomaterials could alleviate resource depletion and environmental contamination (Istiqola & Syafiuddin, 2020). Recycling or regenerating AgNP-based catalysts in catalytic or water treatment systems offers pathways toward circular nanotechnology economy models.

12.4 Risk–Benefit Balancing

Ultimately, the potential benefits of silver nanoparticles—in healthcare, food safety, and beyond—can be significant, provided that rigorous risk assessment and responsible management are in place. Balancing innovation with public and environmental health remains an ongoing challenge and responsibility (Nie et al., 2023).

13. Emerging Trends and Future Prospects

13.1 Personalized Medicine and Theranostics

The convergence of silver nanoparticles with diagnostics and therapy—theranostics—holds promise for personalized healthcare (Kim et al., 2021). Integrated systems can deliver real-time imaging feedback while administering targeted treatments, minimizing harm to healthy tissues.

13.2 Nano–Bio Interfaces and Advanced Functional Materials

Future research may see AgNPs integrated into “smart” materials capable of sensing and responding to biological cues (Namulinda et al., 2024). Multifunctional nanocomposites could simultaneously detect pathogens, release antimicrobial agents, and monitor healing progress.

13.3 Ultra-Small Silver Clusters

Researchers are investigating even smaller silver clusters—sub-nanometer or “Ångström-scale” entities—which may offer unique optical and catalytic properties with potential lower cytotoxicity (Wang et al., 2019). Such ultra-small clusters might revolutionize fields such as biosensing, advanced electronics, and selective catalysis.

13.4 Laser and Plasma-Based Upgrades

Laser ablation and arc discharge techniques continue to evolve, potentially offering greener and more precise control over particle attributes (Sadrolhosseini et al., 2018; Sportelli et al., 2018). Plasma-enhanced approaches may also allow in-situ functionalization, streamlining advanced AgNP production for high-value applications.

13.5 Expanding Antiviral and Pandemic Response

Recent global health crises highlight the urgency of advanced antiviral solutions. Research on AgNP coatings for personal protective equipment and air filtration is likely to expand, supported by more rigorous clinical and environmental validations (Jeremiah et al., 2020; Abulikemu et al., 2022; Noppradit et al., 2023).

14. Conclusion

Silver nanoparticles stand at a crucial intersection between materials science, microbiology, medicine, and environmental studies. Their exceptional antimicrobial, antiviral, antifungal, and anticancer capabilities make them unparalleled in certain applications—from advanced wound dressings and food preservation systems to catalytic pollution remediation. Equally important is their potential in cutting-edge fields such as photothermal cancer therapy, personalized medicine, and advanced nanosensors.

However, unlocking the full potential of AgNPs necessitates a nuanced grasp of their synthesis methods, surface chemistry, and biological interactions. Factors such as size, shape, surface charge, and functionalization converge to define both efficacy and toxicity. As the knowledge base expands, so must regulatory frameworks, ensuring public health and environmental safety. The development of green synthesis protocols, targeted delivery strategies, and lifecycle-based approaches forms a rational path toward responsible innovation.

Looking ahead, emerging research areas—like ultrasmall silver clusters, plasmonic-based sensing, and synergy with viral therapies—promise to reshape the future of nanotechnology. Integrating silver nanoparticles into hybrid, multifunctional materials will broaden their horizon, bridging gaps between diagnostics, therapy, and real-time monitoring. The overarching narrative underscores a balancing act: harnessing silver nanoparticles’ versatile benefits while adopting robust risk assessment and ecological stewardship.

In sum, the evolution of silver nanoparticles embodies nanotechnology’s capacity to transform conventional practices in healthcare, agriculture, environmental management, and beyond. With continued interdisciplinary collaboration, the field is well-positioned to overcome its challenges, delivering safe, efficient, and sustainable nanosilver solutions that address pressing global needs.

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