

Small Silver Nanoparticles: A Multi-Functional Novel Delivery Vehicle For Therapeutics

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Abstract

Small silver nanoparticles (AgNPs) have been increasingly studied as a promising drug delivery platform due to their unique properties, including high surface area, high reactivity, and tunable surface chemistry. In this article, we review recent advances in the use of small AgNPs as a drug delivery vehicle. We discuss the benefits of AgNPs for targeted drug delivery, controlled drug release, and enhanced bioavailability, as well as their potential for use in photothermal therapy, immunotherapy, and gene delivery. We also review the challenges and potential safety concerns associated with the use of AgNPs in drug delivery, and discuss future research directions in this field. Overall, small AgNPs represent a promising platform for the development of novel drug delivery systems with enhanced efficacy and reduced side effects. Silver nanoparticles have gained increasing attention in the field of drug delivery due to their unique physical and chemical properties. These nanoparticles can be used as a carrier for drugs, allowing for targeted delivery and improved therapeutic efficacy. In this review, we will discuss the potential of silver nanoparticles in drug delivery and their current applications.

Introduction

Nanotechnology has revolutionized the way we think and approach various fields of science, including biotechnology, electronics, and environmental science[1]. Among various types of nanoparticles, silver nanoparticles (AgNPs) have gained immense popularity in recent years due to their unique physical, chemical, and biological properties. physicochemical properties that make them useful in a wide range of applications. Silver nanoparticles have a high surface area-to-volume ratio, which means they can interact with other molecules and materials more effectively than bulk silver[2]. This property, combined with their high reactivity, tunable surface chemistry, and optical properties, has made silver nanoparticles an attractive platform for drug delivery, imaging, sensing, and catalysis. In recent years, researchers have made significant progress in synthesizing silver nanoparticles with specific sizes, shapes, and surface chemistries, and in understanding their interactions with biological systems[3]. This has led to a growing interest in the use of silver nanoparticles for medical applications, including drug delivery, imaging, and diagnostics. Small silver nanoparticles, in particular, have shown great promise as a drug delivery platform due to their unique properties, including the ability to passively target tumor tissues and the potential for triggered drug release. However, there are also safety concerns associated with the use of silver nanoparticles, as their small size and high reactivity can lead to toxicity and other adverse effects[4]. As such, ongoing research is focused on developing safe and effective silver nanoparticle-based drug delivery systems, as well as understanding their potential health and environmental impacts. Overall, silver nanoparticles

represent a promising and rapidly developing field of research with potential applications in a wide range of industries and medical fields[5]. This article provides an overview of the properties, synthesis methods, applications, and safety concerns of silver nanoparticles.

Properties of silver nanoparticles

Silver nanoparticles are known for their unique optical, electrical, and catalytic properties. They possess a high surface area-to-volume ratio, which enhances their catalytic activity. Additionally, the presence of free electrons on the surface of silver nanoparticles makes them an excellent conductor of electricity. The unique optical properties of AgNPs are due to their ability to absorb and scatter light at different wavelengths, which makes them useful in various sensing applications[6].

Synthesis of silver nanoparticles

Silver nanoparticles can be synthesized using different methods, including physical, chemical, and biological methods. Physical methods include laser ablation, evaporation, and lithography. Chemical methods include reduction, precipitation, and electrochemical reduction. Biological methods involve the use of microorganisms, such as bacteria and fungi, to synthesize AgNPs[7].

Physical Synthesis of Silver Nanoparticles

Physical synthesis methods involve the use of energy sources to generate nanoparticles. These methods include laser ablation, evaporation, and lithography[8,9].

1. Laser ablation involves the use of a high-energy laser to ablate a silver target in a liquid medium, leading to the formation of AgNPs. This method is useful for producing well-defined and monodisperse nanoparticles.
2. Evaporation involves the use of a high-temperature environment to evaporate silver atoms and form AgNPs. The method is simple and cost-effective, but it often results in irregularly shaped nanoparticles.
3. Lithography involves the use of a patterned template to fabricate AgNPs. This method is useful for generating nanoparticles with specific shapes and sizes.

Chemical Synthesis of Silver Nanoparticles

Chemical synthesis methods involve the use of chemical reducing agents to reduce silver ions to form AgNPs. These methods include the following:

Reduction with sodium borohydride: Sodium borohydride is a common reducing agent used to reduce silver ions to form AgNPs. This method is simple and cost-effective, but it can result in the formation of irregularly shaped nanoparticles[10].

Reduction with citrate: Citrate is a mild reducing agent that produces monodisperse spherical AgNPs. The method is simple and cost-effective but requires precise control of reaction conditions[10].

Biological Synthesis of Silver Nanoparticles

Biological synthesis methods involve the use of microorganisms, such as bacteria or fungi, to synthesize AgNPs. These methods include the following:

Biosynthesis with bacteria: Some bacteria, such as *Pseudomonas aeruginosa* and *Bacillus licheniformis*, are capable of reducing silver ions to form AgNPs. This method is eco-friendly and produces nanoparticles with a narrow size distribution[11].

Biosynthesis with fungi: Fungi, such as *Fusarium oxysporum* and *Aspergillus niger*, can also be used to synthesize AgNPs. This method is eco-friendly and produces nanoparticles with a high degree of uniformity[12].

Applications of silver nanoparticles

AgNPs have found wide applications in various fields, including biomedicine, electronics, and environmental science. In biomedicine, silver nanoparticles have been used for wound healing, drug delivery, and cancer therapy. The unique properties of AgNPs, such as their antibacterial and antifungal properties, have made them an ideal candidate for developing antimicrobial coatings for medical devices[13]. In electronics, silver nanoparticles are used in conductive inks and printable electronics. In environmental science, AgNPs are used for water treatment, air purification, and remediation of contaminated soils. Table 2 shown different application of silver nanoparticles.

Medical Applications: Silver nanoparticles have been extensively studied for their antimicrobial properties and are used in a variety of medical applications. These include wound dressings, surgical tools, and dental materials. They can also be used in drug delivery systems and as diagnostic tools[14].

Wound Dressings: Silver nanoparticles are often incorporated into wound dressings to prevent infection and promote wound healing. They can also be used to treat chronic wounds, such as diabetic foot ulcers and pressure ulcers[15].

Surgical Tools: Silver nanoparticles can be incorporated into surgical tools, such as sutures and catheters, to prevent infection. They can also be used in implantable medical devices to prevent biofilm formation.

Diagnostics: Silver nanoparticles can be used in diagnostic assays to detect a wide range of diseases and infections. They can also be used in imaging applications, such as magnetic resonance imaging (MRI) and computed tomography (CT) scans[16].

Surface-Enhanced Raman Scattering (SERS): Silver nanoparticles can be used as a substrate for surface-enhanced Raman scattering (SERS), which is a powerful analytical technique for detecting and analyzing molecules. When molecules are adsorbed onto the surface of the silver nanoparticles, they experience a significant enhancement in their Raman signal, which can be used for imaging and diagnosis of various diseases[17].

Fluorescence Imaging: Silver nanoparticles can be functionalized with fluorescent dyes or other imaging agents, allowing for their use in fluorescence imaging. When excited with a light source, the nanoparticles can emit fluorescence, which can be detected using specialized imaging equipment. This can be used for the detection and diagnosis of various diseases, such as cancer[18].

Magnetic Resonance Imaging (MRI): Silver nanoparticles can also be used as contrast agents for magnetic resonance imaging (MRI). The nanoparticles can be functionalized with magnetic materials, allowing for their use in MRI. When injected into the body, the nanoparticles can enhance the contrast in MRI images, allowing for the detection of tumors and other diseases[19].

Computed Tomography (CT) Imaging: Silver nanoparticles can also be used as contrast agents for computed tomography (CT) imaging. The nanoparticles can absorb X-rays and enhance the contrast in CT images, allowing for the detection of tumors and other diseases[20].

Dental Materials: Silver nanoparticles can be used in dental materials, such as fillings and dentures, to prevent bacterial growth and improve oral health.

Cancer Therapy: Silver nanoparticles have been studied for their potential as a cancer therapy. They can be used to deliver drugs directly to cancer cells or to destroy cancer cells using photothermal therapy[21].

Eye Care: Silver nanoparticles can be used in eye care products, such as contact lenses and eye drops, to prevent

infection and promote healing.

Environmental Applications: Silver nanoparticles can be used to remove pollutants from water and air. They are effective in degrading organic contaminants and can also be used to remove heavy metals from water[22].

Silver nanoparticles in Drug Delivery

Silver nanoparticles can be used as a carrier for drugs, allowing for targeted delivery and improved therapeutic efficacy. They can also be used in combination with antibiotics to enhance their effectiveness against drug-resistant bacteria.

Targeted Drug Delivery: Silver nanoparticles can be used to target specific cells or tissues in the body. These nanoparticles can be functionalized with ligands or antibodies that bind to specific receptors on the surface of cells, allowing for targeted drug delivery. This targeted approach can improve the therapeutic efficacy of drugs while reducing their side effects[23]. Here are the key steps involved in silver nanoparticle targeted drug delivery:

Functionalization of Silver Nanoparticles: The first step in targeted drug delivery is the functionalization of silver nanoparticles. This involves attaching ligands or antibodies to the surface of the nanoparticles that bind to specific receptors on the surface of cells. The choice of ligands or antibodies depends on the targeted cells or tissues and the desired therapeutic outcome[12].

Interaction with Target Cells: Once the silver nanoparticles are functionalized, they are introduced into the body and interact with the targeted cells. The ligands or antibodies on the surface of the nanoparticles bind to specific receptors on the surface of the cells, allowing for targeted drug delivery[21].

Cellular Uptake: After binding to the targeted cells, the silver nanoparticles are internalized through endocytosis. The nanoparticles are then transported to the cell's intracellular compartments, where they release the drug payload[21].

Drug Release: The release of the drug payload from the silver nanoparticles can be controlled by various mechanisms, such as changes in pH or temperature. This allows for a sustained release of the drug over time, improving its therapeutic efficacy[19].

Therapeutic Effect: The released drug interacts with the targeted cells, producing the desired therapeutic effect. Since the silver nanoparticles are targeted to specific cells or tissues, the drug is delivered directly to the site of action, reducing the potential for off-target effects and improving therapeutic efficacy[13].

Enhanced Drug Solubility

Many drugs have poor solubility, which can limit their therapeutic efficacy. Silver nanoparticles can be used to enhance drug solubility, allowing for improved drug delivery. The high surface area of silver nanoparticles allows for increased drug loading, which can also improve drug delivery efficiency[24]. The following are the mechanisms by which silver nanoparticles enhance drug solubility:

Increased Surface Area: Silver nanoparticles have a high surface area to volume ratio, which allows for increased drug loading. The larger surface area of silver nanoparticles increases the number of drug molecules that can be adsorbed onto the surface of the nanoparticles, thereby increasing the drug's solubility[24].

Hydrophobic and Hydrophilic Properties: Silver nanoparticles have both hydrophobic and hydrophilic properties. This allows them to interact with both hydrophobic and hydrophilic drug molecules, making them more soluble in both water and oil-based solvents.

Nano-Size Effects: Silver nanoparticles are in the nanometer size range, which can lead to changes in the physical and chemical properties of the drugs. These changes can lead to improved solubility of poorly soluble drugs[25].

Electrostatic Interaction: Silver nanoparticles have a high surface charge, which can lead to electrostatic interaction with the drugs. This interaction can increase the solubility of the drugs by preventing them from aggregating and forming larger particles.

Stability of Drug Formulations: Silver nanoparticles can also improve the stability of drug formulations. They can prevent the degradation of drugs by protecting them from external factors such as light, heat, and moisture[26].

Controlled Drug Release

Silver nanoparticles can be used to control the release of drugs over time. These nanoparticles can be functionalized with polymers or other materials that respond to changes in pH, temperature, or other environmental factors, allowing for controlled drug release[27]. The following are the ways in which silver nanoparticles can help in controlled drug release:

Surface Modification: Silver nanoparticles can be functionalized with various ligands, including drugs, to create a drug-loaded nanoparticle. The drug is typically attached to the surface of the nanoparticle through chemical or physical adsorption. The rate of drug release can be controlled by the type of linkage between the drug and the nanoparticle, as well as the chemical properties of the drug[28].

pH-Dependent Release: The release of drugs from silver nanoparticles can be pH-dependent. This is because the pH of the surrounding environment can affect the stability of the drug-nanoparticle complex. By modifying the surface of the nanoparticle with pH-responsive moieties, drug release can be controlled in response to changes in the local pH[20].

Temperature-Dependent Release: The release of drugs from silver nanoparticles can also be temperature-dependent. By modifying the surface of the nanoparticle with temperature-sensitive moieties, drug release can be controlled in response to changes in the local temperature[17].

Photoresponsive Release: Silver nanoparticles can be modified with photoresponsive moieties, such as azobenzene or spiropyran, which can respond to light by changing their conformation. By attaching the drug to the photoresponsive moiety, the release of the drug can be triggered by exposure to light of a specific wavelength[29].

Magnetic Field-Responsive Release: Silver nanoparticles can be modified with magnetic nanoparticles, allowing the release of the drug to be controlled by an external magnetic field. By applying a magnetic field, the drug-loaded nanoparticle can be directed to a specific location, enabling targeted drug delivery[5]. Different types of silver nanoparticles and their reported activities in various research studies shown in table 1.

Table 1: summarizing some of the different types of silver nanoparticles and their reported activities in various research studies

Silver Nanoparticle Type	Reported Activity in Research
Citrate-coated silver nanoparticles	Antibacterial, anti-inflammatory, wound-healing, and anticancer properties [5]
PVP-coated silver nanoparticles	Anticancer, antibacterial, and antifungal properties[6]
Starch-coated silver nanoparticles	Antibacterial, antifungal, and antioxidant properties[4]
Chitosan-coated silver nanoparticles	Antibacterial, antifungal, and anti-inflammatory properties[7]
Polyethylene glycol-coated silver nanoparticles	Anticancer and antibacterial properties[8]
Gelatin-coated silver nanoparticles	Antibacterial and anti-inflammatory properties[9]
Albumin-coated silver nanoparticles	Antibacterial, antifungal, and antiviral properties[12]
Silica-coated silver nanoparticles	Antibacterial and antifungal properties[17]
Polyvinyl alcohol-coated silver nanoparticles	Antibacterial and anticancer properties[21]

Polyvinylpyrrolidone-coated silver nanoparticles	Antibacterial and antiviral properties[5]
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Improved Bioavailability

Silver nanoparticles can improve the bioavailability of drugs by protecting them from degradation in the body. These nanoparticles can also increase the permeability of cell membranes, allowing for better drug uptake[30].

Antibacterial Properties

Silver nanoparticles have potent antibacterial properties, which can be useful in drug delivery. These nanoparticles can be used to deliver antibiotics directly to bacterial cells, allowing for improved therapeutic efficacy against drug-resistant bacteria[26]. The following are the ways in which silver nanoparticles can improve antibacterial properties:

Disruption of Cell Membrane: Silver nanoparticles can interact with bacterial cell membranes and disrupt their integrity, leading to increased permeability and eventual cell death. This is due to the ability of silver nanoparticles to generate reactive oxygen species, which can damage the bacterial cell membrane and other cellular components[31].

Inhibition of Enzymatic Activity: Silver nanoparticles can also inhibit bacterial enzymatic activity, which is essential for the survival and growth of bacterial cells. The interaction of silver nanoparticles with bacterial enzymes can lead to their denaturation, inhibition, or inactivation, thereby reducing bacterial viability[32].

Reduced Antibiotic Resistance: Silver nanoparticles can also help reduce antibiotic resistance by enhancing the antibacterial activity of existing antibiotics. This is because silver nanoparticles can interact with bacterial cells in a different way than antibiotics, and therefore, bacteria may not develop resistance to silver nanoparticles as easily as they do with antibiotics. In combination with antibiotics, silver nanoparticles can help overcome bacterial resistance and improve the effectiveness of antibiotic treatment[32].

Table 2: Application of silver nanoparticles

Application	Description
Targeted drug delivery	Functionalization of silver nanoparticles with specific ligands or peptides can lead to enhanced drug delivery to diseased cells[11]
Controlled drug release	Changing the properties of the silver nanoparticle surface can lead to controlled release of drugs at the site of action, reducing side effects and improving efficacy[14]
Imaging and diagnosis	Silver nanoparticles can be functionalized with imaging agents to allow for visualization and tracking of nanoparticles and their delivery to target sites[16]
Photothermal therapy	Silver nanoparticles have unique optical properties that can be used for localized thermal ablation of diseased cells[17]
Immunotherapy	Silver nanoparticles can be used as a delivery vehicle for antigens or adjuvants to stimulate the immune system against diseased cells[20]
Enhanced bioavailability	Silver nanoparticles can improve the solubility and permeability of drugs, leading to improved bioavailability and efficacy[21]
Antibacterial properties	Silver nanoparticles have strong antibacterial properties, making them useful for the treatment of bacterial infections[22]
Wound healing	Silver nanoparticles can be used to enhance wound healing due to their antibacterial and anti-inflammatory properties[12]
Gene delivery	Silver nanoparticles can be used to deliver genes to target cells for gene therapy[31]
Anti-cancer therapy	Silver nanoparticles can be used for the delivery of chemotherapeutic agents and for photothermal ablation of cancer cells[12]

Others Application of silver nanoparticles

Electronics: Silver nanoparticles have been used in electronics due to their excellent electrical conductivity. They can be used as conductive inks for printed electronics, as well as in the manufacture of touchscreens and other electronic devices[32,33].

Textiles: Silver nanoparticles can be incorporated into textiles to produce antimicrobial fabrics. This can be useful in medical settings, as well as in consumer products like athletic wear and underwear[34].

Food Packaging: Silver nanoparticles can be incorporated into food packaging materials to prevent bacterial growth and increase the shelf life of food [35].

Cosmetics: Silver nanoparticles can be used in cosmetics as a preservative and antimicrobial agent. They can also be used in sunscreens and other products to provide UV protection[32,36].

Energy: Silver nanoparticles have potential applications in the field of renewable energy. They can be used in solar cells and in the production of hydrogen gas from water[37].

Safety concerns

Despite their potential benefits, there are concerns about the safety of silver nanoparticles. AgNPs can enter the body through inhalation, ingestion, or dermal exposure, and can accumulate in different organs, leading to toxicity. Studies have shown that AgNPs can cause oxidative stress, inflammation, and genotoxicity, which raises concerns about their long-term safety[36].

Conclusion

In conclusion, silver nanoparticles (AgNPs) have shown great promise as a novel platform for drug delivery in the pharmaceutical industry. They possess unique physicochemical properties that make them attractive for drug delivery applications, including high surface area, reactivity, tunable surface chemistry, and optical properties. Small silver nanoparticles, in particular, have emerged as a promising drug delivery vehicle with the potential to improve targeted drug delivery, controlled drug release, and enhanced bioavailability, as well as photothermal therapy, immunotherapy, and gene delivery. While the use of silver nanoparticles in drug delivery has many potential benefits, there are also safety concerns and potential toxicities associated with their use. Thus, ongoing research is focused on developing safe and effective silver nanoparticle-based drug delivery systems, as well as understanding their potential health and environmental impacts. Overall, silver nanoparticles have shown great potential for use in pharmaceuticals, particularly in drug delivery applications. Further research is needed to fully realize their potential benefits while also addressing safety concerns, with the ultimate goal of improving patient outcomes and advancing the field of drug delivery.

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