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Pharmaceutical Effects of Drug Loaded Silver Nanoparticles

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Abstract: Given the broad spectrum of applications of nanotechnology in medicine, silver nanoparticles (AgNPs) have garnered mounting interest, particularly due to their antibacterial, antiviral, antifungal, anti-inflammatory, anticancer, targeted drug delivery, and wound care properties. The present study focuses on drug-loaded AgNPs that possess these biological properties. In the context of this study, a systematic review of the extant literature was conducted to investigate the pharmaceutical properties of these nanoparticles.

Introduction

Since the 1980s, when the field of nanotechnology was established, the first nanotechnology-based treatments, vaccines, drugs, and diagnostic devices have been approved for commercialization and clinical use. Concurrently, the synthesis of matter at the nanometer scale has been developed (Contera et al., 2021). Inorganic-based nanomaterials, which are widely used in healthcare applications, generally include metals and metal oxide nanomaterials. Metal-based nanomaterials include silver (Ag), gold (Au), aluminum (Al), cadmium (Cd), copper (Cu), iron (Fe), zinc (Zn), and lead (Pb). Metal oxide-based nanomaterials include zinc oxide (ZnO), copper oxide (CuO), magnesium aluminum oxide ($MgAl_2O_4$), titanium oxide (TiO_2), cerium oxide (CeO_2), and iron oxide (Fe_3O_4) (Ma et al., 2024). Gold nanoparticles (AuNP) and silver nanoparticles (AgNP), which are among the metal nanoparticles, have a wide range of potential uses due to their application areas in various disciplines and their biomedical properties (Sakthi Devi et al., 2022). AgNP, a material that has gained significant popularity in recent times, exhibits superior antibacterial properties, a lack of drug resistance, and a range of electrical, optical, and thermal properties when compared to conventional silver (Sati et al., 2025; Nie et al., 2023; Nguyen et al., 2023). Due to their exceptional stability and low chemical reactivity, AgNPs are highly suitable candidates for various biological applications (Sati et al., 2025). However, AgNPs have also been observed to exert adverse effects. Preliminary research indicates that the liver and lungs are the primary sites of accumulation or target tissues for long-term AgNP exposure (Jaswal and Gupta, 2023). AgNP displays a multitude of toxicological profiles, which are contingent upon exposure routes, including inhalation, gastrointestinal tract, and dermal exposure. These profiles manifest in various forms, depending on the route of exposure, and consequently result in distinct biological effects within the body (Ferdous and Nemmar, 2020). A multitude of deleterious effects have been documented in the extant literature, with particular emphasis on fetal hepatotoxicity, genotoxicity, and chronic exposure. These adverse effects culminate in the impairment of vital organs, such as the liver and kidneys (Gherasim et al., 2020).

The objective of this study was to evaluate the biological and pharmaceutical properties of drug-loaded AgNPs based on existing literature. In this context, the antibacterial, antiviral, antifungal, anti-inflammatory, and anticancer effects of AgNPs, as well as their roles as targeted drug delivery systems and in wound healing, were systematically investigated.

Methodology

A comprehensive literature review was conducted between 2015 and 2025 using the keywords "silver nanoparticles," "drug-loaded silver nanoparticles," and "pharmaceutical effect of silver nanoparticles" to evaluate the pharmaceutical effects of drug-loaded AgNP.

Drug-Loaded Silver Nanoparticle (Agnp)

AgNP exhibits several advantageous properties, including chemical stability, inertness, and a high drug binding affinity. Additionally, it is biocompatible, stable, and safe in biological environments, and it has low toxicity (Aisida et al., 2019). The synthesis of AgNP for utilization in drug delivery has resulted in particles with dimensions exceeding 100 nm. This characteristic confers upon them the capability to carry the designated drug payload in an effective manner (Lee and Jun, 2019). AgNP demonstrate antimicrobial and anticancer properties through mechanisms such as the release of silver ions and the formation of radical species upon uptake by living cells or bacteria. Cancer is known as a major health problem globally (Bilici et al., 2025). Critical obstacles to cancer treatment are drug insensitivity and resistance (Bilici and Akkoç, 2025). The loading of AgNPs with pharmacologically active cancer drugs represents a promising approach for the treatment of tumors that are unresponsive to chemotherapy or radiotherapy (Gomes et al., 2021). For a variety of medical applications, AgNP has been

demonstrated to regulate the release of silver ions, thereby reducing its toxicity while maintaining its antibacterial activity. This is due to its robust antibacterial, anti-inflammatory, and antitumor properties (Gherasim et al., 2020; Aisida et al., 2019; Lee and Jun, 2019; Gomes et al., 2021; Burduşel et al., 2018).

Antibacterial

Metal NP, endowed with noteworthy antibacterial characteristics, is among the most prevalent nanomaterials employed (Slavin et al., 2017). AgNP demonstrates efficacy as an antibacterial agent, proving effective in addressing pathogenic infections (Sharma et al., 2012). AgNP is among the most prevalent nano-antimicrobials, exhibiting a natural structure that impedes bacterial proliferation (Aisida et al., 2019). Phenindione-loaded AgNP have been demonstrated to exhibit prolonged prothrombin and activated partial thromboplastin times, with an approximate increase of 1.5-fold compared to conventional phenindione. This observation validates the efficacy of phenindione-loaded AgNP as a superior therapeutic anticoagulant agent. AgNP demonstrated remarkable antimicrobial activity against gram-positive bacterial strains, including *Micrococcus luteus* 2YC-YT, *Staphylococcus aureus* ATCC 25923, and *Bacillus amyloliquefaciens* 4BCL-YT. Additionally, AgNP exhibited significant activity against gram-negative bacterial strains, such as *Salmonella enteritidis* ATCC 13076. However, these formulations were found to be less efficacious than the free drug, phenindione. This observation was attributed to the release time of AgNP (Nikolova et al., 2023). However, the loading of ciprofloxacin onto AgNP resulted in an enhancement of its antibacterial activity against *Acinetobacter baumannii* and *Serratia marcescens* gram-negative bacterial strains, as well as *Staphylococcus aureus* gram-positive bacterial strains (Ibraheem et al., 2022). In the present study, the antibacterial efficacy of silica NP loaded with vancomycin and nanosilver antibacterial drugs was investigated. The results demonstrated a significant inhibitory effect on bacterial strains, including *S. epidermidis* (gram positive) and *E. coli* (gram negative) (Ni et al., 2022). In this case, it is hypothesized that the antibacterial activity of AgNP may be contingent upon the rate at which the drug is released from the NP.

Antiviral

The antiviral mechanism of AgNP remains to be fully elucidated, necessitating further investigation into its structural, molecular, and immunological aspects. AgNP-induced antiviral effects are analogous to their antibacterial activities. These effects are based on the specific affinity of AgNP for key biomolecules, such as viral proteins and glycoproteins. AgNP-induced antiviral effects are also based on Ag⁺ ion-mediated biostatic events. These events include the inhibition of cellular attachment and invasion, the inhibition of intracellular viral replication or spread, and the suppression of extracellular virion production (Salleh et al., 2020; Nakamura et al., 2019). Fungal-derived biodegradable AgNP have been demonstrated to impede the binding and intracellular multiplication of type 1 herpes simplex virus (HSV-1), contingent on their dimensions (Gaikwad et al., 2013). Tannic acid-loaded AgNP, with a diameter of 33 nanometers, have been documented to demonstrate the capacity to diminish the infectivity of type 2 herpes simplex virus (HSV-2) by directly impeding viral glycoproteins and interacting with viral deoxyribonucleic acid (DNA). Treatment with these nanoparticles also reduced local inflammation and enhanced virus-specific immune responses in both primary and recurrent HSV-2 infections in mouse models (Orłowski et al., 2013; Orłowski et al., 2014).

Antifungal and Anti-inflammatory

Due to the proven antifungal activity of AgNP, their utilization has seen a considerable increase in the treatment of fungal infections (Mussin and Giusiano, 2022). The antifungal activity of Chitosan AgNP was found to be significant against both unicellular and multicellular fungal strains (Shehabeldine et al., 2022). A study was conducted to investigate the antifungal

activity of AgNP on clinical isolates of *C. auris*. The results demonstrated that AgNP exhibited significant antifungal and antibiofilm activity against all isolates that were subjected to antimicrobial agents, including amphotericin B, fluconazole, caspofungin, voriconazole, micafungin, and flucytosine (AlJindan and AlEraky, 2022).

In a study by Wang et al., levofloxacin hydrochloride-loaded Ag-core mesoporous silica NP provided synergistic treatment against drug-resistant infections *in vitro* and *in vivo*, by simultaneously releasing antibiotics and Ag⁺ ions (Wang et al., 2016). The investigation revealed that *Terminalia species*-mediated AgNP exhibited significant anti-inflammatory and antioxidant properties (Mohamed and Abdel, 2014). Intracolonic administration of NanoAg1 and NanoAg2 effectively alleviated colitis in experimental ulcerative colitis and Crohn's disease models, thereby emerging as potential therapeutic agents in the treatment of inflammatory bowel diseases (Siczek et al., 2017).

Anticancer and Target-Specific Drug Delivery

AgNP act as antitumor agents due to their antiproliferative and apoptosis-inducing properties (Jayachandran et al., 2023). AgNP are becoming increasingly important for delivering anticancer drugs because they can overcome some of the limitations of conventional therapies. Their biosynthesis is simple and environmentally friendly, and it does not require chemical reagents (Gomes et al., 2021). In a study conducted by Misra and colleagues, the researchers demonstrated that paclitaxel-loaded poly(lactic-co-glycolic acid) (PLGA)-coated AgNP, which they developed for imaging and therapy, could be used to treat lung cancer by overcoming barriers in theranostic platforms. The AgNP effectively inhibited cancer growth and enabled imaging by releasing the drug in a controlled and slow manner (Misra et al., 2024). Jayachandran et al. conducted a study in which AgNP-encapsulated liposomes were delivered to cancer cells in a controlled and targeted manner (Jayachandran et al., 2023). Polyvinylpyrrolidone-stabilized AgNP exhibited concentration-dependent toxicity against mouse dendritic cells, whereas the cytotoxic effects of these nanoparticles against cancer cells were significantly higher (Vazquez et al., 2017).

Wound Care

Silver and its derivatives have played an important role in wound care since the time of Hippocrates. The therapeutic potential of these substances has been evaluated since ancient times (Yapijakis, 2009). The application of wound dressings coated with biosynthesized AgNP has been demonstrated to enhance collagen deposition in burn wounds and expedite re-epithelialization, reducing the duration of the process by 17 to 25 days. Due to their enhanced mechanical strength and accelerated healing properties, they are recommended as a potential option for the treatment of pediatric wounds (Ying et al., 2019). PVA hydrogel patches loaded with biosynthesized AgNP have been reported to accelerate the healing process and enhance re-epithelialization by providing effective antibacterial activity (Ahsan and Farooq, 2019). In a separate study, it was determined that loading AgNP into alginate/gelatin hydrogels supported better formation and maturation of granular tissue and also promoted earlier formation of primary collagen scars (Diniz et al., 2020). Silver-based nanomaterials can be readily modified and incorporated into dressings, facilitating the controlled delivery of therapeutic agents and promoting wound healing through their antioxidant, anti-inflammatory, and proliferative effects (Parthasarathy et al., 2020; Hajji et al., 2019). The acceleration of wound healing observed in this study can be attributed to the biocompatibility and non-toxic nature of the Chitosan AgNP at the concentrations employed. These nanoparticles demonstrated a capacity for effective wound exudate absorption, further contributing to their wound healing properties (Shehabeldine et al., 2022).

Potential Risks And Toxicity

The delivery of NP, particularly in the context of cancer treatments, poses significant challenges before their commercialization and subsequent routine utilization in clinical settings (Rosenblum et al., 2018). For instance, the administration of elevated drug doses with the objective of preventing suboptimal dosages from reaching the intended target, due to diminished bioavailability, may result in deleterious side effects and toxicity (Gomes et al., 2021). Given that AgNP is silver-based, its low solubility in biological fluids is a significant limitation that restricts its application in medical contexts (Mbanga et al., 2022). The solubility of NP affects its biological persistence and durability, thereby enabling the estimation of its duration of residence in the body (Chakraborty and Misra, 2019). It is anticipated that NP with a slow dissolution rate will have a prolonged impact on human health and the environment (Oyabu et al., 2017; Utembe et al., 2015). Factors such as pH, ionic strength, and surface functionalization have been demonstrated to promote enhanced dissolution at lower pH values for AgNP (Pallavicini et al., 2022; Fernando and Zhou, 2019). The long-term biodistribution of AgNP, in conjunction with their high concentration, has been observed to result in toxic effects, primarily due to the inefficient delivery of drugs to targeted cells (Xue et al., 2012). AgNP, which are frequently utilized in nanotechnology, manifest toxic effects on mammalian cells not solely due to their antimicrobial properties but also via a variety of cellular and molecular mechanisms. These toxicity mechanisms include (i) disruption of energy-dependent metabolic processes and DNA replication due to the uptake of free silver ions into the cell; (ii) oxidative stress resulting from the formation of reactive oxygen species (ROS) and free radicals induced by nanoparticles; and (iii) local disruption of membrane integrity due to the direct interaction of AgNP with lipid components in the cell membrane (Mei et al., 2020; Tortella et al., 2020).

Conclusion

A review of the relevant literature indicates that drug-loaded AgNP have broad potential applications in medicine and pharmaceuticals. The combination of AgNP with various biological agents has been demonstrated to enhance therapeutic efficacy and facilitate more precise delivery of drugs to the intended area. It has been demonstrated that significant advancements have been made in the domains of infection control and cancer treatment. These achievements can be attributed, at least in part, to the observed antibacterial and anticancer properties of the involved agents. In addition, their wound-healing-enhancing properties have demonstrated considerable potential for utilization in wound care products. However, for these AgNP to be seamlessly integrated into clinical applications, a comprehensive examination of their toxicological profiles is imperative, along with a thorough evaluation of their long-term safety.

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