Role of silver nanoparticles in Medicine

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Abstract:
We diagnose, treat, and prevent various diseases in all phases of human life recent advances in nanoscience and nanotechnology drastically changed the way. Among several metallic nanoparticles Silver nanoparticles (AgNPs) are one of the most vital and fascinating nanomaterials that are involved in biomedical applications. AgNPs play an important role in nanoscience and nanotechnology, mostly in nanomedicine. Although several noble metals have been used for various purposes, in cancer diagnosis and therapy AgNPs have been focused on potential applications. In this review, we discuss the application of AgNPs. More importantly, we extensively discuss the multifunctional bio-applications of AgNPs; for example, as antibacterial, antifungal, antiviral and anti-inflammatory. Finally, we conclude by discussing the future perspective of AgNPs.

Keywords: *silver nanoparticles, applications, cancer therapy, antibacterial, antifungal, antiviral*

1. Introduction

Medicinal and preservative properties of silver have been known for over 2,000 years. The ancient Greek and Roman civilizations used silver vessels to keep water potable. Since the nineteenth century, silver based compounds have been widely used in bactericidal applications, in burns and in wound therapy, etc. **[1]**. Nanotechnology is rapidly growing by producing nanoproducts and nanoparticles (NPs) that can have novel and size-related physico-chemical properties differing significantly from larger matter **[2]**. Silver nanoparticles (Ag-NPs or nanosilver) have attracted increasing interest due to their unique physical, chemical and biological properties compared to their macro-scaled counterparts **[3]**. Silver nanoparticles have been the theme of researchers because of their distinctive properties (e.g. size, shape and antimicrobial properties). Ag-NPs have distinctive physico-chemical properties, including a high electrical and thermal conductivity, surface-enhanced Raman scattering, chemical stability, catalytic activity and nonlinear optical behavior **[4]**. These properties make them of potential value in inks, microelectronics, and medical imaging **[5]**. Ag-NPs exhibit broad spectrum bactericidal and fungicidal activity **[6]**.

Silver nanoparticles have attracted much attention and have found applications in diverse areas, including medicine **[7]**, catalysis **[8]**, textile engineering **[9]**, biotechnology and bioengineering **[10]**, water treatment **[11]**, electronics **[12]** and optics **[13]**. Furthermore, currently silver nanoparticles are widely used as antibacterial/antifungal agents in a diverse range of consumer products: air sanitizer sprays, socks, pillows, slippers, respirators, wet wipes, detergents, soaps, shampoos, toothpastes, air filters, coatings of refrigerators, vacuum cleaners, washing machines, food storage containers, cellular phones, etc. **[14]**. Silver nanoparticles are additionally concentrated by material researchers who examine their combination into different materials so as to get upgraded properties, as, in sunlight-based cells where silver nanoparticles are utilized as plasmonic light snares.

Nanosilver can also be utilized either in the textile industry by incorporating it into the fiber (spun) or employed in filtration membranes of water purification systems. In many of these applications, the technological idea is to store silver ions and incorporate a time-release mechanism. According to Woodrow Wilson Centre study, 313 out of 1317 nano-products contain AgNPs, and this figure has increased by more than ten times within five years **[15]**. This rapid increase of AgNPs commercialization raises concern over its potential release to the environment and the consequent adverse effects **[16-17]**. The release of AgNPs to the environment from washing machines, textiles, and paint containing AgNPs has been demonstrated **[18-21]** with significant speciation alteration due to chemical reactions with the detergent and bleaching agent, and also effect of mechanical stresses from the washing machine **[22]**. Number of (eco)toxicology findings has also been reported **[23-24]**, however, establishing an association between NP characteristics and the observed toxic effect was unsuccessful due to the lack of characterization data of most of the NPs used **[25]**.

2. Ag-NPs Role in Medicine

2.1 Antibacterial Properties

The Ag-NPs are famous for its potent antibacterial activity against various strains of bacteria including highly pathogenic bacteria species (gram positive and gram negative bacteria) **[26]**. Sondi and Salopeck-Sondi investigated those antibacterial movements for Ag-NPs against e. Coli once Luria-Bertni agar plates. The e.Coli bacterial strains were utilized Similarly as symbolic species to gram negative microscopic organisms. Then afterward the examination of the gotten comes from those researchers that those antibacterial movement for Ag-NPs against e. Coli might have been dosage indigent (concentration). At optimized experimental parameters, they found out that Ag-NPs were adhered to the cell wall of the gram negative bacteria (E. coli) that caused the destruction of the bacterial cell **[27]**.

In another reported study scientists conducted experiments on the size related properties of the Ag-NPs on different species of gram negative bacterial strains **[28]**. Those outcomes gotten from their investigation proposed that size for Ag-NPs will be a main reason in keeping those bacterial unit cells safe as of their regular functions. Moreover they also accounted that more diminutive molecule effectively follow of the cell wall of the microbial cells in this way hampering their regular conduct technique for example, such that permeability and breath alongside those arrival of the Ag ions from those Ag-NPs molecule. Besides Previously, a in turn distributed study, analysts led trials for elucidating those dosage subordinate properties about Ag-NPs for gram negative Furthermore gram positive bacteria; those writers stated that gram negative microscopic organisms (E. Coli) camwood make hindered toward moderately low focus Concerning illustration contrasted with the gram positive microscopic organisms (S. Aureus) (see figure 5).

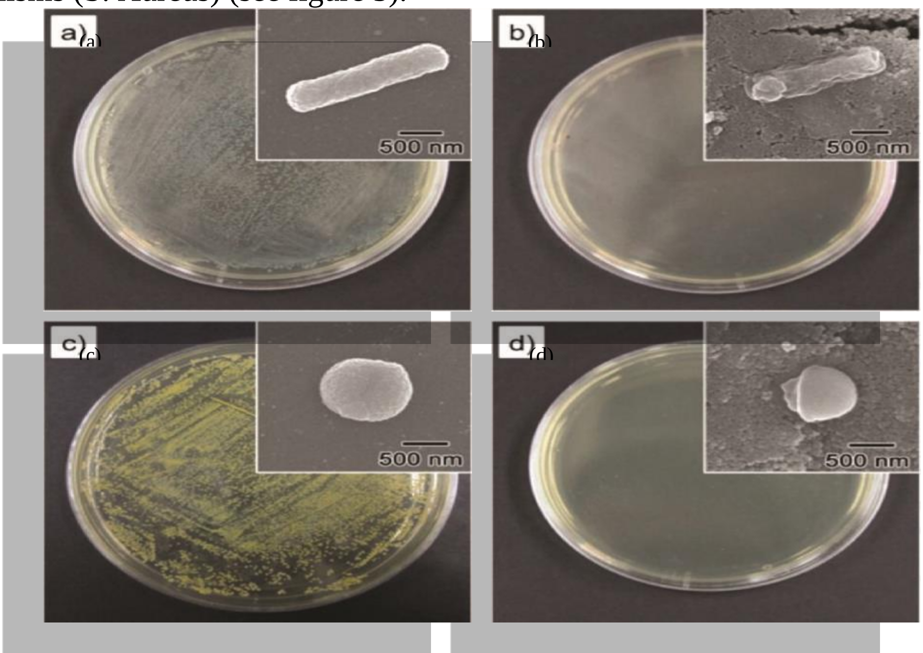

Figure 5 Photographs of colonies of (top) E. coli and (bottom) S. aureus (a, c) without nanoparticles treatment and (b, d) treated with SiO_2 -Ag/PRh nanoparticles. Inset figures show the FE-SEM images of a single bacterial cell (left) in the absence of bactericidal agents and (right) treated with the as-prepared nanoparticles. Reproduce from Song et al. with permission from ACS publishers **[42]**.

Shrivastava et al. revealed that the antibacterial activity of the Ag-NPs is both size and dose dependent; furthermore they also proposed the possible mechanism for the antibacterial activity of AgNPs, which states that the antibacterial activity of the AgNPs is governed by the adhesion and penetration pattern of the Ag-NPs into the cell wall of the bacterial cell, ultimately resulting in abnormal function **[29]**. In a study published by Pal et al., the authors revealed that the antibacterial activity of the Ag-NPs is structure (morphology) dependent **[30]**.

2.2 Antifungal

Fungi are considered to play a vital role in causing fungal infections, especially in hospitals **[31]**. Alongside the antibacterial movements of the Ag-NPs various investigations needed been stated on the antifungal movements for AgNPs, which uncovers that Ag-NPs Might be utilized Similarly as compelling antifungal mediator in light Ag-NPs show phenomenal antifungal properties against Different species of growths.. Previously, An report card distributed toward Kim et al. they tried the antifungal movements of the Ag-NPs against diverse fungous strains for example, trichophyton mentagrophytes (T. Mentagrophytes) What's more open Candida albanicans (C. Albanicans) growths furthermore uncovered that Ag-NPs exhibited great antifungal action. Furthermore they also proposed the possible mechanism for the antifungal activity of AgNPs, which states that Ag-NPs cause abnormalities in the cell wall of the fungi which results in the abnormal functions (retarding the normal budding process) of the fungal cells (C. albanicans) **[45, 31, 32]**.

In another published paper researchers found out that catheters coated with Ag-NPs can result in complete inhibition of fungi (C. albicans). . To an additional published article research scholars found out that catheters covered for Ag-NPs camwood bring about finish restraint from claiming growths (C. Albicans). Recently, researcher stated the antifungal movements of Ag-NPs synthesized toward Tollens process. Starting with the acquired outcomes they uncovered that those yeast cells production might be hindered for those assistance of Ag-NPs along without bringing on any mischief to human fibroblastic cells. Another reported work states that Ag-NPs have exhibited antifungal activities against different strains of fungi such as C. albicans and C. glabrata Trichophyton rubrum (T. rubrum) but the activity is dose dependent **[33]**.

In short because of the informed for expositive expression accessible on the antifungal movement from claiming Ag-NPs, it might be closed that Ag-NPs might be utilized concerning illustration antifungal mediator against different strains (species) for growths and camwood a chance to be supportive previously, overcoming different contagious infections initiated by growths.

2.3 Antiviral Agent

Recently, the increase in infectious diseases caused by virus such as SARS-Cov, influenza A/H5N1, influenza A/H1N1, Dengue virus, HIV, HBV, and new encephalitis viruses, is of prime concern. Recently, those expand done infective maladies brought about eventually virus for example, such that SARS-Cov, flu A/H5N1, flu A/H1N1, dengue virus, HIV, HBV, Furthermore new encephalitis viruses, is of prime concern. These infections can create havoc in no time because of the rapid proliferation (glimpses of destruction caused by these viral infections have been observed in some of the countries and the most dangerous of these viral infections were bird flu, swine flu, and dengue), ultimately resulting in causing severe damage to health and wealth of humans beings **[34]**. Ag-NPs need aid popular to their antimicrobial activities; In specialists bring redirected their consideration and off assessing the vitality from claiming Ag-NPs clinched alongside controlling infective maladies initiated eventually pathogens What's more infections. Then again those amount about stated for meets expectations utilizing Ag-NPs for controlling viral infections is altogether low yet all the even now it could clear those path to other research scholars should indicate their enthusiasm toward managing against viral infections utilizing nanoparticle particularly Ag-NPs.

Elechiguerra et al. distributed their contemplate directed to surveying those impact for Ag-NPs on the HIV-1 infection. The authors concluded and revealed that the interaction between Ag-NPs and virus is size dependent (small sized nanoparticles are more effective against these viruses) **[35]**. They further illuminated those clue that Ag-NPs get adhered of the sulfur available in the gp120 glycoprotein knobs that brings about hampering the typical movements of the infection consequently hindered the typical works of the infection. This mechanism was second by another group of researchers when they published their report after assessing the role of Ag-NPs on HIV virus **[35]**. According to their published article they proposed that Ag-NPs were effective against HIV virus having the capability to bind to the sulfur present at gp120 glycoprotein knobs thus ultimately retarding their normal functions and binding to the hosts **[45, 35]**. Furthermore in a published article the authors reported that Ag-NPs play a vital role in inhibiting the synthesis of HBV RNA and extracellular virions in vitro (hepatitis B virus using HepAD38 cell line) **[45, 36]**.

Sun et al. published their research work in which they conducted experiments on the PVP (polyvinylpyrrolidone) coated Ag-NPs in combination with protein for controlling the infection caused in HEp-2 cell by syncytial virus (RSV) **[37]**. They uncovered that PVP covered Ag-NPs would successful for keeping those RSV infection spoiling. Moreover they suggested those conceivable component which stated that the PVP covered Ag-NPs tie of the G proteins available on the surface from claiming viral cell In this way suppressing those bond of the RSV infection cells to the host cells. Other researchers conducted experiment on Ag-NPs (having different size and geometry) and reported that Ag-NPs are very effective in inhibiting the normal functions of monkey virus **[38]**. De Gusseme et al. reported the usefulness of bio-AgNPs (biogenic Ag-NPs), and they concluded that both AgNPs and ionic Ag+ play very important role in controlling murine norovirus **[39]**.

Xiang et al. conducted experiments for elucidating the inhibiting role of Ag-NPs against H1N1 influenza a virus. In the report the authors revealed that AgNPs are very effective in inhibiting the normal activity of H1N1 influenza a virus **[40]**. Besides they recommended that Ag-NPs might control the apoptosis of MDCK cells initiated by H1N1 flu an infection. In short very nearly all of the stated research papers proposed those same system which states that AgNPs get adhered of the external proteins of the viral cells hence extreme hindering those typical work of the viral units. However authentic mechanism is yet to be established but Ag-NPs are considered to play a pivotal role in future for controlling infectious diseases caused by the viruses **[41]**.

2.4 Anti-Inflammatory Activity

Inflammation is associate early immunological response against foreign particles by tissue, that is supported by the improved production of pro-inflammatory cytokines, the activation of the immune system, and the release of prostaglandins and chemotactic substances like complement factors, interleukin-1 (IL-1), TNF-α, and TGF-β **[221–224]**.

So as to beat inflammatory action, we did like to search out effective anti-inflammatory agents. Among many anti-inflammatory agents, AgNPs have recently contend a very important role in anti-inflammatory field. AgNPs are noted to be antimicrobial, however the anti-inflammatory responses of AgNPs are still restricted. Bhol and Schechter **[225]** reported the anti-inflammatory activity in rat. Rats treated intra-colonically with four mg/kg or orally with forty mg/kg of nano crystalline silver (NPI 32101) showed considerably reduced colonic inflammation. Mice treated with AgNPs showed fast healing and improved cosmetic look, occurring in a very dose-dependent manner. Moreover, AgNPs showed important antimicrobial properties, reduction in wound inflammation, and modulation of fibrogenic cytokines **[226]**. Continued the previous study, Wong et al. **[222]** investigated to achieve any proof for the anti-inflammatory properties of AgNPs, within which they used each in vivo and in vitro models and located that AgNPs able to down-regulate the quantities of inflammatory markers, suggesting that AgNPs may suppress inflammatory events within the early phases of wound healing **[222]**. A porcine dermatitis model showed that treatment with nanosilver considerably will increases apoptosis within the inflammatory cells and reduced the stages of pro-inflammatory cytokines **[227]**. Biologically-synthesized AgNPs will inhibit the assembly of cytokines convinced by UV-B irradiation in HaCaT cells, and additionally reduces the edema and cytokine levels within the paw tissues **[228]**.

3. Conclusions and Future Perspectives

This review comprehensively addressed bio-applications of silver nanoparticles, with antibacterial, antifungal, antiviral and anti-inflammatory agents using AgNPs. Recently, both academic and industrial research has explored the possibility of using AgNPs as a next-generation anticancer therapeutic agent. Although AgNPs play an important role in clinical research, several factors need to be considered, including the source of raw materials, the method of production, stability, bio-distribution, controlled release, accumulation, cell-specific targeting, and finally toxicological issues to human beings. Although various methods are available, the synergistic effects of AgNPs and antibiotics on antibacterial agents or multiple therapeutic agents on anti-cancer activity/tumor reduction are still obscure. Therefore, more studies are required to explain the synergistic effect of the two different cytotoxic agents at a single time point. These kinds of studies could provide understanding, mechanisms, and efficiency of the synergistic effect of two different agents or multiple agents; thus, they would help to develop a novel system bearing multiple components with synergistic effects for the treatment of various types of cancer. Although AgNPs have been focused on therapeutic purposes, further research is inevitable in animal models to confirm the mechanisms and to gain a comprehensive picture of biocompatibility vs. toxicity of AgNPs. Finally, if we succeed in all these studies, it would help the researchers of the nanoscience and nanotechnology community to develop safer, biocompatible, efficient cancer or anti-angiogenic agents containing AgNPs. Eventually, to ensure the biosafety of the use of AgNPs in humans, studies dealing with biocompatibility of AgNPs and their interaction with cells and tissues are inevitable. Finally, the great concern is that the developing nanotechnology-based therapy should be better than available technologies, and it should overcome the limitations of existing treatment techniques. Finally, it has to provide a safe, reliable, and viable treatment of diseases with high accuracy in a patient-friendly manner.

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