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Silver Nanoparticles on the Horizon: Exploring Future Directions in Healthcare

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Abstract

Nanoparticles, consisting of clusters of atoms ranging from 1 to 100 nm, exhibit unique properties attributable to their small size and extensive surface area. This review paper addresses silver nanoparticles (AgNPs), their classification, manufacturing methods, and diverse uses. Nanoparticles are classed into organic, inorganic, and carbon-based categories, with silver nanoparticles (AgNPs) being under the inorganic classification. The discussion covers both top-down and bottom-up approaches for synthesis highlighting their strengths and limitations of each. A significant focus on green synthesis approaches that use biological agents such as plant extracts, microorganisms and enzymes present a promising alternative to chemical methods that often involve toxic chemicals and high energy. AgNPs find versatile applications: in agriculture to boost crop resilience, nutrient uptake and pest management; in aquaculture to combat microbial infection; in textiles, to develop smart, antimicrobial fabrics for medical and industrial uses; in environmental to facilitate dye detoxification and pollution degradation; and in health care, to enable targeted drug delivery, support diagnostic assays and promote wound healing. Overall, this review highlights the significance of AgNPs and their capacity to tackle contemporary challenges in medicine, agriculture and environmental protection, while emphasizing the need for ongoing research to improve synthesis strategies and expand their practical application.

Keywords: *Applications, Medicine, Nanotechnology, Silver Nanoparticles, Synthesis.*

Introduction

Nanotechnology emerges as an exceptionally compelling area of scientific exploration, garnering notable momentum and interest [1]. Nanotechnology can be defined as the application of material and devices with nanometer scale and their design, synthesis, characterization using science and engineering. The prefix "nano," stemming from the Greek word for "dwarf," denotes a minute scale of one billionth (10^{-9}) of a unit. The nano size objects or nanoparticles are cluster of atoms in the size ranging from 10-100 nm [2]. Nanotechnology, leveraging nanomaterials, has ushered in a new technological era that significantly influences all facets of human life. *viz.*, electronics and computers, food and agriculture industry, environment, cosmetics and health care.

The great revolution has been made in the field of medicine and pharmaceuticals by nanotechnology in the twentieth century. Nanotechnologies are categorized into wet, dry, and computational domains. Wet nanotechnology involves utilizing enzymes, tissues, membranes, and cellular components,

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whereas dry nanotechnology focuses on producing inorganic materials like carbon and silicon through methods rooted in physical chemistry. The simulation of nanometer size structures makes the computational nanotechnology [3]. These three approaches depend on each other for optimal functionality. The advances in diagnosis, treatment and prevention of disease will be significantly improved by nanotechnology. In recent years, the unprecedented growth of nanoscience has been witnessed. The novel properties of nanoparticles that depend on their shape, size and morphology that make them to have synergetic association with microbes, plants and animals.

Classification of Nanoparticles

Nanoparticles can be broadly classified into three groups: organic, inorganic, and carbon-based. Organic variants include micelles, liposomes, dendrimers and ferritin. Inorganic nanoparticles encompass metal nanoparticles (e.g., silver and gold) and metal oxides (e.g., titanium and zinc). Finally, the carbon-based category includes fullerens, carbon nanotubes, carbon nanofibers, graphene, and carbon black. Notably, among inorganic metals, silver and gold nanoparticles have attracted considerable research interest [4].

Synthesis of Silver Nanoparticles

Annual production and utilization of silver nanoparticles (AgNPs) are estimated to be around 320 tons, with applications spanning biosensing, food products, and nanomedicine imaging [9]. Silver nanoparticles can be synthesized through both top-down and bottom-up approaches. The top-down method involves breaking down larger particles into nanosized particles, often through destructive means. Common techniques include mechanical milling, thermal decomposition, laser ablation, nanolithography, and sputtering. Conversely, the bottom-up approach is constructive, starting from atoms and gradually building up to clusters and nanoparticles [5].

In the bottom-up approach, silver nanoparticles can be obtained through physical, chemical, or environmentally friendly (green) protocol. Physical method of synthesis includes, air-discharge condensation, physical vapour energy ball milling method and direct current magnetron sputtering. The main demerit of physical method is the consumption of high energy. Chemical method of AgNPs synthesis can be divided in to electrochemical, pyrolysis, chemical reduction and irradiation assisted chemical method. Non biodegradable agents, toxic chemicals and organic solvents were used as reducing and stabilizing agents in all the above-mentioned method. The use of these chemical reagents for the synthesis of AgNPs is potentially dangerous to biological systems and the environment. Moreover, most of these techniques require complicated controlled or hard processing conditions (temperature and pressure), which make them expensive as well [6]. A key challenge in nanotechnology is achieving the precise size, shape, and dispersibility of nanoparticles through the advancement of effective green chemistry synthesis methods [7]. Nature offers a fascinating toolbox for inorganic nanoparticle synthesis. These biological processes remain largely unexplored, presenting a rich frontier for future research. Utilizing biological entities like microorganisms, plants, marine organisms, and their extracts for the green synthesis of nanoparticles represents a growing field within nanotechnology. The primary benefit of utilizing green synthesis for silver nanoparticle synthesis, as opposed to other methods, lies in their lower biohazard risk, ease of enhancement, and simplified nanoparticle formulation process [8].

Applications of Silver Nanoparticles

The medicinal and therapeutic benefits of silver have been known longer than recorded history [9]. The antibacterial property of silver-based compounds make use of them for many centuries for several applications such as water purification, wood preservation, in wound dressing etc., [10]. Unlike many other antimicrobial agents, silver nanoparticles possess the unique ability to function in their solid state. This property offers a significant advantage, yet its exploitation remains limited primarily to traditional oriental medicine. Silver ions and their compounds have low toxicity to mammalian cells but are highly toxic to microbes. This unique property of silver nanomaterials makes them to use in different fields such as nanomedicine, biomaterials, energy and food [11] (Figure.1).

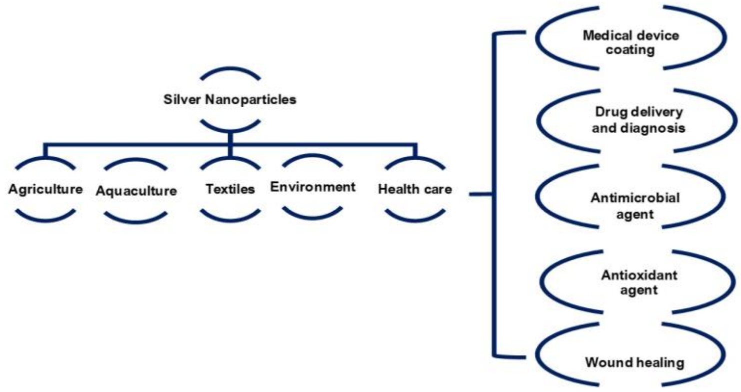

Figure 1. Applications of Silver Nanoparticles in Various Fields with Special Reference to the Health Care Industry

Agriculture

Agriculture stands as a vital and steady sector, supplying basic needs for both food and feed industries. The removal of poverty and hunger can be done only with the development of agriculture. The development of pest and drought-resistant crops holds significant promise for increased crop yields and improved agricultural sustainability. The potential benefits of using silver nanoparticles for agricultural sciences include enhancing food safety and quality, minimizing agricultural inputs, enhanced soil uptake of nutrients at the nanoscale and resilience to plant diseases resistance [12]. Silver and zinc oxide nanoparticles are used in remediating plant growth by helping in the uptake of nutrients by the plants. The predominant destroyer of the agricultural sector found to be insects, pests and its products. The increased solubility, permeability, stability and specificity characteristics of nano pesticides plays important in minimizing pests, insects and microbial pathogens [13]. Research has investigated the use of various nanoparticles, including silver nanoparticles, aluminum oxide, zinc oxide, and titanium dioxide, for controlling rice weevil infestations (caused by *Sitophilus oryzae*), as well as combating grasserie disease in silkworms (caused by *Bombyx mori*) and baculovirus BmNPV (*B. mori* nuclear polyhedrosis virus) [14]. The application of silver for its antimicrobial properties against a wide range of human pathogens has a long history, dating back several decades. However, the potential of silver nanoparticles in agricultural sector is still to be explored. The well-documented antimicrobial properties of silver, coupled with the unique characteristics of nanoparticles, have fueled a surge in research exploring the potential of silver nanoparticles for plant disease management [15].

Aquaculture

In the past twenty years, Asian aquaculture had attained dramatic growth as science-based industry from using traditional practice thereby contributing to economic growth and providing better livelihoods for rural peoples. According to the Food and Agriculture Organization of the United Nations (FAO) 2018, aquaculture will continue to expand over the next years. Aquaculture industry is currently attending different problems that includes diseases to cultured organisms, nutrition and water pollution. As a result, the aquaculture industry is adopting various innovative technologies such as silver nanoparticles to enhance production rates [16]. The omnipresent nature of the bacterium in aquatic environments provides opportunity for fish, amphibians and animals to ingest organisms. The utilization of antimicrobial drugs in aquatic medicine can pose significant environmental challenges due to the rapid dispersion of antibiotics in water. The recognition and commercial utilization of silver nanoparticles as antimicrobial agents are now widespread [17]. Water pollution in aquaculture by excretion products, faeces, chemical products and antibiotics generate high quantity of waste during organism's production. The application of silver bactericidal nanoparticles for disinfection to remediate pollution by eliminating organic matter and waste has been employed, particularly through the use of membranes containing silver nanoparticles [18].

Textiles

Smart textiles are textile fibres coated or impregnated with silver nanoparticles had developed interest than normal textiles because of their capacity to thwart mold and bacteria. These smart textiles have been utilized to create clothing and gowns for hospitals and laboratories, as well as socks, lingerie, and undergarments. The impregnation of AgNPs in textiles for medical applications has brought attention, as these materials were useful for fighting multidrug-resistant bacteria and healthcare-associated infections. The property of AgNPs impregnated textile make them use in reduction of microbial growth in wound dressings materials, medical staff uniforms, bed sheets and others [19].

Environmental Application

AgNPs possess catalytic properties that can be used for the dye detoxification in the paper and textile industry for treatment of effluents. Biosynthesized AgNPs acts as effective catalyst as compared to synthetic AgNPs. Silver nanoparticles' photocatalytic properties have been harnessed for the detoxification of various dyes like methyl orange, congo red, methyl red, methylene blue, and among others [20]. The biogenic AgNPs have been shown to effectively reduce hydrogen peroxide and degrade 4-nitrophenol (4-NP) into 4-aminophenol (4-AP). The World Health Organization has endorsed the utilization of silver nanoparticles in filtration systems for purifying drinking water [21].

Health Care

Silver nanoparticles are extensively utilized in biomedical applications, including treatments, wound dressings, drug delivery, diagnostics, medical device coatings, and contraceptive devices [22].

Medical Device Coating

Pioneering the use of silver in cardiovascular medicine, a prosthetic silicone heart valve was developed to combat both bacterial infections and inflammatory responses on the valve itself. Later the silver nanoparticles have been examined for mechanical, hemodynamic and antibacterial properties for its application in cardiovascular implant coating [22]. Silver nanoparticles have been utilized to coat various catheters, including central venous catheters and neurological catheters. Two commercially available medical catheters, Silverline (Spiegelberg GmbH and Co. KG, Germany) and ON-Q Silver Soaker™ (I-Flow Corporation, USA), utilize silver nanoparticle coatings to mitigate catheter-associated infections [23]. AgNPs also find its use as antibacterial additive in bone cement (Poly (methyl methacrylate) (PMMA) for reducing infection rate to persons undergoing hip and knee replacement surgery [24].

Drug Delivery and Diagnosis

Due to their distinctive surface plasmon resonance and substantial effective scattering cross-section, silver nanoparticles are ideally suited for molecular labelling. The size, shape and dielectric medium surrounding the silver nanoparticles determine the plasmonic properties that can be used for bio diagnosis. AgNPs used for the detection of interaction between amyloid β-derived diffusible ligands (ADDL) and the anti-ADDL antibody that are related to development of Alzheimer's disease [25]. Silver nanoparticles have been used for the detection of head and neck squamous cell carcinoma. AgNPs used to locate and destruct the targeted cancer cells by photothermal therapy [26]. Silica-coated AgNPs used for the detection of bovine serum albumin, while surface-coated AgNPs have been utilized to study interactions between biomolecules like biotin and streptavidin [27]. Silver nanoparticles with cubical or rhombohedral shape were used for detecting protein interactions [21].

Antimicrobial Agent

The rise of multidrug resistance in both Gram-positive and Gram-negative bacteria over recent decades stems from antibiotic overuse/misuse and a lack of new drug development. Facing antibiotic resistance, the medical community explores new and old approaches to combat infections. As previously mentioned, silver has a history of being used as an antiseptic and disinfectant. The antimicrobial property of silver has a long history against over 650 microorganisms [28] including gram negative, positive bacteria, fungi and viruses. During the First World War, silver was commonly used for wounded soldiers to reduce the microbial growth on wounds.

The 19th century saw F. Crede pioneer the use of silver nitrate as eye drops for newborns, preventing blindness from postpartum infections [29]. While the medicinal benefits of silver have been recognized for over two millennia, its application in the form of silver nanoparticles represents a more recent development [30]. The silver nanoparticles had been utilized to increase the surface-to-volume ratio thereby enhancing the bactericidal efficiency over silver [31]. The synthesis of silver nanoparticles for treating microbial disease using environmentally benign materials like plant extracts, fungi, bacteria and enzymes are of great concern as the synthesis process do not need toxic substances and have great compatibility for other pharmaceutical applications [5]. These advantages opened doors for green routes of synthesising nanoparticles and applications for treating microbial infections.

Antioxidants

Free radicals generated due to oxidative stress are toxic and harmful to our bodyFree radicals interact with essential biomolecules like lipids, proteins, and DNA, impacting human health by elevating the risk of heart diseases, degenerative illnesses, and accelerating the aging process [32]. There are two primary categories of harmful free radicals: reactive oxygen species (ROS) and reactive nitrogen species (RNS). ROS encompass a range of highly reactive molecules including superoxide anion, hydroxyl radicals, peroxyl and alkoxyl radicals, as well as non-radical species like hydrogen peroxide and singlet oxygen. These molecules may damage the biological macromolecules, causing cell ageing, oxidative stress and cancer [33]. The nitric oxide and nitrogen dioxide radicals as well as non radicals like N_2O_3, $ONOO^-$, and nitrous acid are collectively known to be termed RNS.

The oxidation reactions facilitated by atmospheric oxygen or reactive oxygen species (ROS) are either postponed or suppressed due to the intervention of antioxidants.

Antioxidants can be categorized in to two types enzymatic and non enzymatic. The non enzymatic antioxidants are important body's antioxidant system components that are mostly low molecular weights and have the ability to directly and efficiently quench ROS and RNS [34]. In recent studies the inorganic nanoparticles proved to be effectively scavenging the oxygen based free radicals. The challenge of assessing individual antioxidants and their interactions led to the creation of assays aimed at quantifying total antioxidant capacity. Evaluating the total antioxidant capacity of all non-enzymatic antioxidants is essential in clinical studies to determine the *in vivo* antioxidant index accurately.

Wound Healing

The skin barrier disrupted by the consequence of trauma, surgery or disease is highly susceptible to bacterial infection. Microorganisms from the surroundings (eg. soil, water) or from mucosal surface (eg. bite) may enter into skin wound [35]. The incidence of wound infections varies between 2 to 17.5% following trauma and between 1 to 1.5% after minor surgical procedures [36]. Infections result in discomfort, inconvenience, and can impede or slow down wound healing, potentially leading to unsatisfactory cosmetic results. The primary goals of wound healing include pain reduction and expediting the restoration process, which must occur in a physiological environment conducive to tissue repair and regeneration [37]. In severe cases of wound infection results in spreading of infection to joint tissues, bone that leads to systemic disease (e.g. Shock). Topical antibiotics such as clioquinol (e.g. LocortenVioform), framycetin (e.g. Sofradex), mupirocin (e.g. Bactroban), metronidazole, fusidic acid (e.g. Foban), ciprofloxacin, gramicidin (e.g. Sofradex), sulfadiazine and chloramphenicol. The use of these antibiotics results in resistance and occasionally, pathogens may develop cross-resistance. The multi drug resistance pathogenic bacteria intricate wound infections are increasing today and these pose a great problem to patients [35].

Furthermore, heightened production of reactive oxygen species, lipid peroxidation, and inadequate scavenging mechanisms are significant factors in skin lesions and in regulating fibroblast proliferation. Skin injuries (cutaneous wounds) experience a decline in their overall antioxidant defenses, leaving them susceptible to damage from harmful oxygen molecules [38]. The use of antioxidants over the injured site found to be effective for wound healing and inflammatory conditions as it involved in the maturation of collagen fibers and fibroblast with good angiogenesis. There has been growing interest on the use of antioxidants for surgery, dermatology and cosmetology as they are natural inducers of wound healing [39]. A new therapeutic modality has been provided by the recent emergence of nanotechnology for the treatment of wounds using silver nanoparticles. The unique physicochemical properties of silver nanoparticles with broad antibacterial activities with antioxidant activity make them as best choice for treating wound infection. Silver nanoparticles promote wound healing by reducing inflammation, regulating cytokine activity, and limiting the infiltration of immune cells like lymphocytes and mast cells. The rapid healing of wounds by silver nanoparticles also improves the cosmetic appearance [40].

Conclusion

AgNPs are prominent nanomaterials for future application in many fields, including nanomedicine. This review discusses the classification, synthesis methods of silver nanoparticles. Green synthesis gains favor due to its environmental friendliness compared to other methods. The promising application of AgNPs in agriculture, aquaculture, textile, environment monitoring and health care discovers comprehensive research. Future research is crucial to optimize synthesis, large-scale production, and evaluate long-term biocompatibility and environmental safety.

Conflicts of Interest

The author declares no conflict of interest.

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