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A Brief Review Bio-Synthesized Silver Nanoparticles and Their Antimicrobial Potential

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Abstract

The synthesis, applications, and antimicrobial investigation of Silver Nanoparticles (AgNPs) have been indicated in several studies. However, only few studies were published characterizing the features of biologically synthesized AgNPs. Silver also, it salts long been employed by the old civilizations without reporting sides effects on the human health. While, Ag NPs has been just recently produced and used in the industrial, agricultural and medical applications. Regarding pharmaceutical applications, AgNPs have been used as antimicrobial and antioxidants agent because of the generation of free radicals (- o2) and reactive oxygen species (ROS), which cell killing/inhibition. The small size of AgNPs is facilitating their diffusion into cell lead to cell wall rupture. However, the small sized-AgNPs are associated with their toxicity, the smaller size nanoparticles, and the more toxic ones. AgNPs toxicity also depends on the environment's pH and concentration, in addition to size. In addition to discussing their antibacterial action and toxicity, this study will cover the numerous AgNPs manufacturing techniques and uses.

Keywords: Silver nanoparticles; Bio-synthesis; Applications; Antimicrobial activity; Toxicity.

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مقال مراجعة موضوع جسيمات الفضة النانوية المصنعة بيولوجيا و فعاليتها المضادة للميكروبات

رند محسن حسين مبارك[1]، عمار رياض قاسم الجبوري[2,3] و حسين سامي اسماعيل المياحي[3]

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الخلاصة

العديد من الدراسات اشارت الى عمليات تصنيع وتطبيقات واختبار فعالية جسيمات الفضة النانوية كمضادات للميكروبات، الا ان هناك عدد قليل فقط من الدراسات التي اشارت ال مميزات جسيمات الفضة النانوية المصنعة بايولوجيا. استخدمت الفضة واملاحها لفترة طويلة من الزمن و قبل الحضارات القديمة دون الاشارة الى اي اثار جانبية على صحة الانسان. ان انتاج واستخدام جسيمات الفضة النانوية في التطبيقات الصناعية والزراعية والطبية قد ظهر حديثا. فيما يتعلق بالتطبيقات الصيدلانية، فقد استخدمت جسيمات الفضة النانوية كعامل مضاد للميكروبات ومضادات الاكسدة بسبب قدرتها على انتاج أنواع من مركبات الاوكسجين التفاعلية والجذور الحرة التي تسبب قتل / تثبيط الخلايا. ان الحجم الصغير لجسيمات الفضة النانوية يسهل عملية انتشارها داخل الخلية ويؤدي الى تحطيم جدار الخلية الميكروبية. ومع ذلك، فانه قد وجد ان الحجم الصغير لجسيمات الفضة النانوية يكون مرتبط بسميتها ، فكلما كانت الجسيمات النانوية اصغر حجما، كانت اكثر سمية. بالإضافة الى الحجم، فان سمية جسيمات الفضة النانوية ترتبط بتركيزها وكذلك درجة حموضة البيئة. الغرض من هذه المقالة هو لمناقشة اكثر واهم وافضل الطرق المستخدمة لتصنيع جسيمات الفضة النانوية وتطبيقاتها، بالإضافة الى فعاليتها البيولوجية و سميتها و كعامل مضاد للميكروبات المرضية.

كلمات مفتاحية : جسيمات الفضة النانوية, تخليق حيوي, تطبيقات, الفاعلية الضد مايكروبية, السمية.

Introduction

The study of manipulating materials at the nanoscale is known as nanotechnology and is an area that is expanding quickly. (1-100nanometers). It involves design, production, as well as the use of tools and materials with unique properties and functionalities. Medicine is one of nanotechnology's most exciting potential uses where it has the potential to revolutionize the way of diagnose and control diseases. [1].

One type of nanomaterial that has gained attention for its antimicrobial properties is AgNPs that are less than 100 nanometers in size. They have been discovered to work well against a variety of bacteria, including bacteria, viruses, and fungi [2]. The antimicrobial active of AgNPs is due to their capacity to penetrate microbial cells and disrupt their membranes and metabolic processes. As a result, cell proliferation is inhibited, which ultimately causes cell death. Additionally, AgNPs have the capacity to produce (ROS) reactive oxygen species., which further contribute to their antimicrobial properties [3]. Silver nanoparticle have demonstrated excellent promise as antimicrobial substances with numerous studies demonstrating their effectiveness against a variety of microorganisms. Additional study is required to completely comprehend their mode of action and create safe and effective applications in medicine and other fields [4].

AgNPs have been employed several applications including, medical, environmental, industrial, foods and electronics. AgNPs was recruited in cancer therapy as a chemotherapeutic drug [5]. In addition, it was used to eliminate pollutants and pathogens from the soil, water and air and degrade the hazardous organic substances [6]. Moreover, it has been used to control food spoilage [7] and in gas sensors and biosensors [8].

1. Features of Silver Nanoparticles

Due to their special features, such as optical, electrical, and magnetic properties that are reliant on shape and small size. AgNPs can be used in a range of products, such as antimicrobial ones, Components for electronics, cryogenic superconductors, biosensor materials, composite fibers, and cosmetics. AgNPs have been produced and stabilized employing a range of biological, chemical, physical, and approaches [9]. Due to their biocidal activity, silver-based compounds have been employed for millennia as non-toxic inorganic several uses for antibacterial agent, such as wood preservatives, hospital water purification, wound or burn treatment, and more. In fact, silver ions and the chemicals are reported as very harmful to pathogenic microorganisms, bacteria and fungus but not to the animal cells. Many scientific fields have been significantly impacted by the revolution of nanoparticles, the synthesis of AgNPs has tended to do so [10]. Due to the special characteristics of nanomaterials, there have been applied in the electrical, nanomedical, biomaterials, food, and energy domains. In reality, Compounds based on silver cost far less than those based on gold and AgNPs are now recognized as a significant class of nanomaterials. They are currently mostly employed as catalysts or antibacterial / antifungal drugs [11].

2. Applications of silver nanoparticles

Silver nanoparticles have garnered significant attention in a variety of fields because of their distinctive qualities, namely its large surface area to volume ratio, biocompatibility, and antimicrobial activity. Some of the applications of AgNPs, include:

- Medical Applications
- Environmental Applications
- Industrial Applications
- Pharmaceutical Applications

Uses in biomedicine, such as medication delivery methods, wound healing, and cancers treatments, AgNPs have undergone significant studies. AgNPs are a suitable molecules for targeting drug delivery since they are tiny and have a high surface area, both of which allow them to enter cells and interrelate with biological elements of the host's cells. Additionally, it has been demonstrated that AgNPs stimulate tissue growth and enhance wound healing by lowering inflammation. AgNPs have been employed in cancer therapy as a radiosensitizer to improve the efficacy of radiation therapy as well as a delivery mechanism for chemotherapeutic drugs [5].

Environmental applications, include water purification, air filtration, and soil remediation are just a few of the environmental applications where AgNPs have been applied. Heavy metals, organic contaminants, and contaminating bacteria can all be successfully removed from water using AgNPs. AgNPs have also been added to air filters to eliminate pollutants and pathogens that are carried in the air. AgNPs have been employed in soil remediation to decrease soil-borne pathogens and decompose hazardous organic compounds [6].

Regarding, packaging for food and in order to improve the antibacterial properties of food packaging materials and increase shelf life of packed foods, AgNPs have been added to prevent the development of bacteria, fungus, and viruses that cause food spoilage [7].

Many different electronic gadgets have been made using AgNPs., include displays, sensors, and conductive inks. Because of their great electrical conductivity, AgNPs can be easily included into inks and coatings to create conductive channels on a variety of surfaces. AgNPs have also been used as sensing elements in gas sensors and biosensors [8].

3. Synthesis of silver nanoparticles

Given their unique physicochemical properties characteristics and myriad applications in industries including catalysis, electronics, medicine, and energy, silver nanoparticles (AgNPs)have garnered a great deal of attention in recent years. There are numerous ways to make AgNPs; biological. Chemical, and physical, methods.

3.1.Physical of methods:

- Laser ablation: this technique, a silver target is ablated with a laser beam in a liquid medium, causing the creation of AgNPs. By changing the laser's pulse duration, wavelength, and fluence, one may regulate the nanoparticles' size and form [12].
- Thermal decomposition: In this technique, AgNPs are produced by heating silver salts in a suitable solvent under controlled conditions. By changing the reaction temperature, pressure, and precursor concentration, Controllable nanoparticle characteristics include size and shape [13].

3.2.Chemical methods:

- Reduction by chemicals: A reducing agent is used in reduction procedures to turn a silver precursor into AgNPs. In this method, citrate, hydrazine, and sodium borohydride are often used as reducing agents. Due to the simplicity and high productivity, this technique is commonly utilized [14].

3.3.Biological methods:

- Microbial methods involve using microorganisms like bacteria, fungus, and algae, to synthesize AgNPs. It has been demonstrated that this technique yields AgNPs with a limited size distribution. and high stability [15].
- Plant-mediated methods entail using plant extracts as stabilizing and lowering agents to synthesize AgNPs. This method have been shown to produced AgNPs characterized by a strong stability and a restricted size distribution [16].
- Enzymatic synthesis, enzymes are used to reduce silver ions and produce AgNPs. Nanoparticles can be regulated in terms of size and shapes. by varying the enzyme concentration and reaction circumstances [17].

4. Synthesis of silver nanoparticles by microorganisms

Presence of reductase enzymes as microbial products may naturally purge heavy metals and transform metals into salts into a narrow size distribution. less polydispersity in nanomaterials [18]. Microbes have been used to produce nanomaterials both within and outside of cells. Metal-resistant peptides, enzymes, reducing co-factors proteins, and genes are essential reducing agents that give nanomaterials their natural capping and stability. [19]. Metal nanoparticles and other inorganic nanoparticles has been produced in large quantities by bacteria. [20].

The bacterial cell-produced nitrate reductase enzyme participates in the bio-reduction of silver performs a crucial part in turning nitrate into nitrite. [21]. When nitrate is regenerated into cluster, AgNPs are synthesized [22]. Temperature, pH, and bacterial species are only a few of the variables that affect the stability and characteristics of produced AgNPs [23]. Bacteria grown in medium are typically first re-suspended in water before being combined with silver salt. According to several reports, silver detoxification results from the surface-bound, tiny periplasmic space-binding proteins that bind silver. The releasing metals are propelled by efflux pumps, which additionally guard the cytoplasm against toxicity [24] According to a paper, amino acid moieties act as nucleation sites for AgNPs to develop in proteins that bind silver in organic matrixes [25]. The extracellular synthesis involves the secretion of AgNPs from the bacterial cell. Obviously, extracellular environments contain metal nanoparticles, Metal ion reduction is catalyzed by secretory or reductive enzymes. [26].

5. Mechanism of action of silver nanoparticles

Silver has become one of the most thoroughly studied oligodynamic materials due to its potent antibacterial properties, efficiency, low toxicity, and wide range of disinfection uses. When heavy metals, in particular, are present in low concentrations, their biocidal effects can be seen, known as the oligodynamic effect are used. AgNPs characterized by; (a) their extensive surface area, (b) possessing the capacity to bind to bacterial biomolecule, (c) having the capacity to infiltrate cells, creating free radicals and (ROS) reactive oxygen species, and d. a moderator's capacity to influence the signaling pathways used by microorganisms, as well as e. having oligodynamic effect [27].

AgNPs in particular, which have a wide range of oligodynamic properties, may have aided in the creation of nanotherapeutics, which have drawn a lot of attention. The oligodynamic effect of nanoparticles can also be influenced by the surface modification of AgNPs that can make these nanoparticles more stable. For instance, polyimide is used to modify AgNPs. The antibacterial activity AgNPs and silver stability can be improved using partially encapsulation technique in polyimide [28] The glass spheres (PDA-HF/GSs) coated with polydopamine and hydrofluoric acid have demonstrated high adherence to *Bacillus* and *E. coli* [29]. Thus, stopping the development of biofilm. A consistent dispersion of NPs was seen after the modification of AgNPs by adding metal oxide using a solution casting technique. These altered nanoparticles also impede the development of biofilm-forming bacteria including *S. aureus and E. coli*. [30]. Comparing AgNPs to other metallic nanoparticles which their antibacterial actions are more complicated but less damaging for cells. There are some metallic nanoparticles, like (CuNPs) copper nanoparticles, are more effective against bacteria than AgNPs, yet they are harmful to cells. The mode of CuNPs action involves the breakdown of bacterial membranes and the transfer of electrons via photocatalytic action [31]. CuNPs have greater antibacterial action, but they are less stable and are more likely to undergo oxidation, turning into CuONPs. In contrast to AgNPs, gold nanoparticles (AuNPs) are more expensive and less effective at preventing the growth of pathogenic bacteria because they lack the intrinsic antibacterial action. They exclusively use electrostatic forces to adhere to the bacterial surface [32].

Antibacterial activity of silver nanoparticles

AgNPs possess antimicrobial potential that attracted the scientists' attention to investigate their activity against various microbial species because of microbial mutations that generate resistance to medications, we urgently need fresh advances in antibacterial products or agents. Moreover, given that they were less reactive than silver ions, AgNPs were ideal for application in clinical and therapeutic settings. [33]. AgNPs have four recognized antibacterial effects.; (1) adherence to a microbial cell's surface membrane, (2) invasion of host cells that disrupts biomolecules and damages intracellular structures, (3) by producing ROS, which causes the cell's oxidative stress, to cause cellular damage and (4) stop cellular signaling pathways are interfered with. The general method of action in bacteria is depicted in Figure (1).

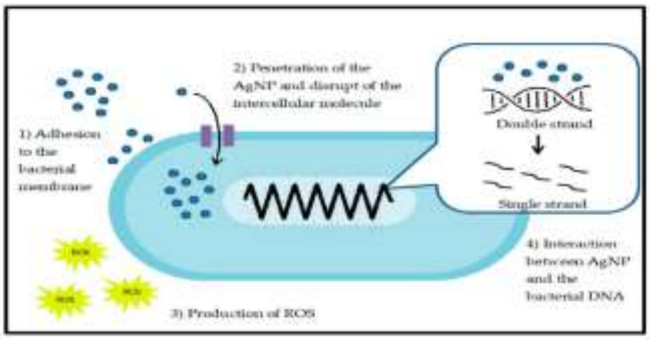

Figure 1: Antibacterial activities of silver nanoparticles [34].

Because of the electrostatic interaction between the silver ions' positive charges produced by the oxidation of AgNPs and the microbial cell membrane's negative charge, the nanoparticles frequently attach to the membrane of the bacterial cell, when it exposed to AgNPs [34]. Furthermore, AgNPs showed a great affinity for binding to the sulfur-containing proteins in microbial cell walls. The structure of the cell membranes is irreversibly altered when AgNPs adhered to the bacterial cell membrane [35]. Consequently, the cell membrane's permeability as well as the integrity of the lipid bilayer are compromised. The whole cell regulation can be affected due to the changes in cell structure leading to an increasing in the membrane permeability [36]. As they bind to the microbial membrane's surface, AgNPs can enter cells and affect crucial biomolecules and cellular activity. Gram negative bacteria with water filled channels, such as *E. coli*, have an outer membrane, Porins, which are responsible for allowing AgNPs into bacterial cells. After penetration of cells, AgNPs binds to the elements that make up cells, including proteins, lipids, and biomolecules like DNA, causing damage to the bacterial internal structures. Ions of silver that have been liberated inside cells binds to the negatively charged proteins, changing their structural makeup and ultimately making them inactive. The findings demonstrated that the respiratory chain dehydrogenase is inhibited by the AgNP. In Gram-positive bacteria like *S. aureus* by changing many enzymes into dihydroxyacetone. This interferes with the normal growth and metabolism of the bacterial cell [37]. Moreover, AgNPs can react with bacterial DNA, denaturing it and preventing microbial cell development [38]. The same polar charges shared by DNA and AgNPs cause electrostatic repulsion, which can reduce the stability of DNA structure [39].

Another method of AgNPs activity is the production of (ROS) reactive oxygen species, which normally causes cellular oxidative stress in bacteria. The word "ROS" refers generation of oxygenated substances comprising hydroxyl radicals, superoxide, and hydrogen peroxide that are involved in a variety of cellular biological processes. AgNPs' antibacterial feature is typically associated with their capacity to generate –o2 free radicals and ROS, which in turn, causes cells to experience more oxidative stress. The intercellular ROS production is associated with breakdown of lipids, leaking of cellular biomolecules, and finally cell death, these events are the most significant signal of the toxicity of nanoparticles [40].

6. Toxicity of silver nanoparticles

Silver nanoparticle are worldwide use in the industrial and medical applications owing to their distinctive biological and physicochemical characteristics. The frequent exposure and usage of nanoparticle in the animal production and in human health, makes ensuring their safety is highly important [41].

According to toxicity evaluation of AgNPs, the biological behavior of organs, tissues, cells, subcellular structures, and proteins can all be affected. Because of their small size, the skin, lungs, and brain can all be easily invaded by nanoparticles. Where they can cause tissues' damage [42]. To verify the safety and antimicrobial potential, at the same time, the *in vitro and in vivo* biological activities of nanoparticle and their cytotoxic effect must be further assessed in animal models [43]. That's why turning to using biological methods to synthesized AgNPs and determine their MICs are essential to avoid their negative side effects of using high concentrations. Real-time reverse transcription PCR and microarray are increasingly being used for analyzes for measuring changes in hundreds of genes' expression across a wide range of experimental circumstances, as these techniques are extremely sensitive and precise [42]. NPs have interesting biological and physiochemical features that make them potential antibacterial and therapeutic agents. They can be applied to overcome several difficulties in the field of nanomedicine [43].

Conclusion

Silver nanoparticles has been just recently produced and used in the medical, agricultural and industrial applications. They are suitable molecules for targeting drug delivery since they are tiny and have a high surface area. In addition, AgNPs was recruited in cancer therapy as a chemotherapeutic drug. Environmentally, it was used to eliminate pollutants and pathogens from the soil, water and air. Despite of their beneficial, the toxicity of NPs in general on viable cells was reported in several studies causing tissues' damage. Verification of the safety and antimicrobial potential of each nano-formulation, *in vivo* and *in vitro* should be confirmed before officially accepted and commercially used That's why turning to use biological methods for synthesizing AgNPs and determine their MICs are essential to avoid their negative side effects of using high concentrations.

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