Journal of University of Babylon for Pure and Applied Sciences, Vol. (28), No. (3): 2020
Online ISSN: 2312-8135, Print ISSN: 1992-0652

Applications of Silver Nanoparticles as Antibiotics for Pathogenic Organisms: Bacteria, Fungi ,Viruses and Algae

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Article Information
Submission date: 8 /11 / 2020
Acceptance date: 3 /12 / 2020
Publication date: 31 / 12/ 2020

Abstract

Silver nanoparticles are used in the medical and engineering fields and are still of interest to scientists, possibly due to their small size compared to their efficiency. Previous research has demonstrated the efficacy of silver nanoparticles in inhibiting microbes as they are used as reducing agents. Silver nanoparticles are manufactured in a variety of chemical or physical ways that may have environmental hazards due to their potential toxicity, or they are manufactured in biological, environmentally friendly and non-toxic ways.
In this review, we first present the properties of nanoparticles and their synthesis methods and then discuss their role as inhibitors of bacteria, fungi, viruses and algae.

Keywords: Silver nanoparticles; Biomedical applications; Efficiency of antibiotics; Nanotechnology.

Introduction

Nanotechnology is the use of matter on an atomic, molecular, and supramolecular scale for industrial purposes. The use of nanoparticles and nanomaterials has developed rapidly in different fields recently due to their possessing improved properties that depend on size and shape, and from these fields their use in health care is also involved in the cosmetics, medicine, health, energy and environmental industries. the size of nanoparticles used in these fields ranges should be from 1 to 100 nanometers [1-3]. Due to the development of many microbial strains and their resistance to antibiotics, metallic nanoparticles have been used to contain anti-bacterial properties due to the large surface area compared to the size[2].

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Online ISSN: 2312-8135, Print ISSN: 1992-0652

The World Health Organization considered that resistance of microbes of bacteria, fungi and viruses to antibiotics is a serious problem, and there are efforts to develop new antibacterial and antiviral drugs. Silver is a disinfectant and sterilizer that has the ability to fuse with disulphide bonds of the glycoprotein or protein of microbes. Silver nanoparticles , silver ions can alter the 3- dimensional formation of proteins through interaction with disulphide bonds and prevent the practical processes of the microorganism [4-6].The reaction between nanoscience and biology line is recognized as Nano biotechnology, while the linkedzonefamousas nanomedicine, where is used with nanostructured materials to diagnose and treat diseases[7,8].Silver nitrate nanoparticles prepared with the addition of plant extracts were used to treat bacteria resistant to multiple antibiotics, including: *Streptococcus pyogens*, *Pseudomonasaeruginosa*, *Bacillus subtilis*, *Escherichia coli* and *Staphylococcus aureus* [9]. Previous studies indicated that AgNPs had kindly antifungal and antimicrobial effects (10-12). Other researcher are reported the growth inhibition of the AgNPs on *Trichophyton mentagrophytes* and *Candida albicans*[12]. In addition the AgNPs had inhibitory effects on the growth of *T. mentagrophytes*, *C. albicans*, *C. tropicalis*, and *C. glabrata*[13].

There are some difficulties including treating viruses with conventional medicines, the building of reservoirs in cellular sites such as the blood-brain barrier[14],the use of RNA interference (RNAi) technology a public molecular process for the therapy of more infectious diseases. The failure of RNA to cross the cell membrane, lead to the great molecular weight and anionic charge[15], fast kidney permission, absorption by phagocytes, and toxicity cause to catalyzed immune response[16], utilizing of treatments containing nanomaterials have the capacity to be wheel through cell membranes[17].Previous research has shown that anti-algae effectiveness was bigger at low pH. AgNPs were studied to mark the function of nanoparticleslinked with *Microcystis aeruginosa* and the influence of silver ions on algaecidal toxicity[18].

This review will provide a summary of nanotechnology and the latest related literature describing the application of nanotechnology to treat harmful bacteria, fungi, viruses and algae and the mechanism of action of nanomaterials on the living cell and microbial cell.

The properties of silver nanoparticles as antibiotic and their function as inhibitor of microorganisms

Silver metal was used in the past and widely used as jewelry and tableware, in addition to its use as an antimicrobial to prevent microbial contamination. Silver has been used as a natural biocide for coating milk bottles by the Phoenicians, and silver is considered to be against a large number of microorganisms such as bacteria, fungi and viruses. water silver nitrate was used in 1884 as eye drops for newborns to prevent the transmission of Neisseria gonorrhea from mothers that Infected with this bacteria . Silver nitrate is less toxic to animal cells. It was also used in the World War to treat soldiers ’wounds to prevent contamination with microbes [19]. The properties of silver nanoparticles as anti-biotic rely on size and environmental situations (size, pH, ionic strength)and capping factors.

The positive charge on silver ions is the vital site for silver's effectiveness as an antibiotic, as silver must be in an ionized state and upon contact with moisture it releases ions[20]. Complexes are formed between the silver ions and the nucleosides of nucleic acids, and silver is added where the ions are slowly released or silver is used in its ionized form[21,22] Previous studies demonstrated the electronic interaction between the negative charge of nanoparticles and the negative charge of bacterial cells[23], and these studies have suggested that nanoparticles can be considered an anti-bacterial[24,25]. When the nanoparticles accumulate, they will penetrate into the cell membrane and then into the cells and this leads to the breakdown of the cell wall and cellular membranes where they connect to the thiols group of cell enzymes that role in generation energy then lead to suppression this enzymes, When silver ions enter the cell, they interfere with the bases of pyrimidine and purine and thus change and denature in a molecule, then the microbial cell lysis, Where the nanoparticles bind with the phosphothyrosine of the bacterial peptide and thus affect the transmission of signals and then inhibit the growth of microorganisms[26].Several experiments were conducted on laboratory mice to study the effect of silver nanoparticles on immunity, where they examined the effect of localized silver nanoparticles on the induction of apoptosis of inflammatory cells and the role of silver nanoparticles in the inhibition of inflammatory cytokines by measuring mRNA expression and protein expression of IL-12 and TNF-a, which was suppressed. The expression of these inflammatory cytokines is significantly via silver nanoparticles[27].

Synthesis of silver nanoparticles

The knowing of the silver nanomaterials making processes is significant due to an overall achievement and field of utilize perspective. The major trouble in making the silver nanoparticles is the control of their physical features like obtaining uniform particle size distribution, similar shape, morphology, nanoparticle coating or stabilizing factor, chemical composition or type and crystal structure. The processes can be categorized that they follow public patterns and the differences like reactants and the reaction conditions. Top-down versus bottom-up, green versus no green, and traditional versus nontraditional synthesis methods have been notified. The traditional synthesis methods contain the use of citrate, borohydride, two-phase systems (water-organic),organic reducers like cyclodextrin, and micelles and/or polymer in the making process. The untraditionalprocessesconsist laser ablation, radio catalysis, vacuum evaporation of metal, irradiation, photolithography, electrodeposition and the electro condensation[28].

Top-down and bottom-up are the two synthesis patterns of metallic nanoparticles involving chemical, physical, and biological means. The common fabrication of the nanoparticles includes chemical and physical processes. The top-down patternutilizes macroscopic initial structures, which can be externally controlled in the processing of nanostructures. The nanoparticles made by mechanical mashing of bulk metals and moreover of colloidal protecting factors are some examples of the top-down method. The bottom-up patterns consist the miniaturization of materials compounds with further self-assembly process. The lowering of metals, electrochemical processes, and decomposition are the examples of the bottom-up processes. Moreover, the making

Journal of University of Babylon for Pure and Applied Sciences, Vol. (28), No. (3): 2020
Online ISSN: 2312-8135, Print ISSN: 1992-0652

patterns can be classified as either green or non-green. Green synthetic systems utilize environmentally friendly factors sugars, plant extracts, bacteria and fungi to form and set Nano silver[28](figure1).

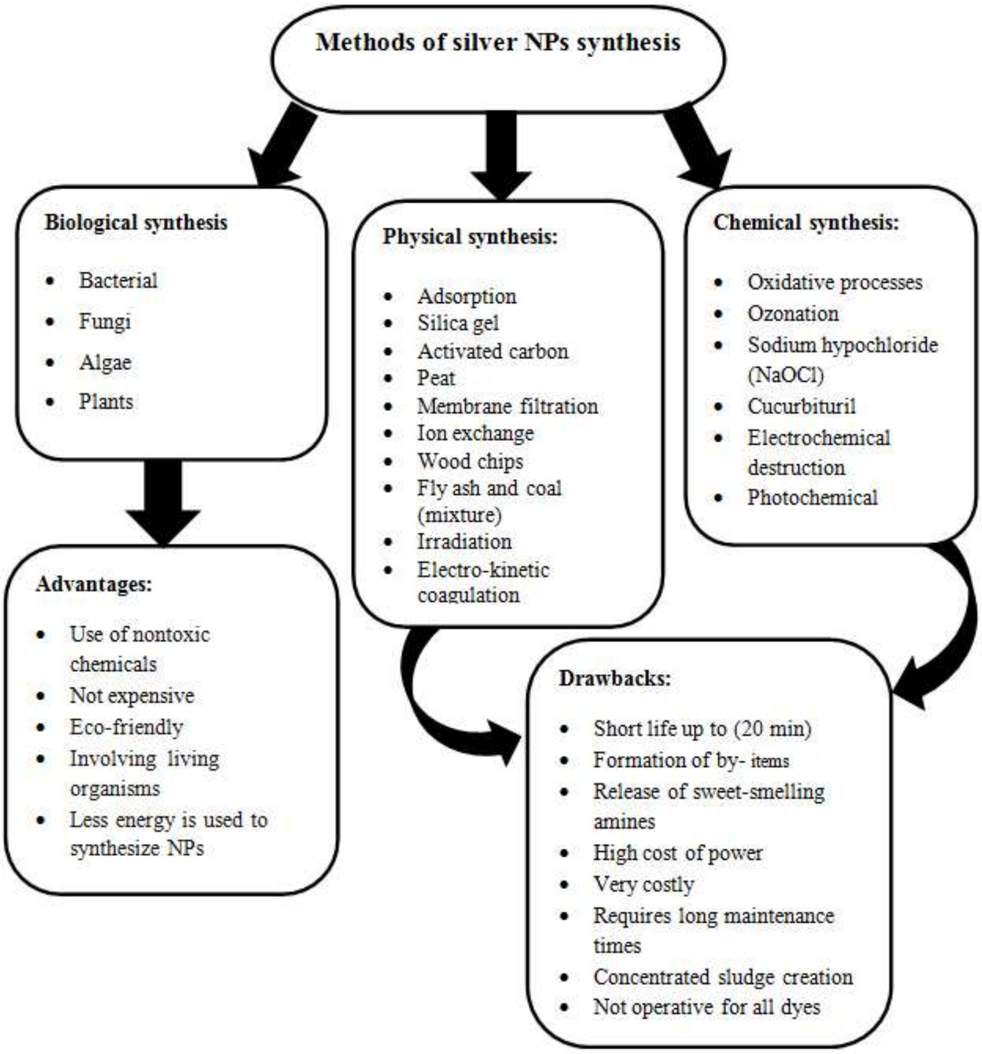

Figure 1: Variousprocesses of silver nanoparticles and its advantages and its shortcomings [29].

The role of nanotechnology in the treatment of bacterial infections

Excessive and incorrect use of antibiotics leads to an increase in the resistance of microbes to those antibiotics, as they were previously sensitive to these antibiotics. Therefore, multiple resistance strains appeared.In recent times, studies have shown the ability of bacteria to possess the characteristic of antibiotic resistance, and this is evidence of the development of the bacteria to multiple mechanisms that gave it the characteristic of resistance. It may be natural, such as its possession of an outer membrane and its function as a barrier that reduces the passage of antibiotics into the inside of the bacterial cell or acquired resulting from a change in the genes or the acquisition of genes Resistant, bacteria become resistant to it[30].Substitutional curative factors such as silver nanoparticles are suggested as a favorite factor to aid administer and block the biofilm formation of various bacterial species. Where a research study showed that making silver nanoparticles (AgNPs) by utilizing *Myrtus communis* leaf extract as anti-biofilm formation factor, utilizing a tube process they have determined the minimum inhibitory concentrations (MIC) value of AgNPs against planktonic growth of *P. aeruginosa* thus inhibiting the growth of these bacteria by inhibiting biofilm formation[31,32].

Previous studies showed that silver nanoparticles have high anti-bacterial activity[33].A study showed that the silver nanoparticles were prepared using green synthesis, It has a clear inhibitory effect on *Esherichia coli* and *Proteus mirabilis* bacteria[34],The reason for the resistance of *E.coli* and *P. mirabilis* bacteria to antibiotics may be due to mutations, and thus the bacteria acquiring resistance to antibiotics or as a result of loss Penicillin Binding Proteins or slow in the permeability of antibiotics or because of the effect on DNA gyrase enzyme , or the ability of bacteria to produce Beta lactamase enzymes[35-37].Gram-positive bacteria are little sensitive to Ag+ than gram-negative bacteria, the reason for this may be due to the components of the Gram-positive bacterial cell wall from the peptidoglycan layer, which is more dense than the Gram-negative bacterial layer of peptidoglycan, and thus the Gram-positive bacterial cell wall is more dense and since the peptidoglycan has a negative charge and the silver ions have a positive charge, they may stick Silver ions with peptidoglycan are more attached to peptidoglycan's Gram-positive bacteria than the Gram-negative bacterial[38].

Based on their results, some studies have stated that the use of silver nanoparticles and their accumulation on the bacterial cell wall leads to inhibition of protein formation and thus to the instability and loss of the ATP molecule[39].Figure 2 shown the silver nanoparticles stick to the bacterial cell wall and later penetrate it, this leads to a change in the structure of the cell membrane, increased permeability of the membrane, and thus cell death[40]. If free radicals is formed, this is prompted membrane harm, NSPs can emit silver ions and connect with the thiol groups of many pivotal enzymes and phosphorus-containing bases[37], consequentlyblockseveral works in cells, such as stop cell division and replication of DNA [41]. also, NSPs may regulate signal transduction by altering the phosphotyrosine that relating with bacterial peptides of the antibacterial mechanism[42].

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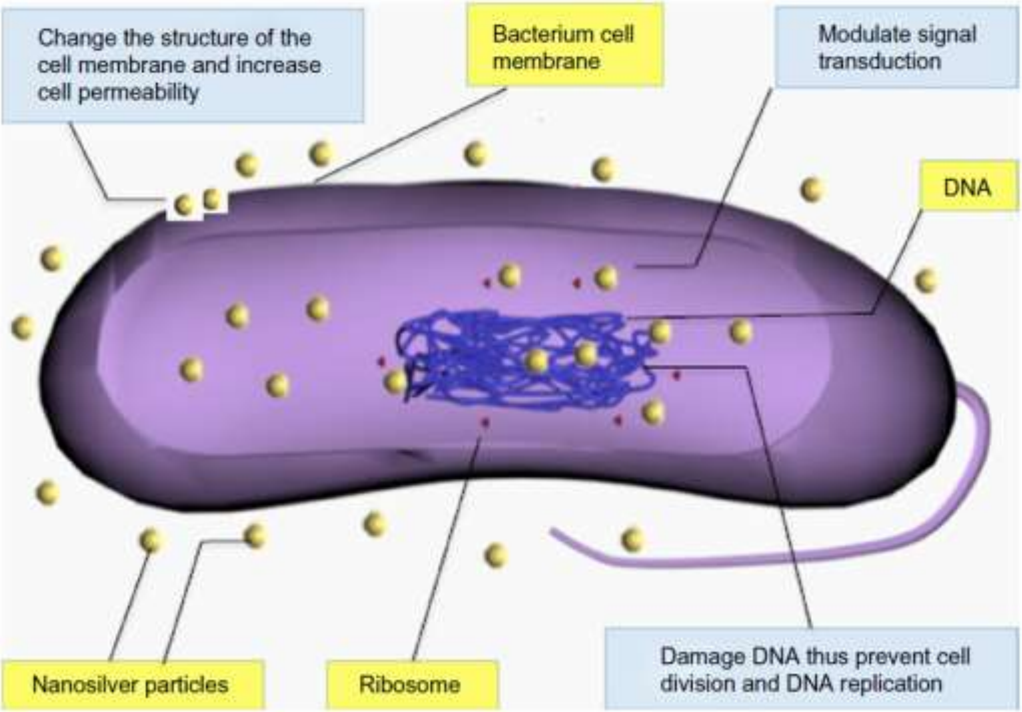

Figure 2: Action of Nano silver particles on bacterial cell [43].

The role of nanotechnology in the treatment of fungi infections

The high dispersal of fungal contagion, the rising in its impedance to drugs, the limited availability of drugs used to treat fungi with minimal side effects, and an increase in morbidity and mortality rates among people, especially in people who are immunocompromised and those with serious diseases[44-49].

AgNps influenced various cellular goals conclusive for drug impedance and pathogenicity in the fungal cells, new cellular targets of AgNps which include fatty acids like oleic acid (figure 3), vital for hyphal morphogenesis of *Candida*[50].Silver nanoparticles is a powerful antifungal with a wide spectrum of fungi inclusive *Aspergillus, Candida and Saccharomyces*[51].

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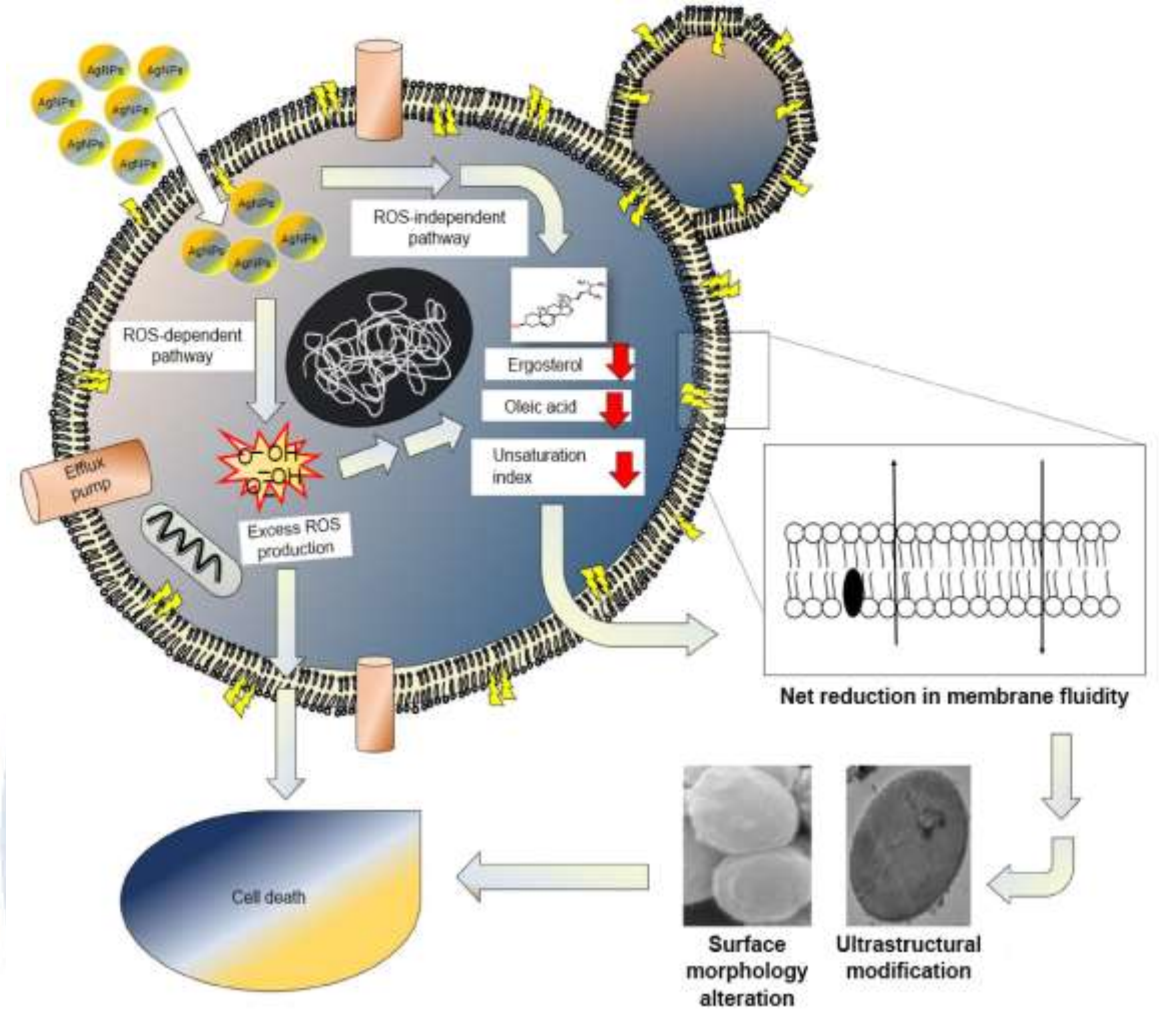

Figure 3: Mechanism of AgNps against *Candida* cells.(Abbreviations: AgNps, silver nanoparticles; ROS, reactive oxygen species).

The role of nanotechnology in the treatment of viral infections

Viral contagion leads to negative effects not only on health, but also on social and economic development[52], as well as the development of viruses and their resistance to drugs impedes the elimination of viral contagion[53], especially in people with HIV[54-57], influenza virus[58],respiratory syncytial virus[59], herpes simplex virus type 1[60], and monkeypox virus[61] , and thus high mortality rates in addition to additional costs for medicines, and this constitutes a burden on public health systems[62].Ag0 (atomic) and Ag (ionic) it is released , whilst silver salts release Ag only this lead to NSPs have higher drug effective against viruses efficiency than silver ions[63].

The anti-HIV action of Nano silver particles is located on the suppression of the primary phases of the HIV-1 cycle.47 NSPs can linked to glycoprotein (gp)120, thus block cluster of differentiation (CD) 4-dependent committing, incorporation, and infection. The role of NPs is an effective virucidal factor to prevent HIV-1 cell-free and cell-related infection[64].NSPs could be investigated to be a broad-spectrum factor versus a types of viruses and are not lead to evolving impedance. the tannic acid changed AgNPs have the capacity to stop HSV-2 infection by direct suppression of virus connection, permeation and next-infection prevalence(figure 4), and considered a good candidates for effective anti-HSV-2 at lower concentrations and creation of an anti-inflammatory response[65].

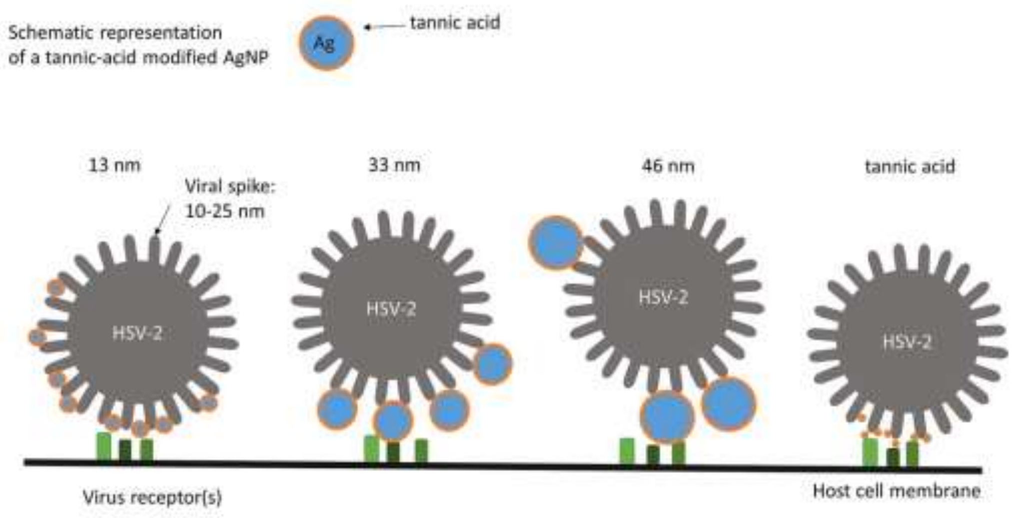

Figure 4 : Connection between tannic acid changed AgNPs or tannic acid and HSV-2 virion.

Silver nanoparticles have mostly perfect features, as they have a great surface from which these ions can be freed. Lab trials have shown that they are active opposite to specific kinds of corona virus family. Researchers are presently examining whether this applies to the creator of the disease COVID-19 and are looking into the utilize of surface coverings with silver nanoparticles in hospitals and public sites. The pandemic of COVID-19 is circulating incorrect due to the loss of active antiviral means. Silver nanoparticles (AgNP) have been studied to have antiviral features and are assumed to prevent SARS-CoV-2. A number of studies have estimated the antiviral influence of AgNPs .It was observed that particles of diameter around 10 nm were influence in preventing extracellular SARS-CoV-2 at concentrations ranging between 1 and 10 ppm while cytotoxic effect was observed at concentrations of 20 ppm and above. Luciferase-based pseudo virus entry assay revealed that AgNPs potently inhibited viral entry step via disrupting viral integrity. These studies suggest that AgNPs are very strong microbicides against to SARS-CoV-2 but should be utilized with warning lead to their cytotoxic effects and their powerful to disrupt environmental ecosystems when incorrectly organized[66].

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The role of nanotechnology in the treatment of algae

Algae are anextremelyvarious group of mostly photosynthetic microorganisms. Watery ecosystems are the generality well-known algae environment. algae also colonize terrestrial habitats with extreme environments. this terrestrial species are known as aerophytes algae [67,68].Through many physiological and biochemical methods aerial algae produce chemical components that corrode building substrates and give them to infiltrate further into thematerial[69-71]. *Apatococcus lobatus* is one species of aerial algae are an significant biological agentleading to biodegradation of facade buildings. silver nanoparticles (AgNP) manufactured with specifications participating to the effecting and toxicity especially that it has a spherical shape and has a small size on the most repeatedly, which includes green algae in aerial biofilms, that considered as biodegradation factor. alters in the chloroplasts shape and the photosynthetic activity of the cells under AgNP submission. This leading to loss in the photosynthetic activity of cells and suppression of aerial algae growth[72](figure 5). The AgNP leaded a remarkable lower in the photosynthetic activity of the aerophytes algal cells. It is extremely possible that this suppression was concerned to a altering the maximum quantum produce for first photochemistry and electron transport activity[73].

In order for drugs established on silver nanoparticles to be used in the therapy of diseases, clinical tests and more future research must be conducted and what are the best physical and chemical methods for manufacturing silver particles, and do microorganisms show resistance to the treatment used in silver nanoparticles and is there a cellular or genetic toxicity. Nevertheless, research conducted so far has suggested that silver nanoparticles can be designed to have antimicrobial activity, stability and decrease stress side effects.

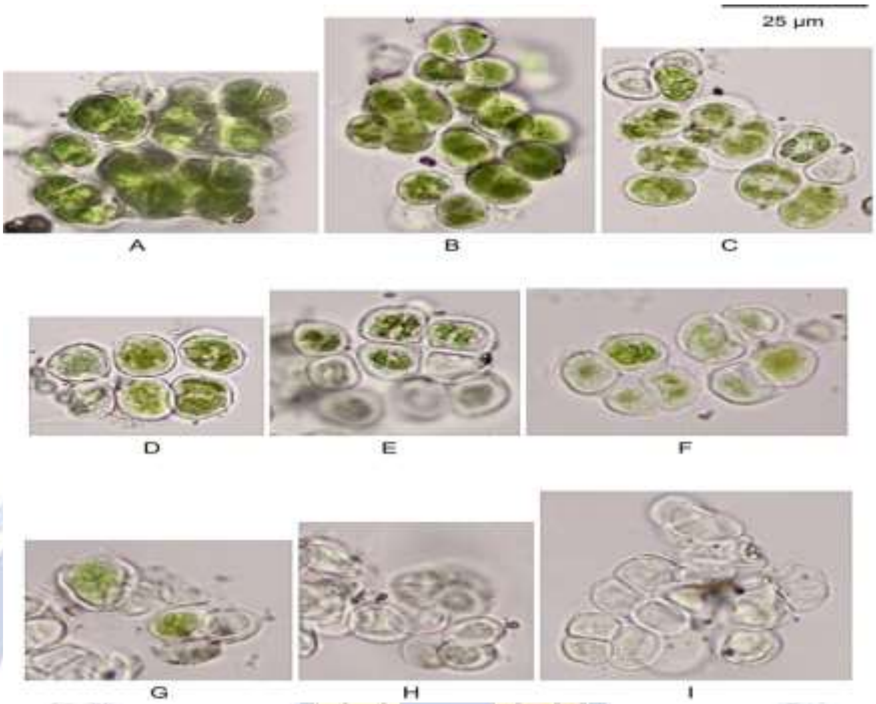

Figure 5: Morphological alters in chloroplast of *Apatococcus lobatus* after addition AgNP(A-B)Controlcellswithaproperlyformedchloroplast;(C-G)followingstagesofchloroplastdeclination; (H-I)defunct cells without chloroplast[71].

Conflict of Interests.

There are non-conflicts of interest .

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الخلاصة

تُستخدم الجسيمات النانوية الفضية في المجالات الطبية والهندسية ولاتزال محل اهتمام العلماء، وقد يكون هذا بسبب صغر حجمها مقارنة بكفاءتها. أثبتت الأبحاث السابقة كفاءة الجسيمات النانوية الفضية في تثبيط الميكروبات حيث تستخدم كعوامل اختزال. يتم تصنيع جسيمات الفضة النانوية بعدة طرق كيميائية أو فيزيائية التي قد يكون لها مخاطر بيئية لاحتمالية سميتها او تصنيعها بطرق بيولوجية وصديقة للبيئة وغير سامة.

في هذه المراجعة، قدمنا أولاً خصائص الجسيمات النانوية وطرق تصنيعها ثم نناقش دورها كمثبطات للبكتيريا والفطريات الفيروسات والطحالب.

الكلمات الدالة: جسيمات الفضة النانوية, تطبيقات الطب الحيوي, كفاءة المضادات الحياتية, تقنية النانو تكنولوجي.