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ORIGINAL

The Role of Nanoparticles in Wound Healing: Synthesis, Characterization, and Mechanisms of Action

El papel de las nanopartículas en la cicatrización de heridas: síntesis, caracterización y mecanismos de acción

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ABSTRACT

As a consequence of its distinctive functioning and diverse set of uses, nanotechnology is a discipline that is expanding quickly. To prevent, cure, diagnose, and control illness, nanomedicine examines the potential applications of nanotechnology knowledge and techniques. Silver nanoparticles with a length between 1 to 100 mm are thought to be the most important in this aspect because of their exceptional property, ability that form different nanostructures, incredible group for antibacterial effects, the space for wound healing and other beneficial ability, and efficiency in production. Research analysis the different biological, chemical, and physical techniques for nanoparticles development are explored. The techniques to employ silver nanoparticles as antibacterial substances, anticancer, in dentistry and bone healing promoter, in wound healing supporters are presented. Research examines the purpose of silver nanoparticles in medical therapies and illness management by examining their method of accomplishment, synthesis techniques characterization.

Keywords: Illness; Wound Healing; Nanotechnology; Nanomedicine; Nanoparticles; Antibacterial.

RESUMEN

Como consecuencia de su funcionamiento distintivo y su diverso conjunto de usos, la nanotecnología es una disciplina que se está expandiendo rápidamente. Para prevenir, curar, diagnosticar y controlar enfermedades, la nanomedicina examina las posibles aplicaciones de los conocimientos y técnicas de la nanotecnología. Se cree que las nanopartículas de plata con una longitud de entre 1 y 100 mm son las más importantes en este aspecto debido a su propiedad excepcional, su capacidad para formar diferentes nanoestructuras, su increíble grupo de efectos antibacterianos, su espacio para la cicatrización de heridas y otras capacidades beneficiosas, y su eficiencia en la producción. Se analizan las diferentes técnicas biológicas, químicas y físicas para el desarrollo de nanopartículas. Se presentan las técnicas para emplear nanopartículas de plata como sustancias antibacterianas, anticancerígenas, en odontología y como promotoras de la cicatrización ósea, así como en el tratamiento de heridas. La investigación examina el propósito de las nanopartículas de plata en las terapias médicas y el tratamiento de enfermedades mediante el examen de su método de realización y la caracterización de las técnicas de síntesis.

Palabras clave: Enfermedad; Cicatrización de Heridas; Nanotecnología; Nanomedicina; Nanopartículas; Antibacteriano.

INTRODUCTION

Bacteria are primary cause of many infections, which often result in mortality and interruption from destroyed nourishment, ruined crops, and polluted tools.[1] Because of long-term hospitalizations failures in therapies, disease determination, and slow wound healing that often results in disability and more fatal infections caused by bacteria enhance medical expenditures and impose stress on healthcare systems.[2] An Antifungal Effects of Silver Nanoparticles (AgNPs), which tends to have a size between 1 to 100nm are the size at which materials with special qualities are reduced to a person molecules and atomic particles.[3] Commercial, industrial, agricultural, and medical applications are the few of the possibility that used these microscopic particles.[4] Nanotechnology provides several benefits for the biomedical profession, including their tiny size, capacity to interact at the subatomic level, and efficient usage in systems to deliver drugs.[5] For being a common ingredient in cosmetics and sunscreen lotions, silver nanoparticles are utilized as a common component in wound bandage, antimicrobials, anticancer medications, and targeted systems in many clinical disorders.[6,7] AgNPs are used in agriculture as a component of nanopesticides and nano fertilizers.[8] Depending on the method of synthesis, these NPs are distinctive and contain variation in outside for dimension ratios. Smaller AgNPs are more effective as antibacterial agents than larger AgNPs' as it have the highest outside to volume ratio that releases more silver cautions.[9,10] To the implications of quantum dimension during the metal nanoparticle production procedure, there is an important ecological difficulty. Research [11] participants have continued their aim at complete extinction or reduction of waste and their execution of sustainable methods through the consent of 12 basic values of green chemistry across the past thirty years, and with the increasing recognition of environmental protection, people were pre-disposed to focus on sustainability in chemistry. The antiviral and antibacterial properties of the AgNPs were attained through methods directed against microorganisms. Based on the research,[12] there were three primary methods for producing AgNPs: chemically, physiologically, and physically. The cytotoxicity, antioxidants, anti-fungal, antibacterial, and topical wound healing properties of copper nanoparticles were chemically examined and evaluated by the article [13] using ascorbic acid and water strawberry fruit extracts as stabilizing and decreasing chemicals. Learning more about zinc ferrite nanoparticles' range, bactericidal potential, antibacterial activity mechanism, compatibility with cells, blood, tissues, and capability for assisting in wound healing were necessary determined in the paper.[14] Systemic antibiotics, that were used to treat these infections could not always successful to the development of microbial resistance were used as the treatment type. The development of nanostructure materials with embedded particles or the utilization of coatings with strong biocompatibility and antibacterial qualities were two solutions that could be used to address those issues.[15] Antibacterial qualities could be included in contemporary bone established to protect against different bacterial infection. It appeared to the primary complication to heal the bone material in medical proficient also dentistry since it caused an implant-associated infection that resulted in the disappearance of the device.[16] Skin injury was repaired and remodeled through wound healing. Biochemical and cellular processes were divided into four overlapping phases. There were overlapping stages in these processes such as hemostasis, inflammation, proliferation, and remodelling. Many cells and growth factor were mixed with these processes. The process of wound healing treated the injuries naturally were determined in the paper.[17] Article [18] discussed the importance of inorganic nanoparticles and wound healing techniques based on nanomaterials, and their mechanistic properties, medical classification, and difficulties. The primary focus was on creating an environmentally safe technique to produce gold nanoparticles using plants by extracting leaves of the insulin-producing plant *Chamaecostuscuspidatus*. Research [19] examined at the ability of gold nanoparticles made of green synthesis to scavenge radicals that were produced. The delivery mechanism could be used in medical application for effective treatment of wounds in diabetic patients and the work [20] demonstrated the utility of AgNPs in wound healing. In the research, the role silver nanoparticles performed as medical therapies and disease therapy was determined the mechanism conducted, synthesis techniques, and morphological description of the particles.

Producing silver nanoparticles

Silver nanoparticles are created via a range of processes, involving chemical, chemical-based, and microbiological processes. It is important to consider that each approach has pros and cons of its own. The microbe decreases Ag^+ to form Ag^0 throughout the naturally occurring manufacture of silver nanoparticles that acting as a wrapping substance decreasing agent, or stabilizing agent. The past few months have seen a growth in the use of biological technologies centered on natural products derived from microbial and botanical sources based on their cheap cost, substantial yields, and minimal impact on humans and the surroundings. In the paragraphs that follow below, several processes for creating silver nanoparticles in detailed.

Chemical methods

There are many ways to create silver nanoparticles. The apparatus needed for chemical techniques is further practical and easy to bring performance than that for genetic approaches, which makes them advantageous. It has been shown that silver ions absorb electron from the substances that reduce and change interested in the metallurgical state, which then assembles to create silver nanoparticles. The $AgNO_3$ constitutes one of the majority frequently used metallic salt since it is inexpensive and it utilized the chemical production of silver nanoparticles. It had successfully reduced the nitrate to create monodispersed silver nanocubes. Silver nanoparticles were created by using $AgNO_3$, which is an antecedent, sodium borohydride, and disodium citrate as stabilizers. Based on the reports, sodium borohydride works efficient as the reducer for creating silver nanoparticles. Disodium the acid citrate, in contrast, efficient dropping for the creation of silver nanoparticles in sixty to one hundred nanometer (nm) sizes ranges. The resulting nanoparticles had a spherical form and had important uses in biotechnology and biological research. The produced silver nanoparticles were found to be round and varied in diameter by a distinct investigation. A silver nitrate solution appears that the constant rise in rate has the biggest effect on the size of the nanoparticles. In contrast, the precursor administration method involves injecting a silver nitrate aqueous solution and relies heavily on the interaction temperatures to reduce particle size and achieve monodispersed. Chemical procedures provide a higher yield than physical ones, which is their principal benefit. Chemical treatments are very costly, and dangerous and poisonous substances including borohydride, two mercaptoethanol, thio glycerol and citrate are utilized in the creation of silver nanoparticles. A further step is necessary to avoid aggregated particles, and it is very difficult to create silver nanoparticles with certain volume. Synthesis results in the production of several poisonous and dangerous intermediates. The hazardous reducing chemicals used in these techniques shown in table 1.

Table 1. Monodispersed and practically spherical silver nanoparticles are produced chemically

Dropping agent	Capping	Precursor	Experimental conditions
Alanine/NaOH	DBSA (dodecylbenzenesulfonic acid)	Silver nitrate	Diameter ≈ 9,10 mm; 'temp ≈ 90° C;time≈ 60 min
Trisodium citrate	Trisodium citrate	Silver nitrate	breadth ≈ 32–98 mm; temp ≈ boiling point; pH ≈ 5,9–11,3
Oleic acid	Sodium oleate	Silver nitrate	breadth ≈ 7-100 mm; temp ≈ 100-160°C; time ≈ 17–122 min
Ascorbic acid	Glycerol/PVP	Silver nitrate	breadth ≈ 22-100 mm; 'temp ≈ 90°C
Trisodium citrate	Trisodium citrate	Silver nitrate	breadth ≈ 12-82 mm; 'temp ≈ boiling point'
Trisodium citrate	Trisodium citrate/Tannic acid	Silver nitrate	breadth ≈ 12–100 mm; temp ≈ 90°C
Ascorbic acid	Daxad 19	Silver nitrate	breadth ≈ 20–100 nm; temp ≈ boiling point

Substantial Method

Appearances of moisture compression and laser ablation are two physical techniques for creating silver nanoparticles. These technology's primary limitations are the massive force used and the long-lasting instance needed for whole operation. From the monodispersed silver Nano crystallites are created during the thermal disintegration of Ag+ oleate combinations. It was discovered that maintaining the heating system's surface temperature over time produced polydispersed nanoparticles. Such silver nanoparticles had a spherical shape and had no clumped together. Present investigations demonstrate that vaporizing polyol with a laser produces spherical nanoparticles of different diameters. Silver nanoparticles were produced to investigate that the laser spectrum affects subdivision range. The way dispersion nanoparticles are produced using pulse and the way effectively it generates colloidal particles with nanosecond laser pulses, nanosized silver particles were made by laser treatment in solution. Femtosecond pulsed have considerably less generative effectiveness than nanosecond impulses. The femtosecond pulses produced colloidal substances that were smaller and less distributed than those produced by nanosecond laser impulses. It demonstrated the immediate physical application of metallic into the triglyceride during the creation of silver nanoparticles. This method was discovered as an effective substitute for laborious chemical operations. Physical procedures include constraints such as solvent contaminating things, low yield, uneven distribution, and significant expenditures on energy depicted in table 2.

Table 2. Silver nanoparticle synthesis

Type	Biological activity	Reducing agent	Characterisation
silver nanoparticles	-	-	-
Silver nanoparticles with PVP coated	-	Sodium borohydride	'UV-Vis, TEM, EDS, DLS, FIFFF
Silver-chitosan nanoparticles	Antibacterial	Polysaccharide chitosan	'TEM, FTIR, 'XRD, DSC, TGA
silver nanoparticles	Antibacterial	Ascorbic acid	'UV-Vis, EFTEM
silver nanoparticles	Antibacterial	D-glucose and Hydrazine	'UV-Vis, TEM
Poly diallyl dimethyl ammonium chloride and polymethacrylic acid generates the capsules	Antimicrobial	Meth acrylic acid polymers	'Ultraviolet (UV)-Vis, reflectance spectro photometry

METHOD

Chemical and physical processes for produce silver nanoparticles are costly, time-consuming, and unsustainable. Since harmful chemicals and other issues related to chemical and physical methods of manufacturing must be avoided, it is crucial to design an ecologically economically acceptable technique. By controlling a variety of biological processes, biological approaches close these gaps and have many applications in managing all aspects of disease. Fungi, which bacterial cells, yeast cells and plant sources are, used in fermentation techniques shows in figure 1. Based on these sources, this method is widely used for nanoparticles uses for medicine. Reports indicate that the use of microbes and plants to produce nanoparticles is a safer, more economical, and less environmentally harmful method of accomplishing compared to applying chemicals. In addition, microbes and plants can take in and store inorganic ions such as metals from their surroundings. The microbes and plant sources are primarily used in the biosynthesis of silver nanoparticles.

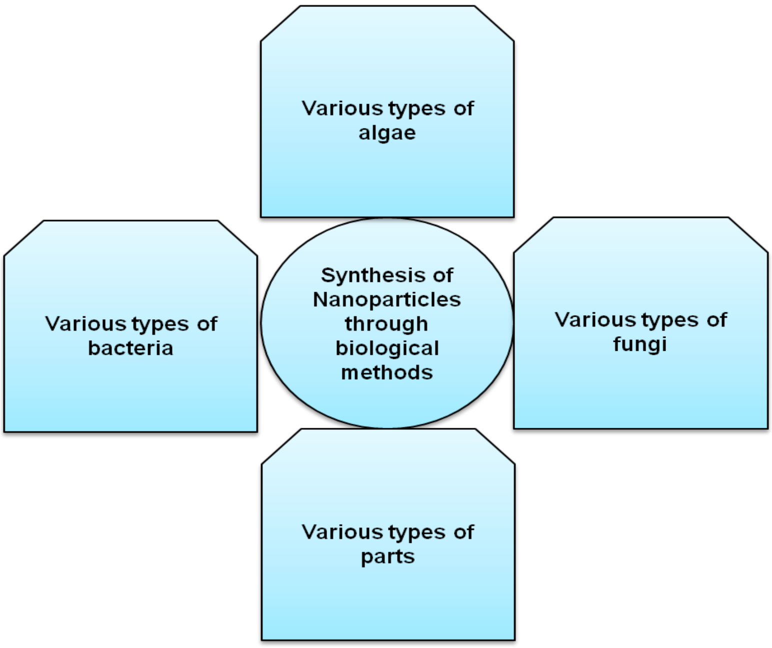

Figure 1. Silver nanoparticle biosynthesis techniques

Production in bacteria

The fermentation the wastes of several bacteria were used in the research to generate silver nanoparticles by dipping aqueous Ag^{+} ions. This method was shown to be quick, since it only took five minutes for silver ions to combine with the cell filtrate to produce silver nanoparticles. It is significant to remember that the accepted material piperitone inhibit the nitro reduction commotion of the bacterium enter several those belonging to the enter strains, including Klebsiella pneumoniae, are thought to partly impede the biological reduction of silver ions to tiny silver particles. Silver nanoparticle was optimized, providing data for the process' bioreductive nature. From dried Bacillus megaterium cells, the creation of nanoparticles. Silver nanoparticles are produced extracellular by an organism's strain. Research demonstrated that intracellular silver nanoparticle production occurred when Bacillus strain CS 11 was treated with $AgNO_3$.

Production in yeast

Silver nanoparticle production by yeast has reportedly determined. The yeast-based technologies for producing silver nanoparticles are economical and environmentally safe. Later the calculation Ag+ ions to the mushroom culture, it was observed that as the incubation period increased, the colorless sample gradually became reddish-brown. The solution's color is depicted as a bright reddish-brown.

Synthesis based plant extract

To the lack of high temperatures, energy, hazardous chemicals, and the detail that it is more economical and environmentally friendly, manufacturing in plants is superior to chemical and physical processes. Aloe vera leaves contain a variety of biologically active substances. These components, which have been shown to have a definite involvement in decreasing the amount of silver ions, consist of a combination of and pectin. The outcome demonstrated that the process of forming silver nanoparticles involved the reduction of Ag^+ ions. When plant extract wasn't present, the same set of conditions showed no change in color. The results demonstrated that silver nanoparticles from $AgNO_3$ solutions could be produced quickly when juice extract was used.

Production in algae

This technology can produce nanoparticles more affordably and environmentally friendly than both chemical and physical processes. It has been shown that living things like sea algae have the power to catalyze certain processes. The color is caused by the strength of silver nanoparticles formed from the modifications of silver ions and it associated with the algal extract. The silver nanoparticles were found to have a deep brown color after 32 hours, indicating a strong correlation between the duration of incubation and the development of color. The results demonstrated that silver nanoparticles were produced as a result of the reduction of Ag+. The inclusion of various quantities of water-based leaf extracts caused the color of the aqueous silver nitrate explanation to shift from a dim radiance to a yellowish-brown shade.

Construction base on fungi

It has been discovered that fungus can produce silver nanoparticles quite quickly. The creation of silver nanoparticles by fungus has been extensively researched. From one research, the association of fungi such as with silver nitrate results in external creation of sphere silver nanoparticles. Silver nanoparticles develop on the top layer of the flavus fungal cell wall as a consequence of the silver nitrate solution's interaction with the wall. Based on the interaction between silver ions and cellular deposition, the data suggests that nanoparticles of silver were produced rapidly.

Characterization techniques for nanoparticles

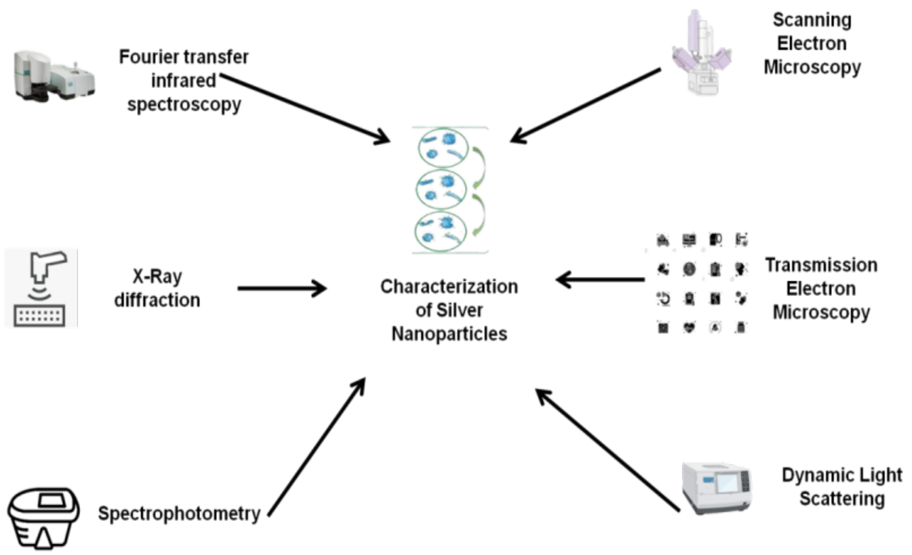

Figure 2. Characterization methods for silver nanoparticles

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The sustainable production of nanoparticles involves many steps, one of which is characterization. Determining the shape, chemical composition of the amount of outside area, every silver nanoparticle is an essential stride displayed in figure 2.

X-ray diffraction analysis (XRD)

A systematic method known as X-ray diffractogram analysis (XRD) is often damaged to research the organization of harsh nanoparticles that are crystallized. The formed nanoparticles' crystalline structure is confirmed by the scattering pattern that results. The formula for determining particle size is D = k/cos, where k the Scherrer is continuous of the X-ray, the greatest size, and D is the particle size (mm). It indicates the angle of diffraction that is parallel to plane of lattice. A wide range of materials like proteins, polymers, glasses, and hyper conductors can have their structural properties examined using the outcome. Researching nanomaterials can be effectively done with the XRD method.

Fourier transforms infrared (FTIR) spectroscopy

From the utilization to analyze various capping agents, FTIR can be used to explore the outside synthesizing nanoparticles are involved in the creation of nanoparticles. In FTIR, the object being examined is subjected to infrared radiation, which is the part wrapped up by it and the rest of which passes through. The generated spectra illustrate the distinct dispersion and absorption of the tested substance. FTIR is a practical, affordable, and non-invasive method for determining the part played by bio-molecules in transformation of silver from nitrates of silver nitrate.

Energy-dispersive X-ray (EDX) spectroscopy

The application of EDX in nanotechnology is well recognized, and this method is crucial for identifying the constituent parts of a sample. Researchers can identify the elements that make each nanoparticle by observing at the peaks in the X-ray range that result from the various atomic arrangements of each component.

Nanoparticle Attributes and Actions in Wound Healing

Table 3. Physicochemical Properties of Nanoparticles in Wound Healing

Property	AgNPs	AuNPs	ZnONPs
Particle Size (nm)	10-50	5-30	20-100
Shape	Spherical, Cubic	Spherical, Rod-like	Hexagonal, Spherical
Surface Charge (Zeta Potential, mV)	−20 to −40	−10 to −30	−25 to −50
Antibacterial Mechanism	ROS Generation, Membrane Disruption	Protein Binding	Zinc Ion Release, ROS Formation
Wound Healing Benefits	Anti-inflammatory, Angiogenesis	Cell Proliferation	Antimicrobial, Epithelialization

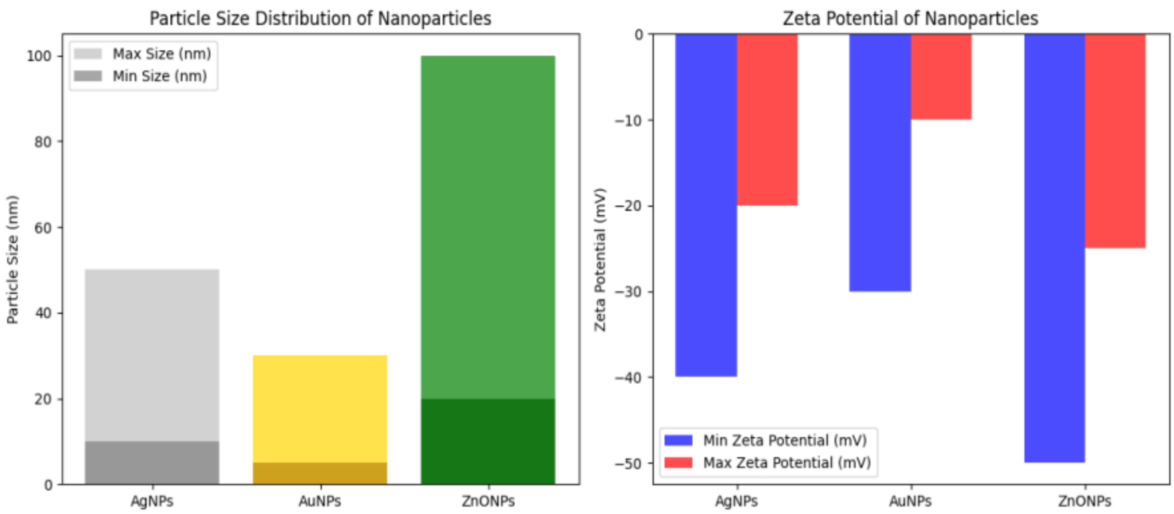

Figure 3. Nanoparticle-Driven Healing in Mechanisms in Tissue Repair

Nanoparticles are extensively used in wound healing due to their unique physicochemical properties, which enhance antimicrobial action, inflammation reduction, and tissue regeneration. As highlighted in table 3, AgNPscombat infections via Reactive Oxygen Species (ROS) genFieration, Gold Nanoparticles (AuNPs) stimulate cell proliferation, and Zinc Oxide Nanoparticles (ZnONPs) promote epithelialization through zinc ion release. Their mechanisms figure 3 presented the accelerate wound repair by enhancing angiogenesis, collagen deposition, and immune modulation. This aligns with research by demonstrating how nanoparticles facilitate faster healing, reduce infection risks, and improve tissue regeneration, making them a promising tool for advanced wound care solutions in modern regenerative medicine.

Silver nanoparticle uses in a range of industries

From their availability, antibacterial and optical qualities, inexpensive manufacturing, processing, and storage costs, and an important material for many different sectors is silver nanoparticles. These factors have led to the adoption of silver nanoparticles as substitutes in the production of products and industries with broad consumer appeal. At present, the silver nanoparticles are being investigated in a number of areas, including medical, biotechnology, material science, energy, and pharmaceuticals. The silver nanoparticles are often employed as a crucial component in commercial items including cosmetics and food processing. Utilizing nanoparticles in the agricultural sector helps to solve the issues with food security brought on by climate change. Silver nanoparticles have given artificial implants, wound dressing, and the avoidance of post-operative microbial contamination new dimensions in the area of medicine. When used as antibacterial agent in the material, healthcare, and food sectors, silver nanoparticles are very significant. A number of material products employ silver nanoparticles. Table 4 depicts the characterization methods for silver nanoparticles.

Table 4. Characterization methods for silver nanoparticles

Applications	Silver nanoparticles utilization
Healthcare	Scar recovery
	Larvicidal
	Anti-microbial
Fabrication	Medical devices and textile
	UV-ray blocking
Water therapy	Wastewater disinfection
	Drinking water
	Ground water cleaning
Biomedical industry	Anticancer
	Anti-inflammatory
	Anti- fungal
	Anti- bacterial
	Antiviral
Sectors of food	Preparation of food
	Packing Food

Antiviral activity

When it comes to treating and limiting the spread of viral infections, nanoparticles provide an alternative to medications. Silver nanoparticles can be biosynthesized to produce strong antiviral medicines that would limit the functionalities of viruses. The operation of the virus is controlled by the numerous gp120 binding sites on biosynthesized nanoparticles that one research found that cell-associated virus can be effectively eradicated using bio-based nanoparticles. Based on this research, monkey pox virus infection in vitro is significantly inhibited by silver nanoparticles. When Tacaribe virus was exposed to silver nanoparticles before infection, the virus was more easily able to replicate in multitude cells. The silver-treat virus produced significantly less viral Ribonucleic Acid (RNA), which proved that silver nanoparticles can prevent arena virus infection in vitro.

Antibacterial activity

Silver nanoparticles are effective antimicrobial substances. It has been shown that silver Nano formulations have a strong power to stop the development of bacteria and other microbes. Silver nanoparticles have strong antibacterial qualities that define the Gram-negative and Gram-positive bacteria. The conclusions indicated that when it used in conjunction with antibiotics the silver nanoparticle that was biosynthesized with a plant extract had significant antibacterial and antibiofilm properties that were visible at the lowest dosage. Based on the research, $AgNO_3$ concentration and nanoparticle size both affect how bacteriostatic polymeric nanoparticles. AgNPs' antibacterial efficacy has been shown against the four bacterial species depicted in figure 4. The MIC50 values against S. epidermis (124,88 µg/mL), salmonella (162,77 µg/mL), E. coli (165,63 µg/mL) and, S. aureus (148,12 µg/mL) indicate the broad-spectrum character of the compound.

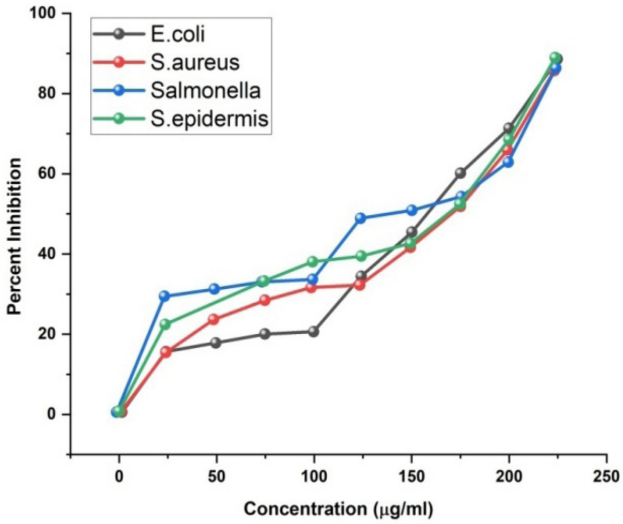

Figure 4. Percent inhibition

CONCLUSIONS

To the more utilization in the food industry, agriculture, healthcare, and as antibacterial and antitumor agents, silver nanoparticles have a considerable impact on managing health. Therefore, bacteria that form biofilms pose a significant threat. Alternative therapy approaches are receiving more global attention as a solution to the antibiotic resistance issue. These alternate methods can make use of silver nanoparticles, outside coating, impregnated with antibiofilm chemicals. The silver nanoparticles are the most researched and used nanoparticles for treating a variety of ailments, counting cancer, wound healing, dental implants, and further therapies including regulating biological activity. The use of new particle in medication resolve provides a standardized stage for the treatment of multidrug difficulty with increased technology.

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None.

CONFLICT OF INTEREST

Authors declare that there is no conflict of interest.

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