Chapter 15

Role of Nanoparticles for the Control of Haemonchosis

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ABSTRACT

Particles that range in size from around 1 to 100 nanometers and are created in various shapes are called nanoparticles (NPs). Nanotechnology is a growing field of study that is expected to open up new possibilities for the control and eradication of germs since it uses substances and networks at the atomic scale. Many individuals worldwide are afflicted with parasitic infections, which are particularly prevalent in developing nations and have significant treatment limits. Some parasites have recently shown signs of medication resistance, which has heightened the demand for safer, more effective treatments to prevent parasitic infections or for pharmaceuticals to be improved. AgNPs possess distinctive physical and chemical characteristics. Multiple studies have demonstrated the advantageous biological impacts of AgNPs on a range of disorders, including antibacterial, anti-inflammatory, antioxidant, antiparasitic, and antiviral activities. AgNPs have gained recognition for their efficacy in combating multi-drug resistant bacteria, positioning them as a promising contender for antibacterial medication development. Plant-extracted AgNPs have recently demonstrated remarkable antiparasitic properties, surpassing typical antiparasitic medications in terms of shorter treatment time and superior capacity to hinder parasite reproduction. This chapter offers a thorough review of the numerous types, unique qualities, and mechanisms of action of AgNPs in the fight against parasitic diseases. The major emphasis is placed on their efficacy in treating *Haemonchus*. The objective is to offer a comprehensive guide for using AgNPs to cure and manage parasitic infections.

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INTRODUCTION

Parasites and parasitic diseases impact a significant number of individuals globally and are associated with numerous challenges in the field of cure and management (Norouzi, 2017; Alvi et al., 2020; Alvi et al., 2021; Alvi et al., 2022; Alvi et al., 2023). Despite the rapid and notable progress in healthcare and health advancements in various parts of the world, intestinal parasitic infections persist as a major health concern with implications for the economy, particularly in developing nations. According to WHO estimates, 3.5 billion individuals globally have parasitic infections, of which 450 million experience clinical symptoms each year. Poor hygiene contributes to the spread of these illnesses, which can lead to gastrointestinal disturbances, malnutrition, problems with nutrient absorption, and a variety of symptoms (Kousha et al., 2011). Severe consequences include cholecystitis, appendicitis, myocarditis, vaginal infections, and abdominal pain can be brought on by intestinal parasites. Intestinal parasite frequency varies from 0.5% to 62.3% across age groups, according to studies, and it is more common in densely populated areas (Momen Heravi M, 2013). Unhygienic surroundings and poor hygiene habits may contribute to the spread of these illnesses (Gamboa et al., 1998). Moreover, it has been discovered that intestinal parasites lead to malnutrition, impede the absorption of nutrients, and interfere with gastrointestinal processes. These consequences include vomiting, sickness, cholera, anemia, avitaminosis, iron deficiency, a weakened immune system, and slowed physical growth (Rehman et al., 2021). Extremely hazardous adverse effects, such as vaginal infections, stomach pain, a condition called appendicitis, myocarditis, intestinal obstruction, and extra-intestinal abscess formation can occasionally result from intestinal infections. Numerous studies have found that intestinal parasite prevalence varies from 0.5% to 62.3% in people of different ages (Tegen and Damtie, 2021). There is a notable incidence of direct and simple transmission of several parasites in the intestines from affected to uninfected people, especially in areas with high societal concentrations (Momen Heravi et al., 2013). *H. contortus* is a highly transmissible gastrointestinal parasite worm that mostly affects ruminants and causes serious anemia, hemorrhagic gastroenteritis, diarrhea, stress, and other ailments. Additionally, it lessens the production of meat and milk, which causes a huge loss of profit for the world economy an estimated USD 120 billion is lost annually (Singh et al., 2017; Qamar et al., 2023). Many animals, including humans, can become infected with *H. contortus* through contaminated soils (Sinnathamby et al., 2018). Blood infections with *H. contortus* have also been reported in a variety of mammals, including humans, goats, sheep, rabbits, and others. These infections can alter immune responses and induce inflammation (Wang et al., 2019). Since over 30% of people globally suffer from parasitic illnesses, parasitic diseases are extremely significant. Furthermore, parasitic illnesses significantly increase the global incidence of mortality and morbidity, particularly in underdeveloped nations (Thurner et al., 2016). Though great progress has been made in recent years to investigate the pathophysiology and pharmacogenomics, causation, and cell biology of the majority of parasite-borne diseases, the condition of therapeutics is disheartening. Since most parasitic diseases do not elicit a robust immune response, there is currently no effective vaccination against any of the major parasitic infections, despite extensive research efforts. Therefore, the sole tool available to combat parasite diseases is an antiparasitic chemotherapy treatment (Sueth-Santiago et al., 2017). On the other hand, the majority of anti-parasitic medications in use today were introduced more than 50 years ago. Despite their effectiveness, the majority of these medicines do not closely resemble the contemporary definition of a "drug" in terms of patient acceptance, therapeutic regimen, duration of therapy, tolerability, or specificity (Dziduch et al., 2022). In contrast to other industries, the parasitic illness segment is not seeing as much advancement or new medication discovery as other industries do; this problem seems to be mostly caused by the lack of funding in this field. Prior to 2000, parasitic infections were considered unimportant, as demonstrated by the reality that just 0.1% of global health research money was allocated to the development of anti-parasitic medications (Norouzi, 2017). The most effective way to solve the previously described calamity associated with parasite infections is to develop innovative delivery methods to enhance the potency, specificity, tolerability, and therapeutic index of already available antiparasitic medications (Sun et al., 2019). Research on new antiparasitic compounds that are more potent, less toxic, more economical, and more active is imperative considering the side effects of antiparasitic drugs and the extent of parasitic illnesses (Mustafa et al., 2024). Because biotechnology and nanotechnology have developed so quickly, integrated them, and become widely used in pharmaceuticals, drug discovery has increased dramatically in recent years (Sarkar et al., 2017; Alfaleh et al., 2023). It is a wise decision to combine nanotechnology with conventional metal inorganic bactericides to create novel antiparasitic medications (Durak et al.,2020) and research on the insecticidal and inhibitory mechanisms of metal nanomaterials serves as a foundation for the creation of further parasite inhibitors (Rai et al., 2014). As a result, we covered an overview of all nanomaterials used to combat parasites in this chapter, with a special emphasis on silver nanoparticles. Particulate materials having more than we refer to one dimensional that is shorter than 100 nm as nanoparticles (Elhefny et al., 2021). Nanoparticles (NPs) can penetrate blood-brain obstacles, penetrate the respiratory tract, and bind to endothelial cells because of their small size and huge surface area, which also increases their colloidal strength and bioavailability (Rizvi and Salah, 2018). Metal oxide nanoparticles (MONPs) possess several advantageous properties, including straightforward preparation methods, excellent stability, and the capacity to functionalize with different molecules, the ability to be designed to precise sizes, shapes, and porosities, minimal fluctuations in swelling, and the capability to integrate into both hydrophobic and hydrophilic systems because of their negatively charged surface. These characteristics make MONPs a promising tool for biomedical properties (Sánchez-Moreno et al., 2018). Silver ions have a multilocation impact and are bactericidal to a wide spectrum of pathogens as inorganic materials (Zhang et al., 2023). Nevertheless, the use of silver-based materials is significantly restricted due to the exorbitant cost of the material, the unpredictable chemical characteristics of free silver ions, and the severe poisoning of conventional silver items (AbuDalo et al., 2019). Nanotechnology-produced sodium silver compounds possess several benefits, including superior pathogen-killing capabilities, reduced germ resistance, lower dosage requirements, and chemical stability (Ullah et al., 2018). Utilizing AgNP materials for parasite control offers the potential for developing novel substances to chemically combat clinical parasitic illnesses. By studying the inhibitory impact of AgNPs on parasites and understanding the fundamental causes of these effects, progress can be made in the creation of AgNP pesticides. The numerous forms and distinctive qualities of (AgNPs) and their usage in treating parasite diseases, especially *Haemonchus*, are the main topics of this study. We will now examine the main way in which it works: by disturbing the smoothness and structure of the parasites cell membrane. Reactive oxygen species, or ROS for short, are released as a result of this disruption, which also makes the membrane more porous and loses its internal content. This leads to inflammation and damage to biological components (Hassan et al., 2019).

History of NP's Birth

Although several techniques have been used to study the formation of nanosized particles from prehistoric times, perhaps even a century ago, the area of nanomedicine as a contemporary field of research was not formally founded until the 1990s. 21st-century research is seeing a rise in the investigation of nanomedicine (Krukemeyer et al., 2015). Nanoparticles (NPs) are artificially created and intricate molecules with precise chemical compositions. They were initially synthesized in the early 1980s. These nanoparticles consist of polymers that are extremely small in size and are constructed from smaller units called branch units. Synthetic nanomaterials possess a multitude of chain ends on their surface, which can be customized to perform specific chemical tasks. This characteristic could potentially be advantageous for catalytic applications. Nanomaterials exhibit significantly enhanced chemical and physical characteristics in comparison to conventional polymers (Krukemeyer et al., 2015). A diverse array of applications reveals novel capabilities and properties of matter. Nanotechnology offers significant novel instruments that are anticipated to have a profound influence on various domains within the field of medical sciences. Polymer-coated functionalized metal nanoparticles have emerged as a dynamic and innovative area of advanced study. For instance, silver is a significant and easily obtainable metal, and its nanoparticles (NPs) are more effective than other nanosized metal particles in terms of their ability to combat microbial growth. Nevertheless, the stability of polar terminal groups, such as hydroxyl groups or amines, is a significant concern and is typically employed to enhance their stabilization (sufi et al., 2022). Three-dimensional nanomaterials have found extensive applications in the past few years in a variety of sectors, including medication delivery, gene therapy, ophthalmic surgery, in vitro testing for cardiac muscle injury, virulence against HIV-1, treatment for cancer, and tumor cell targeting (Chugh et al., 2021).

Categorization of Non-Precursors

Nanoparticles are divided according to their chemical composition as inorganic, organic, or carbon-based **(**Oprică and Bălășoiu, 2019).

Organic NPs

Organic compounds that are smaller than 100 nm are used to create organic nanoparticles or ONPs (Qi and Zhang, 2022). Prominent examples of this category include liposomes, micelles, dendrimers, and ferritin, which are all well-established organic nanoparticles and polymers. Micelles and liposomes are two forms of nanoparticles that exhibit sensitivity to electromagnetic radiation, including heat and light. Additionally, they possess a hollow core referred to as a nanocapsule (Esakkimuthu et al., 2014). They possess non-toxic properties and are also biodegradable. There are superior alternatives for the transportation of medicine because of their distinct attributes. The size, content, surface form, and other characteristics of drug carriers are key factors. Their efficacy and variety of uses, however, are greatly influenced by their therapeutic-carrying capability, stability, and administration methods, such as adsorption or entrapped drug systems (Illes et al., in 2017). The biomedical profession has found several uses for organic nanoparticles, especially in drug delivery systems due to their effectiveness and ability to be accurately administered in specific anatomical locations; this is known as targeted drug administration.

Carbon-based NPs

An essential factor in the growth of human civilization on Earth has been carbon. It forms connections with materials that are incredibly strong. Graphite, oxides of carbon, fullerenes, carbon nanofibers, and carbon black are among the subcategories (Ealia and Saravanakumar, 2017).

Inorganic Nanoparticles

Nanoparticles that lack carbon as a component of their structure are known as "inorganic nanoparticles". Inorganic nanoparticles (NPs) include metal and metal oxide NPs, along with their derivatives.

Metal-Based Oxide Nanoparticles

Investigators have been paying more and more attention to metal oxides in the past few years. Ionic substances known as metal oxides are made up of negatively charged oxygen ions and positively charged metallic ions. Through electrostatic attraction, the positively charged metal ions and the negative oxygen ions create strong and long-lasting ionic bonds (Devan et al., 2012). These oxide-based nanoparticles are being synthesized with the intention of altering the characteristics of their metal-based counterparts. To benefit from their improved capacity for responsiveness and performance (Nikam et al., 2018). Metal oxide nanoparticles that have been artificially produced are widespread. Some of the often-produced oxides include (SiO_2), (TiO_2), (ZnO), and (Al_2O_3) (Bulychev, 2022) (Fayad and Dhahad, 2021) (Song et al., 2021). The most commonly utilized oxide nanoparticles (NPs) for drug delivery systems are zinc oxide (ZnO) and titanium oxide.

Metal-Based NPs

Destructive or constructive methods are used to produce metal-based nanoparticles to nonmetric sizes. Nearly every metal has a synthesizable nanoparticle. Metals such as aluminum (Al) (Muzammil et al., 2020) cadmium (Cd) cobalt (Co) copper (Cu) gold (Au) silver (Ag) (Zhang et al., 2023) are regularly utilized in the creation of nanoparticles. Because of their enormous surface-to-volume ratio and quantum effects, metal nanoparticles exhibit remarkable UV-visible sensitivity as well as electrical, stimulating, heating, and antimicrobial characteristics.

Silver (Ag) NPs

Creation and Possible Uses of Silver Nanomaterials

Characteristics of Silver Nanomaterials

Small particles with widths in one or more dimensions inside a space with three dimensions that vary between 1 to 100 nanometers are called nanoparticles (Ansari et al., 2022). Applications for materials based on nanoparticles are unique and include the volume effect, interface effect, influence of small size, and enormous quantum tunneling effect. Thus, nanomaterials considered unique compounds in the twenty-first century find application in a variety of fields, including energy, national defense, technological innovation, biology, medicine, and the chemical sector. Commercially available AgNPs are the most widely used Nano-compound on the market due to their broad potential for use in a variety of common applications as of right now, AgNPs are present in 435 out of 1814 nanoproducts, which are distributed over 32 nations or regions worldwide. This makes up about 24 percent of all nanoproducts (Vance et al., 2015). AgNP stands for "silver nanoparticles," which are tiny particles consisting of silver atoms and usually ranging in size from one to one hundred nanometers AgNPs experience oxidation on their surface, which releases free silver ions, just like bulk silver compounds do. AgNPs have unique characteristics, like area effect, quantum dimension effects, and tiny size effect, that are not found in typical materials (Naganthran et al., 2022). The greatly accelerated rate of ionized silver emission is caused by the coating and small size effects of nanoparticles. Because AgNPs function as ionized silver and increase the porousness of cell membranes, they can therefore directly harm the membranes of cells. This makes it possible for many cells to enter, which eventually leads to necrosis or apoptosis. These characteristics mean that AgNPs have a far higher bactericidal effect than silver ions. Furthermore, the negative impacts of AgNPs are associated with a range of properties, including form, concentration, chemical coating, surface charge, and others (Akter et al., 2018). AgNPs can have many different morphologies, such as triangle prism, ring, sheet, spherical, conical, disc, rod, cube, and prism (Mukherji et al., 2019). Forms that are uneven and angular increase the risk of physical injury. It was demonstrated in a study that triangular AgNPs had a stronger antibacterial impact than spherical and rod-shaped AgNPs when used to manipulate Escherichia coli (Zhang et al., 2023) or the use of both spherical and flaky AgNPs to manipulate zebrafish embryos revealed that the flaky AgNPs were more harmful (Abramenko et al., 2018). Nevertheless, because it depends on multiple variables rather than just one, the relationship between a particle's form and toxicity is not clearly defined. (Akter et al., 2018). These elements significantly affect the biotoxicity of AgNPs which include the dimension impact, redox impact, and surface stabilizers. In order to prevent aggregation, coatings are commonly placed on AgNP surfaces throughout the production process. This enhances stability and facilitates the dispersion of particles. AgNPs can be coated in a variety of ways to change their form and prevent silver ions from oxidizing. This alteration directly affects the biotoxicity of AgNPs (Zhao et al., 2021). The study discovered that AgNPs, which were altered by citrate and chitosan, exhibited more toxicity towards bacteria compared to the unmodified AgNPs. This increased toxicity is likely due to the ability of these two modifiers to expedite the release of silver ions from the AgNPs (Cavassin et al., 2015). When AgNPs are coated with citrate instead of polyvinyl pyrrolidone and poly ethyl enimine, or when there is no coating at all, their toxicity is reduced (Ivask et al.,2014). The way the coating altered the AgNPs' surface charge characteristics may have contributed to the variations in toxicity amongst the various coverings. Positively charged AgNPs are able to adhere to the negatively orientated microbial cell wall, giving them a greater bactericidal impact than negatively charged AgNPs (Zhang et al., 2023).

The Synthesis of Silver Nanoparticles

There are multiple methods for producing nanomaterials, but the two fundamental approaches currently used are: firstly, breaking down large solids into nanoparticles; and secondly, creating particles by combining individual atoms and carefully managing their growth to ensure they remain at the nanometer scale. The concept of nanoparticle preparation categorizes the ways of creating AgNPs into physical synthesis methods (Cobos et al., 2020), chemical synthesis methods (Fouda et al., 2020) and biological synthesis methods (Fig. 1) (Mohamed et al., 2019).

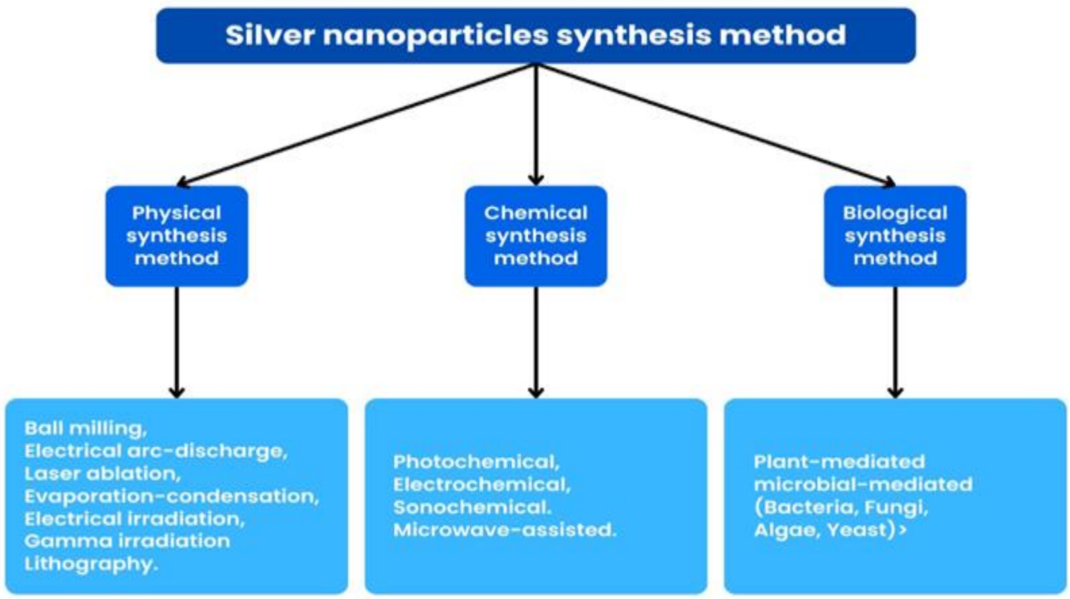

Fig. 1: Synthesis of silver nanoparticles (Mohamed et al., 2019)

A variety of techniques are used in physical synthesis, including lithography, electrical irradiation, irradiation with gamma rays, mechanical grinding, and ablation by laser, and evaporation-condensation. The metal is ground into a very fine powder using the mechanical grinding technique, which creates localized tremendous pressure through high-speed impacts. The abrasion level determines the dimension of the nanoparticles (Nguyen et al 2023). Using arc-discharge equipment, the arc-discharge process may create nanoparticles of silver in clean water without any requirement for any buffer or surfactant (El-Khatib et al., 2020). The production of nanosilver particles through evaporation and cooling plasma can be achieved by applying high voltage to silver electrodes in ionized water or by employing laser ablation in water or organic solvent (Khatami et al., 2018). In the laser elimination process, a silver block immersed in water or a synthetic solvent is quickly burned using a pulsed laser. As the plasma cools down, silver particles form and increase in size, finally resulting in the formation of nanosilver (Sharma and Bharti, 2023). The action of evaporation and later condensation turns metallic silver into particles in the evaporation-condensation technique. These nanoparticles can then further condense into atomic clusters or nano-silver particles (Mandal et al., 2016). Gamma rays have the ability to cause a radioactive breakdown of solvents, resulting in the production of dissolved electrons. These electrons can then react with metal ions, such as $Ag+$, in a solution to create nanoparticles (Bekhit et al., 2020).

Although the physical synthesis process looks simple, it requires exact machinery and is costly to prepare, thus it is not appropriate for large-scale manufacture (Nguyen et al 2023). This method enables the degradation of silver ions to basic silver or silver nanoparticles by electron transfer under certain conditions. Nanosilver preparation can be expedited by chemical techniques that use external energy sources, including photochemical, electrochemical, microwave-assisted, and sonic approaches (Jara et al., 2021). In photochemical processes, light—typically ultraviolet (UV) light is employed to cause silver ions to reduce and become silver nanoparticles. (Jara et al., 2021). Excitation of silver ions and the promotion of the reduction reaction can occur due to photon energy produced by light (dos Santos et al., 2019In order to cause the decrease of silver ions to silver nanoparticles, the electrochemical technique applies an electromotive force. typically, a silver electrode electrochemical cell is used for this. Silver atoms are created when electrons from the applied potential are transferred to silver ions, causing them to congregate into nanoparticles. (Kuntyi et al., 2021In order to facilitate the conversion of silver ions to nanoparticles, microwave energy is used in the process of microwave-assisted synthesis to warm the reaction mixture (Naganthran et al., 2022). Using ultrasonics, bubbles from cavitation in liquids can be produced for the purpose of synthesizing nanoparticles. When these bubbles burst, a great deal of pressure and heat is generated locally, which can turn silver ions into nanoparticles (Bhangu et al., 2020).

Through the application of reducing reagents, metallic colloidal silver particles are created by reducing oligomeric complexes formed when silver atoms and silver ions come together (Mofidfar et al., 2019). Reducing agents that are often utilized include Tollens reagent, ethylene glycol, sodium borohydride, and hydrazine (Suriati et al., 2014). In addition to lowering agents, polymers must be added as moderators during the chemical synthesis of AgNPs in order to increase their durability and keep them from clumping together. Decanethiol, polyvinyl ether, and polyvinylpyrrolidone are a few examples of these polymers. Unfortunately, one major barrier to the chemical production of AgNPs is the harmful effects of chemical reagents. Moreover, the selected stabilizers and decreasing agents have particular harmful qualities to the organism, making the chemically generated AgNPs biotoxic. Consequently, this limits the possible uses for them (Liu et al., 2016). The biological approach includes the use of plant and microbial methods which use carbohydrates, proteins, and antioxidants obtained from organic creatures like microorganisms, yeast, and herbs (including seaweed, mustard, and tea) as a substitute for agents that reduce hazardous compounds and maintain substances (Alves et al., 2022). The synthesis of these substances is potentially achieved through enzymatic and non-enzymatic reductions.

Plant strategy involves using different plant extracts to decrease silver ions into silver nanoparticles. Plant extracts include bioactive chemicals, including phenolic compounds, flavonoids, and terpenoids, which have the ability to function as stabilizing agents and lowering agents typically, the procedure is easy to follow, reasonably priced, and ecologically friendly. With this technique, a large range of plant sources, such as mustard, seaweed, tea leaves, and others, can be used (Xu et al., 2020). Utilizing microorganisms like yeast, fungi, and bacteria to create silver nanoparticles is known as the microbiological technique. It is possible for microorganisms to produce the enzymes needed to conduct the conversion of silver ions to elemental silver. To increase their stability, the nanoparticles in this process are usually coated with a coating of protein. The ability of some bacterial and fungal strains to reduce metal ions and generate nanoparticles has been investigated (Ibrahim et al., 2022). This product is distinguished by its environmentally friendly and sustainable nature, as well as its homogeneous and extremely fine particle size. It exhibits excellent dispersion and is resistant to precipitation (Adnan et al., 2022), however, when the particle size decreases, the number of surface atoms rises, resulting in the agglomeration of nanoparticles (Li et al., 2022). Because AgNPs have tendency to joint together when used alone as an antimicrobial solution, which limits their effectiveness. As a result, AgNPs are frequently mixed with other substances to create AgNPs-hydroxyapatite composites. (Bee et al., 2021), Poly (vinyl alcohol)- AgNP (PVA-AgNP) (Yang et al., 2023), AgNP-TiO2 composites, Ag/ZnO nanocomposites, etc (Kavaliūnas et al., 2022). The incorporation of AgNPs with other materials enhances compatibility for certain applications, hence expanding the range of unique qualities shown by AgNPs. AgNP-TiO2 composites have excellent biocompatibility and demonstrate significant antibacterial activity, as evidenced by a study conducted by researchers (Wang et al., 2018), and The Ag/ZnO nanocomposites, consisting of silver nanoparticles attached to the surface of ZnO, had a suppressive impact on Streptococcus mutans. Furthermore, these nanocomposites show superior antibacterial efficacy compared to ZnO nanorods (Wang et al., 2017).

Prospective Uses for AgNPs

Research into silver nanoparticles, or AgNPs, has shown promising results for application in living things. AgNPs have been shown to possess antibacterial and anticancer effects through in vivo studies. According to studies, AgNPs on Bermuda grass may be able to successfully fight off root-knot nematodes (Khan et al., 2021) as well as the plant-parasitic nematode Meloidogyne graminicola (Baronia et al., 2020). Subsequent research has unequivocally shown that (AgNPs) are effective at eradicating incognita Meloidogyne infestations on aubergine, tomato, and okra plants (Abdellatif et al., 2016). Investigations on animals have shown that AgNPs are effective in treating a variety of diseases, including those that impact the skin, respiratory system, and urinary tract, and are parasite-related (De Silva et al., 2021). Furthermore, studies have demonstrated that AgNPs can impede the development of tumors and enhance the survival rates in animal cancer models (Ansar et al., 2020). AgNPs have different uses in the medical field for curing human ailments, such as bioimaging, cancer therapy, medicine delivery, and dental technology. The unique physicochemical properties of silver nanoparticles (AgNPs) have attracted a lot of interest in the treatment of cancer (Xu et al., 2020). Instead of using conventional anticancer methods, using metal nanoparticles entails mixing therapeutic drugs and treatment candidates with drug carriers. This tactic enables targeted techniques to lessen negative consequences (Andleeb et al., 2021). In research aimed at human cervical carcinoma cells, Nepeta deflersiana (ND) was used to extract AgNPs. The AgNPs that were collected showed face-centered cubic structures that measured 33 nm on averageHeLa, a model organism of human cervical cancer cells, was to be used to assess its anticancer ability. The generation of reactive oxygen compounds (ROS), structural alterations, toxic concentrations on oxidative stress indicators, and mitochondrial membrane potential were among the parameters used to evaluate the cytotoxic reaction. The amount of AgNPs present affected the reported cytotoxicity in various ways. According to the study, ND-AgNPs can potentially cause a reduction in glutathione levels and the mitochondrial membrane, which will ultimately cause cervical carcinoma cells to die. This implies that ND-AgNPs may be useful as a cervical cancer anticancer treatment (Al-Sheddi et al., 2018). Because of their optical characteristics, which enable them to create the best contrast in cellular imaging and other therapeutic applications, nanoparticles are also used in cell biological imaging or cell sensitivity (Pratiwi et al., 2019). Silver nanoparticles (AgNPs) are extensively utilized in dentistry to enhance dental biomaterials by minimizing the formation of biofilm through their antibacterial properties. Additionally, AgNPs are integrated into root canal fillings to decrease the presence of Staphylococcus aureus and Streptococcus mutans (Yin et al., 2020).

Use of AgNPs for Control of Haemonchosis

Globally, G.I.T. parasitic nematodes represent the most economically consequential infectious illnesses (Szewc et al., 2021). They significantly impact babies and preschoolers, who are most vulnerable and are more common in tropical areas. Worm infestations can be fatal in certain age ranges (Stracke et al., 2021). The gastrointestinal tract can become infected with the highly contagious parasitic worm *H. contortus,* which can cause hemorrhagic enteritis, diarrhea, and severe anemia. If these indications are present, cattle may produce less dairy and meat, which could result in financial losses (Singh et al., 2017). *H. contortus* is spread by contaminated soil of different species and has the potential to cause human illness (Salle et al., 2019). Prior therapies for helminths have only utilized a limited number of medicines, including benzimidazole, imidazothiazole, and ivermectin (Dixit et al., 2017). A new medicine needs to be created immediately to fill the vacuum left by the increasing prevalence of parasitic infections, the scarcity of current drugs, and the evolution of drug resistance. Carvacrol-coated chitosan nanoparticles are utilized (Fernandes et al., 2020) for anthelminthic activity against the adult stage of *Haemonchus contortus* (Fernandes et al., 2020). *Lansium parasiticum* is a common plant used for food and timber production in both Bangladesh and India. Indian researchers exploited this plant to manufacture silver nanoparticles (LAgNPs). The use of LAgNPs made from this plant, a unique anthelminthic medication, could lead to new developments in the field of contemporary medicine. The study discovered that all of the males and 80% of the females in the samples passed away after 12 hours of starting LAgNP treatment. In contrast, just 26% of the males and 11.3% of the females in the citric acid-coated AgNPs sample perished after 12 hours, and none of the males or females in the sample became paralyzed after one hour. Consequently, LAgNPs exhibited elevated toxicity and demonstrated greater efficacy against the parasite. When LAgNPs were given to *Haemonchus contortus*, the stress caused by nitric oxide synthase (NOS) and reactive oxygen species (ROS) increased more quickly, which inhibited the growth of the parasite (Goel et al., 2020).

Anti-Parasitic Mechanism of AgNPs

Because of their huge surface area, capacity to release silver ions (Ag+), and generation of reactive oxygen species (ROS), which possess substantial antibacterial and antifungal capabilities, AgNPs have the potential to be extremely successful in battling infections. (Flores-López et al., 2019) The entry of silver ions and the production of reactive oxygen species (ROS) are associated with the effects of AgNPs on parasites. The tiny-sized silver particles have the ability to penetrate the Cryptosporidium oocyst and kill the sporozoites, whilst the released silver ions have the potential to engage with the cell wall and induce leakage (Cameron et al., 2016) Metallic silver can negatively affect a cell by interfering with its membrane or by chemically attaching to and accumulating on its surface. Plasmodium and other parasitic protozoa are among the parasites that are harmful to silver ions released by silver nanoparticles (AgNPs) (Al-Quraishy et al., 2020). The mobility and stability of the parasite's cell membrane may be compromised by the binding of these silver ions. The disturbance ultimately results in the malfunction and demise of the parasite's cells by increasing the membrane's permeability and causing the loss of vital intracellular components (Cameron et al., 2016). Silver nanoparticles (AgNPs) cause cell death and primarily eliminate parasites by producing reactive oxygen species (ROS) (Ahmed et al., 2018). The majority of stress reactions that occur within cells are a result of the harmful effects generated by reactive oxygen species (ROS). Among these responses, oxidative stress is believed to be the primary mechanism responsible for the cytotoxicity induced by silver nanoparticles (AgNPs). The release of silver ions has the potential to cause the parasite to produce reactive oxygen species, which can lead to oxygen consumption and damage to its cellular components. This can ultimately lead to the demise of the parasite cells and the eradication of the parasite (Ullah et al., 2018). Every normal cell has some ROS, but the immune system balances it out. After cells are exposed to AgNP stress, they quickly produce large amounts of reactive oxygen species (ROS). The proteins that eliminate excess reactive oxygen species (ROS) include glutathione (GSH), catalase, or superoxide dismutase (SOD), thioredoxin, vitamin E, and others. Glutathione has the ability to bind to and neutralize reactive oxygen species (ROS). Therefore, it is acknowledged that the glutathione-regulated antioxidant system is an essential defense mechanism for cellular survival (Docea et al., 2020). AgNPs decrease the amounts of GSH by blocking GSH synthase, which results in the cells being unable to efficiently remove intracellular ROS (Zorraquín-Peña et al., 2020). When there is an imbalance between the production of oxygen species that are reactive (ROS) and the antioxidant system's ability to break them down, oxidative stress may result. This imbalance may result in catastrophic events such as lipid and protein peroxidation, mitochondrial damage, DNA damage, and ultimately apoptosis-induced cell death (Flores-López et al., 2019). When cells produce too much reactive oxygen species (ROS), the p53, protein kinase B (AKT), and mitogen-activated protein kinase (MAPK) signaling pathways become active, initiating the apoptotic process. AKT expression is first downregulated when cells are subjected to AgNP stress, which causes them to produce a significant amount of reactive oxygen species (ROS). Pro-apoptotic kinase p38 expression is subsequently elevated as a result of this reduction. Simultaneously, there is a decline in the expression of the DNA repair enzyme PARP, which significantly amplifies the expression of p53. Consequently, the increased p53 expression induces apoptosis (Li et al., 2016)

Moreover, by upsetting the proton transport chain, silver ions can impede metabolism and interfere with the synthesis of ATP. Silver ions have the ability to disrupt the functioning of important enzymes and metabolic pathways in the parasite, resulting in cellular malfunction and ultimately causing its demise (Hamad et al., 2020). The precise mechanism by which AgNPs operate against the parasite is currently being studied, and there might be alternative methods that are equally effective. AgNPs possess the capability to serve as a valuable instrument in combating parasitic illnesses (Ghorbani et al., 2019).

Conclusion

AgNPs have a promising future due to their unique features, which are in high demand for many applications. It is anticipated that they will significantly influence industries like electronics, energy, environmental cleanup, medical applications, and antimicrobial applications. This article has given a succinct summary of the most recent developments in understanding AgNPs' antiprotozoal properties. AgNPs have an antiparasitic effect through a variety of mechanisms, including breaking down the parasite's cellular membranes, lowering metabolism, and preventing proper development. Silver nanoparticles (AgNPs) pose practical challenges. Primarily, when silver is discharged into the environment, it poses a significant risk to human health and environmental safety due to its detrimental effects on humans, animals, and the ecosystem. Silver nanoparticles (AgNPs) may potentially have possible adverse effects on animal health, including hepatotoxicity and nephrotoxicity. Furthermore, the issue of AgNP stability poses an additional hurdle. The effectiveness of AgNPs may diminish over time due to degradation and interactions with other chemicals in the environment. This can result in the development of parasite resistance and a decrease in their ability to effectively combat parasites when used extensively over a long period. Therefore, further research and development are needed to address the concerns regarding the stability, safety, and drug resistance of AgNPs, as well as to ensure the safe and long-lasting use of these materials.

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