Review Article

A review of the antimicrobial and toxic properties of nanoparticles as a new alternative in the control of aquatic diseases

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Abstract

Nowadays, the Aquaculture industry has played a major role in dealing with a broad range requirements for human protein needs. Though environmental pollution and the incidence of the disease have always been the significant challenges in the use of aquatic products. Increasing the antibiotic resistance rate in fish pathogens has attracted attention to searching for alternatives to antibiotics. In this regard, nanotechnology as a new and innovative strategy has a range of applications in aquaculture and preserving sea animals and can provide a reliable way to protect farmed fish from pathogens. The producers, therefore, try to eliminate barriers in food fields using nano-based tools and cause growth, proliferation, aquaculture, and water purification to increase production in the aquaculture industry.

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One of the most outstanding issues that researchers point out nano-scale is finding appropriate methodologies for the synthesis of environment-friendly and non-toxic nanoparticles. The specific chemical, physical and biological properties of nanoparticles have increased the incentive to produce them. Today these agents have found their way into many medical applications, including detection, vaccinations, medicine, and gene transfer. Moreover, the use of nanoparticle-based vaccines for many viral pathogens is a developing field in fish disease research. So, Nanoparticles have been widely taken into consideration as a special and sensitive tool to identify bacterial, fungal and viral diseases in aquaculture. This study focuses on the antimicrobial effects of nanoparticles, especially antibiotic-resistant bacteria, and the nanotechnology applications in fisheries.

Keywords: Nanoparticles, Antimicrobial properties, Toxicity, Aquatic animal diseases, Nanotechnology

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Introduction

Fish is a significant source of food in every country in the world. The presence of essential beneficial compounds for humans makes aquatic proteins as the preferred source of proteins. According to Jafari Porzani "the animal plays an important role in nutrition, food security and livelihood of the human being" (Jafari Porzani *et al*., 2021; Nowruzi and Lorenzi, 2021a; Rodrigues *et al*., 2017). Fish contains the highest quality protein sources and provides a wide range of nutrients, especially essential amino acids and fatty acids and vitamins, and other vital elements such as iodine and selenium that are not found in other foods or meat. Minerals in fish include iron, calcium, zinc, iodine (from marine fish) (Abdel-Tawwab *et al*., 2019), phosphorus, selenium and fluoride. Fish is a potential source of vitamin B complex, and cod liver oil contains a significant amount of fat-soluble vitamins A, E, K and D in addition to other vitamins such as vitamin E, vitamin K and vitamin C. Fish oil is rich in unsaturated fatty acids (PUFAs), especially omega-3 fatty acids, which the human body cannot synthesize. Omega-3 fatty acids such as eicosatetraenoic acid (EPA) and docosahexaenoic acid (DHA) are the building blocks of our nervous system (Nasr-Eldahan *et al*., 2021; Nowruzi and Lorenzi, 2021b; Nowruzi and Porzani, 2021).

As the world's population grows, the demand for fish products is expected to increase, as they are the cheapest and most accessible source of animal protein compared to other protein sources. Fish can be an essential component of nutrition for the poor who are dependent on foods such as corn, rice, and other grains, and can also help improve the calorie ratio; in other words, about 50% of fish protein per 150 grams of fish there is a protein needed by an adult (Kwasek *et al*., 2020). Many studies have shown how the consumption of fish, especially oily fish, reduces the risk of death from cardiovascular disease (CHD) (Mohanty, 2015; Nowruzi *et al*., 2020a; Nowruzi *et al*., 2020b; Porzani *et al*., 2021).

Fish disease

Fish, like other animals, suffer from a variety of diseases, especially young fish with weakened immune systems. Fish diseases are divided into two categories infectious and non-communicable diseases. Non-communicable diseases are not spread through infection or through other fish and are often related to poor water quality, malnutrition, etc. In addition, these diseases cannot be transmitted from one fish to another. Non-communicable diseases due to deficiency of certain nutrients (such as vitamins and minerals), pollutants related disorders (agricultural and industrial), and neoplastic and genetic abnormalities with abnormal growth in any organ that causes loss of function. Infectious disease is a dangerous type of fish disease because it is transmitted from one fish to another and causes a many deaths. In such cases, the fish can protect themselves from any pathogen via their immune system (Rajabpour *et al*., 2019; Safavi *et al*., 2019). Non-specific defenses, include the skin as well as the mucus layer secreted by the skin, inhibit the spread of microorganisms.

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When pathogens penetrate the skin and other physical barriers, a defensive role begins. The fish's immune system increases blood flow to the infected area and transports more white blood cells that try to kill the pathogens, resulting in an inflammatory reaction. When pathogens enter the body of the fish, the antibodies may absorb the bacteria and act as an opsonin to facilitate phagocytosis (Nasr-Eldahan *et al*., 2021; Nowruzi *et al*., 2018a; Nowruzi *et al*., 2018b).

To eliminate and sometimes fight against many diseases, a wide range of chemicals such as hormones, vitamins, antibiotics, and other chemicals have been tested for various therapies in aquaculture operations, which is why control measures have been implemented in recent years. Although they have beneficial effects, they cannot always be prescribed because in their side effects (Shah and Mraz, 2020).

Vaccination is one of the most essential and probably the most significant ways to prevent and control infectious diseases of fish by activating the immune system (Dadar *et al*., 2017; Embregts and Forlenza, 2016). The use of vaccines in aquaculture as a defense mechanism against pathogens has been very important in protecting the host from infection by these pathogens. Many bacterial infections in aquatic animals cannot be treated with antimicrobials alone. Recent advances in fish vaccination have been made. There are several types of vaccines can that can be identified as killed, attenuated, DNA, hybrid peptides, recombinants, and genetically modified vaccines. Immunization of fish began in 1942 with vaccination against *Aeromonas salmonicida* infection. The advantage of vaccination is that it reduces the use of antibiotics in aquaculture and reduces the likelihood of drug resistance. It has been reported that vaccination could control any bacterial or viral disease with no accumulation of toxic waste and environmental effects (Mohd-Aris *et al*., 2019).

Nanoparticles

Today, the aquaculture and fisheries industry provides about 15 percent of the average animal protein intake it continues to grow, with 520 million people earning their livelihood indirectly from the aquaculture and fisheries industries. Newly engineered nano-products improved by nanoparticles (NPs) have been a critical factor in the success of the nanotechnology industry. NPs with a size between 1 and 100 nm offer unique physical and chemical properties, as a higher surface-to-volume ratio leads to greater reactivity (Dar *et al*., 2020). Because of these remarkable properties, NPs are widely used in various fields, such as energy and electronics, wastewater treatment, medicine, and agriculture. Recently, nanotechnology has found several applications in aquaculture, but its implications are still unknown (Table 1) (Vimbela *et al*., 2017).

In the fisheries and aquaculture industry, NPs have many direct and indirect applications. Indirect applications include water and wastewater treatment, sterilization of fishponds, and packaging of fish for commercialization such as barcoding and labeling; direct applications include animal nutrition and health industries, such as fish disease control. Increased production and use of NPs have raised concerns about their safety for human health and the environment.

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While a considerable number of studies have been performed on the potential toxicity of NPs to humans and other living organisms, few studies have examined the effects of nanoparticles on aquaculture. Assessing the potential adverse biological effects of NPs makes it possible to determine the safe limit concentrations used in food production activities such as fisheries and aquaculture does not currently exist. The present study, first examines the antimicrobial properties and potential toxicity of NPs in aquaculture and then provides a summary of recent scientific papers on their potentially hazardous effects (Vimbela *et al*., 2017).

Table 1. Biological activity of bioparticles synthesized biologically (Vimbela *et al*., 2017)

Biological activity	Biosynthesis by	Size	Nanomaterial
Antibacterial activity: Silver nanoparticles attach to the cell membrane surface of gram-negative bacteria, then enter the cell and have the ability to interact with phosphorous and sulfur molecules and DNA.	*Ceropegia thwaitesii*	100 nm	Silver nanoparticles
Inhibition of human lung cancer	*Origanum vulgare*	136 ± 10.09 nm	Silver nanoparticles
Antibacterial and cytotoxic properties against MG-63 osteosarcoma cell line	Tree bark extract	40 & 50 nm	Silver nanoparticles
Antibacterial properties against cold-loving bacteria	Extracellular synthesis using cryogenic bacteria	6-13 nm	Silver nanoparticles
Antibacterial properties against drug-resistant microorganisms	*Bacillus flexus*	12-65 nm	Silver nanoparticles
Antibacterial properties against Vibrio cholerae	*Ochrobactrum rhizosphaerae*	10 nm	Silver nanoparticles
Strong growth inhibition against gram-positive and gram-negative bacteria	Yeast	2-10 nm	Silver nanoparticles / Silver chloride
Controlled size Morphology Controlled cheap nanoparticles without toxic contaminants	Green synthesis using plant extracts	25-40 nm	Zinc oxide nanoparticles

Antibiotic resistance and dangers ahead

In aquaculture, there are several bacterial diseases lead to increased use of antibiotics, still antibiotics have several disadvantages in aquaculture, which are as follows: Estimating the specific concentration of antibiotics used in different countries is not easy. Antibiotics are added to foods that settle in the water, so that they can build up in the fish. An antibiotic may be widely used in aquaculture, but not for all bacteria; even bacteria that may have been initially affected may later become resistant to the antibiotic. The price of these chemical treatments is very high, and it decreases over time and has various side effects. In addition, the researchers stated that antibiotic resistance could be inherited or acquired. In the first or inherited form, an antibiotic has less power to penetrate bacterial cells and reach the target cell site. In the

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latter or acquired case, a bacterial species is usually sensitive to a particular antibiotic. Still, some other bacterial species have antibiotic resistance, and overuse of antibiotics can significantly lead to bacterials resistance to them (antibiotics) (Vimbela *et al*., 2017).

Researchers conducted a study on the use of antimicrobial in fish farms in 25 countries. They found that tetracycline was the most widely used antibiotic in fish farms and that there was a strong association between the emergence of antibiotic-resistant bacteria and the overuse of antibiotics in aquaculture. The emergence of many resistant bacteria, including methicillin-6-resistant *Staphylococcus aureus*, has been reported. Some species of *Aeromonas hydrophila* grown from tilapia were resistant to broad-spectrum antibiotics such as tetracycline, streptomycin, and erythromycin. Antibiotic resistance has been seen in *Aeromonas salmonicida* and *Photobacterium damselae. Piscicida, Yersinia ruckeri, Vibrio Listeria, Pseudomonas* and *Edwardsiella* (Khosravi-Katuli *et al*., 2017).

In addition, the researchers isolated antibiotic-resistant enterococci from fish farms. They suggested that the fish-resistant bacteria could transmit the infection to humans and that the presence of these fish in fishponds became a significant public health issue (Shaalan *et al*., 2016). There are some compounds include disinfectants (such as hydrogen peroxide and green malachite 2), antibiotics (such as sulfonamides and tetracycline), anthelmintics (such as diethylcarbamazine, and ivermectin); Natural is like probiotics, essential oils and herbal biomedicine that were researched as antibiotics alternatives (Nasr-Eldahan *et al*., 2021; Nowruzi *et al*., 2012; Nowruzi *et al*., 2013).

Application of nanotechnology in aquaculture industries

The word nano comes from Nanos, which means "dwarf" in the Greek word. The branch of nanotechnology and nanobiotechnology deals with compounds with dimensions of 1 to 100 nanometers. Many nanomaterials have antibacterial activities derived from metal salts, metal oxides, and biometals, including silver, aluminum, cerium, gold, cadmium, magnesium, nickel, lead, selenium, titanium, and palladium (Mudhafar *et al*., 2020).

Nanotechnology is the science of producing and using nanometer-sized particles. Recently, methods have been developed to understand and control matter at the nanoscale. Particles in this range have unique sizes and properties that pave the way for new applications. There are several methods for describing nanoparticles, which are summarized in Table 2 (Khosravi-Katuli *et al*., 2017).

Nanomaterials can be divided into two large groups: very fine nanoparticles of nanoscale that are usually found in nature and not artificially produced, and the next group, nanoparticles that are engineered and produced in a controlled manner. The application of nanotechnology in connection with the treating humans and animals by designing and using nanoparticles and nanodevices for biomedical applications (Luis *et al*., 2019).

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Table 2. Common survey methods for characterizing nanoparticles (Mudhafar *et al*., 2020)

Descriptive parameters	Method
Absorption spectrum of nanoparticles	Ultraviolet-visible spectroscopy
Size and dispersion of suspended nanoparticles in the liquid phase	Dynamic light scattering / particle size analyzer
Surface charge of nanoparticles in aqueous solutions or suspensions	Zeta potential analyst
Analytical tool for chemical composition	Fourier-transform infrared spectroscopy (FTIR)
Shape and structure of the surface	scanning electron microscope (SEM)
Size, shape and morphology (including internal structure), especially for biological samples	Transmission electron microscopy (TEM)
Shape and morphology of high resolution horizontal and vertical nanoparticles	Atomic force microscopy (AFM)
Atomic-scale surface images / Atomic-scale, molecular / nanometer-scale material changes with high accuracy	scanning tunneling microscope (STM)
A non-invasive method for investigating the migration of nanoparticles to biological barriers, 3D nanoparticle morphology	Laser scanning confocal microscopy (LSCM)
Structure, phase and average particle size	X-Ray Diffraction (XRD)
Chemical composition (both elemental and chemical state), information about the surface of nanoparticles	X-ray Photoelectron Spectroscopy (XPS)
Temperature analysis and phase change studies	Differential Scanning Calorimetry (DSC)
Discover, isolate and determine the properties of nanoparticles / nanomaterials of various sizes	High-performance liquid chromatography (HPLC)

Many types of nanoparticles have been used in medicine, for example, nanospheres, which are nano-sized spherical particles. Due to their small size and high contact area, a particular drug can be dispersed on the surface of nanoparticles to facilitate drug delivery. Nanospheres can also be used to regenerate tissue. Another form of the nanoparticle is a nanocapsule, which consists primarily of an outer nano-shell and an inner core. The kernel may contain a specific drug, while the shell protects the drug from decomposition and hydrolysis. Liposomes, for example, are nanoparticles that have two layers of fat and are ideal for the delivery of lipophilic and hydrophilic drugs because of their similar structure to eukaryotic cell membranes. They are known for their vast surface area and high ability to penetrate cell membranes, which act as micro-needles, making them an ideal means of delivering antitumor drugs (Shaalan *et al*., 2016).

The types of nanoparticles used in the treatment of fish to date are mostly limited to spherical nanoparticles or polymer nanoparticles. Nanoparticles have a wide range of potential applications as antimicrobials, drug delivery and gene transfer, vaccination, and especially for detecting fish pathogens. In the aquaculture and seafood industries, nanotechnology has the potential to be widely used, but there is limited information about its impact on marine species. Numerous studies have shown that carp and young sturgeon grow faster due to the effect of iron nanoparticles. These studies also suggest that a diet containing nano-selenium can increase fish weight, relative growth rate, and antioxidant status of fish and increase glutathione peroxidase activity and muscle selenium concentration in Carasius Giblio 17 (Ansar *et al*., 2017; Khosravi-Katuli *et al*., 2017).

In addition, the study of fish tested by the mentioned nanomaterials showed that the

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presence of nanomaterials can increase fish growth compared to the control group. The direct use of silver nanoparticles in water to treat fungal diseases is harmful to young trout. Filtering water with silver nanoparticles could prevent fungal infections in rainbow trout farming (AYDIN and Şehriban, 2019). In addition, scientists at the Russian Academy of Sciences report that when young carp and caviar are fed iron nanoparticles, they grow faster (30% and 24%, respectively). Research has shown that various sources of selenium (nano-selenium and selenomethionine 18) added to the basal diet can increase final weight, relative growth rate, and antioxidant status. In addition, nano-selenium appears to be more successful in increasing muscle selenium content than organic selenomethionine (Nasr-Eldahan *et al*., 2021).

Nanoparticles are now recognized as a promising new antimicrobial agent against traditional antibiotic-resistant bacteria. Studies have shown that nanoparticles have significant toxic effects against several bacterial strains. According to the results, nanomaterials can be promising in various medical fields, including drug and gene delivery, tissue engineering, and imaging techniques. In addition, nanoparticles can be used as a carrier to deliver a wide range of therapeutic agents, including drugs and antibodies. Paul Ehrlich first proposed the idea of developing drug delivery systems using nanoparticles. For this reason, since early 2005, nanomaterials have been widely studied for medical and pharmaceutical applications. These materials are 100 nm or less in size and can be metal, semiconductor, polymer, or carbon based. Reports of antibacterial activity in root nanomaterials have been observed in biophysical reactions (Nasr-Eldahan *et al*., 2021).

Nanoparticles cause damage to bacterial membranes; in particular, metal nanomaterials (such as silver, gold, copper, and titanium) exhibit desirable physicochemical properties that lead to significant levels of antibacterial activity. In the fisheries sector, nanotechnology is widely used for many purposes such as water purification, fish pond sterilization, fish nutrition and aquatic disease management. Nanotechnology is commonly used in water disinfection in fish farms. The application of nanotechnology in shrimp farming can improve water quality, reduce water exchange rates, and increase the survival and better performance of shrimp. Nanotechnologies are available today to remove contaminants from water. In the aquaculture industry, nanomaterials in the form of active substances, such as carbon or alumina, with additives such as zeolite 21 and iron-containing compounds, can be used to remove ammonia, nitrites, and nitrate contaminants. Nano-scale iron powder can also be used as an essential method for cleaning carbon compounds with less and less toxicity, such as trichloroethane, carbon tetrachloride, dioxins and polychlorinated biphenyls, thus paving the way for nano-aquaculture (Table 3) (Mudhafar *et al*., 2020).

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Table 3. The effect of cytotoxicity of nanoparticles against different bacteria (Ravikumar *et al*., 2012)

Minimum Inhibitory Concentration (MIC)	**Type of bacteria**	**Size**	**Shape**	**Type of silver**
6.25 & 7.5 µg/mL	*E. coli* and *S. aureus*	7 nm	Spherical	AgNPS
13.02 & 16.67 µg/mL	*E. coli* and *S. aureus*	29 nm	Spherical	AgNPS
11.79 & 33.71 µg/mL	*E. coli* and *S. aureus*	89 nm	pseudo Spherical	AgNPS
25 µg/mL	*E. coli*	16 nm	Not reported	AgNPS
8-12 mm	*E. coli*	5-40nm	Cube	AgNPS
9&12 15&6 mm	*B. cereus* & B. subtilis S. aureus & P. aeruginosa	10.78nm	Spherical	AgNPS
12.7&11.3mm	*E. coli* and S. aureus	18.2 nm	Cube	AgNPS
18&11 mm	*K. pneumoniae* & *M. luteus*	55-83nm	Spherical	AgNPS
11&19 mm	*P. aeroginosa* & *S. aureus*	15 nm	Spherical	AgNPS
5mm	*E. coli*	20-90 nm	Spherical	AgNPS
1.5-2.5mm	*E. coli*	20-90 nm	Spherical	AgNPS
31&27mm	*E. coli* and *S. aureus*	16 nm	Spherical	AgNPS
23 &21mm	*E. coli* and *S. aureus*	20nm	Oval	AgNPS
14 &13mm 18 &20 mm	*S. aureus* & *B. cereus* Pseudomonas & *B. subtilis*	46nm	Spherical	AgNPS
15&11 mm	*S. enteric* & *S. aureus*	10-25 nm	Spherical	AgNPS
15.3 mm	*P. aureginosa*	7.3 nm	Spherical	AgNPS
23&27.5mm 26&14mm	*K. pneumonia* & *S. aureus* *P. aeruginosa* & *P. vulgaris*	15 nm	Hexagonal	AgNPS
8.5 &9mm 10.5&10mm	*K. pneumonia* & *M. flavus* *P. aeruginosa* & *B. pumilus*	53.2 nm	Cube	AgNPS
20mm	*E. coli*	40 nm	Spherical	AgNPS
24mm	*E. coli*	40 nm	Triangular	AgNPS
10mm	*E. coli*	40nm	Hexagonal	AgNPS

The fisheries and aquaculture industries can be improved with the help of nanotechnology through tasks such as rapid diagnosis of diseases, increasing the ability of fish to absorb drugs such as hormones, drugs and nutrients. Nanotechnology can protect food products by using various techniques, and packaging them to ensure product safety and prevent enzymatic and microbial spoilage.

It has recently been observed that there is an increasing application of nanoparticles in aquaculture. Nanoparticles of elements such as selenium, iron and chitosan that are added to food sources can improve the fish production. Researchers believe that nanotechnology may be able to provide healthy fish ponds to prevent any contamination and disease. Another application of nanotechnology is using various conservation and packaging techniques to ensure the safety of seafood by avoiding mold and microbial spoilage. Several studies have shown that smaller particles produce more potent immune responses than larger equivalents. The researchers showed that using nano-chitosan increased the growth performance of tilapia indigo, and the stimulating antioxidant activity was also observed. The actions of catalase, superoxide dismutase, and lysozyme were also increased, which led to improved immunity. In addition, the use of nano-chitosan in African catfish improved water quality, increased daily weight and improved food utilization, and increased survival (Shaalan *et al*., 2016).

Circumstances about nano smith still exist and must be addressed before they can be

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implemented on a larger scale. The toxic effects of nanoparticles depend on various factors including an interaction between particle properties such as diameter, shape, surface charge, concentration and particle exposure time, nature of nanoparticles, medium composition, particle management pathway, and immune system of target species. Despite the information available, there are several ambiguities have obscured the use of nanoparticles in aquaculture. First, how nanoparticles are used in aquaculture can be very different: concentrations are sometimes less or more than what is used or expected in aquaculture, resulting in unrealistic results. Therefore, there may be potential side effects that affect the end consumer (Fang *et al*., 2018).

Properties and antimicrobial mechanism of silver nanoparticles

The story of the discovery of silver nanoparticles is not new, as it dates back more than 100 years. In the past, silver nanoparticles were produced by carrying them through a path with a positive electric current through silver rods suspended in water (Dananjaya *et al*., 2016; Hosseini *et al*., 2016). Through this technique, the sizes obtained from silver nanoparticles ranged from 15 to 500 nanometers and were used to treat bacterial infections before the discovery of penicillin in 1928. When silver is reduced in size from nanoparticles, it enhances the physical, chemical, and optical properties of silver. The increase in surface area, leads to increased performance against bacteria and fungi because it penetrates the cell wall of bacteria, which ultimately stops cell metabolism and cell proliferation. The unique optical, mechanical, magnetic, and electrical properties of silver nanoparticles are the main reason for their use in various fields. Applications of silver nanoparticles (Ag NPs) can be classified into four main sections; Scientific, medical, industrial and consumer (Mudhafar *et al*., 2020).

Scientific applications of Ag NPs include enhanced IR absorption spectroscopy, evaluation of fibrinogen in human plasma, colorimetric sensors for histidine, DNA sequencing, glucose sensors for medical diagnosis, optical imaging of cancer, and biosensors for herbicide detection, and optical sensors for zaptomol. Meanwhile, industrial applications of Ag NPs include decomposition, electronics, book materials, brochures, envelopes, and office supplies. In contrast, the consumer uses of Ag NPs include face masks, wipes, slippers, pillows, cell phones, vacuum cleaners, shampoos, washing machines, soaps, air filters, and food storage containers. In medicine, these applications include medical devices, dressings, treatments, drug delivery, medical textiles, contraceptives, scaffolding, diabetic socks, wound dressings, medical catheters, and sterile materials in hospitals (Mudhafar *et al*., 2020).

The use of silver nanoparticles in medicine is due to their antibacterial, antifungal, anti-inflammatory, anti-cancer, antioxidant, anti-biofilm, and surface plasmon intensification properties. In addition to their antibacterial properties, Ag NPs are commonly used in the healthcare industry, food storage, textile coatings, and other environmental applications. Although these nanoparticles have been used for

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years, their toxicity is still unclear (Mudhafar *et al*., 2020).

Silver is used in medicine as an antibacterial reagent to treat wounds and burns. In the early 1940s, with the advent of the antibiotic age, penicillin largely replaced silver. At present, with the emergence and increase of antibiotic-resistant bacterial strains, silver has been introduced as a promising substance in the development of new antibiotics. In recent years, numerous studies have demonstrated the ability of silver nanomaterials to have unique electronic, optical, and chemical properties. Recently, studies have reported that the size and surface coating of silver nanoparticles play a significant role in antibacterial activity (Banasiuk *et al*., 2016).

Silver nanoparticles were highly effective against a wide range of gram-negative and gram-positive bacteria and antibiotic-resistant strains. Gram-negative genera include Vibrio, Salmonella, pseudomonas, *E.coli* and Acinetobacter. These species are associated with a disease that infects the patient during hospital treatment in the medical care unit. Gram-positive genera include critical pathogens such as Streptococcus, Staphylococcus, Listeria, Enterococcus, Clostridium, and Bacillus. Meanwhile, antibiotic-resistant bacteria include strains such as *Enterococcus faecium*, and *Staphylococcus aureus* resistant to vancomycin and resistant to methicillin. Several studies have shown that factors such as size, shape, concentration and type of bacteria can have a significant effect on the activity of silver nanoparticles. Among the various forms of synthesized silver nanoparticles that have been reported are quasi-spherical, cubic, spherical, oval, hexagonal, plate, rod, and triangular (Nayak *et al*., 2016). At the same time, different sizes of silver nanoparticles were reported in the range of 1 to 500 nm due to other synthesis methods. They were very effective against a wide range of bacteria such as E. coli (Mudhafar *et al*., 2020).

The mechanism of silver's antibacterial effect is manifested in both colloidal and ionic forms. The first mechanism suggests that Ag + ions released from silver nanoparticles can bind to thiol groups of proteins and enzymes found at the cellular level, destabilizing cell membranes and degrading the ATP synthesis pathway (Gahlawat *et al*., 2016). The silver nanoparticles may then adhere to the membrane wall, creating holes through which they can later penetrate bacteria and interact with intracellular components or sulfur-containing proteins (Eugenio *et al*., 2016). The second mechanism suggests ROS can be produced in cell membranes and lead to irreversible damage to DNA replication that affects metabolic processes and cell division. Many studies indicate the first mechanism is the most critical damage to bacteria. Bactericidal effects and high potential of silver nanoparticles in water treatment, medical devices, burn dressings and food storage have been proven. For this reason, silver nanomaterials have been the primary sources of attention in the medical and technological fields (Mudhafar *et al*., 2020).

The interaction between silver nanoparticles and the cell surface of different bacteria can occur physically. In gram-negative bacteria, several studies have reported the

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binding of Ag NPs to the bacterial surface. Silver nanoparticles are anchored to the bacterial cell wall and eventually enter it, causing changes in the structure of the cell membrane. This makes the bacteria more permeable. Accumulation of Ag NPs causes a gap in the bilayer of the cell membrane. Cell permeability increases and eventually causes cell death. Studies on 30-electron spin resonance spectroscopy have reported increased free radicals released from silver nanoparticles when they interact with bacteria that cause cell death (Mudhafar *et al*., 2020). Similarly, when silver nanoparticles and free ions combine, they produce vigorous antibacterial activity. In addition, nanoparticles may release silver ions, which can interact with and inactivate thiol groups of various enzymes. When bacterial cells come in contact with silver, silver ions are absorbed, inhibiting cell function and damaging the cells. In addition, reactive oxygen species (ROS) are produced. ROS are oxygen-free radicals from silver ions that have a predominant bacterial activity and attack cells by inhibiting respiratory enzymes. Silver ions damage the structure of germs when they enter them. Ribosomes may inhibit protein synthesis due to their denatured state and block translation and transcription by genetic material or bacterial cells. In one study, researchers exposed some microorganisms to lethal concentrations of silver nanoparticles (500 g / L), which increased ROS production and, consequently, the activity of antioxidant enzymes in the control group. Other researchers exposed *Labeo rohita* to 100 mg of silver nanoparticles for seven days, which resulted in a significant reduction in hematological parameters and a significant increase in antioxidant enzymes in the gills, liver, and muscles. In addition, the antibacterial effect of silver nanoparticles synthesized by *Prosopis chilensis* leaf extract was evaluated after thirty days of exposure to four species of pathogens affecting *Penaeus monodon* shrimp. This study showed that shrimp fed with silver nanoparticles showed a higher survival rate, which is associated with an increased immune system in terms of higher hemocyte count, phenol oxidase and hemolymph antibacterial activity (Khosravi-Katuli *et al*., 2017).

Other researchers report that silver nanoparticles exhibit high antibacterial activity against multidrug-resistant bacterial species. The bactericidal effect of silver nanoparticles against methicillin-resistant *Staphylococcus aureus* has also been reported. Silver nanoparticles synthesized using citrus lemon 32 extracts a reducing agent showed antibacterial activity against *Staphylococcus aureus* and *Edwardsiella tarda* and anti-cyanobacterial activity against Anabaena and Osilatoria species (Table 4). Other researchers used *Rhizophora mucronata* bud extract for the biosynthesis of Ag NPs and then demonstrated its antimicrobial effects against *Pseudomonas fluorescens*, Proteus species and Flavobacterium species. The performance of these synthesized green silver nanoparticles was similar to that of commercial antibiotics. In a study of young shrimp infected with *Vibrio harveyi*, researchers treated shrimp with silver nanoparticles for a long time, reducing mortality by up to 71% at high doses of Ag - NPs. Silver nanoparticles act as an

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antifungal agent with high inhibitory effects against Candida species and have a similar function to commercial antifungal Amphotericin B. Silver nanoparticles also have antiviral properties: they can bind to HIV-1 virus proteins in vitro. Both silver nanoparticles and silver-chitosan nanoparticles are active against the influenza A virus (Latif *et al*., 2015). However, little research has been done on the antifungal and antiviral effects of silver nanoparticles in the treatment of fish (Shaalan *et al*., 2016; Yadollahi *et al*., 2015).

Table 4. Synthesized silver nanoparticles with different strains of cyanobacteria (Mustafa Mudhafar *et al*., 2021)

Specie	Reaction time (hour)	Shape of nanoparticles	Maximum absorption (Nanometers)	Nanoparticle size (Nanometers)
Arthrospira indica PCC7940	45	spherule	446	48
Arthrospira indica SAE-85	45	spherule	468	67
Arthrospira indica SOSA-4	46	spherule	446	48
Arthrospira maxima SAE-49-88	48	triangle	465	61
Arthrospira platensis NEERI	45	triangle	445	46
Chroococcus NCCU-207	120	spherule	447	48
Gloeocapsa gelatinosa NCCU-430	50	spherule	490	88
Lyngbya NCCU-102	120	spherule	452	54
Oscillatoria sp. NCCU-369	360	spherule	485	80
Phormidium sp. NCCU-104	96	Square	446	48
Plectonema sp. NCCU-204	320	spherule	460	61
Spirulina CFTRI	46	hexagon	446	47
Spirulina NCCU-477	45	Square	450	49
Spirulina NCCU-479	45	spherule	451	52
Spirulina-481	45	spherule	466	64
Spirulina NCCU-482	45	spherule	443	42
Spirulina NCCU-483	47	pentangle	450	51
Spirulina platensis NCCU-S5	45	spherule	445	46
Synechocystis NCCU-370	72	spherule	485	80
Anabaena ambigua NCCU-1	72	spherule	446	48
Anabaena variabilis NCCU-441	72	spherule	450	50
Aulosira fertilissma NCCU-443	50	spherule	450	58
Calothrix brevissema NCCU-65	220	Square	443	42
Cylindrospermum stagnale NCCU	250	pentangle	440	38 & 40
Hapalosiphon fontinalis NCCU-339	270	triangle	450	50
Microchaete sp. NCCU-342	30	spherule	440	40
Nostoc muscorum NCCU-442	220	spherule	443	42
Scytonema sp. NCCU-126	350	spherule	470	70
Tolypothrix tenuis NCCU-122	300	spherule	445	44
Westiellopsis prolifica NCCU-331	280	spherule	451	52

Synthesis of silver nanoparticles

Synthesis of silver nanoparticles can be done by chemical or physical techniques (Figure 1) (Park *et al*., 2016a). Chemical techniques include chemical reduction, sonochemical, microemulsion, photochemical, electrochemical, pyrolysis, microwave, heat solvent and co-precipitation. A standard chemical method for producing silver nanoparticles is chemical reduction using organic reducing agents. Several chemical reducing agents such N, N-dimethylformamide (DMF), sodium borohydride (NaBH4), polyethylene glycol, and Tollens reagent are used to reduce silver ions from its salts in non-aqueous solutions. Physical methods include pulsed laser erosion 33, evaporation-density 34,

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ARC35 evacuation, spray pyrolysis 36, ball mill 37, vapor and gas phase 38, pulse wire evacuation 39, and lithography 40 (Mudhafar *et al*., 2020).

Today there is a great desire to find environmentally friendly and economical methods for the synthesis of nanoparticles. Biological methods are considered as the key to this approach. The biosynthesized nanoparticles are derived from three main groups of living organisms: bacteria, fungi, and plants (Figure 1). Bio-synthesis of nanoparticles is a bottom-up method that mainly involves reduction / oxidation reactions. Plant microbial enzymes or phytochemicals act as antioxidants on precursor compounds can produce desirable nanoparticles. The three main components of a synthetic nanoparticle system are a solvent medium for synthesis, an environmentally friendly reducing agent, and a non-toxic stabilizing agent (Table 5) (Mudhafar *et al*., 2020).

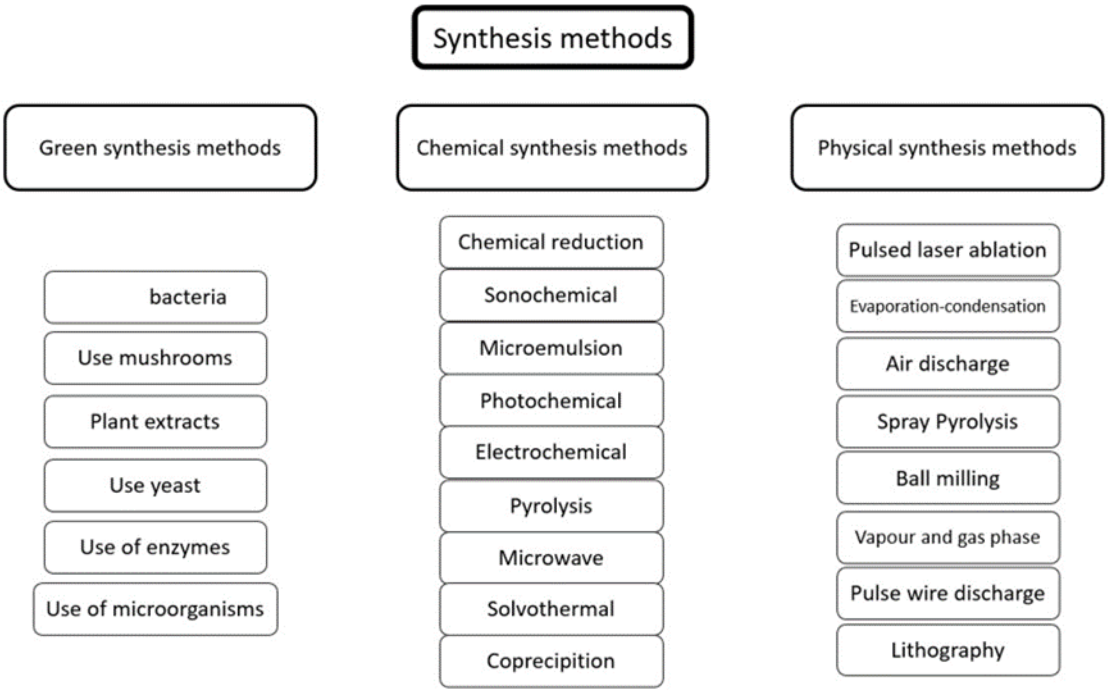

Figure 1. Different methods of nanoparticle synthesis (Mudhafar *et al*., 2021).

Simple, environmentally friendly methods using plant extracts are capable of producing dispersed silver nanoparticles about 20 nanometers in diameter. For example, researchers used marjoram leaf extract to synthesize spherical silver nanoparticles that show cytotoxicity against A549 cell line in human lung cancer. This study showed a direct correlation between increased silver nanoparticle concentrations and cell toxicity against the cancer cell line with 85% cell mortality, although the mechanism of anticancer activity is not yet understood . Using extracts of Ficus benghalensis and Azadirachta indica, the researchers synthesized crystalline and spherical silver nanoparticles and observed antibacterial activity against gram-positive and gram-negative bacteria, as well as against cancer cell lines. The researchers described a new bacterial strain called ocrobacterium rhizobacterium 41 that synthesizes globular silver nanoparticles as antimicrobial

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agents against cholera. Walnut shell extract was used to synthesize green silver and gold nanoparticles, which showed bactericidal activity against several fish pathogens (Khan *et al*., 2019; Park *et al*., 2016b). Silver nanoparticles synthesized using tea leaf extract (Camellia Sinensis) showed potential bactericidal activity in high amounts of nanoparticle against *Vibrio harveyi*. *Aloe vera* leaf extract was used to synthesize green zinc oxide nanoparticles, which had higher bactericidal activity than chemically synthesized nanoparticles. A new method for the biological synthesis of zinc oxide (ZnO) nanoparticles uses the bacterium *Aeromonas hydrophila* as a reducing agent (Ahmed *et al*., 2016; Rafique *et al*., 2017). This method is environmentally friendly and economically feasible and leads to the production of ZnO nanoparticles with antibacterial and antifungal effects (Vimbela *et al*., 2017).

The researchers then isolated the biomolecule in the culture medium responsible for the synthesis and coating of silver nanoparticles and identified it as a glycoprotein exopolymer. The observations showed antibacterial properties, inhibition of bacterial growth and reduced metabolic activity, and cell viability against the pathogen. In addition, researchers have recently identified a single-celled fungus as a promising candidate for the synthesis of silver nanoparticles due to their long-term use in industrial-scale production. In addition, the researchers reduced the synthesis time of silver nanoparticles using commercially available LED lights to significantly reduce energy consumption. In addition, the researchers reported a new green method for stabilizing and reducing silver nanoparticles by fluorescent carbon dots. It has been previously reported that carbon dots, in addition to their stabilizing properties due to the different COOH and -OH groups on their surface, also have reducing and oxidizing properties. With this in mind, the researchers investigated the synthesis of silver nanoparticles using fluorescents as reducing and stabilizing agents and the resulting antibacterial properties. They concluded that the reduction method was highly dependent on pH levels (Vimbela *et al*., 2017).

The specific physicochemical properties of nanomaterials play an essential role in its performance and use. Silver nanoparticles may be produced in metal or composite structures with one or more dimensions at the nanoscale. Structures such as nanocrystals, nanocrystals, and quantum dots are examples of nanostructures with the highest reported antibacterial properties. Due to their very high volume-to-surface ratio, they are particularly promising for medical and drug delivery systems. For example, a study on the physiological reactions of *E.coli* to silver nanoparticles with different zeta potentials and sizes showed that these factors affect its antibacterial mechanism (Handoko *et al*., 2019; Rafique *et al*., 2017; Vimbela *et al*., 2017).

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Table 5. Green synthesis of metal nanoparticles using bacteria, yeasts, microalgae and fungi (Mudhafar *et al*., 2020)

Bacterial species	Metal nanoparticles	zone of synthesis	Size (nanometers)
Shewanella oneidensis	Uranium	Extracellular	150
Pseudomonas aeruginosa	Au	Extracellular	30 – 15
Lactobacillus sp.	Au/Ag	Intracellular	20-50
Acetobacter xylinum	Ag	Extracellular	-
Bacillus selenitireducens	Tellurium	Extracellular	~10
Magnetospirillum magnetotacticum	Fe3O4*Fe3O4*	Intracellular	1/47
Desulfovibrio desulfuricans NCIMB 8307	Palladium	Intracellular	50~
Aquaspirillum	Fe3O4*Fe3O4*	Intracellular	50 – 40
Lactobacillus sp.	Ti	Extracellular	60 – 40
Rhodopseudomonas capsulate	Au	Extracellular	20 – 10
Plectonema boryanum UTEX485	Au	Intracellular	10
Enterobacter cloacae, Klebsiella pneumonia, E. coli	Ag	Extracellular	5 / 52
Gluconacetobacter xylinus	CdS	Extracellular	30
Actinobacter sp.	Magnetite	Extracellular	40 – 10
Yeast species	**Metal nanoparticles**	**Zone of synthesis**	**Size (nanometers)**
Bread yeast	Au	Extracellular	13
Candida albicans	Au	Cell-free extract	5
Candida utilis	Au	Intracellular	-
Yarrowia lipolytica NCIM3589	Au	Cell surface	various
Candida glabrata	CdS	Intracellular & Extracellular	Å 20 &Å 29
Yeast strain MKY3	Ag	Extracellular	5 – 2
Saccharomyces cerevisiae	Sb2O3*Sb2O3*	Intracellular	10 - 2
Schizosaccharomyces pombe	CdS	Intracellular & Extracellular	Å 18 &Å 29
Schizosaccharomyces pombe	CdS	Intracellular	5/1 - 1
Rhodotorula mucilaginosa	Cu	Intracellular	5 / 10
Rhodotorula mucilaginosa	Ni/NiO	Extracellular	5 / 5
Rhodotorula mucilaginosa	Ag	Intracellular	11
Mushroom species	**Metal nanoparticles**	**Zone of synthesis**	**Size (nanometers)**
Aspergillus clavatus	Ag	Extracellular	25 - 10
Aspergillus niger	Ag	Extracellular	30 - 3
Bipolaris nodulosa	Ag	Extracellular	60 - 10
Phoma glomerata	Ag	Extracellular	80 - 60
Mucor hiemalis	Ag	Extracellular	15 - 5
Pestalotia sp.	Ag	Extracellular	40 - 10
Aspergillus terreus	Mg	Extracellular	98 - 48
Aspergillus aculeatus	NiO	Extracellular	89 / 5
Aspergillus niger	Ce02*Ce02*	Extracellular	20 - 5
Hypocrea lixii	Cu	Extracellular	5 / 24
Aspergillus fumigatus	ZnO	Extracellular	8/6 – 2/1
Trichoderma koningiopsis	Cu	Extracellular	5/87
Colletotrichum sp.	Au	Extracellular	40 - 8
Hypocrea lixii	NiO	Extracellular & Intracellular	8/3 & 25/1
Lecanicillium lecanii	Ag	Extracellular	100 - 45
Rhizopus oryzae	Au	Cell surface	10
Aureobasidium pullulans	Au	Intracellular	29
Algal species	**Metal nanoparticles**	**zone of synthesis**	**Size (nanometers)**
Ulva fasciata	Ag	Extracellular	41 - 28
Sargassum plagiophyllum	AgCl3	Extracellular	42 - 18
Caulerpa racemose	Ag	Extracellular	5/2 - 5
Spirulina platensis	Au	Intracellular	5
Galaxaura elongata	Au	Extracellular	13/77 – 85/3
Sargassum wightii Grevilli	Ag	Extracellular	27 - 8
Padina pavonica	Ag	Extracellular	54
Chlorella pyrenoidosa	Ag	Extracellular	15 - 5
Scendesmus abundans	Ag	Extracellular	66 - 59
Chlorococcum humicola	Ag	Intracellular	6 - 4
Bifurcaria bifurcate	Cuo	Extracellular	45 - 5
Amphora-46	Ag	Extracellular	70 - 5
Gracilaria dura	Ag	Extracellular	6
Turbinaria conoides	Au	Extracellular	60

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Bacteria synthesizing green silver nanoparticles

Bacteria synthesizing silver nanoparticles include *Bacillus methylotrophic*, *Pseudomonas putida*, *Vibrio alginolyticus*, Lactobacillus, endosymbiotic bacteria, *Penicillium glabroma*, and the size of these nanoparticles was about 200 nm. The researchers reported that the synthesis of silver nanoparticles using Aeromonas sp. They successfully obtained to obtain silver nanoparticles with a size between 8 to 16 nm and spherical. In addition, *Serratia nematodiphila* was used to produce silver nanoparticles with a size between 10 and 31 nm and spherical. Actinobacteria, Streptomyces spp. and Cyanobacterium *spirulina platensis* were used as precursors to produce silver nanoparticles using AgNO3, and the size of the silver nanoparticles obtained was reported to be between 7 and 15 nm (Mudhafar *et al*., 2020).

Cytotoxicity effects of nanoparticles

The effect that nanoparticles and nanostructures may have on biological organisms must be adequately understood to minimize the potentially destructive effects of these nanoparticles in any application. Recent studies have examined the cytotoxic effects of silver nanoparticles on the human body, particularly on the respiratory and cardiovascular systems, osteoblasts, osteoclasts, DNA, and fetal growth disorders. The researchers studied the physicochemical effects of silver nanoparticles measuring 10, 40, 50 and 75 nanometers, as well as coating them against healthy human lung cells. Although the coating agent responsible for modulating the toxic effects was not found, the release of Ag + into the cell culture medium was directly proportional to the total surface area of the particles and thus their size. The researchers suggest that the high Ag + content inside the cell should result from the intracellular conversion of silver nanoparticles to Ag +. DNA damage occurs with the release of Ag + after a 4-hour incubation period. Mitochondrial damage has also been observed due to exposure to silver nanoparticles. The cytotoxicity of silver nanoparticles on red blood cells (RBCs) is of great interest. The researchers found that the cytotoxic effects of 15, 50 and 100 nm silver nanoparticles were more excellent on RBC when more diminutive in size, while larger nanoparticles showed higher cytotoxic effects (Mudhafar *et al*., 2020).

Zinc Nanomaterials

Zinc and its alloys have broad applications in medicine due to their low toxicity. These materials are promising in imaging and drug delivery due to their electrical, optical, and photocatalytic properties. Recently, the introduction of zinc into biomedical systems has increased and has been very effective in several biological functions, including DNA synthesis and nucleic acid metabolism (Vimbela *et al*., 2017).

Zinc-containing nanomaterials have excellent antibacterial properties. The most common zinc-containing material is zinc oxide nanoparticles. ZnO nanomaterials (ZnO), and biocompatible and biodegradable properties are

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unique in their semiconductor and piezoelectric properties (Manosalva *et al*., 2019; Singh *et al*., 2017). ROS, like superoxide anion, hydrogen peroxide, and hydroxide, can damage lipids and proteins within bacterial cell membranes, at the same time the release of Zn + 2 from zinc oxide nanoparticles can disrupt their metabolic pathways (Vimbela *et al*., 2017). Recent advances in zinc oxide nanoparticle synthesis techniques include the use of precursors (49 coordination polymers and biological extracts). Simple and controlled processes that resulted in the production of nanoparticles without significant impurities and good crystallization but with no homogeneity in nanoparticle size. At the same time, the researchers synthesized nanoparticles using mangrove plant extracts. Nanoparticles produced from Mangrove *Sonaratia aptala* 50 showed relatively higher antibacterial and anti-inflammatory properties. In addition, more research has been done on other applications of zinc oxide nanoparticles in the treatment of prosthetics and dentistry (Kalaiselvi *et al*., 2019; Siddiqi *et al*., 2018). The results showed that zinc oxide nanoparticles are used in optoelectronics 51, cosmetics, catalysts, ceramics, pigments and aquaculture. However, there are conflicting results regarding the effects of zinc oxide nanoparticles concerning separation, contact time, and target organisms. This means that the researchers exposed zebrafish embryos to different concentrations of zinc oxide nanoparticles, which led to a significant reduction in survival, egg production and larval growth rate after 94 hours. Other researchers performed a 30-day study on *C. capio* larvae exposed to zinc oxide nanoparticles that resulted in severe histopathological changes 52 and intracellular oxidative stress (Francis *et al*., 2018; Vimbela *et al*., 2017).

Other researchers have shown that after 90 days of exposure to *Macrobrachium rosenbergii* with zinc oxide nanoparticles leads to reduced growth and survival and changes in the activity of digestive enzymes (protease, amylase and lipase) and biochemical compounds (total protein, total amino acid, Total carbohydrates and total lipids) (Devi *et al*., 2019). In addition, after 96 hours of exposure to *Crassostrea gigas* to a lethal concentration of zinc oxide nanoparticles up to an attention of 30 mg / l, zinc accumulates in the gills and gastrointestinal glands, leading to oxidative damage. Also, short-term exposure (up to 96 hours) to lethal concentrations of zinc oxide nanoparticles up to 10 mg / l had no adverse effect on *California blackworm*, but long-term exposure (up to 28 days) showed toxic effects. The results of zinc oxide nanoparticles on embryonic growth, zinc bioaccumulation, oxidative stress and aquatic behavior have been quite evident. In aquaculture, using zinc oxide particles can contribute to development, increase safety and water quality in fish ponds. However, focused studies are needed to determine the appropriate concentration of exposure to zinc oxide nanoparticles for aquaculture activities (Khosravi-Katuli *et al*., 2017; Vijayan *et al*., 2018).

Zinc oxide nanoparticles have attracted much attention due to their antibacterial and antifungal effects. Antibacterial activity results from the damage that particles do to the bacterial cell membrane, which causes the cytoplasmic

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contents of the cell to leak. In fish diseases, zinc oxide nanoparticles can inhibit the growth of *Aeromonas hydrophila*, *Adorsila tarda*, *Flavobacterium branchiolum*, Citrobacter species. Other researchers have compared the antibacterial effects of zinc oxide nanoparticles with the pathogen Vibrio harveyi and observed the higher bactericidal effects of nanoparticles compared to zinc oxide. In another interesting study, zinc oxide nanoparticles were biologically synthesized using *Aeromonas hydrophila*, and these nanoparticles showed antibacterial activity against the same bacteria and other species such as *Pseudomonas aeruginosa* 58, *Escherichia coli* 59, *Enterococcus faecalis* 60, *Aspergillus canolabi* 61 (Kasithevar *et al*., 2017; Shaalan *et al*., 2016).

Conclusion

Fish is one of the most important source of food containing high quality protein, fatty acids, vitamins and other vital elements such as iodine and selenium that are not found in other products or meat. So fish is a valuable food for most people. However, fish, like other species, suffer from many infectious and non-infectious diseases due to various agricultural and industrial pollutants in ponds. In addition, the increase in environmental stress on fish leads to the rise in the prevalence of diseases and increases the capacity for various diseases (bacteria - fungi - viruses). Therefore, treating fish diseases has received considerable attention in recent years. In addition, the side effects of antibiotics and indirect therapies through the synthesis of natural products have been proven over time. Classical treatments have shown significant disadvantages. Today, using nano vaccines is a new attempt to increase the immunogenicity of vaccines by using nanoparticles as carriers.

Advances in green synthesis techniques for silver nano materials have increased their applications (Gheibi Hayat and Darroudi, 2019). Nano materials can be used as antibacterial agents. New synthesis techniques for silver nanostructures using biogenic methods that include plant extracts, bacteria, fungi, and yeasts as solvents have provided green alternatives to conventional synthesis. In addition, nano materials with other sizes and structures showed different antibacterial properties. For example, synthesized triangular nanoparticles released more considerable amounts of silver ions than nanoparticles of similar size and thus showed higher antibacterial activity. However, nanoparticles with smaller sizes but similar morphological properties showed higher antibacterial activity due to the higher ionization rate of silver ions and the higher probability of nanoparticles entering the bacterial cell wall at a smaller size. In other words, the potential of silver nanoparticles as an antibacterial reagent is undeniable. The antibacterial activity of nanomaterials is due to the observed biophysical interactions between nanoparticles and bacteria, including cell adsorption and accumulation of nanoparticles, which leads to membrane damage and toxicity. In particular, metal nanomaterials (such as silver, gold, copper, and titanium) exhibit desirable

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physicochemical properties that lead to significant levels of antibacterial activity.

Many studies on the antibacterial effects of the mentioned nanomaterials show that the physicochemical manipulations of the nanomaterials affect their antibacterial activity. However, there is still a large gap in the exact mechanisms of this antibacterial activity. That is why more research needs to be done on the morphological and bactericidal effects, especially for materials other than silver nanoparticles.

Today, using nanotechnology in aquaculture has become a comprehensive tool to solve many problems, not only disease diagnosis and treatment but also water quality control, fish nutrition, environmental management and so on. However, the use of nanomaterials and nanotechnology in the aquaculture sector will be a slow process (Idowu *et al*., 2017). However, it is likely that soon this path will be very effective in solving major problems in aquaculture, including disease control, and may even be included in diet formulation in the not-too-distant future. Therefore, the safety of food consumed by humans and the potentially harmful environmental effects of nanoparticles must always be considered during the nanoparticle utilization process. That is why researchers and producers are working to remove barriers to the growth, reproduction and cultivation of species, their health and water treatment to increase production in aquaculture. However, there are still many concerns about nanotechnology that need to be addressed before they can be fully implemented. The effects of nanoparticles depend on several factors, including the complex interaction between particle properties, concentration, placement time, nature of nanoparticles, environment composition, particle management pathway, and the immune system of the target species. This means that sometimes inoculating very low or even very high concentrations of nanoparticles into fishponds can lead to unrealistic results. Therefore, it is not possible to deduce the side effects of nanoparticles on the final consumer. Therefore, the treatment of nanoparticles should be done accurately with a predetermined concentration and short treatment periods of 40 days. The life of fish from the stage of eggs, larvae and maturity should be examined. In addition, becuse aquatic organisms are grown in different environments (for example, freshwater and saline or tropical and temperate regions), nano-coated products can behave very differently as the effects obtained; Therefore, it can be interesting to study how environmental factors such as salinity, pH and temperature affect nanoparticles (Ali *et al*., 2015).

Many nanoparticles are excellent tools for drug delivery, genes and vaccines because of their unique properties. The most significant nanoparticles studied in fish medicine for these applications are chitosan and poly D nanoparticles, L-lactide-co-glycolic acid (PLGA). Various forms of nanoparticles such as nanocapsules, liposomes, dendrimers and nanotubes can theoretically be used in fish disease research. However, the antifungal and antiviral effects of nanoparticles against fish diseases still need to be further investigated.

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Thus there are still many research gaps in the applications of nanotechnology in the treatment of fish diseases. Given the revealed potential of nanoparticles, there is a need for more targeted research on their application in the treatment of fish diseases and improvement of diagnostic methods.

This paper attempts to examine recent advances in synthesizing metal nanomaterials as antibacterial agents, focusing on their toxicity and antibacterial activity based on the structure, dimensions and size of nanomaterials. In addition, the benefits of nanomaterials and medical applications are discussed. It is hoped that the present results of the current review article will take a step towards the need to use as much as possible and, of course, cautiously in the use of nanoparticles in the aquaculture industry.

Conflict of interest

Authors have no conflict of interest on this work.

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