

Recent Insights into the Silver Nanomaterials: an Overview of Their Transformation in the Food Webs and Toxicity in the Aquatic Ecosystem

Syed Zaheer Ud Din \cdot Khadim Shah \cdot Nadia Bibi \cdot Heba H. Mahboub \cdot Mian Adnan Kakakhel $^{\textcircled{0}}$

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Abstract Nanotechnology (NT) in the past and current decade has gained a lot of attention due to its potent antibacterial activities and its unique physicochemical features. NT works based on nanoparticles in which silver nanoparticles (AgNPs) are one of the most vital and fascinating nanomaterials. Therefore, AgNPs have been used for a variety of items, with encouraging outcomes. Besides the significant applications, there is a

S. Zaheer Ud Din International School for Optoelectronic Engineering, Qilu University of Technology (Shandong Academy

of Sciences), 250353 Jinan, China

S. Zaheer Ud Din Laser Institute, Qilu University of Technology, (Shandong Academy of Science), Jinan, 250104, China

K. Shah Institutes and Key Laboratories, Chemistry Department, Tsinghua University, Beijing 100084, China

N. Bibi

Department of Microbiology, Shaheed Benazir University, Peshawar, Pakistan

H. H. Mahboub

Department of Fish Diseases and Management, Faculty of Veterinary Medicine, Zagazig University, P.O. Box 44511, Zagazig, Sharkia, Egypt

M. A. Kakakhel (🖂)

MOE Key Laboratory of Cell Activities and Stress Adaptations, School of Life Sciences, Lanzhou University, Lanzhou 730000, China e-mail: zoology863@gmail.com; dr.kakakhel@icloud.com lot of disagreement over how AgNPs interact with the environment and how hazardous they are to aquatic life. Most worldwide freshwater ecosystems are polluted by AgNPs-containing effluents discharged from sewage and wastewater treatment plants and/or runoff streams. In the aquatic food web, fish acquire higher trophic levels; therefore, AgNPs accumulation in the body is inevitable. The bioaccumulation of AgNPs causes numerous toxic effects such as inflammation, oxidative stress, tissue disruption, and intestinal bacterial dysbiosis which could possibly lead to death. Therefore, this study aimed to describe the fate of AgNPs in the food web, their transformation and accumulation, and their possible consequences in fish. The various causes of toxicity within the fish body and the detrimental impacts on the aquatic ecosystem still require more in-depth study.

KeywordsNanoparticles \cdot Nanotoxicity \cdot Aquaticecosystem \cdot Food web \cdot Fish

1 Introduction

Nanoscience has emerged as an imperative discipline in the past and recent decade and can be defined as the science of nanomaterials (Ashraf et al., 2021). In the recent decade, due to its long history of widespread applications, this technology is growing quickly and has attracted interest in the past decades. It is a multi-disciplinary field (Calipinar et al., 2019). After Nobel laureate Richard P. Feynman introduced "NT" in his well-known 1959 lecture "There's Plenty of Room at the Bottom" ("Plenty of room' revisited" 2009). "Nano" is a word that means one-billionth of a physical unit, yet there has been no agreement on the definition of NT (Satalkar et al., 2016).

Nanoparticles are a diverse class of materials comprising particulate substances with at least one dimension less than 100 nm (Khan et al., 2019). This exclusive size gives them a very large surface area to volume ratio and results in different electronic properties than the conventional bulk counterpart. The emerging interest in NT has been directed to increasing global production and applications of NPs in numerous commercial and industrial sectors, such as cosmetics, biomedical, biosensing, wastewater treatment, electronics, and energy sectors (Mihranyan et al., 2012; Morris et al., 2011). The development of NPs began late in the twenty-first century, after the innovation of the atomic force microscope (AFM) (Brar et al., 2010). With the innovation of AFM, the production of NPs significantly increased for instance, in 2004, the estimated synthesis of NPs was about 2000 tons/year, and it was expected to increase to 58,000 tons/year in 2020 (Joshi et al., 2013; Poursorkhabi et al., 2020). About 1015 commercial products were used by the people, which were manufactured using NPs in 2009 (Kim et al., 2012).

Nanoparticles may be discharged into the environment after using industrial and commercial products made with NPs (Bundschuh et al., 2018). For instance, NPs were well-known products for utilization in wastewater treatment (Singhal et al., 2018), which could possibly introduce into the aquatic ecosystem (Bundschuh et al., 2019). NPs were detected in wastewater treatment plants and sewer systems were considered the primary source of releasing NPs into the environment (Mohana et al., 2021). A recent study has suggested that most NPs discharged into the aquatic ecosystem during wastewater treatment (Naeri et al., 2020). In respect of the above studies, the present review study aimed to provide knowledge to the readers about the introduction of AgNPs and

their profound effects on the aquatic ecosystem: the transformation in the food web, the fate of toxicity, possible damage, and intestinal bacterial dysbiosis by AgNPs in fish.

1.1 Silver Nanoparticles

Silver nanoparticles have gained prominence as a safe material in recent years due to their promising properties. Their main features are due to the high surface-tovolume ratio, allowing the nanomaterial to be broadly exploited in numerous fields, such as electronics, biotechnology, microbiology, medicine, biosensors, food industry, agriculture, and especially in general environmental remediation. The wide use of AgNPs is reflected in the number of global suppliers and worldwide consumption in different fields of life (Temizel-Sekery et al. 2020; Tortella et al., 2020), as shown in Fig. 1. Because novel applications for AgNPs are being explored daily, this ongoing use of AgNPs throughout the globe can be expected to produce more and more. A previous study reported that due to the promising results

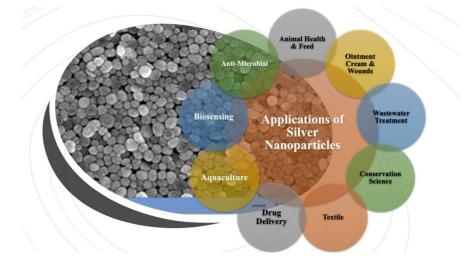


Fig. 1 The graphical representations of the application of the AgNPs

of AgNPs in electrical and electronic applications, demand in this field is expected to increase until 2022 (Syafiuddin et al., 2017). About 2000 tons of nanomaterials are being fabricated nowadays; remarkably, one-fifth (435 nano-products) are silver-based, with a total annual fabrication of about 320–420 tons (Pulit-Prociak et al., 2016). Though the requirement of AgNPs is not restricted to commercial products, however, the AgNPs are also significantly being used in environmental applications, i.e., bioremediation (Mukherjee et al., 2016), and aquaculture (Márquez et al., 2018).

As a considerable quantity of AgNPs is required to satisfy market demands for various applications, the AgNPs have been produced on an industrial scale, mostly using physicochemical approaches, such as gamma radiation (Flores-Rojas et al., 2020), electrochemical technique (Nasretdinova et al., 2015), and chemical reduction method (Khan et al., 2017). Although these techniques are quite successful and efficient, they nevertheless result in hazardous deposits that may be released into the environment and cause extremely harmful environmental toxins (Tortella et al., 2020). Significant efforts have been made in the last decade to overcome these problems to promote the large-scale fabrication of AgNPs by biological means. Biological fabrication is also known as "green fabrication" which includes plants and microorganisms (Rolim et al., 2019), animal blood serum (Kakakhel et al., 2021a, 2021b), and so-called nano factories (Tortella et al., 2020). Moreover, the biological method is comparatively cost-effective and produces less hazardous waste (Duran et al., 2018). Specific biological resources can be used as reductive agents such as plants, bacteria, and fungi. It has been suggested that the biological method for AgNPs is usually less toxic than any other traditional method (de Lima et al., 2012); therefore, the biogenic fabrication method gained significant attention in the last decade. However, the chemical method is still the most used technique due to the greater control on experimental parameters, small sizes, and polydispersity (Syafiuddin et al., 2017).

Certainly, AgNPs took place in our daily life. They are used in everyday life, such as consumer products from clothes and washing machines to medical products and bacterial-resistance antibiotics (Tortella et al., 2020). AgNPs have also been included in medical devices, for instance, bionanomaterials for healing wounds (Kumar et al., 2018), dentistry (Bapat et al., 2018), and as a disinfectant (Deshmukh et al., 2019). NT is one of the recent technologies being significantly used to treat wastewater (Esakkimuthu et al., 2014). Recently, a study was conducted to remove the malachite green dye using AgNPs. Their findings revealed that increases in the concentration of AgNPs increase the removal of malachite green dye (Ismail et al., 2020). Additionally, another study revealed that AgNPs introduce into wastewater and facilitate wastewater treatment during the fabrication and utilization process (Zhao et al., 2021). In addition, the synergetic influence has allowed using AgNPs to increase the effectiveness of antibacterial agents against animal and human pathogenic bacterial species (Kaur et al., 2019). There are many other good applications of AgNPs that have been confirmed in the last decade. However, hazardous waste produced during the fabrication to the disposal process can significantly be discharged into the environment (Tortella et al., 2020). Similarly, sludge discharge from wastewater treatment led to the significant introduction of AgNPs into the environment (Caballero-Guzman et al., 2015) as shown in Fig. 2. The main possible routes probably facilitate the introduction of AgNPs into the environment. After releasing AgNPs into the environment, their transformation and interaction with biotic components can enhance the possibility of ecotoxicity (Khan et al., 2017). Previously, studies reported that some parameters, for instance, fulvic acid or humic acid, organic components, ionic strength, and pH, were identified as interacting agents that could profoundly enhance the toxicity of AgNPs (Chambers et al., 2014; Delay et al., 2011).

Due to the potential environmental effects of industrial silver-based NPs, their widespread use is cause for concern. AgNPs' negative consequences, however, are still not well understood. Therefore, an in-depth investigation into their toxicity, harmful effects on living things, and environmental fate and behavior is required (Li et al., 2017). As there is no prospect for studying the toxicity of compounds in humans and limited possibility in mammalian models, the use of a non-mammalian model is an alternative source that has been developed for many years (Wimmer et al., 2018). The organisms, such as common carp (*Cyprinus carpio*), are selected due to their short life cycle and are easily available. In addition, some are used as complementary vertebrate models,

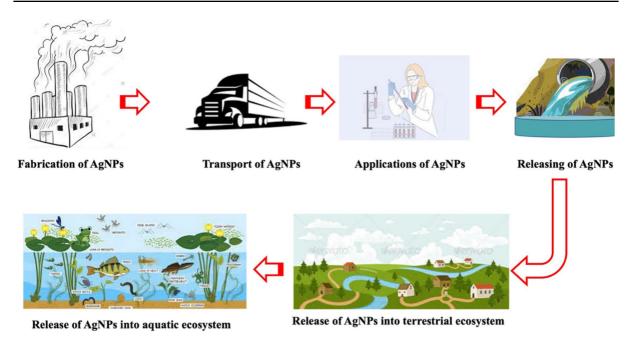


Fig. 2 Possible releasing routes of AgNPs into the environment during their life cycle (fabrication, transportation, and applications) (Cambier et al., 2018; Jorge de Souza et al., 2019; McGillicuddy et al., 2017)

for instance, Zebrafish (*Danio rerio*). Other macro and microorganisms have also been used for the toxicity of AgNPs. Previously, specific methods have been used to evaluate the toxicity of AgNPs. The more traditional method includes lethal concentration (LC_{50}), reactive oxygen species (ROS) generation, oxidative stress, enzymatic expression, and growth inhibition (Griffin et al., 2018; Sharma et al., 2015).

1.2 Transformation of AgNPs into the Ecosystem

The production of silver nanoparticles naturally is another factor contributing to the prevalence of AgNPs in the environment, in addition to industrial waste (Sharma et al., 2019; Tortella et al., 2020). Metallic NPs, for example, Ag, Au, Cu, Ni, and Fi, may be formed during industrial mining processes, in wastewater, or due to microbial activity via extracellular or intracellular processes, including biosorption, precipitation, and bioaccumulation (Adegboyega et al., 2016). Moreover, natural, purposeful, and inadvertent anthropogenic activities can all be sources of NPs. Since the beginning of Earth's history, AgNPs have been present in the environment. They are frequently and extensively distributed in the atmosphere, oceans, soil, surface, and groundwater, even in living things. Forest fires, volcanic activity, weathering, creation from clay minerals, soil erosion by wind and water, or dust storms from the desert are major natural processes that release NPs into the atmosphere. According to estimates, several million tons of natural NPs could be found in atmospheric dust alone within a year (Smita et al., 2012). In the past, geogenic silver traces in water with reducing agents like sulfide ions have been observed to naturally generate AgNPs (Akaighe et al., 2011). Additionally, nano-silver can be formed naturally under dark and light periods, even at low temperatures (Bundschuh et al., 2018). Another element that encourages the creation of AgNPs is the presence of humic acid in the environment. However, humic acid produces fewer AgNPs in terrestrial environments compared to aquatic environments. This is most likely because soil-based aromatic humic acid may have a small lowering capacity (Akaighe et al., 2012). But most probably, the NPs enter the environment and complete their life cycle in three different phases: (1) the AgNPs released into the environment during the production period; (2) release during use; and (3) release after the disposal of AgNPs-containing products, which is called waste handling (Bundschuh et al., 2018).

The fate of AgNPs discharged into the environment, whether intentionally or accidentally, is one of the most crucial factors. This may be investigated by looking at how AgNPs interact with their surroundings as well as their surface, as seen in Fig. 3. These concepts are closely linked since depending on the pressure exerted on AgNPs by the nearby environment, charge, size, shape, and surface coating (David et al., 2020). AgNPs discharges can either be undirected to the environment such as the application of AgNPs as a biocide (Al-Kattan et al., 2015; Zuin et al., 2014). Recently, metal NPs of copper, zinc, aluminum, and silver have been reported as a biocide for the application and conservation of cultural heritage objects (Keller et al., 2013) which could lead to environmental toxicity (Reyes-Estebanez et al., 2018). Directly, the AgNPs introduce through the technical system into the environment, such as wastewater treatment plants or landfills. It has been reported that the AgNPs fate in technical systems, i.e., wastewater treatment plants, determine whether coated, bare, physically, and chemically transformed particles are released (Akaighe et al., 2012). Globally estimation revealed that Page 5 of 20 **114**

the NPs are mostly released into landfills 63–91% followed by soil 8–28%, aquatic ecosystem 7%, and the lowest in the air 1.5%, respectively, of the production volume (Bundschuh et al., 2018; Keller et al., 2013).

AgNPs' behavior is thought to be significantly influenced by ionic strength, which affects both their fate and their hazardous potential. Previously, a study revealed that the AgNPs in an aqueous solution and the presence of organic matter interacted more freely with Na^+ and K^+ than with divalent cations (Delay et al., 2011). With the increase of ionic strength up to 1-10 mM, their size increased, whereas their zeta potential values of AgNPs decreased (Yue et al., 2015). Similarly, another study reported that the AgNPs significantly decreased in the presence of natural organic matter (Dinesh et al., 2012). Increasing silver ions and aggregation of AgNPs have also been shown increased ionic strength, causing toxicity (Chambers et al., 2014). A study reported the interesting findings that the increase in the size of AgNPs due to agglomeration is mainly related to the lower toxicity of AgNPs (Yang et al., 2019). However, high ionic strength also favors silver ion release, increasing toxicity (Odzak et al., 2017; Tortella et al., 2020).

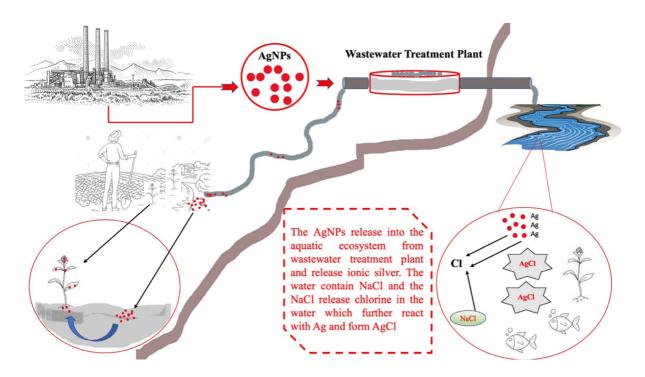


Fig. 3 The fate of AgNPs in the terrestrial and aquatic environment. The chemically fabricated AgNPs are primarily used to treat wastewater, where the AgNPs are released into the aquatic ecosystem which releases ionic silver attached to chlorine and forms AgCl

Additionally, a related researcher noted that the chemical environment or characteristics of the water used in the study had a significant impact on the outcomes. In general, using high chloride concentrations and high ionic strengths increased the release of silver ions, but it also favored the negatively charged $AgClx(x^{-1})^{-}$, which may be less toxic. However, these circumstances do not accurately represent the state of the ecosystem (Klitzke et al., 2015). A recent study reported that small-sized AgNPs (<5 nm) were observed in the water by transmission electron microscope. The finding revealed the increase in toxicity of AgNPs in the aquatic environment (Yu et al., 2013).

Most of the studies evaluated the fate of AgNPs in the aquatic ecosystem, although some studies have reported alterations and movement of AgNPs in the terrestrial and aquatic environment. Interestingly, in a study of the fate of the AgNPs investigated in the terrestrial environment (Devi et al., 2015; Fletcher et al., 2019), the authors reported that the combined effects of two parameters played a vital role in the aggregation of AgNPs. The two parameters are ionic strength and concentrations of NPs. Finally, similar authors reported a decrease in Ag⁺ released from AgNPs, mainly due to the presence of organic coating. Another study reported that the fate of AgNPs also depends on the electrostatic interactions with charged species present in the environment (Pradas et al., 2016). In contrast, in the aquatic and soil ecosystem, AgNPs can readily react with sulfide leading to sulfidation to form Ag₂S, which might reduce their toxicity (Garg et al., 2016; Levard et al., 2013). Previously, a study reported that the AgNPs existed in the sewage sludge and mixed with soil. The soil contains sulfur-rich particles, which lead to exchangeable Ag formation. Although the same study also revealed that the root exudates from plants, the organic matter turns turnover and nutrient mobilization might induce Ag⁺ released in the environment (Fletcher et al., 2019).

AgNPs are generally controlled by environmental parameters such as pH, temperature, organic matter concentrations, and ionic strength, as well as their size, concentration, and capping agent. According to the literature, when AgNPs are introduced into the environment, they are exposed to numerous transformations, such as oxidation, sulfidation, dissolution, chlorination, and aggregations. This release of ionic silver into the environment might be limited or favored if oxidation species such as sulfur and chlorine are present (Wang et al., 2019); at the same time, their toxic effects and toxicity might be changed (Bundschuh et al., 2016). Additionally, AgNPs with naturally occurring negatively charged species may enable an increase in their retention period and, consequently, in their toxicity and harmful consequences. AgNPs readily transform in the environment, which modifies their properties and alters their transport, fate, and toxicity (Levard et al., 2012). Because of the susceptibility of AgNPs to the environmental transformation such as changes in aggregation state, oxidation state, precipitation of secondary phases, and sorption of organic species could be vital to assess the toxicity of the transformed NPs as well as the fresh ones (Xiu et al., 2011). For example, silver is known to react strongly with sulfide, chloride, and organic matter. Because of their small particle size, the kinetics of corrosion of AgNPs is expected to be faster than for bulk silver, reducing greatly the lifetime of the metallic state of Ag in nature. Known silver corrosion agents are ubiquitous, and therefore environmental transformations of Ag-NPs will strongly affect their surface properties and consequently their transport, reactivity, and toxicity in soils and aqueous systems. This review discusses the most important environmental transformations of Ag-NPs released into wastewater streams and ecosystems that may affect their stability and toxicity (Levard et al., 2012; Liu et al., 2010).

1.2.1 Fate of NPs in the Aquatic Food Web

As a basis for the aquatic food web, algae are known to be the major source of food for numerous aquatic organisms, and algae can promote the ingestion of NPs by organisms in the feeding process (Bouldin et al., 2008), thus incorporating NPs into the food chain (Yang et al., 2014), as given in Fig. 4. The transmission of NPs via the aquatic food chain can lead to toxic effects on different trophic levels of organisms in the food chain. Since crustaceans are the primary consumers of algae, several studies reported the transmission of NPs from algae to crustaceans via diet. Previously, it was reported that the quantum dots could be transported with the food chain from Pseudokirchneriella subcapitata studied using the fluorescence technique (Gilroy et al., 2014). When algae were used to feed *Daphnia magna*, the *D. magna* was found to ingest NPs from the suspension via feeding behavior (Kleiven et al., 2018). Previously, an

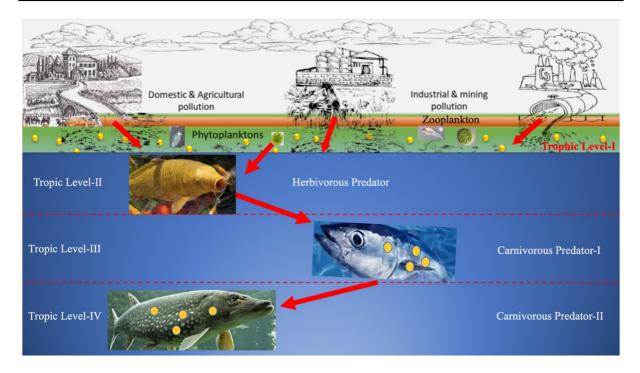


Fig. 4 The graphical representation of AgNPs (yellow color) as toxic AgNPs, and their possible route for bioaccumulation during the aquatic food chain, represents different trophic levels. The AgNPs are introduced into the aquatic environment

experiment was conducted to study the shift of NPs in the food chain. For this purpose, the titanium oxide nanoparticles (TiO₂ NPs) were exposed to Daphnia magna and the Daphnia magna was further exposed to the zebrafish. The obtained findings revealed that TiO₂ NPs concentrations in zebrafish fed with 0.1 and 1.0 mg/L TiO₂ NPs contaminated daphnia were 106.57 ± 14.89 and 522.02 ± 12.92 mg/kg, respectively (Zhu et al., 2010). The results concluded that the food chain transfers TiO2 NPs. Due to sorption to phytoplankton or zooplankton, transfer from water to sediment, and uptake in benthic creatures, which can subsequently be directly swallowed by large vertebrates like fish, ingestion or touch is the primary exposure pathway in the aquatic ecosystem (Persoone et al., 2009). As a result, AgNPs may have harmful effects on suspension or deposit feeders, as well as on shredders, scrapers, and predators (Zhang et al., 2016a, 2016b). AgNPs can build up and interact with other water constituents, just like in terrestrial ecosystems, leading to major changes in the NPs. The characteristics of AgNPs could be significantly altered by

that is absorbed by the zooplankton and phytoplankton. The trophic "level I" is fed by zooplankton and phytoplankton, which are further transferred to other trophic levels in the food web (Gatti et al., 2015; Tsang et al., 2006)

these processes: ecotoxicity, bioavailability, uptake, reactivity, and mobility (Zhang et al., 2016a, 2016b). The trophic level transformation of AgNPs is given in Fig. 4. Different trophic levels had been adopted as a model to evaluate the toxic study of AgNPs. Chlorella vulgaris is primarily used as a model aquatic species for toxic studies as it divides asexually and rapidly in favorable conditions within 24 h (Howe et al., 2013), and it was selected as the first trophic level. On the other hand, the Daphnia magna as a model organism for acute toxicity testing, with characteristics of short-time life span and sensitivity to contamination (Couce-Montero et al., 2015), is considered a second trophic level. Danio rerio and Cyprinus carpio were considered a third trophic level due to the same morphological, histological, and physiological characteristics as humans (Zhu et al., 2010). In addition, the first trophic level comprises phytoplankton or seaweeds, and the second level includes zooplankton, followed by small fish, jellyfish, or crustaceans at the third trophic level. The larger fish (such as salmon) or other carnivorous aquatic animals (such as squids and octopuses) are considered as the higher trophic levels in the aquatic food web (Zhang et al., 2016a, 2016b). Previously, a study checked for brain damage and behavioral disorders in fish induced by NPs delivered through the food chain. The obtained findings revealed that the NPs were taken by *Daphnia magna*. Equipped with the insight obtained from *Daphnia magna*, next set out to study the effects of NPs (53 nm and 180 nm) on the entire food chain and the fish received NPs (53 nm) slowly as compared to 180-nm-sized NPs (Mattsson et al., 2017). Hence, proved that the NPs could possibly be transferred in the food chain.

1.3 Accumulation of AgNPs in Fish

The increasing use of AgNPs in consuming products and their introduction into terrestrial and aquatic ecosystems have gained attention to investigate their toxicity in water, soil, and sediments. Environmental toxic studies of AgNPs have been carried out at different trophic levels using invertebrates, vertebrates, microorganisms, and plants as biomarkers. Different organisms have been chosen for ecotoxicological studies due to their pollutants and sensitivity by following a standard protocol. The following sub-section describes the toxic effects and toxicity of AgNPs in fish. The extensive use of AgNPs has extensively led to their release and presence in the natural aquatic ecosystem (Kleiven et al., 2018). Additionally, they have been used to treat wastewater and bioremediation (Van Den Brink et al., 2019). That could be alarming for aquatic life.

The zebrafish and Cyprinus carpio are widely used as important experimental models to measure aquatic toxicity (Chakraborty et al., 2016). These models have been used in biomedical and taxological research at the embryonic and adult levels (Bilberg et al., 2012). Moreover, the organs and tissues of these fish can be visualized in vivo and instantly examined (Cambier et al., 2018). Different scientists have evaluated the toxicity of AgNPs in fish fauna. For instance, acute toxicity of AgNPs sized between 75 and 81 nm and Ag⁺ in zebrafish after 48-h incubation period. After incubation, LC₅₀ values were 84 and 25 $\mu g \ L^{-1}$ respectively. An increase in surface respiration and a higher rate of operculum movement were observed after the exposure to AgNPs. The findings concluded that the AgNPs were lethal to zebrafish (Vali et al., 2020). As a result, scientists recently tested exposing zebrafish larvae to 20-nmsized AgNPs to see how they affected the developing fish. The findings revealed that no significant impairment of growth was observed after the exposure to AgNPs. The AgNPs exposure has significantly increased the zebrafish larvae' survival. However, the secondary ion mass spectrometry (SIMS) analysis has shown that the AgNPs accumulated in the liver and intestine (Khosravi-Katuli et al., 2018). Early in 2020, a study was conducted in which the Cyprinus carpio were exposed to different concentrations of AgNPs for 96 h. At the end of the experiment, the number of white blood cells (WBCs) was significantly higher in AgNPs-treated fish than in the control, whereas the total serum proteins were profoundly decreased in the AgNPs-treated group of fish compared to the control study (Jang et al., 2014). Similarly, another study was conducted in which the Cyprinus carpio was exposed to AgNPs and silver nitrate (AgNO₃). The investigation found that the AgNPs were more toxic to the fish than AgNO₃. The AgNPs were significantly bioaccumulated in the liver, gill, and intestine. Their accumulation led to histological alterations such as the shortening of lamella and degeneration in targeted organs (Kakakhel et al., 2021a, 2021b; Lee et al., 2012).

This section revealed that various studies have reported AgNPs toxicity in aquatic models such as Cyprinus carpio and Danio rerio. Several studies have found that AgNPs can disrupt maturation, embryogenesis, and offspring development. While our current understanding is limited, these studies demonstrate harm on both a physiological and molecular level. There is no doubt that all this information aided authors in writing about the potential toxicity of AgNPs in fish. Because of differences in study size, concentration, liquid culture, and timing of the various investigations, there may be discrepancies in the comparison analysis. Low LC₅₀ values have been noted concerning artificial settings like deionized water. Therefore, studies in water conditions that stimulate more ionic strength and the organic presence of organic matter are strictly needed to confirm the reproducibility of results obtained under optimal conditions. Interestingly, and in contrast to terrestrial organisms, aquatic organisms such as fish are more pose to the toxicity of AgNPs. However, stimulatory effects on growth have also been suggested when low concentrations of AgNPs were exposed. Therefore,

more studies are worthy to understand the possible mechanism by which the AgNPs cause positive effects.

1.4 Toxic Effects of Accumulated Nanoparticles

Yet, many studies have already investigated the toxicity and toxic effects of AgNPs in model aquatic organisms, for instance, algae, Daphnia, and fish (Ale et al., 2018). But the fish are primarily used as an indicator of aquatic environmental pollution to study the health of aquatic ecosystems (George et al., 2012). However, limited information is available on the aquatic toxicity of AgNPs. When AgNPs encounter fish, these NPs easily penetrate the tissues of the fish and cause severe types of damage (Jung et al., 2014). In 2012, a study revealed that the AgNPs mainly cause toxic effects in the gill of rainbow trout fish (M. S. Khan et al., 2018). These NPs are too small and easily penetrate and can accumulate in the gills, liver, intestine, brain, and muscles of the fish (Mahmoud et al., 2019) exerting diverse toxic effects, for example, hematological and histological alterations (Ale et al., 2018). The AgNPs are toxic to the kidney cells in fish which mainly cause proliferation in the hemopoietic tissue, hypertrophies of glomeruli, dissociation in the renal tubule, and shrinkage of the glomerulus (Khosravi-Katuli et al., 2018). Previously, a study was conducted in which the fish were exposed to AgNPs for toxicity and bioaccumulation. Their findings revealed that the AgNPs were mostly accumulated in the liver followed by the intestine and brain (Park et al., 2011; Piao et al., 2011). Another study summarized that the AgNPs were accumulated in the liver, gills, and intestine, respectively, leading to the histological alteration in the targeted organs; for instance, tissue lesions were observed in the liver, intestine, and gills (AshaRani et al., 2009; Kakakhel et al., 2021a, 2021b).

Several previous studies' findings revealed that AgNPs cause cytotoxicity, DNA damage, and ROS generation in fish (Taju et al., 2014) as shown in Table 1. Previously, Sayed et al., (2017) reported that the increased ROS generation and excess oxidative stress resulted from the intracellular production of hydrogen peroxide and superoxide in AgNPs. A study conducted by Bacchetta et al. (2017) revealed that the biogenic synthesized AgNPs were exposed to *Catla catla* and *Labeo rohita* for 96 h. As a result, DNA

damage and nuclear fragmentation were observed. Another study has also investigated DNA damage in *Clarias gariepinus* after exposure to AgNPs (25 ng/L) (Afifi et al., 2016). A study conducted by Khosravi-Katuli et al. (2018) analyzed the taxological endpoints, for instance, oxidative stress, metal burden, and genotoxicity. Their findings revealed that the AgNPs were significantly bioaccumulated in the brain, followed by the liver and gills. Fish exposed to the highest concentration of AgNPs cause severe alteration at the tissue level with no changes in enzymatic activities. Similarly, another study analyzed cellular and DNA damage in Cyprinus carpio (Song et al., 2015). Measuring the toxicity and accumulation of NPs in fish is very important (Clearwater et al., 2002) because fish play a vital role in the diet of humans (Haug et al., 2010). Therefore, by consuming fish, the NPs might shift from fish to humans (Hosseini et al., 2015) as shown in Fig. 5. The study reported that the NPs are mostly bioaccumulated in pancreatic cells (Pašukonienė et al., 2014) and lymphatic tissue (Teow et al., 2011). This accumulation causes severe destruction to human body cells, for instance, ingested NPs pass the gastrointestinal tract which leads to damage to the digestive gland cell membrane via oxidative stress (Valant et al., 2012). Hence, the above studies proved that measuring toxicity in fish is very important. NPs can enter the environment through human activities and can be transferred from one place to another place with the help of water, air, and soil (Khan et al., 2019). This transformation process of AgNPs might be accumulated by plants and can lead to AgNPs toxicity in plants (Cvjetko et al., 2017) (Table 2).

Humans get exposed to AgNPs via respiratory exposure, oral exposure, skin exposure, and by consuming contaminated fish with NPs (Gambardella et al., 2015). Especially, the urban and industrial sewages of AgNPs were introduced into the aquatic ecosystem and accumulated inside the food web (Valodkar et al., 2011). Therefore, the presence of AgNPs in dietary supplements, water contamination, and fish and other aquatic organisms' consumption are significant sources of oral exposure (Wang et al., 2017) as shown in Fig. 5. On the other side, the accumulation of AgNPs in the human lung can be toxic to the human carcinoma A549 cells (Bin-Jumah et al., 2020). The AgNPs are also toxic to human sperm. A study revealed that the AgNPs might cause abnormalities

Fabrication method	Features	Size	Findings	Reference
Chemical	PVP coated	0.62–1	The AgNPs were accumulated in the liver, intestine, brain, and blood in <i>Cyprinus carpio</i>	Ale et al. (2018)
Chemical	Citrate-caped AgNPs were exposed	> 100 nm	Glutathione-S-transferase, super oxidase dismutase, and catalase were decreased after exposure to AgNPs in <i>Cyprinus carpio</i>	Mansour et al. (2021)
Chemical	Glucose oligomers caped AgNPs	20–40 nm	The amount of bacterial col- ony-forming unit (CFU) was significantly decreased in the skin mucous of streaked prochilod fish	Auclair et al. (2019)
Biological synthesis		Starch-mediated silver nanoma- terials	Severe changes in RNA were observed, whereas the expression of antioxidant genes was significantly suppressed, and enzymatic activity was inhibited in Nile tilapia	Xiang et al. (2020)
Chemically fabricated	PVP coated	50 nm	The findings revealed that the AgNPs damaged the hepatic DNA in rainbow trout fish	Ma et al. (2018)
Chemical	PVP coated AgNPs	12–15 nm	The exposure to AgNPs caused telangiectasia and epithelial cell hyperplasia in <i>Cyprinus</i> <i>carpio</i>	Dang et al. (2021); Sohn et al. (2015)
Chemical		Diameter of AgNPs < 150 nm	The AgNPs are potentially a health risk for fish through gut bacterial dysbiosis. The AgNPs exposure sig- nificantly disturbed the gut microbiota in zebrafish	Naguib et al. (2020)
Biological	Sheep blood plasma-induced AgNPs	20–50 nm	B-AgNPs significantly decreased intestinal bacte- rial composition. However, the genus <i>Cetobacterium</i> increased which plays a vital role in ethanol metabolism	Kakakhel et al. (2023)

 Table 1
 The variant toxicity and toxic effects of AgNPs in various fish species

such as damage to the sperm head and disruption of chromatin in human sperm cells (Hussain et al., 2001). In addition, the higher concentrations of AgNPs cause ROS that can change the cell (Kim et al., 2006). NPs absorbed through the respiratory tract may reach the lymph stream and blood circulation (Kashiwada, 2006). Some studies revealed that the AgNPs can pass through the blood–brain axis (Sambale et al., 2015) and the cell membrane (Akter et al., 2018) and can, therefore, accumulate in different organs and interact with biological systems (Korani et al., 2015). Because of the ability of AgNPs to cross the tight junction of the blood-brain barrier, they are considered potential neurotoxins. Studies reported that blood-brain barrier permeability in the brain micro-vessel endothelial cells causes neuronal degeneration (Rosenman et al., 1979). Liver biomarkers, for instance, aspartate aminotransferase, alanine aminotransferase, and histopathological changes, were elevated after exposure to NPs (Gritz & Bhandari 2015). In an occupational study, a group of workers was exposed to AgNPs. During the experiment, an increase in the N-acetyl-B-D

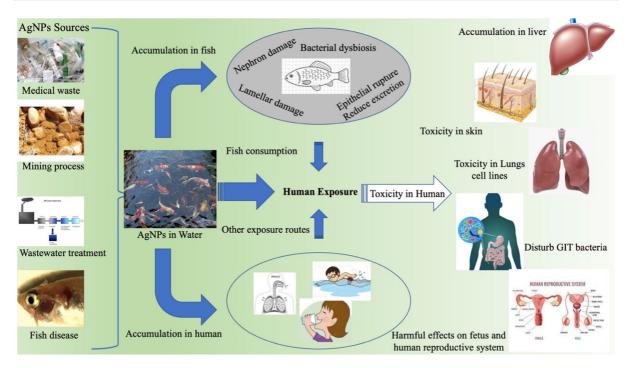


Fig. 5 The schematic representation of major sources of AgNPs and their transformation cycle from the environment to fish (Dang et al., 2021), and from fish to human (Ghobashy

glucosaminidase and a decrease in creatinine level were observed (Brinkmann et al., 2020).

1.4.1 Intestinal Bacterial Dysbiosis

The gut is also stated as a "super organ" and "hidden organ" which encompasses approximately trillions of microorganisms, and their diversity varies among organisms (Ali et al., 2021). It is vital in the maintenance of organisms' health and development as well as the structural integrity of the gut, performs diverse biological functions related to metabolism and neurological responses, and is also capable of immunomodulation (Bäumler et al. 2016; Montalban-Arques et al., 2015). While at risk of the negative consequences of dysbiosis, some microorganisms may interact with antimicrobial NPs, potentially reducing the NPs toxicity to the host (Brule et al., 2016). However, the exposure of the intestine to these NPs or contaminants damages the structure of the gut, causing a leaky gut condition, and disturbs the gut microbial community as given in Table 3. Reduction in the gut microbial population also facilitates the entry and growth of pathogens in the intestine.

et al., 2021), where the AgNPs cause severe toxicities and damage to several vital organs (Lai et al., 2020)

Pathogens such as *Aeromonas hydrophila* can induce oxidative stress in the gut via reactive oxygen species (ROS) generation, and additionally, it may increase the abundance of native pathogenic bacterial strains (such as *Halomonas, Vibrio, Aeromonas*, and others) in the host gut (Meng et al., 2018). Due to the strong antibacterial activity, the ingested AgNPs might disturb the intestinal bacterial structure and composition which is considered a metabolic organ with numerous physio-pathological functions (Pubo et al., 2021) as shown in Fig. 6.

Their entry into the gut affects the α -diversity and β -diversity indices of the microbiome (Yan et al., 2016). Recently, a study was conducted, in which the AgNPs were exposed to zebrafish for 15, 45, and 75 days. The findings revealed that the alpha diversity was significantly decreased. The relative abundance results explored that the bacterial taxa such as Actinobacteria and *Gemmata* were significantly decreased after exposure to the highest concentration of AgNPs. Moreover, the study revealed the influence of AgNPs on fish intestinal bacterial structure and composition and provided insights into maintaining host-microbiome stability during environmental pollution (Xiao et al., 2021). The mechanism

		•••					
Fish	NPs type	Concentration selection method	Duration	Organs analyzed	Histological study	Bioaccumulation	Reference
Cyprinus carpio	AgNPs	0.04, 0.08 mg/L	96 h	Gills, liver, and intestine	Epithelial lifting, telangiectasia in second- ary lamellae, and epithelial necrosis	Mostly in the liver and intestine	Griffitt et al. (2007)
Zebrafish, rain- bow trout fish	CuNPs	1 mg/L	96 h	Gills	Damage to gill filaments	N/A	Xiang et al. (2020)
Epinephelus coioides	CuNPs	100 μg/L	25 days	Gill, intestine, liver, and muscle	Cell apoptosis in gill and liver	Liver, gill, intestine, and muscles	Hao et al. (2013)
Cyprinus carpio	AgNPs	0.75 mg/L	14 days	Gill	Telangiectasia and epithelial cell hyperpla- sia in fish gills	N/A	Johari et al. (2020)
Cyprinus carpio	ZnONPs	50 mg/L	30 days	Gill, liver, intestine, and brain	Irregular cell outline, abnor- mal pyknotic nuclei, shrink- age of cell	Mostly accu- mulated in the liver and gills	Ferdous and Nem- mar (2020)
Cyprinus carpio	CuNPs	N/A	21 days	Gill, intestine, and liver	N/A	Mostly accu- mulated in the liver and intestine	Gambardella et al. (2015)

Table 2 The toxic effects of various types of NPs on fish histology

Table 3 The exposure of model animals to NPs and alteration induced by NPs on the intestinal bacterial structure and composition in different animal models

Model organism	Type of NPs	Exposure time (days)	Bacterial dysbiosis	Reference
Mice	Chemical AgNPs	28	Firmicutes and Bacteroidetes ↑	Khorshidi et al. (2016)
Cyprinus carpio	Commercial AgNPs	35	Fusobacteria and Proteobacteria ↑	P. Chen et al. (2022)
Cyprinus carpio	Dietary AgNPs	60	Lactic acid bacteria and Enterobacte- riaceae ↓	Javurek et al. (2017)
Zebrafish	TiO ₂ , ZnO, and Se NPs	90	Fusobacteria \uparrow and Proteobacteria \downarrow	Patsiou et al. (2020)
Rats	AgNPs	14	Cyanobacteria sp. and Aggregatibacter pneumotropica ↓	Perez et al. (2021)
Zebrafish	Dietary PbNPs	4 days post fertiliza- tion and 14 days of exposure	Alphaproteobacteria ↑ and Gam- maproteobacteria ↓	H. Chen et al. (2017)
Mice	Dietary AgNPs	4 weeks	Cyanobacteria \uparrow and Tenericutes \downarrow	Jami et al. (2015)
Mice	TiO ₂ NPs	7 days	Bacteroidetes and Firmicutes ↓ <i>Lactobacillus</i> ↑	Sanchez et al. (2012)

 \uparrow = increased and \downarrow = decreased

leading to aquatic fish intestinal microbiota can be surely unlike those of terrestrial animals. Oviparous fish get heritable microorganisms from their mother as those viviparous mammals delivered vaginally (Talwar et al., 2018). A recent study found that the fish gut microbiome was closely correlated with host genetics, immunology, physiology, and ecology (Yang et al., 2021). A study suggested that the bacterial phyla have a significant role in

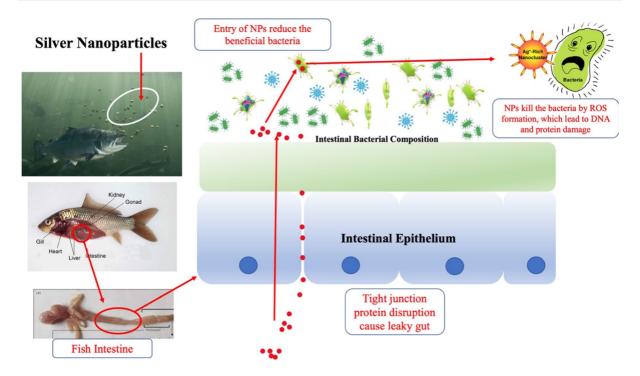


Fig. 6 Diagrammatic presentation of the toxicity in the intestinal bacterial composition by the entry of AgNPs. Herein, the AgNPs enter the bacterial cell in the intestine and cause ROS, leading to DNA and protein damage

fish growth, development, and marinating health status (Ng et al., 2018), including phyla Bacteroidetes and Firmicutes which almost comprises 90% of the fish intestinal microbiota (Gómez & Balcázar 2008), that maintain the inflexible quantity of bacteria in the fish gut (Talwar et al., 2018). A study reported that the phylum Bacteroidetes play a role in innate immune response in fish fauna (Xu et al., 2003) and instructs the host immune system to protect the fish species against pathogens (Yang et al., 2017). Another study reported that the Bacteroidetes phylum can break the polysaccharides and convert them into sugar and convert complex molecules into the simplest molecules in the intestine of fish (van den Brule et al., 2016). However, when these bacterial phyla are reduced, disease-causing microbes can enter and multiply in the fish digestive tract. Aeromonas hydrophila and other pathogenic bacteria can produce reactive oxygen species (ROS) in the intestine, causing oxidative stress. In addition, it may increase the abundance of native pathogenic bacterial strains, for instance, Vibrio Aeromonas, Halomonas, and others (Ma et al., 2018).

Actinobacteria are a well-known bacterial taxon found in the intestine of fish that can produce secondary metabolites, many of which are active against pathogenic microorganisms. A study revealed that 33 selected antimicrobial isolates were obtained from fish intestinal microbiota and tested against nine Gram-positive pathogenic bacteria. The data indicated that the strains with the ability to produce antimicrobial compounds belong to four genera such as *Nocardiopsis*, *Saccharomonospora*, *Micromonospora*, and *Streptomyces* (Butt & Volkoff, 2019). Although Actinobacteria are commensal to the genus *Bifidobacterium*, it has been shown to regulate interleukin-10 production in healthy hosts (Ansar et al., 2020). Other previous studies strongly suggested that the fish intestinal microbiota influences the overall health of the host fish regarding overall digestion, physiology, reproduction, stress response, and the immune system (Haghighat et al., 2021).

2 Methodology Section

In this review article, the relevant literature was collected using online tools and different databases including PubMed, Google Scholar, ScienceDirect, Springer, Frontiers, etc.

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3 Conclusion

The new and updated literature demonstrates that there is an urgent need for practical approaches to evaluating the ecotoxicity of synthesized NPs such as silver nanoparticles. This review broadens our understanding of AgNPs based on previous research into their use, the pathways through which they are released into the environment during their life cycle (during fabrication, transportation, and application), and their ultimate fate in both terrestrial and aquatic environments. The aquatic food chain bioaccumulation pathway, the transformation and bioaccumulation pathway in fish, the key sources and their transformation cycle from the environment to fish, and the toxicity of the intestinal bacterial makeup are also discussed. We first talked about AgNPs bioaccumulation in the liver, then in the gills. Fish exposed to the highest concentration of AgNPs exhibit significant physiological and molecular abnormalities, but no or only minor changes in enzymatic activity. AgNPs harm tissue in the gastrointestinal tract by causing a leaky gut and disrupting the normal bacteria population. In the future, research on the likely mechanism of AgNPs contamination in fish should concentrate on the transcriptomics and proteomics levels.

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Data Availability The dataset generated and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Competing Interests The authors declare no competing interests.

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