



Reviews of the toxicity behavior of five potential engineered nanomaterials (ENMs) into the aquatic ecosystem



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ABSTRACT

Presently, engineered nanomaterials (ENMs) are used in a wide variety of commercial applications, resulting in an uncontrolled introduction into the aquatic environment. The purpose of this review is to summarize the pathways and factors that controlling the transport and toxicity of five extensively used ENMs. These toxicological pathways are of great importance and need to be addressed for sustainable implications of ENMs without environmental liabilities. Here we discuss five potentially utilized ENMs with their possible toxicological risk factors to aquatic plants, vertebrates model and microbes. Moreover, the key effect of ENMs surface transformations by significant reaction with environmental objects such as dissolved natural organic matter (DOM) and the effect of ENMs surface coating and surface charge will also be debated. The transformations of ENMs are subsequently facing a major ecological transition that is expected to create a substantial toxicological effect towards the ecosystem. These transformations largely involve chemical and physical processes, which depend on the properties of both ENMs and the receiving medium. In this review article, the critical issues that controlling the transport and toxicity of ENMs are reviewed by exploiting the latest reports and future directions and targets are keenly discussed to minimize the pessimistic effects of ENMs.

1. Introduction

The ecosystem, particularly the aquatic ecosystem has profoundly become a major sufferer of environmental pollution via extensive use and disposal of ENMs in everyday life [1]. In recent years, nanotechnology has become a major innovative approach for scientific and economic growth. Nevertheless, its epidemic usage and high dose introduction have effectively produced a detrimental effect on the aquatic ecosystem. In addition, the uncontrolled release of these manufactured ENMs from the industrial waste and sewage sludge is heterogeneous and largely an unknown phenomenon, which consequently produces a hallmark concern towards its ecological toxicity. ENMs, in relation to their widespread application, are synthesized in various forms, shapes, sizes and surface functionalities and they enter the ecosystem either intentionally or unintentionally with varying particle morphology and elemental composition.

The examples of some widely utilized ENMs are silver nanoparticles (AgNPs) [2,3], graphene oxide nanoparticles (GONPs) [4–6], zinc oxide nanoparticles (ZnONPs) [7–9], titanium dioxide nanoparticles (TiO₂NPs) [10–12], and single-walled or multi-walled carbon nano-

tubes (CNTs). Recently, the production and use of these ENMs have seen a peak for making a high risk of environmental release. ENMs, due to their marvelous physicochemical properties compared to their bulk counterparts, are the reason for their increased use in products. However, at the same time, these unique properties have ultimately prompted concerns in eliciting ecological toxicity [13].

In order to investigate the toxicity of ENMs, recent efforts are focused on the exploration of ecosystem toxicity related to these nanomaterials. In addition, many recent reports have considered the ecological behavior of ENMs including their transport and toxicity to investigate and promote the sustainable use of these novel materials. One of the major drawbacks in determining the sustainability of direct environmental applications, either in wastewater treatment plant [14] or effluent and sludge treatment [15] is the ENMs modifications. Likewise, transformations of ENMs such as agglomeration, dissolution, sedimentation or surface change by interacting with naturally occurring moieties could greatly alter the pathways and extent of their environmental release. These transformations of ENMs from their original state have greatly controlled their toxicity in the environment; thus making it more critical to understand and characterize the toxicity of ENMs

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[13,16].

In addition to metallic ENMs [17], carbon-based materials including carbon nanotubes [18,19], graphene oxide [20] are found to be toxic towards the aqueous ecosystem. Increased applications and uncontrolled production of these materials to a large extent will likely lead to the release in the environment and ecosystem, causing damage at the cellular level. Moreover, long-term stability studies showed that graphene oxide is highly unstable in natural surface water and readily interacts with other environmental surfaces which play a key role in the transformation of these emerging materials. Despite significant researches done on graphene-based applications, research on their environmental behavior is in its initial stage. Hence, transport behavior and toxicity of these emerging materials need to be investigated for sustainable environmental implementation [4].

Although certain literatures are emerging in the past few years reporting ecotoxicological data on synthesized ENMs, the mechanistic basis of exposure and adverse effects generated are poorly understood, especially in the aquatic environment. Moreover, there are many challenges and controversies that exist, but knowledge transfer from toxicology, colloidal chemistry, as well as detailed material sciences will facilitate to move forward in this new multidisciplinary field.

Till now, only a few critical reviews have been produced about the hazards [21,22] and ecological toxicity [16,23] of ENMs in the aquatic ecosystem, and none have elaborated on the potential impact of all five ENMs in a single report. Herein, the presenting review will be focused on the adverse effects generated by the five potential ENMs including metallic carbon-based materials with special emphasis on those materials that achieved high volume of industrial production. Furthermore, their main ecotoxicological factors will be addressed with the future needs of a safe and sustainable aquatic ecosystem.

2. Factors affecting ENMs transport

Although hundreds of reports to date are available on the fate and transport of ENMs, there is still a lack of accurate toxicological knowledge in relation to the utilization and disposal of these materials. The gap between ENMs synthesis and its toxicological data has urged the scientific community to introduce robust, stable, and ecofriendly methods for a safe synthesis [24] and safe disposal. The in-bound characteristics of ENMs greatly affect their transport into the environment. For example, the toxicological effect belongs to the doped ENMs primarily due to their high stability toward aggregation, low photobleaching, and slow photodegradation. In addition, some latest reports [25] proved that the transport and toxicological impact of ENMs are solely attributed to the dissolved ion concentration rather than the nanomaterial itself or its aggregated form.

Nonetheless, the aggregation is directly related to the transport of ENMs and the stability towards aggregation plays a crucial role in the long-term transport and toxicity of ENMs. This behavior impulsify the importance of imperative precaution measures for the development or production of safer ENMs while keeping their physical and chemical properties intact [8]. Past studies have shown that the behavior of ENMs may vary critically under different environmental conditions. Certain environmental factors such as pH of the solution, concentration of salt, type of electrolyte and organic acids such as humic acid produce huge impact in the dissolution and aggregation of ENMs in the aquatic ecosystem [9,26,27].

Previous studies indicated that among all of the above mentioned factors, the organic acid concentration, particularly the humic acid, influences the transport of ENMs such as ZnONPs by largely reducing its aggregation (Fig. 1). Similarly, the anionic charges carried by these humic substances also play a key role in the aggregation of ZnONPs [28].

The type of organic acid adsorbed onto the surface of nanoparticles imparts steric hindrance because of the surface functionality and chemical nature of the particles. The humic acid increases the dissolu-

tion of ZnONPs regardless of the ionic strength and pH. In contrast, the pH has a minor effect on aggregation; typically, the maximum aggregation is achieved at the pH close to its isoelectric point, whereas in the presence of higher salt concentration, the larger aggregates of ZnONPs are formed.

Large volumes of commercial production of Ag nanoproductions in textile, antiseptic sprays and in medical commodities have ushered a potential concern towards environmental hazards and to human health. For a better understanding of AgNPs toxicity and bioavailability, it is critically suggested to investigate the behavior of AgNPs in the complex natural environment.

The reactivity of AgNPs depends on the physicochemical properties [29] i.e. size, pH of the solution, surface coating, agglomeration properties and dissolution ability. Certain studies showed that environmental factors like sunlight, pH, inorganic salts and dissolved natural organic matter affect the chemical nature, dissolution and leads to the significant transformation of AgNPs. For example, Yu et al. [30], proposed the three stage pathway for the transformation of AgNPs. According to this study, the UV-light from the sun induced the aggregation of AgNPs, resulting in larger particle symmetry, self-assembly, and particle fusion processes. In addition, sunlight through oxidative reductive mechanisms stimulated the dissolution of AgNPs which is considered to be the major toxicity related to any metallic ENMs. These dissolved ions then may adsorb on the surface of dissolved organic species, resulting in the reconstitution of smaller particles which cross-linked together to form coarse aggregates as can be seen from Fig. 2. Therefore, imperative measures should be taken to minimize the rational effects of these unforeseen impacts of ENMs.

Dissolution is one of the main factors that control the behavior of AgNPs in an aquatic system through oxidation, which results in an ionic Ag^+ release into the solution. Several studies have shown that the size of AgNPs has a dominant effect on the dissolution behavior in natural water [31]. A group of researchers [32] investigated the size dependent oxidative dissolution and the effect of pH on the thiol functionalized methoxyl polyethylene glycol silver nanoparticles (PEGSH-AgNPs). They found that the extent of PEGSH-AgNPs dissolution in acetic acid was higher compared to water due to the protonation of the surface Ag_2O layers. Protonation led to weakening and breaking of the surface Ag_2O bonds, thus resulting in more Ag^+ release into the acidic solution. They also experienced that like the previous report [31,33], solubility of AgNPs increased as their sizes decreased, both in the neutral and acidic medium.

According to this study, after dissolution, the particle morphology did not change when observed under TEM analysis. Nevertheless, other factors like dissolved organic species, type of ligand and suspended particulate materials may alter the morphology and aggregation properties in the aquatic ecosystem. These observations showed that irrespective of the particle sizes, medium pH, and change in solution chemistry, AgNPs could be considered as non-reactive towards oxidative dissolution. In addition to size, surface charge and concentration also play a major role in the toxicity of AgNPs. Previously, a group of researchers [33] examined that surface coating or organo-coating imparts stability to the ENMs and causes of the inhibition of aquatic vertebrate models growth by suppressing certain biologically important enzymes. Moreover, certain aquatic plants were also susceptible to the dissolved AgNPs through uptake and bioaccumulation into the different plant parts.

TiO_2 due to their unique characteristics like unusual shape, size and other morphological and structural properties, have gained substantial impact on their transport and behavior in the ecosystem [34]. TiO_2 show huge toxicity to the environment [35,36] by bio persistence and non-degradable properties which make them a potent candidate for possible long term chronic effects [37]. However, TiO_2 are often reported as less toxic than many other ENMs during species sensitivity distributions [38].

Fu et al. [39], determined the transformation and destabilization of

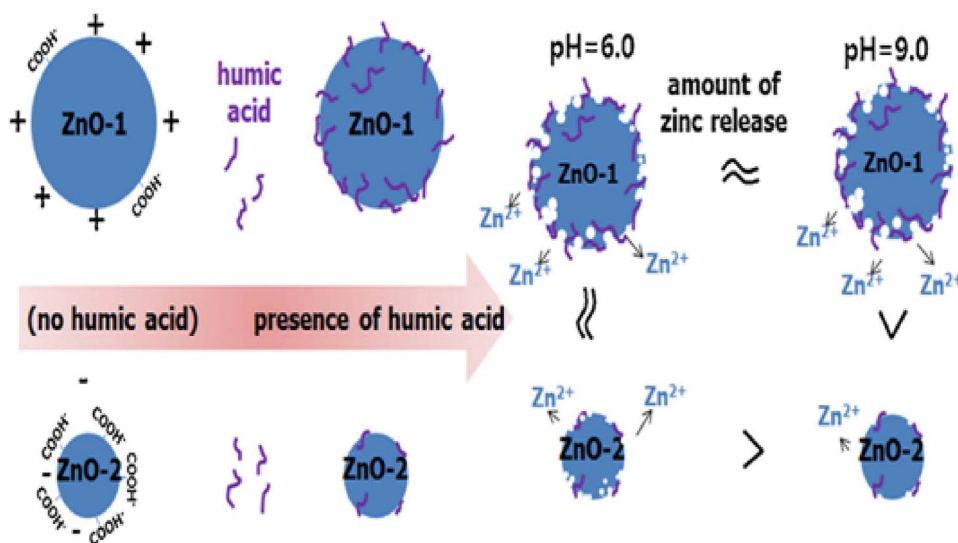


Fig. 1. Effect of Humic acid on the aggregation, dissolution, and release ionic Zn²⁺ from ZnONPs. The presence of humic acid and pH greatly influence the ionic release. [adopted from Ref. [26]].

GO nanoparticles in a natural reducing environment containing sulfides. They found that in the concentration of sulfide as low as 0.5 mM, the GO were significantly destabilized by the reduction of oxygen-containing groups at the surface. Whereas, in the presence of humic acid, GO became stabilized due to steric hindrance. GO is adsorbed at the surface of humic acid through electrostatic interaction and through π - π stacking interactions. These interactions significantly blocked the GO oxygen-containing groups at the surface and inhibited the oxidation-reduction process.

To assess the aqueous behavior of GO more precisely, Ren et al. [40], studied the effect of Al₂O₃ on the aggregation and deposition of GO. According to the results obtained from this study, the aggregation of GO by dissolved Al₂O₃ depends on the ionic strength as well as the pH of the solution. The study showed that the GO became destabilized in the high concentration of metal chlorides due to effective charge screening, whereas the presence of poly(acrylic acid) or NaH₂PO₄ increased the pH of the solution and stabilized the GO, either by electrostatic interaction or by steric repulsion. Therefore, the presence of abundant electrolytes and dissolved organic species in the natural aquatic environment could effectively alter the behavior of GO and these exacerbates must be taken into account while determining the

crucial insights of toxicity.

Furthermore, several studies have reported to support GO as a degradable material through photo-Fenton degradation; however, the toxicity of their degradable products such as polycyclic aromatic hydrocarbons may have toxicological implications to human and to the environment [41]. GO in the form of nanocomposites are widely used in sensor technology [42,43]. Generally, metals nanoparticles combine on the surface of graphene materials to achieve higher reactivity. However, these composites are much more lethal than the individual metal nanoparticles and can cause greater cytotoxicity when introduced internally into the cells.

Similarly, the morphology or the surface properties of GO nanomaterials play a crucial role in toxicity production. For example, Chng et al. [44], investigated that GO nanoribbons exhibited greater toxicity than GO nanoplatelets. The insights of this investigation revealed that GO nanoribbons, due to its higher amount of functional carbonyl group at the surface, as well as greater length, eventually show more cytotoxicity. Therefore, considering these aspects, future synthetic protocols, carbon precursors and functionalization process should be taken into stress carefully before any biomedical application.

Presently, CNTs possess numerous exciting commercial and indus-

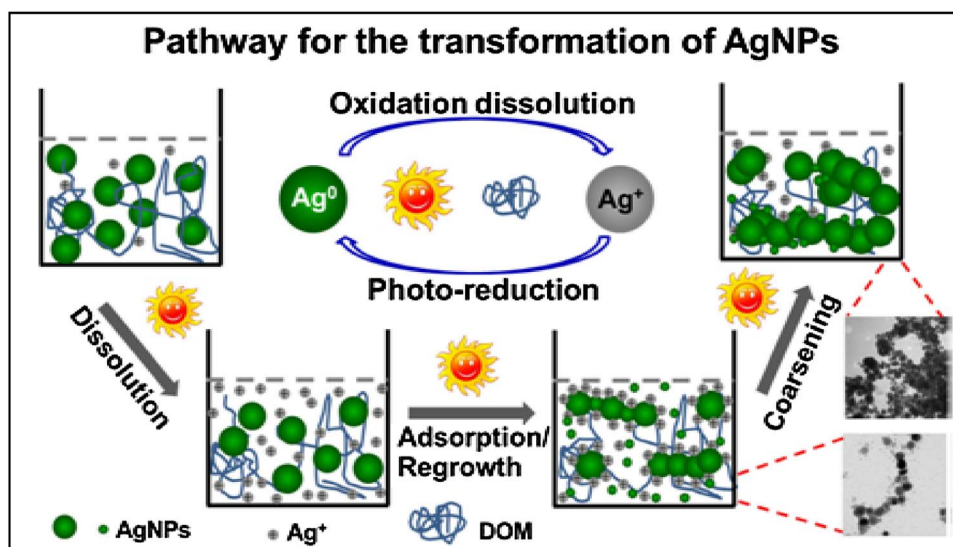


Fig. 2. Transformation pathways of AgNPs in aquatic ecosystem under the influence of sunlight and dissolved natural organic matter (DOM). [adopted from Ref. [30]].

trial applications. In recent years, due to the fluorescent nature, electronic structure [45] and surface properties of CNTs, they are profoundly used in the field of nanomedicine [46,47]. The global market outlook of CNTs produces a risk of industrial waste through different channels into the aquatic life and causes many toxicological effects, not only to aquatic life but also to human health through direct and indirect exposures. The stability of CNTs into the water, soils, sediments and other porous media often make its fate and transport critical. The surface functional groups often drive the transportation of CNTs into the aqueous environment, respective of the medium ionic strength. However, their transport tendency is directly related with surface hydrophobicity and inversely correlated with the presence of minerals in the case of soil and sediments [48,49]. Two groups of researchers [50,51] studied the uptake, transport and elimination of CNTs into earthworm and bacteria respectively. They studied the effect of surface coating, ionic charge and ion valence on CNTs uptake and found that the uptake, elimination, and sorption by soil were independent of these properties. However, the presence of bacteria in suspension increased the transportation and decreased the deposition in porous media. The overall factors highlighted in this review are summarized in Scheme 1, which control the behavior and transport of ENMs in natural aqueous system.

3. ENMs toxicity to aquatic ecosystem

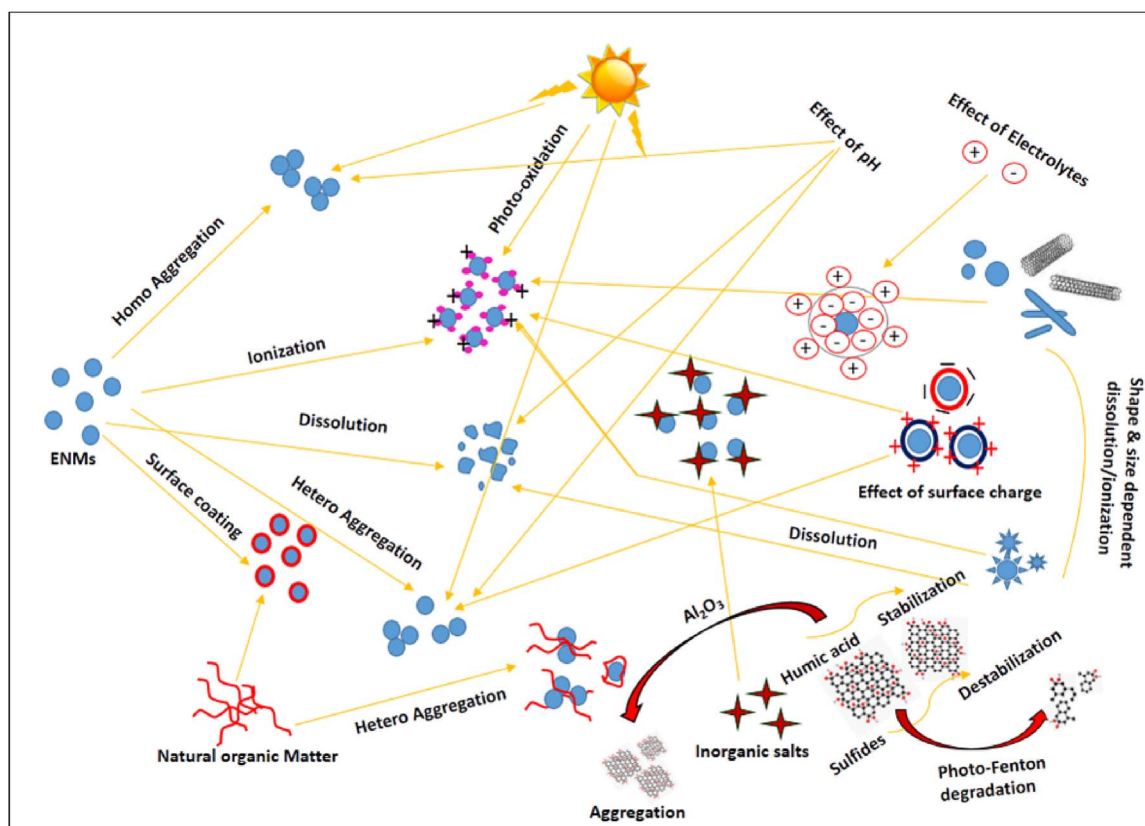
Previous report [52], manifested that the huge utilization of ENMs rooted out the toxicological effects in the aquatic ecosystem [53], where they caused major toxicity related to aquatic plants, aquatic microbes, and vertebrates. For instance, several studies showed that [54–56] the accumulation of Zn^{+2} ions into the aquatic vertebrates, plants and microbes are responsible for the toxicity directly related to the ZnONPs. A considerable number of publications have been reported in an effort to understand the interaction and toxicity of ZnONPs. Fig. 3,

summarizes the number of reports published to investigate the toxicological impacts of ZnONPs to aquatic plants, aquatic vertebrate models and microbes. As can be seen in the line diagram, the maximum toxicity of ZnONPs was reported to aquatic plants in the year range of 2006–2016. In the bulk of the analyzed reports, the toxicity was mainly attributed to the dissolved Zn^{+} ions which resulted in accumulation and translocation in plants, microbes, and vertebrates.

3.1. Toxicity to aquatic plants and algae

Plants are essential components of all ecosystems and play a critical role in the fate and behavior of ENMs. However, the toxicological impacts of ENMs to aquatic plants are not well documented and limited number of reports are available in literature. For example Jiang et al. [57], examined the concentration dependent nanotoxicity of AgNPs through bio accumulation and generation of reactive oxygen species (ROS) into the aquatic plant *Spirodela polyrrhiza*. They observed the dose dependant increase in ROS level when exposed to AgNPs. In another study Movafeghi et al. [58], elaborates the toxicity of TiO_2 NPs to *Spirodela polyrrhiza*. They found significant reduction in growth parameters, photosynthetic pigment and the activity of certain oxidative stress controlling enzymes after exposure to TiO_2 NPs. The oxidative stress was produced in response to the entry of nanoparticles into the plant tissues.

Similarly, Ouakarroum et al., [59] determined the effect of pH on the cellular toxicity of AgNPs on green alga *Chlamydomonas acidophila*. They observed that AgNPs size distribution was pH dependent and higher solubility was observed on pH-4 compared to that of pH-7. The results indicated that a 24 h exposure of AgNPs caused a decrease in chlorophyll content and reduced cell viability due to the pH-dependent dissolution and generation of reactive oxygen species (ROS). Another group of researchers [60] examined the toxicity of TiO_2 NPs on algae. After exposure to 72 h, they observed that algal growth due to ROS



Scheme 1. Factors effecting the transport of ENMs in the natural aqueous environemnt.

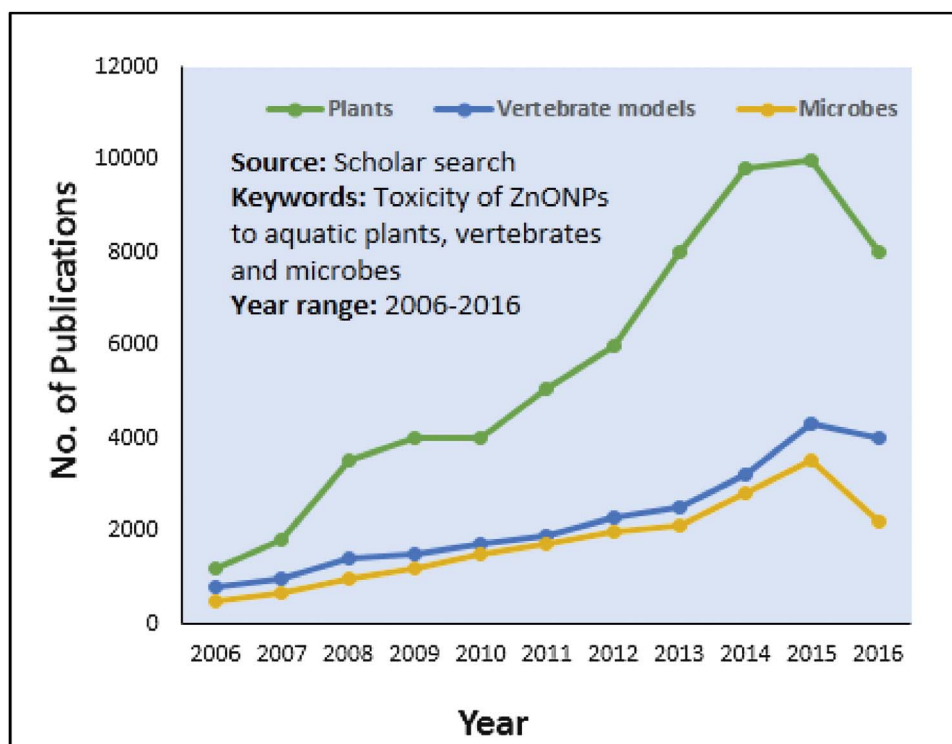


Fig. 3. Line diagram of the toxicity related publications of ZnONPs to aquatic plants, aquatic vertebrate models and microbes over the year range of 2006–2016.

production resulted in anti-oxidant enzymes disbalance and growth retardation. However, the results obtained in these in-vivo experiments may be artifacts while studying TiO₂ genotoxicity with the comet assay; therefore, control experiments are needed to support the results obtained [61,62].

In addition to this, Zhao et al. [63] determined the toxicity of GONPs to freshwater algae. Results from this study indicated that the GONPs owing to its physical penetration by algal cells induced oxidative stress that lead to membrane damage and nutrient depletion. They suggested that this nutrient depletion was of comprehensive importance to assess the negative effect of GONPs. Nonetheless, the findings from this laboratory based investigation may differ under natural aqueous environment that provoke the significance for future investigations. Zhang et al. [64] studied the toxicity potential of freshly synthesized and aged ZnONPs to the aquatic microalga, i.e. *Chlorella vulgaris*. They found that the toxicity varied with the aging time, i.e. the toxicity of aged ZnONPs for 30 days showed the higher toxicity to the green alga than the fresh ZnONPs. This indicated that the toxicity of ZnONPs was mainly due to the release of zinc ions.

3.2. Toxicity to aquatic vertebrate models

In determining the toxicity of ENMs, water has been declared as a major point of entry for these materials, as these materials are used, degraded, disposed of and eventually enter into the aquatic environment [65]. In the aquatic ecosystem, both plants [66] and animals [67] are susceptible to these contaminants. Recently, a group of researchers [67] determined the tissue uptake, distribution, and depuration of common carp (*Cyprinus Carpio*) after exposure to AgNPs. They investigated the toxicokinetic studies of AgNPs into the 7-day exposed and 2-weeks depurated common carp. After the exposure period, tissues of fish (brain, gills, skeletal, muscle, liver, GI tract and blood) were excised and digested in acid and their total silver concentration were examined. Interestingly, there was no evidence of silver accumulation as AgNPs; instead, it was observed as an ionic form in all tissues. This study provides important information about the mode of silver accumulation

in different tissues of exposed fish which will be helpful in the assessment of ecological risk produced by dissolved silver ions.

Another study [68], described the genotoxicity of AgNPs to the aquatic organism mussel *Mytilus Galloprovincialis*. 10 mg/L AgNPs were exposed to mussels for 15 days to evaluate the genotoxic effect using comet assay. Results of this study indicated that the time response induced DNA damage due to oxidative stress generated by Ag⁺ ionic species. However, this study failed to determine the actual mechanism of DNA damage by the generation of oxidative stress. Siller et al. [69], observed that AgNPs were more toxic than their equivalent AgNO₃ when exposed to sea urchin *Paracentrotus lividus*. They found that AgNO₃ released Ag⁺ more instantly by reacting with halides in the solution, while citrate stabilized AgNPs were unstable in the presence of halides and slowly released Ag⁺ in solution with the passage of time. Exposure to 0.3 mg/L of AgNPs caused development defects such as shortened or irregular arms, asymmetric body, and changes in swimming patterns. However, the similar defects were not observed when the sea urchins were exposed to an equivalent amount of Ag⁺ dose.

Cunningham et al. [70], described the exposure outcome and acute toxicity of AgNPs in developing zebrafish embryos (*Danio rerio*). They determined the effects of size, shape, surface charge, internalization of AgNPs by adsorption on exposure of embryos and highlighting the dissolution rate of AgNPs as a key factor contributing its potential toxicity. This study concluded that both nano size range and dissolved form of Ag⁺ have the capability to cause health and ecotoxicological effects when subjected to release in the environment.

In addition to this Bai et al. [71], investigated the toxicity of ZnONPs to zebrafish embryos. They found that nano-ZnO at concentration (50 and 100 mg/L) killed the zebrafish embryos, (1–25 mg/L) retarded the embryo hatching and caused body malformation.

Among other nanomaterials, TiO₂NPs shows potent toxicity to aquatic vertebrates such as zebrafish [72–74] and daphnia magna [75,76] etc. Previously, extensive toxicological research has been done on zebrafish vertebrate model because of their optical clarity, rapid uptake defects developments and similarity to other vertebrates including humans. A research group [72], determined the mortality rate of

zebrafish at ppb concentration of TiO₂NPs. Zebrafish were exposed to these nanomaterials for a period of 23 days and were illuminated artificially with a metal halide lamp that mimicked solar irradiation. This irradiation reacted with TiO₂NPs and generated (ROS) in a dose-dependent manner.

These ROS accumulated in the different organs and caused stunted growth, organ pathology, delayed metamorphosis and DNA damage. The study revealed that zebrafish was susceptible to TiO₂NPs, even at a low concentration of ng/mL and when illuminated, produced cumulative toxicity. However, at this place, it is important to recognize that although this study tends to provide natural aquatic environment toxicity to zebrafish, the study lacks the consideration of other factors like flow, depth, temperature and presence of natural organic matter which play key roles in toxicity and may involve the dissolution or aggregation of TiO₂NPs and make the condition of ecosystem more complex.

Kim et al. [73], studied the effect of particle sizes on the toxicity of citrate-stabilized TiO₂NPs on zebrafish embryos. By using citrate-functionalized TiO₂NPs of 6, 12 and 15 nm, zebrafish exposure to toxicity is determined either in sunlight illumination or in the dark. They found that TiO₂NPs caused photo-dependent toxicity in all three sizes, particularly in the 6 nm size (Fig. 4) with higher defects in development than larger particles under sunlight illumination. These defects included pericardial edema, yolk sac edema, craniofacial malformation, and opaque yolk in zebrafish embryos. This is due to the fact that the smaller particles due to their large surface area can generate a higher level of ROS in both in-vivo and in-vitro studies. The study concluded that mechanism of toxicity is mainly dependent on the surface area rather than the concentration of TiO₂NPs.

To determine the effect of metal doping, recently, a research group [74] determined the effect of metal doped TiO₂NPs on zebrafish embryo. In this study, zebrafish embryos were exposed for 72 h to 4 mg L⁻¹ metal doped TiO₂NPs and their morphological features and survival rate percentile were determined. According to a previous report [77], the doped metal- TiO₂ materials showed higher energy efficiencies than pure TiO₂ because the doped metal is closely related to oxidative stress generation and it is potentially more toxic to the aquatic ecosystem. The study indicated that the doped TiO₂NPs penetrated into the cells and caused cellular toxicity such as apoptosis and necrosis.

Yang et al. [78], investigated the effect of humic acid on the toxicity behavior of TiO₂NPs to developing zebrafish. They determined the toxicity behavior of TiO₂ nanoparticles in the presence of Suwannee river humic acid (HA), both in the presence and absence of sunlight. They observed that TiO₂NPs were more toxic in the presence of sunlight, causing photocatalytic degradation of HA and making the suspension more unstable which resulted in the toxicity and death of exposed zebrafish. While in the absence of sunlight, only small lethal effects were observed in which lipid peroxidation caused a small mortality effect to the zebrafish.

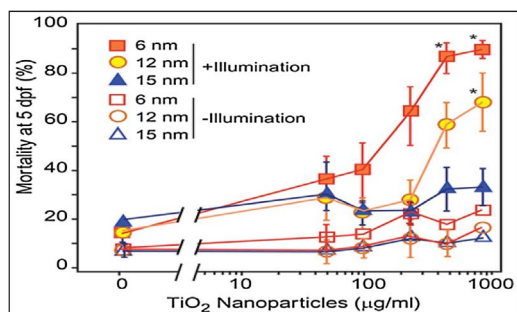


Fig. 4. Toxicity of citrate functionalized TiO₂ nanoparticles (6, 12 and 15 nm sizes) to zebrafish embryos with and without illumination and their mortality pattern. [Taken from Ref. [73]].

Moreover, the results showed that HA coating on the surface of TiO₂NPs resulted in more toxicity compared to uncoated particles. Although this is the first report to investigate the impact of HA on the toxicity of TiO₂ nanomaterials, the concentration of TiO₂NPs used in this study (100 mgL⁻¹) was much higher than those currently predicted (0.002–0.01 µg.L⁻¹) in the natural environment. Therefore, further studies are required to examine the toxicity of TiO₂ nanoparticles in true environmental concentration and in the presence of other environmental factors (sunlight illumination, pH and dissolved natural organic matter, etc.).

Certain in vivo studies have been conducted to demonstrate the toxicity of CNTs in aquatic vertebrates, concluding that the non agglomerated dispersed form of CNTs is the major source of toxicity compared to the agglomerated form [79]. The concept lies in the fact that agglomeration alters the electronic interaction between the tubes in terms of π -electrons and affects the reactivity of CNTs into the biological system as a result of distorted network formation [79]. Water borne contamination of CNTs still remains a challenge and has been a subject of many recent investigations [80,81]. Meas et al. [82], studied the bioaccumulation effect of multiwall carbon nanotubes (MWCNTs) in a different compartment of an adult zebrafish with respect to the exposure time. During this study, they observed that CNTs mainly accumulated in the gut of all fish and remained constant. This may be due to fact the that CNTs do not translocate outside of the gut tract of organisms at detectable concentrations [83] and there is also strong evidence to suggest against biomagnifications [84,85]. While going on a deep insight into the mechanism of CNTs toxicity in biological systems, it is recognized that CNTs induced the cytotoxicity by the generation of oxidative stress, accompanied by the depletion of antioxidants [86].

Besides current progress in determining the bioavailability of ENMs, till now, only a handful of studies have been conducted to track the quantity and uptake of carbon-based materials in the aquatic vertebrate model. For example, [87] detected and quantified the SWCNTs in an aquatic vertebrate model using near infrared fluorescent detector (NIRF). In this study, the vertebrate model was first exposed to the carbon nanomaterials. Then, their distribution and quantification in different tissues were tracked by using an NIRF detector. However, there are certain limitations with this technique to investigate the accurate distribution of SWCNTs into different parts of the vertebrates, majorly due to the differential nano sized carbon-based materials [88] fluorescence quenching [89] and transformation ability of ENMs by reacting with natural organic matter to form modified complexes and thereby supposedly lowering its bio availability in the aquatic ecosystem [90].

3.3. Toxicity to aquatic microbes

In addition to aquatic vertebrate models, TiO₂NPs also caused dominant toxicity to aquatic microorganism. Although previous reports confirmed that doping increases the toxicity of these ENMs, some studies claimed that the doping of ENMs effectively reduces their toxicity [91] to aquatic vertebrate models and microbes with increased light absorption [92]. Pathakoti et al. [93], investigated the photo inactivation phenomenon of *E. coli* by singly and doubly doped TiO₂NPs (sulfur doped S-TiO₂ and nitrogen-fluorine co-doped N-F-TiO₂NPs) under the influence of solar and visible light irradiation. Results of this study showed that the toxicity of TiO₂NPs mainly depended on the generation of ROS like \cdot OH radicals or oxidative stress in *E. coli* rather than the particle size and surface area which did not influence the phototoxicity under light irradiation.

Moreover, they concluded that visible light activated doped TiO₂NPs did not show photocatalytic activity towards *E. coli* inactivation when compared to undoped TiO₂NPs.

In another study [94], it was demonstrated that pH dependent dissolution of Ag⁺ is the main dominant factor responsible for the

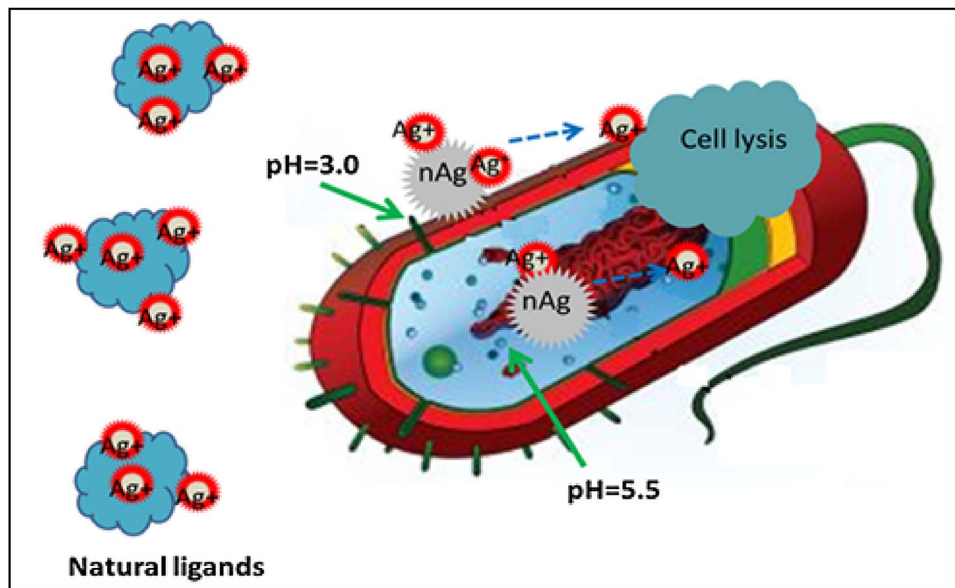
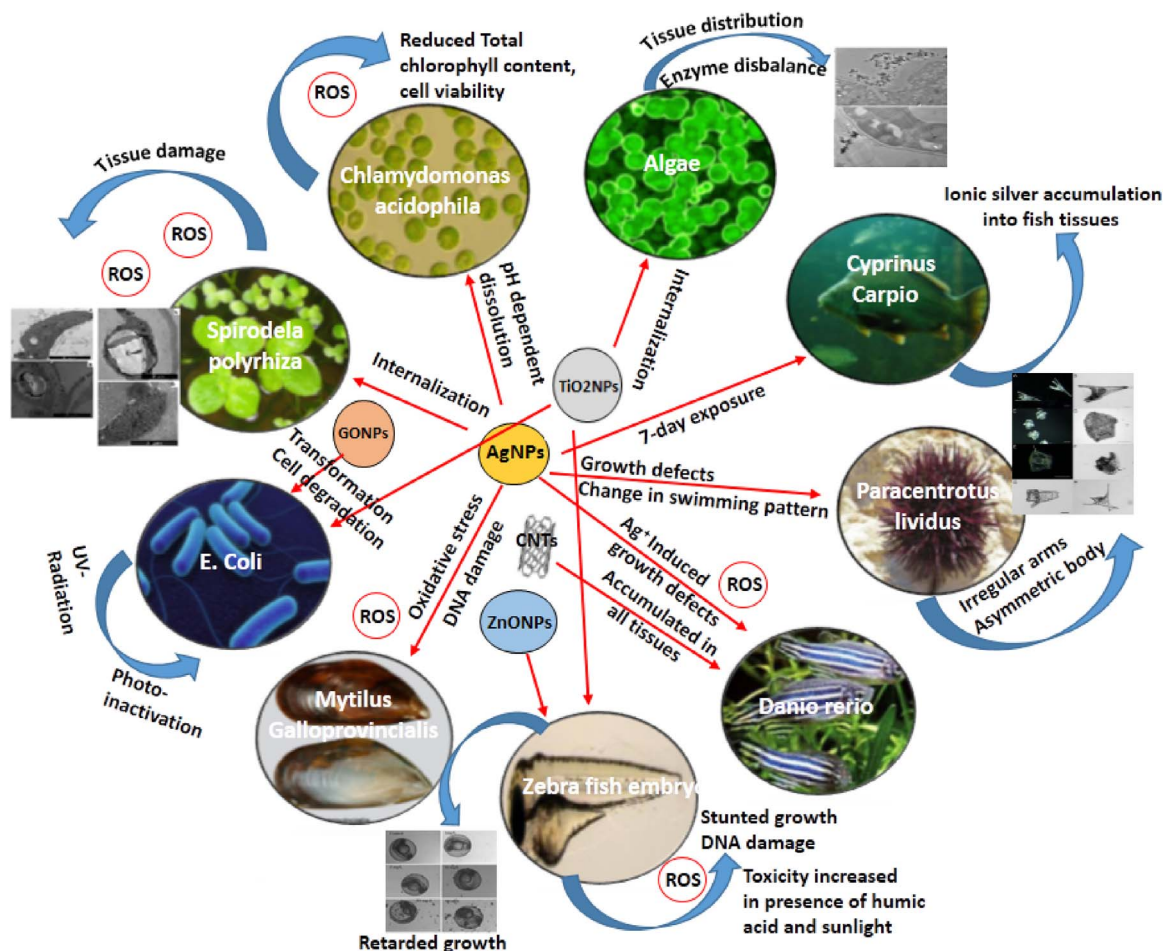


Fig. 5. Schematic representation of AgNPs (Ag⁺ vehicle) which binds with cell cytoplasm at PH-3 and releases Ag⁺ ions resulting in bacterial cell lysis [Taken from Ref. [94]].



Scheme 2. Schematic representation of the toxicity of ENMs to aquatic plant, microbe and vertebrate models.

toxicity to *E. coli* (Fig. 5). The dissolved Ag⁺ binds with the cell cytoplasm and resulting in cell death because of the oxidative stress generated by Ag⁺ ions. However, certain environmental transformations like reaction with organic and inorganic ligand, reaction with chloride ions, and sulfidation also play key roles in the stability, short term, and long term toxicity of AgNPs [95]. The toxicity of TiO₂NPs to

E. coli in the dark is studied by [96]. They found that TiO₂NPs caused the depolarization and membrane loss integrity in *E. coli*, resulting in K⁺ and Mg²⁺ cellular leakage when exposed in the dark. The membrane increased permeability, which resulted in osmotic stress generation and introduction of nanoparticles into the cell. The induced osmotic stress upgraded several genes or proteins involved in the

defence mechanism against oxidative stress. The concomitant increase in the oxidative stress produced free radicals which appeared to play a role in the induced toxicity and deregulation of certain genes or proteins.

The fate and behavior of GONPs into the aquatic system were well studied by Zhao et al. [97]. According to this study, transformation of GONPs was greatly altered by their adsorption and dispersion/aggregation characteristics. However, the solution chemistry, presence of colloidal and biocolloidal particles in the aquatic system also impact their toxicity to aquatic organisms such as aquatic plants, vertebrates and bacteria.

Wu et al. [98], described the impacts of ZnONPs to ammonia-oxidizing bacteria, *Nitrosomonas europaea*. The study demonstrated that, ZnONPs exerted dose-dependent impairment to the bacterial cells. Interestingly, they observed dose and time dependent toxicity to ZnONPs exposure. For instance, the 50 mg/L ZnONP exposed cells displayed potential recoverability which was negatively correlated with the NP exposure time. The cells were nearly completely restored in a 12-h recovery incubation in terms of cell density, membrane integrity, and the nitrite production rate. The findings of this study provide better understanding of the impact of ZnONPs and microbial recovery potentials and provide fundamental knowledge about the risk assessments of the growing NPs in the future.

Scheme 2, representing the overall summarized toxicological data obtained from different aquatic plants, microbes and vertebrates models discussed in this review.

In regards to all of the above, despite the considerable beneficial approach of ENMs in various fields of science and technology, they are proven to be a double-edged sword and their toxic effects are lethal to the aquatic ecosystems. In this review, the summarized data represents that both the physicochemical properties (shape, size, surface charge) and environmental factors (pH, temperature, ionic strength, UV light, dissolved NOM and presence of electrolytes and other contaminants) control the transformation, transport, and toxicity of ENMs. Overall, these materials through the production of ionic species including ROS have become a spontaneous source of damage to aquatic ecosystem. However, to date, an in-depth understanding of the ENMs physicochemical properties, prediction of their true concentration in the environment, their transport and transformation behavior, and evaluation of benefits and risks are still critical and need to be discussed in detail. There should be more detailed case-by-case toxicity evaluations of ENMs to build a sophisticated predictive model which can estimate and quantify their long-term existence in the ecosystem, as long-term studies provide a more realistic and holistic approach for determining the impact of ENMs in the aquatic environment. Furthermore, the toxicity, fate and behavior of ENMs from a large-scale synthesis to industrial application and disposal should be the main focus of concern and steps should be taken in all three departments, i.e., (a) ENMs synthesis and modification parameters (b) determination of ENMs source or point of entry, and (c) to fill up the safety regulatory gaps which are highly recommended. More precisely, there should be regulatory models and tools to predict the true concentration, long-term environmental fate, transport, and transformation of ENMs into the environment and the ecosystem.

We believe that this review will add significant information to help regulators, engineers, and scientists in this field to understand the transport, toxicity and the interactions of ENMs with the contaminants in natural aqueous system. We have summarized the transport and toxicity data with the assistance of the latest publications, and the knowledge gap and future research needs are recognized. Furthermore, the key challenges in evaluating the behavior and transport of selected ENMs in aquatic plants, vertebrate models and microbes are discussed.

Conflict of interest

None.

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