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Toxicity of zinc nanoparticles in fish: a critical review

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Abstract

Nanotechnology has noticeably developed with potential effects in every science specially by using nanoscale element. Among the nano material, ZnO-NPs have got more intention due to its special properties and its fewer hazards to the environment. Like most of the nanoparticles, ZnO is also toxic to organisms; however the toxicity of these nanoparticles can be used for antibacterial, antiviral, antifungal, and antialgal. To reduce the hazardous effects of nanoparticles, some manufacturers use chemical particles such as Nanoscale zero-valent ion that can enhance the environmental remediation of polluted water, soil and sediments. In the present study, the effect of ZnO Nanoparticles on fish model has been reviewed in detail.

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Introduction

Metal-based nanoparticles are increasingly implemented in materials, cosmetics and technical applications (Brun *et al*., 2014). Zinc oxide, with its unique physical and chemical properties, such as high electrochemical coupling coefficient, high chemical stability, high photo stability and broad range of radiation absorption is a multifunctional material (Segets *et al*., 2009). In material science, ZnO is classified as semiconductor in group II-VI, whose covalence is on the edge between covalent and ionic semiconductors. A broad energy band (3.37 eV), high bond energy (60 meV) and high thermal and mechanical stability at room temperature makes it attractive for potential use in electronics, optoelectronics and laser technology (Wang *et al*., 2005;Bacaksiz *et al*., 2008). The piezo and pyroelectric properties of ZnO mean that it can be used as a converter, sensor, energy generator and photocatalyst in production of hydrogen (Wang, 2008; Chaari and Matoussi, 2012). Because of its rigidity and piezoelectric and hardness, it is an important material in the ceramic industry while, it's low toxicity, biocompatibility and biodegradability make it a material of interest for biomedicine (Ozgür *et al*., 2005; Ludi and Niederberger, 2013). It might also be used in semiconductors, solar panel devices, personal care products (sunscreens), paints and even in waste water treatment (Zimmermann *et al*., 2012). Being large use of ZnO nanoparticles; consequently, they may be ultimately released into the environment during production, use and disposal (Brun *et al*., 2014).

Due to different physico-chemical properties or behaviours of nanoparticles than bulk materials change their fate (Li *et al*., 2013, 2014). Zinc is also an essential trace element for organisms but induces toxicity at elevated concentrations. Partially but relatively quickly, ZnO-NPs dissolve in water, and the release of free zinc ions has been previously known to be the primary source of toxicity (Buerki-Thurnherr *et al*., 2013; Blinova *et al*., 2010; Franklin *et al*., 2007). However, in other studies ZnO-NPs showed higher toxicity (Bai *et al*., 2010; Hu *et al*., 2009; Fernández *et al*., 2013), or induced additional effects (Poynton *et al*., 2011) than dissolved Zn(II) alone. Thus, there are conflicting observations and further research is needed to resolve these discrepancies. In organisms, cellular zinc ion fluctuations are mainly regulated by zinc binding metallothioneins (MT). Both, Zn (II) and ZnO-NPs induce reactive oxygen species (ROS) formation (Dineley *et al*., 2003; Heng *et al*., 2010; Sensi *et al*., 1999). ROS production triggers an oxidative stress response has become a widely accepted paradigm for cellular effects of nanoparticles (Nel *et al*., 2006; Sharma *et al*., 2012; Song *et al*., 2010; Zhu *et al*., 2009; Khan *et al*., 2015a). Excessive production of ROS can induce pro-inflammatory and cytotoxic effects (Nel *et al*., 2006). ZnO-NPs and associated may ultimately lead to apoptosis (Buerki-Thurnherr *et al*., 2013) and acute toxicity at high concentrations. In zebra fish, adverse effects of ZnO-NPs include reduce hatching of embryos and ROS production (Bai *et al*., 2010; George *et al*., 2011; Ong *et al*., 2013; Xia *et al*., 2011; Zhao *et al*., 2013; Zhu *et al*., 2009). However, induction of inflammatory responses has not yet been investigated in fish. So the present review was aimed to summarize the toxic effects of ZnO-NPs on the fish model.

Applications of Zinc Oxide

Because of its diverse properties, in chemical and physical aspects, zinc oxide is widely used in different areas of life. It plays an important role in a very wide range of applications, including tires, ceramics, pharmaceuticals, agriculture, paints and some other chemicals. Table 1 provided the different uses of ZnO-NPs and Fig.1 shows worldwide consumption of zinc oxide by region.

Toxic Effects to Fish

Recently, due to ecological changes and degradation of their natural spawning ground in most water body, the number and variation of fish species have been decreased sharply. The scientist has much attention in biological study and inducing artificial spawning to prevent diminishing of some valuable and endangered fish species (Yousefian *et al.*, 2008a; Yousefian and Mosavi, 2008).

Nanoparticles (NPs) including ZnO have a potential environmental danger. The researchers tried to find out the consequence of nanoparticles in animal models, e.g. Khan *et al.,* (2015b) sum up the toxicity of silver nanoparticles in fish and in this review toxicity of ZnO-NPs to fish model studied. The applications of ZnO-NPs suggested that these materials are likely to be in effluents, or released into the environment directly during use and their known toxic effects in mammalian models raises concerns about other vertebrates including fish (Handy *et al.*, 2008). For living organisms in the aquatic environment, there is huge uncertainty on exposure because of a lack of data about the effect of nanoparticles in behavior, physiology and bioactivity of organism in the water.

Table 1. Some important industrial uses of ZnO nanoparticles.

Sr	Industry	Applications
1	Rubber industry	Filter, activator of rubber compounds
2	Pharmaceutical and cosmetic industry	Component of creams, powders, dental paste etc., absorber of UV radiations
3	Textile industry	Absorber of UV radiation
4	Photo-catalyst	Photo-catalyst
5	Miscellaneous application	Used in production of zinc silicates, typographical and offset inks, criminology, biosensor, process of producing and packing meat and vegetables products etc.

There are several studies that supported the adverse effects of nanoparticles on fish. Dietary nanoparticles have previously been seen to cause lipid peroxidation in the liver and heart of African catfish (Baker *et al.*, 1999). An increase in intracellular reactive oxygen species (ROS) was observed in zebra fish embryos exposed to ZnO-NPs and implemented some toxic effects (Zhu *et al.*, 2009b). The emerging studies reported that nano-metals can cross the chorion and suggested that the nano-forms ZnO-NPs may be more toxic to embryos or juveniles, than the equivalent metal salt (Shaw and Handy, 2011). There are also studies on the oral administration of nanoparticles and supported the absorption of fine ZnO and TiO2 particles across porcine skin (Gamer *et al.*, 2006; Wang *et al.*, 2007). In an experiment with medaka fish (*Oryzias latipe*) and their embryos the effects of ZnO-NPs were examined. The finding of these studies revealed that both the exposed embryos and medaka adults showed dose dependent toxicity. SOD and glutathione (GSH) activity were found to decrease significantly in liver and brain samples taken from the adults, but at the time of exposure increased, the adults appeared to recover from the exposure by adjusting the levels of antioxidant enzymes (Li *et al.*, 2009). The adults were also examined for possible histopathological and morphological changes. The gills and intestine samples showed a considerable change, but the liver and brain samples did not show significant change. At exposures of 5 and 50 µg mL^{-1} of ZnO-NPs, gill samples were found with swollen epithelium cells, black particles deposited on the surface and missing scales (Gavaskar *et al.*, 2005).

Baker *et al.*, 1997, determined the effect of increased iron intake on growth and lipid peroxidation in African catfish (*Clarias gariepinus*) juveniles of mean weight 32.25 g. The fish were fed a ratio of 2% body weight per day, for 5 weeks on fishmeal based diets containing iron in a dry diet (as $FeSO_4.7H_2O$). Ingestion of the dietary iron in high ratio resulted in decreased growth in the catfish by accumulating in the tissues. Greater iron accumulation was found to occur during exposure to commercial iron sulphate liquor. Respiratory disruption occurs due to physical clogging of the gills is suggested as a possible mechanism for iron toxicity (Dalzell and MacFarlane, 1999). In integrative biological and physicochemical studies on the uptake of unmodified commercial nanoscale metal oxides, zinc oxide (ZnO), cerium dioxide (CeO_2), and titanium dioxide (TiO_2), from the water and diet to determine their potential ecotoxicological impacts on fish as a function of concentration were reported by Johnston *et al.* (2010). Significant uptake of nanomaterials was found only for cerium in the liver of zebra fish exposed via the water and ionic titanium in the gut of trout exposed through the diet. For the aqueous exposures, formation of large NP aggregates (up to 3 μm) occurred and it is likely that this resulted in limited bioavailability of the unmodified metal oxide NPs in fish. The toxicity of ZnO-NPs in some fish groups are described below.

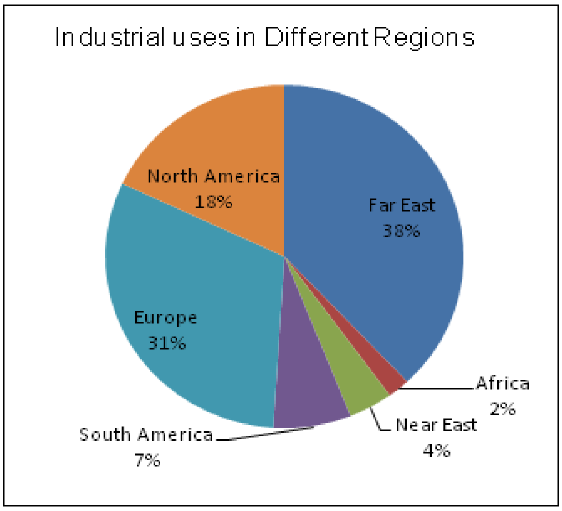

Fig. 1. Industrial uses of ZnO in different Regions.

Zebrafish (Danio rerio)

The experimental results of different studies showed that the NPs inhibited both the body length and hatching rate of zebrafish larvae. The particles with smaller size exhibited more toxicity. Studies on enzyme activity showed that the NPs reduced the glutathione content and inhibited catalase and superoxide dismutase activities, resulting in shortening the body length, lower hatching success, and lowering reproduction of zebrafish larvae (Liu *et al.*, 2014). Upon Exposure the zebrafish embryos and Eleuthero-embryos lead to an accumulation of zinc. Dose-dependent adverse effects of hatching and expressional changes of genes associated with oxidative stress and inflammation reaction occurred. These findings confirmed the inhibitory effect of ZnO-NPs on hatching of embryos (Bai *et al.*, 2010; Zhao *et al.*, 2013). The effects were mainly related to the release of Zn (II) from nanoparticles, and they were more pronounced in embryos than Eleuthero-embryos. There is still a debate on this question, as there are supporting reports (Song *et al.*, 2010; Buerki-Thurnherr *et al.*, 2013), as well as reports showing that zinc ions only partly contributed to the effects of ZnO-NPs (Bai *et al.*, 2010; Ong *et al.*, 2013; Zhao *et al.*, 2013; Zhu *et al.*, 2009).

Common Carp (Cyprinus carpio)

Subashkumar and Selvanayagam (2014) showed acute toxicity of ZnO nanoparticles for common carp (*C. carpio*) at 4.897 mg/L and this is well in accordance with the acute toxicity of ZnO nanoparticle in zebra fish (96 h LC50 of 4.92 mg/L). The principal toxic mechanisms were probably associated with the physical and chemical characteristics of ZnO nanoparticle and also reported as nanoparticles will cause toxic effect (Xionf *et al.*, 2011). Fish gill is a crucial organ of respiration (Korai *et al.*, 2010), osmoregulation and there is a close relationship between gill morphology and stress (Saber, 2011). Histological study of the gills showed a typical structural organization of the lamella in the control group. In the study by Saber *et al.* (2011), the treated group showed progressive architectural distortions like alteration in secondary structure, congestion of blood, marginal channel dilation of lamellae, hyperplasia in epithelial cells, lamellar fusion, epithelial lifting, desquamation and necrosis, aneurism, acute cellular swelling, lamellar disorganization, curling and loss of secondary lamellae at 21 days exposures were observed due to ZnO-NPs toxicosis. Pathological alterations like hyperplasia of epithelial cells, epithelial lifting and lamellar fusion may increase the space of contact of toxicants with the vascular system of the gill, resulting in impairment of respiration as well as fish health. Aneurism was observed due to collapse of pillar cells in the secondary lamellae and rupture of blood vessels, releasing large quantities of blood resulting in the lamellar disorganization. Desquamation and necrosis are the direct deleterious effects induced by ZnO.

Nile Tilapia (Oreochromis niloticus)

The gills of fish received ZnO-NPs had a severe vacuolation and necrosis pavement and epithelial cells with dilated mucous cells (Alkaladi *et al.*, 2014). These cells were separated from secondary lamella by edema containing fibrin and inflammatory cells (Linhua *et al.*, 2013). The swollen and disrupted gill cells exposed to ZnO-NPs might reduce the contact surface and affect the exchanges of air and ion (Alkaladi *et al.*, 2014). Some black blocks accumulated in the mucus of chloride cell, which was suspected as ZnO-NPs aggregates, showing that ZnO-NPs might directly enter into the fish body through the injured epithelial cell membrane and induce the undesirable toxic effects (Linhua *et al.*, 2013). Gill is the major target organ for chemical pollutants to elicit toxic effects. Previously, some researchers defined two types of gill injuries: the first type of injury results from defense response, including hyperplasia of the gill filaments epithelium, edema of gill lamellae; the second type is the direct injury in the form of necrosis and shedding of the gill epithelium (Jinyuan *et al.*, 2011).

Conclusion

Nanotechnology has been shown to be an important of high technologies that can be used in a wide range of human activities. It is used in industry, agriculture and medicine therapy. The development of nanotechnologies also has a negative impact on the environment. Exposure of nanomaterials into the aquatic environment causes a serious effect on the environment and living organisms including fish. Therefore, it is suggested that exposure of this nanoparticle like others should be limited in the aquatic environment.

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