Aquatic Toxicology 161 (2015) 117–126

Contents lists available at ScienceDirect

Aquatic Toxicology

journal homepage: www.elsevier.com/locate/aquatox

Review

Effects of titanium dioxide nanoparticles on lead bioconcentration and toxicity on thyroid endocrine system and neuronal development in zebrafish larvae

Wei Miao[a], Biran Zhu[b,c], Xiaohong Xiao[d], Ying Li[a], Niguse Bekele Dirbaba[a], Bingsheng Zhou[b], Hongjuan Wu[a,*]

[a] School of Environmental Science and Engineering, Huazhong University of Science and Technology, Wuhan 430074, China
[b] State Key Laboratory of Freshwater Ecology and Biotechnology, Institute of Hydrobiology, Chinese Academy of Sciences, Wuhan 430072, China
[c] Graduate University of Chinese Academy of Sciences, Beijing 100039, China
[d] College of Mechanical and Electronic Engineering, China University of Petroleum (East China), Qingdao 266580, China

ARTICLE INFO

Article history:
Received 22 October 2014
Received in revised form 30 January 2015
Accepted 2 February 2015
Available online 7 February 2015

Keywords:
Pb
Titanium dioxide nanoparticles
Bioconcentration
Thyroid disruption
Developmental neurotoxicity
Zebrafish larvae

ABSTRACT

Nanoparticles (NPs) have attracted considerable attention because of their wide range of applications. Interactions between heavy metals (e.g., Pb) and NPs in aquatic environments may modify the bioavailability and toxicity of heavy metals. Therefore, this study investigated the influence of NPs (e.g., nano-TiO_2) on the bioavailability and toxicity of Pb and its effects in the thyroid endocrine and nervous systems of zebrafish (*Danio rerio*) larvae. Zebrafish embryos (2-h post-fertilization) were exposed to five concentrations of Pb alone (0, 5, 10, 20, and 30 μg/L) or in combination with nano-TiO_2 (0.1 mg/L) until 6 days post-fertilization. Results showed that the bioconcentration of Pb was significantly enhanced when combined with nano-TiO_2 than when used alone. Zebrafish exposure to Pb alone at 30 μg/L significantly decreased the thyroid hormone levels (T_4 and T_3), whereas nano-TiO_2 treatment alone did not produce detectable changes. The levels of T_4 and T_3 were further decreased when Pb was combined with nano-TiO_2 than when used alone. The transcription of the thyroid hormone-related factor *tg* gene was remarkably down-regulated by Pb treatment alone but up-regulated when Pb was combined with nano-TiO_2. The significant up-regulation of *tshβ* gene and the down-regulation of *TTR* gene expression in the hypothalamic–pituitary–thyroid were observed in Pb with or without nano-TiO_2 treatment groups. In addition, the transcription of genes involved in central nervous system (CNS) development (*α-tubulin*, *mbp*, *gfap* and *shha*) were significantly down-regulated by Pb and nano-TiO_2 co-exposure as compared with Pb exposure alone. The locomotion activity analyzes confirmed that nano-TiO_2 might enhance the toxicity of Pb to CNS development. These results suggest that nano-TiO_2 increase bioconcentration of lead, which lead to the disruption of thyroid endocrine and neuronal system in zebrafish larvae.

Contents

* Corresponding author at: School of Environmental Science and Engineering, Huazhong University of Science and Technology, No.1037 Luoyu Road, Wuhan, Hubei 430074, China. Tel.: +86 27 87792363; fax: +86 27 87792101.
E-mail address: hongjuanwu@hust.edu.cn (H. Wu).

http://dx.doi.org/10.1016/j.aquatox.2015.02.002
0166-445X/

1. Introduction

With the rapid development of nanotechnology, titanium dioxide nanoparticles (nano-TiO_2) have attracted considerable attention because of their unique properties (small size, chemical composition, surface structure, solubility, shape and aggregation) and widespread use in the production of sunscreen, toothpaste, surface coatings and water treatments (Nel et al., 2006; Chen and Mao, 2007). Their increased production and use may cause the release of nanoparticles (NPs) into the environment (Kaegi et al., 2008). The potential health hazards and environmental impacts of manufactured NPs are of great concern. As of 2009, more than 140 companies worldwide have been engaged in NPs manufacturing (Sun et al., 2009). The estimated worldwide production of nano-TiO_2 was approximately 5000 t/year in 2006–2010 and 10,000 t/year in 2011–2014; its production is expected to reach 2.5 million metric tons/year by 2025 (United Nations Environment Programme, 2007; Robichaud et al., 2009). The predicted environmental concentration of nano-TiO_2 in Switzerland waters is 0.7–16 μg/L, which is higher than the predicted no effect concentration (1 μg/L), the predicted no effect concentration was measured based on toxicological studies, the concentration at which no adverse effect on organisms (and ecosystems) is to be expected (Mueller and Nowack, 2008).

Heavy metal pollution has received much attention as an important source of pollution worldwide (Toscano and Guilarte, 2005). Lead is a major heavy metal that has been used for over 8000 years to produce glass, pigments, make-up, wine, antiknock fuel additives, electronic components and batteries as well as for water transport and cooking (Ahmed et al., 2014). Additional Pb pollution has been derived from agricultural, urban and industrial wastes (Environmental Protection Agency, 2009). Thus, Pb is one of the top toxic pollutants of environmental concern (Gonzalez et al., 2006). The water concentration of Pb is approximately 5–15 μg/L in the Guangzhou segment of the Pearl River, which is one of China's most developed regions; the Pb concentration of some areas in Guangzhou is higher than the median values of the world's freshwater (Liu et al., 2014). The Pb concentrations in *Oreochromis mossambicus* and *Channa asiatica* from the Pearl River estuary of China are higher than 8 and 6 μg/g dry weight (dw), respectively (Kwok et al., 2014). Meanwhile, the Pb concentration in freshwater fishes (common carp, rainbow trout and Siberian sturgeon) from Szczecin is 0.002–0.021 mg/kg wet weight (Brucka-Jastrzebska, 2010).

Previous studies have reported the bioaccumulation of Pb even at very low concentrations (Hollis et al., 1999; Bu-Olayan and Thomas, 2005). The level of Pb exposure negatively correlates with the serum levels of thyroid hormones (THs) in humans (Singh et al., 2000; Lopez et al., 2000). Ibrahim et al. (2011) showed that Pb can reduce TH levels in rats. A similar study reported related negative effects in fish; that is, the TH levels of model organisms are significantly decreased after exposure to Pb at 20 μg/L (Spieler and Weber, 1991). In addition, the altered TH levels may cause several developmental defects, particularly to the central nervous system (CNS). There were also some results had demonstrated lead could cause an damage to the CNS (Guilarte and McGlothan, 2003; Reddy et al., 2007; Ahmed et al., 2014; Hu et al., 2014). The mechanisms behind the known effects of Pb on the CNS have not been fully explained, but several studies have reported that Pb exposure may alter the hypothalamic–pituitary–thyroid axis and thus, affect the CNS (Meeker et al., 2009; Singh et al., 2000 Singh et al., 2000). The absorbed Pb can accumulate in the choroid plexus and markedly decrease the transthyretin (*TTR*) level in the cerebrospinal fluid of human (Zheng et al., 2001).

Heavy metals and nano-TiO_2 are simultaneously released in the environment; the higher surface area-to-volume ratio of nano-TiO_2 relative to that of traditional TiO_2 particles allows the NPs to absorb heavy metals and modify their toxicity (Pettibone et al., 2008; Cho et al., 2010). Some reports have studied the possible combined effects from the interaction of nano-TiO_2 with other pollutants (Sun et al., 2009; Hu et al., 2011; Fan et al., 2012). For instance, a previous study focused on the bioconcentration of the e-waste (BDE-209) that can be absorbed by nano-TiO_2 (Wang et al., 2014). Several previous studies focused on the enhanced bioaccumulation of metals mixed with NPs in aquatic ecosystems (Fan et al., 2012; Tan et al., 2012). Their results showed that the increasing concentration of Cadmium and Zinc is related to NPs adsorption in *Daphnia magna* experiments. Although previous studies have examined the potential effects of nano-TiO_2, those that specifically studied the ecotoxicity of nano-TiO_2 are limited on acute and chronic experiments (Hund-Rinke and Simon, 2006; Federici et al., 2007; Heinlaan et al., 2008; Wiench et al., 2009). Therefore, the present study investigated the carrier effect of nano-TiO_2 in the aquatic environment and described the ecotoxicological effects of concomitant exposure to Pb and nano-TiO_2. We hypothesized that the presence of nano-TiO_2 facilitates the entry of metal pollutants into aquatic organisms and observed the potential toxic effects of heavy metals combined with nano-TiO_2.

Zebrafish (*Danio rerio*) was selected as the model animal in our study. The advantages of zebrafish relative to rodent models for studying developmental neurotoxicity is mainly for the zebrafish neuronal cells can be conveniently observed via microscopy because of their optical transparency during early developmental stages. Additional advantages include their small size, rapid embryonic development and short life cycle. The aim of the present study was to identify the interaction between nano-TiO_2 and Pb