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A review on the ecotoxicological effects of heavy metals on aquatic organisms

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Review

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ABSTRACT

In recent years, with the rapid development of the global economy, heavy metals have been widely used in industrial production and daily life because of their unique properties. This, however, has simultaneously led to heavy metal pollution due to several reasons. After entering the aquatic environment, heavy metals are not easily decomposed by microorganisms and become toxic when they reach a certain concentration. Heavy metals can easily enter the liver and other vital organs of aquatic organisms, where they accumulate and severely affect the growth and reproduction of these organisms. They can also threaten human health through the food chain. Therefore, heavy metal pollution has potential ecological and health risks. This paper summarizes the sources and hazards of heavy metals in water, the pattern of enrichment of heavy metals in aquatic organisms, the toxic effects of heavy metals on aquatic organisms, the tolerance mechanism of aquatic animals to heavy metals, and the factors affecting the toxicity of heavy metals. The authors put forward three feasible suggestions for the study of ecotoxicological effects of heavy metals on aquatic organisms in the future. The results of this study have considerable significance for aquaculture and environmental management and even for humans.

Keywords: Heavy metal, Aquatic environment, Aquatic organisms, Toxicity, Ecosystems

1.INTRODUCTION

Water is one of the most important resources for the natural environment, industrial production, and life. However, at present, all major river basins in China have been affected by several types of water pollution, especially pollution due to heavy metals (Harguinteguy et al. 2014). Pollution by heavy metals has become one of the major environmental problems because of their persistence in the environment, biological toxicity, nondegradability, and ability to enter the food chain. They can also induce redox reactions with some substances and convert them into more toxic pollutant compounds (Yohannes et al., 2013; Fu et al., 2016). Aquatic organisms such as aquatic animals, aquatic plants, and aquatic microorganisms can accumulate heavy metals in their body (Rose et al., 2015). However, when the concentration and toxicity of heavy metals in water exceed the regulatory capacity for aquatic organisms, it will have a severe negative impact on their related functions and even life activities and can lead to genetic alteration and changes in species diversity. Heavy metals in the aquatic environment can be transmitted to humans through various food chains, and hence, heavy metal pollution poses a serious threat to human health. For example, heavy metals cannot be easily eliminated from the human body. Once they exceed the physiological regulatory limits for the human body, they will cause damage to the physiological system of the body, resulting in acute or chronic harm. Heavy metals such as zinc (Zn), cadmium (Cd), mercury (Hg), selenium (Se), and nickel (Ni) are teratogenic. In an environment with a high concentration of heavy metals, excessive intake of heavy metals by animals will cause poisoning and even serious consequences (Zhao, 2010)

2. Pollution status of heavy metals in water

The pollution of heavy metals in water has become a global environmental problem and is also a very prominent issue in China. The results of water quality monitoring in recent years show an increase in heavy metal pollution of major lakes and rivers in China. For example, in the Pearl River of China, approximately 3000 tons of Pb, 15000 tons of Zn, 300 tons of Cd, and 1000 tons of as are discharged into the waters every year, through ship maintenance, metal corrosion, and pesticide application (Yang, 2015). The Yellow River basin, Jiulong River, Poyang Lake, and other aquatic systems have also been polluted to varying degrees (Fan et al., 2008; Li et al., 2010; Yang et al., 2011). The distribution pattern of different heavy metals in the sediments of Poyang Lake is lake area > inlet area > outlet area, indicating that heavy metals are concentrated in the sediments of the lake area. The content of different heavy metals in Poyang Lake is much lower than that in its sediments, indicating that heavy metals in water can easily settle and accumulate in sediments (Li et al., 2010). Cr, Cd, Pb, Cu, and Zn have also been detected in waters near Kosovo. The content of Cr exceeds European water quality standards, especially in sediments (Maloku et al., 2015). From the results of the investigation of heavy metal pollution in water in China and abroad, it was found that the pollution of heavy metals in water occurred as composite pollution due to the coexistence of several heavy metals. Moreover, heavy metals in water are easily adsorbed on the sediments, thereby making sediments a pollutant source that releases heavy metals for a long time. Consequently, there is long-term persistence of heavy metal pollution in water.

3. Sources and hazards of heavy metals in water

Heavy metals can be divided into essential metals (copper, zinc, iron, magnesium, nickel, etc.) and non-essential metals (aluminum, cadmium, mercury, tin, lead, etc.). The sources of heavy metals in water include industrial sources, agricultural sources, and urbanization sources. A large number of heavy metals in the waste gas generated by chemical, electroplating, mining, and metal smelting industries enter the atmosphere and then enter the water bodies through rainfall. Heavy metals such as Cu, As, Hg, and Pb enter the soil through the application of fertilizers and pesticides and then enter the water bodies through rainwater leaching. With the acceleration of urbanization, heavy metals from waste incineration and automobile exhaust can also enter the water bodies through dry and wet deposition (Zhang et al., 2018). Tables 1 and 2 list the sources, hazards, maximum contaminant level (MCL) of some heavy metal pollutants, and the limits of GB 3838–2002 environmental quality standard for surface water (Class III).

Table 1. Sources of some heavy metals in water environment

Heavy metals	Sources
As	Pesticides, fungicides, sedimentary rocks, geothermal water and weathered volcanic rocks, human activities such as mining, manufacturing, gold treatment and wood preservation.
Pb	Paint, pesticide, smoking, automobile exhaust, coal combustion, etc.
Hg	Mineral resources, fossil fuels, ores, pesticides, batteries, paper industry.
Cd	Steel and plastics industry, cooling tower, metal electroplating and coating operation, nickel cadmium battery, cadmium film, solar cell, pigment, galvanized pipe, welding, fertilizer and nuclear emission device.
Cr	Industrial wastewater is discharged into the environment, cooling tower blowdown, electroplating and metal electroplating and coating operations.
Cu	Pesticide industry, mining, metal pipeline, chemical industry.
Zn	Brass mapping, wood pulp production, grinding and newsprint production, iron and steel plants with zinc lines, zinc and brass metal products, refineries and pipelines.
Se	Water loss, rock weathering, rainfall and decomposition of organisms, combustion of coal and oil, agricultural irrigation, use of phosphate pesticides and fertilizers.
Ni	Battery manufacturing, alloy production, zinc base casting, printing, electroplating, silver refinery.

Table 2. Potential toxic effects of heavy metals and the maximum harmful concentration levels (MCL) and GB3838-2002 in China

Heavy metals	Hazards	MCL (mg/L)	GB 3838-2002 In China (mg/L)	References
As	Cancer of the skin, lungs, bladder, and kidneys; cancer and other internal tumor diseases; vascular diseases and diabetes; infant mortality and weight loss of newborns; hearing loss; developmental abnormalities and neurobehavioral disorders; reproductive toxicity; blood diseases; nervous system diseases.	0.05	0.05	Baskan et al., 2011. Ntim et al., 2012
Pb	Anemia; cancer; kidney disease; neurological impairment; mental retardation; mental impairment and behavioral problems in children.	6×10^{-3}	0.05	Salem et al., 2011. Qu et al., 2013
Hg	Damage to the immunity of the renal reproductive system; damage to the blood, cardiovascular and respiratory systems and the brain.	3×10^{-5}	0.0001	Shamsijazeyi et al., 2010; Natale et al., 2011
Cd	Renal cancer damage; bronchiolitis; chronic obstructive pulmonary disease; emphysema; fibrotic bone damage	0.01	0.005	Arias et al., 2002. Vukovi et al., 2010
Cr	Severe diarrhea; vomiting; pulmonary congestion; liver and kidney damage.	0.05	0.05	Liu et al., 2011. Ihsanullah et al., 2016
Cu	Increased blood pressure and breathing; kidney and liver damage; convulsions, spasms, vomiting.	0.25	1.0	Awual et al., 2013，Al-Rashdi et al., 2013
Zn	Gastric nausea; skin irritation; spasms; vomiting and anemia.	0.8	1.0	Deliyanni et al., 2007
Se	Gastrointestinal discomforts; hair and nail loss; fatigue; cardiac arrhythmia and nerve injuries.	—	0.01	Li et al., 2017
Ni	Dry coughing; bone, nose, and lung cancer; shortness of breath; chest tightness and chest pain; nausea and vomiting; dizziness and headache.	0.2	—	Reddad et al., 2002. Yavuz et al., 2003

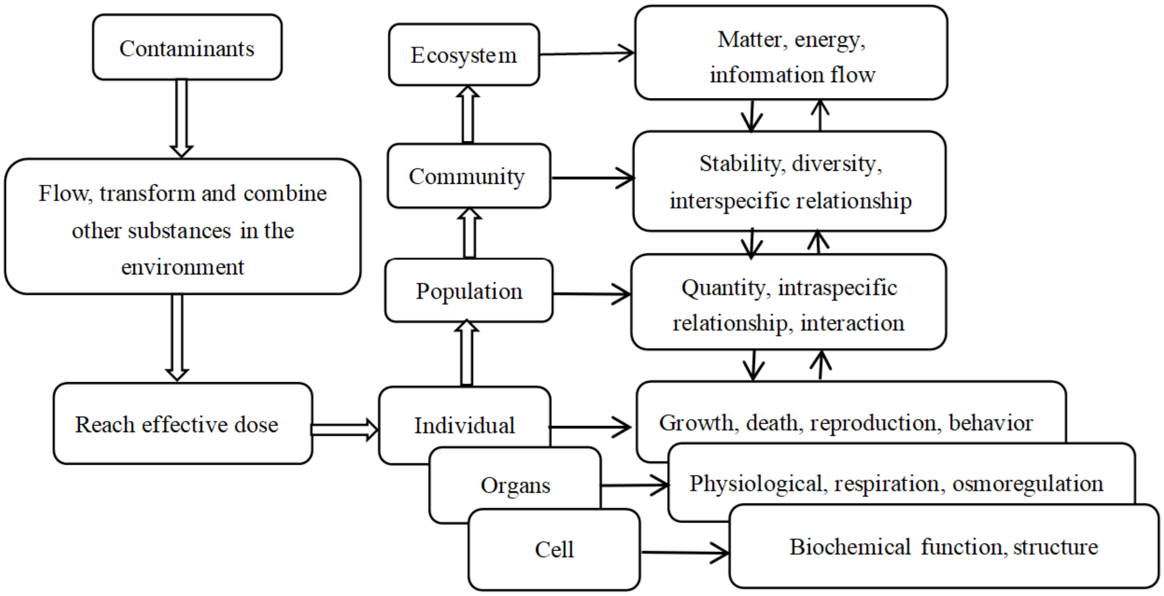

Fig. 1. The toxicological effects of heavy metal pollution on organisms at different levels

4. Pattern of enrichment of heavy metals in aquatic organisms

Heavy metals in water cannot be easily metabolized by aquatic organisms, and therefore, these metals tend to get enriched in organs such as the liver and kidney. Studies have shown that heavy metals can enter aquatic animals through their gills or during feeding and bind with metallothioneins and other substances in the body (Yang, 2015). The pattern of enrichment of heavy metals, however, varies according to the enrichment ability of different aquatic species. In the aquatic environment of the Pearl River Delta of China, the content of Pb in tilapia muscle was found to be higher than that of other species (Leung et al., 2014). At the same concentration, the accumulation of Pb in crucian carp tissues showed the following trend: viscera > gills > fins > muscles, and the content of Pb was significantly higher in viscera (Wang et al., 2015). Zheng et al. (2014) found that the enrichment level of the essential trace elements Fe, Zn, and Cu in the hepatopancreas of fish was higher than that in other tissues. In addition, in the Meizhou area of Guangzhou, the pollution level of heavy metals in fish showed the following trend: Pb > Cr > Cd > Cu. These findings show that fish species encounter the problem of composite pollution of heavy metals rather than pollution of a single metal element.

5. Toxic effects of heavy metals on aquatic organisms

Heavy metals in water enter aquatic organisms in three ways. First, aquatic animals absorb heavy metal ions in water through gill tissues and then transport them to various tissues of the body. Second, aquatic animals absorb heavy metals into their bodies by ingesting food contaminated with heavy metals. Third, heavy metals enter the bodies of aquatic animals by osmotic exchange through subcutaneous absorption (Long et al., 2016). Figure 1 shows the toxicological effects of heavy metal pollution on organisms at different levels.

Some heavy metals entering aquatic animals can promote the growth, metabolism and enzyme activity of aquatic animals within an appropriate concentration range. However, with the extension of exposure time, due to the accumulation effect of metal ions on aquatic animals, when its concentration reaches a certain threshold, it also produces a series of toxicological effects on the growth, physiology and biochemistry, genetic gene expression, behavior, metabolism and other processes of aquatic animals. Moreover, the potential risks of heavy metals to different kinds of aquatic animals are also different. Du et al. (2013) compared the sensitivity of marine vertebrates and invertebrates to eight kinds of heavy metals and the acute ecological risk of different heavy metals, indicating that the ecological risk of heavy metals to crustaceans is greater than that to fish. Bian et al. (2016) showed that aquatic animals of benthic oligochaetes are more sensitive to heavy metal pollution, followed by leeches, gastropods and insects. The enrichment of heavy metals by aquatic animals is related to specific factors such as age, geographical distribution, season, species differences and the form of heavy metals. Moreover, the distribution of different kinds of heavy metals in different tissues of aquatic animals is also different, so it will cause different ecotoxicological effects on aquatic animals.

5.1 Bioaccumulation of heavy metals

Once heavy metals enter the aquatic organisms, they are difficult to be decomposed, metabolized, and excreted and are thus very easily enriched in animal organs such as the liver and kidney. Olivares et al. (2016) confirmed that binding with metal binding proteins such as metallothioneins is the main mechanism of heavy metal accumulation in organisms. Rainbow et al. (1992) found that the process of heavy metal intake by organisms does not require energy expenditure and that heavy metals are not easily excreted and thus show the cumulative effect of toxicity. Qin et al. (2015) studied the acute toxic effects of six types of heavy metals on three species of mariculture organisms and found that the content of heavy metals in three species increased significantly after 96 h of treatment. Sun et al. (2015) investigated the enrichment characteristics of heavy metals in sediments and marine organisms in the sea area of Zhanjiang port and found that except for Cd, the contents of other heavy metals in sediments were higher than those in marine organisms. Cu, Zn, and Cd were highly enriched in organisms in the Zhanjiang port basin. Mollusks and crustaceans showed the same accumulation ability for Hg and Pb; mollusks exhibited a stronger enrichment ability for Sn and Cd and a weaker enrichment ability for Cu than crustaceans. Rzymski et al. (2014) showed that bivalves have a high accumulation ability for Cu and Cd. Topcuoglu et al. (2002) reported the highest enrichment of Pb, Cd, and Cr and the lowest enrichment of Fe and Zn in mollusks and shellfish from the Black Sea, Turkey.

5.2 Effect of toxicity of heavy metals on early biological development

The early embryonic and larval development stages of fish are prone to be affected by heavy metals. After the heavy metal pollutants enter the larvae of aquatic organisms, they react with nucleic acids, enzymes, vitamins, hormones, and other substances in the organisms; alter their chemical structure and biological activity; and then disrupt the functions of multiple systems such as the endocrine and central nervous systems, resulting in various diseases and even death (Tolins et al., 2014; Jakubowski et al., 2015; Meng et al., 2018). Guo et al. (2015) studied the toxicity of heavy metals in water samples from the Three Gorges Reservoir area on the embryonic development of zebrafish (*Danio rerio*). The results showed that after seven days of exposure, although there was no significant difference in the hatching rate, relative survival rate, and deformity rate in all zebrafish embryos, there was a significant decrease in the expression levels of genes related to reproduction and neurodevelopment in juveniles. Zhang et al. (2010) measured the toxic effects of Cu and Cd on embryonic development by using zebrafish early embryonic development technology; the authors found that both Cu and Cd had toxic effects on zebrafish embryos in terms of death and inhibition of embryo hatching at 24 h and 72 h, respectively. García et al. (2014) noted that a certain concentration of Ag ions significantly increased the mortality and distortion rate of eel (*Nereis succinea*) embryos. Munley et al. (2013) found that the embryonic growth of aquatic snails was inhibited after 28 days of exposure to Co, Cu, Pb, and Ni, and the oviposition was inhibited after 56 days. Cu, Pb, and Zn can also significantly interfere with the development of early biological embryos, resulting in delayed embryonic development (Salvaggio et al., 2016).

5.3 Immunotoxicity of heavy metals to aquatic organisms

Low concentrations of heavy metals or short-term exposure to heavy metals can stimulate the immune response of organisms and enhance the phagocytic activity of blood cells (Rickwood et al., 2004; Hannam et al., 2009). However, high concentrations of heavy metals or long-term exposure will significantly reduce the phagocytic capacity of body cells, mainly because heavy metals change the fluidity of the cell membrane and the permeability of ion pumps on the cell membrane and reduce the stability of the cell membrane, thereby leading to a decrease in phagocytic activity (Grundy et al., 1996; Camus et al., 2002). Paul et al. (2014) studied the immunotoxicity of Pb in freshwater fish and found that Pb ions significantly reduced the level of tumor necrosis factor in serum. Qin et al. (2012) reported that Cd exposure affected the enzyme activity in river crab (*Potamidae*). Vijayavel et al. (2009) showed that Ni exposure promoted hemolymph phagocytosis of green crab and significantly inhibited the activity of phenoloxidase. Chandurvelan et al. (2013) revealed that Cd exposure increased the level of basophils and eosinophils in mussel blood, resulting in DNA damage.

5.4. Heavy metals affect gene mutation and variation

After the heavy metal pollutants from the environment enter the organisms, they tend to accumulate in various organs of the organisms. When their concentration exceeds a certain level or after long-term exposure to these heavy metals, they cause damage to the tissue, induce the production of a high amount of reactive oxygen species (ROS) and electrophilic metabolites, and then combine with DNA molecules; consequently, the cells are subjected to oxidative attack from the external environment, resulting in multiple reactions of lipids in the organism, such as peroxidation, alterations in genetic material, and ribose oxidation, which leads to cell death or carcinogenesis (Waisberg et al., 2003; Pan et al., 2005; Thomas et al., 2007). Hix et al. (1999) revealed that DNA is highly methylated when organisms are attacked by a large number of methyl radicals induced by Fe ions. Leszkowicz et al. (1987) also showed that heavy metal ions can significantly inhibit the activity of methyltransferase. For example, Pb, Cu, and Zn ions can inhibit the activity of 5-methyltransferase. Rossiello et al. (1991) also reported that Pb can cause low methylation of DNA. Tang et al. (2013) found that both single and combined toxicity of Cu and Pb caused DNA damage in the eggs of *Misgurnus anguillicaudatus*, thus showing these metals induced genotoxic effects. Xing et al. (2016) also showed that Pb and Cr exerted genotoxic effects on loach in varying degrees, and the toxic effects increased with the increase in treatment concentration and treatment time under certain conditions; moreover, the toxic effects were inhibited after reaching a certain concentration and time.

5.5. Endocrine-disrupting toxicity of heavy metals

One of the mechanisms of metabolic diseases induced by heavy metal exposure is the disruption of the endocrine system by heavy metals. In vivo, heavy metals can interfere with hormone synthesis and secretion and induce endocrine-disrupting toxicity; for example, Cd, Mn, and Cr were found to increase the incidence rate of metabolic disorders. Exposure to metal endocrine disruptors can increase the risk of oxidative stress and induce mitochondrial dysfunction (Rafa et al., 2010). Exposure to sublethal concentrations of Pb and Cd caused a significant increase or decrease in blood steroid concentration, ovarian steroid secretion activity, and ovarian development. Mu (2017) showed that Cd exposure interfered with thyroid hormone levels in the plasma of carp (*Cyprinus carpio*). Luo (2015) found that Cd increased the level of estradiol in serum but had no effect on the level of testosterone. At the gene level, Cd exposure increased the expression of estrogen receptor (ER) in the ovary but inhibited the production of vitellogenin. In the testis, Cd inhibited the development of spermatids and sperm by increasing the expression of the glucocorticoid receptor. Li et al. (2014) found that after minnow larvae were exposed to Hg for four days, the gene expression of the adrenocorticotropic hormone-releasing hormone, thyroglobulin, and thyroid receptors α and β were significantly induced, and the contents of thyroxine T3 and T4 increased.

6. Tolerance mechanism of aquatic animals to heavy metals

Living in the environment stressed by heavy metal ions for a long time, some aquatic animals can adjust some physiological and biochemical indexes to improve their stress and tolerance to heavy metal ions. For example, after Daptmia magna was exposed to high-dose Zn^{2+} for two generations, the reproduction and growth of larvae slowed down, but after three generations of exposure, the growth and reproduction of larvae did not decrease significantly, indicating that multi generations of heavy metal exposure tended to increase the tolerance of Daphnia magna to heavy metals (Vandegehuchte et al., 2010). In aquatic animals, the antioxidant enzyme system composed of SOD and CAT forms the first defense line against heavy metal toxicity, which can alleviate the oxidative damage caused by heavy metals; The second antioxidant damage defense line composed of glutathione and glutathione related enzymes plays an important role in cell metabolism and free radical scavenging. SOD can disproportionate superoxide anion free radicals to produce H_2O_2, which can remove harmful free radicals; CAT can catalyze H_2O_2 to produce harmless H_2O and O_2 and cooperate with SOD and POD to remove excess free radicals and peroxides in the body; GPX can convert H_2O_2 into H_2O and O_2, to reduce the damage of H_2O_2 to body tissues.

Metallothionein widely exists in aquatic animals. Because it is rich in cysteine, the sulfhydryl group on the side chain of cysteine residues can strongly chelate with toxic metal ions, and can combine with 18 metal ions to form non-toxic or low toxic complexes, so as to play the role of detoxification, alleviate the toxicity of heavy metals and protect against oxidative stress (Ryvolov et al., 2011;Sheng et al.,2014). Mao et al. (2012) analyzed the MT gene sequence and protein structure of Charybdis japonica, detected the temporal and spatial expression pattern of MT mRNA during spermatogenesis, and found that Charybdis japonica MT had more non conservative Cys at the C -terminal, which may be helpful to resist heavy metal pollution. The antioxidant enzyme system and antioxidant non enzyme system in aquatic animals will also play a series of detoxification action when aquatic animals are stressed by heavy metals. Kim et al. (2014) found that when Tigriopus japonicus is exposed to water polluted by a certain concentration of Ag, As, Cd, Cu and Zn ions, its antioxidant enzyme system can be effectively activated and can alleviate the damage of reactive oxygen species to itself. Liu et al. (2008) found that low concentration of Ce^{3+} can increase the contents of SOD, CAT, GSH-Px, vitamin and GSH, reduce the accumulation of reactive oxygen species and inhibit lipid peroxidation. Some aquatic animals secrete abundant mucus under heavy metal stress, which can improve their tolerance to metals to a certain extent. For example, the acute toxicological test of striped bass by Tripathi et al. showed that when stressed by heavy metal Cd2+, rich mucus played a good protective role against the harm of toxic heavy metals (Tripathi et al., 2012). Rhee et al. (2013) showed that exposure of Daphnia japonicus to water polluted by a certain concentration of Ag, As, Cd and Cu would significantly increase its GST sigma protein, thus improving its ability to detoxify heavy metals and adapt to the environment. At the same time, the physiological protection mechanism of some marine shellfish and the antagonism between metal ions can also reduce the damage of heavy metal ions to shellfish (Sun et al., 2015). In addition, heat shock protein (HSP) and transferrins (TF) are also one of the important tolerance mechanisms against heavy metal stress (Ding et al., 2012; Yang et al., 2015).

Damaged DNA can be self-repaired by organisms under normal physiological conditions to ensure the stability of genetic genes and reduce the probability of gene mutation. However, when the concentration of heavy metals in the body exceeds a certain threshold or the retention time of heavy metals in the body exceeds a certain time, the repair function will be damaged, resulting in gene mutation; In addition, heavy metals can also interfere with the normal repair process of DNA damage, so that DNA cannot be repaired in time after damage, resulting in the destruction of body tissues. The results showed that DNA damage of digestive gland and gill tissue cells increased with the increase of Cd^{2+} concentration and exposure time within 12 hours; However, within 24 hours, the degree of DNA damage in both tissues decreased in varying degrees, showing a certain repair function to DNA; However, at 96 h, the damage degree of high concentration group began to increase, and at the same concentration, the DNA damage degree of gill tissue was higher than that of digestive gland cells (Lu et al., 2011).

7. Physical and chemical factors affecting the toxicity of heavy metals

Many factors affect the biological toxicity of heavy metals, such as temperature, pH, hardness of water, dissolved oxygen, light, and salinity. In addition, the existing form of heavy metals, the existence of other metals or contaminants, and biological conditions play an important role in affecting the toxicity of heavy metals.

7.1 Temperature

Temperature is one of the regulatory factors of metal ion concentration in the environment and metal toxicity to algae. The toxicity of heavy metals to algae is positively correlated with temperature. Klotz et al. (1981) found that the toxicity of Cu to *Scenedesmus* decreased below the optimum temperature but increased at the optimum temperature. The toxicity of Zn to *Nitzschia linearis* and *Cyclotella meneghiniana* increased with the increase in temperature from 22 °C to 30 °C, while the opposite was true for *Scenedesmus quadricauda* and *Chlamydomonas*. The same results were obtained in the acid sulfate ion toxicity test. The maximum toxicity occurred at the temperature with the most vigorous metabolism. This may be because the increase in temperature enhances respiratory activity, which promotes the absorption of metals by algae. Klotz et al. (1981) showed that temperature change significantly affected the toxicity of Cu to *Scenedesmus* and *Chlorella* and the toxic effect of Cu on algal cell division. The division rate of *Chlorella* cells treated with 0.15 ppm Cu decreased at 6 °C.

7.2 pH and redox potential

pH and redox potential are two important physical and chemical factors that affect the migration and transformation of heavy metals in water. They play a decisive role in the migration and transformation of Zn, Fe, Mn, and Cu. Under acidic and reducing conditions, Fe and Cu exist as easily soluble compounds of Fe^{2+} and Cu^{2+}, while under alkaline or near neutral and oxidizing conditions, insoluble Fe^{3+} and Mn^{4+} oxides and hydroxides are formed. Rai et al. (1990) showed that heavy metals induce high toxicity under acidic conditions, but their toxicity is reduced under alkaline conditions. Their analysis showed that metals exist as free ions at acidic pH, while at alkaline pH, they form insoluble carbonate, phosphate, sulfate, oxide, or hydroxide precipitates. The precipitation of different metals requires different potential and pH values, especially for those metal cations with more than one valence state. The valence state, morphology, and bioavailability of heavy metal ions are restricted by environmental pH and redox potential. Therefore, at acidic conditions, most metals are free cationic, organic matter can be most utilized and toxic; Under alkaline conditions, the opposite is true (Les et al., 1984). Peterson et al. (1990) showed that the toxicity of Cd to crescent algae increased by eight times for each unit of pH increase, but the change in the toxicity of Cu was smaller. At pH 6, the toxicity of Cd was 500 times lower than that of Cu, while at pH 10, the toxicity of Cd was twice that of Cu.

7.3 Dissolved oxygen

When the temperature and contaminant concentrations are constant, the toxicity of toxic substances tends to increase with the decrease in dissolved oxygen concentration. This is because when the level of dissolved oxygen is insufficient, to obtain adequate oxygen, the respiratory and circulatory systems increase their activity, and the amount of water flowing through the gill filaments increase; consequently, the amount of toxins entering the body increases, and these toxins are transported to each sensitive organ through the blood, resulting in enhanced toxicity. Dissolved oxygen also has an important effect on the redox state of water, which will significantly change the presence of chemical elements with variable valence in water, thus affecting their biological effectiveness. For example, the concentration of heavy metals in sediment interstitial water with extremely low dissolved oxygen content and anaerobic microorganisms is ten times higher than that in upper clear water, resulting in greater toxicity to aquatic organisms residing in the sedimental region.

7.4. Hardness of Water

It is believed that water hardness affects the toxicity of heavy metals through the formation of insoluble carbonate or calcium carbonate absorption. However, the increase in Ca^{2+} and Mg^{2+} plasma concentration can reduce the toxicity of heavy metals; hence, it is considered to have a protective function. Pellegrini et al. (1993) systematically studied the detoxification of Ca^{2+} on Cd, Cu, and Zn in brown algae. They designed a series of experiments and found that Ca^{2+} had a protective effect in all experiments, but the detoxification mechanism was not clear. Bjerselius et al. (1993) conducted the acute toxicity test of Atlantic salmon to Cu and found that when the concentration of Ca^{2+} and Mg^{2+} increased, the toxicity of Cu decreased. Jayaraj et al. (1992) studied the effects of Ca, Mg, and Fe on the toxicity of Cu, Cd, and Ni in algae. They found that the increase in Ca^{2+} and Mg^{2+} concentration reduced the toxicity of these heavy metals before their concentration reached 100 mg/L, but the opposite situation occurred when the concentration continued to increase further. Although it has been suggested that the effect of common ions such as Ca and Mg on heavy metal toxicity is related to the competitive reaction of metal ions at the active site, this view needs to be further discussed.

7.5. Organic matter

Many studies have shown that organic complexes can reduce the toxicity of heavy metal pollutants because the combination of heavy metals and organic complexes reduces the concentration of free metal ions. Oikari et al. (1992) found that humic acid (HA) increased the toxicity of Cd and Cr to *Daphnia magna*. Stackhouse and Benson (1989) reported that when 0.5 mg/L HA was added to water, *Daphnia magna* could enrich more Cd, while the metal enrichment decreased when HA concentration was higher (5–50 mg/L). This shows that the effect of HA on metal toxicity is multifaceted, and its mechanism remains to be discussed. The biological toxicity of heavy metal complexes has also been reported, such as the secretion of copper and algae, copper and citric acid, and ethylenediamine complexes. Tubbing et al. (1993) confirmed that regardless of how high the EDTA concentration is, a small amount of copper can cause changes in the structure and function of bacteria and algae. All these findings show that the EDTA complex copper is also toxic to bacteria and algae.

7.6. Biological factors

Biological factors that affect the toxicity of heavy metal ions in water include biological age, size, weight, growth period, and tolerance. For example, the 96-h 50% lethal concentration of Cd is 2, 5, and 7 μg/L for carp younger than 10 days, carp aged 10–20 days, and carp aged more than 20 days, respectively.

CONCLUSION

When heavy metals enter the natural water environment, they can only migrate and transform among various forms through adsorption-desorption, dissolution-precipitation and oxidation-reduction, and finally stay in the water environment for a long time in one or more forms, resulting in permanent potential harm (Zhou et al.,2005). With the change of environmental conditions, the toxicity of some heavy metals may be strengthened or weakened. For example, the granular heavy metals deposited in the sediment will be re-released into the water body when the redox potential changes, resulting in secondary pollution (Daniele et al., 2008). The toxicity of heavy metals to aquatic organisms is a complex process, and the combined toxicity between heavy metals and between heavy metals and other organics is even more complex. Therefore, the research on the toxicity of heavy metals to aquatic organisms has a long way to go; At the same time, the research on the tolerance mechanism of aquatic organisms will also be of far-reaching significance in the prevention of heavy metal pollution.

With the development of science and technology and the deepening of ecotoxicological research on heavy metals in water, it is believed that some new tolerance mechanisms of aquatic organisms to heavy metals will be put forward. Especially in the low-dose and long-term exposure of heavy metals, it is of great significance to deeply understand the toxic mechanism of heavy metals and the health status of aquatic animals. The following suggestions are put forward for the future research on the ecotoxicological effects of heavy metals on aquatic organisms: (1) Due to the significant internal relationship between sediment particles and suspended particles in water and the enrichment, migration and bioavailability of heavy metals, the research on the bioaccumulation model of heavy metals in sediment and suspended particles in water can be strengthened and further study, predict and understand the response and change of organisms to heavy metals in water environment. (2) Because the harmful effects of some aquatic organisms are the result of the long-term effects of toxic heavy metals, the concentration of heavy metals in the water environment is usually lower than the acute poisoning dose and is difficult to detect, but even low concentration levels can have a significant impact on the growth, reproduction and survival of aquatic organisms (Sfakianakis et al., 2015). Therefore, we should conduct comprehensive research on acute toxicology test, subacute toxicology test and chronic toxicology test, analyze and establish a database of various diseases caused by aquatic organisms over time, to provide more basis for formulating water environmental sanitation standards. (3) Strengthen multidisciplinary cooperation, conduct in-depth research on the ecotoxicological effects of different forms of heavy metals and compound pollution coexisting with other pollutants on aquatic organisms and the tolerance mechanism of aquatic organisms themselves, and accurately locate the key factors of heavy metal injury and biological tolerance. It is of great significance for the formulation of environmental quality standards for heavy metals, the establishment of a complete and reliable water quality risk assessment system, the remediation and treatment of heavy metal pollution in water, biological evolution and improvement, etc.

Author contribution statement

Yanli Wang: Conceptualization, Investigation, Writing – original draft, Writing – review & editing.
Qi Li: Conceptualization, Writing – original draft, Writing – review & editing.
Xiao Yun: Resources, Writing – review & editing.
Jie Zhou: Resources, Writing – review & editing.
Jiting Wang: Conceptualization, Methodology, Writing – review & editing, Project administration, Supervision.

Declaration of interest statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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