Eco. Env. & Cons. 26 (1) : 2020; pp. (180-184)
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ISSN 0971–765X

Biological and ecological impact of iron and iron nanoparticles across diverse array of fish models: A review

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(Received 11 August, 2019; accepted 29 September, 2019)

ABSTRACT

The present literature reviews concerns the ecological and biological impact of iron and iron nanoparticles across diverse array of fish species in aquatic ecosystem around the globe. Iron and its derivatives such as sulphates, oxides, chlorides, nanoparticles etc have been reported to have a deleterious effect on embryology, hematology, physiology, biochemistry, metabolism and histological parameters in fish. Different species of fish like *Danio rerio, Labeo rohita, Catla catla, Oncorhynchus mykiss, Salmo trutta* and their response to iron toxicity has been extensively discussed in the review. Finally based on studies performed by many research groups, we can conclude that iron and iron nanoparticles pose a serious threat not only to fish, but ecology and environment as a whole.

Key words: *Ecology, Environment, Fish, Iron, Nanoparticles*

Introduction

Greater part of water bodies around the world is contaminated due to human and industrial interference. The pollutants of concern are heavy metals, pesticides, nanoparticles, herbicides, pharmaceutics etc. Perhaps among the above, heavy metals poses a grave threat to aquatic ecosystem, which sequentially affects the principal source of nutrition that is, fish. Reports on biotransformation of xenobiotic molecules in fish have been focused on definite metabolite formed, because the following metabolic reactions influence the distribution, accumulation and toxicity of metals and their derivatives (Lech and Bend, 1980). Fishes are susceptible to frequent uptake of heavy metals and their derivatives through gills and other tissues like skin, thus leading to bioaccumulation of metals in different tissues of the fish (Fatima and Usmani, 2013). Iron is abundantly found in earth's crust and also naturally occurring in aquatic ecosystem, however due to human activity the concentration of iron in aquatic environment is found to be more than desirable. Alleviating the accumulation and their effects is challenging due to their complex speciation, which is determined by redox potential, dissolved oxygen, pH and organic matter (Vuori, 1995). In aqueous ecosystem, iron exists in two oxidation states, reduced ferrous ion (Fe II) and oxidized ferric ion (Fe III). In fresh water rich in oxygen, ferrous ion oxidizes to ferric ions. In waters (pH > 6.5), ferric ions are insoluble and vigorously precipitate as hydroxides and oxyhydroxides (Hem, 1985; Kimball *et al.*, 2007). Thus different forms of iron are detrimental

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to aquatic organisms in diverse aquatic conditions. In the present literature we discuss the effect of iron and their derivatives including nanoparticles on different array of fishes.

***Danio rerio*: Zebra fish**

Zebra fish is one among the main model organism that has been used extensively. Zebra fish presents the perfect fish model over other vertebrates due to its early morphology, size and maintenance. Zebra fish eggs are transparent from fertilization to proliferation and pigmentation, which is initiated at 30-72 h post fertilization (hpf); this facilitates unhindered observations of the development phase (Chakraborty et al. 2016). There is also a high percentage (75%) similarity between zebrafish and human genomes, with high genomic homology, making it a perfect model organism for research (Hafiz *et al.,* 2018). Hafiz *et al.* investigated the effect of iron oxide nanoparticles on zebra fish. The fish in the studies were exposed from 8 hpf to 7 dpf to 1, 5, 10, 50 and 100mg/L iron oxide nanoparticles. The results demonstrated LC_{50} of 10 mg/L to iron oxide nanoparticles. Further both concentrations of 50 mg/L and 100 mg/ L demonstrated developmental toxicity in the embryos leading to mortality and delay in hatching. The research indicates that appropriately dissolved nanoparticles and particles which is extremely small can effortlessly pass through the chorion pores, thus causing blockage of oxygen transport to embryos and subsequently leading to mortality. Zhu *et al*., 2012 reported the ecological effect of iron oxide nanoparticles on early life stages of zebrafish. The studies were performed to understand the effects of nanoparticles on embryonic development of the fish. The results revealed that e" 10 mg/L of iron oxide nanoparticles triggered developmental toxicity in the embryos, leading to hatching delay, mortality and malformation.

***Labeo rohita:* Rohu**

L. rohita is a fresh water fish of the carp family. It is a large omnivore used in aquaculture and extensively consumed. Remya et al. 2015 reported the chronic effects of iron oxide nanoparticles (Fe_2O_3NPs) of 500mg/L concentration on hematological, ionoregulatory and physiological parameters of *L. rohita.* The results showed remarkable increase in hemoglobin (Hb), red blood cell (RBC), haematocrit (Ht) values when compared to control groups, throughout the analysis period of 25 days. On the other hand, mean cellular volume (MCV), mean cellular hemoglobin (MCH) and mean cellular hemoglobin concentration (MCHC) and white blood cell (WBC) levels were found to be deceasing during the entire period of study. Interaction of iron oxide nanoparticles in fish biology also lead to variations in ion regulation resulting in hyponatremia (Na^+), hypochloremia (Cl^-) and hypokalemia (K^+). A dual phase characteristic was observed in gill Na^+/K^+-ATPase activity. The results summarize the toxicological impact of iron oxide nanoparticles on the physiology and metabolism on *L.rohita*. Keerthika et al. 2016 reported behavioral changes in *L. rohita* when exposed to iron oxide nanoparticles. The study showed changes in behavior patterns such as bottom resting, surface separation and jerk movement at sub lethal concentrations (300 ppm and 30 ppm).

***Catla catla*: Catla**

Catla catla is a major fresh water carp, rich in protein source and is reported to attain a length and weight of 185 cm and 50 kg (Ilavazhahan *et al.,* 2012). It is known to be a surface and mid water feeder, feeding mainly on phytoplankton, decomposed organic matter and phytoplankton. Because of its high nutritive source, it's widely consumed. Ilavazhahan *et al.,* 2012 reported toxicological impact of ferrous sulphate (iron sulphate) on *C. catla.* Biochemical analysis in different tissues such as liver, brain, muscle and kidney revealed remarkable variations in sugar, protein and lipid levels in theses organs compared to control. This observation is interpreted as stress induced on fish, due to heavy metal toxicity. Sub lethal concentration of iron sulphate to *C. catla* was observed to be 2.1 ppm (LC_{50}) during the 96 h observation. The undesirable changes were also attributed to significant changes in metabolism processes such as gluconeogenesis and fatty acid synthesis.

***Oncorhynchus mykiss*: Rainbow trout**

Rainbow trout belongs to species of salmonid and is widely distributed in cold water tributaries of the Pacific Ocean in Asian and North America. Özgür *et al.,* 2018 reported the ecological impact of iron oxide nanoparticles on rainbow trout spermatozoon. They subjected the different doses of iron oxide nanoparticles (50, 100,200,400 and 800 mg/L) at 4 °C for 24 h on *O. mykiss* (rainbow trout) spermatozoon. They observed significant ($p < 0.05$) decrease in the velocities of spermatozoon after exposure to 400 mg/L of iron oxide nanoparticles. They also reported decrease in catalase (CAT) and superoxide dismutase (SOD) activities when exposed to 100 mg/L of iron oxide nanoparticles for 24 h. Total glutathione and malondialdehyde levels were also reported to increase when exposed to 400 and 800 mg/L respectively of iron oxide nanoparticles. From the above observations Özgür *et al.* concluded that imbalance between the antioxidant system and oxidative stress lead to oxidative damage in turn caused the exposure of spermatozoon fur to iron oxide nanoparticles (> 200mg/L).

***Salmo trutta*: Brown trout**

S.trutta (brown trout) is a species of salmonid fish originating in Europe. Though from Europe, the brown trout has been extensively introduced into different aquatic ecosystems globally. Dalzell and Macfarlane, 1999 studied the impact of two types of iron (i) commercial iron (III) sulphate liquor (ii) analar grade iron (III) sulphate on brown trout for 96 h. The LC_{50} of the above iron types were reported to be 28 mg total Fe/L (0.05 mg soluble Fe/L) and 47mg total Fe/L (0.24 mg soluble Fe/L) respectively. Both sublethal and lethal exposure to different kinds of iron showed gill accumulation, indication of iron toxicity. However higher accumulation, couple with prominent gill tissue damage was reported in commercial iron sulphate liquor. However the further uptake of accumulated iron in gills was not found during tissue examination. The authors concluded that respiratory disruption due to physical clogging of iron particles may be the likely mechanism for iron toxicity.

***Oreochromis mossambicus*: Mozambique tilapia**

The *O. mossambicus* is a tilapiine cichlid fish found chiefly in Southern Africa region. However due to human introduction it can be seen in many tropical and subtropical ecosystem around the world. Karthikeyeni *et al.,* 2013 reported the changes in hematological parameters in *O. mossambicus* upon exposure to iron oxide nanoparticles. *O. mossambicus* were exposed to different concentrations of iron oxide nanoparticles (0.5, 5 and 50 ìg/mL). Significant variations were reported in hematological (RBC, WBC, HCT, Ht) levels and biochemical variables (SGPT and SGOT) during the 96 h exposure period. Biochemical experiments reiterated that iron oxide nanoparticles were relatively less toxic, up to 50 ìg/mL concentration in *O. mossambicus.* However they also reported elevated levels of SGPT (serum glutamatic pyruvic transaminase) and SGOT (serum glutamic oxaloacetic transaminase) till 48 h period, suggesting hepatic tissue damage due to accumulation iron oxide nanoparticles in fish. Vidya and Chitra, 2019 established the irreversible histopathological damage in *O. mossambicus* upon exposure to iron oxide nanoparticles. Sublethal concentrations of iron oxide nanoparticles (15 mg/L) were treated to *O. mossambicus* for acute (96 h) and chronic (60 days) exposure. Histopathological modifications revealed vacuolization, loss of secondary lamella, mucous deposition and blebbing of gill epithelium. Fish liver displayed tendency of necrosis and aggregation of melanomacrophages, segmentation of hepatocytes, vacuolization and spindle shaped nucleus. Lesions were observed in the brain tissue accompanying degeneration and significant loss of granular cells, aggregation of gliosis after chronic exposure. However the observed histological modifications remained unchanged even after withdrawal of the treatment. This study confirms the irreversible damage caused by iron oxide nanoparticles on *O. mossambicus.*

***Rutilus kutum*: Caspian Kutum Fish**

The Caspian kutum belongs to cyprinidae family of fish, found widely in brackish water habitats of the Caspian Sea and its tributaries. Zahedi *et al.,* 2014 demonstrated the accumulation and acute toxicity of iron on kutum fish. Kutum fish was esposed to iron at several concentrations (105, 111, 117, 123, 129 and 135 mg/L) and observed for 96 h to establish LC_{50}. For sublethal examinations kutum fish was exposed to 12.3 mg/L of iron. Probit analysis revealed the 96 h LC_{50} value for iron to be 122.98 mg/L. The research also showed accumulation of iron in the gill tissue of kutum fish.

***Leporinus friderici:* Threespot leporinus**

L. friderici belongs to Characiformes order and Anostomidae family and is mostly found in the Neotropical region. It is one of most widely distributed fish in the various aquatic ecosystems in the Amazon and also has a economic importance (Olovatti *et al.,* 2011). Da costa *et al.,* 2019 reported iron toxicity in *L. friderici.* They reported the toxicity both forms of iron ions (Fe^{2+} and Fe^{3+}) in juveniles of *L. friderici.* They observed toxicity impact through the acute toxicity, hematology and opercular beat analysis. Buffer solutions of Fe^{2+} and Fe^{3+} ions were treated to juvenile fish at different concentrations (1, 3, 7.5, 15 and 30 mg/L) for 96 h. Both the iron ions displayed varied degree of toxicity and lethality to *L. friderici,* but both showed 100% lethality to fish at 30 mg/L. Fe^{3+} showed lethality at even 7.5 mg/L and 15 mg/L. Their studies reported decreased glutathione levels (GSH), and elevated levels of hemoglobin and methemoglobin in fish treated with both the iron ions.

***Gonoproktopterus kolus*: Kolus barb**

G. kolus belongs to ray finned fish species and Hypselobarbus genus, found extensively in the Western Ghats region of southern India. Karanjkar and Deshpande, 2016 studied the iron induced alterations in biochemical variables in *G. kolus.* The studies were perfomed on the fingerlings of *G. kolus* which were exposed to ferric chloride for 96 h. LC_0 and LC_{50} were reported to be 1.370 ppm and 1.928 ppm. They analyzed the glycogen, protein and and lipid in liver, gill, intestine and muscle of juvenile *G. kolus.* They inferred that the glycogen and total lipid in all the tissues decreased when compared to the control during acute exposure. They also reported depletion in protein levels in all tissue except in kidney.

***Heteropneustes fossilis*: Shingi fish**

H. fossilis belongs to the species of airsac catfish found extensively in the sub continent aquatic environment. Findings of Jahan *et al.,* 2015 on bioaccumulation and toxicity of iron on *H. fossilis* and its possible impact on human health has been discussed below. *H. fossilis* were exposed to ferrous sulphate and LC_{50} was found to be 109, 68 and 45 mg/L for 24, 48 and 72 h. They reported that the moisture content in the fish was elevated due to the release of toxicant during metabolism. Their findings suggest decrease in protein and lipid concentrations and increase in the ash content with the increase in the duration of exposure. They concluded that exposure of iron salt at toxic doses led to bioaccumulation of iron in fish tissue.

Conclusion

In conclusion, the studies discussed in the literature review have suggested that iron and its derivatives, in the form of ions, oxides, chlorides, sulphates, nanoparticles pose a grave threat to the aquatic ecosystem of the fish, when present in abnormal concentrations. They seem to intervene with the developmental phase, spermatozoon, tissue growth, hematology, physiology, ion regulation and metabolism of the various species of fish. Thus it can be concluded that a suitable regulation in place is very essential for not only alleviating the present issue of iron accumulation and damage but also to avert its danger in forthcoming years.

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