Review Article

# Bioaccumulation of heavy metals in various tissues of fish and their Human health risk assessment


## Abstract

Heavy metals are being utilized in a variety of ways in industries, agriculture, and food processing and household in many forms. Metals are unique environmental and industrial pollutants in the sense that they are neither created nor destroyed by human beings but are only transported and transformed into various products. The aim of the present review paper to find various effects of heavy metals on fish and other aquatic. The polluted areas receiving effluents from industrial, agricultural, municipal and domestic wastes. The order of abundance of the metals were as fellow; Fe > Zn > Cu > Mn > Cd > Pb > Cr > Ni > Hg > As. Most studies showed that essential metals (Fe, Zn, Cu, and Mn) in aquatic organisms are much high, but the quantities of non-essential metals are found to be less. This review has shown that fish and other aquatic organisms are used as bio-monitoring species in heavy metal pollution. It is suggested that such investigations should be continuous in terms of both human health and determination of metal pollution in aquatic environment.



**Keywords:** Metals, Pollution, Species, Human health and Bio-monitoring


## Introduction

The toxic pollutants such as heavy metals that are released from point and nonpoint sources have a severe impact on health and ecological integrity of the aquatic ecosystem. The contamination of aquatic ecosystem has emerged as an environmental issue in the last few decades (Maurya and Malik 2016b). In the recent years, world consumption of fish has increased simultaneously with the growing concern of their nutritional and therapeutic benefits. In addition to being an important source of protein, fish typically have rich contents of essential minerals, vitamins, protein, and unsaturated fatty acids (Medeiros et al. 2012).

The bioaccumulation may therefore depend on the food sources, the physiological state of the fish, and the toxicological dynamics of the species. The occurrence of metals in higher concentrations is a serious threat because of their toxicity, long persistence, and bioaccumulation and biomagnification in the food chain (Eisler 1993; Has-Schon et al. 2006; Maurya and Malik 2016c). Fish are considered to be the most significant bio-monitors in aquatic systems for the estimation of metal pollution level (Rashed 2001; Authman 2008). They offer several specific advantages in describing the natural characteristics of aquatic systems and in assessing the changes to habitats (Lamas et al. 2007). In addition, fish are located at the end of the aquatic food chain and may accumulate metals and pass them to human beings through food, causing chronic or acute diseases (Malik et al. 2015b). Fish play a major role in the human diet as they bring a good amount of proteins. Numerous studies on toxic pollutants and on metal pollution in different species of edible fish have been carried out (Kucuksezgin et al. 2002; Lewis et al. 2002; Prudente et al. 1997). There are five main pathways for the entry of the heavy metals in fish tissues. These include ingestion of food through gills, skin, and vocal cavity through the intake of water and integument (Kotze et al. 1999). Metals get absorbed into blood and are transported to various organs for either storage or excretion. The level of trace metals in different organs is used as an index of metal pollution in an ecosystem, which is considered as an important tool for highlighting the health of an organism. Due to feeding and living in the aquatic environments, fish are particularly vulnerable and heavily exposed to pollution because they cannot escape from the detrimental effects of pollutants (Yarsan and Yipel 2013; Saleh and Marie 2014). Fish, in comparison with invertebrates, are more sensitive to many toxicants and are a convenient test subject for indication of ecosystem health (Adams and Ryon 1994). Heavy metals are produced from a variety of natural and anthropogenic sources (Bauvais et al. 2015; Gupta et al. 2015; Yadav et al. 2017a). Heavy metals analyzed in the present study included cadmium (Cd), chromium (Cr), lead (Pb), zinc (Zn), and copper (Cu), which are required in very less quantity for the functioning of different biological systems. Pb and Cd are known to produce adverse effects in biological system. The aim of this study was to examine the accumulation of heavy metals in the selected fish species and their impact assessment regarding human health risk. The selected fish species were obtained from different places of river Ganga at Kanpur, Allahabad and Varanasi. The occupational exposure to cadmium, chromium, lead, and copper caused respiratory problems and effects, lung function, and changes in the nasal mucosa. The histopathological examination of respiratory tract tissues revealed chronic inflammation of the lung. Heavy metal toxicity does not only have adverse effects on human health but also affects animals, plants, and aquatic microorganisms (Yadav et al. 2018). Metal toxicity depends on the absorbed dose, the route of exposure, and the duration of exposure, such as acute or chronic. This can lead to various disorders and can also result in excessive damage due to oxidative stress induced by free radical formation (Jaishankar et al. 2014). Deliberate consumption of arsenic in the case of suicidal attempts or accidental consumption by children may also result in cases of acute poisoning (Mazumder 2008). Lead is an extremely toxic heavy metal that disturbs various plant physiological processes, and unlike other metals, such as zinc, copper, and manganese, it does not play any biological functions (Jaishankar et al. 2014). High doses may lead to death, usually 2–4 weeks after the onset of symptoms. Even at low concentrations, lead treatment was found to cause huge instability in ion uptake by plants, which, in turn, leads to significant metabolic changes in photosynthetic capacity and ultimately in a strong inhibition of plant growth (Yadav et al. 2017a).

**Table 1: Heavy metals permissible concentration ppm in water.**

| **Heavy metals** | **Limiting concentration in water (ppm)** |
|---|---|
| Aluminum | 0.05 - 0.2 |
| Arsenic | 0.01 |
| Mercury | 0.002 |
| Lead | 0.015 |
| Chromium | 0.1 |

ppm= part per million

**MAIN SOURCES OF HEAVY METALS:**

Contaminations of heavy metals in water also lead to changes in the chemical components of the aquatic environment, usually influences the behavioral, physiological, and bloodstream patterns, cell structures ionic balance (Oikari and Soivio 1976), liver function, and carbohydrate metabolism (Oikari and Soivio 1976; Oikari and Nakari 1982) of fishes. Earlier studies, showed that anthropogenic activities and domestic effluent constitute huge sources of heavy metal which contribute to the steadily increasing metallic pollutant in aquatic environment in most part of the world (Jibiri and Adewuyi 2008; Ates et al. 2015). Recent development and advancements in the agricultural sector, industrialization, and urbanization have contributed substantially to elevated heavy metal pollution in freshwater and marine environments. Anthropogenic activities such as mining and smelting (Chen et al. 2015), combustion of fossil fuel refining (Muradoglu et al. 2015), discharge and disposal of domestic and municipal wastes

(Khan et al. 2016), using pesticides in agricultural sector (Ogunlade and Agbeniyi 2011), sewage irrigation in some countries (Sun et al. 2013), fertilizer and urea application (Atafar et al. 2010), dust (Chen et al. 2011) contribute to spread the levels and concentrations of dangerous heavy metals in the aquatic environments. The major sources of heavy metals are summarized in Table 1. Generally, metals can be categorized as biologically essential and nonessential. The nonessential metals (e.g., lead (Pb), mercury (Hg), cadmium (Cd), aluminum (Al), and tin (Sn)) no study has proven their biological function (also called xenobiotics elements or foreign elements), and their effects and toxicity rise with increasing the levels and concentration of these metals, on the other hand essential metals (e.g., zinc (Zn), iron (Fe) copper (Cu), cobalt (Co), nickel (Ni), chromium (Cr) and molybdenum (Mo)), have a known their biological role, and their effects and toxicity occur either at metabolic deficiencies or at high levels and concentrations of these metals (Sfakianakis et al. 2015). The deficiency of an essential metal can lead to adverse health effects, whereas the high levels of essential elements can also lead to negative effects which are equivalent to or worse than those effects caused by non-essential metals (Kennedy 2011; Sfakianakis et al. 2015). The most commonly investigated and found heavy metals in fish and other aquatic organisms in many studies are Zn, Cu, Pb, Cr, Cd, Ni, Hg, Co, Sn, and Mo.

**HEAVY METAL AND HUMAN HEALTH:**

Consumption of contaminated food is the main source of exposure of humans to the risks of heavy metals (Liu et al. 2010). The presence of heavy metal in commercial fish can pose potential health risks to humans (Cid et al. 2001; Castro-gonzález and Méndez-armenta 2008; Saeedi et al. 2012; Ullah et al. 2017). Hence, it is important to know the level and concentration of heavy metal contents in aquatic organisms in order to ensure that it does not expose any hazard to the human and maintain concentration under permissible level (Sivaperumal et al.

2007; Uysal et al. 2008; Palaniappan and Karthikeyan 2009; Dehghani et al. 2017; Pal et al. 2018). Heavy metal pollution is increasingly recognized as a serious, environmental issue by environmentalists, high levels of toxicity, persistence, and potential for accumulation inside human body pose a serious health threat to the residents of urban areas (Karim et al. 2015; Mohmad et al. 2015; Hwang et al. 2016; Gope et al. 2017; Khan and Strand 2018; You et al. 2018; Liu et al. 2019; Men et al. 2019; Tian et al. 2019). Many organizations and institutions such as the Food and Agriculture Organization (FAO), World Health Organization (WHO) and European Union (EU) from different countries have been established about the maximum permitted concentration of heavy metals in foodstuffs including fish and other seafood (Chary et al. 2008; Xue et al. 2012). For example, European Union (2006) reported that the maximum tolerable limit (MTL) of lead (Pb) in the edible tissues of fish is 0.3 mg/kg where Cd and Hg were about 0.05-0.30 and 0.5-1.00 mg/kg wet weight respectively depends on the type of fish. Heavy metals such as Pb, Cd and Hg are categorized as nonessential elements and they are very toxic and harmful to individuals and aquatic organisms, even at small levels (Thomas et al. 2009; Zheng et al. 2011; Bourliva et al. 2018). While, Zn, Mn, Cu, and Ni are essential elements due to their important function in biological systems (Stern et al. 2007; Fernandes et al. 2008). The dose-response curve for essential metals is U-shaped due to those metals that have both deficiency and copper excess which produce adverse health (Stern et al. 2007).

**ACCUMULATION OF HEAVY METALS AND THE ECOLOGICAL STATUS OF AQUATIC ORGANISMS:**

The rapid development of industry and agriculture has resulted in an increase in the pollution of coastal areas with heavy metals, which have been identified as a significant environmental hazard for invertebrates, fish, and humans. ) Significant quantities of heavy metals in waster water are discharged into aquatic environments. These metals can be strongly accumulated and biomagnified along water, sediment, and aquatic food chains, thus resulting in sublethal effects or death in local fish populations and other aquatic animals (Yi and Zhangc 2012). Heavy metals like copper and zinc are essential for fish metabolism, while others such as mercury, cadmium, and lead have no known role in biological systems (Yi and Zhangc 2012; Ates et al. 2015). Therefore, it is important to better understand the relationships between ecological status of aquatic organisms and the concentrations of both essential and nonessential metals. Heavy metal pollution of water and sediment in the Karachi Coast has attracted much attention from researchers (Ahmed et al. 2017b).

**Heavy metal exposure in natural fish populations**

The studies of natural fish populations' exposure to heavy metals have not been conducted under controlled laboratory conditions and therefore precision in details of important parameters (such as the metal's exact concentration, the possible synergistic effect of other pollutants present in the area etc.) is lacking. Those studies are based on the metal's tracing primarily on fish tissues or secondarily in the water or sediment of the natural habitat.

As far as fish deformities are concerned, it is well established today that they mostly appear in cultured populations mainly due to the environmental conditions prevailing and secondarily due to other factors such as genetics, general husbandry etc. (Boglione et al., 2013, Sfakianakis et al., 2006, Sfakianakis et al., 2013b). In some cases, the incidence of deformities in fish populations under aquaculture conditions has been reported to be over 80% (Sfakianakis et al., 2006). Wild populations on the other hand, are considered to be ideal and therefore – in general – free of deformities (Sfakianakis et al., 2004). Consequently, when natural fish populations bearing deformities are discovered, the first assumption always is that there must have been – at some level – an exposure to certain pollutants (usually organic compounds or heavy metals) (Bengtsson and Larsson, 1986, Bengtsson et al., 1985, Bengtsson et al., 1979).

**Discussion and Conclusion:**

The pathway through which heavy metals induce deformities in fish is not quite clear yet and it seems to be different for each metal. Sassi et al. (2010) argue that Cd induces disturbance of the Ca balance in the cellular bone tissue of *G. affinis* and that in turn would probably lead to a situation in which hypocalcemia is compensated by an increased release of Ca from skeletal bone. As a result, the spinal column would become more fragile and increasingly susceptible to deformities. Cd may also directly induce bone deformities by negatively affecting the bone matrix or the bone tissue itself, disturbing bone remodeling and mineralization. In addition, Cd may interfere with the crystallization of the main bone mineral hydroxyapatite and osteoblast activity (Blumenthal et al., 1995, Suzuki et al., 1989). According to Muramoto (1981), cadmium induced body deformities in fish, were related to a decrease in Ca and P content. Developmental deformities may also originate from genotoxic action of Cd and Cu (Cavas et al., 2005). The delay of hatching which is very common in heavy metal exposure has been attributed to the effect of the metals on mitotic divisions (Perry et al., 1988).

Concerning fish larvae, decrease in fish growth caused by copper or cadmium intoxication may be a result of various metabolic disturbances. Couture and Kumar (2003) reported a direct inhibition of mitochondrial enzymatic activity and oxidative metabolism in *Perca flavescens* exposed to copper and cadmium. Detoxification is a process which requires high metabolic costs and may also reduce growth of fish exposed to Cd and Cu. According to Wu and

Hwang (2003), Cu and Cd exposures induced metallothionein synthesis in *O. mossambicus* larvae. These metals also cause ionoregulatory disorders in fish which may again cause increased metabolic cost of the compensatory osmoregulation and also lead to growth reduction due to the inevitable energetic deficiency (Witeska et al., 2014).

According to other authors (Kennedy, 2011), the effect of heavy metal poisoning could also be indirect; vertebral deformities can be the result of a nutritional deficiency as fish exposed to heavy metals stop feeding (which results in vitamin C deficiency etc.).

Regarding fish, it is well established that the younger the stage, the more sensitive the organism is. A recent study on heavy metals (Zhu et al., 2011) contradicts this general knowledge as it has shown that the Chinese rare minnow (*Gobiocypris rarus*) – when exposed to 3 different heavy metals (Cu, Zn and Cd) – was more sensitive during the larval stage rather than the embryonic one. The same conclusion is reached in 2 earlier studies concerning the effect of cadmium and copper on Common carp (Witeska et al., 1995, Jezierska et al., 2009b).

In teleost species, it is generally accepted that skeletal deformities can be environmentally induced in two ways: (i) by alteration of biological processes necessary for maintaining the biochemical integrity of bone, or (ii) through neuromuscular effects, which lead to deformities without a chemical change in vertebral composition (Avyle et al., 1989). Most of the deformities reported in fish are in the vertebral column or its predecessor – in fish development –, the notochord. The notochord is the primary axial structure on which many other tissues depend for their proper formation and differentiation. Toxicants that disrupt normal development and differentiation of the notochord may therefore result in permanent skeletal deformities, muscle abnormalities, and neurological dysfunction. Axial structures may also be malformed by uncontrolled muscle spasms (Nguyen Thi Hong et al., 1997).

Apart from their negative effects, it is common knowledge that certain heavy metals (and in certain concentrations) play a positive role on fish development. Nguyen et al. (2008) tested different combinations of Artemia enrichment with zinc and manganese (Mn) – both essential metals for fish – before feeding red sea bream (*P. major*) larvae and concluded that the presence of these metals acts beneficially to growth and skeletal deformities.

Environmental parameters such as water temperature, oxygen concentration, hardness, salinity, alkalinity and dissolved organic carbon may affect metal's toxicity to fish (Benaduce et al., 2008, Linbo et al., 2009, Sassi et al., 2010). Hypoxic conditions, temperature increase and acidification usually render the fish more susceptible to intoxication, whereas increase in mineral content (hardness and salinity) reduce metal toxicity (Witeska and Jezierska, 2003). Moreover, interactions among various metals present in the water may also modify their toxicity and synergistic, additive or antagonistic effects may also occur (Witeska and Jezierska, 2003). Bao et al. (2008) studied the synergistic toxic effects of zinc pyrithione and copper to three marine species and concluded that in order to properly protect the marine life, water quality criteria should be established in such a way that would take into account the synergistic effects of the studied metals.

Besides heavy metals, fish populations encounter a number of other hazardous conditions. Murl Rolland (2000) states that there has been an unprecedented decline in commercial marine fisheries and in freshwater fish species world-wide, prompting a search for the causes of these declines and a growing concern for the future viability of fishery resources. Commercial fishery species have been subjected to tremendous pressure from overfishing which has caused rapid declines in some populations. Together with eutrophication, introduction of exotic species, habitat alterations, exposure to aquatic pollution, and (potentially) the effects of global climate change, it is apparent that fish populations are faced with a wide variety of stressors generated by human activity. Reversal of the current decline in many fish populations and successful management in the future depends upon identifying the risks posed by all factors currently impacting the health and survival of these populations.

In literature, there are a lot of available studies on other contaminants such as selenium (Kennedy et al., 2000) and on nutritional aspects such as vitamins deficiencies (Darias et al., 2011, Mazurais et al., 2009) but there is little information on the effects of heavy metal poisoning accompanied by precise monitoring of the consequences on the fish. Although in the past years quite a few publications on the subject appeared, the effect of the different heavy metals on various fish species still needs to be studied more thoroughly. Moreover, the precise effect on fish deformities has not been studied since all studies – or most of them – examine their samples at hatching or a few days afterwards. Additionally, it is crucial to have – in a documented form – the exact concentrations (threshold), above which the heavy metal contamination poses a threat to the organism (reduction of welfare or death), to the fisheries and aquaculture industry (through fish that are unmarketable bearing deformities) and of course to the consumer's health (through the food chain).

Barbee et al. (2013) state that toxicological research has recently been shifting from the traditional focus on the lethality of toxicants to organisms, to an increased emphasis on the sublethal impacts of contaminants. The sublethal effects of environmental pollutants may be latent, and thus harder to detect, yet can have significant consequences for the long-term growth, reproduction and survival of individuals. Therefore, there is a need of future studies which will focus on using lower exposure concentrations (non-lethal) thus enabling the fish to reach adulthood (or at least the juvenile stage), in order to fully understand the long-term consequences of heavy metals poisoning on fish organisms.

Moreover, as stated many times previously (Au, 2004, Kessabi et al., 2013b, Sun et al., 2009), the presence of deformities in wild fish populations could serve as an excellent indicator of water pollution (in this case, heavy metal contamination). The effects of sublethal concentrations of metals on fish could offer information about the contamination level of certain environments and thus facilitate the use of fish deformities as biomarkers of environmental pollution. In order, however, to achieve this use, tolerant fish species should be used in addition to the cause-and-effect relationships between biomarkers and the various pollutants being well established (Antunes and Lopes Da Cunha, 2002, Sun et al., 2009).

There are quite a few studies on wild fish deformities but most of them simply hypothesize that the causative factor is probably the presence of heavy metals on the natural habitat. Only a limited number of articles in the recent literature directly correlate the presence of fish deformities with heavy metals either on fish tissues or on the habitat's water or sediment.

Kessabi et al. (2009) sampled populations of the Mediterranean killifish, *Alphanius fasciatus*, from different unpolluted and polluted sites off the coast of Tunisia and discovered that the deformed specimens (originating only from the polluted sampling areas) presented higher Cd concentrations in their livers and spinal columns when compared to the normal ones. Moreover, they reported that the bioaccumulation factors of Cd in the liver in deformed fish were also significantly higher than in normal fish, thus suggesting that the ability of fish to accumulate large amount of Cd may represent a potential risk to induce spinal deformities. In a follow up study by the same authors in the same species (Kessabi et al., 2010), quantitative RNA biomarkers were used and it was suggested that a combined effect of both heavy metals and organic pollutants is what actually leads to the presence of deformities.

Sun et al. (2009) studied Tilapia (*Oreochromis* spp.) populations collected from different rivers in Taiwan. They discovered the presence of many different skeletal deformities in the vertebral column, cranium, operculum, fins and jaws. They correlated these deformities with the severe pollution of the rivers with heavy metals (Hg, Zn, Pb, Cu and Cr) and organic compounds. In this study, there seems to be a slight correlation between certain deformities and certain pollutants but nothing is definitive. The authors argue that Tilapia is quite tolerant and presents more deformities than other species and could therefore serve as a reliable biomarker of the environment pollution in general.

In a recent study (Kessabi et al., 2013a), skeletal deformities in the vertebral column of Mediterranean killifish specimens, collected from the Tunisian coast, were linked with high concentration of heavy metals (Cd, Cu and Zn), various polycyclic aromatic hydrocarbons (PAHs) and estrogenic compounds discovered in water and sediment of the sampling areas. The incidence of deformed specimens reached up to 18% in a certain polluted sampling area while it did not exceed 5% in the unpolluted reference area. The authors did not discriminate between the different xenobiotics discovered and therefore the direct effect of only the heavy metals remains unknown.

Besides sampling fish from their natural habitats, Skinner et al. (1999) had the idea of exposing hatched eggs of two species (Japanese medaka, *O. latipes* and Inland Silverside, *Menidia beryllina*) to different percentages of storm water sampled in an urban area and contaminated with various pollutants (including Cd, Cu, Pd, Zn, Cr and Ni). Their findings showed that the contaminated storm water induced various deformities in the hatched larvae of both species with the most prominent ones being the abnormal swimbladder inflation, the spinal curvatures and the reduction of pigmentation. The presence of significant adverse effects in this study did not correlate significantly with any of the individual pollutants that were traced in the storm water, but did correspond with total toxic metal pollutants in the samples (especially Cd, Cu, Pb and Zn).

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