Journal of Stress Physiology & Biochemistry, Vol. 21, No. 3 2025, pp. 184 - 193 ISSN 1997-0838

REVIEW

OPEN ACCESS

Heavy Metal Pollution and Its Impact on Fish: A Review on Lead Toxicity

Harshada Mohankar, Mahek Rakhde, Janvee Bhagat, Varsha Dhurvey*, Aashik Nagwanshi, Dharita Joshi, Ankita Sharma

[1] *Department of Zoology, RTM Nagpur University, Nagpur-440033, MS, India*

*E-Mail: *varshadhurvey@yahoo.com*

Received March 26, 2025

Freshwater ecosystems are increasingly threatened by anthropogenic activities, with heavy metal contamination, particularly Lead (Pb). Lead is a persistent environmental pollutant, that accumulates in aquatic organisms especially fish, which serve as bioindicators of ecosystem health. This review examines the histopathological, biochemical and molecular effects of lead toxicity on fish, focusing on the liver, gills and intestines. Lead exposure disrupts liver function, leading to cellular degeneration, necrosis and oxidative stress. In gills, it induces structural deformities, impairs respiratory efficiency and alters gene expression related to stress and osmoregulation. The intestinal tract suffers from villi degradation, inflammation and compromised nutrient absorption due to enzymatic and genetic disruptions. Additionally, hematological alterations, such as anemia and immune dysregulation, exacerbate systemic toxicity. Understanding these toxicology effects is crucial for assessing environmental pollution and developing mitigation strategies. This review highlights the urgent need for stringent regulatory policies and sustainable environmental practices to minimize lead contamination in aquatic ecosystems and safeguard biodiversity.

Key words: lead (Pb), freshwater ecosystems, fish, heavy metal contamination, histopathological effects, liver toxicity, gills, oxidative stress, environmental pollution

Freshwater plays a crucial role in sustaining life on earth, constituting only 1% of total surface water. Natural and anthropogenic impacts the quality of surface water, these activities negatively affect the aquatic organisms (Sharma *et al*., 2021). Several factors including population growth, industrialization, urbanization, deforestation, lack of environmental awareness among society, inadequate policy implementation, improper enforcement of regulations, effluent discharge from various industries and so on, leads to pollution in the aquatic ecosystem and ultimate loss of aquatic organisms (Malik *et al*., 2020).

Toxic heavy metals such as lead, thallium, cadmium and antimony, are among the most common pollutants released through industrial operations (Karbowska, 2016). Among these Lead is regarded as a potent occupational toxin and particularly concerning due to its well documented toxicological effects. Lead's nonbiodegradable nature is the prime reason for its prolonged persistence in the environment (Flora *et al.,* 2012). It is characterised by its soft malleable nature and relatively low melting point.

Lead exposure primarily occurs in occupational settings like mining, smelting, welding, lead painting and battery production. Even low to moderate exposure can occur in the glass industry, while the highest levels are seen near lead mines and smelters. Airborne lead emissions further contribute to soil and water contamination, allowing lead to enter the food chain and pose risks to human health (WHO, 1995).

Fish, at the top of the aquatic food chain, are highly susceptible to biomagnification of heavy metals, which can transfer toxins to humans (WHO/FAO, 1989). The growing demand for protein in third-world countries has led to increased fish farming, often using recycled water from industrial, agricultural, or sewage sources, raising safety concerns (Wong *et al.,* 2001). Fish exposed to polluted water accumulate heavy metals in their tissues, with accumulation varying based on factors such as metal concentration, exposure duration, water conditions (e.g., temperature, pH, hardness and salinity) and fish age and feeding habits. The highest accumulation is typically in the liver, kidneys and gills, while muscle tissues have the lowest levels (Barbara *et al.,* 2006). Fish species serve as environmental health indicators and metallothionein transcripts in fish provide a method for assessing contamination (Evans *et al.,* 2001). Fish are not only early warning indicators of environmental degradation but also biomarkers for harmful substances like toxins, carcinogens and mutagens (Khan, 2003).

Histological effects of lead on liver

A study by Suicmez *et al.,* (2006) found that exposure to lead acetate for 72 hours caused degeneration of hepatic tissues in *Oncorhynchus mykiss*, leading to vacuolation, tubular degeneration and necrosis of the liver.

Chavan (2016) studied the toxic effects of lead on the liver of *Cirrhinus mrigala*. Fish samples were exposed to different concentrations of lead acetate for 30 days, revealing a loss of liver architecture, parenchymal disorganization, cell death and venule dilation. Degeneration of hepatocytes resulted in a decreased cell population.

Another study observed hepatocellular degeneration, characterized by swollen liver cells, vacuolar degeneration and fatty changes (Suicmez *et al.,* 2006; Ibrahim and Mahmoud, 2005). Prolonged exposure to lead can cause hepatic necrosis, leading to liver cell death. In some cases, it also results in the formation of congested blood vessels and sinusoidal dilatation (Rashed, 2001; Patnaik *et al.,* 2011). Histological evidence of liver damage includes the accumulation of hemosiderin, indicating blood cell destruction and inflammatory cell infiltration, which further deteriorates the tissue (Yacoub and Satar, 2003; Olojo *et al.,* 2004). Long-term exposure to lead may also lead to severe conditions such as cirrhosis, characterized by fibrosis and the destruction of normal liver architecture (Ibrahim and Mahmoud, 2005).

Biochemical effects of lead on liver

El-Khadragy (2017) conducted a study on 80 *Oreochromis niloticus* exposed to four different concentrations of lead acetate for 12 days. The results showed increased levels of creatinine, uric acidandliver enzymes (ALT and AST). Studies have also reported a

significant rise in oxidative stress markers, such as lipid peroxidation (malondialdehyde levels), indicating cellular membrane damage (Suicmez *et al.,* 2006; Adegbesan and Adenuga, 2007).

Furthermore, exposure to lead reduces the activity of enzymes such as δ-aminolevulinic acid dehydratase (ALA-D), which is crucial for heme synthesis. It also affects metallothionein-like proteins, which play an essential role in detoxification processes (Schmitt *et al.,* 2005; Atli and Canli, 2003). The inhibition of ALA-D and other enzymes disrupts normal liver functions and impairs detoxification mechanisms, ultimately affecting the overall health of fish (Schmitt *et al.,* 2005; Yacoub and Satar, 2003).

Histopathological Effects of Lead on Gills

Histopathological changes in the gills are among the most prominent indicators of lead toxicity in fish. Lead exposure has been shown to cause significant structural alterations, including epithelial lifting, lamellar fusion, hyperplasia and necrosis. For instance, Younis *et al.,* (2020) observed dose-dependent histopathological changes in the gills of *Clarias gariepinus* exposed to lead nitrate, including deformed lamellae, increased vascular spaces and hyperplasia. Similarly, Aldoghachi *et al.,* (2015) reported that lead exposure disrupted the normal histoarchitecture of gills in hybrid red tilapia, leading to epithelial cell damage and fusion of adjacent lamellae. These structural alterations impair the gills' ability to facilitate gas exchange and regulate ions, ultimately compromising the fish's respiratory efficiency.

Further evidence of histopathological damage has been documented in zebrafish (*Danio rerio*) exposed to environmentally relevant lead concentrations. Curcio *et al.,* (2022) reported significant histological alterations, including osmoregulatory dysfunction, increased oxidative stress and epithelial lifting. The severity of these changes was directly correlated with lead concentration and exposure duration. Moreover, Mishra and Behera (2023) observed progressive degeneration in gill tissues of *Clarias batrachus* exposed to mercury and lead, emphasizing the cumulative impact of heavy metals on aquatic organisms.

Chronic exposure to lead also results in long-term structural damage. Kaur *et al.,* (2021) used transmission electron microscopy to examine ultrastructural changes in the gills of *Labeo rohita* exposed to sub-lethal lead nitrate concentrations. They reported extensive cellular damage, including nuclear deformation, vacuolation, chromatin clumping and mitochondrial swelling. These findings underscore the importance of gills as sensitive biomarkers for assessing environmental lead contamination.

Biochemical Effects of Lead on Gills

Lead toxicity disrupts the biochemical balance in fish gill tissues by impairing enzymatic activities and inducing oxidative stress. Enzymes like Na^+/K^+-ATPase and Ca^{2+}-ATPase, critical for ion transport and osmoregulation, are particularly affected. Ay *et al.,* (1998) demonstrated that exposure to lead significantly reduced the activity of branchial Na^+/K^+-ATPase in *Tilapia zillii*, highlighting the metal's inhibitory effects on essential physiological processes. This enzymatic disruption leads to ionic imbalance and increased metabolic stress, further exacerbating gill dysfunction.

Oxidative stress is another major consequence of lead exposure. Increased levels of reactive oxygen species (ROS) and lipid peroxidation markers, such as malondialdehyde (MDA), have been reported in fish exposed to lead. Nayak *et al.,* (2023) observed elevated phosphatase enzyme activity and increased protein content in the gills of *Anabas testudineus* following lead exposure. These biochemical changes indicate cellular damage and a compromised antioxidant defense system.

Additionally, lead bioaccumulation in gills exacerbates systemic toxicity. Studies on goldfish (*Carassius auratus*) revealed that gills accumulate higher concentrations of lead compared to other tissues, making them a primary site for metal uptake (Fawad *et al.,* 2016). This accumulation not only impairs gill function but also facilitates the systemic distribution of lead, affecting other vital organs.

Effect of Lead on Gene Expression in Gills

Lead exposure significantly alters the expression of genes associated with stress responses, inflammation and apoptosis in gill tissues. Curcio *et al.,* (2022)

reported that lead exposure upregulated genes involved in oxidative stress, such as superoxide dismutase (SOD)and osmoregulatory function, including Na^+/K^+-ATPase and aquaporins. These genetic changes reflect the gills' adaptive responses to counteract lead-induced damage.

In zebrafish, Gonzalez *et al.,* (2005) found that cadmium and lead exposure induced the differential expression of nine out of fourteen genes related to cellular stress and immune responses. The upregulation of metallothioneins and heat shock proteins indicates an attempt by the gills to mitigate metal toxicity. However, prolonged exposure often overwhelms these protective mechanisms, leading to irreversible damage.

Lead exposure also affects genes related to structural integrity and cell repair. For example, studies on Nile tilapia showed downregulation of tight junction proteins and upregulation of inflammatory cytokines like TNF-α, suggesting impaired barrier function and heightened inflammatory responses (Wong and Wong, 1999). These findings highlight the complex interplay between genetic regulation and lead-induced toxicity in gill tissues.

Hematological Effects of Lead on Gills

The hematological effects of lead toxicity on gills are closely linked to structural and functional impairments. Lead-induced damage to the gill vasculature often results in hemorrhage, edema and hypoxia. Mishra and Behera (2023) reported significant blood congestion and necrosis in the gills of *Clarias batrachus* exposed to lead, emphasizing the impact of vascular damage on oxygen transport efficiency.

Hemoglobin levels and erythrocyte counts are also adversely affected. Tabche *et al.,* (1990) observed reduced hemoglobin concentrations in tilapia exposed to sub-lethal lead concentrations, correlating with impaired respiratory efficiency. Similarly, studies on *Catla catla* exposed to heavy metals revealed significant reductions in red blood cell count and hematocrit values, indicative of anemia (Hussan *et al.,* 2016). These hematological changes exacerbate the systemic effects of lead toxicity, further compromising the fish's health and survival.

In addition to anemia, lead exposure can trigger immune-inflammatory responses. Increased neutrophil counts and altered lymphocyte populations have been reported in fish exposed to lead, reflecting an immune response to tissue damage (Naz *et al.,* 2021). These hematological parameters provide valuable insights into the physiological stress experienced by fish in polluted environments. (Table 2)

Table 1. Biochemical effects of lead on liver

Type of toxicity	Organism	Names of genus and species	Doses	Duration	Effects	References
Hepatotoxicity due to lead	Fish	*Oncorhynchus mykiss*	0.1, 1.0, 10 mg/l	24, 48 and 72 hours	Hepatic tissue degeneration, tubular degeneration, necrosis and dilation of hepatic sinusoids in the liver	Suicmez *et al.,* (2006)
		Cirrhinus mrigala	14.1 ppm and 28.2 ppm	30 days	Loss of liver architecture, parenchymal disorganization, cell death and dilation of vennules degeneration of hepatocytes	Chavan (2016)
		Oreochromis niloticus	50, 100, 150, 200 mg/L	96 hrs	Increased levels of creatinine, uric acid and liver enzymes (ALT and AST)	El-Khadragy (2017)

Table 2. Hematological Effects of Lead

Toxicant	Organism	Name of genus and species	Doses	Duration	Effects	References
Lead	Fish	*Ctenopharyngodon idella*.	16.12 mg/L, 32.24 mg/L and 48.37 mg/L	96 hours	Alterations in cartilaginous matrix, deformed and shortened lamellae, increased vascular spaces, extra cartilaginous matrix and lamellar hyperplasia.	Younis *et al.,* (2020)
		Clarias gariepinus	5.5 mg/L	96 hours	Disrupts the normal histoarchitecture of gills, causing changes in the epithelial cells.	Aldoghachi *et al.,* (2015)
		Danio rerio	2.5 and 5 µg/L		Osmoregulatory dysfunction, altered gene expression, increased oxidative stress and significant histological changes.	Curcio *et al.,* (2022)
		Labeo rohita	11.4, 6.84, 4.88 and 3.42 mg/L	15, 30, 45 and 60 days.	Cytoplasmic loss, vacuolation, nuclear deformation, ruptured nuclear membranes, chromatin clumping, enlarged intercellular spaces, cell debris, disorganized epithelial cells.	Kaur *et al.,* (2021)
		Anabas testudineus	1.291, 1.936, 3.873 mg/L		Severe toxicity found in gill tissue	Nayak *et al.,* (2024)
		Tilapia	31 mg, 47 mg, 63 mg, 78 mg and 94 mg Pb^{2+}	72 hours	Increased lysosomal membrane lability in gill tissue, indicating subcellular damage and stress	Tabche *et al.,* (1990)

Table 3. Hematological Effects of Lead

Toxicant	Organism	Name of genus and species	Doses	Duration	Effects	References
Lead acetate	Rat		50 mg/kg body weight	7 days	Enhanced alkaline phosphatase expression reduced sucrose expression.	Kapur *et al.,* (2004)
Lead nitrate	Fish	*Clarius gariepinus*	20% of LC50 (16.12mg /l) 40% of LC_{50} (32.24mg/l) 60% of LC_{50} (48.37 mg/l)		Damage intestinal tissue, particularly affect enterocytes and villi structure	Abdel and Warith (2020)
Lead	Mice		Cd (5,20,100mgl) Pb (100,500mg)	4, 8 and 12 weeks	Effects in transport oxidative stress and inflammation in gut epithelium	Breton *et al.,* (2013)
	Fish	*Carassius auratus gibelio*	0, 0.05, 1 mg/L	60 days	Reduced antioxidant enzyme activity	Yin *et al.,* (2018)
		Sebastes schlegelii	0, 30, 60, 120 and 240 mg/kg	4 weeks	Lead accumulation increased in tissue	Kim and Kang (2016)
		Danio rerio	0.1 µg/L, 1 µg/L, 10, 20 and 100 µg/L	30 days	Increase intestinal villi and cell numbers	Ngo *et al.,* (2021)

Histopathological Effects of Lead on the Intestine

Histopathological studies reveal that lead exposure induces significant structural alterations in the intestinal tissues of exposed organisms. Research on African catfish (*Clarias gariepinus*) exposed to sublethal concentrations of lead nitrate showed villi destruction, enterocyte disruption, inflamed lamina propria and goblet cell proliferation (Abdel-Warith *et al.,* 2020). Similarly, zebrafish (*Danio rerio*) exposed to varying lead concentrations exhibited increased intestinal villi and cell numbers, along with disruptions in digestive function (Ngo *et al.,* 2021).

Lead-induced histological changes often correlate with oxidative stress and inflammation. Studies on freshwater fish like crucian carp (*Carassius auratus gibelio*) reported decreased mucosal fold lengths, swollen endoplasmic reticulum and nearly obliterated intestinal microvilli, highlighting severe structural damage (Yu *et al.,* 2021). In Nile tilapia (*Oreochromis niloticus*), lead exposure caused atrophy of villi, epithelial desquamation and necrosis in intestinal tissues (Younis *et al.,* 2015).

Chronic exposure to lead exacerbates these effects. In juvenile rockfish (*Sebastes schlegelii*), higher dietary lead concentrations led to more pronounced intestinal degeneration, necrosis and hyperplasia (Kim and Kang, 2015). These findings underscore the role of histopathological changes as reliable indicators of lead toxicity in aquatic species. The degree of damage can also depend on other environmental factors, such as water hardness, pH and presence of other pollutants.

Moreover, studies in rats have revealed similar pathological changes, with lead exposure causing necrosis, mucosal edema and goblet cell hyperplasia. These findings suggest that the intestinal response to lead is consistent across different species, emphasizing its broad toxicological impact.

Biochemical Effects of Lead on the Intestine

Lead exposure disrupts intestinal biochemical homeostasis by impairing enzyme activities and inducing oxidative stress. Key digestive enzymes such as sucrase, lactase, maltase and leucine aminopeptidase exhibit reduced activities upon lead exposure, as observed in rat models (Kapur *et al.,* 2005). Elevated levels of alkaline phosphatase were noted, suggesting compensatory responses to intestinal damage. These enzymatic alterations impair nutrient absorption and overall digestive efficiency.

In aquatic species, lead-induced oxidative stress disrupts the balance of reactive oxygen species (ROS) and antioxidant defenses. *Crucian carp* exposed to lead showed increased malondialdehyde (MDA) levels, a marker of lipid peroxidation and decreased antioxidant enzyme activities, including superoxide dismutase (SOD) and catalase (Yu *et al.,* 2021). These biochemical changes impair nutrient absorption, damage cellular integrity and weaken intestinal barrier function.

Studies on silver carp (*Hypophthalmichthys molitrix*) demonstrated elevated digestive enzyme activities (trypsin and lipase) and upregulated immune genes such as TNF-α and IL-8 following lead exposure. However, structural gene expression, including Claudin-7 and Villin-1, was reduced, indicating compromised intestinal barrier function (Liu *et al.,* 2022). This interplay between biochemical alterations and structural damage exacerbates the overall impact of lead on intestinal health.

Interestingly, lead exposure has been shown to alter gut microbiota composition, which plays a crucial role in maintaining biochemical and immune homeostasis. Changes in microbial diversity and abundance further contribute to oxidative stress and inflammation, creating a vicious cycle that worsens intestinal damage.

Effect of Lead on Gene Expression in the Intestine

Lead toxicity alters the expression of genes involved in oxidative stress, apoptosis and immune responses. In *Cyprinus carpio*, lead exposure downregulated miR-17-5p and upregulated TXNIP expression, promoting pyroptosis-related genes such as NLRP3 and CASP1 (Miao *et al.,* 2022). These molecular changes contribute to inflammation and cellular apoptosis.

Breton *et al.,* (2013) investigated the impact of chronic lead ingestion on intestinal gene expression in mice. The study revealed upregulated markers of oxidative stress and inflammation, including heat shock proteins and pro-inflammatory cytokines. Concurrently, essential nutrient transporter genes showed altered expression, indicating lead's interference in nutrient absorption and gut homeostasis.

In fish, lead exposure has been linked to disrupted immune gene expression. For instance, in *Carassius auratus gibelio*, genes like TNF-α and IL-10 were differentially expressed, reflecting immune dysfunction and inflammatory responses (Yin *et al.,* 2018). These findings highlight the molecular pathways through which lead exerts toxic effects on intestinal health.

Furthermore, lead exposure can modulate the expression of genes related to cell proliferation and repair, thereby impairing the intestine's ability to recover from damage. Studies in rat models have shown that genes regulating tight junction proteins, crucial for barrier integrity, are downregulated following lead exposure. This highlights the potential for long-term intestinal dysfunction even after the cessation of exposure.

Hematological Effects of Lead on the Intestine

Lead toxicity also impacts hematological parameters related to intestinal health. In juvenile rockfish, lead exposure significantly reduced red blood cell count, hemoglobin levels and hematocrit values, indicating anemia (Kim and Kang, 2015). Reduced oxygen transport capacity exacerbates tissue hypoxia, further impairing intestinal function.

In *Catla catla*, chronic exposure to lead resulted in decreased erythrocyte counts, hemoglobin levels and lymphocyte populations, alongside elevated neutrophil counts (Naz *et al.,* 2021). These changes suggest an immune-inflammatory response to lead toxicity. Additionally, lead disrupts iron metabolism, as observed in studies on rats, where lead ingestion altered plasma iron levels and increased duodenal DMT1 expression (Molina *et al.,* 2011).

Lead-induced anemia and immunosuppression can indirectly impact intestinal health by reducing the availability of nutrients and oxygen required for tissue repair. Studies also suggest that lead exposure may affect the production of erythropoietin, further exacerbating anemia and its associated complications. This interplay between hematological dysfunction and intestinal damage underscores the systemic nature of lead toxicity. (Table 3)

Summary and Conclusion

Lead contamination in freshwater ecosystems poses a severe threat to aquatic life and biodiversity. Lead bioaccumulates in fish organs such as the liver, gills and intestines, causing cellular damage, oxidative stress and metabolic dysfunction. Histopathological and biochemical studies reveal severe tissue damage, enzyme inhibition and genetic disruptions, compromising fish health and survival. Hematological changes further weaken immune responses and oxygen transport, exacerbating toxicity.

Addressing lead pollution requires stringent regulations, environmental monitoring and sustainable industrial practices. Molecular biomarkers and histopathological assessments can improve early detection of heavy metal toxicity in aquatic organisms. Future research should focus on bioremediation strategies and eco-friendly alternatives to reduce lead contamination, ensuring the protection of aquatic ecosystems and food safety.

CONFLICTS OF INTEREST

The authors declare that they have no potential conflicts of interest.

REFERENCES

Abdel-Warith, A. W. A., Younis, E. M., Al-Asgah, N., Ebaid, H., & Elsayed, E. A. (2020). Lead Nitrate induced histopathological alterations in the liver and intestine of African Catfish Clarias gariepinus exposed to sublethal concentrations. *Journal of Scientific & Industrial Research 79, 552-557.*

Adegbesan, B. O. and Adenuga, G. A. (2007). Effect of lead exposure on liver lipid peroxidative and antioxidant defense systems of protein-

undernourished rats. *Biological trace element research*, *116*, 219-225.

Aldoghachi, M. A., Azirun, M. S., Yusoff, I. and Ashraf, M. A. (2016). Ultrastructural effects on gill tissues induced in red tilapia *Oreochromis* sp. by a waterborne lead exposure. *Saudi Journal of Biological Sciences, 23(5), 634-641.*

Atli, G. and Canli, M. (2003). Natural occurrence of metallothionein-like proteins in the liver of fish *Oreochromis niloticus* and effects of cadmium, lead, copper, zincandiron exposures on their profiles. *Bulletin of Environmental Contamination and Toxicology*, *70*(3).

Ay, Ö., Kalay, M., Tamer, L. and Canli, M. (1999). Copper and lead accumulation in tissues of a freshwater fish *Tilapia zillii* and its effects on the branchial Na, K-ATPase activity. *Bulletin of Environmental Contamination and Toxicology, 62, 160-168.*

Barbara, J. and W. Malgorzata, (2006). The metal uptake and accumulation in fish living in polluted waters. *Soil and Water Pollution Monitoring Protection and Remediation, 69: 107-114.*

Breton, J., Le Clère, K., Daniel, C., Sauty, M., Nakab, L., Chassat, T. ... and Foligné, B. (2013). Chronic ingestion of cadmium and lead alters the bioavailability of essential and heavy metals, gene expression pathways and genotoxicity in mouse intestine. *Archives of toxicology, 87, 1787-1795.*

Chavan, V. R. (2016). Effect of lead on morphological and biochemical profile of fish liver. *Int J Adv Sci Res*, *1*, 19-22.

Curcio, V., Macirella, R., Sesti, S., Ahmed, A. I., Talarico, F., Tagarelli, A. and Brunelli, E. (2022). Morphological and functional alterations induced by two ecologically relevant concentrations of Lead on *Danio rerio* gills*. International journal of molecular sciences, 23(16), 9165.*

El-Khadragy, M., Al-Olayan, E. M., Abou Arab, A., Sebaee, S. E., Abou Donia, M. A. and Elamin, M. H. (2017). Effect of sub lethal concentrations of cadmium and lead on *Oreochromis niloticus*. *Biomed Res*, *28*(4), 1-8.

Evans, C.W., Wilson D.A. and Mills G.N., (2001). Quantitative competitive RT-PCR as a tool in biomarker analysis. *Biomarkers, 6: 7-14*.

Fawad, M., Yousafzai, A. M., Haseeb, A., Rehman, H. U., jan Afridi, A., Akhtar, N. ... and Usman, K. (2017). Acute toxicity and bioaccumulation of chromium in gills, skin and intestine of goldfish (*Carassius auratus*). *Journal of Entomology and Zoology studies, 5(1), 568-571.*

Flora, G., Gupta, D. and Tiwari, A. (2012). Toxicity of lead: a review with recent updates. *Interdisciplinary toxicology*, *5*(2), 47-58.

Gonzalez, P., Baudrimont, M., Boudou, A. and Bourdineaud, J. P. (2006). Comparative effects of direct cadmium contamination on gene expression in gills, liver, skeletal muscles and brain of the zebrafish (*Danio rerio*). *Biometals, 19, 225-235.*

Ibrahim, S. and Mahmoud, S. (2005). Effect of heavy metals accumulation on enzyme activity and histology in liver of some Nile fish in Egypt. *Egyptian Journal of Aquatic Biology and Fisheries*, *9(1), 203-219.*

Kapur, P., Kaur, K. and Mahmood, A. (2005). Expression of brush border enzymes in response to lead exposure in rat intestine. *Journal of Applied Toxicology: An International Journal, 25(5), 361-364.*

Karbowska, B. (2016). Presence of thallium in the environment: sources of contaminations, distribution and monitoring methods. *Environmental monitoring and assessment*, *188*, *1-19.*

Kaur, M.and Brraich, O. S. (2021). Ultrastructural alterations in the gills of cyprinid, Labeo rohita (Hamilton) exposed to Lead nitrate. *Indian Journal of Experimental Biology (IJEB), 59(08), 570-575.*

Khan, R.A., (2003). Health flat fish from localities in Placentia Bay, New Found Land, contaminated with petroleum and PCBS. *Archives of Environmental Contamination and Toxicology, 44: 485-492.*

Kim, J. H.and Kang, J. C. (2015). The lead accumulation and hematological findings in juvenile rock fish

Sebastes schlegelii exposed to the dietary lead (II) concentrations. *Ecotoxicology and environmental safety, 115, 33-39*.

Liu, H., Qian, K., Zhang, S., Yu, Q., Du, Y.and Fu, S. (2022). Lead exposure induces structural damage, digestive stress, immune response and microbiota dysbiosis in the intestine of silver carp (*Hypophthalmichthys molitrix*). *Comparative Biochemistry and Physiology Part C: Toxicology and Pharmacology, 262, 109464.*

Malik, D. S., Sharma, A. K., Sharma, A. K., Thakur, R.and Sharma, M. (2020). A review on impact of water pollution on freshwater fish species and their aquatic environment. *Advances in environmental pollution management: wastewater impacts and treatment technologies*, *1*, 10-28.

Miao, Z., Miao, Z., Teng, X.and Xu, S. (2022). Melatonin alleviates lead-induced intestinal epithelial cell pyroptosis in the common carps (Cyprinus carpio) via miR-17-5p/TXNIP axis. *Fish and Shellfish Immunology, 131, 127-136.*

Mishra, A., & Behera, B. (2023). Effect of mercury on histological alterations in gill, liver and stomach tissues of Indian catfish, Clarias batrachus. *Journal of Applied & Natural Science, 15(2). 685 - 691*

Molina, R. M., Phattanarudee, S., Kim, J., Thompson, K., Wessling-Resnick, M., Maher, T. J.and Brain, J. D. (2011). Ingestion of Mn and Pb by rats during and after pregnancy alters iron metabolism and behavior in offspring. *Neurotoxicology, 32(4), 413-422*.

Nayak, P., Sharma, S. N., Nayak, S., Pradhan, S. P., Nayak, S.and Patnaik, L. (2024) Biochemical changes in the gill, liver and muscle tissue of *Anabas testudineus* on exposure to varying concentration of Lead acetate*. Environmental Quality Management, 33(4), 217-228.*

Olojo, E. A. A., Olurin, K. B., Mbaka, G.and Oluwemimo, A. D. (2005). Histopathology of the gill and liver tissues of the African catfish *Clarias gariepinus* exposed to lead. *African Journal of Biotechnology*, *4*(1), 117-122.

Patnaik, B. B., Howrelia, H., Mathews, T.and Selvanayagam, M. (2011). Histopathology of gill, liver, muscle and brain of *Cyprinus carpio communis* L. exposed to sublethal concentration of lead and cadmium. *African Journal of Biotechnology*, *10*(57), 12218-12223.

Rashed, M. N. (2001). Cadmium and lead levels in fish (*Tilapia nilotica)* tissues as biological indicator for lake water pollution. *Environmental monitoring and assessment*, *68*, 75-89.

Schmitt, C. J., Whyte, J. J., Brumbaugh, W. G.and Tillitt, D. E. (2005). Biochemical effects of lead, zinc and cadmium from mining on fish in the tri-states district of northeastern Oklahoma, USA. *Environmental Toxicology and Chemistry*, *24*(6), 1483-1495.

Sharma, A. K., Sharma, M. and Navneet, S. (2021). M.: A review on impact of water pollution on aquatic ecosystem. *Current Research and Innovations in Life Sciences, Eds. Sharma, AK, Thakur, R., Sharma, M. and Sharma, M*, 129-148.

Suiçmez, M., Kayım, M., Köseoğlu, D.and Hasdemir, E. (2006). Toxic effects of lead on the liver and gills of *Oncorhynchus mykiss* WALBAUM 1792. *Bulletin of Environmental Contamination and Toxicology*, *77*(4).

WHO, (1995). Lead: Environmental Health Criteria. Vol. 165. Geneva: World Health Organization Program on Chemical Safety (IPCS), India.

WHO/FAO, (1989). Evaluation of food contaminants. 33 Report of the Joint FAO/WHO Expert Committee rd on Food Additives. Technical Report Series 776, Geneva, Switzerland. Wong, C.K., P.P.K. Wong and L.M. Chu, 2001. Heavy metal concentration in marine fish collected from culture sites in Hong Kong. *Archives of Environmental Contamination and Toxicology, 40: 60-69.*

Wong, C. K.and Wong, M. H. (2000). Morphological and biochemical changes in the gills of tilapia (*Oreochromis mossambicus*) to ambient cadmium exposure. *Aquatic Toxicology, 48(4), 517-527.*

Yacoub, A.and Abdel Satar, A. (2003). Heavy metals accumulation and macronutrients in the livers of

some fish species of Bardawil Lagoon and their histological changes. *Egyptian Journal of Aquatic Biology and Fisheries*, *7*(4), 403-422.

Yin, Y., Zhang, P., Yue, X., Du, X., Li, W., Yin, Y., ... and Li, Y. (2018). Effect of sub-chronic exposure to lead (Pb) and Bacillus subtilis on *Carassius auratus gibelio*: bioaccumulation, antioxidant responses and immune responses*. Ecotoxicology and environmental safety, 161, 755-762.*

Younis, E., Abdel-Warith, A. W., Al-Asgah, N.and Ebaid, H. (2015). Histopathological alterations in the liver and intestine of Nile tilapia *Oreochromis niloticus* exposed to long-term sublethal concentrations of cadmium chloride. *Chinese journal of oceanology and limnology, 33(4), 846-852.*

Yu, Y., Tong, B., Liu, Y., Liu, H.and Yu, H. (2021). Bioaccumulation, histopathological and apoptotic effects of waterborne cadmium in the intestine of crucian carp *Carassius auratus gibelio. Aquaculture Reports, 20, 100669.*