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Evaluation of Heavy Metal Pollutants of Water on Fish Health and its Impact on Human Health

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Abstract

This review provides a summary of the toxic effects of heavy metals on fish. In the aquatic environment, these metals are important pollutants and are found in all ecosystems and are found in large quantities. Some heavy metals such as Cadmium, iron, copper, zinc and lead have the advantage of accumulating in tissues and poisoning fish. These minerals can effectively affect biological processes, fish reproduction, impair the immune system, and cause pathological changes. Therefore, heavy metals play an important role as a vital predictor of pollutants affecting the health and life of fish environments. These minerals cause organ damage even at low levels of exposure, so they have recently been classified as carcinogens. For all the above-mentioned reasons, this review has been written to contribute to the role of heavy metals in the environment, the toxic mechanism, the toxic effects on fish and the health of the human consumption of fish. Also, this article reviews the Histopathological change and biomarkers when exposed to heavy metal contamination.

Keywords: Fish; Pollutants; Heavy Metals; Health; Histopathological

Introduction

Heavy metals are highly persistent and toxic in trace amounts, and can cause severe oxidative stress in aquatic organisms. Hence, these pollutants are very important in terms of environmental toxins. As it is not subjected to bacterial degradation, and therefore remains permanent in the aquatic environment, it may have devastating effects on the ecological balance [1]. Heavy metal contamination of water creates a serious problem due to the dumping of household and industrial waste into the water. They reach a dangerous level and pose a threat to the health of aquatic organisms, as well as humans. It is important to know the concentration of toxic metals in fish to avoid these problems [2]. Heavy metals are naturally found in the deep layers of the earth and are found in sediments of high concentrations. In addition, geological weather factors and human emissions from crude oil mines may lead to increased concentrations of heavy metals in the aquatic environment [3]. Aquatic animals have the ability to accumulate heavy metals in their tissues through absorption through the layer of gills, liver and intestine to levels higher than those in the environment. Cadmium, mercury and lead have no known essential role in living organisms; however, they exhibit significant toxicity at low exposure levels and are considered fundamental threats to all life forms, especially human health. The biological accumulation of toxic substances depends on the availability and persistence of pollution in water and food, and their physical and chemical properties. Some studies have shown that the degree of accumulation of these minerals in fish depends on the types of minerals, fish species, and tissues, respectively [4,5]. In aqueous environments, heavy metals produce their pollutants from direct precipitation from the atmosphere, or through the disposal of agricultural and industrial wastes, as well as through the plants where sewage wastes are treated [6]. Heavy metals accumulate in the aquatic environment, then affect fish and build up in their bodies. Marine water fish are less susceptible to heavy metals than freshwater fish. This is because freshwater fish tend to gain water and lose salt, unlike marine water fish, which tend to lose water and gain salt. Heavy metals enter the body of the fish through a process known as ion exchange by the gills and skin, or adsorption by fish tissues. Metal accumulation in different parts of the body depends on many factors such as water solubility, feeding behavior, environment, and physiology including species, age, size, reproductive status, fish health, bioavailability and different habitats [7].

The Main Sources of Water in Egypt

River Nile

It is estimated that 85 % of the water flowing from the Aswan High Dam is used for irrigation, and the remaining 15 % is used in industry, water supply, hydropower and fisheries. Adopting new irrigation techniques through sprinkler and drip irrigation will reduce the total volume of agricultural wastewater significantly [8].

Groundwater

Groundwater is found within the sandstone aquifer. They occur at great depths and the aquifer is generally non-renewable. Therefore, the use of this water depends on the costs of pumping and its depletion against the potential economic return in the long run [9].

Rain Water

It cannot be relied upon for expanded agricultural production or other uses, due to its spatial and temporal fluctuation.

Others Water Resources

This includes agricultural drainage water, treated wastewater, cloud seeding and seawater desalination. Every resource has its limits on usage. These restrictions relate to quantity, quality, location, time, and cost of use [10]. This is shown in (Table 1) and (Figure 1).

Water supplies	1990	2000	2025
Nile water	55.5	57.5	57.5
In the desert	2.6	5.1	6.3
Reuse of agricultural drainage water	5.2	7	8
Treated sewage water	0.2	1.1	2.4
Management and saving wasted water	–	1	–
Total	63.5	71.7	74.2

Table 1: Shows the water resources in Egypt (billion / m^3) between the last years from 1990 to 2025 [11,12].

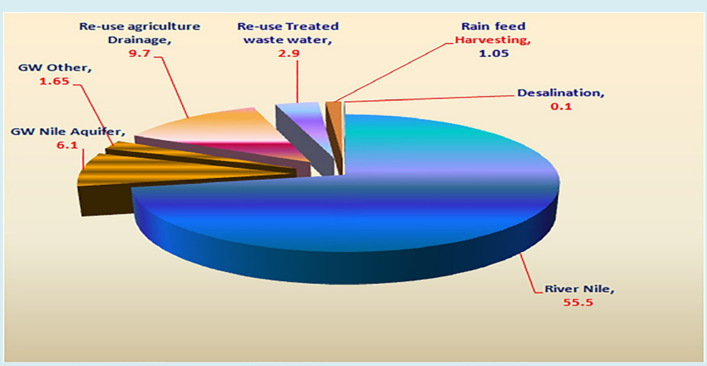

Figure 1: Water rates and resources in Egypt (billion/ m^3) (Ministry of water resources and irrigation, MWRI) [13].

Water Pollution

Water pollution is defined as human direct and indirect interference with various substances in the water environment, which leads to harm to human public health, deterioration of fish activities, and damage to water components. Pollution also occurs from human activities that supply some foreign substances in fresh water or sea water [14]. Agricultural wastewater, industrial effluents, and municipal wastewater are disposed of recklessly into the Nile, gradually making its waters unfit for human consumption. There are many areas in Cairo that empty into the Nile without treating the water. Agricultural drainage water contains pesticide and herbicide contaminants. Industrial effluents are often highly toxic, and contain heavy metals that can combine with suspended solids in household wastewater to form slurries. This water entering the river makes it very polluted in the future [15].

Water pollution with heavy metals

Identification of heavy metals

Heavy metals are defined as mineral elements with a relatively high density compared to water, and human exposure to them has increased dramatically as a result of the massive increase in their use in many industrial, agricultural and technological applications [16]. The sources of heavy metals are many in different environments, including the industrial and agricultural environment, liquid waste and air sources [17]. Heavy metals are considered pollutants due to their toxicity, persistence in the environment, and their ability to integrate and bioaccumulation within food chains [18]. Heavy metals can accumulate in freshwater and marine systems which pose a potential health concern for consumers and may lead to financial losses if concentrations in the water exceed Maximum Pollutant Levels (MCL). Moreover, the uptake of heavy metal contaminants may lead to concentrations in fish or edible plant tissues that exceed standards, contributing to economic losses, environmental degradation and negative impacts on human health [19].

Classification of heavy metals

Essential heavy metals

Copper, chromium, zinc, nickel, cobalt and iron are essential minerals required for all vital processes within the body at an ideal level. If it exceeds the permissible limits it causes various diseases and high level toxicity [20].

Non-essential heavy metals

These have no biological roles and are also called xenobiotics. When it increases in concentrations, it will cause toxoplasmosis effects in the tissues. They include aluminum, mercury, lead, cadmium, and others. [21].

Source of heavy metals in water

Heavy metals in surface waters such as rivers and lakes are influenced by soil type and water velocity. So metals on the surface of the soil are derailed and end up in reservoirs and wastewater. Rainwater is polluted as it passes through the atmosphere. Water sources are polluted as various industrial liquid wastes flow into them. This industrial and liquid agricultural waste contains many heavy metals, as mentioned in Table 2. Groundwater is polluted from landfills, from deep wells, and from industrial waste [22].

Metal	Sources
Fe	Pigments and paints; fuel; refineries; textile.
Mn& Zn	Batteries and electrical; pigments and paints; alloys and solders; pesticides; glass; fertilizers; refiners; fuel.
Pb	Batteries and electrical; pigments and paints; alloys and solders; pesticides; glass; fertilizer; refiners; fuel; plastic.
Cd	Batteries electrical; pigments and paints; alloys and solids; fertilizers.
Ni	Electrical; pigments and paints; alloys and solids; fuel; catalysts; fertilizers.
Cu	Batteries and electrical; pigments and paints; alloys and solid; fuel; pesticides.
Cr	Pigments; fertilizers; textile.

Table 2: Industrial and agricultural sources for metals in the aquatic environment [23].

Heavy metals are natural elements found in the Earth's crust. Pollution with these metals occurs as a result of the activities embodied in the following Mining and industrial production and the use of minerals containing chemical compounds that are used for agricultural and domestic purposes. These sources have been reported by several researchers. The potential sources of environmental pollution with heavy metals are shown in Figures 2 & 3. The toxic properties of heavy metals are characterized by many causes including persistence of the metal in the soil and bioaccumulation [24]. Heavy metals in the aquatic ecosystem are a serious pollutant of global concern due to their high bioaccumulation and severity of toxicity, which cause severe damage to organisms present in the aquatic environment. Contamination of riverine ecosystems with heavy metals has become a major problem and is a natural result of industrial growth and other man-made activities [25]. Heavy metals enter rivers and lakes from natural and human sources through erosion, leaching, and rock weathering [26]. New techniques have been developed to treat heavy metals present in wastewater in order to achieve a reduction in the harmful effects of heavy metals on the ecosystem [27].

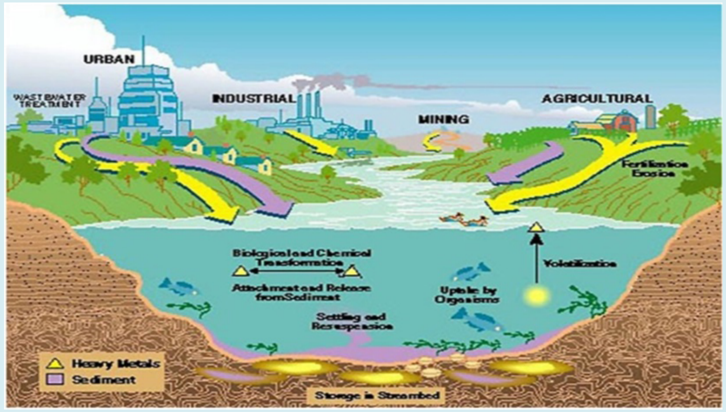

Figure 2: Different sources of heavy metals in surface waters [28].

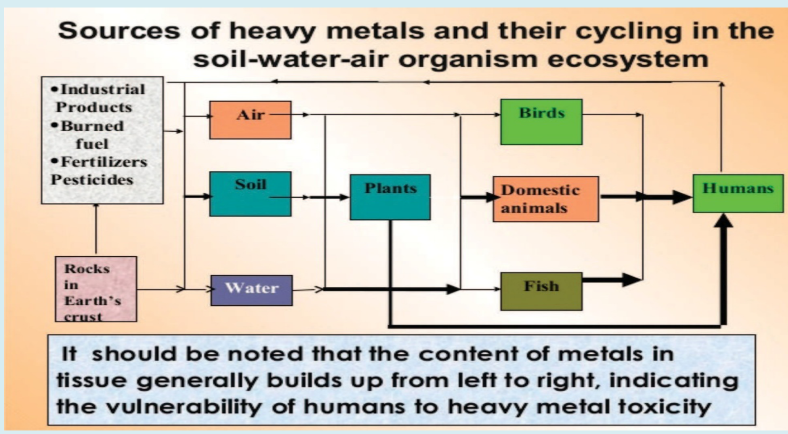

Figure 3: A schematic diagram showing the source of heavy metals and their cycle in the aquatic ecosystem [29].

Contamination of water with heavy metals

Heavy metals are present in the environment in various forms as solids, solutions and free ions that are absorbed by solid colloidal particles. Concentrations in the environment are due to natural sources such as rock weathering, dissolution of water-soluble salts, as well as human sources [30]. The essential and non-essential elements thereof are of particular importance in environmental toxicology because they are of high persistence and are highly persistent and have the potential for virulence [31]. The presence of metal contaminants in excess of the permissible limits has become a problem of concern. This situation arose as a result of the increase in population and the different activities of human life on earth and the lack of environmental regulations [32]. Industrialization and urbanization are the biggest reasons for the increase in water pollution with heavy metals, which leads to accumulation in the soil and sediments of water bodies [33]. The level of toxicity of heavy metals depends on several factors, including exposure of living organisms such as fish for a long time, their nature, and their biological role. It is may exist naturally in the aquatic environment and cause toxicity and pathological changes in fish tissues when it's permissible restricted concentration increases as a result of agricultural and industrial activities [34].

The role of heavy metals in fish organs

Heavy metals such as Fe, Mn, Pb, Zn and Cu, have a direct role in affecting fish health as the biological and toxic roles of minerals have been extensively studied in recent years. Figure 4 shows the presence of some heavy metals in different tissues of fish. It has an influential role in biological functions in living organisms such as iron, and it is necessary for almost all living organisms to carry out phytological functions [35]. Manganese is found in surface waters, but high concentrations of it are very toxic to various systems in fish [36]. For aquatic organisms, zinc is an essential nutrient and environmental pollutant. The intestine is possibly the most important method for zinc absorption, but little is known regarding the zinc absorption pathway in fish [37]. Zinc does not form free radical ions and has antioxidant properties [38]. Copper is the main source for the food chain in a state of natural growth [39]. High concentrations of copper can be fatal to fish and other organisms in the aquatic environment [40]. Nickel has a significant role in inhibiting a number of enzymes and binds to some proteins, including albumin and metallothionine [41]. The different valences of chromium present play a fundamental role in its toxicity [42]. The toxic effect of lead can be avoided by various factors that affect its concentration. Cadmium is a heavy metal with unknown biological functions in aquatic organisms [43]. In general, free ions of heavy metals are toxic to organisms in the ecosystem if they exceed the internationally permissible limits [44].

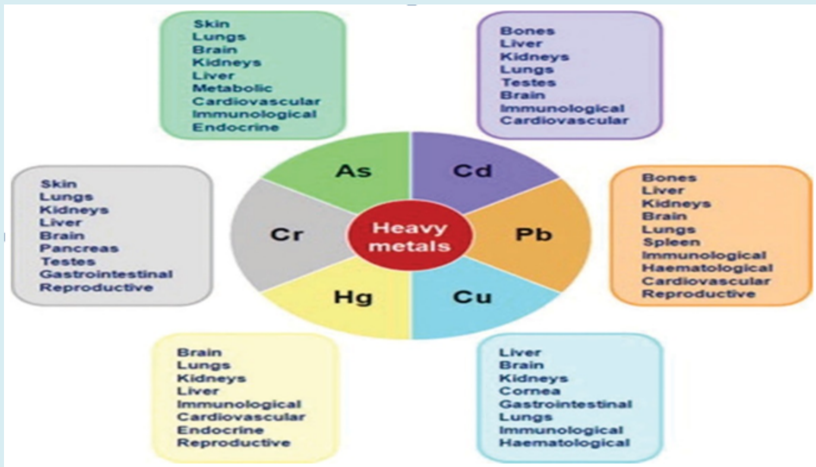

Figure 4: Schematic diagram showing the role of heavy metals in the different tissues in fish [45].

Mechanism of toxicity and uptake of heavy metals by fish tissues (Bioaccumulation)

Heavy metals enter aquatic environment mainly in three ways (!) Gills, then to other organs. Also, they accumulate on the skin surface cells or transfer to different tissues of the body through their blood. (!!)Its digestive tracts from food intake and more. (!!!) Subcutaneous layers and through osmotic exchange. Once heavy metals enter aquatic organisms, they cannot easily metabolize and degradation of various body organs occurs over time, as they easily accumulate in organs such as the liver and kidneys of animals. Bioaccumulation can be defined as the process by which certain toxic substances such as heavy metals occurring in the environment accumulate in the living organisms and their uptake is considered to be passive and involves diffusion gradients created by adsorption or binding of the metal to the tissue and cell surfaces. The bioaccumulation of heavy metals in fish depends on a large variety of factors such as the physical and chemical properties of water, its bioavailability, and concentration in the water [46,47]. Bioaccumulation is also dependent on size, age, sex and special differences, according to species with sensitivity to different minerals and cumulative metabolic activity [48,49]. Heavy metals are both organic and inorganic pollutants in the aquatic environment and their concentrations in different parts of the organism's bodies are determined as a biomarker on the level of pollution in the aquatic environment [50]. Heavy metals discharged into seas and rivers have the potential to harm aquatic species and the ecosystem. It also has the potential to cause changes in water quality that affect aquatic organisms and fish. Exposure to these toxins cannot be avoided as a solid or dissolved in water [51]. Heavy metals in fish move through the blood in different organs and thus accumulate to varying degrees [52]. Exposure to metals at very low concentrations has been studied to identify morphological and biotic changes in tissues that may directly affect fish quality [53]. There is an increase in the concentrations of a chemical in an organism over time compared to the concentration of chemicals in the environment. Therefore, bioaccumulation occurs when an organism absorbs the toxic substance at a greater rate than the loss of that substance. Whereas, it results from the dynamic balance between exposure from the external environment and absorption into the body of an organism [54]. Fish are one of the most important vital monitoring devices in the aquatic system for estimating mineral pollution concentration. Because it provides many specific advantages in describing the physical properties of aquatic systems and in evaluating the changes that take place in them [55,56]. Various minerals accumulate in the body of fish in indifferent quantities. These differences result from the affinity of the different minerals with fish tissue, and the difference in the uptake and excretion sedimentation [57]. Heavy metals in natural waters are in the form of water-insoluble particles or substances, including variable and fixed elements, and modified compounds are more dangerous to fish. The amounts of minerals in the variable fractions and the different metal ions depend on the surrounding environmental conditions. Fish at the top of the aquatic food chain and can accumulate in different tissues and organs because they have the ability to accumulate minerals several times higher than those found in sediments and water [58,59]. Also, minerals accumulate in their different bodies and tissues and enter the human body through consumption, causing various diseases. Also, minerals may accumulate in fish in higher concentrations than in water because these minerals are not identifiable in water samples taken permanently [60,61]. Figures 5 & 6 show the bioaccumulation sequence of heavy metals and how they are present in the food chain. Fish that live in polluted waters are characterized by the accumulation of heavy metals in their tissues. In general, fish can regulate mineral concentrations after bioaccumulation has occurred [62]. Therefore, the ability of each organ to regulate or accumulate minerals can be directly related to the total amount of minerals accumulated in that specific organ and when minerals reach high concentrations in the cells of the body they can alter the physiological performance of fish [63,64]. Heavy metals are toxic if they are concentrated in high quantities in the tissues of the organism, and they can cause severe damage and become fatal for most organisms because they are capable of bioaccumulation and biomagnification [65].

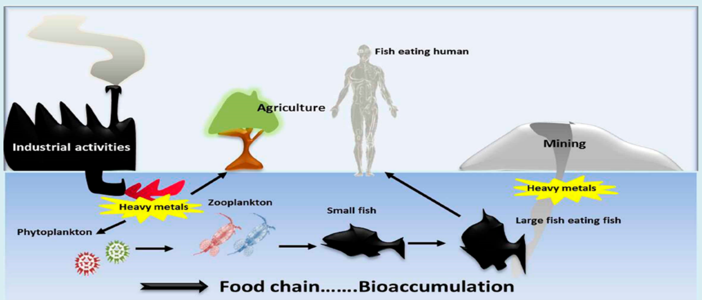

Figure 5: Bioaccumulation of heavy metals due to different activities and its effect on the food chain in the aquatic environment [66].

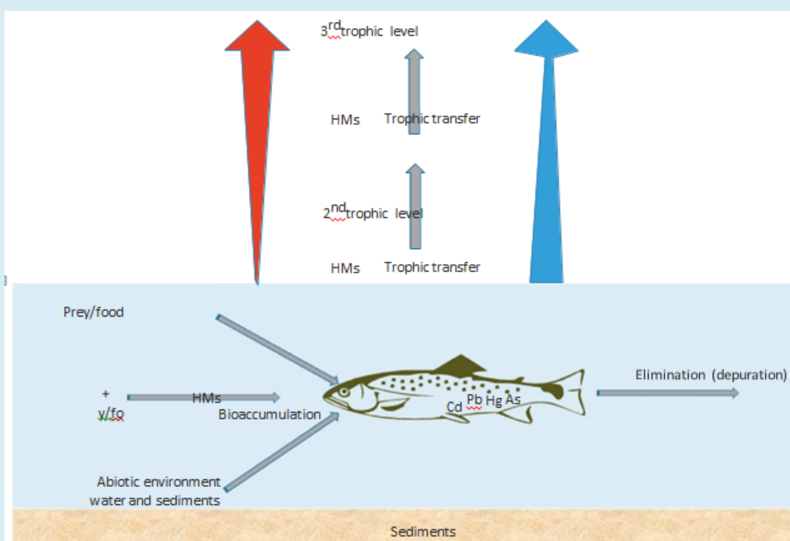

Figure 6: Schematic diagram of heavy metals and how they are in the food chain [67].

Fish absorption of heavy metals from the environment occurs primarily through gills, food, and skin. The concentration of the toxic component in fish depends on the sex and age of the fish, the season and the location. Pollution of water sources through human activities leads to water loss and thus disturbance in the balance of the food chain [68]. Metals accumulated in fish tissues up to toxic concentrations depend on specific environmental conditions such as food chain, predation competition, water chemistry such as pH, and water hardness, moreover, interaction between minerals may also affect the accumulation [69]. Some other environmental and biological factors such as hypoxia, excessive storage, famine, growth, development and reproduction affect heavy metal accumulation negatively through altering metabolic, Biochemical and physiological functions [70,71]. Topcuoglu C, et al. [72] studied heavy metal content levels in aquatic organizations. The results showed that heavy metals Pb, Cd and Cr were the most accumulated in the tissues of molluscs and shellfish, while iron and zinc were the least accumulated. Olga S, et al. [73] studied that toxic effects of minerals cause loss of nervous system functions and great damage to the content of blood, liver and other organs. Also, mineral accumulation in different organs of fish may cause functional disorders in them. In general, it was found that heavy metal toxicity causes changes in the condition parameter and the somatic liver index, and the occurrence of various diseases that appear upon dissection of diseased tissues [74]. To cause serious environmental damage. Ionic oxidizing forms of these minerals work with living environmental regulators to form corresponding toxic compounds where oxidation states play important roles in increasing the bioaccumulation of heavy metals [75]. The toxic effects of minerals mainly cause loss of nervous system function, and significant damage to the content of blood, liver and other organs. This damage results in physical weakness, allergic skin reactions, high blood pressure, and other symptoms, and fish growth may be impeded. One of the most obvious symptoms of the metal's toxic effect on fish larvae is growth inhibition. Therefore, fish body length and mass are indicators of environmental conditions [76]. Table 3 shows the organs that can be targeted due to the accumulation of heavy metals in them and the emergence of some signs of disease in these organs.

Metal	Primary Sources	Target Organs	Clinical effects
Arsenic	Industrial Dusts, Medicinal Uses of Polluted Water	Pulmonary Nervous System, Skin	Perforation of Nasal Septum, Respiratory Cancer,
Cadmium	Industrial dust and Fumes and Polluted Water And Food	Renal Skeletal Pulmonary	Proteinuria,Glucosuria, Osteomalacia,
Chromium	Industrial dust and Fumes and Polluted Food	Pulmonary	Ulcer, Perforation of Nasal Septum, Respiratory Cancer
Manganese	Industrial dust and Fumes	Nervous System	Central and Peripheral Neuropathies
Lead	Industrial dust and Fumes And Polluted Food	Nervous System, Hematopoietic System, Renal	Encephalopathy, Central Nervous Disorders, Anemia.
Nickel	Industrial dust, Aerosols	Pulmonary, Skin	Cancer, Dramatis
Mercury	Industrial dust and Fumes And Polluted Water	Nervous System, Renal	

Table 3: Shows the organs that can be targeted due to the accumulation of heavy metals and the emergence of some signs of disease in these organs [77].

Aquatic organisms, such as fish, accumulate pollutants in them from the water indirectly through the food chain. The use of chemical fertilizers containing traces of heavy metals results in contamination of fish with these minerals [78]. The larvae of common carp showed under laboratory conditions in lead or copper water. It slowed the growth rate and decreased the survival rate. Exposure to copper inhibited ossification of the skeleton, while lead caused scoliosis [79]. Another study conducted on the same adult fish, with the fish being exposed to heavy metals, showed that red blood cell concentrations, blood glucose and total cholesterol increased significantly. The level of iron and copper in the blood has been increased. The results showed decreased vitamin C activity during chronic exposure to toxic heavy metals, indicating the presence of reactive and induced oxygen species in the oxidation process [80]. Long-term exposure to cadmium of 20 days or longer showed reduced growth of juvenile and adult rainbow trout [81]. Fish mortality increased with increased concentration and exposure to heavy metals. Perhaps this was due to these toxic minerals that directly affected the respiration of the tilapia fish. Similar results are shown by Chen AWY, et al. [82]. Heavy metal toxicity increases due to reduced gill diffusion capacity, decreased oxygen consumption, physiological imbalance and decreased respiratory rate. Moreover, small species that have not reached the sexual maturity are more sensitive to acute toxicity than larger species [83]. When fish are exposed to toxic substances that contain those heavy metals, an imbalance occurs and leads to changes in the metabolic processes of the fish that may affect the survival of aquatic life, such as the concentration of minerals in the cell membranes that cause their destruction as well as the biological processes that activate some enzymes in the synthesis of metabolites of compounds Organic in fish [84,85]. Heavy metals accumulate in gills rapidly due to the large amount of water passing through them to increase oxygen under toxic pressure [86]. In a recent study, it was found that there is a strong relationship between heavy metal pollutants and parasites. It was found that parasites strengthen the toxic effects of heavy metals through the mechanisms used to protect fish, and this leads to negative effects on the physiological balance of fish. That study showed that some types of parasites can accumulate heavy metals in them several thousand times compared to those found in fish [66]. Table 4 shows the average permissible limits for some heavy metals in fish tissues.

Metal	Permissible	References
Copper	1.00 ppm	WHO [87]
Lead	0.05 ppm	WHO [87]
	0.1 mg/kg	Egypt "E.O.S.Q.C. [88]
	0.5 ppm	FAO/WHO [89]
Cadmium	0.005 ppm	WHO [87]
	0.05 ppm	FAO/WHO [89]
	0.1 mg/kg	Egypt "E.O.S.Q.C. [83]
Mercury	0.001 ppm	WHO [87]
	0.05 mg/kg	Egypt "E.O.S.Q.C. [88]
	0.05 ppm	FAO/WHO [89]

Table 4: Permissible limits of various some heavy metals) [53].

Hazard of Some Heavy Metals on Fish and Human Health

Iron (Fe)

Iron is a predominant component of industrial effluents discharged into aqueous environments. Ferrous Fe2+ is more toxic to fish than the form of iron Fe^{3+} [90]. Abbas HH, et al. [91] confirmed that the highest iron concentration in fish tissues was in the liver and gonads, and lowest in the brain, muscles and heart. It was found that respiratory disturbance was due to physical obstruction of the gills as a possible mechanism of iron toxicity. Since the surface of the gills of fish tends to be alkaline. Precipitated iron compounds have the dangerous effect of reducing the gill space available for breathing and damaging the respiratory epithelium, leading to fish strangulation and death. Also, iron in tilapia causes secondary platelet enlargement and necrosis through the study [92]. Collapsed nostrils reduce the diffusion distance between water and blood and reduce oxygen consumption. Also, iron compounds can be deposited on the surface of fish eggs, causing non-hatching [93]. (Fe) is an essential mineral for every living cell, the synthesis of hemoglobin and some enzymes. Iron deficiency leads to weakness and lack of focus, and anemia such as malaria is one of its most common deficiencies. Anemia leads to poor performance in the blood transfusion process and also reduces the supply of oxygen to the muscles, and reduces efficiency due to reduced hemoglobin content and poor endurance [94,95].

Lead (Pb)

Lead has the potential to bioaccumulation in aquatic ecosystems, due to its persistence in the environment. Lead accumulates in fish tissues such as bones and gills during the gas exchange through the gills into the bloodstream. Some of the effects of lead poisoning include a decrease in cognitive abilities due to the destruction of nerve cells, abdominal pain and weak bones where lead replaces calcium and causes anemia due to reduced enzymes involved in red blood cell synthesis [96-98]. It is a neurotoxin that causes behavioral deficits in fish and also leads to reduced survival, growth and metabolism rates, as well as increased mucus formation in fish [99].

Increased levels of lead in water have harmful effects in most aquatic organisms as it leads to changes in the nervous system and blood components of fish and other organisms. It is considered a dangerous environmental pollutant because it has become the subject of many researchers due to its great risks to the health of aquatic organisms and humans [68]. The effect of lead on Nile tilapia (*Oreochromis niloticus)* has been studied in terms of HSI and GSI; it caused a decrease in the HSI of fish while it had no effect on the GSI. The decrease in HSI was due to the consumption of energy reserves in the liver cells [71]. High exposure to lead may be fatal as it damages the nervous system of the unborn child. However, exposure to lead during childhood affects behavior and intelligence, and can lead to miscarriage and infertility (both in men and women) .Generally, lead affects children more than adults [100].

Children are most susceptible to lead infection because their renal excretion is weak, and more absorption occurs in the gastrointestinal tract, and the fetal brain shows greater sensitivity to the toxic effects of lead compared to the mature brain. In addition to symptoms of intestinal spasms and anemia, it can also cause neurotoxicity and nephrotoxicity [101-103].

Zinc (Zn)

It is the most abundant element after iron and is an essential element, it is present in almost every cell and participates in the synthesis of nucleic acids and is found in an abundant amount of enzymes. Zinc is involved in more complex functions, such as transmitting nerves, the immune system, and cell signalling. Zinc residue has direct toxicity to fish when water levels are increased [104]. The primary target of zinc toxicity is the gills, where calcium absorption is disrupted, which leads to hypocalcemia and ultimately death. Also, the fish kidney is a target organ for zinc accumulation [105]. Zinc is one of the essential elements important to humans and plants. It is considered as a cofactor for most of the enzyme involved in DNA metabolism. It is also important to stabilize a large amount of proteins, when there is an excess of it, it becomes toxic, as for zinc deficiency can lead to many functional disorders such as poor pregnancy outcomes, the development of chronic diseases, vascular diseases and cancers as well [106-108]. Zinc causes death, respiratory changes, reduced ovulation, and other harmful effects that threaten fish survival, and damage gills, skeletal muscles, and liver [109]. In a study of Nile tilapia exposed to zinc sulfate, the gills were congested. The gill sutures are swollen with a hollow epithelial covering of gills [110]. Exposure to zinc has been shown to cause pathological histological changes in the ovary of Nile tilapia, liver changes in *Oreochromis mossambicus* such as hyaline, hepatocyte emptying and vascular congestion [111].

Cadmium (Cd)

Cadmium is widely distributed in the environment, and can be found in many food items, including some seafood products. Cadmium is a carcinogen and is toxic to the kidneys. Cadmium is a trace element that tends to bioaccumulate in organisms often at high levels [112]. It has been shown that this mineral accumulates in the kidneys, livers and gills of freshwater fish, but it can also be deposited in the heart and other tissues and cause uneven pathological changes in those organs [110,111]. Cadmium is one of the most toxic elements that humans are exposed to in the environment. Once absorbed, the human body retains it, as it accumulates throughout life without symptoms appearing on the living organism. It is primarily toxic to the kidneys and especially to the adjacent tube cells. It can cause bone demineralization either through direct or indirect bone damage [100]. Fish that were exposed to cadmium developed disturbances in blood components. Where it destroys red blood cells and reduces hematocrit and hemoglobin concentration in addition to anemia. The cadmium present in the plasma of the goldfish significantly increased the activities of glutamic acid in the plasma. Cadmium alters carbohydrate metabolism, causing the blood sugar level to rise in some freshwater and marine fish [91]. The high doses of cadmium caused visible external lesions such as discoloration and necrosis of the skin (*Cyprinus carpio*, and *Oreochromis mossambicus*). Cadmium inhibits calcium absorption in the gills and may alter the metabolism of essential elements by affecting the normal tissue distribution of trace elements such as zinc and copper [113]. It is considered an endocrine irritant and can cause breast and prostate cancer in humans, as well as kidney damage, high blood pressure and impaired reproductive function [114]. Cadmium is a dangerous environmental pollutant in fish. It can cause anemia and vertebral fractures, osmotic regulation problems that reduce the efficiency of the digestive system. Stunted growth, irregular swimming, and deaths [115].

Copper (Cu)

Copper (Cu) is a micronutrient of cellular metabolism in living organisms due to it being a major component of metabolic enzymes, yet it can be highly toxic to intracellular mechanisms in aquatic animals in concentrations exceeding normal levels [116]. Copper accumulates in fish through the diet and the environment. Even at low environmental concentrations, the accumulation of copper in the fish shows significant pathological changes, including the presence of mucus on the surface of the body, under the gill cover, and between the strings of the gills [117]. (Cu) is essential for enzymes and essential for hemoglobin synthesis. Poor copper conduction can lead to decreased bone and blood vessel activity, as well as anemia and osteoporosis. Poor copper metabolism can result from two inherited diseases, mine disease and Wilson's disease. Wilson's disease can also be caused by a build-up of copper in the brain and eyes in the form of a Kayaer-Fleischer ring. Excessive copper intake may also damage the kidneys [118,119]. Heavy metals such as copper reduced the respiration rate and metabolism of freshwater fish. Also, the decrease in glycogen number, tissue oxygen consumption and pyruvate level of the whole body of *Cyprinus carpio* due to stress from copper exposure was determined [120]. Copper reduces resistance of fish to diseases by disrupting altering swimming, causing oxidative damage, impairing respiration, disrupting osmoregulation structure and pathology of vital organs such as gills, kidney, liver and other stem cells [121]. Copper exposed different fish species posed behavioural changes such as decrease in swimming ability and food intake and increase in operculum movements [70]. Some pathological signs appeared in the different tissues of the fish upon exposure to copper. The exposure of Nile tilapia (*Oreochromis niloticus*) to sublethal levels of copper showed tissue changes such as gills and liver. Also, *Oreochromis mossambicus* exposed to copper showed pathological alterations in the testis (necrosis of testicular hemorrhage, sclerosis, dissociation of primary sperm and interstitial tissue [122].

Mercury

The different forms of mercury are symptoms of many different diseases. It causes spontaneous abortion, congenital anomalies, and gastrointestinal disorders such as esophagitis, intoxication, abnormal irritation and allergic reactions characterized by rashes, peeling of hands and feet, gingivitis, stomatitis and neurological disorders [123]. Mercury has no known beneficial role in human metabolism, and its ability to influence the distribution and retention of other heavy metals makes it one of the most toxic metals. The relatively high solubility and stability of some mercury salts in water enable them to be easily absorbed and bio-converted to methyl mercury by certain fish. Therefore mercury is found in its highest concentrations in carnivores such as sharks and some tuna. These forms are easily absorbed through the digestive system and have become a major source of human exposure to mercury. Although humans can excrete a small amount of mercury in urine or feces as well as through sweating, they lack a robust, active mechanism for excreting mercury, which allows levels to build up with chronic exposure. When ingested, mercury can spread to many organs, but it may be concentrated in the brain and kidneys. It can also cross the placenta and is found in breast milk. Mercury exerts its toxic effects by competing with and displacing iron and copper from the active site of enzymes involved in energy production. Mercury may also build up in Thyroid gland and increased risk of autoimmune disorders [124-126]. All heavy metals in surface waters are present in a colloid in particle and dissolved phases, although the solute concentrations are generally low. The solubility of heavy metals in surface waters is affected by the following factors, mostly water pH, the type and concentration of bonds on which the metal can be absorbed, the oxidation state of mineral components and the oxidation-reduction environment. Figures 7-9 illustrate the dynamics of heavy metals in fish tissues and their effect on human health.

Different Methods of Detecting Heavy Metals in the Organs of Different Fish (updates)

Techniques in determining metals concentration to include the

- Atomic Absorption Spectrometer (AAS),
- X-Ray Fluorescence (XRF),
- Particle Induced Gamma Ray Emission (PIGE),
- Instrumental Neutron Activation Analysis (INAA),
- Particle Induced X-ray Emission (PIXE)
- The Inductively Coupled Plasma Optical Emission Spectrometry Technique (ICP OES) [127].

Figure 7: Effects of heavy metals on human health [128].

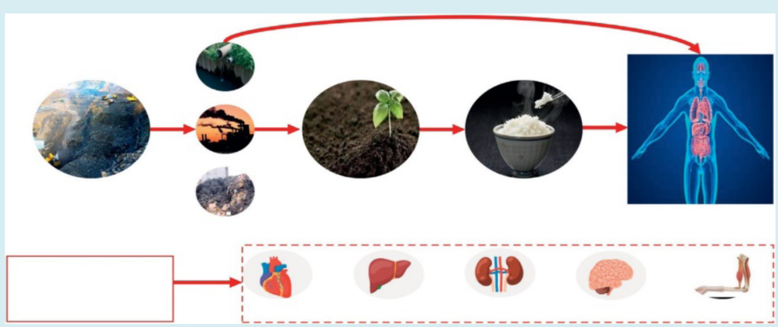

Figure 8: Sources of heavy metals and its hazard to the human body [129].

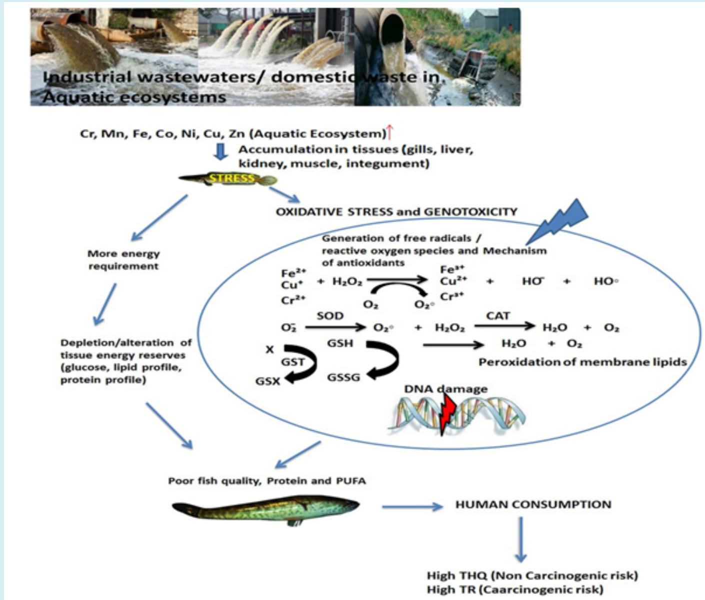

Figure 9: Illustrates the impact of heavy metal-loaded industrial waste on general health of fish and fish consumers [130].

Histopathological Change and Biomarkers

Detection of pathological changes by heavy metals in fish tissues

Pathophysiology provides a faster way to detect traces of heavy metals and pathogens in the organs of different fish, and can be considered as an indicator of many abnormal states of the fish ecosystem. However, heavy metal diseases vary according to duration of exposure, mineral concentration, and genetic susceptibility. When studying the histopathological effects of heavy metals such as cadmium, lead, and zinc in water and fish, the characteristic pathological and cumulative changes were in the gills, liver and kidneys. Changes in the gills were lamellar epithelial hyperplasia, fusion, necrosis, and filament separation. Hepatic and renal changes were vacuoles and hydrophobic degeneration of both hepatocytes and renal epithelial cells that were separated [131,132]. Another study showed the effect of some metals on other fish species, emptying of gill epithelial cells and intestines, lipoid enteritis, lamellar necrosis and infiltration of mononuclear cells [133,134]. Figure 10 illustrate the pathological changes that occur in the gills to infer the pathological effects and changes of heavy metals.

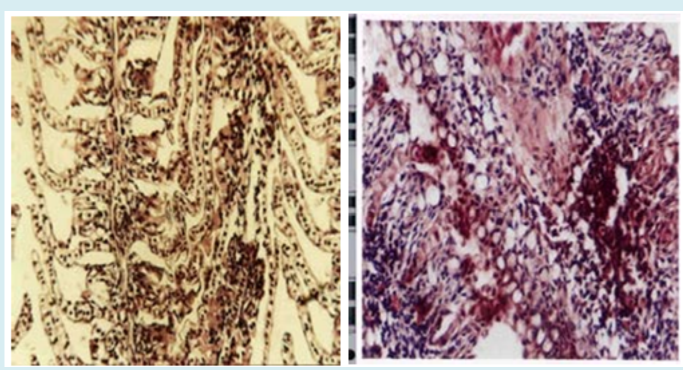

Figure 10: The gills of tilapia appear in areas heavily contaminated with heavy metals, showing lamellar necrosis [135].

Biomarkers, Fish Health and Impact of Heavy Metals

Biomarkers are powerful tools for detecting the effect of exposure to near-lethal concentrations of a specific substance or complex chemical mixtures, and for evaluating the less obvious effects on organisms that respond to environmental pollution by altering life functions or the accumulation of toxins in their bodies, such as fish, shellfish, algae, protozoa, large plants and bacteria [136]. Fish has become a favorite subject for biomarker research due to its sensitivity to changes in temperature, natural environment and water quality. Water degradation and pollution also negatively affect fish health, which can lead to mortality and ecosystem degradation [137]. Fish biomarker including assessment of molecular, cellular and physiological change that was used to monitor the biological effect of toxic substances, especially exposure to heavy metals. Interest in biomarkers of heavy metal impact was identified in parallel with the development of a biomonitoring program. Some studies showed fish livers the highest popularity in studying heavy metal toxicity, followed by muscle, gills, kidneys and brain. Types of fish biomarkers in aquatic organizations are widely used in assessing the quality of environmental pollutant systems [138]. Toxic pollutants often cause characteristic responses in an infected organism by providing evidence of exposure to one or more chemical pollutants because they are a biological marker of contamination in the organism's body [139]. Fish are sensitive to the effects of a complex mixture of chemicals because they cause they usually have a wide range of effects and responses in them ranging from the cellular and biochemical level to the level of behavior, growth and reproduction during low and limited exposure to toxic substances. Heavy and prolonged exposure may lead to a series of functional and structural changes that impair vital functions. Tissue chemical concentrations are therefore excellent indicators of the environmental load of a specific toxin but do not usually reflect physiological and environmental outcomes directly [140]. Heavy metals from direct contact have been shown to bioaccumulate by inhalation in hepatocytes prior to distribution to fish tissues and cause abnormalities such as homeostatic imbalance, enzyme inhibition and growth retardation at an elevated level [141]. Heavy metals such as copper reduce the respiration rate and metabolism of freshwater fish. Significant reduction in glycogen count, tissue oxygen consumption and disk level of the whole body of *Cyprinus carpio* due to stress induced copper exposure. Further studies can be done based on fish biomarkers which can aid in estimating the level of toxicity by monitoring fish behavior, cellular change, enzyme and protein response. [120,142].

Conclusions and Future Expectations

Although some heavy metals are essential for animals, plants, and many other organisms, their toxic effects are seen through metabolic interference and mutations. Heavy metals can have toxic effects on various organs [143,144]. They can get into the water across drainage, atmosphere, soil erosion and all human activities in different ways. Heavy metals are the most pollutants in both aquatic and terrestrial ecosystems and toxic environmental chemicals that are persistent and bio- accumulative are more dangerous. Heavy metals are dangerous due to these three properties: persistence, bioaccumulation, and toxicity. The most environmentally hazardous heavy metals include Fe, Cu, Zn, Cd, and Pb. The food transport of these elements in aquatic and terrestrial food chains has important implications for human health. It is extremely important to assess and monitor the concentrations of potentially toxic heavy metals and metals in different environmental sectors as well as in living organisms. Steps must be taken to minimize the impact of these elements on human health and the environment the following recommendations:

- The concentrations of heavy metals present in the water environment must be documented, as they are considered a reference for all researchers in this field.
- Levels of potentially toxic heavy metals in water, sediments, soil and living organisms should be assessed and monitored.
- Efforts should be made to reduce heavy metal pollution in the aquatic environment which threatens the health of fish and subsequently the health of consumers.
- The consumer public should be educated about the harmful effects of toxic heavy metals on human health and the environment.
- Industrial wastewater must be effectively analyzed before being discharged into natural water bodies.
- Encourage scientific research on environmental assessment of toxic chemicals, including toxic heavy metals, to protect human health and the environment.

References

1. Ayandiran TA, Fawole OO, Adewoye SO, Ogundiran MA (2009) Bioconcentration of metals in the body muscle and gut of Clarias gariepinus exposed to sublethal concentrations of soap and detergent effluent. Journal of Cell and Animal Biology 3(8): 113-118.

2. Vardi V, Chenji V (2020) Bioaccumulation of heavy metal lead (Pb) in different tissues of brackish water fish *Mugil cephalus* (Linnaeus, 1758). Journal of Applied Biology & Biotechnology 8(2): 1-5.

3. Waheed R, El Asely AM, Bakery H, El-Shawarby R, Abuo-Salem M, et al. (2020) Thermal stress accelerates mercury chloride toxicity in *Oreochromis niloticus* via up-regulation of mercury bioaccumulation and HSP70 mRNA expression. Sci Total Environ 718: 137326.

4. Korkmaz Gorur F, Keser R, Akcay N, Dizman S (2012) Radioactivity and heavy metal concentrations of some commercial fish species consumed in the Black Sea Region of Turkey. Chemosphere 87(4): 356-361.

5. Petrovic Z, Teodrorovic V, Dimitrijevic M, Borozan S, Beukovic M, et al. (2013) Environmental Cd and Zn concentration in liver and kidney of eropean hare from

different Serbian region: age and tissue difference. Bull Environ Contamin Toxicol 90 (2): 203-207.

6. Maier D, Blaha L, Giesy JP, Henneberg A, Köhler HR, et al. (2014) Biological plausibility as a tool to associate analytical data for micropollutants and effect potentials in wastewater, surface water, and sediments with effects in fishes. Water Research 1(72): 127-144.

7. Anandkumar A, Nagarajan R, Prabakaran K (2017) Trace metals dynamics and risk assessment in the commercially important marine shrimp species collected from the Miri coast, Sarawak, East Malaysia. Reg Stu Mar Sci 16: 79-88.

8. Rassoul EMA (2006) Prospects of water reuse in Egypt. IWTC10, Alexandria, Egypt.

9. Abdel-Shafy, Aziza H (2016) Groundwater in Egypt Issue: Resources, Location, Amount, Contamination, Protection, Renewal, Future Overview Egypt. J. Chem 59(3): 321-362.

10. Abdel Ghaffer E (2006) Non-Conventional water resources management. IWTC10, Alexandria, Egypt. 81-92.

11. Abdel Dayem S (1994) Water quality issues in Egypt. Italian Egyptian Study Days on the Environment pp: EL-Kassas MA (1998) Freshwater Problem in Egypt in Land, Water and Soil. In: El-Razaz M (Ed.), Educational Palace General Organization Publ. Cairo.

12. Radwan G Abd Ellah (2020) Water resources in Egypt and their challenges, Lake Nasser case study Egyptian Journal of Aquatic Research 46(1): 1-12.

13. Clark RB (2001) Metals. In: Marine pollution. Oxford University Press, Oxford 5th (Ed.), pp: 98-125.

14. Dakkak A (2013) Egypt's Water Crisis-Recipe for Disaster. Middle East, Water.

15. Bradl H (2002) Heavy Metals in the Environment: Origin, Interaction and Remediation. Academic Press, UK, 6.

16. Yang H, Stoffella PJ (2005) Trace elements in agro-ecosystems and impacts on the environment. J Trace Elem Med Biol 19(2-3): 125-140.

17. Armitage PD, Bowes MJ, Vincent HM (2007) Long-term changes in macro invertebrate communities of a heavy metal polluted stream: The River Nent (Cumbria. UK) after 28 years. River Research 23: 997-1015.

18. Mendiguchia C, Moreno MP, Manuel-Vez, Garcia Vargas M (2006) Preliminary investigation on the enrichment of heavy metals in marine sediments originated from intensive aquaculture effluents. Aquaculture 254(1-4): 317-325.

19. Sivaperumal P, Sant V, Nant V (2007) Heavy metal concentration in fish, shellfish and fish products from internal markets of India vis-à-vis international standards Food Chem 102(3): 612-620.

20. Salamat N, Movahedinia A, Etemadi E, Mohammadi Y (2015) Pike (Esox Lucius) Bio-indicator of heavy metal pollution in Anzali Wetland. Water Qual. Exposure Health 7(2): 251-254.

21. Oyeku OT, Eludoyin AO (2010) Heavy metal contamination of groundwater resources in a Nigerian urban settlement. Afr J Environ Sci Technol 4(4): 201-214.

22. Rahman PKSM, Bastola S (2014) Biological reduction of iron to the elemental state from ochre deposits of Skelton Beck in Northeast England. Front Environ Sci 2: 22-25.

23. Fifield FW, Haines PJ (2000) Environmental analytical chemistry. Wiley-Blackwell, USA.

24. Manzetti S, Spoel ER, Spoel D (2014) Chemical properties, environmental fate, and degradation of seven classes of pollutants. Chem Res Toxicol 27: 713-737.

25. Arefin MT, Rahman MM, Wahid-U-Zzaman M, Kim JE (2016) Heavy metal contamination in surface water used for irrigation: functional assessment of the Turag River in Bangladesh. J Appl Biol Chem 59: 83-90.

26. Paul D (2017) Research on heavy metal pollution of river Ganga: a review. Ann Agrar Sci 15(2): 278-286.

27. Dhir P, Sharmila, Saradhi PP (2009) Potential of aquatic macrophytes for removing contaminants from the environment. Critical Reviews in Environmental Science and Technology 39(9): 754-781.

28. Garbarino JR, Hayes HC, Roth DA, Antweiler RC, Brinton TI, et al. (1995) Contaminants in the Mississippi River: Heavy metals in the Mississippi River. Reston, Virginia, US, pp: 1133.

29. Brady D, Stoll AD, Starke L, Duncan JR, (1994) Bioaccumulation of metal cations by Saccharomyces cerevisiae. Applied Microbiology and Biotechnology 41:149-154.

30. Güven DE, Akinci G (2008) Heavy metals partitioning in the sediments of Izmir Inner Bay. J Environ Sci-China 20(4): 413-418.

31. Storelli MM, Storelli A, D'ddabbo R, Marano C, Bruno

R, et al. (2005) Trace elements in logger head turtles (Carettacaretta) from the eastern Mediterranean Sea: Overview and evaluation. Environ Pollut 135(1): 163-170.

32. Shirkhanloo H, Zavvar H, Rouhollahi A (2011) Preconcentration and determination of heavy metals in water, sediment and biological samples. J Serb Chem Soc 76 (11) 1583-1595.

33. Musilova J, Arvay J, Vollmannova A, Toth T, Tomas J (2016) Environmental contamination by heavy metals in region with previous mining activity. Bulletin of Environmental Contamination and Toxicology 97(4): 569-575.

34. Shahbaa K AL-Taee, Karam H, Hana Kh Ismail (2020) Review on some heavy metals toxicity on fresh water fishs ournal of Applied Veterinary Sciences 5(3): 78 -86.

35. Bury N, Grosell M (2003) Iron acquisition by teleost fish. Comp Biochem Physiol 135(2): 97-105.

36. Krauskopf KB, Bird DK (1995) Introduction to geochemistry. London, McGraw-Hill, pp: 647.

37. Glover CN, Hogstrand C (2003) Effect of dissolved metals and other hydrominerals on in vivo intestinal zinc uptake in freshwater rainbow trout. Aquat Toxicol 62(4): 281-293.

38. Powell SR (2000) The antioxidant properties of zinc. J Nutr 130(S5): 1447S-1454S.

39. Kamunde CN, Clayton C, Wood CM (2002) Waterborne vs. dietary copper uptake in rainbow trout and the effect of previous waterborne copper exposure. Am J Physiol 283(1): R69-R78.

40. Cogun HY, Kargin F (2004) Effects of PH on themortality and accumulation of copper in tissues of *Oreochromis niloticus*. Chemosphere 55: 277-282.

41. Dallas HF, Day A (1993) The effect of Water Quality variables on Riverine ecosystems: A Review. Water Research commission Report 351: 40.

42. Steihagen (2004) Effect of hexavalent carcinogenic chromium on carp *cyprinus carpio* immunecells. Dis Aquat Org 62: 155-161.

43. Xie l, Klerks Pl (2004) Changes in cadmium accumulation as a mechanism for cadmium resistance in the least killifish *Heterandria formosa*. Aquat Toxicol 66: 73-81.

44. Aardt WJ, Venter lR (2004) The effect of lead, water hardness and pH on oxygen consumption, plasma chlorides and bioaccumulation in the freshwater fish Tilapia sparrmanii. Afr J Aquat Sci 29: 37-46.

45. García-Niño WR, Pedraza-Chaverrí J (2014) Protective effect of curcumin against heavy metals induced liver damage. Food and Chemical Toxicology 69: 182-201.

46. Long YJ, Luo J, Xiao (2016) Research advances in effects of heavy metals stress on fish. Journal of Southern Agriculture 47(9): 1608-1614.

47. Olivares NM, Lagos CJ, Gutierrez (2016) Assessment oxidative stress biomarkers and metal bioaccumulation in macroalgae from coastal areas with mining activities in Chile. Environmental Monitoring & Assessmen 188(1): 1-11.

48. Merciai RH, Guasch A Kumar, Sabater S, García Berthou E (2014) Trace Metal Concentration and Fish Size: Variation among Fish Species in a Mediterranean River. Ecotoxicology and Environmental Safety 107: 154-161.

49. Yancheva V, Stoyanova S, Velcheva I, Petrova S, Georgieva E (2014) Metal Bioaccumulation in Common Carp and Rudd from the Topolnitsa Reservoir, Bulgaria. Archives of Industrial Hygiene and Toxicology 65(1): 57-66.

50. Sivakumar R, Natesan M (2011) Impact of metals on histopathology and expression of HSP 70 in different tissues of Milk fish (Chanos chanos) of Kaattuppalli Island, South East Coast, India. Chemosphere 83(4): 415-421.

51. Gad (2009) Determination of glutathion related enzymes and cholenisterase activities in *Oreochromis niloticus* and *clarias gariepinus* as bioindicator for pollution of Lake Manzala. Global Veterinaria 2 (1): 37-44.

52. Kalay M, Canli M (2000) Elimination of Essential (Cu, Zn) and Nonessential (Cd, Pb) Metals from Tissues of a Fresh Water Fish, Tillapia zilli. Turk J Zool 24: 429-436.

53. Kaoud HA, El-Dahshan AR (2010) Bioaccumulation and Histopatho logical Alterations of the Heavy Metals in *Oreochromis Niloticus* Fish. Nature and Science 8(4): 147-156.

54. Zhou R, Zhu L, Chen Y, Kong Q (2008) Concentrations and characteristics of organochlorine pesticides in aquatic biota from Qiantang River in China. Environ Pollut 151(1): 190-199.

55. Begum A, HariKrishna S, Khan I (2009) Analysis of Heavy metals in Water, Sediments and Fish samples of Madivala Lakes of Bangalore, Karnataka: International Journal of ChemTech Research 1(2): 245-249.

56. Lamas S, Fernàndez JA, Abdal JR, Carballeira A (2007)

Testing the use of Juvenile Salmotrtta L as biomonitors of heavy metal pollution in fresh water. Chemosphere 67: 221-228.

57. Jovanovic B, Mihaljev E, Maletin S, Palic D (2011) Assesement of heavy metal load in chub liver (*Cyprinida. leuciscuscephalus*). from the Nisava river (Serbia) Biol Nyssana 2(1): 1-7.
58. Al-Weher SM (2008) Levels of Heavy Metal Cd, Cu and Zn in Three Fish Species Collected from the Northern Jordan Valley, Jordan. Jordan Journal of BiologicalSciences 1(1): 41-16.
59. Sönmez AY, Hisar O, Yanık T (2012) Karasu Irmağında Ağır Metal Kirliliğinin Tespiti ve Su Kalitesine Göre Sınıflandırılması. Atatürk Üniv Ziraat Fak Derg 43(1): 69-77.
60. Al-Yousuf MH, El-Shahawi, Al-Ghais SM (2000) Trace metals in liver, skin and muscle of Lethrimus lentjan fish species in relation to body length and sex. The science of the total Environment 256(2-3): 87-94.
61. Olaifa F, Olaifa A, Adelja A, Owolabi A (2004) Heavy metals contamination in *clarias gariapinus* from alake and fish farm in Ibadan, Nigeria African. Bio med res 7: 145- 148.
62. Heath AG (1995) Water pollution and fish physiology. In: 2nd (Edn.), Lewis Publisher. New York and London, UK, pp: 359.
63. Filipovic V, Raspor B (2003) Metallothionein and metal levels in cytosol of liver, kidney and brain in relation to growth parameters of Mullussurmuletus and Liza aurata. From the eastern Adriatic Sea Water Res 37(13): 3253-3262.
64. Akoto O, Bismark Eshun F, Darko G, Adei E (2014) Concentrations and Health Risk Assessments of Heavy Metals in Fish from the Fosu Lagoon. Int J Environ Res 8(2): 403-410.
65. Govind P, Madhuri S (2014) Heavy Metals Causing Toxicity in Animals and Fishes. Research Journal of Animal, Veterinary and Fishery Sciences 2(2): 17-23.
66. El-Sayed E, Asmaa F, Samar S, Mohamed E, Mohammed AE, et al. (2020) Biomonitoring of Heavy Metal Pollution Using Acanthocephalans Parasite in Ecosystem: An Updated Overview. Animals 10(5): 811.
67. Ali H, Khan E (2018) Trophic transfer, bioaccumulation and biomagnification of non-essential hazardous heavy metals and metalloids in food chains/webs: concepts and implica- tions for wildlife and human health. Human and Ecological Risk Assessment: An International Journal, in Press.
68. Afshan S, Ali S, Ameen US, Farid M, Bharwana SA, et al. (2014) Effect of Different Heavy Metal Pollution on Fish. Res J Chem Env Sci 2(1): 74-79.
69. Cicik B (2003) Bakır-çinko etkileşiminin sazan (Cyprinus carpio)'nın karaciğer, solungaç ve kas dokularındaki metal birikimi üzerine etkileri. Ekoloji Çevre Dergisi, Cilt 12, Sayı 48: 32-36.
70. Arslan M, Karaytuğ S, Cicik B (2006) Bakırın Clariaslazera (Valenciennes, 1840)'da Doku Glikojen ve Serum Glukoz Düzeyi Üzerine Etkileri. E.Ü. Su Ürünleri Dergisi 23(1/1): 23-27.
71. Çiftçi N, Korkmaz C, Ay Ö, Karayakar F, Ccik B (2017) Bakır ve Kurşunun Oreochromis niloticus' Hepatosomatic İndecs, Gonadosomatic İndecs ve Kondüsyon Faktörü Üzerine Etkileri. Süleyman Demirel Üniversitesi Eğirdir Su Ürünleri Fakültesi Dergisi 13(1): 12-18.
72. Topcuoglu S, Kirbasoglu C, Gungor N (2002) Heavy metals in organisms and sediments from Turkish coast of the Black Sea, 1997-1998. Environment International 27: 521-526.
73. Olga K, Violetta S, Michaela S, Karel N, Jozef K, et a. (2009) Sunflower plants as bioindicators of environmental pollution with lead (II) ions. Sensors 9(7): 5040-5058.
74. Javed M, Usman N (2013) Assessment of heavy metal (Cu, Ni, Fe, Co, Mn,Cr,Zn) pollution in effluent dominated rivulet water and their effect on glycogenmetabolism and histology of Mastacembelus armatus. Springer Plus 2: 390.
75. Joseph l, Jun BM, Flora JRV, Park CM, Yoon Y (2019) Removal of heavy metals from water sources in the developing world using low-cost materials: A review. Chemosphere 229: 142-159.
76. Babel S, Kurniawan TA (2003) Low Cost Adsorbents for Heavy Metals Uptake from Contaminated Water: A Review. Journal of Hazardous Materials 97(1-3): 219-243.
77. Mahurpawar M (2015) Effects of heavy metals on human health. International Journal of Research 3(9).
78. Sun LN, Zhang YF, He LY, Chen ZJ, Wang QY, et al. (2010) Genetic diversity and characterization of heavy metal-resistant-endophytic bacteria from two copper-tolerant plant species on copper mine wasteland. Bioresource Technology 101(2): 501-509.

79. Stomiñska I, Jezierska B, (2000) The effect of Heavy metals on post embryonic development of COMMON CARP, *Cyprinus carpio* L. Fisheries & Aquatic Life 8(1): 1119-1128.

80. Vinodhini R, Narayanan M (2009) The impact of toxic heavy metals on the hematological parameters in common CARP (*Cyprinus carpio* l.). Iran J Environ Health Sci Eng 6(1): 23-28.

81. Hayat S, Javed M, Razzao S (2007) Growth performance of metal stressed: Pakistan Veterinary. Journal V 27(1): 8-12.

82. Chen AWY, Lin CJ, Ju YR, Tsai JW, Liao CM (2012) Assessing the effects of pulsed waterborne copper toxicity on life-stage tilapia populations. Sci Total Environ 417-418: 129-137.

83. Grosell M, Nielson C, Bianchini A (2002) Sodium torn over rate determines sensitivity to acute copper and silver exposure in fresh water animals. Comp Biochem Physiol Part C Toxic Pharma 133(1-2): 248-333.

84. Tan F, Wang M, Wang W, Lu Y (2007) Comparative evaluation of the cytotoxicity sensitivity of six fish cell lines to four heavy metals in vitro. Toxicol Vitro 22(1): 164-170.

85. Fidan A, Ciğerci I, Konuk M, Kücükkurt I, Aslan R, et al. (2008) Determination of some heavy metal level and oxidative status in *Carassius carassius* L 1758 from Eber Lake. Environ Mon Assess 147(1-3): 35-141.

86. Karuppasamy R (2004) Evaluation of Hg concentration in the tissue of fish *Channa punctatus* (Bloch.) in relation to short and longterm exposure to phenylmercuric acetate. J Plant Jubilee AU 40, pp: 197-204.

87. World Health Organisation (1984) Guidelines for drinking water quality WHO Geneva 111.

88. EOSQC (1993) Egyptian Organization for Standardization and Quality Control, Maximum Residue Limits for Heavy Metals in Food. Ministry of Industry No. 2360/1993, 5.

89. FAO/WHO (1992) Food Contamination Monitoring and Assessment Programme. WHO, Geneva 5, UNEP, Report of the Third Meeting of the GEMS/Food.

90. Dalzell DJB, Macfarlane NAA (1999) The toxicity of iron to brown trout and effects on the gills: a comparison of two grades of iron sulphate. J Fish Biol 55(2): 301-315.

91. Abbas HH, Ali FK (2007) Study the effect of hexavalent chromium on some biochemical, cytotoxicological and histopathological aspects of the Oreochromis spp. Fish Pak J Biol Sci 10(22): 3973-3982.

92. Baker RTM, Martin P, Davies SJ (1997) Ingestion of sub-lethal levels of iron sulphate by African catfish affects growth and tissue lipid peroxidation. Aquatic Toxicology 40(1): 51-61.

93. Sepe A, Ciaralli L, Ciprotti M, Giordano R, Funari E, et al. (2003) Determination of cadmium, chromium, lead and vanadium in six fish species from the Adriatic Sea. Food Additives & Contaminants 20(6): 543-552.

94. Anderson J, Fitzgerald C (2010) Iron: An Essential Nutrient Review.

95. Erdman Jr JW, Macdonald IA, Zeisel SH (2012) Present Knowledge in Nutrition. 10th (Edn.), A John Wiley & Sons, Ltd., publication.

96. Miller JR, Allan R, Horowitz AJ (2002) Metal Mining in the Environment, Special Issue. The Journal of Geochemistry: Exploration Environment Analysis 2: 225-233.

97. Lars J (2003) Hazards of heavy metal contamination. British Medical Bulletin 68(1): 167-182.

98. Anim AK, Ahialey EK, Duodu GO, Ackah M, Bentil NO (2010) Accumulation profile of heavy metals in fish samples from Nsawam, along the Densu River, Ghana. Research Journal of Environmental and Earth Sciences 3(1): 56-60.

99. Weber DN, Dingel WM, Panos JJ, Steinpreis RE (1997) Alterations in Neurobehavioral Responses in Fishes Exposed to Lead and Lead-Chelating Agents. American Zoologist 37(4): 354-362.

100. ATSDR (2005) Lead toxicity. Georgia: Agency for Toxic Substances and Disease Registry, U.S. Department of Health and Human Services.

101. Schnaas L, Rothenberg SJ, Flores MF, Martinez S, Hernandez C, et al. (2006) Reduced Intellectual Development in Children with Prenatal Lead Exposure. Environmental Health Perspectives 114(5): 791- 797.

102. Umar A, Umar R, Ahmad MS (2001) Hydrogeological and Hydrochemical Frame Works of Regional Aquter System in Kali-Ganga Sub-Basin, India. Environmental Earth Sciences 40(4): 602-611.

103. García-lestón J, Mendez J, Pásaro E, Laffon B (2010) Genotoxic Effects of Lead : An Updated Review. Environment International 36(6): 623-636.

104. Niyogi S, Wood CM (2006) Interaction between dietary calcium supplementation and chronic

waterborne zinc exposure in juvenile rainbow trout, Oncorhynchus mykiss. Comp Biochem Physiol C 143(1): 94-102.

105. Farombi EO, Adelowo OA, Ajimoko YR (2007) Biomarkers of oxidative stress and heavy metal levels as indicators of environmental pollution in African cat fish (*Clarias gariepinus*) from Nigeria Ogun River. Int J Environ Res Public Health 4(2): 158-165.

106. Song Y, Elias V, Loban A, Scrimgeour AG, Ho E (2010) Marginal Zinc Deficiency Increases Oxidative DNA Damage in the Prostate After Chronic Exercise. Free Radical Biology and Medicine 48(1): 82-88.

107. Afridi HI, Kazi TG, Kazi N, Kandhro GA, Baig JA, et al. (2011) Interactions between Cadmium and Zinc in the Biological Samples of Pakistani Smokers and Nonsmokers Cardiovascular Disease Patients. Biol Trace Elem Res 139(3): 257-268.

108. Chasapis CT, Loutsidou AC, Spiliopoulou CA, Stefanidou ME (2012) Zinc and Human Health: An Update. Arch Toxicol 86(4): 521-534.

109. Gabet-Giraud V, Miége C, Choubert JM, Ruel SM, Coquery M (2010) Occurrence and removal of estrogens and beta blockers by various processes in wastewater treatment plants. Sci Total Environ 408(19): 4257-4269.

110. Margot J, Kienle C, Magnet A, Weil M, Rossi L, et al. (2013) Treatment of micropollutants in municipal wastewater: Ozone or powdered activated carbon? Sci Total Environ 461-462: 480-498.

111. Margot J, Kienle C, Magnet A, Weil M, Rossi L, et al. (2013). Treatment of micropollutants in municipal wastewater: Ozone or powdered activated carbon? Sci. Total Environ 461-462: 480-498.

112. Valipour M, Mousavi SM, Valipour R, Rezaei E (2012) Air, water, and soil pollution study in industrial units using environmental flow diagram. J Basic Appl Sci Res 2(12): 12365-12372.

113. Chowdhury MJ, McDonald DG, Wood CM (2004) Gastrointestinal uptake and fate of cadmium in rainbow trout acclimated to sublethal dietary cadmium. Aquat Toxicol 69(2): 149-163.

114. Žikić RV, Štajn AŠ, Pavlović SZ, Ognjanović BI, Saičić ZS (2001) Activities of superoxide dismutase and catalase in erythrocytes and plasma transaminases of goldfish (*Carassius auratus* gibelio Bloch.) exposed to cadmium. Physiol Res 50(1): 105-111.

115. Hao Y, Chen L, Zhang X, Zhang D, Zhang X, et al. (2013) Trace Elements in Fish from Taihu Lake, China : Levels, Associated Risks, and Trophic Transfer. Ecotoxicology and Environmental Safety 90: 89-97.

116. Abdel-Mohsien HS, Mahmoud MAM (2015) Accumulation of Some Heavy Metals in Oreochromis niloticus from the Nile in Egypt: Potential Hazards to Fish and Consumers. Journal of Environmental Protection 6(9): 1003-1013.

117. Jezierska B, Witeska M (2006) The metal uptake and accumulation in fish living in polluted waters. Soil and Water Pollution Monitoring, Protection and Remediation, pp: 107-114.

118. Pieterse GM (2004) Histopathological changes in the testis of *Oreochromis mossambicus* (Cichlidae) as a biomarker of heavy metal pollution.

119. Failla ML, Johnson MA, Prohaska JR (2001) Copper. In: Present Knowledge in Nutrition. Washington D.C: Life Sciences Institute Press, pp: 373-383.

120. Angelova M, Asenova S, Nedkova V, Koleva Kolarova R (2011) Copper in the Human Organism. Trakia Journal of Sciences 9(1): 88-98.

121. Reddy S, Venkata Reddy M, Radhakrishnaiah K (2008) Impact of copper on the oxidative metabolism of the fry of common carp, *Cyprinus carpio* (Linn.) at different pH. Journal of Environmental Biology 29(5): 721-724.

122. Woddy CA, O Neal SL (2012) Effects of Copper on Fish and Aquatic Resources. The Nature Conservancy. Alaska, pp: 1-27.

123. Grosell M, McDonald MD, Walsh PJ, Wood CM (2004) Effects of prolonged copper exposure in the marine gulf toadfish (Opsanus beta) II: copper accumulation, drinking rate and Na+/K+-ATPase activity in osmoregulatory tissues. Aquat Toxicol 68(3): 263-275.

124. Duruibe JO, Ogwuegbu MOC, Egwurugwu JN (2007) Heavy metal pollution and human biotoxic effects. International Journal of Physical Sciences 2(5): 112-118.

125. Galanis A, Karapetsas A, Sandaltzopoulos R (2009) Metal-induced carcinogenesis, oxidative stress and hypoxia signaling. Mutation Research 674(1-2): 31-35.

126. Yuan CG, Shi JB, Liang IN, Jiang GB (2004) Speciation of heavy metals in marine sediments from the East China Sea. The Environment 30(6): 769-783.

127. Peterson SA, Vansickle J, Herlihy AT, Hughes RM (2007) Mercury concentration in fish frim streams

and rivers throughout the Western United States. Environmental Science and Technology 41(1): 58-67.

128. Achide SA, Omame AO (2017) Bioaccumulation of Heavy Metals on Some Organs of *Oreochromis Niloticus*. International Journal of Applied Science and Mathematical Theory 3(1): 31-37.

129. Selvi A, Rajasekar A, Ananthaselvam A, Jayaram T, Sathish kumar K, et al. (2019) Integrated Remediation Processes Toward Heavy Metal Removal/Recovery From Various Environments-A Review Removal/Recovery From Various Environments-A Review. Front Environ Sci 7: 66.

130. Ya-jun Hong, WeiLiao, Zhen-fei Yan, Ying-chen Bai, Cheng-lian Feng, et al. (2020) Progress in the Research of the Toxicity Effect Mechanisms of Heavy Metals on Freshwater Organisms and Their Water Quality Criteria in China. Journal of Chemistry 2020: 12.

131. Mehjbeen Javed, Nazura Usmani (2019) An Overview of the Adverse Effects of Heavy Metal Contamination on Fish Health. Proc Natl Acad Sci India Sect B Biol Sci 89(2): 389-403.

132. Ahmed NF, Sadek KM, Soliman MK, Khalil RH, Khafaga AF, et al. (2020) Moringa Oleifera Leaf Extract Repairs the Oxidative Misbalance following Sub-Chronic Exposure to Sodium Fluoride in Nile Tilapia *Oreochromis niloticus*. Animals 10(4): 626.

133. Abalaka SE (2015) Heavy metals bioaccumulation and histopathological changes in *Auchenoglanis occidentalis* fish from Tiga dam, Nigeria. J Environ Health Sci Eng 13: 67.

134. Sabra FS, Mehana E (2015) Pesticides toxicity in fish with particular reference to insecticides. Asian J Agric Food Sci 3(1): 40-61.

135. Dhevakrishnan R, Zaman G (2012) Cauvery river pollutants induced histopathological changes in kidney and muscle tissues of freshwater fish, *Labio rohita* (Hamilton, 1822). Online Int Interdiscip Res J 2(5): 9-19.

136. Velcheva E, Tomova D, Arnaudova D, Arnaudov A (2010) Morphological investigation on gills and liver of fresh water fish from Dam Lake “Studen Kladenets”. Bulgarian Journal of Agriculture Sciences 16(3): 364-368.

137. Bascinar NS (2009) Benthics creatures and bioindicator species. Central Fisheries Research Institute.

138. Skouras A, Broeg K, Dizer H, von Westernhagen H, Hansen PD, et al. (2003) The use of innate immune responses as biomarkers in programme of integrated biological effects monitoring on flounder (Platichthys flesus) from the southern North Sea. Helgoland Marine Research 57: 190-198.

139. Zhou Q, Zhang J, Fu J, Shi J, Jiang G (2008) Biomonitoring: an appealing tool for assessment of metal pollution in the aquatic ecosystem. Analytical Chemistry Acta 606(2): 135-150.

140. Depledge M, Amaral-Mendes JJ, Daniel B, Halbrook RS, Loepper-Sams P (1993) The conceptual basis of the biomarker approach. Biomarkers: Research and Application in the assessment of Environmental Health, NATO ASI Series H: Cell Biology. Springer Verlag, Berlin 68: 15-29.

141. Bryan GW, Langston WJ (1992) Bioavailability, accumulation and effects of heavy metals in sediments with special reference to United Kingdom estuaries: a review. Environmental Pollution 76(2): 89-131.

142. Lauer MM, de Oliveira CB, Yano NL, Bianchini A (2012) Copper effects on key metabolic enzymes and mitochondrial membrane potential in gills of the estuarine crab *Neohelice granulata* at different salinities. Comparative Biochemistry and Physiology 156(3-4): 140-147.

143. Sukumaran M, Manikandan SR, Nathiya N, Muthukumaravel K (2013) Impact of pesticides monocrotophos on histological changes in the liver of *Mystus vittatus*. International Journal of Current Research 5(10): 3244-3247

144. Xu J, Chen Y, Zheng L, Liu B, Liu J, et al. (2018) Assessment of Heavy Metal Pollution in the Sediment of the Main Tributaries of Dongting Lake. China Water 10(8).