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Heavy Metal Pollution in Iraqi Rivers and Impact on Human and Fish Health: A Review

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Abstract: The Euphrates and Tigris rivers are the main vital water sources in Iraq, and therefore many studies have been conducted on them to find out the reasons for their pollution, and the most important sources of pollution are heavy metals. Heavy metals are usually present in nature. Some of them are necessary for life, but they can become toxic through their accumulation in living organisms, as they cannot be eliminated in ecosystems through natural processes, unlike most organic pollutants, where these elements are one of the dangerous pollutants that enter the freshwater environment and cause an imbalance in the ecological system. This is directly or indirectly reflected on the human beings. These elements enter the plant and animal bodies through the soil, water and air which have been categorized by their ability to bio-accumulate in the tissues of animals and elevate their concentration in the tissue and body fluids. Such bioaccumulation causes toxicity to living organisms and may affect human public health. Fishes are the most susceptible among the aquatic animals to the toxicity of heavy metals. They are a basic food source and animal protein, cheap and economical, with a high nutritional value and the human body needs them on a permanent and continuous basis. Fishes are also commonly used in assessing the health of aquatic organisms. This review is focused on the pathological effects of heavy metals in both fishes and humans.

Keywords: Toxicity, Heavy metals, Iraqi rivers, Fish health

Introduction

The elements which have a density of more than 5 gram/cm^3 are called heavy metals (HV). Heavy metals have two categories: essential and non-essential elements. Essential elements like selenium (Se), cobalt (Co), chromium (Cr), zinc (Zn), manganese (Mn) and copper (Cu) are required for basic cellular functions, particularly enzymatic reactions, in all living cells at low levels. Their toxicity and disturbance of physiological homeostasis may come from exposure to higher levels

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(Ali & Khan, 2018). The essential elements are nontoxic metals which have harmless effects but cause toxicity when their concentrations are excessed such as the chromium. Non-essential elements and toxic metals do not have vital functions and have toxicity effect to living cells as metalloids comprising mercury, cadmium and lead (Roy, 2010).

HVs, both essential and non-essential are found in various quantities in aquatic systems. Metal concentrations that are too low have unfavorable physiological, histological and morphological impacts (Al-Taee et al., 2020). Contaminant levels in fishes are of special concern because they represented hazards for human and public health (Al-Sarraj, 2013; Jasim, 2017).

Sources of Heavy Elements in the Aquatic Environment

1- Natural Sources: These minerals arrive from the natural source, which is rocks and sediments, to the aquatic environment, and these released minerals which are dissolved or suspended in rainwater drifting on the surface ground or suspended in the air to be moved by the wind from one place to another one. Also, volcanic activities are among the most important natural sources that lead to pollution of the aquatic environment (Papagiannis et al., 2004; Butu & Iguisi, 2013).

2- Anthropogenic sources: Manufacturing activity is a major source of pollution with heavy metals in the environment, including the petroleum industries, oil refineries, iron and steel factories, copper, glass, aluminum, tanning factories, fertilizers, pesticides, gasoline ....etc. (Rashed, 2001; Al-Edreesi et al., 2002).

When fishes are exposed to heavy metals through their skin, gills and intestinal tract, such heavy metals cause, as a result of their pathway in fish systems, loss of vital functions, combined with bioaccumulation in the tissues. Hence, fishes represented a good bio-indicator for observing pollution of the aquatic environment.

Contaminated Iraqi Rivers

Euphrates and Tigris rivers are the biggest Iraqi rivers and both are the main important source for the development of fish culture. For years, they were used for human, agriculture and industrial activities. They are naturally polluted leeding to damage the aquatic environment while potentially posing a health risk to humans. Many toxic exogenous elements are introduced to the aquatic environment as organic pesticides, polynuclear aromatic hydrocarbons PAHs, phytoplankton, algae, overconcentration of chemotherapeutic agents and sodium chloride NaCl (Al-Taee et al., 2021). Heavy metals which are the main problem in the aquatic organisms (Authman et al., 2015), biological degradation cannot destroy the heavy metals so they are sedimented in the aquatic ecosystem and concentrated in the aquatic plants or animals (Oguzie, 2003), or they may interact with other water column components leading to the formation of more toxic compounds.

According to the recommendations of USEPA (2011), the levels of heavy metals in main Iraqi rivers are lesser than in other Iraqi aquatic environments. These variations may be affected by several factors such as increase water flow and

dilution, increase degraded and flow exogenous material from upper to low river, drainage directly from farmland, factories: dissolution of sediments, sewage disposal plants, heavy phytoplankton in the water, accumulative, adsorption interact with other organic matter forming new complexes and some heavy metals present in very low concentration it is difficult to estimation them (Kaiser et al., 2004).

Many previous studies were done to estimate the types and concentration of heavy metals in Iraqi rivers. Kassim et al. (1997) revealed that the Cd, Ni, Pb, Zn, and Cu have more concentrations in the Tigris river than the limitation. Al-Taee et al. (2007) reported that heavy metal concentration in the Hilla River in Babylon Province were Al/ 434, Cd/ 114, Pb/ 36 and Hg/ 76 µg/l, while Hassan et al. (2010) found Cd, Co, Cr, Cu, Fe, Mn, Ni, Pb and Zn in low concentrations at Euphrates sediments as compared with USEPA (2011) guidelines.

Mensoor & Said (2018) reported the high concentration of Cd and Cr in the Tigris river in Baghdad and these metal accumulation in the muscle of two fish species: *Mesopotamichthys sharpeyi* (reported as *Barbus sharpeyi*) and *Luciobarbus xanthopterus* (reported as *Barbus xanthopterus*) which are consumed by human and affected public health, so the pathological alteration in these fishes is considered as a bio-indicator for monitoring aquatic environment pollution with HMs. In 2018, there was high mortality in fish cages in the middle Euphrates region in Iraq. Jaber et al. (2021) indicated that one of the causes of such death may be due to bioaccumulation of As, Zn, Fe, Pb, and Cu in the muscles of the fishes. These results come from concentrated heavy metals in the declining water rivers and other chemical factors.

Shatt Al-Arab River represents the confluence of the Tigris and Euphrates rivers at Qarmat Ali City. Therefore, many studies were conducted to assess the presence of pollutants, which may enter and be concentrated in the Shatt Al-Arab River. Nasir et al. (2011) indicated that the concentration of Cd, Co, Ni, Pb, Cu and Fe in the Qarmat Ali, Mufti, Siba and Ras Al-Bishah regions is higher than the permissible limit. Alhello et al. (2020) estimated the heavy metal concentration in different sites in Shatt Al-Arab River as in the following orders: Iron> Manganes> Nickel> Zinc> Copper> Lead> Chromium> Cobalt> and Cadmium. The following Table 1 demonstrates the concentration of some HVs in Iraqi rivers.

Table 1: Concentration of heavy metals in contaminated waters in comparison with Iraqi environmental law No. 65/1967 (Salim, 2015).

Metals	Permissible limited concentration (mg/l)	Concentration in the pollution water (mg/l)
Ni	0.10	0.19
Fe	0.3	3
Mn	0.1	0.55
Cu	0.05	0.199

Biological Effects and Toxic Mechanisms of Heavy Metals

Fishes are exposed to heavy metals in two ways: indirectly through the skin and gills, or directly through the consumption of polluted water or food (Rajeshkumar & Li, 2018). As a result, impacts of heavy metals can affect the intestine, liver and others organs even at low concentrations, causing tissue damage (Jaber et al., 2021; Yousif et al., 2021). The bioaccumulation of these metals in fish tissue depends on the types of heavy metals, concentration, route of exposure and absorption, types of fishes, age, nutritional and physiological status as well as the physical-chemical characteristic of the aquatic environment (Begum et al., 2009; Tchounwou et al., 2012). As a result, fishes can be used as a biological indicator for heavy metal toxicity and aquatic environmental pollution (Gaim et al., 2015).

Heavy metals have been shown to disrupt cellular components and structure, including the cell outer and inner membranes, lysosomes, mitochondria, endoplasmic reticulum, nuclei, enzymes that important for metabolisms, detoxification and damage repair (Wang & Shi, 2001). According to Farombi et al. (2007), the main toxic mechanisms of heavy metals are their ability to induce oxidative stress and release reactive oxygen species (ROS). Ions of metals are classified as carcinogenic for fishes and humans and cause apoptosis because their toxic mechanisms interact with a genetic component, DNA, and nuclear proteins and lead to disturbances in the cell cycle (Beyersmann & Hartwig, 2008) as illustrated in Figure 1.

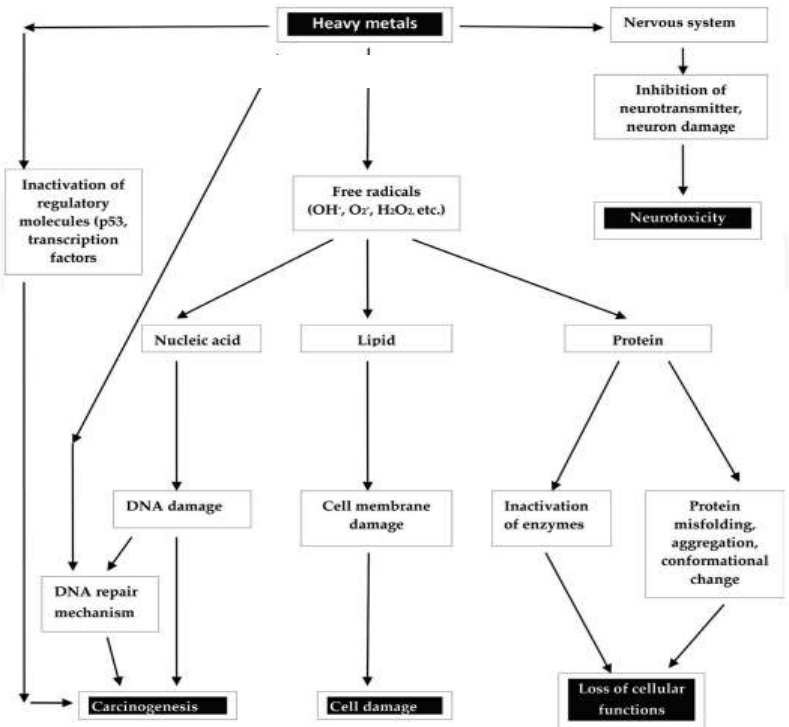


Figure 1: Pathways toxicity mechanisms of heavy metals in fishes and humans (Engwa et al., 2019).

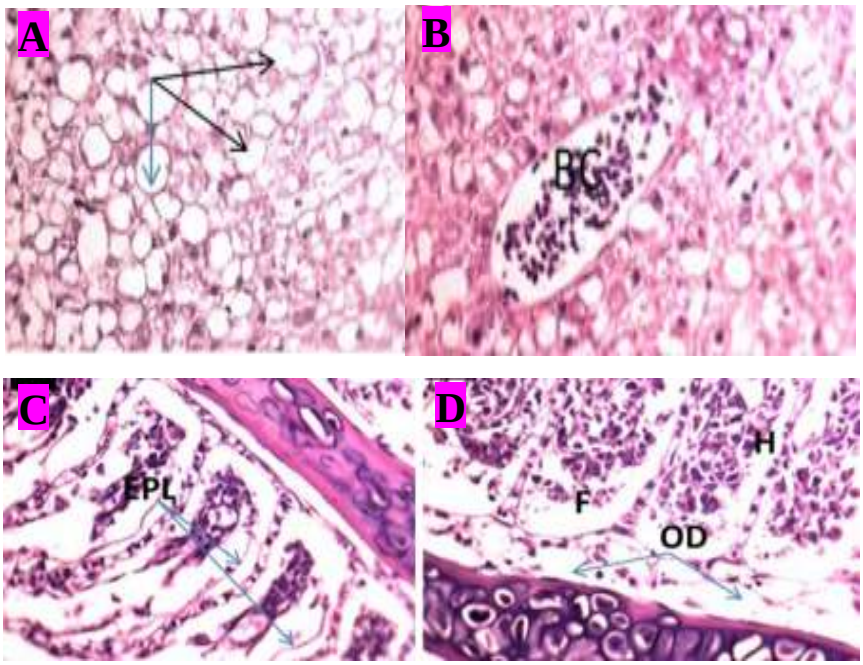
Heavy metals cause histopathological alteration in variable fish organs which are variable in their grade (Table 2), such as in the gills and livers of both *Cyprinus carpio* and *Carasobarbus luteus* in Tigris River contaminated with Cd, and Pb (as in Figure 2) which caused hepatocyte vacuolization and congestion of central vein the lesions in the gills, edema and epithelial lifting with adhesion between secondary gills filaments (Mustafa et al., 2020).

In general, these alterations are either edema, hyperplasia or necrosiases. When fishes exposed to heavy metals, many organs, mainly the gills, will be destructed.

Edema and degeneration will occur with lifting epithelial cells are the main pathological changes which are biomarkers for aquatic pollution (Osman et al., 2009).

Hyperplasia: Epithelial cells that undergo lamellal fusion and hyperplasia can result in a significant reduction in gill surface area available for respiration. It also causes gill blood flow to be disrupted, metabolism to be altered and fish mortality to occur (Purwanti et al., 2019). Some researchers recently distinguished between two types of gill damages. The first type forms of injury are caused by a defense reaction and comprises hyperplasia of gill epithelium filaments, whereas the second type is caused by direct traumas and includes gill epithelium shedding and necrosis (Fanta et al., 2003).

Necrosis: Accumulative heavy metals in the hepatocytes and kidneys lead to degeneration and blood flow disturbances which cause necrosis in hepatic tissue and necrosis in the epithelium lining renal tubules due to oxygen deficiency with shrinkage of glomerulus and dilated Bowman's pace (Mohamed, 2001; Onita et al., 2021).



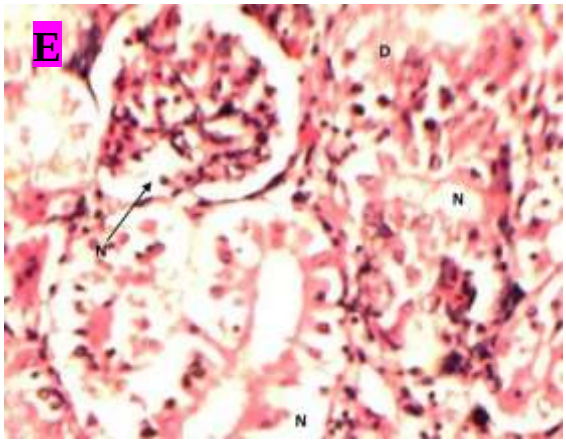


Figure 2: Histopathological examination of the liver of *C. luteu*s habits in contaminated environment shows hepatocyte vacuolation (A- three rows) and central vein congestion (B- BC), gills of *C. carpio* showing epithelial cell lifting (C- EPL), edema (D- OD), hyperplasia (D- H) with lamellae fusion (D-F. H&E, 400X, (E) necrosis in the glomerulus (black arrow), necrosis in the renal tubule (E-N) and degeneration (E-D), H&E, 400X (Mustafa et al., 2020 for A, B, C and D, and El-Hais et al., 2017 for E).

Table 2: Grade of pathological lesions as a result of heavy metals toxicity in fishes according to Onita et al. (2021) with some modifications.

Organs	Grade	Description	Pathological alteration
Gills	I	Disturbances of cell growth and circulatory, abnormal morphology	Hyperplasia and hypertrophy in the gill epithelium, congestion, fusion in the epithelial cells and lifting of the lamella and lamellar disorganization
	II	Abnormal morphology	Partial closure of the secondary filaments, partially epithelium lifting and desquamation
	III	Abnormal morphology and circulatory disturbances	Lamellar circulatory disorder (aneurysm), epithelial cells damage, hemorrhage, a fusion of the primary gill filaments, damage of the lamellar epithelium
Kidneys	I	Morphology disturbances	Small dilated renal tubuli normal feature of hematopoietic tissue
	II	Morphology disturbances	Mild dilated tubular with glomeruli contraction
	III	Disturbances cell growth	Hypertrophy of the epithelial cells lining renal tubule and damaged, glomerular contraction, development of connective tissue, shrinkage of the hematopoietic tissue
Liver	I	Morphology and circulatory disturbances	Dilatation of sinusoid normal aspect of hepatic architecture
	II	Circulatory disturbances	Slightly dilatation of sinusoid expansion of connective tissue
	III	Disturbances of cell growth and circulatory	Hypertrophic of hepatocytes with vacuolated degeneration, dilatation of sinusoid

Heavy metals are also affected enzyme activities of fishes so they are of a diagnostic method for environmental pollution. *C. luteus* populating in contaminated environment with Cu, Ni, Fe, Co, Mn showed elevation in the levels of AST, ALT and ALP which are enzymes for liver function (Salman, 2011). The same result was reported by Abedi et al. (2013) in *C. carpio* and by Zorriehzahra et al. (2010) in *Oncorhynchus mykiss.* Also, they cause DNA damage and genotoxicity, lipid peroxidation with disturbances in antioxidant defense mechanisms (Gjorgieva et al., 2013).

Nickel (Ni)

This metal enters the water environment and increases its concentration through alloy, steel, sanitation, Ni-Cd batteries and medical materials. Imarah et al. (2006) reported that the concentration of Ni in branches of Shatt Al-Arab River was affected by the seasons also. Mahmood & Alkhafaji (2016) reported its concentration in Tigris and Diyala rivers as above the acceptable limits, causes pollution to the aquatic environment. These elements enter the body through inhalation, oral and dermal exposures, cause toxic behavior to organisms and systemic disorders (immunological, reproductive, neurological, circulatory and developmental even mucus membrane and chromosome disorders) and considered as carcinogenic agents leading to death (Palaniappan & Karthikeyan, 2009; Buxton et al., 2019; Purwanti et al., 2019).

The toxic mechanism was producing oxidative stress, ion regulatory diminishing (interruption Ca^{2+} which is important in formation of shell and exoskeleton rather than interacting with Mg^{2+} and Fe^{2+} homeostasis which they disorder with Ni toxicity, other mechanisms include an allergic-type response of respiratory epithelia leading to embarrassment of respiration (Blewett & Leonard, 2017). Exposing rainbow trout, *O. mykiss* to 34-51 µM caused gills edema, decrease arterial oxygen with increasing CO_2 in its content and increase ventilation rate (Brix et al., 2017).

Oxygen extraction efficiency and arterial oxygen content increased arterial CO_2 and reduced blood pH. Compensatory responses included an increase in ventilation rate and ventilation volume (Pane et al., 2004; Brix et al., 2017). Ahmed (2021) pointed out to the high concentration of nickel in Khor Al-Zubair, and thus its concentration in the muscles of the common carp at 2.75 mg/kg body weight which constitutes a food source for the Iraqi individual and therefore may have a toxic effect on human health.

Ni has specificity organs and tissue lesions, so exposed silver carp (*Hypophthalmichthys molitrix*) to concentration of 5.7 mg/l for a long period, showed variable histopathological alteration as decrease space between secondary gill filaments, complete closure, fusion and mucus secretion, loss of arrangement and vacuolation of hepatocyte, disturbances of blood circulation with dense chromatine in the nuclear hepatocyte and severe interstitial nephritis and nephrosis in the kidney of *C. carpio* as in Figure 3 (Athikesavan et al., 2006; Bhatkar, 2013).

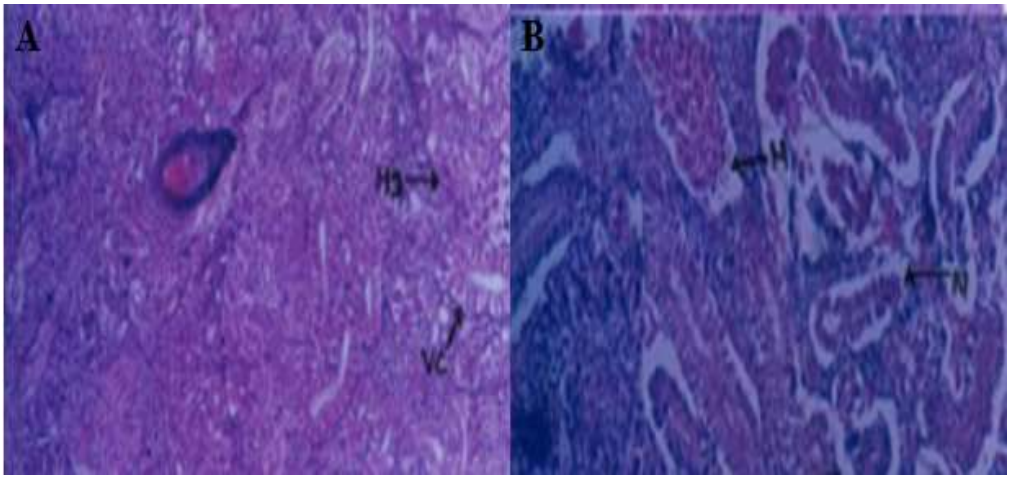


Figure 3: Microscopic examination presentation of the kidney of common carp exposed to 4 mg/l Nickel chloride shows: A- hydropic degeneration of epithelial cells lining tubules (Hg) and vacuolated tubule (VC), B- heamorrahge in the glomeruli (H) and nephrosis (N). H&E, 400X (Bhatkar, 2013).

Iron (Fe)

Iron is an essential elements for tissue and cell structure in animals. fishes require Fe in ranges of 30-170 mg/kg. It is the main component of hemoglobin as it deficiency leads to many disturbances and anemia while elevated concentrations cause increased mortality and physiological, immunological and cellular disturbances in *Leporinus friderici*, reduced growth reduces feed utilization with accumulation in the tissue (Bury et al., 2012; Gemaque et al., 2019).

Pathway Mechanisms of Fe in Fishes

The mean iron toxic concentration ranged between 150-1000 µg/l. Its toxicity depends on water temperature, salinity, pH and presence of organic materials (*Aris & Tamrin*, 2020). There are two forms of iron present in the environment: ferrous ion F^{2+} which is oxidation to ferric ion Fe^{3+} under the effects of pH which is precipitates to form ferric hydroxide ($Fe(OH)_3$). Ferrous iron has more availability in the aquatic environments and inters fish body through the gills and cause pathological changes which involve circulatory disturbances as aneurysms and edema in addition to cell adaptation as epithelial hyperplasia, hypertrophy lead to lamellar fusion, epithelial lifting and necrosis as a final stage of cell injury. This pathological alteration causes imbalanced osmoregulation and insufficient transport oxygen to the tissues (Flores-Lopez & Thomaz, 2010; B'ey, 2015).

Also, Fe accumulates in other organs and causes histopathological changes such as alteration in the architecture of liver characterized by damage of blood vessels and hemorrhage, vacuolated degeneration and necrosis (Aris & Tamrin, 2020) as in Figure 4.

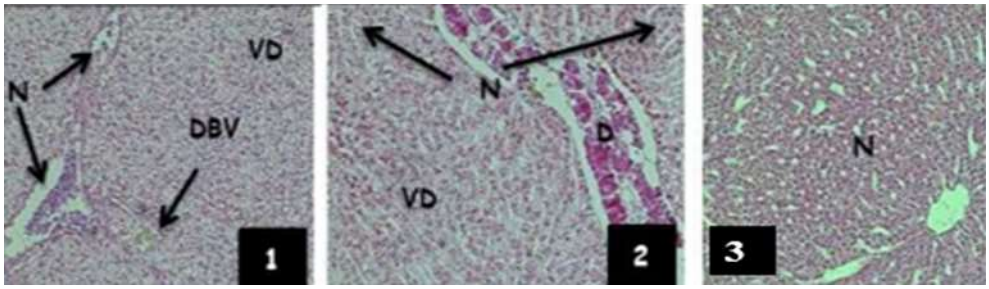


Figure 4: Microscopic examiantion of liver in *Plectropomus leopardus* (1), *Lutjanus griseus* (2) and *Lutjanus campechanus* (3) showing necrosis (N), vacuolar degeneration (VD), damage of blood vessels (DBV) and degeneration (D). H&E, 400X (*Aris & Tamrin*, 2020).

Manganese (Mn)

Manganese is essential for energy and protein synthesis and metabolism, bone mineralization, glycosaminoglycan production, antioxidant defense mechanisms, and metabolic activity (Aschner & Aschner, 2005). In addition, it is an activator for many enzymes as lyases, kinases, hydrolases, decarboxylases and ligases. It is required in fish diet from 2.5-25 mg/kg (Lall & Kaushik, 2021).

Mn toxicity is affected by physical-chemical properties of water as hardness, acidic, and low Ca concentration which may increase toxic Mn availability that leads to decrease calcium and phosphor absorption, a disorder in carbohydrate metabolisms, sodium imbalance with loss metal homeostasis, tissue damage with inflammation, and neurodegeneration (Ye et al., 2009).

Mn is more common accumulated in gills, intestine and less in muscle than skin and bones of *C. carpio* treated with a sub lethal concentration of $MnSO_4$ (1.12) mg/l. Also, it exhibits elevated Hb, PCV, RBC, WBC and platelet with increase enzymatic levels during 24-72 hour. After exposure, there was an elevation in the triglycerides (231.21±0.04), serum uric acid (4.81±0.33), high-density lipoprotein (HDL) (39±0.07), glutamic pyruvic transaminase (SGPT) (40.6±0.4), blood urea (13±0.1) and albumin increases the concentration of cholesterol (Ali et al., 2021).

Copper (Cu)

Copper is an important and essential element for growing and physiology development. It is required by a wide variety of cell components, enzymes, cell respiration, connective tissue and hemoglobin synthesis, having vital functions in all living organisms and bio-effects added to improve healing of tissue damage and reducing the Nano-ZnO toxicity in *C. carpio* (Al-Taee & Al-Hamdani, 2014), but very high intakes can cause adverse health problems (Demirezen & Uruc, 2006; Ajani & Akpoilih, 2012). Copper induce to the fish culture through the dietary or waterborne way as a result of industrial and human activity or even when copper component as $CuSO_4$ used as anti-microorganism or reduce the toxicity of Nano-ZnO (Carneiro et al., 2005; Reddy et al., 2006; Al-Taee & Al-Hamdani, 2015).

Copper occurs naturally in aquatic environment at low concentration. It is important for growth and metabolic activity, but it has harmful effects when it is

concentration has been elevated. Also, copper can interfere adsorption with other water column component and forms complexes (Eisler, 2000).

The mechanisms of copper pathway toxicity are: insensitive to exterior copper concentrations, copper transporter 1 (a transmembrane protein), sensitivity to external concentration of copper. and it is the ability to competition apical Na^+ sited at branchial epithelial cells inhibit the activity of the membrane-bound Na^+/K^+-ATPase also lead to elevated plasma ammonia, acid-base imbalance olfactory, smell sense in salmons and hair cells in lateral line impairment as well and induce oxidative stress (MacKenzie et al., 2004; Linbo et al., 2006; Sandahl et al., 2007; Green et al., 2010; Eyckmans et al., 2011) lead to architectural and structural alterations with hyperemia and hypertrophy (Figure 5).

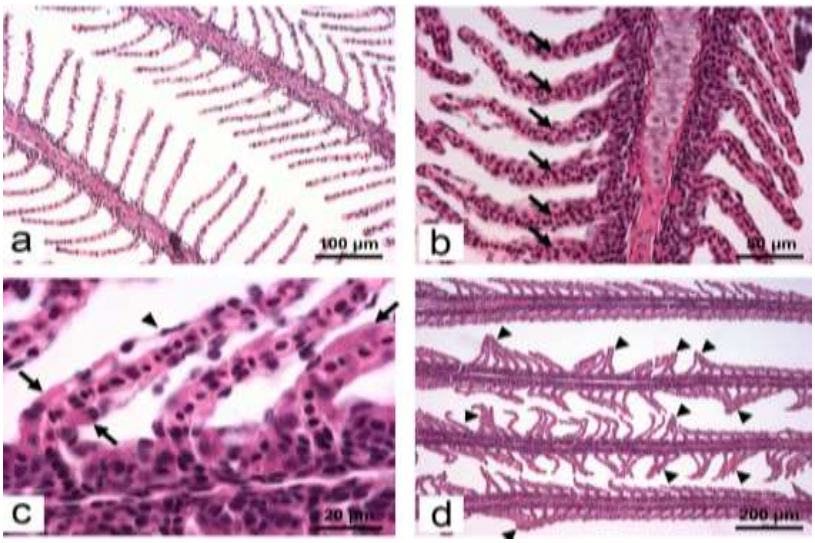


Figure 5: Microscopic examination of gills of *C. carpio* shows normal structure (a). 200X, H&E, (b) widespread hyperemia on 2nd filament, 400X, H&E, (c) enlargement of the epithelial cell lining secondary filament (black arrow), normal epithelial cell (black arrowhead) 1000X, H&E and (d) curling and fusions in the secondary filaments (black arrowhead) 100X, H&E. (Delahaut et al., 2020).

Fish Roles in Human Risk

Aquatic organisms, mainly fishes, are the principal source of human consumption protein. According to the recommendation of the American Heart Association (AHA) that fishes should be taken at less twice weekly (Javed & Usmani, 2019), so they represented risk hazard for humans because their exposure to pollution from industrial activity and deposit in the tissue (marine and freshwater organisms) which transferred to the human (Goretti et al., 2016).

United States Environmental Protection Agency (USEPA, 2011) reported that these metals may be carcinogenic or non-carcinogenic for human health. Target cancer risk (TR) and target hazard quotients (THQ) are measurement terms useful for determining the effects of HVs on social health, THQ should not reach 1, and if

it does, there is a probability that it will cause non-carcinogenic risk. The categories of TR are determined by New York State Department of Health (NYSDOH, 2007) as in Table 3.

Table 3: Categories of target cancer TR risk.

Target Cancer (TR)	
Categories	Range
Low	$\leq 10^{-6}$
Moderate	10^{-4} - 10^{-3}
High	10^{-3} - 10^{-1}
Very high	$\geq 10^{-1}$

Heavy metals poses a greater risk to pregnant women, breastfeeding mothers and children (Javed & Usmani, 2016). In a risk assessment, based on *Mastacembelus armatus* consumption, it was shown that accumulation of Ni (58.98 mg/kg dry weight) approaches non-carcinogenic risk to both adult sexes, whereas the carcinogenic risk of Ni for male and female was in the range of 3.43 x 10^{-3} and 3.91 x 10^{-3}, respectively (Javed & Usmani, 2016). Ni, Mn, Fe and Cu are essential elements and necessary for metabolic activity and biological function in variable systems in the organism's body (Sivaperumal et al. 2007; Gemaque et al., 2019). The U-shape is doing response curve for these elements, because the excessive and deficiency of essential minerals cause adverse health effects (Stern et al., 2007; Fernandes et al., 2008).

Fishes may be a source for Ni which is known to cause inflammation and lung emphysema, tumor and fibrosis. It is also considered as a carcinogenic agent (Forti et al., 2011). Some metals, such as Fe, are bonded to protein and lead to neurodegenerative pathogenesis in humans such as Parkinson's disease and Alzheimer's (Koslowski et al., 2012). Wilson disease has resulted from excessive intake of Cu which accumulates in the brain and eyes, causes damage to kidney and also causes Mense disease which is a fetal disorder (U.S. Department of Health and Human Services, 2004; Ameh & Sayes, 2019). Mn has important ability to prevent cardiac arrest, heart attack and stroke, but it becomes a risky mineral for humans by taking it at high concentration and causes neurologic and psychologic syndromes (Saha & Zaman, 2013).

Conclusion

Iraqi river waters are exposed to heavy metal contamination, which leads to pathological tissue and enzymatic changes in fish body, which is one of the important vital diagnostic methods for pollution of the aquatic environment. Fishes may play a significant role in transporting heavy metals accumulated in their tissues to humans, and thus poses a threat to public health.

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