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Heavy Metal in Aquatic Ecosystem Emphasizing its Effect on Tissue Bioaccumulation and Histopathology: A Review

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ABSTRACT

From several decades environmental pollution is considered as a major global problem for both human and animals. The industrial effluents are the major source of pollution that are discharged into the water bodies posing serious threat to the aquatic animals like fishes. If the concentration of the metal is not in permissible limit as per World Health Organization (WHO) and Federal Environmental Protection Agency (FEPA) guidelines then these heavy metal accumulate in fishes and may cause serious human health hazard. Among the various toxic pollutants, heavy metals like Lead (Pb), Chromium (Cr), Nickel (Ni), Zinc (Zn), Cadmium (Cd), Cobalt (Co), Titanium (Ti), Iron (Fe) and several mixture of these heavy metals have severe action due to their tendency of bioaccumulation in fish tissues. In this review, a wide survey of bioaccumulation of heavy metals in fish tissue in relation to its effect on fish histopathology which is a sensitive biomarker of overall fish health and ecology of water bodies, has been studied. Fish being sensitive to xenobiotics can be used as ecological indicator of freshwater pollution and thus this review is useful in biomonitering studies. Also, some recent studies enlightened that fishes that live in polluted water bodies accumulate different concentration of heavy metals and thus is depleting the quality of major protein rich food item that is fish.

Key words: Pollution, heavy metal, fishes, bioaccumulation, bioindicator

INTRODUCTION

Several water bodies present throughout the world have being contaminated by anthropogenic activities. The pollutants are in form of pesticides, heavy metals, personal care products and pharmaceuticals etc. However, among these pollutants heavy metal poses serious effect to the ecology of water body primarily influencing one of the major protein source that is, fish (Table 1). Recent studies on the biotransformation of xenobiotic chemicals in fish have been focused on the specific metabolites produced, since these metabolic reactions affect distribution, accumulation and toxicity of chemicals majorly heavy metals (Lech and Bend, 1980). Xenobiotic chemicals may also affect the distribution, accumulation and toxicity of other chemicals by modifying the activity of enzymes that carry out these biotransformation processes (Lech *et al.*, 1982). These heavy metals bring about histopathological alterations, however, they take place at later stages. At initial stage the metabolic activity of the fish is disturbed for instance, the mechanism of action of several xenobiotics could initiate the formation of a specific enzyme that causes changes in metabolism,

Table 1: Assessment of heavy metal in different water bodies and its bioaccumulation and effect on different organ of fishes

Fish model	Source	Pollutants	Affected organ	Parameter used	Conclusion	References
Channa punctatus, *Clarias gariepinus* and *Labeo rohita*	Rasalganj fish market, Aligarh, India	Cu, Ni, Fe, Co, Mn, Cr and Zn	Muscle, liver, kidney, gills and integument	Atomic absorption spectrophotometer used to analyse metal concentration in fish tissue	Metals accumulated in tissues and exceeded permissible limits	Javed and Usmani (2011)
African cat fish (*Clarias gariepinus*)	Acclimatized in laboratory	Pb	Gills and liver	Histopathology	Pb is stored in gills and liver that effect fish health	Olojo *et al.* (2005)
Alburnus alburnus	Arda river, South Bulgaria	Heavy metal (Pb, Zn, Cd)	Blood cells	Atomic absorption spectrophotometer, morphological modifications of blood cells by staining Ramanovsky-Geimsa dye, leukograms	Combined impact of Pb, Zn and Cd on blood cells underlined negative effect on fish health	Baltova and Velcheva (2005)
Anabas testudineus	Exposure study	Titanium effluent	Blood samples and liver	Hematological parameter, hepatosomatic index, biochemical studies of liver	Enourmous reduction in the size of liver and kidney due to titanium dioxide exposure	Nair *et al.* (1984)
Bleak, Rudd and Perch	Dam lake (Studen klad enets), Bulgaria	Heavy metal mixtures	Gills and Liver	Histopathology	Histopathological changes were found indicating heavy metals in water	Velcheva *et al.* (2010)
Brown Trout (*Salmo trutta*)	Exposure study	Cd and Zn	Kidney and gills	Histopathology	Severe degeneration found in kidney epithelial cells due to Cd and Zn in high concentration	Besirovic *et al.* (2010)
Carassius auratus gibelio (Silver crucian carp)	Exposure study	Mercury	Gills, skin, intestine, muscle, cord, brain, liver, kidney	Physico-chemical parameter, atomic absorption spectrophotometer	Mercury found accumulated in every tissue	Nicula *et al.* (2009)
Catla catla and *Labeo rohita*	Cauvery river, Karnataka, India	Fe, Pb, Zn, Ni, Mn, Cu, Cr and Cd	Liver, gill and muscle tissues	Atomic absorption spectrophotometer used to analyse metal concentration in fish tissue	Both accumulated heavy metals in tissues but *C. catla* accumulated more heavy metals than *L. rohita*	Raju *et al.* (2013)
Catla catla, *Labeo rohita*, *Cirrhina mrigala* (Carps)	River Ravi, Pakistan	Heavy metal Pb, Ni, Co	Kidney, liver, gills, muscles	Atomic absorption spectrophotometer used for analyzing these heavy metal in fish organ	Accumulation of all metals in fish body organ showed positive correlation	Javed (2005)
Channa punctatus	Water bodies near Annamalai University, India	Zinc	Gills, liver, kidney, intestine and muscle	Atomic absorption spectrophotometer done for measuring Zn concentration in fish organ	Zinc is found in the organs of *C. punctatus*	Murugan *et al.* (2008)

Table 1: Continue

Fish model	Source	Pollutants	Affected organ	Parameter used	Conclusion	References
Channa punctatus	Panethi pond, Aligarh, India	Cu, Ni, Fe, Co, Mn, Cr and Zn	Gills, liver, kidney, muscle and integument	Atomic absorption spectrophotometer used to analyse metal concentration in fish tissue	Fe found to be abundant metal in pond and accumulated most in all tissues	Javed and Usmani (2012)
Channa striatus and *Heteropneustes fossilis*	Yamuna River, India	Cr, Ni and Pb		Bioaccumulation and histopathological alteration	Cr accumulated most and all other metals exceeded permissible limits	Fatima and Usmani (2013)
Clarias batrachus	Exposure study	Mercuric chloride	Blood samples	Hematological parameter	Increase RBC and WBC level, decrease haemoglobin	Maheswaran *et al*. (2008)
Clarias gariepinus (African catfish)	Exposure study	Copper sulphate	Gills	Histology, histopathology	It is found that gill histopathological alterations are due to toxicity of copper sulphate	Wani *et al*. (2011)
Clarias gariepinus African catfish	River Nile, Egypt	Pb, Cd, Zn, Cu, Cr, Fe, Hg, Mn	Liver	Histopathology and enzymatic activity	It is found that enzymatic level and histopathological alteration seen in selected tissues	Osman *et al*. (2010)
Commercial marine fish (*Rastrellinger kanagurta, Epinephelus sexfaciatus, Lates calcarifer, Decapterus maruadsai*)	Kalang valley, Malaysia	Cd and Pb	Brain, gills, intestine, kidney, liver, flesh muscle	Flame atomic absorption spectrophotometer done for Cd and Pb analysis	Both metals were found in edible organs of fishes in permissible limit	Nor Hasyimah *et al*. (2011)
Common carp (*Cyprinus carpio*)	Exposure study	Heavy metals (Cd, Pb, Cr, Ni)	Acclimatized in gills, liver, kidney and flesh	Histopathology	Histopathological changes were found in fish indicating heavy metals in water	Vinodhini and Narayanan (2009)
Ctenopharyngodon idella Grass carp	Lake Balaton and local fish farm, Hungary	Ni, Cu, Zn, Cd, Pb and Hg	gills, liver, kidney, muscle and gut	Atomic absorption spectrophotometer used to analyse metal concentration in fish tissue	Highest metal concentration found in liver and kidney tissues	Vigh *et al*. (1996)

Table 1: Continue

Fish model	Source	Pollutants	Affected organ	Parameter used	Conclusion	References
Cyprinid fish (*Cyprinus carpio* and *capoeta* sps)	Kor river, Iran	Heavy metal Hg, As, Cd and Pb	Liver, kidney, muscle, gonad and brain tissues	Induction coupled plasma method used for assayed these metal concentration	The study shows that not only heavy metal effect fish health as well as steroidal pattern too effected	Ebrahimi and Taherianfard (2011)
Cyprinus carpio	Tumkur tank, Karnataka, India	Heavy metals Zn, Pb, Cd, Ni, Cu, Cr, Fe	Muscle	Atomic absorption spectrophotometer done for metal concentration analysis	Heavy metals accumulated in the fish muscle	Sreedhara Nayaka *et al*., (2009)
Cyprinus carpio	Avsar dam Lake Turkey	Cd, Cr, Cu, Fe, Ni and Pb	Some tissues	Fish sample analyzed by inductively coupled plasma spectroscopy	Fe found more accumulate in fish tissue	Ozturk *et al*. (2009)
Cyprinus carpio (Common carp)	Exposure study	Heavy metals (Cr, Ni, Cd, Pb)	Gills, liver, kidney, flesh	Atomic absorption spectrophotometer for heavy metal analysis	The bioaccumulation of Pb and Cd was significantly increase in tissues	Vinodhini and Narayanan (2008)
Cyprinus carpio, Barbus capito, Chondrostoma regium	Seyhan river, Turkey	Heavy metals (Cd, Pb, Cu, Cr,Ni)	Gill, liver and muscle	Atomic absorption spectrophotometer used for heavy metal analysis	High level of heavy metal in fish gills, liver and muscle tissue are found	Canli *et al*. (1998)
Euryglossa orientalis, Psettodes erumei	North coast of Persian gulf	Heavy metal (Ni, V)	Liver	Histopathology	Major histopathological changes were found in liver	Khoshnood *et al*. (2010)
Fin fish (*Oreochromis mossambicus*)	Jannapura Lake, Karnataka, India	Cu, Zn, Pb, Cd, Ni and Co	Muscle and gill	Fish sample analyze by atomic absorption spectrophotometer	Human activity in jannapura lake increase heavy metal load that effect the fish health	Puttaiah and Kiran (2007)
Freshwater fishes (Perch, roach, silver bream, semi bream, chub, smelt, tench and pike)	Fresh water bodies, Lithuania	Cd, Pb, Ni, Cu, Cr, Mn, Zn, Fe and V	Flesh, bone, liver, gill and intestine	Metal concentration in fish organ analysed by using ICP-MS model element	All these metal are found in higher concentration	Staniskiene *et al*. (2006)
Hammour fish (*Epinephelus areolatus*)	Local market in jeddah city Saudi Arabia	Heavy metals (Cr, Zn, Cu, Fe, Pb, Mn, Cd, As, Co and Hg)	Muscle, gills, brain and viscera	Atomic absorption spectrophotometer done for measuring these metal in fish organ	High concentration of heavy metals found in this fish	Ganbi (2010)
Hemichromis fasciatus	Obga river, Nigeria	Heavy metals (Cr, Cu, Mn, Ni, Pb)	Fish as whole	Atomic absorption spectrophotometer used to measure heavy metal concentration in fish	It is found that some of metal exceeded WHO and FEPA recommended limit in fish	Obasohan (2008)
Heteroclarias spp.	Ughelli town, Delta state, Nigeria	Zn	Blood samples	Hematological parameter	Zn shows changes in blood cells	Kori-Siakpere and Ubogu (2008)

Table 1: Continue

Fish model	Source	Pollutants	Affected organ	Parameter used	Conclusion	References
Heteropneustes fossilis	Yamuna river Delhi to Allahabad, India	Heavy metals (Cd, Co, Cr, Cu, Fe, Mn, Ni, Pb, Zn)	Fish as whole	Atomic absorption spectrophotometer used for heavy metal analysis	High level of heavy metal are found in fish organ	Ajmal *et al*. (1985)
Labeo rohita	Exposure study	Cr	Gill and liver	Histopathology	Gill shown fusion, hypertrophy and degeneration of epithelium while liver shown vacuolization and disintegration of hepatocytes	Muthukumaravel and Rajaraman (2013)
Labeo rohita, Tilapia zilli, Chrysichthys nigrodigatatus	Yamuna river, Delhi, India	Metals (Al, B, Ba, Cd, Co, Cr, Cu, Fe, K, Mg, Mn, Na, Ni, Pb, Sb, Sn, Si, Pb, K)	Fish as whole	Inductively coupled plasma-optical emission spectroscopy (ICP-OES) used for analysis	Fish sample are not in ranged of maximum acceptable limits per WHO	Sen *et al*. (2011)
Lutjans coccineus, Tigeratooh croaker, Cyprinus carpio	Isfahan, Iran	Pb, Cr, Cd, Ni, Hg	Whole fish	Concentration of toxic metal analyse by atomic Absorption spectrophotometer	Heavy metals concentration found in permissible limit	Pourmoghaddas and Shahryari (2010)
Mugil cephalus, Trachurus mediterraneus	Iskenderum Bay, Turkey	Fe, Cu, Ni, Cr, Pb and Zn	Skin, muscle, gonad	Fish tissues, skin, gonad and muscle analysed by atomic absorption spectrophotometer	Some metal exceeded the permissible limit	Yilmaz (2002)
Mystus vittatus, Tilapia mossambica, Heteropneustus fossilis, Ctenopharyngodon idella and Saurida undosquamis	Kollidam River, Tamil Nadu, India	Heavy metals (Cd, Pb, Cr, Zn, Cu)	Liver, gills, intestine, kidney and muscle	The heavy metal assayed by double beam atomic absorption spectrophotometer	It is found that maximum tendency to accumulate copper and minimum accumulation of Zn in the muscle tissue of fish	Ambedkar and Muniyan (2011)
Nile Tilapia (*Oreochromis niloticus*)	Exposure study	Zn	liver	Liver histopathology	Damage seen in liver	Abdel-Warith *et al*. (2011)
Oreochromis aureus, Cyprinus carpio, Clarias lazera	Jordan valley, Jordan	Cd, Cu, Zn	Muscle, bone, skin and gills	Flame atomic absorption spectrophotometer used for analysing heavy metal concentration	All the heavy metals studied in these fishes are at acceptable levels	Al-Weher (2008)

Table 1: Continue

Fish model	Source	Pollutants	Affected organ	Parameter used	Conclusion	References
Oreochromis mossambicus	Indus river, Pakistan	Mn, Pb, Cu, Zn, Hg and Cr	Gill and liver	Bioaccumulation and histopathological alteration	Pb and Hg were above MPL of WHO. Gill and liver shown histopathological alterations	Jabeen and Chaudhry (2013)
Oreochromis niloticus (Nile Tilapia)	Edku, Borollus and Manzala lakes, Egypt	Heavy metals (Fe, Zn, Cu, Mn, Cd and Pb)	Muscle, gills and liver	Atomic absorption spectrophotometer done to measure the metal concentration in selected fish organ	Great concentration of heavy metals in water as well as in tissue of the fish mainly Cadmium	Saeed and Shaker (2008)
Oreochromis niloticus, *Lates niloticus*	Lake Nasser, Egypt	Pb, Fe, Zn, Cu, Cd, Co	Liver, gills, intestine, testis, heart and muscle	Bioaccumulation and histopathological alteration	All organs have high concentration of these heavy metals	Mohamed (2008)
Oreochromis niloticus, Teleost fish	Exposure study	Ni	Gills and blood	Physiological parameter, gill structure	Histological changes are found in fish gills	Al-Attar (2007)
Persian sturgeon (*Acipenser persicus*)	Exposure study	Mercuric chloride	Gills	Histopathology	Fish gills are most significant to find environmental pollution by mercury content	Khoshnood *et al*. (2011)
Prochilodus lineatus, Neotropical fish	Exposure study	Pb	Gill morphology and blood count	Gill histopathology and blood analysis, LC50	Rapid destruction of gill lamellae, histopathological lesions, hyperglycemia to lower lipids	Martinez *et al*. (2004)
Sleek unicorn fish (*Naso hexacanthus*)	Jeddah coast of Red Sea, KSA	Cd, Cu, Zn and Pb	Liver, gills	Liver and gill sample histopathology, histomorphometrical examination and MT gene expression assays	Highly damage gills and liver	Montaser *et al*. (2010)
Three Major carp (*Catla catla*, *Labeo rohita*, *Cirrhina mrigala*)	River Ravi, Pakistan	Heavy metals (Cadmium and copper)	Liver, gills, kidney, skin, muscle and scale	Atomic absorption spectrophotometer done measuring Cd and Cu in fish organ	Both Cd and Cu accumulated in the liver of these Indian major carp	Rauf *et al*. (2009)
Tilapia	Athi-Galana-Sabaki tributaries, Kenya	Pb, Ni, Mn, Zn, Cd and Cr	Gills	Atomic absorption spectrophotometer used to analyse metal concentration in fish tissue	All metals above maximum permissionable limit of WHO	Muiruri *et al*. (2012)

Table 1: Continue

Fish model	Source	Pollutants	Affected organ	Parameter used	Conclusion	References
Tilapia and cat fish	Okumeshi river, Nigeria	Trace metals (Pb, Ni, Cr, Mn, Cd)	Fish tissues	Atomic absorption spectrophotometer used to analyse metal concentration in fish tissue	Maximum accumulation found in gill and liver	Ekeanyanwu *et al*. (2010)
Tilapia fish (*Oreochromis niloticus*)	Langata, Cempaka, Engineering lake Malaysia	Heavy metals Pb, Cd, Cr, Cu, Ni, Zn	Liver, gills and muscle	Inductively coupled mass spectrometer for analysing metal concentration	Heavy metals in fish found in allowable limits	Taweel *et al*. (2011)
Tilapia fish (*Tilapia nilotica*)	Wadi Hanifah, Saudi Arabia	Heavy metal Pb, Cd, Hg, Cu and Cr	Muscle, liver, kidney, gill and intestine	Atomic absorption spectrophotometer used for determining these heavy metal concentration in tissues	Kidney have high concentration of heavy metals	Abdel-Baki *et al*. (2011)
Tilapia mossambic	Dams in Ekiti state, Nigeria	Zn, Fe, Pb and Mn	Fish as whole	Atomic absorption spectrophotometer used to analyse metal concentration in fish tissue	Heavy metals in water and fish were within the international permissible level	Adefemi (2013)
Tilapia zilli	Lake Manzalah, Egypt	Heavy metals Cu, Zn, Cd, Pb	Flesh, gills, liver and gonads	Atomic absorption spectrophotometer was used for determining these heavy metal	Pb is in high concentration in different organs of the fish	Zyadah (1999)
Tilapia zilli (Tilapia), *Chrysichthys nigrodigatatus* (catfish)	Epe and Badagry lagoons, Nigeria	Heavy metals (Zn, Ni, Fe)	Head, trunk, gills and intestine and water sample	Atomic absorption spectrophotometer done for heavy metal analysis	High concentration of zinc and Fe found in fish parts, Zn, Ni and Fe were detected in water sample	Olowu *et al*. (2010)
Tilapia zilli and *Clarias gariepinus*	River Benue, Nigeria	Heavy metals (Cr, Zn, Cu, Fe, Pb, Mn, Cd)	Gills, intestine and tissues	Atomic absorption spectrophotometer done for metal concentration analysis in fish organ	Both fishes contain high concentration of heavy metals	Eneji *et al*. (2011)
Tilapia zilli, Clarias anguillaris, Protoptenus, Oreochromis niloticus, Eutropius niloticus, Synodentis budgetti	Chad lake, Nigeria	Heavy metals (Pb, Fe, Cd)	Bone, liver, stomach, gills and kidney	Atomic absorption spectrophotometer done for metal concentration analysis in different organ	Heavy metals have shown heavy bioaccumulation in the liver tissue of fish	Akan *et al*. (2009)
Wallago attu, Labeo dyocheilus	Kabul river, Pakistan	Zn, Ni, Cr, Cu, Cd and Pb	Skin, gills, intestine, liver and muscle	Fish organ having heavy metal analyse by atomic absorption spectrophotometer	Labeo dychelius accumulate more metal than Wallago attu	Yousafzai *et al*. (2010)

further leading to cellular intoxication and death at a cellular level. This is manifested as necrosis at the tissue level (Bailey *et al.*, 1996). Histological and histopathological changes produced by pollutants in organs and tissues can occur before they produce irreversible effects on the biota. Histological methods can be used in conjunction with other ecotoxicological bioindicators as an early warning system for the survival of the species, as well as for environmental protection (Khoshnood *et al.*, 2010). Histopathological biomarkers are closely related to other biomarkers of stress since many pollutants have to undergo metabolic activation in order to be able to provoke cellular change in the affected organism. The simplest explanation for aquatic data showing greater concentrations at higher trophic levels (up to fish) is that of passive uptake by diffusion through body surfaces including gills, with elimination rates decreasing with increased body size (Gray, 2002).

Since field studies account for both waterborne and dietary metal exposures, bioaccumulation factor data compiled from field are more ecologically important as all the routes of exposure (e.g., dietary absorption, transport across the respiratory surface) are contributing in field data (Gobas and Morrison, 2000; DeForest *et al.*, 2007).

MECHANISM OF METAL BIOACCUMULATION IN FISHES

Fishes are continuously exposed to waterborne and particulate heavy metals due to continuous flow of water through gills and through food sources. Metals bioaccumulated in different tissues follow different patterns of bioaccumulation factors (Fatima and Usmani, 2013). The mechanism of bioaccumulation of heavy metal in fish includes different processes in dynamic manner. Both physiological/biochemical responses and metal geochemistry are responsible for the differences in metal concentrations observed in different populations of aquatic species. It was confirmed that the internalization of metals into the cells of gills and internal epithelia follows similar mechanisms from different bioaccumulation studies (Noegrohati, 2006).

Since decades, study of metal bioaccumulation has led to the formulation of many models. The Free Ion Activity Model (FIAM), proposed in the 1980s, gives an insight in the study of metal uptake in different species of aquatic organisms (Campbell, 1995). Few years later, the Biotic Ligand Model (BLM), was introduced which is based on the interaction of the free metal ion with the proposed biological site of action, fish gill being the initial site of action (Paquin *et al.*, 2002). Then came Subcellular Partitioning Model (SPM) which directly addresses toxicity within organisms in terms of subcellular components of accumulated metal, a variation of a tissue residue approach (Wang and Rainbow, 2007). A simple biokinetic model including all the processes that potentially leads to metal bioaccumulation, quantitatively given by Wang and Rainbow (2008). Thus, metal bioaccumulation in an organism is controlled by the balance between uptake and elimination:

$$dC_t/dt = K_u \times C_w + AE \times IR \times C_f - (k_e + g) \times C_t$$

where, C_t is the metal concentration in an animal at time t, K_u is the uptake rate constant from the dissolved phase (L g^{-1} day^{-1}), C_w is the metal concentration in the dissolved phase (μg L^{-1}), AE is the metal assimilation efficiency from the dietary phase, IR is the weight-specific ingestion rate of the animal (g g^{-1} day^{-1}), C_f is the metal concentration in the dietary phase (μg g^{-1}), K_e is the efflux rate constant (day^{-1}) and g is the growth rate constant of the animal (day^{-1}).

A number of factors such as sex, age, season, spawning period, variability of food habitats and pollutant exposure and phylogenetic differences in regulatory mechanisms, may influence the uptake, retention and bioaccumulation of trace contaminants in fish tissues (Nesto *et al*., 2007). Zhao *et al*. (2012) shown correlation of heavy metals in the tissue of fish to their living environments both qualitatively and quantitatively and there was diverse metal bioaccumulation characteristics which was significantly affected by environment factors and living habits. The bioaccumulation model showed that Uptake Efficiency factor of essential heavy metals such as Cu and Zn decreases as exposure concentration increases, due to homeostasis regulation while for non essential heavy metal Hg, it is increases as the exposure concentration increases and excretion was observed as manifestation of homeostasis regulation (Noegrohati, 2006).

MECHANISM OF HISTOPATHOLOGICAL DAMAGE

Histopathological damage in tissues is outcome of various biochemical and physiological interactions within cell owing to exposure to various xenobiotics. Heavy metals generates Reactive Oxygen Species (ROS) which damages protein, lipid and DNA content of exposed animal which on gross level can be visualized through histopathology. Heavy metals grouped as Redox active (Fe, Cu, Cr etc) undergo redox cycling whereas redox inactive metals (such as Pb, Cd and Hg) undergo covalent electron sharing with cells major antioxidant enzymes (Thiols). Both types lead to the production of ROS as hydroxyl radical (OH), Superoxide radical (O_2^-) or hydrogen peroxide (H_2O_2) which deplete cells intrinsic antioxidant defense. ROS lead to lesions to lipid, protein and DNA which can be visualized through cross index i.e., histopathology of tissues (Ercal *et al*., 2001). Histopathology is a broader term and mirror of effects of exposure to a variety of anthropogenic pollutants (Hinton *et al*., 1992). Histological responses are relatively easily recognized provided that proper reference and control data are available (Hinton, 1994). Histopathology thus is a long term and reliable biomarker of toxicant exposure. Heavy metals undergo metabolic activation that induces a cellular change in affected fish. The tissue lesions and apoptosis arises from bioaccumulation stimulate necrotic alterations in the fish with an inflammatory defensive reaction (Roganovic-Zafirova *et al*., 2003). Below are given few mechanistic insight of metal toxicity leading to microscopically visible alterations.

Heavy metal ions can enter blood vessels some of them are carried by proteins like albumin and can be taken up by endothelial cells lining the vessels. Heavy metal ions induce mechanisms of gene activation in endothelial cells as do pro inflammatory mediators, indicating that corroding metal ion containing biomaterials can provoke inflammatory reactions by known, as well as by yet unknown, intracellular signalling pathways (Wagner *et al*., 1998). And thus blood profile changes with respect to heavy metal exposure and become sensitive bioindicator of heavy metal pollution as also shown by many workers (Baltova and Velcheva, 2005; Kori-Siakpere and Ubogu, 2008; Maheswaran *et al*., 2008). Teleost liver is major organ for heavy metal metabolism thus frequently studied by many workers (Canli *et al*., 1998; Javed, 2005; Vinodhini and Narayanan, 2008) to observe different deformities. Fish hepatocyte has relatively more glycogen/lipid content which lead to hepatocytes more vacuolated (Weber and Gingerich, 1982). Macrophage aggregates act as repositories for product of cell membrane and erythrocyte breakdown include lipofuscin, ceroid, hemosiderin and melanin (Wolke, 1992). Reason behind hepatocellular enlargement is organelle proliferation (hypertrophy), failed mitotic divison of hepatocytes (megalocytosis) and vacuolar swelling of endoplasmic reticulum cisternae (hydropic degeneration) (Hinton *et al*., 1992). Toxic chemicals lead to increased number of organelles as myelinated bodies, mitochondria, glycogenosomes, peroxisomes and lysosomes and changes in rough endoplasmic reticulum. Due to toxicology of chemicals, hepatocytes hypertrophy is accompanied by basophilia (as result of loss in glycogenic vacuolization and increased mRNA content (Wester *et al.*, 2003). Kidney is another target organ for metabolism and removal of waste from blood and studied for metal bioaccumulation (Akan *et al.*, 2009; Ambedkar and Muniyan, 2011; Fatima and Usmani, 2013) followed by heavy metal exposure kidneys follow specific metabolic process. Macrophages are the key defensive cells dealing with foreign materials and debris (Blazer *et al.*, 1994). The macrophage comprise lipofuscin, melanin and hemosiderin pigment in heavy metal toxicated kidney tissues i.e., contaminants influence macrophage pigment composition (Kruger *et al.*, 1996).

Gills are another organ for the concern of heavy metal toxicology as it shows significantly high bioaccumulation factor owing to the fact that gills have larger surface area and comes in direct contact with heavy metal laden water. It has been studied by several workers that various deformities such as epithelial lifting, interstitial oedema, leucocytic infiltration, hyperplasia of the epithelial cells, lamellar fusion, vasodilatation and necrosis are caused due to heavy metals (Martinez *et al.*, 2004; Al-Attar, 2007; Taweel *et al.*, 2011; Fatima and Usmani, 2013). Muscle and integument are the least effected tissue in terms of bioaccumulation and BAF studied by many workers (Javed, 2005; Al-Weher, 2008; Nicula *et al.*, 2009; Rauf *et al.*, 2009; Javed and Usmani, 2011) as these are major edible parts and relished as protein diet. Other workers (Ajmal *et al.*, 1985; Obasohan, 2008; Pourmoghaddas and Shahryari, 2010; Sen *et al.*, 2011) estimated heavy metal in fish taken as whole. The muscle and integument are of prime concern as the fish may not only be consumed by local population but may be transported to other region for economy.

CONCLUSION

Every heavy metal has its own bioaccumulation dynamics, depend to the metal studied and environmental conditions. It is imperative to say that histological biomarkers are the indicators of pollutants in overall health of the entire population in a waterbody since all fishes are exposed to same physico chemical environment. In this review, we have illustrated possible mechanism of heavy metal bioaccumulation in fish tissues and its effect on histopathology because as different species have contrasting patterns of accumulating and eliminated metals. There remains a substantial need to understand the subcellular controls of metal accumulation and toxicity for different metals in different species of fishes as it form major source of protein all around the world. Fish bioaccumulated substantial amount of heavy metals in short exposures and thus form acute ecological indicator of water pollution and later, histopathology of fish tissues can be another tool for chronic effect of exposure used in biomonitering studies. Here, this data is also useful for the understanding and awareness as how we are contaminating our most natural resource of protein through anthropogenic activities and thus appropriate guidelines and policies should be laid down to protect our water resources. Further, human health hazard studies can be encouraged based on difference between fish species bioaccumulation mechanism.

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