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Health Risks of Potentially Toxic Metals Contaminated Water

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Abstract

Groundwater which fulfills globally 50–80% need of drinking water, due to Anthropogenic and geologic activities, has been continuously contaminated by potentially toxic metals, causing a range of effects to animals and citizenry. In the developing countries, about 80% of diseases are waterborne diseases. Bio accumulation of these metals in citizenry due to intake of contaminated vegetables, fruits, fishes, seafood and drinking water and beverages causes a serious threat to citizenry. Toxicity of these metals is due to metabolic interference and mutagenesis, interference in the normal functioning of structural proteins, enzymes, and nucleic acids by binding them, adversely affecting the immune and hematopoietic systems in citizenry and animals. The toxic metals also enrich antibiotic resistant microbes particularly bacteria by Co-selection (occurring by Co-resistance and cross-resistance) as it promotes antibiotic resistance in bacteria even in absence of antibiotics. These metals in living cells cause cytotoxicity, oxidative stress resulting in the damages of antioxidants, enzyme inhibition, loss of DNA repair mechanism, protein dysfunction and damage to lipid per oxidase. Endocrine disruption, neuro-developmental toxicity, biosynthesis of hemoglobin, metabolism of vitamin D, renal toxicity, damage to central nervous system, hearing speech and visual disorders, hypertension, anemia, dementia, hematemeses, bladder, lung, nose, larynx, prostate cancer, and bone diseases are some other health's risks to human.

Keywords: pollution, human, potentially toxic metals, health risks, heavy metals resistance, fishes

1. Introduction

Water the “life-blood of the biosphere” may be an alcahest which dissolves different chemicals and environmental pollutants. Globally, groundwater is the main source of domestic drinking water both in rural and urban areas and fulfills approximately 80% need of drinking water in the rural areas and 50% of urban water need. As surface water infiltrates to unconfined aquifers easily, these aquifers are contaminated very easily. The pollution of groundwater causes significant alteration in the environment. The most sources of lakes, rivers, ponds, and streams are the groundwater. When contaminated groundwater is supplied to those sources, the surface water is additionally contaminated which causes harm to birds, animals, and plants. Because of population growth over the last 50 years, the abstraction of groundwater has increased leading to reduce natural discharge flows and groundwater quality. Groundwater quality is additionally suffering from recharge rate and recharge quality. Existence of human on earth without potentially toxic metals is not possible.

These potentially toxic metals (Cd, Cu, Pb, Zn, Cr (III), Cr (VI), and Hg) have high relative atomic mass and density. Hindu Business on Feb 20, 2019 reported that “more than forty million people in rural India drinks to water contaminated by heavy metals, arsenic, fluoride, etc.” The results are devastating. Diarrhea, often caused by exposure to fecal matter, kills 600,000 Indians per annum and waterborne diseases throughout the Ganges basin. In India, 25% of water sources is River Ganga. These metals participate within the redox reactions and are an important part of enzymes. Cobalt is a constituent of vitamin B₁₂, and manganese acts as an activator of the enzymes within the physical body [1]. Copper is important for enzyme ascorbate oxidase, cytochrome oxidase, plastocyanin oxidase, and photosynthesis in plants. As these metals cannot be degraded, they persist in the environment (in soils, industrial effluents, groundwater) for a long period; easily bio accumulated and bio magnify within the food chains poses a significant threat to the consumer and pollution of water sources by potentially toxic metals became a worldwide problem [2]. The toxic effect of these metals could also be because of metabolic interference and mutagenesis. These metals interfere in the normal functioning of structural proteins, enzymes, and nucleic acids by binding them. Even a smaller amount of potentially toxic metals/metalloid arsenic, lead, cadmium, nickel, mercury, chromium, cobalt, and zinc beyond their permissible limit in body became harmful. These metals also enrich antibiotic resistant microbes even in the absence of antibiotics. This study discusses the health risks of potentially toxic metals contaminated water to the citizenry accumulated via intake of contaminated vegetables, fruits, fishes (freshwater or marine), drinking water, and beverages. The consequences of those metals on antibiotic resistant genes and bacteria have also been discussed.

2. Potentially toxic metals

Potentially toxic metals are essential in a small amount for various biochemical and physiological functions within the plants, animals, and humans. These metals participate in the redox reactions and are an important part of enzymes. A number of researchers [3–6] have reported that natural contaminates of natural water are potentially toxic metals and organometallic compounds. Based on their health importance, the potentially toxic elements are classified into four groups, (i) essential: Cu, Zn, Co, Cr, Mn, and Fe. These metals beyond their permissible limit become toxic, (ii) non-essential: Ba, Al, Li, (iii) less toxic: Sn, and (iv) highly toxic: Hg, Cd, Pb, As (metalloid).

2.1 Routes of uptake

Routes of uptake of those toxic metals by human and animals are:

- i. Ingestion: it occurs via gastrointestinal route, that is, through the mouth by eating contaminated food, vegetables, fruits, seafood including fish, and by drinking contaminated water and beverages.
- ii. Dermal: dermal uptake means absorption through skin/gills, the aquatic animals' bio accumulates these toxic metals via dermal contact.
- iii. Inhalation: inhalation uptake occurs via inhalation of the polluted air as dust fumes and through exposure at work place. In the fish, these metals enter the body directly from water or sediments via the gills/skin or via its alimentary tract from the fish food/prey.

3. Sources of potentially toxic element contaminants within the water

Contamination of the environment by potentially toxic metals has increased after war II because of rapid industrialization and urbanization and increased rate of mobilization and transport [7]. The main sources of groundwater of contamination by heavy metals are:

3.1 Natural

Rock weathering, forest fires, volcanic eruptions, biogenic sources, and wind born soil particles are the natural sources of potentially toxic metals within the environment. Within the rocks, these metals are present as hydroxides, sulphides, oxides, silicates, phosphates, and chelated with organic compounds.

3.2 Anthropogenic activities

Industrial manufacturing of products to satisfy with the stress of the massive population like to cement production, iron industry, steam power plants, glass production, paint, and tanning industries is one among the causes of environmental pollution because of human activities. Agricultural activities (use of sewage sludge as manure), irrigation by sewage wastewater, mining, and metallurgical processes, garbage and waste mud incineration facilities, combustion of fuels, surface emission, and traffic and runoffs are other ways to release the pollutants within the different environmental compartments. The main route of the groundwater and aquatic contamination by potentially toxic metals are the leaching from toxic industrial waste dumps and municipal landfills and leaching of agricultural chemicals from soils into the upper aquifers [8].

As the concentration of potentially toxic metals within the environment is continuously increasing, and therefore, the soil retention capacity of those metals is decreasing and the resultant is the leaching of those metals within the groundwater [9]. Fertilizers and pesticides applied within the fields contain these potentially toxic metals (Cr, Cd, Cu, Zn, Ni, Mn, Pb, and As) as impurities [7]. Another source of groundwater contamination by potentially toxic metals is the urban runoffs which contain Pb, Cu, Zn, Fe, Cd, Cr, and Ni. The intrusion of seawater in aquifers also causes a rise in concentration levels of potentially toxic metals in the groundwater. Another anthropogenic source of the heavy metals in the environment is the burning of wastes at residential levels and dumpsites.

4. Potentially toxic metals within the ground, surface water, and sediments

The pollution of water resources by potentially toxic metals affects plants, animals, and human health adversely [10]. These metals even at a low concentration are toxic to aquatic organisms as these metals alter the histopathology of the tissues of the organisms [11, 12]. The one among the main sources of potentially toxic metals within the aquatic environment are the sediments which act as a sink and reservoir of those metals [13].

4.1 Potentially toxic metals within the drinking, ground, and surface water

A review of the literature showed that globally number of groundwater, drinking water, and surface water samples contains the potentially toxic metals beyond their permissible limit which affects adversely the human and ecological health. The arsenic concentration in the groundwater samples ranged from 0.0005 to 1.15 mg/L [14–16]. Author himself [17, 18] studied the concentration of potentially toxic metals in the groundwater samples for 20 years (1986–2005) and found that (i) concentration of those metals are increasing with time, (ii) concentration of those metals decreased with depth, and (iii) the concentration became beyond the permissible limit after the year 2000. The concentration of the toxic metals in the groundwater, drinking water, and surface water samples are recorded in **Table 1**.

4.2 Potentially toxic metals within the sediments

The accumulated amounts of the potentially toxic metals in the sediments are reported in **Table 1**.

5. Bioaccumulation of probably toxic metals in vegetables and fruits irrigated by contaminated ground and surface water

A long-term study made by the author himself [17, 18] found that the concentration of potentially toxic metals in the soils of agricultural fields of Aligarh irrigated by sewage effluent is continuously increasing, and therefore, the concentration of those metals in edible parts of the crops grown such soils were beyond toxic limits, and maximum accumulation was within the potato followed by maize [53]. Bansal [53] during their studies on the concentrations of Pb, Cd, Ni, Cr, Zn, and Cu in the vegetables palak, cabbage, brinjal, lady's finger, tomato, bitter gourd, radish, and cauliflower grown in the soils of periurban areas of Aligarh irrigated by sewage effluent water found that the concentration of the metals Cd, Pb, and Ni in all the studied vegetables were beyond their permissible limits for human consumption. The Target Hazard Quotient (THQ) values also denote that consumption of those vegetables will cause a potential risk for human health risk. Kabir and Bhuyan [54] found that the concentration of Cu in the hen's egg yolk (1.85–3.65 mg/kg) and albumin (0.5–1.15 mg/kg) were beyond permissible limits. The concentrations of these metals in the vegetables grown globally are given in **Table 1**.

6. Bioaccumulation of potentially toxic metals in freshwater fish, marine fish aqueous flora and fauna

Bioaccumulation of the potentially toxic heavy metals within the ecosystem of the Riverine has a negative impact on the ecological health of aquatic animals and causes decrease in their populations [55, 56]. Several researchers have reported fish deformities, decline of fish populations, and reduce in their growth rates if the concentration of potentially toxic metals increased beyond their tolerable limit [57, 58]. The concentrations of those metals in freshwater fish are reported in **Table 2**. The info in **Table 3** denotes the concentration of those metals in marine fish and other organisms.

Sample	Source	Concentration of metal (mg/L) or (mg/kg)							Reference
		Cd	Cr	Cu	Zn	Pb	Ni	As	
Drinking water	Lagos state, Nigeria	0.0	0.009–0.021	0.027–0.060	0.11–0.41	0.098–0.14	0.72–1.02		[19]
Drinking water and surface water	Yobe State, Nigeria		0.0074–0.99	0.001–0.12	0.012–0.087	0.024	0.0		[20]
Surface water	Nile River and its canals	0.001–0.048				0.054–0.329			[21]
Drinking water	Egypt	0.002–0.049				0.09–0.41			
Drinking water	Nigeria	0.02–0.124;		0.009–0.057	0.08–20.1	0.04–0.57		0.091–0.485	[22]
Surface water	Pearl River, China	0.0005–0.0075	0.0035–0.011	0.003–0.005	0.0165–0.0607	0.0006–0.0011	0.0014–0.0045		[4]
Surface water	Dares salaam, Tanzania	0.32	0.59	0.03	1.14	0.46–0.55			0.99–1.26 (Fe) [23]
Surface water	Ganga River, India	0.0–18.55	0.003–6.28	2.25–63.56	4.70	0.166–107.34	0.06–5.9	4.73	[5, 6, 24]
Ground water	Chembarambakkam lake (India)	0.00–1.32	0.00–0.19	0.018–0.088	0.008–2.45,	0.172–0.486	0.00–0.03		[25]
Surface water		0.00–1.5	0.00	0.01–0.03	0.01–0.70	0.16–0.22	0.00		
Surface water	Tamilnadu		0.229–1.484	0.001–0.128	0.001–0.65	0.031–0.781;	0.01–0.695		[26]
Surface water	Solan district (India)	0.00–0.00004			0.0021–0.0072	0.0 0–0.0041,		0.00–0.0014	[27]
Ground water		0.00001–0.00033			0.0006–0.0015	0.0001–0.0029		0.0–0.0009	
Surface water	Bodo Creek water	0.03–0.06				1.03–1.63			[28]
Surface water	Kenya	0.31–0.53		1.37–1.92		0.57–2.43			[29]

Sample	Source	Concentration of metal (mg/L) or (mg/kg)								Reference
		Cd	Cr	Cu	Zn	Pb	Ni	As	Others	
Ground water	Maru Town, Nigeria		0.0–0.99	0.0–0.33	0.012–0.087		0.00–0.0056			[30]
Groundwater	Albania	0.0–0.0006		0.0075–0.078		0.001–0.0058		0.008–0.009		[31]
Groundwater	Iran	0.006				0.09				[32]
Ground water	Singhbhum, India	0.01–0.08	0.04–0.28			0.08–0.42	0.03–0.14		0.07–4.45 (Fe)	[33]
Sediments	River Raohe, Chia	0.00–1.60	13.5–97.1	15.6–793.5	11.2–52.9	16.0–222.2	18.4–66.4	12.9–318.0		[13]
Sediments	Mashavera Basin Georgia	1.5–1.7	26.4–28	347.8–410.7	423.3–458.9	29.6–37.2	22.3–22.5		0.00–0.02 (Hg)	[34]
Sediments	Kabul	4.4–7.1	75.5–92.5	10.9–15.3	8.1–88.3	32.8–54.6	69.1–85.1			[35]
Sediments	River of Philippines		32.8–131.8	29.4–217.1	76.8–263.3		12.1–98.1		4.1–25.3 (Co)	[36]
Sediments	River Gomati	1.9–8.4		9.0–95.4		35.8–90.9		3.7–15.0		[37]
Sediments	River Ghaghara	0.21–0.28	61.3–84.7	2.8–11.7	13.3–17.6	10.7–14.3	15.3–25.6		11.4–18.4 (Co)	[38]
Sediments	River Ganga	1.7	69.9	29.8	67.8	26.7	26.7			[39]
Sediments	Bay of Bengal	0.03–0.06	0.61–0.79	0.38–0.66		0.01–1.42	0.01–0.23			[40]
Vegetables	Bangladesh	0.03–2.4	0.03–22.6	0.4–52.3	0.33–95.5	0.0.02–61.5	0.03–1.02	0.63–1.33	0.02–32 (Mn)	[41–43]
Vegetables	Supermarket of the Florida	0.002–0.040	0.012–0.223	0.13–2.47	1.31–3.95	0.0019–0.065	0.012–0.291	0.002–0.020	0.0005–0.033 (Co)	[44]
Vegetables		0.0006–0.028	0.009–0.126	0.22–2.65	1.12–3.88	0.0005–0.07	0.010–0.096	0.0012–0.016	0.0012–0.0065 (Co)	

Sample	Source	Concentration of metal (mg/L) or (mg/kg)								Reference
		Cd	Cr	Cu	Zn	Pb	Ni	As	Others	
Vegetables	Iran	0.030.55		0.85–4.1		0.5–1.5			0.69 (Co)	[45, 46]
Vegetables	Pakistan	0.045–0.39	2.72–6.62	22.2–65.2	19.5–41		1.8–5.0		18.7–137.3 (Mn)	[47]
Vegetables	Nigeria	0.11–0.43	5.1–9.9	4.7–75	38.1–335.2	2.6–9.2			19.3–33.3 (Mn)	[48]
Vegetables	Local vegetables, Iraq	1.5–6.0	1.02–1.13	7.3–37.2	25.3–43.8	0.5–1.48	6.3–7.9	4.73	2.83–3.09 (Co)	[49]
Vegetables	Imported vegetables, Iraq	1.6–5.8	1.03–1.15	17.3–33.5	17.3–33.5	0.32–1.55	7.1–10.3		3.08–3.10 (Co)	
Vegetables	China	0.004–0.51		0.015–1.31	1.4–24.2	0.004–1.16		0.014–0.66		[50]
Vegetables	Indonesia		0.0–152.8	4.3–150.1	5.1–90.7	11.1–347.5				[51]
Vegetables	Germany	0.01–0.79	0.03–4.69	3.2–23.2	11.7–122.8	0.1–31.3	0.03–1.93			[52]

Table 1.
The concentration of different potentially toxic metals (mg/L) in drinking, ground, and surface water and in sediments and vegetables (mg/kg).

Fish species	Source	Tissue	Concentration of metal (mg/kg)						Reference
			Cd	Cr	Cu	Zn	Pb	As	
<i>Cyprinus carpio</i>	Sardaryab, tributary of River Kabul	Gills		0.154	0.024	0.074	0.041		[59]
		Liver		0.188	0.089	0.07	0.142		
		Muscles		0.024	0.016	0.018	0.000		
<i>Labeo rohita</i>	Sardaryab, tributary of River Kabul	Gills		0.133	0.018	0.058	0.024		
		Liver		0.165	0.071	0.088	0.161		
		Muscles		0.019	0.01	0.02	0.000		
<i>Cyprinus carpio</i>	Indus River Mianwali, Pakistan	Gills		2.9–9.4	0.77–1.4	—	0.5–1.87		[60]
		Liver		3–5.4	2.5–3.4	—	0.45–1.1		
		Kidney		1.55–3.5	1.4–2.5	—	0.48–0.9		
		Muscles		1.03–2.63	1.1–1.67	—	0.46–1.9		
<i>Wallago attu</i>	Indus River Mianwali, Pakistan	Gills		4.5–9.5	3–5.9	—	0.45–1.92		
		Liver		12.5–20	11.5–21	—	0.9–1.0		
		Kidney		2.0–6.5	1.4–3.5	—	0.0–0.5		
		Muscles		6.5–15.2	2.9–5.5	—	0.83–2.0		
<i>Labeo rohita</i>	Kolleru Lake, India	Gills	0.38	0.19	0.09	0.19	0.3	0.05	[61]
		Liver	0.62	0.69	1.06	1.04	1.48	0.27	
		Kidney	0.25	0.72	0.23	0.94	0.55	0.07	
		Muscles	0.32	0.02	0.09	0.38	0.22	0.04	
<i>Channa striatus</i>	Kolleru Lake, India	Gills	0.32	0.59	0.03	1.14	1.30	0.12	
		Liver	0.48	0.33	0.99	1.01	1.35	0.20	
		Kidney	0.16	0.47	1.03	1.21	1.33	0.25	
		Muscles	0.45	0.85	0.53	0.46	1.30	0.14	

Fish species	Source	Tissue	Concentration of metal (mg/kg)							Reference
			Cd	Cr	Cu	Zn	Pb	As	Hg	
<i>Oreochromis niloticus</i>	Burullus Lake, Egypt	Muscles	0.45	0.85	0.39	4.70	0.46			[62]
<i>Finfish</i>	Lower Gangetic Delta, India	Whole Body	0–1.32		1.3–53.1	2.0–111.5	0–3.05			[63]
<i>Shrimp</i>	Lower Gangetic Delta, India	Whole Body	0–1.5		6.2–109.2	11.7–213.7	0–10			
<i>Oyster</i>	Lower Gangetic Delta, India	Whole Body	BDL		8.7–69.1	21.4–202.8	0–8			
<i>Tilapia zillii</i>	Niger River, Nigeria	Gill	0.094			8.92	ND		ND	[64]
		Muscle	0.049			5.42	ND		ND	
		Intestine	0.119			12.20	ND		ND	
<i>Malapterurus electricus</i>	Niger River, Nigeria	Gill	0.056			5.77	ND		ND	
		Muscle	0.032			3.74	ND		ND	
		Intestine	0.049			5.74	ND		ND	
<i>Clarias gariepinus</i>	Niger River, Nigeria	Gill	0.055			5.55	ND		ND	
		Muscle	0.04			3.38	ND		ND	
		Intestine	0.033			6.6	ND		ND	
<i>Clarias batrachus</i>	Local fish ponds of Ludhiana city and Sutlej River	Liver	3.74	3.69	3.48	67.78	11.12	3.13		[58]
		Muscle	0.24	2.10	3.79	29.42	4.48	0.68		
		Kidney	4.45	2.14	4.65	56.83	8.04	3.09		
<i>Barbuss harpeyi</i>	Tigris River in Baghdad	Gills	2.3–2.4	2.2–2.5	1.1–1.2	1.05–1.1	1.5–1.6			[65]
		Liver	1.3–2.9	2.5–2.7	0.5–0.8	0.9	2.05			
		Muscle	0.97–1.2	1.6–1.6	0.6–0.7	0.80	1.05			
<i>Barbus xanthopterus</i>	Bodo Creek, Niger Delta, Nigeria	Gills	2.2–2.5	2.1–2.5	1.2–1.3	1.1–1.2	1.3–1.6			
		Liver	2.7–2.8	2.2–2.6	0.7–0.8	0.7–0.9	1.8–2.1			
		Muscle	0.8	0.5–1.6	0.7–0.8	0.7–0.8	1.1			

Fish species	Source	Tissue	Concentration of metal (mg/kg)						Reference	
			Cd	Cr	Cu	Zn	Pb	As		Hg
<i>Callinectes amnicola</i>	Bodo Creek, Niger Delta, Nigeria	Leg	0.43–3.78				0.3–1.13			[27]
		Gill	0.38–2.02				0.01–0.42			
		Muscle	0.00–1.13				0.01–0.62			
		carapace	2.4–5.43				0.00–0.47			
<i>Chrysichthys nigrodigitatus</i>	Densu River, Ghana	Muscles			0.59	2.34		0.19	0.37	[11]
<i>Alosa immaculata</i>	Danube River	Whole Body	0.09		5.34		0.65			[66]
<i>Cyprinus carpio</i>	Danube River	Whole Body	0.084		5.10		0.58			
<i>Cyprinus carpio</i>	Danube River, Belgrade, Siberia	Whole Body	0.014		0.207		0.036			[67]
<i>Silurus glanis</i>	Danube River, Belgrade, Siberia	Whole Body	0.08		0.235		0.014			
<i>Silurus glanis</i>	Danube River	Whole Body	0.09		0.07		0.17	0.33		[68]
<i>Sander lucioperca</i>	Danube River	Whole Body	0.04		0.11		0.23	0.3		
<i>Tilapia mossambica</i>	Water bodies of Aurangabad, India	Gill		3.66–4.58	0.32–0.46					[69]
		Skin		1.80–2.74	0.19–0.26					
		Liver		1.56–2.16	0.29–0.36					
		Muscle		2.98–4.23	0.26–0.32					
<i>Oreochromis niloticus</i>	Lakes of Coimbatore, India	Muscle	1.26–1.59		8.49–9.69	18.38–25.94	5.91–9.69			[70]
		Gill	1.47–1.85		9.9–11.3	21.05–29.71	6.89–11.30			
		Liver	1.76–2.22		11.74–13.42	25.08–35.4	8.07–13.24			
<i>Lutjanus griseus</i>	Pearl Delta river China	Whole Body	0.03				0.03	0.39		[71]
<i>Lutjanus stellatus</i>	Pearl Delta river China	Whole Body	0.07				0.04	1.53		
<i>Thunnus albacares</i>	Egypt	Whole Body	0.06				0.32			[72]

Fish species	Source	Tissue	Concentration of metal (mg/kg)							Reference
			Cd	Cr	Cu	Zn	Pb	As	Hg	
<i>Oncorhynchus mykiss</i>	Hamadan Province, Iran	Whole Body	0.17–13.74				0.34–70.17			[73]
		Muscle	0.17–11.88				0.34–35.19			
		Liver	0.17–13.74				1.29–70.17			

Table 2.
The concentration of different potentially toxic metals in different parts of freshwater fish.

Fish species	Source	Tissue	Concentration of metal (mg/kg)						Reference
			Cd	Cr	Cu	Zn	Pb	As	
<i>Mullet</i>	Southeast Coast of Indian Ocean	Gills	0.013		0.092	0.087	0.043		[74]
		Gonad	0.001		0.192	0.284	0.302		
		Muscle	0.013		0.034	0.074	0.009		
		Skin	0.010		0.016	0.018	0.000		
		Whole Body	0.005		0.085	0.176	0.026		
<i>Crab</i>	Southeast Coast of Indian Ocean	Muscle	0.027		0.243	0.228	0.237		
		Gonad	0.060		0.330	0.244	0.150		
		Whole Body	0.004		0.061	0.259	0.013		
<i>Shrimp</i>	Southeast Coast of Indian Ocean	Skin	0.001		0.082	0.233	0.268		
		Whole Body	0.001		0.2	0.088	0.007		
<i>Euthynnus affinis</i>	Tok Bali Port, Malaysia	Whole Body	0.007		0.70	62.4	0.3		[57]
<i>Pampus argenteus</i>	Tok Bali Port, Malaysia	Whole Body	0.004		0.038	4.83	0.024		
<i>Decapterus macrosoma</i>	Tok Bali Port, Malaysia	Whole Body	0.003		0.064	5.29	0.001		
<i>Leiognathus daura</i>	Tok Bali Port, Malaysia	Whole Body	0.004		0.018	5.45	0.003		
<i>Fenneropenaeus indicus</i>	Tok Bali Port, Malaysia	Whole Body	0.04		0.34	14.4	0.008		
<i>Lates calcarifer</i>	Red Sea, Jeddah Coast, Saudi Arabia	Whole Body	0.007		0.49	6.5	0.20		[75]
<i>Johnius belangerii</i>		Whole Body			1.35	23.33	1.45		[76]
<i>Chirocentrus dorab</i>		Whole Body			1.45	22.91	1.0		
<i>Arius maculatus</i>		Whole Body			1.15	25.95	0.85		
<i>Parastromateus niger</i>		Whole Body			2.55	22.29	1.0		
<i>Oyster</i>	Gulf of Chabahar	Soft tissue	0.08–0.45	12.7–38.0	59.2–133.5	87–191	2.36–17.5		[77]

Fish species	Source	Tissue	Concentration of metal (mg/kg)						Reference
			Cd	Cr	Cu	Zn	Pb	As	
<i>Liocarcinus depurator</i>	Samsun coasts of the Black Sea Turkey	Soft tissue	0.07		7.7	19	0.48		[78]
<i>Rapana venosa</i>		Soft tissue	0.085		4.3	9	0.12		
<i>Mytilus galloprovincialis</i>		Soft tissue	0.08		9.2	14	0.50		
<i>Otolithes ruber</i>	Persian Gulf, Iran	Soft tissue	0.21–0.47				1.98–2.98		[79]
<i>Lutjanus johnii</i>	Persian Gulf, Iran	Soft tissue	0.17–0.38				2.53–3.12		
<i>Lagocephalus sceleratus</i>	North-eastern Mediterranean part of Turkey	Muscle	0.045–0.139	0.20–0.36	0.276–0.518	51.4–86.63	1.46–2.56		[80]
		Skin	0.113–0.217	0.10–0.15	0.168–0.209	3.34–6.45	0.34–0.58		
<i>Hirundichthys coromandelensis</i>	Southeast coast of India	Soft tissue	0.02		0.26–0.28	3–3.28	0.20–0.24		[81]
<i>Cypselurus spilopterus</i>	Southeast coast of India	Soft tissue	0.02		0.26–0.33	2.15–3.30	0.17–0.19		
<i>Sardina</i>	Algerian coasts, Algeria	Soft tissue	0.55			2.13	0.62		[82]
<i>Xiphias gladius</i>	Algerian coast, Algeria	Soft tissue	0.57			3.90	0.56		
<i>Brachydeuterus auritus</i>	Fishing Habour Ghana,	Muscle			0.42	2.28		0.2 0.31	[11]
<i>Pennahia anea</i>	Coastal Waters, Malaysia	Muscle	0.03–0.21		0.94–4.38	17.7–26.3	0.14–0.41		[83]
		Liver	0.44–0.69		6.7–19.8	7–114.4	0.96–1.26		
		Gill	0.02–0.21		1.08–6.52	48.2–115.7	0.45–1.96		
<i>Arius maculatus</i>		Muscle	0.04–0.09		0.83–3.68	23–48.6	0.15–0.36		
		Liver	0.23–0.98		17.94–55	356–558	0.1–1.16		
		Gill	0.02–0.19		1.65–6.95	282–528	0.24–0.5		
<i>Decapterus maraudsi</i>	Terengganu Coastal Area, Malaysia	Soft tissue	0.2		0.64	7.97	0.17		[84]
<i>Megalaspis cordyla</i>	Terengganu Coastal Area, Malaysia	Soft tissue	0.31		1.16	10.42	0.02		
<i>Bramidae</i>	Terengganu Coastal Area, Malaysia	Soft tissue	1.53		0.98	15.14	0.09		

Fish species	Source	Tissue	Concentration of metal (mg/kg)						Reference
			Cd	Cr	Cu	Zn	Pb	As	Hg
<i>Selaroides leptolepis</i>	Terengganu Coastal Area, Malaysia	Soft tissue	0.66		0.68	11.28	0.14		
<i>Epinephelus lanceolatus</i>	Terengganu Coastal Area, Malaysia	Soft tissue	0.64		0.83	12.51	0.11		
<i>Rastrellige</i>	Terengganu Coastal Area, Malaysia	Soft tissue	0.25		0.5	9.39	0.73		
<i>Nibea soldado</i>	Terengganu Coastal Area, Malaysia	Soft tissue	0.12		0.29	5.91	ND		
<i>Pristipomoides filamentosus</i>	Terengganu Coastal Area, Malaysia	Soft tissue	0.08		0.25	4.88	ND		
<i>Priacanthus tayenus</i>	Terengganu Coastal Area, Malaysia	Soft tissue	0.08		0.42	6.63	0.13		
<i>Siganus canaliculatus</i>	Terengganu Coastal Area, Malaysia	Soft tissue	0.10		0.68	11.60	0.15		
<i>Thunnus obesus</i>	Western and Central pacific ocean	Soft tissue							0.929
<i>Trichiurus lepturus</i>	Coastal Waters of Ondo State, Nigeria	Muscle	0.0	0.0	0.0	0.34	0.09		[85]
		Head	0.21	0.32	0.0	0.38	0.20		
		Eye	0.37	0.35	0.0	0.38	0.20		
		Gill	0.48	0.49	0.87	0.51	0.15		
		Bone	0.32	0.35	0.59	0.10	0.12		
<i>Pentanmius guigarius</i>		Muscle	0.0	0.0	0.58	0.35	0.1		
		Head	0.26	0.37	0.0	0.36	0.34		
		Eye	0.49	0.62	0.0	0.65	0.14		
		Gill	1.14	1.28	1.88	1.29	0.40		
		Bone	0.32	0.38	0.59	0.39	0.11		
<i>Pseudolithus senegalensis</i>		Muscle	0.0	0.0	0.46	0.36	0.10		
		Head	0.27	0.26	0.38	0.38	0.71		
		Eye	0.29	0.32	0.39	0.39	0.04		

Fish species	Source	Tissue	Concentration of metal (mg/kg)						Reference
			Cd	Cr	Cu	Zn	Pb	As Hg	
<i>Pseudotolithus typus</i>		Gill	0.81	0.86	0.94	0.94	0.27		
		Bone	0.31	0.38	0.39	0.39	0.12		
		Muscle	0.31	0.36	0.0	0.36	0.07		
		Head	0.28	0.23	0.0	0.38	0.16		
		Eye	0.30	0.37	0.0	0.39	0.01		
		Gill	0.32	0.37	0.62	0.42	0.12		
		Bone	0.32	0.37	0.59	0.38	0.11		
<i>Cyprinus carpio L,</i>	Ala gul wetland (Iran)	Muscle	0.0–0.140		1.23–39.4	1.15–47.7	0–21.86		[86]
<i>Cyprinus carpio L,</i>	Alma gul wetland (Iran)		0.0–0.02		1.23–4.4	19.15–117.4	2.1–8.7		

Table 3.
The concentration of different potentially toxic metals in different tissues of marine organisms.

7. Potentially toxic metals-resistance

The potentially toxic metals (Cd, Cu, Pb, Zn, Cr (III), Cr (VI), and Hg) aren't only toxic to human health but also enrich antibiotic resistant microbes particularly bacteria. Co-selection of an antibiotic and metal resistance in bacteria is extremely important because it promotes antibiotic resistance in bacteria even in the absence of antibiotics. Co-selection occurs by two mechanisms:

- i. Co-resistance: when antibiotics and these metals co-exist within the same environment, these metals influence some antibiotic resistant bacteria to survive in more polluted environment. Co-resistance occurs when two or more different resistant genes are present on the same genetic elements (plasmid, transposon, Integron) or are present within the same bacterial strain which provides resistant to different compounds. The rise of antibiotic resistant genes is directly correlated with the concentration of those metals [87].
- ii. Cross-resistance: cross resistance occurs when antibiotics and potentially toxic metals target the same microbes leading to generic detoxification of genes by reducing intracellular concentration of antibiotics and metals, and enhanced efflux occurs during cross-resistance [87].

Besides these two mechanisms, co-selection is additionally promoted by co-regulatory mechanism which occurs when different resistant genes is controlled by one regulator gene [88]. The impact of the potentially toxic metals on the antibiotic resistant bacterial strain is a given in **Table 4**.

8. Toxicity of potentially toxic metals

World Health Organization has reported that globally in the year 2015 approximately 8.8 million deaths were due to cancer, presence of potentially toxic metals beyond permissible limits within the environment is one among the main factors of the death because the endocrine system is disrupted by these metals. When the food or drinking water containing potentially toxic metals beyond their maximum tolerance concentration is ingested, the metabolism of living cells in the body is negatively affected [122]. The immune and hematopoietic systems in human and animals also are adversely affected on exposure to the mixtures of those metals [122]. Li et al. [123] reported that the main cause for human bone diseases is the presence of the potentially toxic metals beyond their permissible limit within the aquatic environment. Potentially toxic metals Pb, Hg, Cd, As, and Cr in living cells causes cytotoxicity [124] and oxidative stress [124], leading to the damages of antioxidants, enzyme inhibition, apoptosis (programmed cell death), loss of DNA repair mechanism, protein dysfunction, and damage to lipid peroxidase and of the membrane.

8.1 Cadmium

Cadmium in human causes Itai-Itai disease, liver/kidney lesions, hepato-colic effects [125], carcinoma, prostatic adenocarcinoma, osteoporosis, hypertension, disorder, and kidney lesions including enlargement, nuclear, and mitochondrial damages, and histological changes; decreased antioxidant power of kidney also

Toxic metal	Mechanism of action	Mechanism of resistance	Antibiotic categories / generic names	Pathogen(s)
Cu	Produces superoxide radicals by interaction with cell membrane. Enzymatic activities are inhibited and cellular functions are disrupted.	Resistant genes are located on plasmids and transposons and transfers in between bacterial species.	Tetracycline	<i>Klebsiella</i> spp. [89, 90]; <i>Fecal Enterococci</i> [91]; <i>E. coli</i> [92]; <i>E. faecium</i> [93]
			Carbapenem	<i>Pseudomonas aeruginosa</i> [94]
			Vancomycin, Amphenicol	<i>Enterococcus faecium</i> [93, 95]
			Chloramphenicol	<i>Bacillus</i> spp. isolated from ship [96]
			Erythromycin	soil bacteria of Scotland [90]; <i>Enterococcus faecium</i> [95]
			Fluoroquinolone	<i>E. coli</i> [92]; <i>E. faecium</i> [93]
			Quinolone; Sulphonamide	<i>E. coli</i> [92]
			Cephalosporin	<i>Fecal Enterococci</i> [91]
			Penicillin; Cephalosporin; Nitrofurantoin	<i>Enterobacter</i> spp.; <i>P. aeruginosa</i> [97]
Hg	Hg inactivates the enzymatic activities, interferes in the protein synthesis and DNA function, and disrupts cell membrane. Destroys the biological membranes as the mercuric ions are lipid soluble so easily passed through biological membranes.	Hg resistant genes are located on plasmids and transposons. The resistance mechanism involves the reduction of Hg ²⁺ ions to Hg in the cytoplasm of the bacteria by the enzyme mercuric reductase which is encoded with the merA gene.	Macrolide	<i>E. faecium</i> [98]
			Sulphonamide, Chloramphenicol, Ampicillin, Streptomycin, Augmentin	<i>Salmonella enterica</i> [99]; Fecal Gram-negative bacteria [100]
			Fluoroquinolone, Quinolone	<i>E. coli</i> , <i>Citrobacter</i> spp., <i>Klebsiella</i> spp. [101]
			Penicillin	<i>Salmonella</i> spp. [102]; <i>Serratia</i> spp. [103]
			Tetracycline	<i>E. coli</i> ; <i>Citrobacter</i> spp.; <i>Klebsiella</i> spp. [104]; <i>E. faecium</i> [105]
			Teicoplanin	<i>Salmonella</i> spp. [102]
			Sulphonamide; Cephalosporin; Macrolide	<i>E. coli</i> ; <i>Citrobacter</i> spp.; <i>Enterobacter</i> spp.; <i>Klebsiella</i> spp.; <i>Proteus</i> spp. [106]
			Cephalosporin	<i>E. coli</i> [107]; <i>Citrobacter</i> spp.; <i>Enterobacter</i> spp.; <i>Klebsiella</i> spp.; <i>Proteus</i> spp. [106]

Toxic metal	Mechanism of action	Mechanism of resistance	Antibiotic categories / generic names	Pathogen(s)
Zn	Due to affinity of Zn to thiol group, the Zn metal is toxic to bacteria, retards glycolysis, transmembrane proton translocation and acid tolerance in the bacterial cell. Also decreases the biomass causing growth inhibition.	Resistance to Zn is found in Gram negative and gram positive bacteria and resistance is mainly via <i>czrC</i> gene	Aminoglycoside	<i>E. coli</i> ; <i>Citrobacter</i> spp.; <i>Enterobacter</i> spp.; <i>Klebsiella</i> spp.; <i>Salmonella</i> spp.; <i>P. aeruginosa</i> [108]
			Vancomycin	<i>E. faecium</i> [100]
			Norfloxacin, Augmentin, Gentamicin, Ampicillin	Bacteria isolated from the soil of Kenya [109]
			Carbapenem	<i>Pseudomonas aeruginosa</i> [94]
			Penicillin, Teicoplanin	<i>Salmonella</i> spp. [102]
			Fluoroquinolone, quinolone	<i>E. coli</i> ; <i>Citrobacter</i> spp. [101]
			Methicillin	<i>Staphylococcus aureus</i> [110]
Cr	Due to strong oxidizing potential the metal Cr damages the cells of the microbes, inhibits the oxygen uptake, growth and elongation of lag phase.	Cr in microbes affects basal energy metabolism, protein oxidative stress protection, DNA repair, detoxification of enzymes, efflux pumps, homeostasis	Tetracycline, Carbapenem	Soil bacteria of Scotland [90]
			Penicillin	<i>Enterobacter</i> spp. [97]
			Cephalosporin, Tetracycline	<i>P. aeruginosa</i> [97]
			Nitrofurantoin, Teicoplanin	<i>Salmonella</i> spp. [102]
			Quinolone, Vancomycin	<i>E. coli</i> [111]
			Sulfonamide	<i>Klebsiella</i> spp. [112]
Cd	Cd in bacteria denatures the protein, interacts with calcium metabolism, damages the cell membrane, hinders cell division and transcription, and also affects the nucleic acid.	Resistance to Cd in Gram negative bacteria affects <i>Czc</i> and <i>Ncc</i> genes and encoding <i>dsbA</i> gene needed for disulphite formation while in Gram positive bacteria resistance to Cd is with the <i>CdA</i> pump	Augmentin, Ampicillin	Bacteria isolated from the soil of Kenya [109]
			Ampicillin	Bacteria isolated from ship [96]
			Fluoroquinolone, Quinolone	<i>E. coli</i> ; <i>Citrobacter</i> spp.; <i>Klebsiella</i> spp. [101]
			Penicillin, Tetracycline	<i>P. aeruginosa</i> [113]
			Amphenicol, Cephalosporin, Methicillin, Sulfonamide, Aminoglycoside	<i>E. coli</i> ; <i>Citrobacter</i> spp.; <i>Klebsiella</i> spp. [112]
			Macrolide	<i>E. faecium</i> [98]

Toxic metal	Mechanism of action	Mechanism of resistance	Antibiotic categories / generic names	Pathogen(s)
Pb	Lead induces mutagenicity, inhibits enzyme activities and transcription. Pb in the bacteria destroys the nucleic acid.	Resistance mechanism is due to adsorption of lead by extracellular polysaccharides, cell exclusion and ion efflux to the cell exterior.	Aminoglycoside	<i>Citrobacter</i> spp. [104]
			Macrolide, Quinolone	<i>E. coli</i> [111]
			Penicillin	<i>Enterobacter</i> spp. [107]
			Teicoplanin	<i>E. faecium</i> [105]
			Quinolone	<i>Klebsiella</i> spp. [106]
			Sulphonamide	<i>Proteus</i> spp. [106]
			Vancomycin	<i>Enterobacter</i> spp.; <i>Klebsiella</i> spp. [106]
			Amphenicol	<i>Salmonella</i> Spp. [114]
			Fluoroquinolone	<i>P. aeruginosa</i> [115]
Ni	Ni replaces the essential metals from metalloprotein. The activity of the enzymes is retarded as Ni binds the catalytic site of the enzyme. Ni causes oxidative stress which results in the enhanced DNA damage, protein impairment, and lipid peroxidation.	The resistance mechanism is due to energy-dependent Ni efflux pump induced by <i>cnr</i> which is promoted by a chemo-osmotic proton-antiporter system.	Tetracycline	<i>Shigella</i> spp. [116]
			Quinolone	<i>E. coli</i> [111]
			Tetracycline	Soil bacteria of Scotland [90]
			Penicillin	<i>Salmonella</i> spp. [102]
			Amphenicol	<i>E. faecium</i> [105]
As	Disrupts enzymatic functions in the cell and interferes in the phosphate uptake and utilization.	Activation of efflux pumps due to cross resistance between arsenic and antibiotics is the main mechanism	Sulfonamide	<i>Citrobacter</i> spp. [112]
			Penicillin	<i>E. coli</i> [107]
			Sulfonamide	<i>Salmonella</i> spp. [117]
			Tetracycline	<i>E. coli</i> [118]
Co	Produces non B ₁₂ cobalt protein.	The gene <i>Czc</i> , affects the inner and outer membranes and removes the cobalt from the cytoplasm	Amphenicol	<i>Salmonella</i> spp. [119]
			Aminoglycoside	<i>Citrobacter</i> spp. [106]
			Macrolide	<i>Enterobacter</i> spp. [120]
			Penicillin	<i>Salmonella</i> spp. [102]
			Quinolone	<i>E. coli</i> [111]
			Sulfamethoxazole	<i>P. aeruginosa</i> [121]
			Vancomycin	<i>Enterobacter</i> spp.; <i>Klebsiella</i> spp. [106]

Table 4.
Impact of potentially toxic metals on some bacterial strain resistant to antibiotics.

disrupts mineral balance within the body, causing dysfunctions of sexual glands and skeletal diseases. A psychomotor function of the brain is bogged down in the presence of Cd. The toxicity of cadmium to cell is because Cd can displace vitamin C and E from their metabolically active sites, decrease in absorption of calcium by intestine and enhanced dissolution of bone calcium causing disorder in the normal bone metabolism processes. Cd an endocrine disrupter causes neuro-developmental toxicity. Toxicity of Cd in fishes includes immune suppression and immune dysfunction.

8.2 Lead

Out of about four million tons of lead used per annum globally about three million tons is discharged within the environment. In the physical body, 90–95% of the intruding lead is accumulated within the bones which combine with bone minerals and organic matter causes rise in the blood lead level. Accumulation of lead within the bones affects the acid-base equilibrium causing calcium deficiency. Pb within the body lowers the active vitamin D₃ level and parathyroid level within the plasma affecting somatic cell function viz., decrease in the secretion of γ -carboxyglutamic acid containing protein. Clinical studies have shown that if the extent of Pb in the drinking water is 50 $\mu\text{g/L}$, the blood lead level within the human is going to be about 30 $\mu\text{g/L}$; if the extent increased further, the lead level within the breast fed babies are enhanced causing hindrance within the bone development. If the blood lead level in children exceeds 75 $\mu\text{g/L}$, it causes coma, convulsions, and eventually death. Pb also affects central systema nervosum, renal, cardiovascular, neurological, and musculoskeletal systems. Pb influences the heme synthesizing enzymes by replacing Zn within the heme synthesis. Lead disrupts biosynthesis of hemoglobin, metabolism of Fe, Zn, and Cu, and of vitamin D within the body, and also causes cognitive impairment. Pb in physical body also acts as nephrotoxicants. Lead in fish's body also affects immune system [122]. Long-term exposure to the low concentration of a mix of Cd, As, and Pb in human and other animal cause hepatotoxic (damage to the liver) effects [123].

8.3 Chromium

The annual output of Cr globally is approximately 7.5 million tons. The secretion of Collagen-Type I which helps in the bone fracture healing is suppressed in the presence of chromium ion. Chromium in human causes nose ulcers, asthma, DNA damage, hemolysis, damage to liver, kidney, and carcinoma.

8.4 Arsenic

Smith et al. [126] after their research studies reported that if the person get 50 $\mu\text{g/L}$ of arsenic (daily) then 13 out of 1000 individuals will suffer with lung, liver, kidney or bladder cancer. Skin lesions are by the uptake of 0.0012 mg/kg/day of arsenic. Bhattacharya et al. [125] found that low concentration of arsenic for long period damages liver in human and other animals. Enlargement of kidney, nuclear, and mitochondrial damages, histological changes, and decreased antioxidant power of kidney is additionally caused by arsenic in human. Arsenic also causes neurotoxic effects in human with the assembly of the reactive oxygen species which incorporates death of neuronal cells, cognitive dysfunction, and Alzheimer's disease. Cognitive impairment, deafness, hypertension, anemia dementia, hematemeses, and

bladder cancer also is caused by As. The prolonged exposure to arsenic also affects central systema nervosum.

8.5 Mercury

Mercury is the third top hazardous substance. Aquatic organisms convert inorganic mercury to methyl mercury which inactivates Na^+/K^+ ATPase. Hg with the production of reactive oxygen causes neurotoxic effects in human including death of neuronal cells, cognitive dysfunction, and Alzheimer's disease. As Hg is an endocrine disrupter, during pregnancy exposure to metal causes long-term damages to new born as mercury disrupts the influences the maternal-fetal balance. Minamata disease, renal toxicity, skin, nose irritation, damage to central systema nervosum, hearing speech, and visual disorders are another health risks to human.

8.6 Copper

Copper an integral part of several enzymes in small amount (0.9 mg daily uptake) is an essential metal for animals and plants. Deficiency of copper in human causes anemia, a low number of leucocytes, defects in animal tissue, and osteoporosis in infants. The copper within the body beyond its permissible limit causes hematemesis, jaundice, melena, damage to central nervous system, liver, and kidney problems. Wilson's disease a genetic disease is additionally caused by copper.

8.7 Nickel

Nickel, a natural occurring metal, exists in a number of mineral forms and is an ingredient of chocolate, steel, and other metal products, pigments, valves and of batteries. Excess uptake of nickel by human causes asthma, pneumonia, allergies, heart disorder, skin rashes, and miscarriage. Chances of development of carcinoma, nose cancer, larynx cancer, and prostatic adenocarcinoma also are enhanced.

8.8 Cobalt

Cobalt is an essential metal for the life as it is the integral part of vitamin B_{12} (cobalamin). Human when exposed to the higher concentration of cobalt causes decreased pulmonary function, asthma, interstitial lung disease, wheezing, and dyspnoea and reduces pulmonary function. Respiratory tract hyperplasia, pulmonary fibrosis, increase in number of red blood cells, emphysema, paralysis of the systema nervosum, seizures, growth retardation, and thyroid deficiency are diseases occurs in human at a really high concentration of the metal.

8.9 Zinc

As zinc plays a crucial role in number of metallo enzymes viz., dehydrogenase, alkaline phosphatase, carbonic anhydrase, leucine amino peptidase, superoxide dismutase, and deoxyribosenucleic acid (DNA) and ribosenucleic acid (RNA) polymerase is an essential metal in humans and animals. Over exposures to zinc in human causes dry or pharyngitis, chest tightness, headache, increased indices of pulmonary inflammation, nausea, decrease in the activity of copper metallo enzyme, decreased HDL-cholesterol level, immuno toxicity, and gastrointestinal effects.

9. Conclusions

- Contamination of ground and surface water by potentially toxic metals is a worldwide problem.
- The major route of the groundwater and aquatic contamination by potentially toxic metals are the leaching from toxic industrial waste dumps, municipal landfills, and leaching of agricultural chemicals from soils into the upper aquifers.
- Potentially toxic metals contaminated vegetables and fruits; fishes, seafood, and drinking water are the most sources of the ingestion of those metals by the citizenry.
- A number of biological and biochemical processes are disrupted in the physical body by accumulation of those metals. These metals also cause developmental abnormalities in the children.
- These potentially toxic metals promote the spread of antibiotic resistant genes which causes the ineffectiveness of broad- spectrum antibiotics.

Declaration


No original data is utilized in this review; all information is accessed from published work.

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