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Risk Assessment of Heavy Metals in Fish in Saudi Arabia

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Abstract: Heavy metals such as arsenic, cadmium, mercury and lead constitute a serious threat to human health. Generally, regular consumption of fish is recommended because it is a good source of omega-3 fatty acids, which have been associated with health benefits. However, flesh of some fish species contains heavy metals in high concentration, which may pose health risk for individuals that consume them in significant quantities. Therefore, over the last few years, evaluation of heavy metals in fish has become a matter of great global concern and especially in Kingdom of Saudi Arabia.The aim of the present work was toassess the concentration of the most toxic heavy metals present in fish caught along the eastern and western coasts of Saudi Arabia, which was achieved through several studies. Results yielded by analyzing 73 fish species and 1,027 edible fish part samples from 12 sampling sitesrevealed considerable variation in metal concentrations across the sampling locations and fish species. Amounts of some of heavy metals were below the maximum allowed limit. Moreover, high hazard index (HI > 10) was obtained for the consumption of some fish species caught at specific sites, which indicates a high probability of consuming populations experiencing adverse health effects.

Keywords: Health Risk Assessment, Fish, Contamination, Heavy Metals, Red Sea, Arabian Gulf

Introduction

Fish seems to be the perfect healthy food, since many species are rich in the polyunsaturated fatty acid Omega-3, which is widely acclaimed as beneficial the human health and optimal heart functioning. However, eating too much fish can cause a buildup of heavy metals, such as arsenic (*As*), cadmium (*Cd*), lead (*Pb*), mercury (*Hg*), chromium (*Cr*) and nickel (*Ni*). In fact, heavy metals accumulate in different vital parts of smaller fish, including heart, liver and tissues, by different natural or accidental causes (Paulino *et al*., 2014; Jayaprakash *et al*., 2015; Dural *et al*., 2006; Fernandes *et al*., 2007). As the contaminated small fish species are food source for bigger fish, which are eaten by even bigger fish and so on, this results in bio-accumulation (Malik *et al*., 2010; Al-Kahtani, 2009). Consequently, these heavy metal elements bio-accumulate at high doses in bigger species, like shark or swordfish (*Xiphias gladius (Linnaeus, 1758)*). Commonly consumed fish, e.g., grouper and emperor fish, can contain significant concentrations of these toxic elements as well. For most people this is not

a problem, as the benefits derived from fish consumption far outweigh any adverse effects. However, consumption of contaminated fish during pregnancy could harm vital organs and processes in a developing fetus. Exposure to heavy metals might be linked to Attention Deficit Hyperactivity Disorder (ADHD) issues in young population, i.e., infants and children, according to one study published in the Journal Archives of Pediatrics and Adolescent Medicine (Stratakis *et al*., 2016). To avoid these adverse effects, the Food and Drug Administration (FDA) suggested that pregnant and breastfeeding women limit consumption of fish species that contain the highest levels of mercury, such as swordfish (*Xiphias gladius)*, shark, tilefish (*Lopholatilus chamaeleonticeps*) and kingfish (*Scomberomorus cavalla*) (Burger, 2009; Lando and Lo, 2014). *FDA* further recommends eating Albacore tuna *(Thunnus alalunga)*no more than twice a week. This prompts the question: "*Where do all these heavy metals come from?*" Heavy metals are natural elements found throughout the environment. Some scientists are of view that they form naturally in the Earth's core and emerge to the surface through

hydrothermal vents (Minic *et al.*, 2006) or volcanic eruptions (Calabrese *et al.*, 2015). While this is likely the case, human activity results insubstantial quantities of heavy metal waste from power plants and manufacturing industries, such as mining activities, oil refinery or urban wastewater treatment plants. While some safeguards are in place, some facilities discharge their waste into the environment resources (sea, soils, river, etc.) without adequate preprocessing. Once these toxins reach seas and oceans, they enter fish metabolism and build up in their tissues. Fish body mechanism turn the most known toxic element mercury into a high toxic form, *methylmercury*. According to the United States Environmental Protection Agency (US *EPA*) (USEPA, 2005), "*Nearly all fish and shellfish contain traces of methylmercury*" (Mahaffey *et al.*, 1999). Other underwater ecosystems like coral are also affected, confirming that heavy metals pose a serious environmental threat. In fact, Kingdom of Saudi Arabia has a unique geographical location characterized by 2,640 km of coastline belt along the Red Sea in the west and the Arabian Gulf in the east. According to *FAO* Fisheries and Aquaculture Department statistics, the Kingdom produced about 23,880 tons of marine products in 2014 (FAO, 2016). Thus, the country is an important source of a wide range of fish suitable for commercial exploitation and local population consumption. Recent studies on Saudi population consumption patterns (Burger *et al.*, 2015; Selvanathan *et al.*, 2015; Burger *et al.*, 2014a) show that marine products, fish in particular, are widely consumed. Hence, to avoid the adverse health effects associated with heavy metal contamination, the *GCC* Standardization Organization (*GSO*) (GSO-GCC, 2016) has established technical standards and regulations for maximum levels of contaminants and food toxins (Dreyer *et al.*, 2007; Al-Rubaie *et al.*, 2014). To evaluate the health risk the Saudi people are exposed to through consumption of marine products, many researchers working in academic institutions throughout the Kingdom have attempted to assess heavy metal levels in fish (Al-Misned and Mortuza, 2015; Idris *et al.*, 2015; Kamal *et al.*, 2015; Burger *et al.*, 2014b; Mahboob *et al.*, 2014; Said *et al.*, 2014). Different fish species and sampling locations were studied (Al-Misned and Mortuza, 2015; Idris *et al.*, 2015; Kamal *et al.*, 2015; Burger *et al.*, 2014b; Mahboob *et al.*, 2014; Said *et al.*, 2014). Burger *et al.* (2014b) examined traces of heavy metals in 13 different fish species collected from three fishing sites and a local fish market in Jeddah, Saudi Arabia. Their findings revealed high levels of arsenic in *Epinephelus tauvina*, as well as *Aphareus rutilans*, *Carangoides bajad* (C. bajad) and *Plectropomus areolatus*. Mercury and methylmercury traces were also

detected in high levels in the Jeddah coastal area in four fish species (*Cephalopholis argus*, *C. bajad*, *Variola louti* and *Lethrinus lentjan*). Thus, the authors concluded that mercury poses the greatest risk associated with fish consumption, while arsenic is also of concern (Burger *et al.*, 2014b). Many researchers have also performed comparisons with international permissible limits and have estimated health risks (Al-Misned and Mortuza, 2015; Idris *et al.*, 2015; Kamal *et al.*, 2015; Burger *et al.*, 2014; Mahboob *et al.*, 2014; Said *et al.*, 2014). However, to the best of our knowledge, formal risk assessments performed by using site-specific experimental data, along with site-specific information on consumption patterns using exposure scenarios is presently lacking. In addition, very few authors have attempted to evaluate the health risk related to heavy metals when found in trace amounts in fish consumed by Saudi population. In their work, Idris *et al.* (2015) calculated human risk indices as Average Daily Dose (*ADD*) and Hazard Index (HI) using the *US EPA* classical calculation method with a fixed Ingestion Ratio (*IR*) and an average body weight equal to 70 kg for normal adults. This approach does not take into account the real consumption patterns of Saudi people and, as it is age independent, it does not specifically address vulnerable population groups. In this study, these shortcomings are overcome by conducting a complete survey pertaining to all heavy metal elements (As, Cd, Pb, Hg, Cr, Ni and MeHg) currently recognized as potentially highly toxic,which are present in fish species commercially fished from the eastern and western Saudi coastal belt. All the reported data are discussed and subjected to the standard Risk Assessment (RA) approach, which comprises of four standard steps, i.e., (1) Hazard Identification; (2) Hazard Characterization; (3) Exposure Assessment and (4) Risk Characterization.

Survey on Heavy Metal Contamination of Fish

Since the effects of industrial human activities on the environment are becoming increasingly pronounced, national (*SASO*, *SFDA*), regional (*GSO*) and international governmental agencies and organizations (*WHO*, *USEPA*, *FAO*, *JECFA*) are dedicating substantial efforts to the protection of human health and environment. This is typically achieved by establishing strict policies and standards in order to limit and reduce the environmental contaminants in the human food chain. Four heavy metals-arsenic (As), cadmium (Cd), lead (Pb) and mercury (Hg)-are classified by *WHO* in the top 10 chemicals of "*major*

public health concern" (WHO, 2016). Table 1 presents the maximum permissible limits and Provisional Tolerable Weekly Intake (PTWI) of arsenic, cadmium, lead, mercury, methylmercury, chromium and nickel based on different international and national standards. These limits and specifications can vary depending on fish species and edible parts, as noted in Table 1.

In the present study, data pertaining to fish heavy metal contamination were collected from 10 peer-reviewed papers related to the Saudi Arabian case. Table 2 provides a summary of the findings reported in these scientific resources for the western (Red Sea fisheries) and eastern (Arabian Gulf fisheries) Saudi Arabian coastal belts.

Eastern and Western Saudi Arabian Coasts

Saudi Arabia is bordered by the Red Sea and the Arabian Gulf. The surface area of the Red Sea is about 438,000 km^2; it is 2,250 km long and measures 355 km at its widest point. Several industrial activities, such as desalination plants, chemical facilities, refineries, *etc.,* are located in the coastal areas of the Red Sea and the ArabianGulf. These industries are considered as the

most important threats for the quality of the environment in this region, Saudi Arabia in particular (Al-Balwai *et al.*, 2013). Therefore, there is an increasing concern about the quality of seafood and especially fish, caught in these waters. One of the major threats human health stems from heavy metals due to their ubiquitous presence as well as potential to enter aquatic organisms, resulting in bio-accumulation and bio-magnification in the food chain (Dhanakumar *et al.*, 2015). Many research studies have been conducted to assess the concentrations of heavy metals in several fish species (Al-Misned and Mortuza, 2015; Idris *et al.*, 2015; Kamal *et al.*, 2015; Burger *et al.*, 2014b; Mahboob *et al.*, 2014; Said *et al.*, 2014). As a part of our investigation, 11 publications were studied in detail. The first part of the literature review highlights the concentration of some heavy metals in fish species located in the Red Sea. As shown in Fig. 1, 37 fish species were collected from three different sites across the coastal area of the Red Sea. Nearly 733 fish samples were analyzed in order to assess concentrations of arsenic, cadmium, lead, mercury, nickel and methylmercury. Table 3 shows the three fish sampling sites and their corresponding geographic locations.

Table 1. Permissible maximum limit and Provisional Tolerable Weekly (PTWI) intake for the most toxic heavy metals (As, Cd, Pb, Hg, MeHg, Cr, Ni) as reported by different standards

| Heavy metal | Guidelines and specifications | |
	Maximum limit (ppm ww*)	PTWI (ppb bw*)
As	1[3, 4, 5]	15[2, 3]
	3[2]	
Cd	0.05[1, 2]	6.7-7[2, 3]
	0.5[4]	
Pb	0.2[2]	25[2, 3]
	0.3[3]	
	0.5[1]	
	2[4]	
Hg	0.5[1, 2]	5[3]
	1[3]	
MeHg	0.5[3]	
	(Small predators and non-predators)	1.6[3]
	1[3]	
	(Large predators)	
Cr	N.D	N.D
Ni	30[7]	
	55[6]	N.D

[1]EC (Regulations No 1881/2006 and No 629/2008); [2]JECFA (FAO/WHO Joint Expert Committee on Food Additives); [3]GSO (Gulf Standard 2013); [4]SASO 1997; [5]SFDA; [6]FAO 2000; [7]WHO 2000; *ppm ww: Part per million wet weight; *ppb ww: Part per billion wet weight

Table 2. Published data for heavy metal contamination of fish in the western (Red Sea) and eastern (Arabian Gulf) Saudi Arabian coastal belts

| Saudi Coast | Number of peer-reviewed papers | Number of sampling locations | Number of species | Number of samples | Rate of heavy metal analysis reported [%] | | | | | | |
					As	Cd	Pb	Hg	Cr	Ni	MeHg
Western	3	3	37	733	66	66	66	66	33	33	33
Eastern	7	9	36	294	42	100	100	28	0	57	0

Table 3. Fish sampling sites on the western coast of KSA with the corresponding geographic locations (Longitude/Latitude)

Site number	Site name	Geographic location	References
1	Djeddah, KSA	21°22'26.7" N 39°11'29.6" E	Burger *et al.* (2014b)
2	Ras-Gharib to Ras Bonas	28°21'09.7" N 33°04'47.4" E 23°54'95.4" N 35°27'58.1" E	Hanna (1989)
3	Red Sea (not specified)	N.D.	Al-Ghanim *et al.* (2015)

Table 4. Fish sampling sites along the eastern coast of KSA with the corresponding geographic locations (Longitude/Latitude)

Site number	Site name	Geographic location	References
1	Al-Dammam, Saudi Arabia	26°29'39.9"N 50°13'00.7"E	Al-Saleh and Shinwari (2002)
2	Maniefa, Saudi Arabia	27°38'18.5"N 49°03'08.3"E	Al-Saleh and Shinwari (2002)
3	Dareen, Saudi Arabia	27°17'04.0"N 49°37'36.2"E	Al-Saleh and Shinwari (2002)
4	Coastal Areas of Bahrain, Saudi Arabia	26°12'28.4"N 50°26'44.6"E	Madany *et al.* (1996)
5	Qateef, Eastern province of Saudi Arabia	26°35'25.9"N 50°01'47.3"E	Ashraf (2005)
6	Bandar Abbas, Iran	27°10'12.1"N 56°16'57.6"E	Saei-Dehkordi and Fallah (2011)
7	The northern part of Persian Gulf	N.D	Pourang *et al.* (2005)
8	Khuzestan Province, Iran	30°25'27.9"N 49°03'58.7"E	Hosseini *et al.* (2015)
9	The Kharg island, Bushehr province	29°16'10.1"N 50°16'56.5"E	Abadi *et al.* (2015)

Fig. 1. Fish sampling sites for the assessment of heavy metal in fish along the western coast of Saudi Arabia
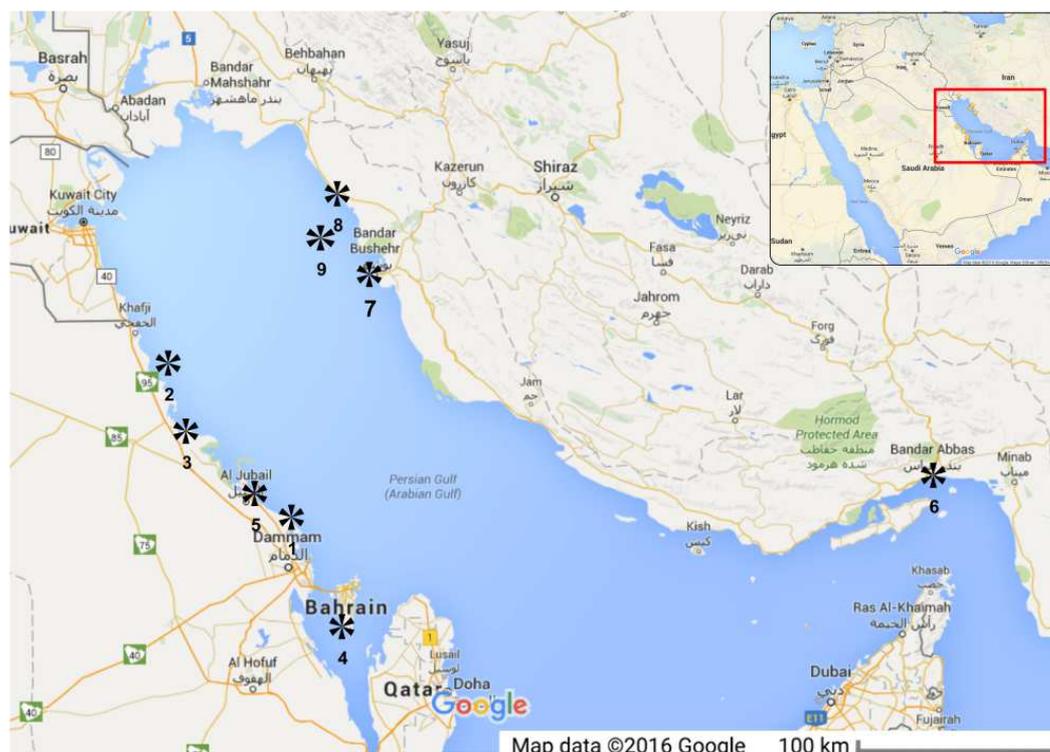
Fig. 2. Fish sampling sites for the assessment of heavy metal in fish along the eastern coast of Saudi Arabia

In the eight peer-reviewed publications included in this review that focused on the eastern Saudi Arabian coast, 36 fish species were collected from 9 different fish sampling sites, as shown in Fig. 2. Table 4 summarizes these sites with their geographic coordinates. It is evident that these sampling sites are well distributed across the Arabian Gulf, thus providing a complete survey on heavy metal concentration in fish.

In order to determine arsenic, cadmium, lead, mercury and nickel concentrations, 413 fish simples were analyzed using different experimental methods, including Polarized Zeeman Atomic Absorption Spectrophotometry (PZ-AAS) (Al-Saleh and Shinwari, 2002), potentiometric stripping analysis (Saei-Dehkordi and Fallah, 2011), or Inductively Coupled Plasma Mass Spectrometry (*ICP-MS*) (Pourang *et al*., 2005).

*Heavy Metal Concentrations*

Arsenic Concentration

Much of the arsenic in fish is present in the form of organic compounds, such as arsenocholine $(C_5H_{14}AsO^+)$, tetramethylarsonium and arsenobetaine $(C_5H_{11}AsO_2)$ ions, rather than as inorganic arsenic. In the present study, published data on the concentrations of total arsenic are reported. The quantitative data on arsenic concentrations and speciation in fish are limited, with organic rather than inorganic forms usually reported. The available data on arsenic in fish are presented in Fig. 3 for 23 different fish species and five sampling sites. All data are reported in terms of wet mass. As shown in Fig. 1, concentrations in fish were presented in $\mu g\ g^{-1}$ (wet weight) and ranged from 0.0674 $\mu g\ g^{-1}$ in *Dammam* to 5.54 $\mu g\ g^{-1}$ in the coastal area of *Bahrain*. In the reported data, arsenic levels varied depending on the fish species and sampling locations. The highest arsenic levels were observed in the coastal area of *Bahrain* in the Southwest (SW) and the *Kharg* Island in the South East (SE) of the Arabian Gulf. At the *Kharg* island sampling site, in 12 fish species, arsenic levels exceeded the maximum tolerable limit of 1 ppm recommended by *GSO*, *SASO* and *SFDA*. On the other hand, only three fish species (*Cuttle fish, Snapper* and *Otolithes Ruber*) at the *Kharg* island sampling site contained arsenic in the amounts above the maximum tolerable limit of 3 ppm recommended by the FAO/WHO Joint Expert Committee on Food Additives.

Figure 3b shows heavy metal levels at three sampling sites along the Red Sea coastal area. We noted low variation in the As concentration values, as the mean levels of As ranged between 0.18 and 10.04 $\mu g\ g^{-1}$ of wet fish weight. The highest mean arsenicconcentration was recorded for *Epinephelus tauvina* at the Djeddah site.
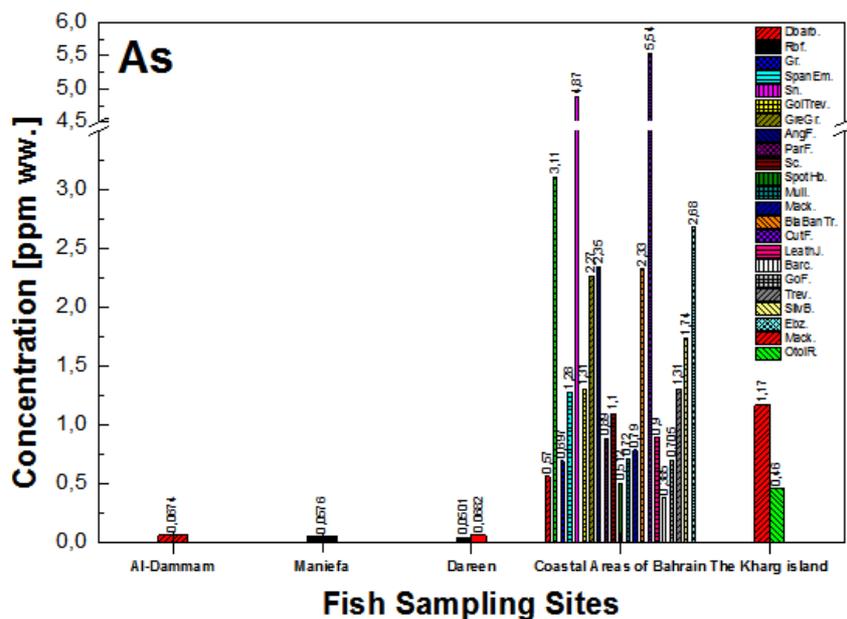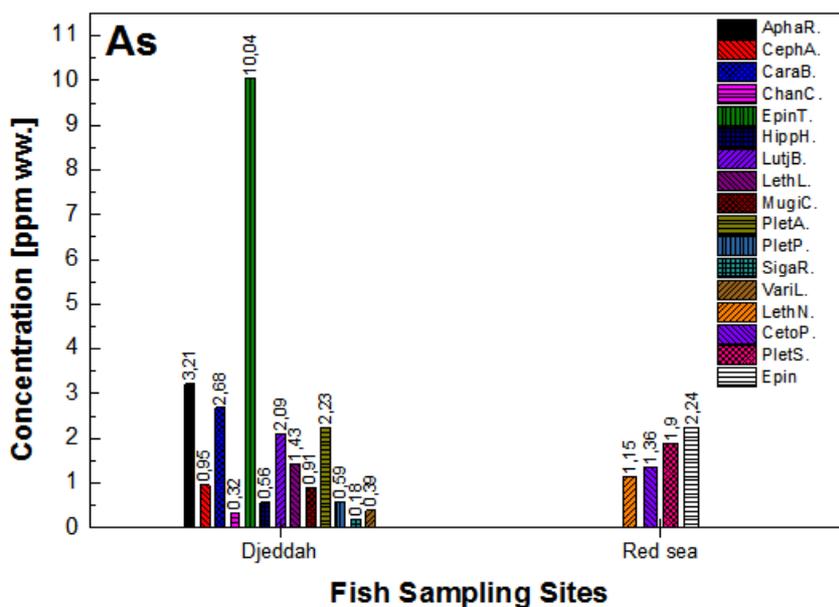
Fig. 3. Arsenic levels in fish based on literature-reported values for (a) eastern coast of KSA and (b) western coast of KSA. All data are presented in ppm for wet weight (ww)

Cadmium Concentration

Cadmium is an environmental pollutant and a highly toxic metal that could pose serious threat to the human internal organs (Järup and Åkesson, 2009). It remains in the human body for decades as it cannot be efficiently removed or metabolized. As a result, it may contribute to a variety of illnesses, including heart disease, cancer and diabetes (Järup and Åkesson, 2009). Findings yielded by recent studies (Larsson *et al*., 2015; Tilley and Fry, 2015; Das *et al*., 2014) suggest that cadmium exposure may produce adverse health effects at lower exposure levels than previously predicted, including increased risk of hormonal cancers. For example, researchers on Long Island (Gallagher *et al*., 2010) estimated that about 40% of breast cancer cases recorded in the U.S. might be associated with elevated cadmium levels. Fish consumption is a dominant route of human exposure.
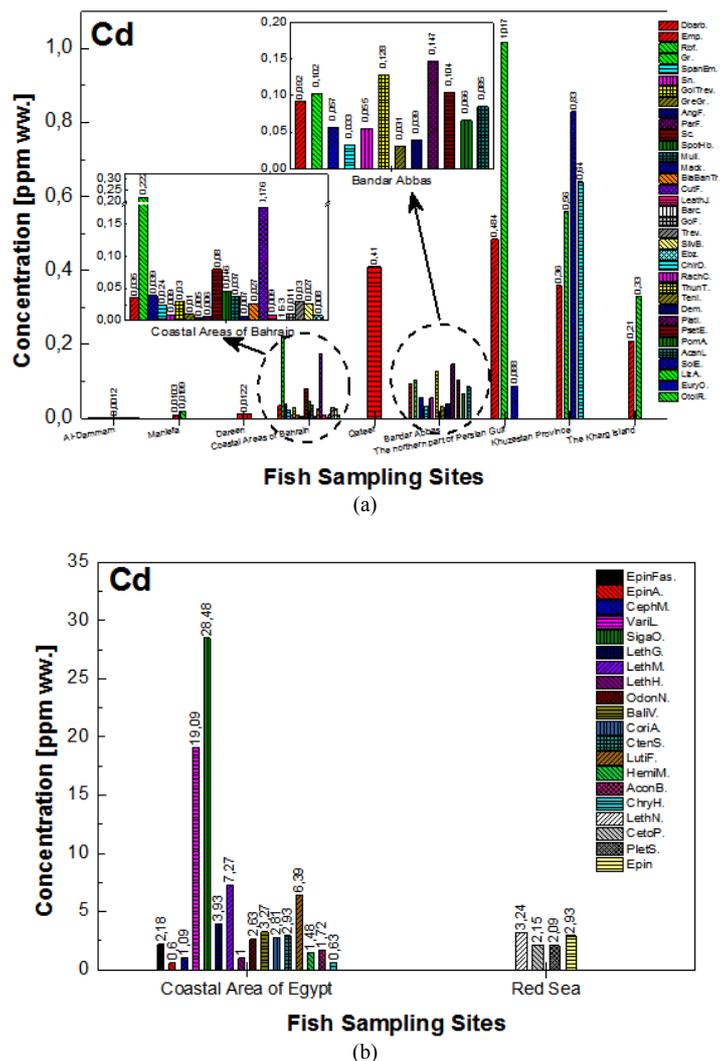
(a)

(b)

Fig. 4. Literature-reported cadmium (Cd) levels in (a) eastern coast of KSA and (b) western coast of KSA. The inset plots pertain to the data collected from the coastal area of Bahrain and Bandar Abbas sites. All data are presented in ppm for wet fish weight (ww)

Based on the reported data for the Arabian Gulf, average cadmium levels in 35 fish species from nine sampling sites were calculated, as shown in Fig. 4. The highest cadmium levels are observed in the northern part of the Arabian Gulf for Greasy-grouper with 1.017 ppm. According to the *SASO*, the maximum tolerable limit for cadmium content in fresh fish is 0.5 ppm. In comparison with this standard, at two sampling sites-northern part of the Persian Gulf and Khuzestan province, which are located in the Northeast (NE) of the Arabian Gulf-*Greasy-grouper*, *Chirocentrus Dorab* and *Solea Elongate* fish species contain cadmium levels above this threshold.

Figure 4b shows the mean concentrations of cadmium in the analyzed fish species in the Red Sea. Levels of Cd ranged between 0.6 and 28.4 µg g^{-1} of wet weight, while the highest mean concentration of cadmium was determined for *Siganus oramin* in the coastal area of Egypt.

Mercury Concentration

Mercury is one of the most lethal substances known to man (Graeme and Pollack, 1998; Rana, 2014). It is one of the heavy metals with the highest level of toxicity. It accumulates in the brain, nervous system, heart and kidneys and can cause depression, autoimmune disorders, memory loss, tremors, anemia and heart attacks, among other health issues. A study conducted at the University of Calgary (Seite, 1956) has shown that, when mercury comes into contact with nerve tissue, it can dissolve the myelin sheath that serves as nerve insulation, causing the nerve to disintegrate within

seconds. Madany *et al*. (1996) analyzed fresh samples of 21 species of marine fish by electro thermal atomic absorption spectrophotometric method to determine mercury traces in fish tissues. Average concentration ranged from 0.037 to 0.3 ppm, as presented in Fig. 5, which is below the European Commission and JECFA recommended limit of 0.5 ppm. Another recent study performed by Hosseini *et al*. (2015) provided mercury concentrations for different fish species caught in Khuzestan province coastal area located in the North East (NE) of the Arabian Gulf. Their findings revealed that the measured mercury concentrations exceeded the *EC* and the *JECFA* guidelines for *Euryglossa Orientalis*, *Otolithes Ruber* and *Psettodes Erumei*, at 1.42 ppm, 0.82 ppm and 0.61 ppm, respectively (Fig. 5).

Figure 5b shows the mean Hg concentrations in the analyzed fish species in the Red Sea. The average concentration ranged from 0.00 to 0.51 ppm. With the value of 0.51 $\mu g\ g^{-1}$ of wet weight, *Plectorhynchus schotaf* exhibited the highest mean values for mercury, whereas *Siganus rivulatus* had the lowest mean values at 0.02 $\mu g\ g^{-1}$ of wet weight.
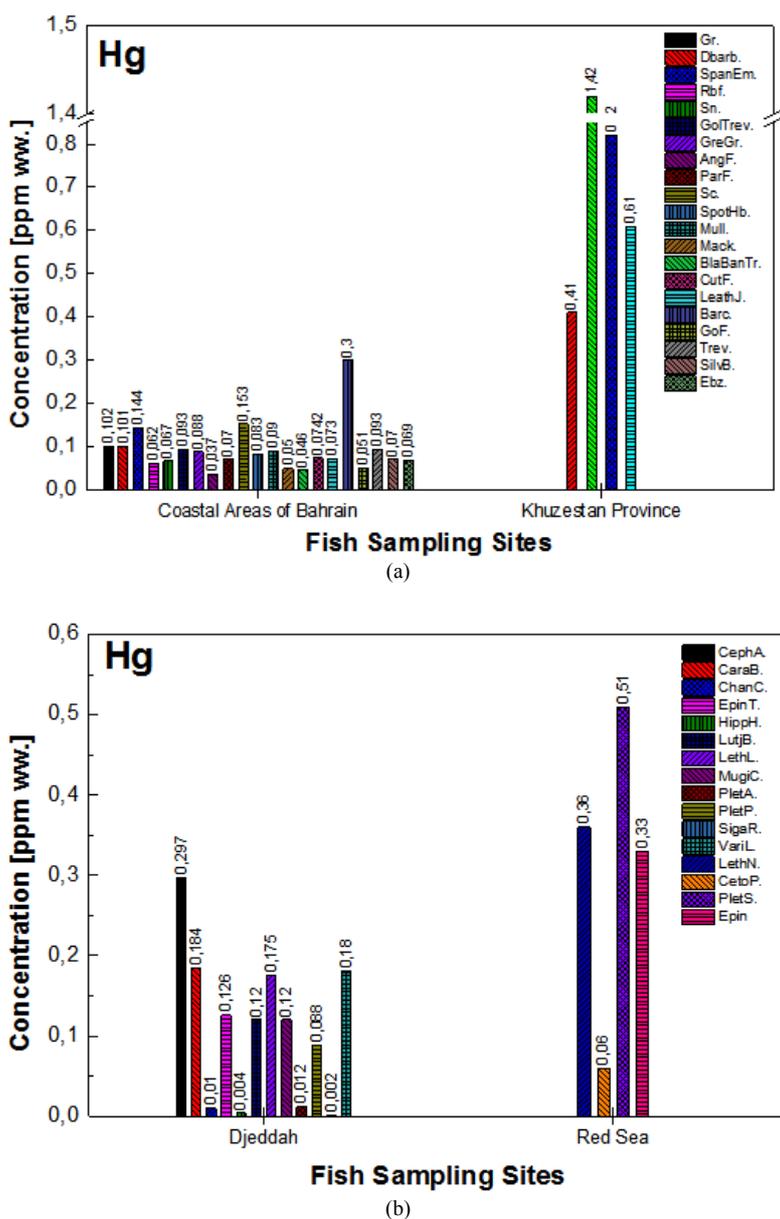

(a)

(b)

Fig. 5. Literature-reported mercury (Hg) levels in (a) Eastern coast of KSA and (b) Western coast of KSA. All data are presented in ppm for wet fish weight (ww)
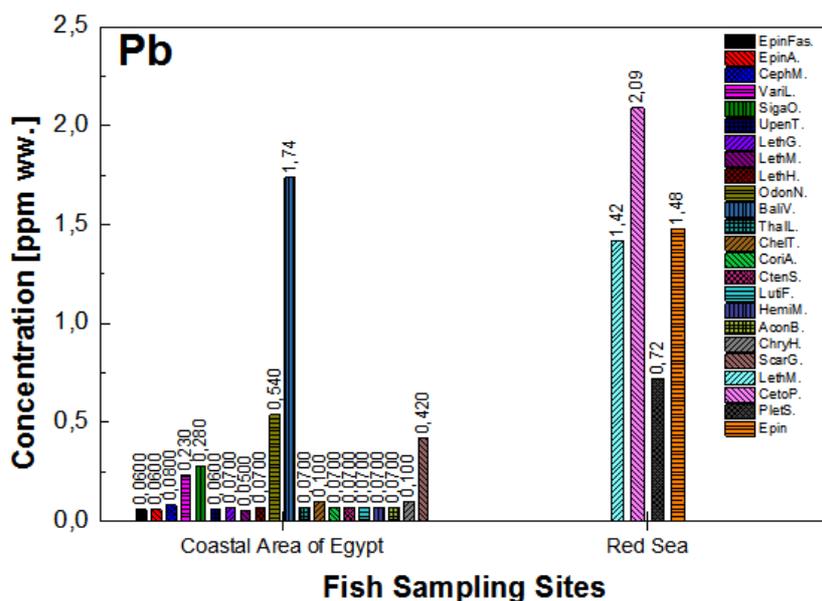
Fig. 6. Literature-reported lead (Pb) levels in fish caught along the Western coast of KSA. All data are presented in ppm for wet fish weight (ww)
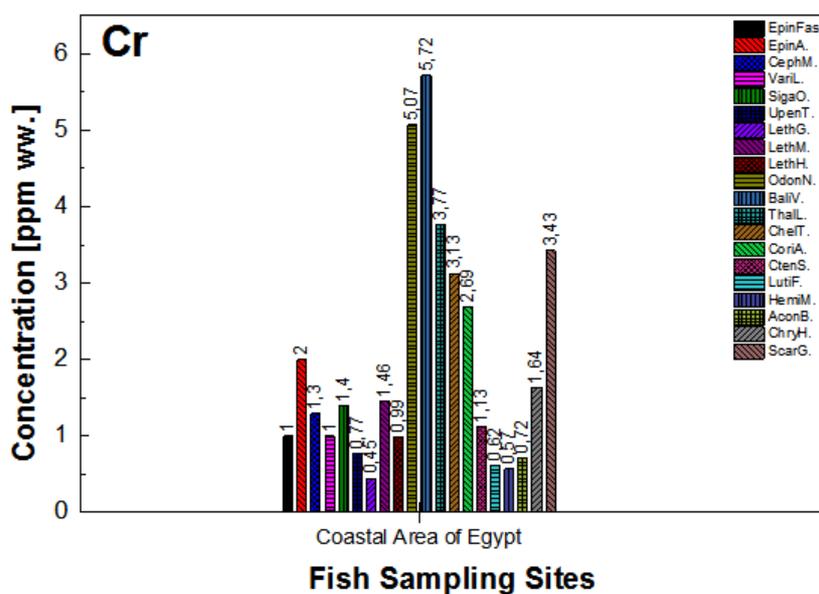

Fig. 7. Literature-reported chromium (Cr) levels in the fish species caught along the western coast of KSA. All data are presented in ppm for wet fish weight (ww)

As shown in Fig. 6, lead concentrations varied significantly between the two Red Sea sites. The mean Pb concentration in different fish species ranges between 0.05 and 2.09 ppm on the wet weight basis. The highest and the lowest mean level of lead on the wet weight basis was observed in *Cetoscarus pulchellus* and *Lethrinus mahsena*, with 2.09 and 0.05 µg g^{-1}, respectively. Lead concentrations in the fish samples analyzed in the study conducted by Al-Ghanim *et al.*

(2015) were much higher (except *Balistoides Vridiscens*) than those observed in the study of Hanna.

Chromium Concentration

Chromium levels in the examined samples ranged from 0.57 ppm to 5.72 ppm on the wet weight basis. Among the analyzed samples, *Balistoides Vridiscens* shows the highest mean concentration of chromium (Fig. 7).
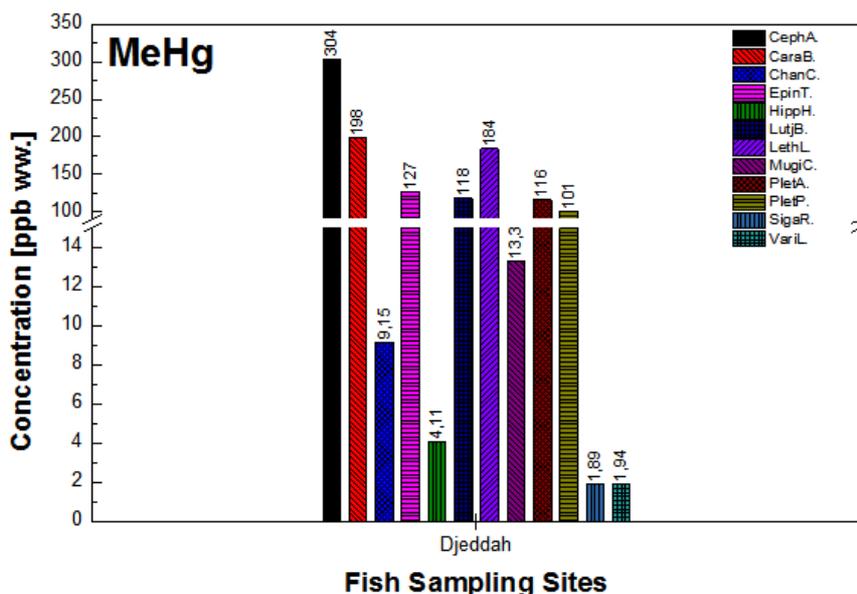
Fig. 8. Literature-reported methylmercury (MeHg) levels in fish species along the western coast of KSA. All data are presented in ppm for wet fish weight (ww)

Methylmercury Concentration

Methylmercury is the most important form of mercury in terms of toxicity and adverse health effects due to environmental exposure (Järup, 2003). Unfortunately, literature pertinent to the determination of this heavy metal concentration in fish is limited. As shown in Fig. 8, *Cephalopholis argus* exhibited the highest mean methylmercury values, while *Siganus rivulatus* showed the lowest mean values for both mercury and methylmercury (Burger *et al*., 2014b).

Risk Assessment

Hazard identification

In the 1930 s, the Chisso Chemical Corporation built a factory in Minamata, located in southwest Japan. It was erected between the Minamata River and the Minamata Bay. It produced chemicals such as *acetaldehyde* (CH_3CHO), which is not inherently dangerous. It is used as a precursor for a chemical reaction required for obtaining vinegar. However, the processes employed were based on an enzyme that contained heavy metal traces, including mercury. As this factory released waste products directly into the bay, methylmercury entered the food chain. These methylmercury traces gradually propagated through the food chain and could be found in fish caught for human consumption. Local residents started to develop the Minamata disease, the cause of which was eventually traced to this factory. Over 2,000 people developed the Minamata disease before this link was established. This case raised awareness of pollutants that enter ecosystems, as many can result in disease. While exposure to harmful products can result in a chronic disease, health issues could also be acute. Chronic and acute diseases can also be induced by pollution. In other words, heavy metal traces that enter the environment become toxic substances with serious consequences for human health. According to the WHO, based on their human health mechanisms of toxicity, toxins can be classified as: (1) Carcinogens, which are probably the best know toxin substances, as they are cancer-causing chemicals that disrupt the human cellular metabolic processes; (2) neurotoxins, which attack the brain and the nervous system and tissues; (3) teratogens, as they lead to congenital anomalies in an embryo or fetus, manifesting as dextrocardia disease; (4) endocrine disruptors, which impact the endocrine system or hormones; and (5) allergens that cause an allergic reaction. Table 5 provides a summary on heavy metal and metalloid classification, along with their human risks for oral route of exposure, which is relevant to fish consumption. As shown in Table 5, arsenic, mercury and methylmercury are neurotoxins that are usually present in doses exceeding safe limits. These toxins can damage parts of the brain, especially the prefrontal cortex.

Hazard Characterization

To conduct a comprehensive risk assessment process, safety factor approach is used for establishing acceptable and tolerable intakes of heavy metals for which toxicity thresholds are established. These safe intake levels are recommended by local (SASO, SFDA), regional (GSO)

and international (EC, FAO, WHO, JECFA) institutions, as shown in Table 1. However, tolerable maximum limits have not yet been established for all heavy metals. As heavy metals accumulate in the human body, JECFA uses the term PTWI, or provisional tolerable weekly intake, to highlight the importance of limiting exposure over a fixed period of time. PTWI values for the most common heavy metals are presented in Table 1.

Table 5. Heavy metal health adverse effects and corresponding toxicological category

Heavy Metal	Adverse effect on human health	Toxicological category			
		Neurotoxin	*Carcinogen*	*Teratogen*	*Endocrine disruptors*
Arsenic (CAS: 7440-38-2)	- Cardiovascular and peripheral vascular disease - Developmental anomalies - Neurologic and neuro-behavioral disorders - Diabetes - Hearing loss - Hematologic disorders - Cancer: lung, bladder, skin, encephalopathy	√	√		
Cadmium (CAS: 7440-43-9)	- Lung cancer - Proteinuria - Osteomalacia - Non-descended testes in young males	√		√	
Lead (CAS: 7439-92-1)	- Encephalopathy - Abdominal pain - Nephropathy - Foot-drop/ wrist-drop				
Mercury (CAS: 7439-97-6)	- Nausea - Gingivo-stomatitis - Tremor - Neurasthenia - Nephrotic syndrome - Gastrointestinal toxicity	√	√		
Chromium (CAS: 7440-47-3)	- Pulmonary fibrosis - Lung cancer (inhalation) - Cardiovascular, renal, gastrointestinal, hematological and neurological effects	√	√		
Nickel (CAS: 7440-02-0)	- Occupational (inhaled): Pulmonary fibrosis, reduced sperm count, nasopharyngeal tumors	√		√	
Methyl-mercury (CAS:22967-92-6)	- Harmful to infant's developing nervous system - Damage the fetus - Nephrotoxicity and gastrointestinal toxicity	√		√	

Exposure Assessment Equations

To assess the impact of hazardous heavy metals on human health, authors of extant studies have adopted several calculation approaches (Ravankhah *et al*., 2016; Xu *et al*., 2016; Pelfrêne *et al*., 2014; Dumitrescu *et al*., 2012) based on the exposure estimation to a metal by oral ingestion. This oral exposure is expressed as the Average Daily Dose (*ADD*) in mg kg^{-1} day^{-1} using the following expression:

$$ADD = \frac{C_m \times C_F \times IR \times EF \times ED_{Tot}}{BW \times \overline{AT}} \qquad (1)$$

where, C_m is the investigated metal concentration in fresh fish (ppm wet weight), C_F is the conversion factor from wet to dry weight (0.33), IR is the ingestion rate (g person^{-1} day^{-1}), *EF* is the exposure frequency over the average lifetime (365.25 days year^{-1}), ED_{Tot} is the total exposure duration over the average lifetime (74.34 years as life expectancy for individuals in Saudi Arabia), BW is the body weight (73 kg for an 74.34-year-old individual) and $\overline{AT}$ is the average exposure time over the average lifetime (365.25 day/year ×74.34 years). In order to calculate the *ADD* correctly, *IR* should be estimated using an exact consumption pattern for fish by individuals. This consumption pattern depends on several parameters, including fish species, frequency of consumption of particular species (average meal size), age category and gender. In a recent study, Burger *et al*. (2015) carried out a survey of 975 households and concluded that Saudis were eating 2.2 fish-based meals/week, whereby Grouper fish (including both *Epinephelus* and *Cephalopholis*) was most widely consumed, followed by *Plectropomus pessuliferus, Hipposcarus harid* and *Lethrinus lentjan*.

In contrast to this survey-based approach, four standard exposure scenarios are adopted (US EPA) in the present study.

Equation 1 is only suitable for non-carcinogen estimation of ADD. As shown in Table 5, most of heavy metals and metalloids are categorized as carcinogenic substances. Hence, to investigate the increased cancer risk from a lifetime oral exposure to a heavy metal agent, the following equation is used:

$$CR = \frac{C_m \times C_F \times IR \times EF \times ED_{Tot} \times CSF}{BW \times \overline{AT}} \qquad (2)$$

where, *CSF* is the carcinogenic oral slope factor, which depends on the metal type. *CFS* can be estimated from the integrated risk information system database for different metals.

Heavy metal Hazard Index (HI) can be estimated for each metal type by using the following equation:

$$HI = \frac{ADD}{OR_f D} \qquad (3)$$

where, $OR_f D$ is the oral reference dose (mg^{-1} kg^{-1} day^{-1}).

Risk Characterization (Potential for Human Exposure)

Based on all studies selected for review; Fig. 9a shows the number of samples that exceeded the permissible limit for the Arabian Gulf and Red Sea fish sampling sites. Maximum allowed limits were recommended by national (SASO, SFDA), regional (GSO) and international institutions (WHO, FAO, JECFA). In the studies conducted on western Saudi Arabian coast, 40 samples exceed permissible limit for all metals, which corresponds to 11.76% of all analyzed fish samples. More specifically, As, Cd and Pb concentrations were above the limit in 10, 20 and 9 fish samples, respectively. The mercury levels were higher than the 0.5 µg g^{-1} wet wt. limit proposed by EC (Regulations No 1881/2006 and No 629/2008) and JECFA (FAO/WHO Joint Expert Committee on Food Additives) for only one sample (*Plectorhynchus schotaf*). In sum, the Red Sea sampling site seems to be the most contaminated among the three studied areas. Among the 16 examined samples, 13 exceed permissible limit. This finding is confirmed by the radar plot in Fig. 9b.

On the eastern Saudi Arabian coast, 413 fish samples (36 fish species) were collected from nine different fish sampling sites. Figure 10b provides the number of samples above the permissible limit for these studied sites. As it can be seen, for heavy metals, there were significant differences in the number of samples that exceeded the permissible limits across the six investigated sites. Moreover, about 15% of the analyzed samples (40 samples) exceed permissible limit of different heavy metals. Specifically, at all sites, some samples (1 to 9 samples) contained Pb levels that exceeded the permissible limit of 0.2 µg g^{-1} provided by 2 JECFA (FAO/WHO Joint Expert Committee on Food Additives). Regarding mercury, only three fish species (*Euryglossa orientalis, Otolithes ruber and Psettodes erumei*) with Hg levels higher than the allowed limit (0.5 ppm, wet weight) were detected at the Khuzestan Province site. In addition, at this site, some samples where characterized by exceedence for four of the five heavy metals investigated in this study.
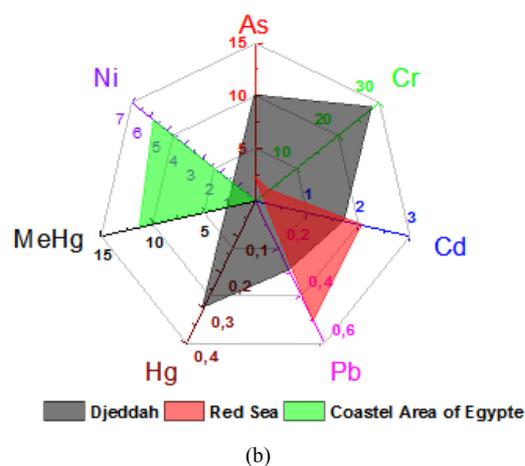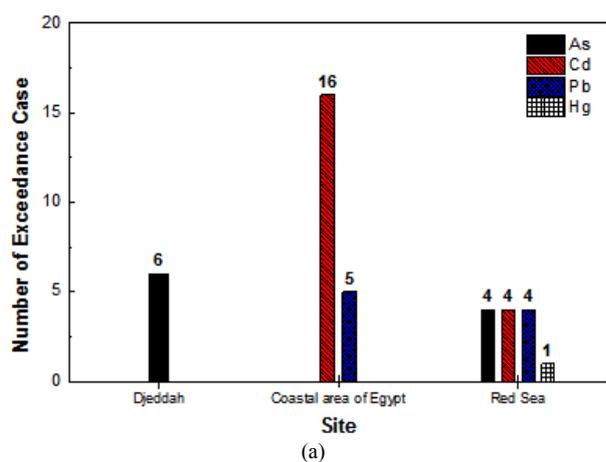

(a)

(b)

Fig. 9. Number of exceedance cases (a) and maximum metal concentrations (b) in fish caught at Saudi western sites
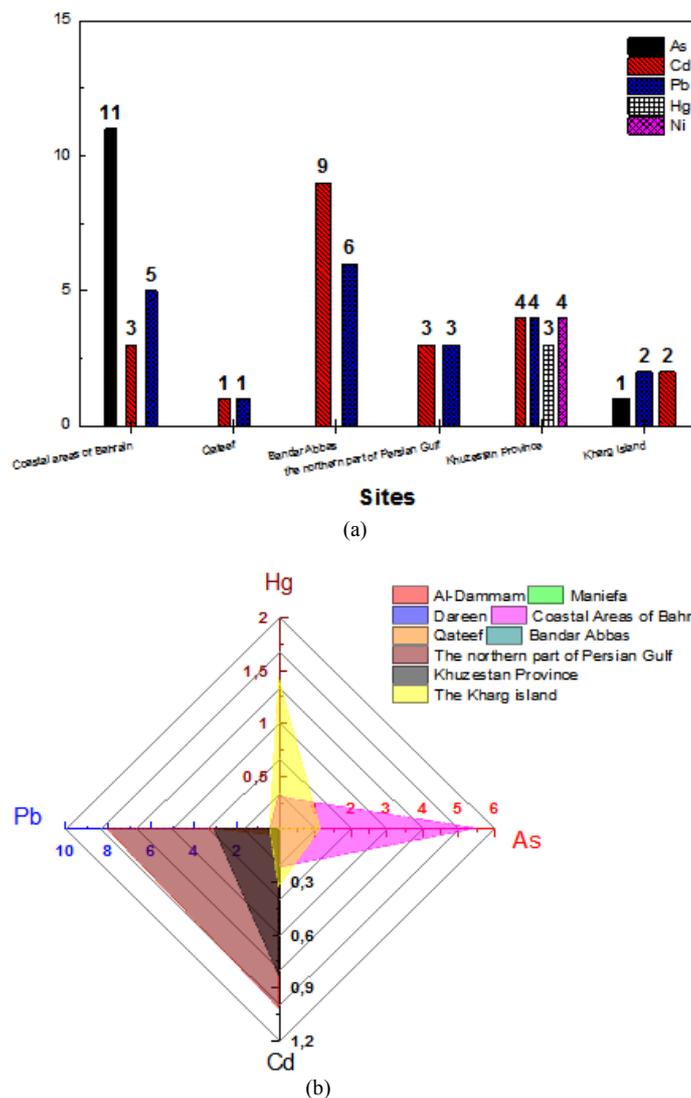
(a)

(b)

Fig. 10. Number of exceedance cases (a) and maximum metal concentrations (b) in fish for Saudi Eastern sites

Table 6. Scenario 1, high fish consumption/high metal concentration (IR = 250)

	Western Coastal Areas								
	Djeddah Coastal			Area of Egypt			Red Sea		
Metal	FS	C_M	HI	FS	C_M	HI	FS	C_M	HI
As	EpinT.	10.04	37.82	--	--	--	Epin	2.24	8.43
Hg	--	--	--	--	--	--	PletS.	0.51	1.92
Pb	--	--	--	BaliV.	1.74	0.49	CetoP.	2.09	0.59
Cd	--	--	--	SigaO.	28.48	32.18	LethN.	3.24	3.66

	Eastern Coastal Areas																	
	Coastal Area of Bahrain			Qateef			Bandar Abbas			The northern part			Khuzestan Province of Persian Gulf			Kharg Island		
Metal	FS	C_M	HI	FS	C_M	HI	FS	C_M	HI	FS	C_M	HI	FS	C_M	HI	FS	C_M	HI
As	CutF.	5.54	20.86	--	--	--	--	--	--	--	--	--	--	--	--	Mack.	1.17	4.40
Hg	--	--	--	--	--	--	--	--	--	--	--	--	EuryO.	1.42	5.34	--	--	--
Pb	Barc.	0.39	--	EpinM.	3.19	0.9	AcanL	0.534	0.15	PsetE.	8.02	2.26	EuryO.	3.01	0.85	Mack.	0.41	0.11
Cd	Gr.	0.222	0.25	EpinM	0.41	0.46	PlatI.	0.147	0.16	PsetE.	1.017	1.14	EuryO.	0.83	0.93	OtolR.	0.33	0.37
Ni	--	--	--	--	--	--	--	--	--	--	--	--	EuryO.	63.02	3.56	--	--	--

Table 7. Scenario 2, high fish consumption /average metal concentration (IR = 250)

Western Coastal Areas

Metal	Djeddah FS	C_M	HI	Coastal Area of Egypt FS	C_M	HI	Red Sea FS	C_M	HI
As	LethL.	1.43	5.38	--	--	--	LethN.	1.15	4.33
Hg	--	--	--	--	--	--	CetoP.	0.06	0.22
Pb	--	--	--	VariL.	0.23	0.064	PletS.	0.72	0.20
Cd	--	--	--	EpinA.	0.6	0.67	PletS.	2.09	2.36

Eastern Coastal Areas

Metal	Coastal Area of Bahrain FS	C_M	HI	Qateef FS	C_M	HI	Bandar Abbas FS	C_M	HI	The northern part of Persian Gulf FS	C_M	HI	Khuzestan Province FS	C_M	HI	Kharg Island FS	C_M	HI
As	Sc.	1.1	4.14	--	--	--	--	--	--	--	--	--	--	--	--	Mack.	1.17	4.40
Hg	--	--	--	--	--	--	--	--	--	--	--	--	PsetE.	0.61	2.29	--	--	--
Pb	SilvB.	0.21	0.05	EpinM.	3.19	0.9	PlatI.	0.211	0.05	Mack.	2.8	0.79	LizA.	2.11	0.59	OtolR.	0.28	0.07
Cd	Sc.	0.8	0.9	SilvB.	0.41	0.46	RachC.	0.055	0.006	SolE.	0.088	0.09	PsetE.	0.36	0.4	Mack.	0.21	0.23
Ni	--	--	--	--	--	--	--	--	--	--	--	--	PsetE.	53.12	3	--	--	--

Table 8. Scenario 3, average fish consumption/high metal concentration (IR = 90.58)

Western Coastal Areas

Metal	Djeddah FS	C_M	HI	Coastal Area of Egypt FS	C_M	HI	Red Sea FS	C_M	HI
As	EpinT.	10.04	14.19	--	--	--	Epin	2.24	3.05
Hg	--	--	--	--	--	--	PletS.	0.51	0.69
Pb	--	--	--	BaliV.	1.74	0.17	CetoP.	2.09	0.21
Cd	--	--	--	SigaO.	28.48	11.66	LethN.	3.24	0.33

Eastern Coastal Areas

Metal	Coastal Area of Bahrain FS	C_M	HI	Qateef FS	C_M	HI	Bandar Abbas FS	C_M	HI	The northern part of Persian Gulf FS	C_M	HI	Khuzestan Province FS	C_M	HI	Kharg Island FS	C_M	HI
As	CutF.	5.54	7.56	--	--	--	--	--	--	--	--	--	--	--	--	Mack.	1.17	1.59
Hg	--	--	--	--	--	--	--	--	--	--	--	--	EuryO.	1.42	1.93	--	--	--
Pb	Barc.	0.39	0.039	EpinM.	3.19	0.32	AcanL.	0.534	0.05	PsetE.	8.02	0.82	EuryO.	3.01	0.3	Mack.	0.41	0.04
Cd	Gr.	0.222	0.09	EpinM.	0.41	0.16	PlatI.	0.147	0.06	PsetE.	1.017	0.41	EuryO.	0.83	0.33	OtolR.	0.33	0.13
Ni	--	--	--	--	--	--	--	--	--	--	--	--	EuryO.	63.02	1.29	--	--	--

Table 9: Scenario 4, average fish consumption/average metal concentration (IR = 90.58)

Western Coastal Areas

Metal	Djeddah FS	C_M	HI	Coastal Area of Egypt FS	C_M	HI	Red Sea FS	C_M	HI
As	LethL.	1.43	1.95	--	--	--	LethN.	1,15	1.56
Hg	--	--	--	--	--	--	CetoP.	0,06	0.08
Pb	--	--	--	VariL.	0.23	0.02	PletS.	0,72	0.07
Cd	--	--	--	EpinA.	0,6	0.24	PletS.	2,09	0.85

Eastern Coastal Areas

Metal	Coastal Area of Bahrain FS	C_M	HI	Qateef FS	C_M	HI	Bandar Abbas FS	C_M	HI	The northern part of Persian Gulf FS	C_M	HI	Khuzestan Province FS	C_M	HI	Kharg Island FS	C_M	HI
As	Sc.	1.1	1.5	--	--	--	--	--	--	--	--	--	--	--	--	Mack.	1.17	1.59
Hg	--	--	--	--	--	--	--	--	--	--	--	--	PsetE.	0.61	0.83	--	--	--
Pb	SilvB.	0.21	0.02	EpinM.	3.19	0.32	PlatI.	0.211	0.02	Mack.	2.8	0.28	LizA.	2.11	0.21	OtolR.	0.28	0.02
Cd	Sc.	0.8	0.32	SilvB.	0.41	0.16	RachC.	0.055	0.02	SolE.	0.088	0.03	PsetE.	0.36	0.14	Mack.	0.21	0.08
Ni	--	--	--	--	--	--	--	--	--	--	--	--	PsetE.	53.12	1.08	--	--	--

Using Equation 1 and 3, *ADD* and *HI* are calculated for all the exceedance cases based on four exposure scenarios for high and average fish consuming populations (Table 6-9). The calculated HI values reveal

that arsenic presents the greatest risk for adverse health effects (HI > 10) for high and average consuming populations of *Epinephelus Tauvina* and *Cuttle fish* species caught in *Djeddah* and coastal area of Bahrain sites, respectively. Moreover, there is a high probability that cadmium would induce adverse health effects for high and average consuming populations of Siganus Oramin fish caught in Coastal Area of Egypt. It should be noted that HI > 1 indicates that adverse health effects are possible, although not assured. Conversely, HI < 1 implies that no adverse effects are expected as a result of exposure. Hence, big consumers of *Epinephelus Tauvina* and *Cuttle fish* species caught in *Jeddah* (Saudi Arabia) and coastal area of Bahrain sites ingest high doses of arsenic and can experience the appearance of pattern of skin changes for a long time exposure. Absorbing arsenic has also been reported to increase the risk of cancer in the liver, bladder and lungs. On the other hand, big consumers of Siganus Oramin fish, caught in coastal area of Egypt, are exposed to high level of cadmium contamination that can causes birth defects and affects the skeleton in the developing young. This risk assessment study can serve as a status report for policy makers to limit industrial discharges in common coastal fishing areas and to prohibit fishing in contaminated areas. A consumption advisory can be established by Saudi national health regulatory and standardization organizations, i.e., the Ministry of Health (MOH) as a recommendation to limit or avoid eating these heavy metal contaminated fish species in these areas and to raise the population awareness about their consumption.

Conclusion

Over the recent years, the consumption of different types of fish by Saudi Arabian population has increased. Consequently, the intake of trace elements, especially heavy metals, through fish consumption has become of high concern for human health. Mean concentrations of arsenic, cadmium, mercury, lead, chromium and methylmercury were collected from 11 peer-reviewed publications related to the Red Sea and the Arabian Gulf in order to assess the level of health risk associated with fish consumption among the Saudi consumers. As a part of this investigation, 73 fish species and 1,027 edible fish part samples from 12 sampling sites were studied and analyzed. The results yielded by this study indicate that consumption of some species of fish, due to their higher bio-accumulated metal concentrations, could be a threat for human health. Furthermore, consumption of some fish species collected from specific areas is highly likely to induce adverse health effects in humans. More specifically, high hazard index (HI > 10) was obtained for some fish species as *Epinephelus Tauvina* and *Cuttle fish* species caught in *Djeddah* and coastal area of

Bahrain sites, respectively. Consequently, very close monitoring of heavy metal levels in different regions of KSA is recommended in order to assess the risks to consumer health. Further investigation on methyl mercury (MeHg) concentrations in edible fish parts should be performed in order to estimate consistent exposure and assess adverse health effects.

Ethics

Author declares no conflict of interest.

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