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REVIEW ARTICLE: HUMAN HEALTH RISK ASSESSMENT IN RELATION TO HEAVY METALS INTAKE DUE TO CONSUMPTION OF CLAM SPECIES FOUND FROM MALAYSIA WATERS

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ABSTRACT
The current systematic review paper discusses the levels of the six important heavy metals concentrations in different clam species from various sites of Malaysian river coasts. The concentrations (μg/g dry weight) of these heavy metals ranged around 0.18–8.51, 0.13–17.20, 2.17–7.80, 0.84–36.00, 24.13–368.00, and 177.82–1912.00 for Cadmium (Cd), Lead (Pb), Nickel (Ni), Copper (Cu), Zinc (Zn) and Ion (Fe) respectively. Human body requires some of heavy metals such as Cu, Zn, and Fe in small quantity, it was observed that the concentrations of heavy metals slightly depend on the different clam species but mostly depend on the habitat site/ locations. According to the Malaysian Food Regulation organization, about 30% and more than 50% of these sites are free from heavy metals' contamination; pose by chemical elements as Cd and Pb respectively; which are very toxic to the human health conditions, for their presence may consequently lead to certain chronic health risks. Generally the clam species based on the other populations researched were safe for further human daily consumptions.

Keywords: *Aquatic Environment, Clam Species, Environmental Pollution, Heavy metals, Health risk*

INTRODUCTION
One of the most diverse marine habitats on earth, Malaysia Waters stands as a home to 37% of the world's reef species and 76% of the world's coral species. It has abundant natural resources that provide such opportunities with regards to fisheries and tourism, indicating its potentiality in providing the neighboring countries with a great economic value.

However, the water body seems to be contaminated by natural gas and some oil deposits [24]. Moreover, the extensive human activities carrying out on the water coast, is believe to be the cause for the release of pollutants into the local environment that threaten marine organisms; given the situation of the significant growth in fishing and farming operations in the South China Sea and the rapid socioeconomic development of nearby districts[20, 24]. Additionally, the fish and the rest of aquatic organisms found within this water body are consumed by people in the neighboring nations, this raises concerns about possible health dangers [40]. However, despite the fact that it is now becoming a serious issue that both freshwater and marine environments are being contaminated with a variety of pollutants, there is still a dearth of information regarding the quantity and origin of metals in fish found from coastal waters[19]. It is believe that the aquatic ecosystems have been negatively impacted in recent decades by domestic, industrial, and other anthropogenic activities that have increased the heavy metal contamination in the water bodies [16, 47].Because of their high toxicity and accumulative nature, pollutants introduced into the water system result in significant alterations that either directly or indirectly affects the ecological balance of the environment, resulting in extensive harm and even mass extinctions of aquatic organisms[37].

The concentration of heavy metals may rise to a dangerous level, which could potentially harm the ecological environment [4]. The risk of contamination in living tissue is considerable when organisms start accumulating higher amounts of heavy metals than the level of excretion because the natural concentrations of these metals in sea water are extremely low[11]. Because they inhabit various tropic levels and range in size and age, fish are among the aquatic species with the highest investigated content of heavy metals; this is because aquatic organisms serve as strong indicators of heavy metal contamination in aquatic systems[21, 7]. Variable aquatic species may have variable levels of heavy metals due to ecological requirements, differences in metabolism, feeding habits, and body size[29]. Because of the increased rate of assimilation by aquatic creatures like clam and fish species, such heavy metal deposition has an impact on people via the food web [42]. Human consumption of such aquatic organism exposes people to high levels of heavy metals contamination, which pose certain major health risks to the entire human race[6]. The body's homeostatic balance typically has an impact on how heavy metals enter the system of living organisms, the process of homeostatic can no longer work if a metal concentration range surpasses the body's limit load, leading to toxic consequences on the body that can be either immediate or chronic [3]. For example, while Cd and Pb have no known function in biological systems, metals like Cu and Zn are necessary for organism metabolism[51]. Prior research has demonstrated that heavy metals may change the physiological processes and biochemical markers in both tissues and blood [42]. One of the most significant areas of food production is sea foods, which provides all of humanity with protein, the Food and Agriculture Organization (FAO) claims that during the past ten years, consumer health consciousness has dramatically increased demand for sea foods[18, 31].

Given these concerns, the current study was started to measure the level of heavy metal bioaccumulation in several commercially significant sea foods from Malaysia's coastal region, by consuming infected clam species and other aquatic foods from this environment, humans may become contaminated by organic and inorganic pollutants linked to aquatic systems; the presence of some heavy metals in the sea foods could turn what would otherwise be an excellent source of nutrition for humans into some chronic illnesses[45]. Through food chain and the water, dangerous trace metals can be ingested by marine organisms like clam species, they are also one of the most important toxicological indicators[42]. Muscles is the primary portion of aquatic organisms that humans eat, making it the tool of choice for determining the risk metal pollution poses to the public's health, is the major way that people are exposed to heavy metals, which can be harmful in higher doses through their diet[8]. The content of heavy metals in aquatic organisms has been widely examined in various parts of the world during the past few decades[27].The primary goal of this research is to investigate the levels of heavy metals in several kinds of clams from Malaysian beaches. In this study, 12 species of clams from various sites around the Malaysian coast were examined for the presence of heavy metals (Cd, Pb, Ni, Cu, Zn, and Fe), and the hazards to human health were evaluated in relation to international food safety standards.

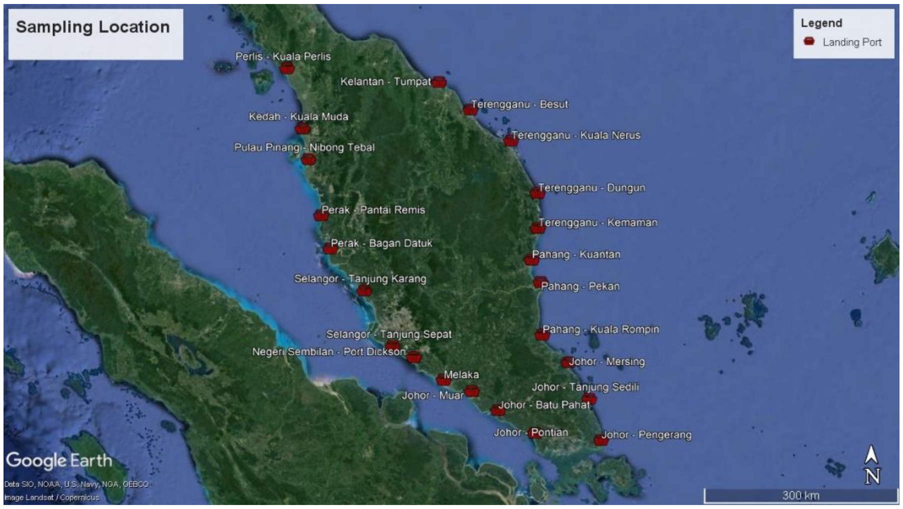

Figure 1: Map of Malaysia River Coasts Showing Different Locations

Figure 2: Marine/Salt Water Clam Species

DISCUSSION

The heavy metals such as Cd, Pb, As, and Hg are known as nonessential heavy metals, they are toxic even in small amount and harmful to human health, those harmful heavy metals released by the human activities will be accumulated in marine organisms through the food web. Hence, human health risks might be caused by consumptions of seafood contaminated with toxic heavy metals, normally, human body requires some of these heavy metals such as Cu, Zn, Fe, and Ni in small amount although sometimes Ni acts as toxic metal. These metals are known as essential metals. However, the essential metals can be toxic if taken in large quantities [5, 22]. In this study, heavy metals such as Cd, Pb, Ni, Cu, Zn, and Fe in total soft tissues of 12 clam species from different sites (Figure 1) of Malaysian river coasts have been discussed.

Cadmium (Cd)

It was observed that the range of Cd concentration was 0.18–8.51 μg/g (dry weight) in different clam species from different river coasts of Malaysia (Table 1). The highest value was observed in *Scapharcabroughtonii* from PantaiRemis (Perak), while the lowest value was observed in *Anadaragranosa* from Tumpat (Kelantan). The Cd levels in clam species from most of the sites exceeded the maximum permissible limits set by Malaysian Food Regulation [25]and International Council for the Exploration of the Seas [23].But the species from Bandar Baharu (Kedah), Merlimau (Malacca), Semerah (Johor), Tumpat (Kelantan), Pekan and Tanjung Lumpur (Pahang), Bandar Permaisuri (Terengganu), and Desa Moyan and Serpan (Sarawak) exhibited lower values than safety limits. Only three (3) species from Kampung Sungai Berembang and Pulau Ketam, Perlis, and Pantai Remis, Perak, exceeded the maximum permissible limit set by Brazilian Ministry of Health [33], but were lower than the permissible limits for human consumption set by Food and Drug Administration of the United States [39], and the Australian Legal Requirements for Food Safety [15] (Table 2). However, it was observed that Cd in clam species from six (6) sites is within the lowest safety limits (1.01–2.00 μg/g) set by Malaysian Food Regulation [25], International Council for the Exploration of the Seas[23], and Hong Kong Environmental Protection Department [38], while Cd in clams from seventeen (17) sites is within the second highest safety limits (2.01–5.00 μg/g) set by Brazilian Ministry of Health [33]. On the other hand, only three (3)fish species from Kampung Sungai Berembang (Perlis), Pulau Ketam (Perlis), and PantaiRemis (Perak) are within the highest safety limits (5.01–10.00 μg/g) set by the Australian Legal Requirements for Food Safety [15].

Lead (Pb)

The concentration ranges from 0.13 to 19.10 μg/g (dry weight) (Table 1). The highest value was observed in *Scapharcabroughtonii* from PantaiRemis (Perak), while the lowest value was observed in *Anadaragranosa* from Pekan (Pahang). The Pb levels in clams from fourteen (14) sites exceeded the maximum permissible limits set by Malaysian Food Regulation [25] and International Council for the Exploration of the Seas[23] while species from nine(9) sites exceeded the maximum permissible limits set by Brazilian Ministry of Health [33], and Ministry of Public Health, Thailand [13]. But six (6) clam species from

Pantai Remis (Perak), Pasir Panjang (Negeri Sembilan), Telok Mas 1 (Malacca), Parit Jawa and Kampung Pasir Putih (Johor), and Muara Tebas (Sarawak) exceeded all of the maximum permissible limits (Table 2). However, it was observed that Pb levels in clams from more than 50% sites are below the safety limits (Table 1) but in Sungai Sarawak (Sarawak) and Sekinchan and Kuala Selangor (Selangor) are within the lowest safety limits (2.01–6.00 μg/g) set by Malaysian Food Regulation [25], International Council for the Exploration of the Seas[23], and Hong Kong Environmental Protection Department [38], and only in three (3) species from Pantai Remis (Selangor), Sungai Sepang (Selangor), and Pantai Remis (Perak) are within the highest safety limits (6.01–11.50 μg/g) set by Ministry of Public Health, Thailand [13], Food and Drug Administration of the United States [39], and Brazilian Ministry of Health [33], while that from six (6) sites mentioned earlier exceeded all of those safety limits (Table 2).

Nickel (Ni)

Normally occurs at very low concentrations in the environment, it was observed that the range of Ni was 1.25–7.80 μg/g (dry weight) in different clam species from different coasts of Malaysia (Table 1). The highest value was observed in *Polymesodaerosa* from Parit Jawa, Johor, and the lowest value was observed in *Pholasorientalis* from Sekinchan, Selangor. Ni in clams from Sungai Sepang (Selangor), Pantai Remis (Selangor), Kampung Pasir Putih (Johor), Parit Jawa (Johor), and Pantai Remis (Perak) were higher than 5.00μg/g.

Copper (Cu)

Cooper (Cu) is an essential element for human health, the range of Cu concentration was 0.84–36.00 μg/g (dry weight) in different clam species from different coasts of Malaysia (Table 1). The highest value was observed in *Polymesodaexpansa* from KampungPasir (Johor) and the lowest value was observed in the same species from Sungai Sarawak (Sarawak). The Cu levels from all of the sites were below the maximum permissible limits set by Malaysian Food Regulation [25], Ministry of Public Health, Thailand [13],Australian Legal Requirements for Food Safety [15], International Council for the Exploration of the Seas[23],Food and Drug Administration of the United States [39], and Brazilian Ministry of Health [33], while Cu in the same ones from

Kampung Pasir Putih (Johor) exceeded the maximum permissible limits set by Malaysian Food Regulation [25] (Table 2).

Zinc (Zn)

Zinc (Zn) is also an essential element like copper, it was observed that the Zn concentrations in different clam species from different coasts of Malaysia ranged widely from 24.13 to 368.00μg/g (dry weight) (Table 1). The highest value was observed in *Polymesodaexpansa* from KampungPasirPutih(Johor), while the lowest value was observed in *Meretrixmeretrix* from Sungai Sarawak (Sarawak). The Pb levels of clam species from almost ten (10) sites exceeded the maximum permissible limits set by Malaysian Food Regulation [25] and only *Polymesodaerosa*and *Polymesodaexpansa* from Sungai Sepang, Selangor, and KampungPasir, Johor, respectively, exceeded the second highest maximum permissible limits set by Brazilian Ministry of Health [33], but Zn levels from all of those sites were below the highest maximum permissible limits set by Ministry of Public Health,Thailand [13], and Australian Legal Requirements for Food Safety [15] (Table 2). However, Zn concentration in clams from six (6) sites was within the lowest safety limits (100.01–250.00 μg/g) set by Malaysian Food Regulation [25] and Brazilian Ministry of Health [33], while Zn in clams only from KampungPasir(Johor) and Sungai Sepang (Selangor) was above this lowest safety limit but below the highest safety limits (667.01–750.00 μg/g).

Iron (Fe)

Iron (Fe)is an essential mineral/nutrient metal required for the every living organisms and important for the certain body enzymes, lack of Iron (Fe) generally lead to the weakness of the organisms body and inability to develop well, and gives low performance in circulatory transport and also reduces oxygen supply to the muscle/tissues. It was observed that the Iron (Fe) concentrations ranged widely from 177.82 to 1912.00μg/g (dry weight) in different clam species from different river coasts of Malaysia (Table 1). The highest value was observed in *Polymesodaerosa* from Telok Mas 1 (Malacca), while the lowest value was observed in the *Solenregularis* from Sungai Sarawak (Sarawak). However, the very high values of few are observed in clams species from Telok Mas 1 (Malacca), KampungPasir (Johor), ParitJawa (Johor), and Sungai Sepang (Selangor) which were 1912, 1454, 1307, and 1111μg/g respectively[2].

Table 1: Mean Concentration of Metals (ug/g dry weight) in Muscles of Different Clam Species from Malaysia

Sample Locations	Clam Species	Cd	Pb	Ni	Cu	Zn	Fe	Ref.
Perlis: Kampung Sungai Berembang Pekan KampungBehorToiKampung Sungai Berembang PulauKetam	 *GlauconomeVirens* *Marcia marmorata* *Marcia marmorata* *Marcia marmorata* *Marcia marmorata*	 - 3.40 1.90 7.10 5.20	 - - - - -	 1.25 - - - -	 8.76 22.80 14.90 23.90 24.70	 74.63 88.70 77.50 89.70 116.50	 572.60 - - - -	 26 49
Kedah: Bandar Baharu Sungai Layar	 *Anadaragranosa* *Glauconomevirens*	 0.67 -	 0.16 -	 - 2.19	 2.01 11.05	 57.20 119.28	 - 706.60	 10 26
Penang: Butterworth PantaiTeluk Air Tawar	 *Anadaragranosa* *Glauconomevirens*	 3.43 -	 1.08 -	 - 2.05	 3.27 11.02	 98.79 132.06	 - -	 10 26
Perak: Kerian Kuala Terong Pangkor Sungai Perak PantaiRemis PantaiRemis	 *Anadaragranosa* *Anadaragranosa* *Anadaragranosa* *Anadaragranosa* *Scapharcabroughto nii* *TrisidosKiyonoi*	 2.60 2.49 2.14 1.49 8.51 2.64	 0.92 0.93 0.79 1.33 19.10 8.00	 - - - - 5.26 4.93	 1.67 3.18 2.42 2.57 4.54 5.84	 56.43 77.21 73.41 69.82 67.80 61.50	 - - - - 782.00 501.00	 10 50
Selangor: Sungai Ayer Tawar Sungai Besar Kuala Selangor Sekinchan PantaiRemis Sungai Sepang	 *Anadaragranosa* *Anadaragranosa* *Anadaragranosa* *Pholasorientalis* *Pholasorientalis* *Polymesodaerosa*	 2.67 4.43 2.66 2.31 1.75 2.96	 1.78 1.61 3.04 3.96 8.21 6.80	 - - - 2.17 6.17 5.07	 3.07 2.17 2.94 16.86 22.55 15.70	 136.03 158.00 99.70 40. 43 37.76 343.00	 - - - 291.15 292.75 1111.0	 10 50
Negeri Sembilan: PasirPanjang	 *Donaxfaba*	 3.96	 12.60	 3.65	 7.23	 51.20	 654.00	 50
Malacca: Merlimau Telok Mas 1	 *Anadaragranosa* *Polymesodaerosa*	 0.62 4.23	 0.91 11.60	 - 4.29	 9.10 5.91	 98.72 249.00	 - 1912.0	 10 50

Johor:								
Semerah	*Anadaragranosa*	0.82	1.43	-	1.96	53.22	-	
Senggarang	*Anadaragranosa*	1.45	0.60	-	2.67	65.91	-1307.0	10
ParitJawa	*Polymesodaerosa*	3.34	12.20	7.80	6.50	222.00	1454.0	
KampungPasirPutih	*Polymesodaexpansa*	3.59	17.20	6.04	36.00	368.00		50
Kelantan:								
Tumpat	*Anadaragranosa*	0.18	0.99	-	1.84	41.80	-	10 7
Pahang:								
Pekan	*Anadaragranosa*	0.65	0.13	-	4.92	104.02	-	10
Tanjung Lumpur	*Solenbrevis*	0.67	1.61	-	8.64	87.74	415.20	41
Terengganu:								
Bandar Permaisuri	*Anadaragranosa*	0.35	0.45	-	2.19	64.50	-	10
Sarawak:								
MuaraTebas	*Solen spp.*	1.64	13.47	-	4.11	82.82	522.07	44
DesaMoyan	*Solenregularis*	0.85	-	-	6.75	-	263.50	
Serpan	*Solenregularis*	0.88	-	-	8.05	-	601.25	41
Sungai Sarawak	*Polymesodaexpansa*	1.15	2.89	-	0.84	62.24	295.31	
Sungai Srawak	*Meretrixmeretrix*	2.15	2.23	-	1.57	24.13	250.73	13
Sungai Sarawak	*Solenregularis*	2.35	4.85	-	2.21	27.08	177.82	

Table 2: Guidelines on heavy metals (μg/g dry weight) for food safety set by different countries

Different Countries Standard Limit of Heavy Metals	Cd	Cu	Pb	Zn	Ni	Fe
Malaysian Food Regulation	1.00	30.0	2.00	100.00	-	-
Ministry of Public Health Thailand (MPHT)	-	133	6.67	667.00	-	-
Brazilian Ministry of Health (ABIA)	5.00	150	10.0	250.00	-	-
International Council for the Exploration of the Seas (ICES)	1.80	-	3.00	-	-	-
Food and Drug Administration of the United States (USFDA)	25.0	-	11.50	-	-	-
Australian Legal Requirements for Food Safety (NHMRC)	10.0	350	-	750.00	-	-
Hong Kong Environmental Protection Department (HKEPD)	2.00	-	6.00	-	-	-

Sources: [13, 15, 23,25,33,38 and 39].

Health Risk Assessment:

In this review study, an assessment on human health risks has been conducted by the process of comparing the levels of the heavy metals found in the total soft muscles/tissues of clam species (Table 1) with the food criteria set by different countries heavy metals standard limits (Table

2). Cadmium is one of the most environmental contaminants which can promote serious damage to the human health. It was observed that Cd levels within the lowest safety limits (1.01–2.00 μg/g) may be due to the fact that most of those samples sites were within the vicinity of agricultural areas of mostly large oil palm plantations heavy in pesticides and herbicides used [10,41], although the levels are within the second (2nd) highest safety standard limits (2.01–5.00 μg/g). On the other hand, Cd levels within the highest safety limits (5.01–10.00 μg/g) may be due to the Influence of external discrete sources like industrial activities, agriculture runoff, and other anthropogenic inputs [48, 49]. From this study, it is revealed that Cd may cause possible toxicological risks and heavy metal related diseases, such as Parkinson's and Wilson's diseases [14], due to long term consumption especially for the population of Kampung Sungai, Berembang (Perlis), PulauKetam (Perlis), and PantaiRemis (Perak).

Lead (Pb) is also one of the environmental contaminants. It was observed that Pb levels in clam species from more than 50% sites are below the safety limits (Table 1) but those from Sungai Sarawak (Sarawak) and Sekinchan and Kuala Selangor (Selangor) are within the lowest safety limits (2.01–6.00 μg/g) which indicated that these sites are slightly polluted. Only three (3) clam species from PantaiRemis (Selangor), Sungai Sepang (Selangor), and PantaiRemis (Perak) are within the highest safety limits (6.01–11.50 μg/g) set while Pb levels in clams from six (6) sites mentioned earlier exceeded all of those safety standard limits (Table 2) and this maybe resulted from burning of fossil fuels from boats used for fishing and leisure activities [44, 50]. This may be the cause of neurological deficits such as mental retardation in children and kidney disease such as interstitial nephritis to adults and also contribute to hypertension and cardiovascular disease [35], to the consumers in these coastal areas after long term consumption.

Nickel normally occurs at very low concentrations in the environment and it can cause variety of pulmonary adverse health effects [9]. The levels of Ni in clams from Sungai Sepang (Selangor), PantaiRemis (Selangor), KampungPasir (Johor), ParitJawa (Johor), and PantaiRemis (Perak) were higher than 5.00μg/g (Table 1). The causes may be that of human activities such as metal mining, smelting, refining, fossil fuel combustion, and solid waste disposal are the significant sources of this metal discharge to the environment and large amount may be transferred to marine

environment through municipal sewage effluent containing industrial waste [1, 26, and 50]. Ni has no definite safety limits but high valuesmay lead to serious health problems, including respiratory system cancer, and it can also cause a skin disorder known as nickel-eczema [30].
Copper (Cu) is an essential nutrient and is necessary for the synthesis of hemoglobin[52]. And its deficiency can result in blood and nervous system disorders [46]. It was observed that Cu in clams fromall sites was below the safety limits (Table 1) indicating that it should not pose an acute toxicological risk to the consumers. But Cu only in *Polymesodaexpansa* from KampungPasir, Johor, exceeded the maximum permissible limits set by Malaysian Food Regulation[25], (Table 2). This higher value may come from the paddy field activities where pesticides are used to prevent the insects' attack [49, 50] and can cause liver and kidney disease [12] and it may lead to stunted human growth due to long term consumption [28].

Zinc (Zn) is also an important metal in human nutrition and fulfills many biochemical functions in human metabolism. Zinc deficiency in human organism leads to several disorders, but an excessive Zn intake can cause acute adverse effects [17]. However, Zn value in calms from six (6) sites is within the lowest safety limits (100.01–250.00μg/g) indicating that these sites may be close to boating activities, fish landing, restaurants, and sightseeing view place [49], while Zn in clams only from KampungPasir (Johor) and Sungai Sepang (Selangor) is above the lowest safety limit but below the highest safety limits (667.01–750.00 μg/g). This may be from antifouling paint and incidental discharges of fuel, oil from boats, ship, and also municipal sewage [32], because Zn has been used as an anticorrosion agent and its ability to get speedy oxidation might enhance the level of zinc in these two sites. This will lead to a tendency in the organism to accumulate the high amount of Zn in its soft tissue [41]. In addition these sites are all in the vicinity of ports busy with navigational activities and cargo handling particularly petroleum and petroleum products [10]. Thus, high levels of zinc result in decreased cytochrome oxidase activity in the heart and liver as well as catalase in the liver [34], due to long term consumptions.

Iron (Fe) is an essential nutrient metal required for human but its deficiency is frequently associated with anemia [2, 23]. Smelting and refining of metals, steel manufacturing, and metal plating that mobilized iron by human activities may lead to the Fe contamination in marine environment [1]. However, very high values of Iron (Fe) were observed in clams from Telok Mas 1 (Malacca), Kampung Pasir (Johor), ParitJawa (Johor), and Sungai Sepang (Selangor) which was 1912, 1454, 1307, and 1111 μg/g, respectively [50]. It has no definite safety limits like other metals but very high values due to the tendency of Iron (Fe) to bind with organic matter in marine environment [33, 34], and also from those human activities. In this study, it was found that the levels of metal slightly depend on species (Table 1). It was evidenced that different organisms display a range of capacities for the accumulation of metals, varying from accumulators to accumulators of certain elements [13, 36, 43 and 50]. Although, the bioavailability of contaminants in the environment is complicated issue which involves many chemical, physical, and biological factors[38, 53], the use of the soft tissues of different clam species might provide a better insight into the bioavailability of metals. On the other hand, it was observed that the levels of metal mostly depend on site locations (Table 1). However, according to Malaysian Food Regulation [25], about 30% sites are safe from Cd contamination while more than 50% sites are safe from Pb contamination.

CONCLUSION

In the present study of review article, it was found that the clam species from different sites of study area accumulated heavy metals content at different concentrations. It was also observed that the concentrations of heavy metals slightly depend on different clam species but mostly depend on the particular site location. The results revealed that the clams species from mentioned sites have higher values than the food safety limits which should be avoided in order to control and safeguard any possible toxicological risks and heavy metals related diseases, such as Parkinson' disease (Brain disorder), Wilson's disease (Inherited disorder), and Hallervorden-Spatz disease (Neurodegenerative disorder), which may probably occur subsequent to the long term consumptions of certain particular clam species. On the other hand, according to Malaysian Food Regulation [25], about 30% and more than 50% different sites are safe from Cd and Pb contamination, respectively, and also the fresh or marine water clam species from the other population of researchers were safe and very clean for consumptions without any additional hindrances.

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