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REVIEW

Health risks of heavy metals in the mediterranean mussels as seafood

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Abstract In recent years, mussels have already become commercially important seafood species worldwide. Mussels accumulate a wide range of metals in their soft tissue. Thus, the determination of accumulated concentrations of heavy metals, such as Pb, Cd, Hg, and As, in mussels is essential because of their usage as seafood and the potential adverse effects of their consumption on human health. In this review, these issues are presented and discussed using the Mediterranean mussel *Mytilus galloprovincialis* as an example. *M. galloprovincialis* is very efficient at converting low value victuals into high quality animal protein. The production of *M. galloprovincialis* in Mediterranean countries has been increasing rapidly, but Spain is still the largest producer of mussels. Only China has a larger production of these mussels than Spain. *M. galloprovincialis* is a filter feeding animal and accumulates a wide range of metals from their environment. The metal concentrations in the soft tissue of *M. galloprovincialis* are indicators of marine ecosystems contamination. In the same time, the bioaccumulation of heavy metals remains an issue concerning the consumption of mussels. Thereby, the Cd, Pb, Hg, and As concentration measurement in mussel soft tissue as a seafood have become significant. A review of literature data revealed large variations in the Cd, Pb, Hg, and As concentrations in *M. galloprovincialis* from their endemic areas, e.g., Mediterranean, Adriatic, and Black Sea, and the concentrations of these toxic metals were generally in the following order: As > Pb > Cd > Hg. The guidelines on heavy metals for seafood safety set by different countries and associations are reviewed. Comparison of the published data with European legislation showed that the levels of the heavy metals generally did not exceed the existing limits in all the mussels analyzed, excluding mussels from hot spots, such as lagoons and harbors, in the Mediterranean, Adriatic, and Black Sea.

Keywords Mediterranean mussel · Seafood · Heavy metals · Risks · Human health

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Introduction

This manuscript is a abridged version of our chapter published in the book Environmental Chemistry for a Sustainable World (Stankovic et al. 2011a, b), which is related to the distribution, biology, and ecology of the Mediterranean mussel, properties and sources of the heavy metals, bioaccumulations and levels of the heavy metals in the mussel, such as their regulations, the mussel production, and health benefits and risks by their consumption.

The Mediterranean mussel *M. galloprovincialis* is raised mainly in the Mediterranean, and farming of this species is common along the coastlines in the Mediterranean region, (Ozden et al. 2010). The culture of *M. galloprovincialis* in the Black Sea region has recently been developing but is not yet widespread, (Karayucel et al. 2010). It is well known that the metal concentrations in the mussel *M. galloprovincialis* can provide a measure pollutants in marine environments, (Gorbi et al. 2008; Deudero et al. 2009; Fernández et al. 2010; Bartolomé et al. 2010; Jovic et al. 2011a; Joksimovic and Stankovic 2011), and information of direct ecological significance (Costas-Rodríguez et al.

2010; Tsangaris et al. 2010; Joksimovic et al. 2011) and potential relevance to human health (Culha et al. 2008; Stankovic et al. 2011a, b; Jovic et al. 2011b). Through feeding, mussels accumulate a wide range of Pb, Cd, Hg, and As from coastal waters. The levels of these heavy metals in mussels are important because of their negative effect on human health, but on the other side, seafood is a major source of animal protein and very rich sources of mineral components, (Fuentes et al. 2009; Ozden et al. 2010). The health benefits associated with the consumption of seafood products are particularly important for the prevention of heart-related diseases (Christophoridis et al. 2009). Although consumption of these mussels provides proteins, essential minerals, and vitamins, and thus, some protection from certain diseases, the risks and benefits of their consumption are still hard to assess. Accumulation of toxic metals to above permissible limits in *M. galloprovincialis* would certainly create a notorious food image from the public health point of view, as it is well known that chronic exposure to heavy metals, such as Cu, Pb, and Zn, is associated with Parkinson's disease and the metals might act alone or together over time to cause the *disease*, as well as other health problems (Gorell et al. 1997). Zn appears to have a protective effect against the toxicities of Cd and Pb, and its toxicity is rare (Sivaperumal et al. 2007). As(V) causes damage to the heart and blood vessels cells (Luong and Rabkin 2009). A link between traditional food sources high in Cd and diabetes has been postulated in Australian Aborigines (Satarug et al. 2003), and high Cd concentrations have also been associated with prostate cancer (Vinceti et al. 2007), while high Hg and low Zn concentrations have been linked to autism (Yorbik et al. 2004). Although the consumption of these mussels provides proteins, essential minerals, and vitamins, and thus, some protection from certain diseases, *e.g.*, myocardial infarction (Yuan et al. 2001), the relative risks and benefits of seafood consumption are hard to assess (Whyte et al. 2009), since mussels as filter feeders are known to bioacumulate Cd, Pb, Hg, and As from their surrounding environment, accumulated in mussels can also be accumulated in the food chain and to accumulate with time in the human body, causing health problems (Malik et al. 2010).

The Mediterranean mussel: *Mytilus galloprovincialis*

The Mediterranean mussel is known from classical texts of Greek antiquity and their use in diet and medicine by humans in the Mediterranean coastal areas (Voultsiadou et al. 2010). The Mediterranean mussel, *M. galloprovincialis*, is endemic to the Mediterranean Sea, the Adriatic Sea, and the Atlantic Ocean from Ireland to Morocco (Gosling 1992). The Mediterranean mussel is a warm-water invasive species (Branch and Steffani 2004), frequently transported by human activities (Anderson et al. 2002). From its source in the Mediterranean, *M. galloprovincialis* has colonized the sea waters of China, Korea, southeast Australia, Hawaii, Mexico, California, the west and east coast of Canada and arrived in South Africa (Branch and Steffani 2004). It is known that *M. galloprovincialis* is able to out compete and displace native mussels and has become the dominant mussel species in certain localities because *M. galloprovincialis* may grow faster than native mussels (Branch and Steffani 2004). Thus, *M. galloprovincialis* is both ecologically invasive and a source of "genetic pollution" that may threaten the genetic integrity of a native mussel species over much of its geographic range (Hilbish et al. 2010).

It is dark blue or brown to almost black. In its native range, *M. galloprovincialis* can be found from exposed rocky outer coasts to sandy bottoms. Only the Mediterranean mussel occurs on open coasts, while all other kind of mussels are restricted to bays and estuaries (Carlton 1992). The Mediterranean mussel tends to grow up to 15 cm, although typically only 5–8 cm. A 5-cm long mussel can filter 5 L water/h. While mussels grow to optimum size in sea water of temperature 15–25°C, their biological activities are decreased over 25°C. They are resistant to 5–40‰ salinity, but the optimal degree of salinity is between 20–35‰ (Braby and Somero 2006). The mean density in the most crowded beds may reach 24,000 mussels/m^2 (Voultsiadou et al. 2010). Mussels feed on organic matter and phytoplankton and can move with the aid of a foot. The foot of a mussel is an important organ because it enables the mussel to attach itself by byssus threads to a solid substrate. Byssal attachment is an important, sometimes critical, factor in mussel aquaculture (Beaumont et al. 2007). The two main reproductive cycles of *M. galloprovincialis* vary greatly according to geographic region and are characterized by one or two major spawning events per year, in spring and autumn, but depending on environmental temperature and food availability, mussels may spawn just once or several times each year (Beaumont et al. 2007). Immediately after the reproduction process, a mussel can lose up to 70% of its soft tissue (Cossa 1989). The sexes are separate in mussels, but there are no morphological differences between males and females (Beaumont et al. 2007). Factors such as water temperature, nutrient availability, and the reproduction cycle of mussels can influence meat yield and biochemical composition of these mussels (Vernocchi et al. 2007). Meat weights can approach 50% of the total wet weight when the mussels are in their best condition. When a large percentage of the mussels are close to spawning or just past spawning, harvesting should be postponed until they are in better condition.

As mussels feed by filtering large amounts of water, mussels are known to have a high capacity for metal accumulation, as reported in various National and Regional mussel monitoring programs (Stankovic et al. 2011a, b), making them potentially very dangerous for consumers. Therefore, strict metal controls are required in order to guarantee the safety of the product. Cd, Pb, Hg, and As are non-biodegradable inorganic chemicals that cannot be metabolized and do not break down into harmless forms (Kromhout et al. 1985). The measurement of their concentration in mussel soft tissue has become increasingly significant, and the regional program called the Mediterranean Mussel Watch (MMW) was established for the detection of radionuclides and trace contaminants in sentinel organisms using the mussel *M. galloprovincialis* as the bioindicator species in the coastal waters of the Mediterranean and Black Sea (Rodriguez y Baena and Thébault 2006).

Heavy metals

All metals are potential toxins at some concentration for humans, but Cd, Pb, Hg, and inorganic As are particularly toxic at relatively low doses. People consuming very frequently mussels with a high accumulation of one or more of these considered toxicants could be exposed to health risks. These heavy metals accumulated in the human body with time might act alone or together over time causing different health problems or diseases. Metals may accumulate in marine organisms up to levels, which may affect the mussels directly affecting their quantity and quality. Moreover, because the heavy metals are potentially detrimental to human health, their presence can limit the quantity of mussels' humans can consume (Stankovic et al. 2011a, b; Jovic et al. 2011b; Joksimovic et al. 2011). In addition, the heavy metals concentrations in the mussels *M. galloprovincialis* are used as an indicator of marine pollution (Joksimovic and Stankovic 2011; Jovic et al. 2011a; Stankovic et al. 2011a, b). The major routes of exposure of the general population to heavy metals almost always follow the cyclic order: industry, atmosphere, soil, water, fish, and humans (Suseno et al. 2010). The variability of these heavy metals concentrations in marine organisms depends on many factors, either environmental, such as metal concentrations in sea water, temperature, salinity, dissolved oxygen, pH, or purely biological *i.e.*, species, tissues, organs, feeding conditions (Sunlu 2006). The Mediterranean Mussel Watch program suggests that a dominant source of heavy metals contamination is from urban and industrial activities and less important inputs are from continental and agricultural origins (Sunlu 2006).

The heavy metals, such as Cd, Pb, Hg, and As, have no known biological function in organisms and exert their toxicity by competing with essential metals for active enzyme or membrane protein sites. Moreover, *Mytilus* species are able to synthesize the metal-binding protein, metallothionein, for metal detoxification (Kohler and Riisgard 1982). For example, the main routes of aqueous Cd uptake in aquatic organisms are via the gills or gut; subsequently, it binds to low-molecular-weight proteins metallothioneins and accumulates in the liver and kidneys, making Cd difficult to extract (Widmeyer et al. 2004). The general population is exposed to Pb through food, water, and air. Absorption of Pb from ingested food and water greatly depends on the levels of other element present in the diet, such as calcium, iron, and zinc. It was shown that dietary deficiencies in these essential elements enhance Pb absorption (Goyer 1995). The main source of Hg in the diet is fish. Hg accumulated in the tissues of seafood usually takes the form of Me-Hg, which is largely responsible for the accumulation of Hg in organisms *i.e.*, bioaccumulations, and the transfer of Hg from one trophic level to another *i.e.*, biomagnifications. Bioaccumulated organic Hg is more toxic to higher organisms, including humans, than inorganic Hg. Hg can affect productivity, reproduction, and survival of coastal and marine organisms and the population living near the coast and on islands runs a greater risk of ingesting this highly toxic substance (Kehrig et al. 2006).

In *Mytilus* species, metals are likely to be absorbed from water and from ingested phytoplankton and other suspended particles, and a Me–Hg to total Hg ratio of about 40% in the Mediterranean mussel was reported (Mikac et al. 1996). Mussels presented higher Hg and Me-Hg concentrations in their soft tissues than oysters, but they accumulate less Me–Hg than fish and hence apparently present a smaller risk to human consumers (Claisse et al. 2001). This is possibly related to their capacity to select particle size and composition of the ingested food they assimilate. On other hand, in estuarine and coastal environments, various environmental factors, including pollutant input, salinity, temperature, and food availability, can vary widely. These external factors are known to influence metal bioaccumulation in organisms (Suseno et al. 2010).

As is an element that occurs naturally in seawater and rocks of the Earth and commonly is used in industry of pesticides, herbicides, and insecticides. Arsenic in an environment is increasing at a rate to suggest potential public health risks (Luong and Rabkin 2009). In some areas, the concentration of As in water can attain levels of 1 mg/L, while in seawater, the concentration ranges from 2.0 to 4.0 μg/L (Devesa et al. 2008). These high concentrations are either due to the presence of As-rich rocks and minerals in aquifers or of anthropogenic contributions (Devesa et al. 2008). In water, As occurs in both inorganic and organic forms (Stankovic et al. 2011a). The form of As in water depends on pH, organic content, suspended solids, dissolved oxygen, and other variables. The inorganic forms of As are the most toxic, whereas most organic forms are considered non-toxic (Sloth and Julshamn 2008). Seafood is known to be the most significant source of As in the diet and, consequently, the total human intake of As depends on the quantity of seafood consumed (Stankovic et al. 2011a; Jovic et al. 2011b). Both organic and inorganic As compounds are absorbed almost completely in the gastro-intestinal tract and predominately eliminated from the body via the kidneys as urine (Sloth and Julshamn 2008). The majority of As in seafood is present in the organic arsenobetaine, less toxic form (Shiomi 1994). The percentages of inorganic As in seafood are 1–5%, while in bivalve mollusks, they are 1.9–6.5%, and mussels contain approximately 1–2% of inorganic As compounds (Sloth et al. 2005). The potential risks associated with the consumption of arsenobetaine containing seafood seem to be minor (Sloth and Julshamn 2008). The literature results indicate that arsenobetaine and As(V) are the dominate species in dry seafood products, while all other As species are present in relatively low concentrations (Cao et al. 2009). The International Agency for Research on Cancer classifies As as a carcinogenic agent for humans–category 1 (Sirot et al. 2009).

In *M. galloprovincialis*, heavy metals such as Cd, Pb, Hg, and As can be absorbed from water and from ingested phytoplankton and other suspended particles. These toxic metals can accumulate with time, becoming an ever greater toxic threat as their concentrations increase, but it should be noted that for some toxic elements, such as Cd and Hg, *Mytilus* species are able to synthesize the metal-binding protein for their own detoxification, metallothionein, neutralizing the harmful influences of exposure to them. Since it is edible and marketed commercially, the determination of heavy metals levels in mussel species provides a means of assessing the possible toxicant risk to public health. The mussel, *M. galloprovincialis,* is well known to accumulate a wide range of metals in their soft tissue. Pb, Cd, As, and Hg are widely distributed in coastal environments, from both natural geological processes and anthropogenic activities. Some metals, such as Cd and Pb, have long been known to accumulate within the aquatic food chain and mussels can simply accumulate metals through time (Mubiana and Blust 2007). They are good bioindicator for Cd, Pb, Hg, and As (Szefer 2002). The distribution of contaminants in mussel organs is known to vary as a result of the differing affinities of pollutants for binding sites and the different rates of pollutant accumulation in and excretion from tissues (Fernández et al. 2010). It has been reported that metals such as Hg, Cd, and Pb accumulate in mussels more rapidly and to a greater extent in the gills than in tissues, such as the mantle, muscle, or digestive gland, while the digestive gland and mantle tissues accumulate higher levels of organic pollutants than gills (Fernández et al. 2010). In addition, the spawning season of the mussels and environmental factors may contribute to the wide variability of pollutant metal concentrations in the total soft tissues of mussels (Yap et al. 2006).

Heavy metals accumulations by the Mediterranean mussel

Several studies demonstrated the presence of significant seasonal and spatial variations of the content of heavy metals in the total soft tissue of the Mediterranean mussels. The Cd, Pb, As, and Hg concentrations determined in the soft tissues of the Mediterranean mussels, *M. galloprovincialis*, mainly in last decade all over the world where exist are given in Fig. 1, including the sites and the years of sampling, such as the corresponding bibliographical references (Stankovic et al. 2011a, b). Metal concentrations are given in mg/kg dry wt. Some concentrations were determined over several years and others result from several samples in a single year. However, some metal concentrations are given with respect to the fresh weight in the original references such as: Sunlu (2006), Klaric et al. (2004), Ünlü et al. (2008), and Ozden et al. (2010). The data from the period 1991–2009 are grouped by countries and seas in order to enable the easiest comparison of the concentrations of the toxic metals (Stankovic et al. 2011a, b). Since *M. galloprovincialis* are aqua cultured and collected from the Mediterranean and Atlantic coast of Spain and France, from Adriatic and Greece, from Italy—Adriatic and Mediterranean, and in the last 10 years from Turkish coasts, the concentrations of Cd, Pb, Hg, and As are primarily compared for these regions in the reference (Stankovic et al. 2011a, b).

Some large variations in the Cd, Pb, Hg, and As concentrations in *M. galloprovincialis* from this extensive analyzed region were observed due to the different ages, feeding behaviors, and different geographical areas with different natural and anthropological impacts. Important factors that modulate the bioavailability and tissue burden of these heavy metals include fluctuations of temperature, phytoplankton blooms and organic matter, the presence of nutrients, waters fluxes and circulation, up-welling phenomena, freshwater inputs, and also intrinsic species-specific features, such as the phase of reproductive cycle and the associated changes in the relative tissue composition (Fattorini et al. 2008).

The concentration results of heavy metals, Cd, Pb, and Hg, in the investigated mussels were of the same order of magnitude in the case of the Spanish Atlantic and the Mediterranean coast, but significantly higher concentrations were observed in the case of As, especially in Galicia, Cantabria, and the Basque Country, as well as in mussels

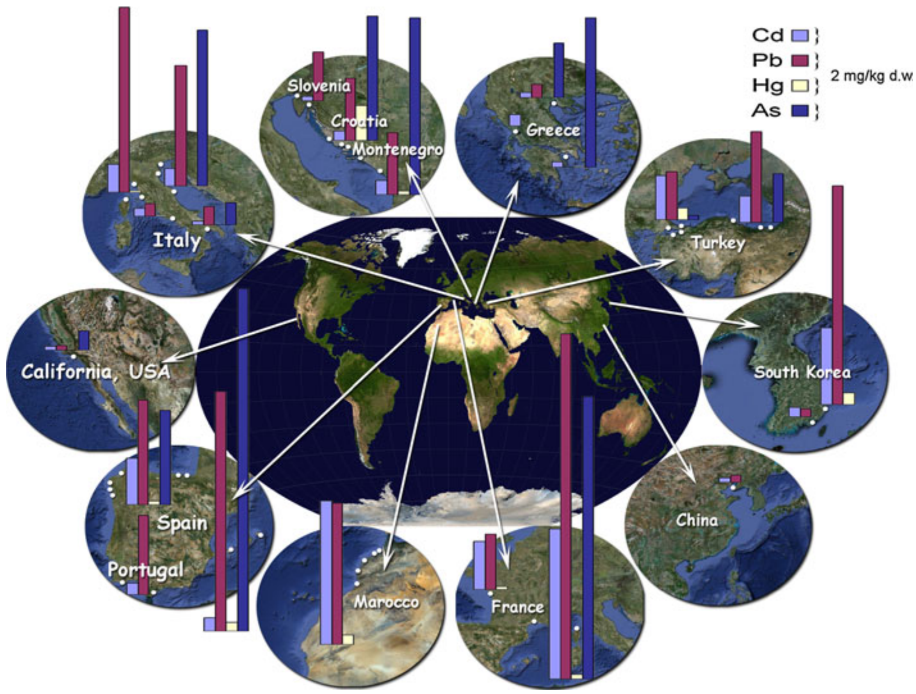

Fig. 1 Heavy metals distributions in *M. galloprovincialis* over the world including hot spots (Stankovic et al. 2011a, b)

from Spanish Mediterranean coast (Bartolomé et al. 2010; Fernández et al. 2010). The temporal variation had no specific trend, and the concentrations were quite constant over a wide range of sites and during time on both sides of the Spanish coastline. The highest mean concentrations were found for As, between 13 and 25.6 mg/kg d.w., in the mussel from both Spanish coastlines, the Atlantic and the Mediterranean. Lower mean concentrations were found for Pb, mainly between 2.0 and 5.0 mg/kg d.w., and Cd, between 0.4 and 2.0 mg/kg d.w., and the lowest were found for Hg, between 0.05 and 0.35 mg/g d.w (Bartolomé et al. 2010; Fernández et al. 2010). Significant downward trends were observed for the concentrations of Pb and Hg in mussels from a large number of sampling stations along the coast of Spain, while the Cd concentrations in the mussels showed upward trends (Benedicto et al. 2003). The mean concentrations of Pb in mussels were lower than those determined in previous studies that were performed in the same area. The concentration of excess Pb in marine organisms is directly linked to human activities (Besada et al. 2002). A study of the spatial distribution of chemical contaminants realized using mussels allowed the identification of clear hot spots along the Spanish coastline (Fattorini et al. 2008). Along the French Mediterranean coast, the Cd concentrations were in the same order of magnitude as in the open sea and in lagoons (mean value: 1.1 mg/kg), with the exception of one lagoon with concentrations of up to 4.5 mg/kg. The Hg background level was stable and below 0.1 mg/kg with high levels in some lagoons (0.15 mg/kg) (Andral et al. 2004, 2007). The Pb background level was 1.13 mg/kg, with extreme values in one lagoon (4.86 mg/kg) and in the coastal waters of large urban areas (3.5 mg/kg), but the mean As value was 20 mg/kg (Andral et al. 2004, 2007). It is oblivious that the concentrations of As, Pb, Cd, and Hg in *M. galloprovincialis* from the Mediterranean part of Spain were higher on average than those in the mussels from the Mediterranean coast of France (Stankovic et al. 2011a, b). The mussels along the Spanish Mediterranean coast were collected in May–June 2003, in the pre-spawning period (Fernández et al. 2010), while those from the French Mediterranean coast after the spawning period, in July 2000 (Andral et al. 2004). In the case of Atlantic coast, the mussels from Spanish and French waters contained similar concentrations of these metals (Stankovic et al. 2011a, b). It is interesting to note that the mean concentrations of As, Cd, and Hg were generally higher in mussels from the Mediterranean coast, but the Pb concentration was lower than in the mussels from the Atlantic coast (Stankovic et al. 2011a, b). Exceptions were mussels from some "hot spots" on the Mediterranean coast, in which very high concentrations of Pb were found, whether they were from the French or Spanish coast (Stankovic et al. 2011a, b). The overall trends observed along the French coasts for 1979–1999 confirmed decreasing values for Cd and Pb, while for Hg, the local decreases were about twice (Stankovic et al. 2011a, b). In both cases, on the French and Spanish coastal areas, the pollutant metal concentrations in the mussel *M. galloprovincialis* were in the order: As $>$ Pb $>$ Cd $>$ Hg (Stankovic et al. 2011a, b).

The results for the heavy metal concentrations in the whole edible soft tissues of mussels from the Spanish and French regions are also compared with the results of studies from different locations of the Mediterranean Sea, such as Italian, Hellenic, and Turkish coastal regions (Stankovic et al. 2011a, b), since they are producers of this mussel. The mean concentration of Pb in mussels from the Ionian Sea, Italy, was higher than in mussels from the Tyrrhenian Sea in Italy, but the opposite was true for the Cd concentrations (Stankovic et al. 2011a). Results from the northern Adriatic Sea in Italy showed higher levels of Cd, Pb, and As, when compared with studies from the Ionian Sea and Tyrrhenian Sea (Stankovic et al. 2011a). Mussels from the Italian Adriatic coast have higher Cd and Pb levels than mussels from the eastern part of the Adriatic Sea at hot spots (Stankovic et al. 2011a, b). The highest concentrations of As, Pb, and Cd in mussels from the northern Adriatic Sea could be correlated to the industrial development of the Venetian region over the last 20 years and the impact of the River Po (Licata et al. 2004). From 1986 to 2003, the Italian National Mussel Watch showed national decreasing trends of the Cd concentrations in mussels, but other trace metals exhibited only local or regional variations with trends in the concentrations in bivalves more or less evenly split between increases and decreases (Fattorini et al. 2008).

Quite limited data are available for the As concentrations in Mediterranean mussels. The results obtained in the investigation of Stankovic et al. (2011a, b) generally indicated higher values of As in Adriatic mussels (Stankovic et al. 2011a; Jovic et al. 2011b; Joksimovic et al. 2011), than in organisms from unpolluted sites of the French and Spanish Mediterranean and the Tyrrhenian coasts, except two hot spot locations with high levels of As on the Mediterranean Spanish and French coast (Stankovic et al. 2011a, b). The highest measured As levels are in the mussel from the Adriatic and Aegean Sea, and the lowest in the mussel from the Marmara and Black Sea (Stankovic et al. 2011a, b). The high level of As in the mussels of the eastern Adriatic could be explained by the exhibited high concentrations of As (1–19 mg/kg) found in the sediments of the southern Adriatic (Dolenec et al. 1998).

Basal levels of trace elements in mussel can also exhibit geographical differences, such as those related to site-specific geological or environmental features. Well-known examples include the Hg anomaly in the Tyrrhenian Sea, which is responsible for the elevated bioavailability of this element (Fattorini et al. 2008). The total Hg values in the Mediterranean and the Marmara Sea (Bosphorus) species were generally higher than those found in the Atlantic (Stankovic et al. 2011a, b). The levels Hg in mussel from the French and Spanish Mediterranean coast, including hot spots, are in the range, 0.02–1.24 and 0.03–2.21 mg/kg d.w., respectively, while in the Atlantic and Adriatic Sea, they are in the range, 0.01–0.88 and 0.02–0.50 mg/kg d.w., respectively (Stankovic et al. 2011a, b). Only on the eastern Adriatic coast, there were two hot spots with high levels of Hg in the mussels in Croatia, Kastela Bay (Kljakovic-Gaspic et al. 2007) and in Montenegro the harbor Bar (Stankovic et al. 2011a, b). In the Marmara Sea, *M. galloprovincialis* from Bosphorus Asian and European side had very high levels of Hg, 1.03–2.94 and 0.14–2.86 mg/kg (Kayhan 2007). The higher Hg levels are deemed to be the result of the region being in the Mediterranean—Himalayan mercuriferous belt (Shoham-Frider et al. 2002).

In mussels from the Turkish seas, the highest levels of Cd and Hg were found in mussels from the Bosphorus and Cd concentrations in the soft tissue of *M. galloprovincialis* from the Bosphorus were high and in general displayed significant variation from station to station (Kayhan et al. 2007). From Bosphorus European and Asian side, there were very high concentrations of Cd up to 8.95–10.68 mg/kg d.w (Kayhan et al. 2007), which are similar to the Cd levels in mussels from the French Atlantic coast, up to 11.70 mg/kg d.w. (Deudero et al. 2007). Along the Turkish coastline, the highest Pb concentrations were found in mussels from the eastern Black Sea, up to 22.0 mg/kg (Çevik et al. 2008).

It could be concluded that the highest concentrations of Cd and Pb were found in mussels from hot spots on the French and Spanish Mediterranean coast, up to 36.2 mg/kg d.w. and 83.2 mg/kg d.w., respectively. Mussels from the Adriatic Sea, Croatia, had the highest concentrations of Hg, up to 8.58 mg/kg d.w, than mussels from the Atlantic coast, Mediterranean and Black Sea, but again at hot spots (Stankovic et al. 2011a). Generally, the levels of Cd, Pb, and Hg were the lowest in mussels from the Aegean Sea, compared to the others investigated seas, but a very high level of As was found in Aegean Sea. Generally, Hg was present in low concentrations; higher average Hg levels were observed in *M. galloprovincialis* from the Marmara Sea, Bosphorous (Stankovic et al. 2011a, b).

In Mediterranean mussel from the all investigates Seas, the concentrations of these pollutant metals were in the following order: As $>$ Pb $>$ Cd $>$ Hg (Stankovic et al. 2011a, b).

Despite the considerable seasonal and inter-annual variations, data on the heavy metal concentrations in *M. galloprovincialis* presented in Stankovic et al. (2011a, b) are generally within the range of mean values more recently reported for Mediterranean mussels sampled or translocated in unpolluted sites of the French coast, the NW Mediterranean, the Spanish Mediterranean coast, the North Tyrrhenian Sea, the North Aegean Sea, the Turkish Aegean Sea, the Black Sea, and the Croatian coast, if the hot spots would be excluded. Most of the examined metals showed a seasonal decrease in July and the highest values in February and April (Stankovic et al. 2011a, b). A similar seasonal trend was described by other authors (Nesto et al. 2007).

The Mediterranean mussel as seafood

The world aquaculture production has grown tremendously over the past 50 years. The world production of mussels, including both, aquaculture and wild harvest production, is given in Fig. 2 (FAO 2006). China is the largest producer of mussels, including aquacultured and wild harvested mussels, 67.3%, and Western Europe contributed with 4.2% and rest is from the other world regions Fig. 2 (FAO 2006).

In the last 20 years, the world production of cultivated mussels has been almost 100% higher than that of wild harvested mussels. Denmark is the only country that still produces very large quantities of wild harvest mussels and Spain is by far the greatest producer of mussels by aquaculture in Europe (FAO 2006). In Europe, the production of cultivated mussels is almost five times higher than wild collected mussels. The Mediterranean mussel *M. galloprovincialis* (L.) is mainly cultured in coastal waters from NW Spain to the northern shores of the Mediterranean Sea. The production of the mussel *M. galloprovincialis* in Spain contributes approximately 25% to the total world production (over 200,000 t year^{-1}); only China has a greater production (about 600,000 t year^{-1}) (Costas-Rodríguez et al. 2010). The Mediterranean mussel farming and harvesting has an important economic impact in many Mediterranean countries. In Spain, mussel is the principal seafood product, while in Italy, this mussel is harvested, which represents more than 75% of the total shellfish production (Vernocchi et al. 2007). *M. galloprovincialis* has been cultivated in French Mediterranean lagoons. The French mussel industry produces around 60,000 t on a yearly basis, with 13% from Mediterranean coast (Prou and Goulletquer 2002). Expansion of *M. galloprovincialis* mariculture in the Mediterranean occurs in areas of Greece and Turkey, *i.e.*, in areas of the Aegean Sea, and also Marmara and the Black Sea (Stankovic et al. 2011a, b). In the last 20 years, the contribution of European countries to the total world production of mussels has decreased due to increased production outside Europe and space limited extension of mussel culture in traditional areas of Europe. Mussels produced in Europe are predominantly consumed within Europe (Smaal 2002).

Regulations

The interactions between the seas and human health are increasing, in part, due to the increasing numbers of humans living within close proximity of the world's seas. The necessity for monitoring metal pollution of coastal waters is therefore important worldwide from the commercial and resource sustainability points of view. Contamination of seafood by toxic contaminants from coastal waters represents a serious threat to human health and is a major economic concern. In order to protect the health of seafood consumers, many countries and associations have set guidelines for the maximum permissible levels of toxic pollutants in seafood. Mussel culture is regulated by EU directives with regard to quality for the consumer in terms of pathogenic bacteria, biotoxins and chemical contaminants (Stankovic et al. 2011a, b). The sanitary quality and level of contaminants are monitored according to national rules, based on EU directives, but not in all countries. Different countries and world associations defined legal

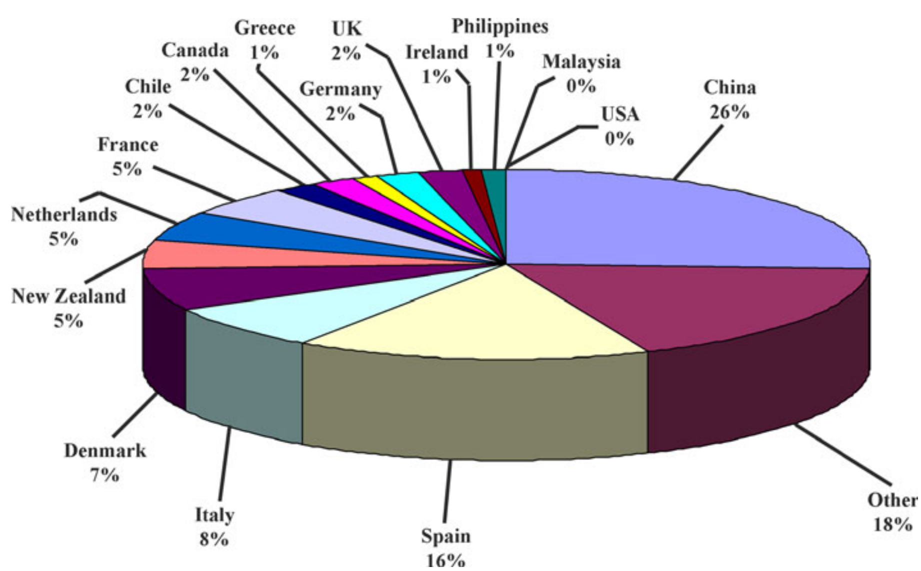

Fig. 2 Share of world production of mussels of all species, including both aquacultured and wild harvested production. The shares are calculated as the average for each country during 1997–2001 (FAO 2006)

limits on permissible concentrations of Cd, Pb, Hg, and As in mussels on a dry or wet weight basis. To prevent health risk from exposure to pollutant trace elements, the European Commission established in the past years maximum levels permitted for Cd, Pb, and Hg in seafood (EC 2006). The guidelines on the heavy metals for seafood safety set by different countries and associations were reviewed in Stankovic et al. (2011a, b): the defined legal limits on permissible concentrations of Cd, Pb, Hg, and As, that are toxic in traces, in mussels on a wet weight basis in mg/kg are in the ranges for Cd from 0.1–4.0; for Pb from 1.0–6.0; for Hg from 0.05–10 mg/kg and for As from 0.5–86 mg/kg. The values of Cd, Pb, Hg, and As in the mussel from Mediterranean were generally much lower than the limits established for mussel consumption by the regulation (EC 2006; Stankovic et al. 2011a, b). The analyzed Provisional Tolerable Weekly Intake (*PTWI*) values appear to support the conclusion that risk to human health from dietary exposure to the investigated elements from the Mediterranean mussels is relatively low (Stankovic et al. 2011a, b). People consuming large amounts of contaminated mussels may have elevated concentrations of the pollutant trace elements in their tissues compared to the general population. Comparison of the published data in Stankovic et al. (2011a, b) with European legislation showed that the levels of Cd, Pb, and Hg generally did not exceed the existing limits in all the mussels analyzed, excluding mussels from hot spots, such as lagoons and harbors in Mediterranean, Adriatic, and Black Sea. Overall, the assessment in this work indicates that the investigated toxic elements may pose a health risk to pollutant mussel consumers, especially related to the levels of Pb and Cd in *M. galloprovincialis* from hot spots in the all investigated Seas (Stankovic et al. 2011a, b).

Impact of mussel consumption to human health

By 2002, fish fisheries and aquaculture products contributed 12% to the total protein for human consumption, although there are no detailed global statistics on the provision of other essential minerals and components, (FAO 2006). The total content of minerals in raw marine fish and invertebrates is in the range of 0.6–1.5% wet weight (Ozden et al. 2010). An epidemiological study in Japan showed that seafood was the largest source of vitamin B6 (16–23% of the total intake) and B12 (77–84%) in the diet (Yoshino et al. 2005). Many species of fish and shellfish are rich sources of Omega 3 fatty acids (Ackman 2000), and the health benefits associated with the consumption of seafood products are particularly important for the prevention of heart-related diseases, for bone mineral density and for children development and growth (Cozzolino 2001; Zalloua et al. 2007; Christophoridis et al. 2009).

In *M. galloprovincialis*, proteins contribute about 60% to the dry weight of the soft tissues (Karayucel et al. 2003). Mussels are very important for marine ecology and for the human diet. They are a cheap source of proteins and essential minerals, Ca and Fe, and vitamins, such as niacin, thiamine, and riboflavin, for human consumption (Amiard et al. 2008; Fuentes et al. 2009; Ozden et al. 2010). They are very important components in human diets as their deficiency and excess may cause serious health problems. All metals are potential toxins at some concentration and the heavy metals, such as Hg, Pb, Cd, and As, are particularly toxic at relatively low concentrations (Çevik et al. 2008). The toxicity effect of heavy metals in living marine organisms was recognized after tragic events of the Minamata and Itai-itai poisoning cases, with Hg and Cd, respectively, which erupted in Japan around the middle of the 20th century (Malik et al. 2010). These tragic Japanese incidents spurred research on the fate and impact of metals in marine environments and their negative effects on human health. These non-essential elements, such as Cd, Pb, Hg, and As, are non-biodegradable chemicals that do not have any positive effects on organisms and are harmful already at low doses. They cannot be metabolized into harmless forms and accumulate with time in the human body and might act alone or together over time to cause the disease, as well as other health problems. Thus, people consuming mussels could be exposed to these potentially dangerous to health metals. Cd, a metal with high toxic effects, which is strongly bioaccumulated in mussels, has an elimination half-life of 10–30 years and accumulates in the human body, particularly the kidney (Amiard et al. 2008). Cd may act as an acute and chronic type of poison. In chronic exposure, the first sign is kidney damage, usually diagnosed by increased excretion of low-molecular-weight proteins (Widmeyer et al. 2004). Over time, Cd can accelerate osteoporotic process, suggesting the role of Cd in development of bone softening due to decalcification, a characteristic of ltai-itai disease (Han et al. 2000). Absorbed Pb is bound to erythrocytes in the blood and initially distributed to the liver, kidney, and heart, where it preferentially binds to cell membranes and mitochondria (Widmeyer et al. 2004). Most forms of Pb are then distributed and stored in the bones. Pb is known to cause both acute and chronic adverse effects in the hematopoietic, nervous, gastrointestinal, and renal systems (Widmeyer et al. 2004). Acute poisoning causes gastrointestinal colic, often resulting in mortality, while chronic poisoning causes anemia due to a decrease in the hemoglobin levels leading to organs damage (Gilbert 2004), but Pb is not-carcinogenic (Chang 1996). Hg and Me-Hg are highly toxic and extremely damaging to cellular and tissue function (Crinnion 2000; Fleisher 2001). Both forms of Hg are immunotoxic, although they differ quantitatively and qualitatively in their effects on the immune system. Me-Hg accumulates mainly in the kidneys, liver, and brain (Fleisher 2001). Elemental Hg may accumulate in the brain, lungs, fatty tissues, kidney, liver, and digestive tract. Over time, Me-Hg accumulates and is slowly converted into inorganic Hg (Crinnion 2000). As inorganic Hg, it binds to sulfur-containing molecules, such as hemoglobin in the blood and the powerful antioxidant glutathione, thus depleting their levels. The increased danger associated with Me-Hg is that it can also have a direct effect on cells without being converted into the inorganic Hg form. Both forms of Hg affect the following systems: nervous system, cardiovascular system, immune system, and reproductive system (Crinnion 2000; Fleisher 2001). The effects of As, mainly caused by inorganic As, may produce inhibition of growth, skin discoloration, respiratory problems, or even death (Eisler 1994). As(III) compounds are bound by red blood cells and affect the activity of many enzymes, particularly those involved in the respiratory process (Eisler 1994). There are a number of potential mechanisms by which As affects tissues that might lead to cell death, but intracellular calcium or enzyme systems regulated by calcium may alter the toxicity of arsenate (Luong and Rabkin 2009). Organic As neither causes cancer nor is it thought to damage DNA, but exposure to high doses may result in nerve injury and stomach problems (Eisler 1994). Adverse health effects, for example, may involve the respiratory, gastrointestinal, cardiovascular, and hematopoietic systems and may range from reversible effects to cancer and death, depending partly on the physical and chemical forms (Luong and Rabkin 2009).

Conclusions

A review of literature data related to the concentrations of Cd, Pb, Hg, and As in *M. galloprovincialis* from their endemic areas, *e.g.*, Mediterranean, Adriatic, and Black Sea, revealed that the concentrations of these toxic metals were in the following order: As > Pb > Cd > Hg. The levels of Cd, Pb, and Hg were the lowest in mussels from the Aegean Sea, compared to the others investigated Seas, but a very high level of As was found. Levels of Pb, Cd, Hg, and As in the mussel are of the same order of magnitude in the Atlantic, Mediterranean, the Adriatic, Aegean, and Black Sea regions. The highest values of heavy metals in *M. galloprovincials* were in the hot spots of the urban areas, near the mouth of rivers, harbors, and lagoons of the Mediterranean and Atlantic coast, such as in the Bosphorus European and Asian side and the Izmir Bay in the Aegean Sea. If the mussels from the hot spots are excluded, in this whole native region of *M. galloprovincials*, all the investigated metals were not of great health concern, including As, which is present in mussels mostly in the organic form, which is not toxic to humans. Some large variations in the Cd, Pb, Hg, and As concentrations in *M. galloprovincialis* from their endemic regions were observed probably due to different age, feeding behavior, natural impacts, anthropological impacts, and geographical areas, as well as factors that modulate the bioavailability of these toxic metals: temperature fluctuation, waters fluxes and circulation, freshwater input, phytoplanktonic blooms and organic matter, the presence of nutrients, and the phase of reproductive cycle.

As the Black Sea and the Mediterranean Basin will potentially be the largest producers of the Mediterranean mussels in the future, health of the mussel consumers will depend on integrated management of the land and nearshore components of the coastal zone. Human health impacts caused by the consumption of contaminated seafood were nearly always related to the quality of the environment where the aquaculture products were produced or harvested. For this reason, it is important to provide sustainable management of shellfish harvesting waters and, simultaneously, maintain public health. The production and management of cultivated mussels also require integrated work between health, food regulators, and environmental and the commercial and casual exploiters of mussel resources.

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