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Mercury in aquatic fauna contamination: A systematic review on its dynamics and potential health risks

Paloma de Almeida Rodrigues¹, Rafaela Gomes Ferrari^{1,2}, Luciano Neves dos Santos⁴,
 Carlos Adam Conte Junior^{1,2,3,*}

1. Molecular and Analytical Laboratory Center, Department of Food Technology, Faculty of Veterinary, Universidade Federal Fluminense, Niterói, Brazil

2. Chemistry Institute, Food Science Program, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

3. National Institute of Health Quality Control, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil

4. Laboratory of Theoretical and Applied Ichthyology, Department of Ecology and Marine Resources, Universidade Federal do Estado do Rio de Janeiro, Rio de Janeiro, Brazil

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ABSTRACT

Mercury is an important pollutant, released into aquatic ecosystems both naturally and by anthropogenic action. This element is transferred to aquatic organisms in different ways, causing potential health risks. In addition, mercury can be accumulated by humans, especially through the consumption of contaminated food. This systematic review aims to present mercury pathways, the major routes through which this element reaches the aquatic environment and its transformations until becoming available to living animals, leading to bioaccumulation and biomagnification phenomena. The key biotic and abiotic factors affecting such processes, the impact of mercury on animal and human health and the issue of seafood consumption as a source of chronic mercury contamination are also addressed. A total of 101 articles were retrieved from a standardized search on three databases (PubMed, Emabse, and Web of Science), in addition to 28 other studies not found on these databases but considered fundamental to this review (totaling 129 articles). Both biotic and abiotic factors display fundamental importance in mediating mercurial dynamics, i.e., muscle tropism, and salinity, respectively. Consequently, mercurial contamination in aquatic environments affects animal health, especially the risk of extinction species and also on human health, with methylmercury the main mercury species responsible for acute and chronic symptomatology.

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* Corresponding author. E-mail: carlosconte@id.uff.br. (Carlos Adam Conte Junior).

Contents

| | |
|--|-----|
| Introduction | 206 |
| 1. Material and methods | 208 |
| 1.1. Focus questions | 208 |
| 1.2. Information sources | 208 |
| 1.3. Risk of bias assessment | 208 |
| 2. Results | 208 |
| 2.1. Mercury bioaccumulation and biomagnification of mercury influence factors | 209 |
| 2.2. Bioaccumulation and magnification in different tissues | 210 |
| 2.3. Mercury in animal health | 211 |
| 2.4. Dynamics of mercury in the human body | 212 |
| 2.5. Risk of consumption of seafood contaminated by mercury | 212 |
| 3. Conclusions | 214 |
| Acknowledgments | 214 |
| References | 214 |

Introduction

Aquatic systems comprise a complex network of relationships between biotic and abiotic factors, each playing a fundamental role in the food web organization (or structure). In this sense, one of the most important concerns regarding the ecological integrity of aquatic environments is contamination by toxic elements, especially Mercury (Hg). This non-essential metal is extremely toxic and widespread through aquatic ecosystems. Its presence occurs both due to natural causes, such as weathering, atmospheric volcano emanations, continental degasification and Hg evasion from the oceans, as well as anthropological drivers, such as mining, chlor-alkali industry, paint factory and metallurgical activities, dental residues and mineral coal burning of (Azevedo et al., 2011, 2012; Balshaw et al., 2007; Condini et al., 2017; Delgado-Alvarez et al., 2014; Díez, 2009; Harayashiki et al., 2018; Hintelmann, 2010; Hossenli et al., 2013; Hutcheson et al., 2014; Kojadinovic et al., 2006; Murphy et al., 2007; Onsanit and Wang, 2011; Ruus et al., 2015; Sadhu et al., 2015; Ward et al., 2010).

Mercury may occur in three forms in nature, such as elemental mercury (Hg^0); inorganic mercury, mainly in the form of mercuric (HgCl_2 , HgS) and mercurous (Hg_2Cl_2) salts; and organic forms, such as ethyl ($\text{C}_2\text{H}_5\text{Hg}^+$) and methylmercury [(CH_3Hg^+)] (Azevedo et al., 2011; Balshaw et al., 2007; Bjørklund et al., 2017; Díez, 2009; Hong et al., 2012; Rice et al., 2014; Sunderland and Selin, 2013). Elemental mercury is liquid at room temperature and highly volatile, often released as a vapor into the atmosphere. As a result, it may be transported over large distances, and deposited and sedimented, either directly or through rainfall in the oceans (Bjørklund et al., 2017; Park and Zheng, 2012; Rice et al., 2014; Sadhu et al., 2015; Sunderland and Selin, 2013). Elementary mercury may also undergo oxidative processes, in addition to combining with elements such as chlorine, sulfur or oxygen, thus becoming inorganic mercury. The, ethylation process can change inorganic mercury to its organic form (Fig. 1) (Bjørklund et al., 2017; Hintelmann, 2010; Hong et al., 2012; Murphy et al., 2007; Park and Zheng, 2012; Rice et al., 2014; Sadhu et al., 2015; Sevillano-Morales et al., 2015; Sunderland and Selin, 2013).

Mercury is able to accumulate in animal tissues, leading to the phenomenon of bioaccumulation. Its concentrations may increase throughout high trophic levels, with animals at the top of the food web presenting higher concentrations than those in lower trophic levels. This trophic biomagnification phenomenon occurs because the organic form of mercury, Methylmercury (MeHg), is more bioavailable than other forms, and is quickly absorbed and slowly excreted. In aquatic animals, this absorption occurs through branchial respiration and, mainly, feeding (Arcagni et al., 2018; Azevedo et al., 2011, 2012; Belger and Forsberg, 2006; Chen et al., 2018; Díez, 2009; Hintelmann, 2010; Ruus et al., 2017; Mallory et al., 2018; Panichev and Panicheva, 2014; Rice et al., 2014; Ruus et al., 2015; Sevillano-Morales et al., 2015; Taylor and Calabrese, 2018; Voegborlo et al., 2011; Ward et al., 2010; Zhang et al., 2012; Zmozinski et al., 2014). As aquatic biota presents a direct relationship with the environment, MeHg can be used as a bioindicator of the presence of mercury (Condini et al., 2017; Kehrig et al., 2011; Taylor and Calabrese, 2018). The persistence of this metal in the aquatic environment affects both animal and human health (Dadar et al., 2016; Díez, 2009; Ha et al., 2017; Hong et al., 2012; Hutcheson et al., 2014; Ruus et al., 2017; Murphy et al., 2007; Park and Zheng, 2012; Rice et al., 2014; Sheehan et al., 2014; Sevillano-Morales et al., 2015; Taylor and Calabrese, 2018; Zmozinski et al., 2014).

MeHg is generated by the action of sulphate-reducing anaerobic bacteria that methylate the metal present in the surface layers of aquatic sediments (Bisi et al., 2012; Evers et al., 2008; Gilmour and Henry, 1991; Hintelmann, 2010; Roman et al., 2011; Ruus et al., 2015; Taylor and Calabrese, 2018). Estuarine and coastal environments, due to anthropogenic action, undergo accelerated rates of methylation. This is due to the constant presence of inorganic Hg, favorable abiotic conditions (e.g., anoxia, high levels of organic material and sulphates) and active bacterial communities (Chen et al., 2018; Fitzgerald et al., 2007; Taylor and Calabrese, 2018). In such favorable conditions, when pellets contaminated with inorganic Hg are resuspended, they are methylated and dissolve in the water. Aquatic organisms are, thus, highly exposed to dissolved MeHg, accumulating this contaminant in their

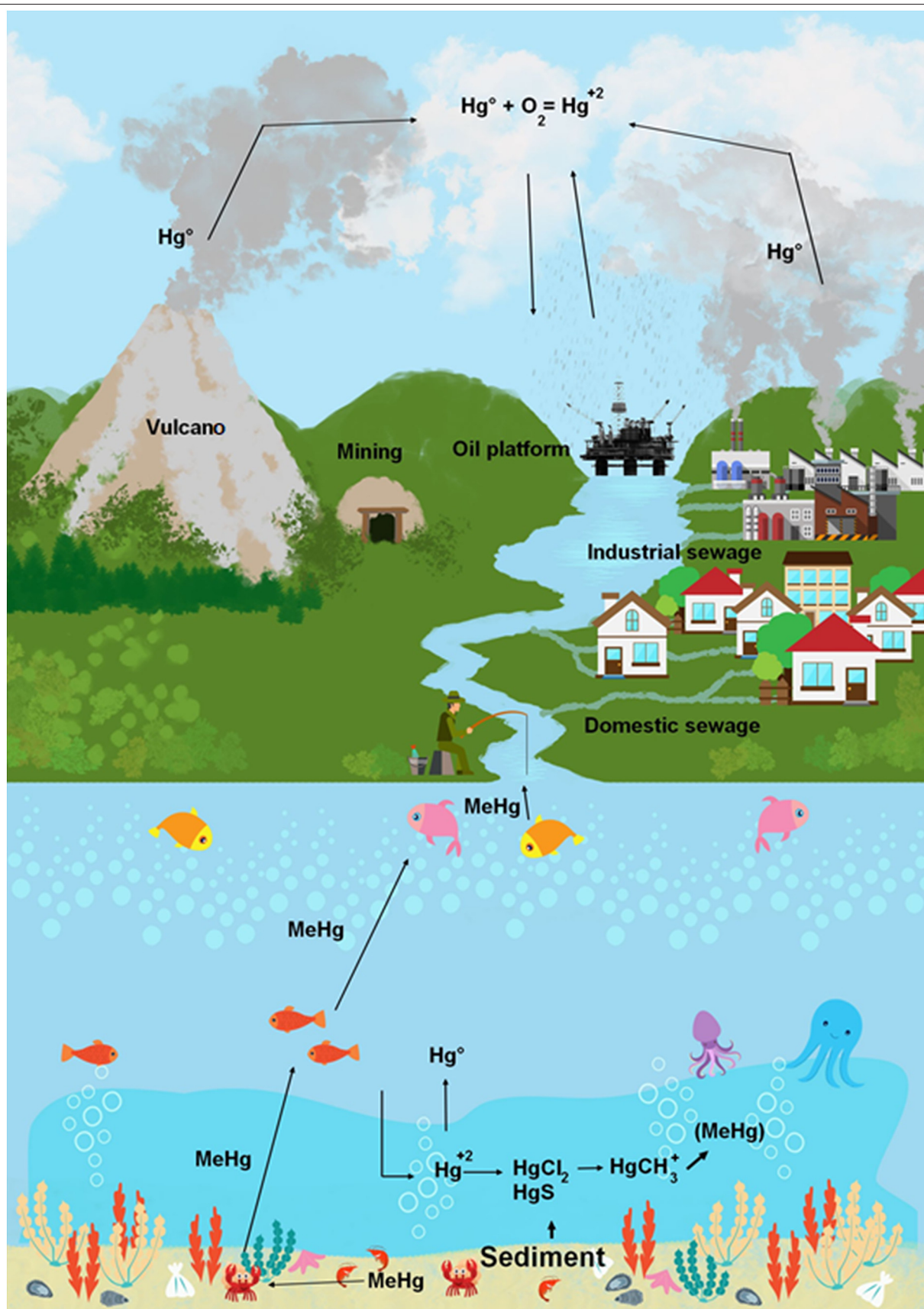


Fig. 1 – Mercury cycle. Mercury can be released by atmospheric volcano emanations, mining, chlor-alkali industry, paint factory and metallurgical activities, mineral coal burning, and domestic and industrial sewage. Hg° is highly volatile, being released into the atmosphere as vapor, and being transported over large distances and deposited directly or through rainfall in the ocean sediment. It may then undergo oxidative processes (Hg^{+2}), in addition to combining with elements such as chlorine, sulfur or oxygen, thus becoming inorganic mercury (HgS , HgCl_2). Subsequently, the methylation process by the action of sulphate reducing bacteria gives rise to the organic form of mercury in the sediment (HgCH_3^+ / MeHg).

tissues, and, mainly, in their muscle tissue, the main edible portion in human consumption (Arcagni et al., 2018; Bisi et al., 2012; Ruus et al., 2017).

MeHg is considered a potent neurotoxic compound, with glial cell predilection, inducing oxidative stress and neuroinflammation. This can also adversely affect the genome, reproduction and various body systems in both humans and animals (Arcagni et al., 2018; Bjørklund et al., 2017; Chen et al., 2008; Hong et al., 2012; Rasinger et al., 2017; Rice et al., 2014; Schoeman et al., 2009; Sevillano-Morales et al., 2015; Sheehan et al., 2014). Therefore, the contamination of aquatic organisms by mercury is of concern both ecologically and in a public health context (Evers et al., 2008; Ha et al., 2017; Hintelmann, 2010; Hosseini et al., 2013; Hutchesson et al., 2014; Ruus et al., 2017; Kütter et al., 2009; Mallory et al., 2018; Murata et al., 2011; Murphy et al., 2007; Sevillano-Morales et al., 2015; Zmozinski et al., 2014). Mercury, when ingested, is released from the alimentary matrix into digestive fluids, followed by absorption by the intestinal epithelium. However, not all released mercury is absorbed. Thus, the term “bioavailable” refers to the concentration of the pollutant that is, in fact, ready to be absorbed. MeHg bioavailability Hg is generally lower than that of inorganic mercury. Concerning food habits, herbivores, detritivores, and omnivores display overall less mercury bioavailability than carnivores (He and Wang, 2011).

The purpose of this systematic review is address the main issues related to mercury contamination of aquatic animals, through a refined search carried out on three research platforms (Embase, PubMed, and Web of Science). The different mercury forms are evaluated, with focus on the factors that affect their bioaccumulation and biomagnification, their affinity with different animal tissues, their effects on animal health, and, finally, the effects of mercury contamination on human health and risks to seafood consumers.

1. Material and methods

Following four sequential stages, two authors (P.A.R. and R.G.F.), first conducted the preliminary selection of identified abstracts and paper titles, independently. Abstracts were then removed in this initial screening if the papers did not investigate the association between animal/matrix (seafood) and the presence of mercury. The search was limited to English and the date delimitation was set as between 2005 and 2018. Editorials, letters, and Ph.D. theses were excluded. Some studies considered essential to compose the revision that was not included in any of the research bases were added, such as those that address illnesses that mercurial intoxication causes in human and animals. These articles were added later and are fundamental, not only because of the differential content addressed but also because of the impact of the journal in which they were published. Finally, regarding the risk of intoxication due to seafood consumption, studies and legislation concerning this subject were also added. The results are reported in agreement with the Preferred Reporting Items for Systematic Review and Meta-Analyses statement (PRISMA).

1.1. Focus questions

The question was developed according to the population, intervention, comparison, and outcome (PICO) method. The following questions were formulated: what are the abiotic and biotic factors that interfere in mercury bioaccumulation and bioaccumulation, and how does this occur? Which animal tissue displays the greatest affinity for the accumulation of this metal among different aquatic species? How does mercury affect human and aquatic animal health?

1.2. Information sources

A literature search was performed using Medical Subject Headings (MeSH) terms on the Pubmed, Web of Science, and Embase databases. The initial screening process was performed from January to April 2018. Further directed searching was also carried out by checking the reference list of relevant articles.

Search Component 1 (SC1) – Population search: Seafood Or Marine fish Or shellfish OR Batrachoidiformes OR catfishes OR Characiformes OR Cypriniformes OR eels OR Elasmobranchii OR Esociformes OR flatfishes OR Gadiformes OR hagfishes OR Osmeriformes OR Perciformes OR bass OR perches OR sea bream OR tuna OR Salmonidae OR Beloniformes OR Cyprinodontiformes OR Tetraodontiformes OR Takifugu OR “Aquatic food Chain.”

Search Component 2 (SC2) – Intervention search: Mercury OR Methylmercury OR “Organic Mercury.”

After retrieving the Search Component results, the boolean operator “AND” was used to combine SC1 and SC2.

1.3. Risk of bias assessment

Possible sources of bias include: inclusion/exclusion criteria, the impact of missing data, missing primary results.

2. Results

A total of 2138 articles were identified at PubMed, 931 at Embase and 334 at Web of Science, totaling 3403 papers. Of these, 1069 were duplicates or triplicates and excluded. A total of 2334 remained after exclusion of repeated papers. After reading the titles and abstracts, only 101 papers were adequate for the purpose of the study, since they dealt with both environmental and animal health aspects, as well as the risk of mercury contaminated seafood consumption (Fig. 2). Priority was given mainly to articles that presented differential information, such as the influence of abiotic factors (e.g., the relation of pH, organic matter and climate in the dynamics of the mercury in the aquatic environment) on mercury methylation and bioaccumulation and biomagnification processes. Most papers dealt with these aspects and discussed the same topics but did not provide consolidated explanations or additional information compared to other papers that deserved attention, so they were discarded. A further 28 articles were added in addition to those found on the research platforms. Some of these documents were used to fill in the

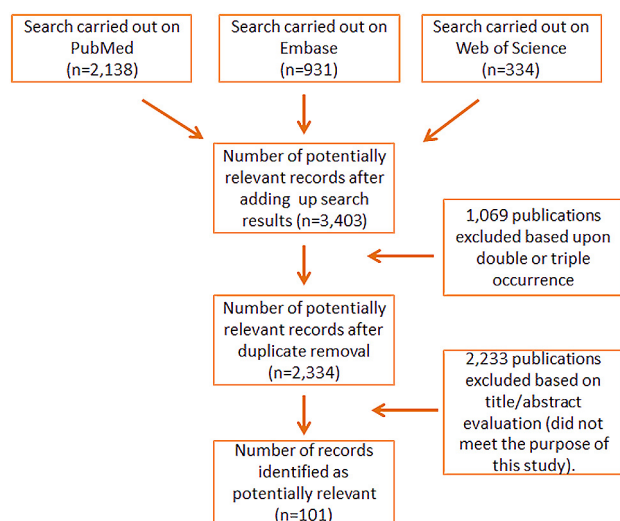


Fig. 2 – Flow diagram displaying the results of the literature search (PubMed, Embase, Web of Science).

lack of explanations of other articles selected in the databases, such as those that addressed the clinical aspects of mercurial intoxication. Additional documents were included those that covered the limits allowed by international authorities regarding the mercury content in seafood and the tolerable permission for weekly intake.

2.1. Mercury bioaccumulation and biomagnification of mercury influence factors

The greatest concern about mercury in seafood is related to the presence of methylmercury. This compound, in addition to bioaccumulating in human and animal tissues, also undergoes biomagnification processes, thus increasing thus concentrations in animals belonging to higher trophic levels (Ando et al., 2010; Auger et al., 2005; Azevedo et al., 2012; Ruus et al., 2017; Panichev and Panicheva, 2014; Sadhu et al., 2015; Sevillano-Morales et al., 2015; Taylor and Calabrese, 2018). Bioaccumulation and biomagnification processes can be affected by both biotic and abiotic and ecological factors, such as age, size, sex, growth rate, trophic position, food web size, population density, position in the water column, water pH, organic matter richness, oxygen saturation, salinity and temperature (Arcagni et al., 2018; Boyd et al., 2017; Chasar et al., 2009; Chen et al., 2018, 2014; Chouvelon et al., 2017; Evers et al., 2008; Henderson et al., 2012; Ruus et al., 2017; Matulik et al., 2017; Panichev and Panicheva, 2014; Reinhart et al., 2018; Sadhu et al., 2015; Taylor and Calabrese, 2018; Tuomola et al., 2008).

In relation to animal size, weight, and age, researchers indicate that larger and heavier animals tend to bioaccumulate more mercury than smaller animals, as well as animals who live longer, which are, consequently, exposed to mercury sources for longer, thus accumulating more mercury (Belger and Forsberg, 2006; Bergés-Tiznado et al., 2015; Bosch et al., 2016; Khoshnamvand et al., 2013; Murphy et al., 2007; Ordiano-Flores et al., 2011; Pethybridge et al., 2010; Sackett et al., 2013;

Sadhu et al., 2015; Sevillano-Morales et al., 2015; Souza-Araujo et al., 2016; Storelli et al., 2006; Teffer et al., 2014; Tuomola et al., 2008; Watanabe et al., 2012).

Regarding sex, differences in accumulation of males and females are expected, mainly due to metabolic differences and dietary characteristics. It is expected that females, in order to meet the reproduction demands, would present higher mercury concentrations due to the increase in food consumption during the reproductive period (Murphy et al., 2007). However, several studies indicate no statistical difference regarding Hg bioaccumulation between sex. Usually, the difference tends to be related to other factors, such as species. For example, Madenjian et al. (2011), when studying a trout species, found that males presented higher Hg concentrations in relation to females. The researchers, although aware of the main cause, attributed this difference to the crude growth rates of a male being higher than in females. However, other studies report that, in some cases, a certain sex presented a greater tendency to bioaccumulate Hg, a fact probably related to animal physiology (Adams and Engel, 2014; Bastos et al., 2015; Endo et al., 2009; Kojadinovic et al., 2006; Licata et al., 2005; Murphy et al., 2007; Ordiano-Flores et al., 2011).

Regarding growth rates, Arcagni et al. (2018), carried out a study in Nahuel Huapi Lake, Patagonia, on different seafood species with different eating habits. The authors observed that, due to the low temperature of the lake, the growth rate of the animals was slower, leading to greater bioaccumulation. Seafood with accelerated growth rates tend to present less Hg accumulation since they grow faster than they accumulate Hg, so a dilution of the concentration of this element with growth is observed (Arcagni et al., 2018; Dong et al., 2016; Dsikowitzky et al., 2013).

Climatic conditions can also affect mercury concentrations. Seasonality will influence not only water temperature and processes, but also alter the centesimal composition of the animal muscle, the tissue with the highest affinity for Hg. Among these changes, protein content, to which MeHg is strongly bound, is the most affected, resulting in shifts in the concentrations of this element in the animal organism (Murphy et al., 2007). Metabolism acceleration also leads to greater mercury excretion and, consequently, decreased accumulated concentrations (Ando et al., 2010). In contrast, higher temperatures directly favor mercury methylation processes in the environment, as well as indirectly, through the reduction of dissolved oxygen, thus generating a favorable anoxic environment for this process (Chen et al., 2018; Murphy et al., 2007; Pack et al., 2014).

Trophic level and food web length are positively correlated, i.e., the higher the trophic level and the larger the food web, the greater the biomagnification process (Azevedo-Silva et al., 2016; Chen et al., 2014; Costa et al., 2008; Dsikowitzky et al., 2013; Evers et al., 2008; Karouna-Renier et al., 2007; Ruus et al., 2017; Maggi et al., 2009; Panichev and Panicheva, 2014; Sadhu et al., 2015; Taylor and Calabrese, 2018; Teffer et al., 2014). Hg⁰ and MeHg, formed in the sediments, are primarily captured directly through benthic infauna gills and by feeding on sediment deposits. Moreover, mercury can also be absorbed through the water column by organisms belonging to different trophic levels, by the advection, diffusion or desorption of resuspended sediments. Indirectly, mercury

and methylmercury acquisition occur through transfer, namely predation, between trophic levels (Chen et al., 2014; Hosseini et al., 2013). However, the efficiency of direct uptake of the MeHg present in the medium through gills is low, approximately seven-fold lower than compared to food intake (Chen et al., 2014). This underscores the importance of mercury acquisition through the food chain, given that, among different mercury forms, MeHg is the best acquired and transferred along trophic levels (Chen et al., 2014). Animal diet also influences Hg concentrations, with carnivorous animals presenting higher Hg content than herbivores and detritivores (Balshaw et al., 2007; Costa et al., 2008; Hosseini et al., 2013; Ruus et al., 2017; Karouna-Renier et al., 2007; Panichev and Panicheva, 2014; Rasinger et al., 2017; Sadhu et al., 2015; Taylor and Calabrese, 2018; Teffer et al., 2014).

In the case of pH, acidic environments are more propitious for methylation, since Hg will be more bioavailable at lower pH values, leading to higher absorption by sulfate-reducing bacteria and, consequently, increased methylation (Dong et al., 2016; Wang et al., 2010). However, Dong et al. (2016) reported that advanced demethylation and volatilization activities of elemental Hg have been observed in this same acidic pH decreasing the methylation process. These findings indicate that the relationship between pH and Hg is complex and still requires further studies. The relationship between organic matter (OM) and Hg is also complex. Dong et al. (2016) found that the higher OM content in the sediment, the greater the methylation since this provides more carbon for sulfate-reducing bacteria. However, other studies have found that increases in dissolved water column organic carbon led to significant inhibition of organic mercury absorption, due to binding with carbon, leading to the reduction of Hg bioavailability. In contrast, its reduction increases methylmercury absorption rates up to two-fold. The opposite is also true, where the reduction of dissolved organic carbon leads to increases in Hg absorption, but lower methylation rates (Chen et al., 2014; Pickhardt et al., 2006; Wang and Wang, 2010; Wang et al., 2010).

Concerning salinity, it is expected that higher salinity environments will present lower total mercury concentrations. In addition, the methylation process is also reduced in marine water. This may occur due to the binding of the sulfide present in the salt water with inorganic mercury, making it less bioavailable for the methylation process (Reinhart et al., 2018). High salinity is also assumed to increase the amount of loaded inorganic mercury species ($\text{HgCl}^{-3}/\text{HgCl}_4^{-2}$) with respect to unloaded ones (HgCl_2). However, unloaded forms are easier to diffuse through the plasma membrane and reach bacteria cytoplasm, where methylation occurs, indicating that lower salinity environments are more prone to the methylation process. Salinity may also negatively interfere with the activity of sulfate-reducing bacteria, due to the increased sensitivity of some species to salinity (Boyd et al., 2017).

In relation to the position in the water column, New Zealand researchers observed that oceanic animals, living in the middle and basal zones, presented higher mercury content than those in the superficial zone, related to photoreduction of MeHg in Hg^0 occurring on the surface. In contrast, deep water presents higher decomposition rates and lower oxygen content, which contributes to methylmercury

production (Sadhu et al., 2015). Further research indicates that bioaccumulation in pelagic organisms is greater than in benthic organisms, suggesting that the fact that mercury persists in the water column may be more important in determining concentrations in higher trophic levels than what is acquired from the sediment. However, the important role of mercury in sediment plays is undeniable, indicating the need for further studies on the subject (Chen et al., 2014; Evers et al., 2008).

2.2. Bioaccumulation and magnification in different tissues

Studies indicate that THg is present almost 100% in the form of MeHg in animal tissues (Adams and Engel, 2014; Chen et al., 2008; Costa et al., 2008; Mallory et al., 2018; Onsanit and Wang, 2011; Souza-Araujo et al., 2016; Taylor and Calabrese, 2018; Wang et al., 2010; Watanabe et al., 2012). THg is distributed by affinity to certain tissues, particularly in muscle and liver (Adams and Engel, 2014; Azevedo et al., 2016; Murillo-Cisneros et al., 2018; Penicaud et al., 2017; Raimundo et al., 2010; Taylor and Calabrese, 2018; Turnquist et al., 2011).

Regardless of the animal species, several studies have compared mercury concentrations in muscle tissue to different organs, such as liver (Azevedo et al., 2016; Khoshnamvand et al., 2013; Le et al., 2010; Licata et al., 2005; Mallory et al., 2018; Murillo-Cisneros et al., 2018; O'Bryhim et al., 2017; Watanabe et al., 2012), hepatopancreas (Storelli et al., 2010), kidney, liver and skin (Pethybridge et al., 2010), digestive gland (Raimundo et al., 2010), shell (Turnquist et al., 2011), kidney, spleen, heart and epigonal organ (O'Bryhim et al., 2017), brain (Bastos et al., 2015), gills (Azevedo et al., 2016), ovary and eggs (Nowosad et al., 2018), and, in the study of Adams and Engel (2014) to all other tissues of a swimming crab (*Callinectes sapidus*). Most studies indicated higher concentrations of this metal in muscle. However, Turnquist et al. (2011) reported that, when comparing the shell and muscle tissue of a marine turtle, the shell presented higher Hg concentrations. The authors were not able to explain this result but suggested that the shell captures mercury accumulated over the years, while muscle mirrors recent contamination. Azevedo et al. (2012) and Hosseini et al. (2013) identified that Hg concentrations in fish liver were higher than those found in muscle and gills. Azevedo et al. (2012) suggested that this finding is related to the detoxification function of the liver, leading to a higher elemental turnover and higher Hg concentrations indicating recent contamination exposure, while muscle tissues could better represent long-term accumulation. Hosseini et al. (2013) suggest that higher liver concentrations are related to the high levels of the protein metallothionein present in this tissue, which plays a key role in Hg regulation and detoxification. This protein contains a high percentage of amino, nitrogen and sulfur groups that are used to sequester metals. In their study, the authors propose that lower muscle concentrations are related to the low concentration of metallothionein in this tissue, while gills acquire the metal present in the water.

It is known that muscle tissue presents lower metal clearance rates compared to other organs such as the liver, which can explain higher Hg concentrations in this tissue. In addition, the affinity of mercury for muscle tissue is also

related to the binding of MeHg to aminoacid thiol ligands that are, in turn, transported to muscle tissue. The liver, in contrast, presents high metal clearance rates, considering its detoxifying role, converting MeHg to less cumulative inorganic forms, and also contains high lipid content, which may affect tissue accumulation (Murillo-Cisneros et al., 2018; Onsanit and Wang, 2011).

On this subject, Raimundo et al. (2010) conducted a study with octopus (*Octopus vulgaris*) from three regions of the Portuguese coast, determining Hg and MeHg in the digestive gland and mantle. The digestive gland has the ability to absorb, assimilate and store Hg, and is an important detoxifying organ. As Hg metal enters the digestive gland, part is stored and then accumulated in the mantle. The authors identified that MeHg percentages were higher in the mantle compared to the digestive gland, due to higher metal clearance rates in the gland (Raimundo et al., 2010). Thus, most of the mercury found in the digestive gland is in its inorganic form, while the mantle muscle tissue harbors mostly the organic form (Penicaud et al., 2017).

Murillo-Cisneros et al. (2018) carried out a study on elasmobranchs (*Myliobatis californica*, *Pseudobatos productus*, and *Zapteryx exasperata*), to evaluate Hg content in liver and muscle tissue. Although the muscle tissue presents, in general, a higher amount of mercury compared to the liver, the liver accounted for higher Hg content in the largest elasmobranchs. The authors attributed their findings to differences in nutritional composition, energetic intake, ontogenetic changes in diet and the metabolic activity of this organ in larger animals.

Azevedo et al. (2016) evaluated four fish species (*Pimelodus fur*, *Pachyurus adspersus*, *Oligosarcus hepsetus*, *Pimelodella lateristriga*) concerning bioaccumulation in muscle and liver, and also studied the gills. Even if gills had a concentration of MeHg lower than muscle tissue and statistically the same as the liver, nevertheless concentrations were considered high and attributed to the close contact of the assessed species with contaminated sediment.

Regarding the difference between the type of muscle tissue, Bosch et al. (2016) carried out a study in Yellowfin tuna (*Thunnus albacares*) evaluating Hg concentrations (inorganic, organic and total). The results indicate that inorganic and total Hg concentrations are higher in dark muscle compared to white. A significant difference in concentrations (inorganic and total Hg) was also observed among dark muscles tissue. In contrast, MeHg concentrations did not vary significantly between dark muscle types and between dark and white muscle tissue. No significant variation for any form of mercury (organic, inorganic and total) was observed among white muscle tissue. The study suggests that the higher concentration noted in dark muscle may be related to the composition and development of muscle fibers. Additionally, the authors report that Hg tends to accumulate in higher amounts in the predominant muscle tissue of the animal, as well as in places where the muscle type is more developed. Finally, the study concluded that, in order to obtain reliable results concerning mercury toxicity, the ideal action when evaluating THg is to collect white muscle samples, since this muscle type presents less Hg variations. In contrast, dark muscle concentrations may lead to

overestimates concerning mercurial toxicity, as well as presenting greater Hg variations.

One study compared the mercury content in the musculature, ovaries, and eggs of European eel (*Anguilla anguilla*) (Nowosad et al., 2018). Although ovary and eggs had a lower concentration of mercury in the musculature, they found that after ovulation there was an increase in Hg content in these organs. After the second spawn, the mercury content increased again. The work explains that during gonadal maturation of the female, there is a transfer of proteins and lipids from the muscle to the gonads and a small amount of mercury is translated together. In eggs, the amount of the metal is relatively small, suggesting a protective mechanism against the transfer of Hg from the ovary to the oocyte. This mechanism is based on the fact that during vitellogenesis the proteins are transported with the vitellogenins to the egg, where it is used for the formation of the yolk, but due to the low sulfur content and a small number of sulfhydryl bonds, vitellogenins bind to MeHg, making the translocation of the element to the egg difficult.

2.3. Mercury in animal health

Mercury is not only a challenge in terms of environmental or human health, but it also significantly affects animal health (Balshaw et al., 2007; Bakar et al., 2017; García-Medina et al., 2017; Hassaninezhad et al., 2014; Hatef et al., 2011; Lepak et al., 2016; Macirella and Brunelli, 2017; Mallory et al., 2018; Rasinger et al., 2017; Van Hees and Ebert, 2017; Zhang et al., 2016). These studies confirmed that the accumulation of mercury in the animal organism leads to changes in lipid metabolism, cellular transport (Richter et al., 2011), behavioral changes, effects on gene expression and affect the growth and characteristics of plasma and blood (Lepak et al., 2016). They also identified circulatory disorders, gills hazards, and degenerative lesions in the liver and gonads (Naija et al., 2016; Safahieh et al., 2012; Zhang et al., 2016). Other researchers have observed significant alterations in antioxidant enzymes that induced oxidative stress and genotoxicity, leading to DNA damage and micronucleus formation (indicative of mutagenic action) (Garcia-Medina et al., 2017; Zhang et al., 2016) and changes in Na⁺/K⁺ ATPase expression standards and metallothioneins (MTs) (Macirella and Brunelli, 2017). Furthermore, these changes can occur from the embryonic period, leading to neurological changes, reducing fetal reproduction and success, causing morphological defects and increasing the mortality rate (Van Hees and Ebert, 2017). With regard to the neurological effects, they are the cerebral proteome disturbance, reduction of the global swimming activity due to the reduction of the number of coils of the tail, and reduction of the heartbeat, alteration of the shoaling and avoidance behavior of predatory animals. In addition to the motor impairment, the proteins, lipids, carbohydrates and nucleic acids of the larvae are also affected (Bakar et al., 2017; Rasinger et al., 2017). In relation to the reproductive system, they identified changes in sexual indexes and somatic-gonadal indices, inhibition of growth and development of gonads, disturbance of hormonal balance by interrupting the transcription of HPG (Hypothalamic Pituitary Gonadal) axis genes, and stimulation of sex change, decreased viability of

sperm, decreased sperm motility, decreased sperm motility, and decreased sperm motility (Hatef et al., 2011; Nowosad et al., 2018).

While MeHg has an affinity for binding to the erythrocyte, inorganic mercury binds to components of the plasma fraction of blood. Thus, the mobility and distribution of MeHg by the organism are more efficient than the inorganic form. The organic form is first concentrated in the liver and kidney and then it is distributed to other reservoirs. Inorganic Hg, with less mobility, is more concentrated in internal organs, being the first place of accumulation the gills. This forms a stable binding with mucoproteins present in the organ, which prevents mass diffusion of the element into the gill and entry into the circulatory system (Balshaw et al., 2007).

2.4. Dynamics of mercury in the human body

Elemental Hg comes into contact with the body primarily through inhalation, with exposure being very low through intestinal and dermal absorption. The absorption of Inorganic Hg (mercury salts) ranges from 7% to 15%, and occurs after ingestion of contaminated food, dental amalgam after abrasion, or can be absorbed via epidermis, sweat glands, sebaceous and hair follicles, when exposure occurs through the use of cosmetics containing mercury salts, topical medications or handling of agricultural products (Díez, 2009; Hong et al., 2012; Park and Zheng, 2012). As for the forms of exposure of elemental and inorganic mercury, they can be classified as acute or chronic. Acute exposure to elemental Hg occurs mainly in cases of occupational accidents, where a significant amount of the element is inhaled, leading to severe lung damage, including death due to hypoxia, as well as neurological symptomatology. In the case of chronic exposure, which is also usually occupational, the target organs of symptomatology are the central nervous system and kidney (Park and Zheng, 2012; Rice et al., 2014). Acute exposure to inorganic mercury, which occurs primarily through ingestion, is characterized by abdominal pain, hypotension, vomiting, acute respiratory distress syndrome, chest burn, severe gastrointestinal conditions due to extensive corrosive power (caustic gastritis), mercury stomatitis and renal failure. Dermal, can lead to dermatitis and corrosion of mucous membranes. Chronic intoxication occurs less frequently, mainly generating renal symptoms (Dias et al., 2016; Park and Zheng, 2012).

The main organic form of mercury, methylmercury, can be acquired by humans mainly through the ingestion of contaminated food, especially seafood, or even through the use of vaccines, which have the preservative thimerosal that is rapidly metabolized to Ethylmercury (Bjørklund et al., 2017; Conдини et al., 2017; Dórea et al., 2013; Hong et al., 2012; Krata et al., 2016; Rice et al., 2014; Rumbold et al., 2018; Ruus et al., 2017; Sadhu et al., 2015; Taylor and Calabrese, 2018). Its intestinal absorption is about 17 to 35 times faster than compared to the absorption of inorganic mercury and almost 100% of what is ingested, can be absorbed (Hong et al., 2012). Both ethyl and methylmercury present high liposolubility, easily crossing the blood and placental barriers, generating a neurological clinical condition that can be fatal, besides having an effect on the fetal development, immunological

and cardiovascular compromise (Björkman et al., 2007; Crowe et al., 2017; Díez, 2009; Dórea et al., 2013; Farina et al., 2011; Gutiérrez-Mosquera et al., 2017; Kuntz et al., 2010; Roman et al., 2011; Yin et al., 2017). During its metabolism, MeHg is converted to bivalence inorganic mercury and undergoes oxidation and reduction. Methylmercury releases oxygen radicals at decomposition and this causes severe damage to cells by activating the chain of lipid peroxidation of the cell membrane. It also compromises intracellular calcium and altering glutamate homeostasis (Farina et al., 2011; Hong et al., 2012).

The forms of exposure may also be acute or chronic. The first form is related to the intake of a large amount of such element and the latter form mainly related to long-term intake of contaminated food. In acute cases, blurred vision, hearing impairment, olfactory and gustatory disturbance, ataxic gait, psychiatric disorders, may lead to death. In chronic cases, paraesthesia of the extremities and lips, somatosensory disorders, reproductive disorders and cerebellar ataxia (Ekino et al., 2007). Regarding the effect of MeHg in cases of prenatal exposure, studies indicate that pregnant women who have a diet rich in seafood, especially of species with higher concentration of Hg, present the possibility that the child is born with neurological deficits (Bjørklund et al., 2017; Trasande et al., 2006). As for this prenatal exposure, a study was carried out in the German infant population born in 2014 with mental retardation due to methylmercury. In 98% of cases, there was a mild delay, while 2% had a severe some cases, with the individual's untimely death (Lackner et al., 2018).

2.5. Risk of consumption of seafood contaminated by mercury

The main route of mercury acquisition for humans is through the consumption of contaminated seafood, especially in the MeHg form, as mentioned previously. Monitoring of elemental concentrations in aquatic organisms used for human consumption is therefore of paramount importance. The organizations of each country, as well as organs related to health and food, then established the limits of Hg and MeHg in seafood (Table 1).

In addition to the established restrictions concerning Hg concentrations in seafood, global health organizations have developed an index to determine the safe limit of weekly Hg intake, called the Provisional Tolerable Weekly Intake (PTWI). This index is expressed on a weekly basis per kilogram of body weight and represents an estimate of the amount of mercury that can be consumed and bioaccumulated in the human body without presenting significant health risks. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) has determined the borderline value of 1.6 µg/kg of body weight for MeHg and 4 µg/kg of body weight for inorganic and total mercury (FAO, 2016). This value was established based on epidemiological studies concerning the effect of Hg on neonatal health when mothers were exposed to this metal (FAO, 2011). This value is set as is 1.3 µg/kg body weight for the European Food Safety Authority (EFSA)), for both forms of mercury. In addition, the organization recommends the maximum consumption of 3–4 portions and 1–2 weekly portions of seafood for adults and children, respectively

Table 1 – Types of seafood and their limits of mercury and/or methylmercury in different countries.

| Country | Seafood | Limits | Reference |
|-----------------|---|--|---------------------------|
| Australia | - Fish are known to contain high mercury levels, such as swordfish, southern bluefin tuna, barramundi, ling, orange roughy, rays, shark | - 1 ppm Hg/Kg | UNEP (2002) |
| Brazil | - All other fish species, crustaceans, and molluscs - Predators - Other non-predatory fish, crustaceans, molluscs, cephalopods, and bivalve molluscs | - 0.5 ppm Hg/Kg - 1 ppm Hg/Kg - 0.5 ppm Hg/Kg | Brasil (2013) |
| Canada | - All fish except shark, swordfish or fresh or frozen tuna (expressed as total mercury in the edible portion of the fish) - The maximum permissible limit for those who consume high amounts of fish, such as Aboriginal people | - 0.5 ppm THg - 0.2 ppm THg | UNEP (2002) |
| China | - Freshwater fish | - 0.3 ppm Hg/Kg | UNEP (2002) |
| Croatia | <i>Fresh fish</i> - Predatory fish (tuna, swordfish, molluscs, crustaceans) - All other fish species <i>Canned fish (tin package)</i> - Predatory fish (tuna, swordfish, molluscs, crustaceans) - All other fish species | - 1.0 ppm Hg/Kg and 0.8 ppm MeHg/Kg - 0.5 ppm Hg/Kg and 0.4 ppm MeHg/Kg - 1.5 ppm Hg/Kg and 1.0 ppm MeHg/Kg - 0.8 ppm Hg/Kg and 0.5 ppm MeHg/Kg | UNEP (2002) |
| European Union | - Fishery products, with the exception of those listed below - Anglerfish, atlantic catfish, bass, blue ling, bonito, eel, halibut, little tuna, marlin, pike, plain bonito, portuguese dogfish, rays, redfish, sail fish, scabbard fish, shark (all species), snake mackerel, sturgeon, swordfish, and tuna | - 0.5 ppm Hg/Kg wet weight - 1.0 ppm Hg/Kg wet weight | EU (2006) |
| Georgia | - Fish (freshwater) and Fishery products - Fish (Black Sea) - Caviar | - 0.3 ppm Hg/Kg - 0.5 ppm Hg/Kg - 0.2 ppm Hg/Kg | UNEP (2002) |
| India | - Fish | - 0.5 ppm THg | UNEP (2002) |
| Japan | - Fish | - 0.4 ppm THG/Kg and 0.3 ppm MeHg | UNEP (2002) |
| Korea | - Fish | - 0.5 ppm Hg/kg | UNEP (2002) |
| Philippines | - Fish (except for predatory species) - Predatory fish (shark, tuna, swordfish) | - 0.5 ppm MeHg/kg - 1.0 ppm MeHg/kg | UNEP (2002) |
| Slovak Republic | - Non-predatory freshwater fish and derived products - Predatory freshwater fish - Non-predatory marine fish and derived products - Marine predatory fish | - 0.1 ppm THg/kg - 0.5 ppm THg/kg - 0.5 ppm THg/kg - 1.0 ppm THg/kg | UNEP (2002) |
| Thailand | - Seafood - Other food | - 0.05 ppm Hg/g - 0.02 ppm Hg/g | UNEP (2002) |
| United Kingdom | - Fish - Fish, shellfish and other aquatic animals (FDA) - States, tribes, and territories are responsible for issuing fish consumption advise for locally-caught fish; Trigger level for many state health departments | - 0.3 ppm Hg/Kg - 1 ppm MeHg - 0.5 ppm MeHg | UNEP (2002) FDA (2011) |
| WHO/FAO | - All fish except predatory fish - Predatory fish (such as shark, swordfish, tuna, pike, and others) | - 0.5 ppm MeHg/Kg - 1 ppm MeHg/Kg | FAO (2016) |

(EFSA, 2015). The United States, through the US EPA, has established a limit of 0.7 µg/kg/week (US EPA, 2001). Research evaluating Hg concentrations in seafood and based on population consumption has determined consumer health risks, suggesting that some types of seafood in certain regions exceed the PTWI and, therefore, pose risks to consumer health, especially in children and pregnant women (Ceccatto et al., 2016; Cheung et al., 2008; Lena et al., 2018; Spada et al., 2012; Storelli et al., 2006).

Different studies have reported Hg concentrations and its major forms in seafood and their risk to public health. Xue et al. (2015) carried out a study comparing MeHg exposure of the North American Indian population (that maintain seafood

as the basis of their diets) with non-indigenous populations and observed that tribal MeHg exposure is 3- to 10-fold higher than the general population. Due to the variations in Hg concentrations among different fish species, researchers believe that about 50% of such exposure can be reduced by replacing the consumption of species with higher MeHg content for others presenting lower concentrations. Concerning the assessment of mercury content in different seafood species, Llull et al. (2017) assessed consumer risks by measuring MeHg and THg in 32 fish species from the Western Mediterranean Sea, and observed that some species highly very consumed by the population, occupying the second and third trophic level (i.e., carnivorous species), exceed the

maximum Hg levels established by the European legislation. However, fish belonging to the first trophic level was below the established limit. Taking into account studies carried out in open ocean waters, Sunderland and Selin (2013) evaluated mercury concentrations in the North Pacific, which provides a substantial amount of seafood to the world market. The study warns that, in the short term, in order to reduce Hg exposure risks, public health authorities should recommend the consumption of smaller, younger seafood from less contaminated sites. Finally, Sevillano-Morales et al. (2015) reported the importance of consuming species known to present lower mercury content, which, consequently, depends on more local-scale studies evaluating both highly consumed species and the frequency of their consumption.

3. Conclusions

Mercury contamination is of high concern in many countries and has been a frequent object of research, in order to monitor and alert consumers to high concentrations of this toxic element. Several biotic and abiotic factors are fundamental to understand the dynamics of mercury and methylmercury in the aquatic environment and, consequently, in aquatic organisms. These include trophic level and, consequently, type of feeding, age, length, growth rate, water pH, organic matter content, oxygen saturation, salinity and temperature.

Many studies have yet to be developed to better elucidate the relationships between factors influencing contamination, bioaccumulation and mercury magnification, since much information has not yet been consolidated, and contrasts in several studies, such as the influence of pH, organic matter, temperature, animal metabolism, and why no significant difference between sex is observed. However, some relationships between biotic and abiotic factors and the favoring of methylation and bioaccumulation and biomagnification processes have already been established, such as size, age, and weight, growth rate, trophic position, food chain length, salinity and oxygen saturation. Another well-established aspect is greater Hg affinity by muscle tissue and liver, while another relevant point is related to the importance of sediment contamination as an initial source for Hg transfer to aquatic organisms. Some scarce studies, highlight that, regardless of the amount of mercury present in the sediment, the amount of MeHg is not always proportional, since sediment must be resuspended for the methylation process to take place. Thus, the concept of bioavailability enters as a key to determine Hg concentrations in aquatic organisms, since not every element present is bioavailable to be methylated.

Regarding animal health, the fact that Hg affects reproductive success generates an alert regarding species maintenance in their habitats and their risk of extinction. Concerning human health, mercurial contamination is a reality in different areas around the world, and its effects are evidenced from newborns exposed during pregnancy, to elderly people, as a bioaccumulation reflex of Hg exposure throughout life. Regardless of values detected in surveys being below or above

those stipulated by the legislation, the existence of Hg contamination must be taken into account and serves as an alert for the generation of new research and campaigns. With the purpose of disclosing the importance of reducing exposure to this metal and its chemical forms, health-oriented organizations will protect the health of the current population and future generations. Studies involving risk analysis, especially risk coefficient calculation, should also be stimulated in the scientific community, since they determine in fact how harmful the consumption of seafood from a certain region is, as they take into account important variables, such as consumption frequency and the amount of seafood ingested by the studied population, allowing for a prospection concerning human accumulation of this contaminant over the years.

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