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Metals, As and Se determination by inductively coupled plasma-mass spectrometry (ICP-MS) in edible fish collected from three eutrophic reservoirs. Their consumption represents a risk for human health?

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ABSTRACT

This study evaluated the concentration of Al, V, Cr, Mn, Zn, Fe, Ni, Cu, As, Se, Sr, Mo, Ag, Cd, Hg and Pb measured in muscle of *Odontesthes bonariensis* (silverside fish) captured from three eutrophic reservoirs in the Province of Córdoba (Argentina). For this purpose, an alternative digestion method was optimized for the mineralization of samples, and then inorganic elements were determined by ICP-MS.
Potential human health risks, associated with the consumption of these elements, have been assessed estimating the average daily intake (EDI) in children and adults. Additionally, we evaluated the target hazard quotient (THQ) and the carcinogenic risk (CR) in both general population and fishermen. The consumption of edible muscles of *Odontesthes bonariensis* from three reservoirs pose a toxicological risk for humans, being Hg, As, and Pb the main elements increasing health risks through fish consumption. Furthermore, for both, general population and fishermen, the risk of cancer caused by As is greater than the acceptable lifetime risk of 10^{-4}. Our current results indicate that fish consumption from studied reservoirs should be extremely limited to minimize the potential health risks to consumers. Results from this study are helpful for pollution control and risk management of metals, mainly As, not only in Argentina but also in other areas around the world, with similar health problems associated with this metalloid consumption.

1. Introduction

Due to anthropogenic and natural emissions, metals have long been recognized as one of the most important pollutants in ecosystems, because they can be readily assimilated and bioaccumulated in organisms, posing a potential risk to human health through the consumption of contaminated food. The main source of human exposure to different metals and metalloids is via the food chain through food consumption, which can contribute to achieving the recommended daily intake levels of these elements [1].

With an increasing incidence rate of cancers among human populations in the world, more efforts should be made to prevent and control cancerous diseases [2]. In recent years, there has been a growing interest within the scientific community to know the potential risks to human health derived from the consumption of fish exposed to individual contaminants or groups of contaminants occurring in the environment coming from natural or anthropogenic sources [3].

Studies of heavy metals in fish have been widely reported in the literature [4]. Many reported studies have confirmed that contamination from metals and metalloids via the food chain can cause human health problems [5,6].

One of the major pathway of human exposure to metal/loids is the fish consumption, reaching >90% compared to other routes of exposure, like dermal contact and inhalation [7]. Over the past decade, levels of contamination with metal/loids in water, soil, vegetables and fish, has reached unprecedented values in some parts of the world [8].

Therefore, risk assessment of metal/loids via dietary intake is an important issue. These elements can be classified as carcinogen and non-carcinogen, which lead to carcinogenic and non-carcinogenic effects on organisms [9]. The USEPA has propounded several methods for the assessment of potential human health risk assessment for them [10].

In eutrophic lakes, microalgae are primary producers, they can absorb and enrich metals, As and Se directly from water, they have high metal sorption efficiency even when the concentrations of metals in the environment are low [11]. These intracellular metals would be released into surrounding waters when the cells decompose, leading to an increase in metals concentration in the lake area. As a result of human influence, the occurrence of phytoplankton blooms with high metals concentrations in eutrophic lakes has become a significant global concern [12].

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San Roque Lake (SRL) (Córdoba, Argentina) is the main drinking water supply for Córdoba city, as well as a source of hydroelectric power. Soil removal from agricultural practices and the use of fertilizers has contributed to increased contamination in water column, thus leading to increased eutrophication of the lake [13]. Cyanobacterial blooms have occurred for about 30 years, as either mixed or single blooms, it is so, SRL has been classified as a hypertrophic reservoir [14]. Biota pollution in the region, mainly by Ag, Al, Cr, As, Hg, and other metals, was registered [15]. In addition, like is a tourist area, people visit the area throughout the year, doubling the population during the summer.

Los Molinos Lake (LML) is an artificial water body located 65 km SW of Córdoba city (Argentina), it has been classified as a eutrophic lake, with recurrent blooms of cyanobacteria [16]. It was constructed for the purposes of providing drinking water, hydroelectrical power, irrigation, and flood control. In the last decade, there has been an important urban development in the lakeshore area, as well as tourism growth. Currently, this water body represents a major touristic attraction for the region, and is also used for recreational activities like fishing and water sports. The main activities performed in the basin are related to agriculture (soybean, corn and potato) and livestock, different animals (cows and horses) graze in the west coast of the reservoir and use it as a drinking trough [17], providing a direct discharge of their manure into the water body. According to a census carried out in 2008 (Censo Provincial de Población, 2008—Provincia de Córdoba), the treatment of domestic wastewater in the San Roque and Los Molinos lakes is made through septic tanks and cesspools, which result inefficient due to the soil characteristics of the area, and the proximity of the dwellings to the reservoir (<50 m from the coast for some buildings) [17]. Moreover, in some cases, the direct discharge of domestic effluents, i.e. without previous treatment, is performed.

Embalse Río Tercero (ERT) is located 85 km SW of Córdoba city. During 2013, a deterioration in its water quality was observed, taking it to a progressive state of eutrophication, from a mesotrophic lake to a eutrophic one [18]. The reservoir was built for flood control, irrigation, drinking water supply and hydroelectric purposes. It is characterized as a touristic site with surrounding cultivation areas. The reservoir includes a nuclear power plant of 600 MW, which uses its water for cooling purposes, the outflow is directed through an open cooling channel of 6 km, and discharges into the southern sector of the reservoir. The thermal plume could influence the biota's distribution and biodiversity [19].

The silverside (*Odontesthes bonariensis*) is a characteristic fish from the central region of Argentina in South America (presently it is found in the area from the Titicaca Lake in Bolivia and south of Brazil down to the Colorado River in Argentina). This species is of economic importance, because is widely used for commercial and sport fishing, being for Argentina and Uruguay the second most important fishery resource for local consumption and also for exportation [20].

On a previous work [6], we reported evidence of cancer risk by As for fishermen and the general population (risk of developing cancer over a human lifetime is 5.6 in 10,000, and 1.4 in 10,000, respectively) who consume silverside from SRL only once per week or once per month. These alarming results led us to expand the study to other lakes with similar eutrophic characteristics and to extend the number of inorganic elements studied.

The present study aims to analyze the presence of Al, V, Cr, Mn, Zn, Fe, Ni, Cu, As, Se, Sr, Mo, Ag, Cd, Hg and Pb in muscle of silverside from SRL, LML and ERT, in two hydrological stations, and to assess the human health risks associated with fish consumption. For this, we evaluated: 1- the daily intake per meal for adults and children comparing it with the provisional tolerable daily intake established by the USEPA's regional screening level [21]; 2- the target hazard quotient (THQ) [21], in order to evaluate a possible alert regarding adverse effects; 3- cancer risk caused by As (within an acceptable lifetime risk 10^{-4}); and 4- the number of eligible meals per month in order to minimize chronic systemic effects [21]. At present, there is no information published about metals, As and Se concentration in muscle of silverside from LML and ERT, as well as the extent of human exposure, and potential health consequences. Groundwater pollution by As is a worldwide problem with high impact on the poorest regions of the world [22]. Argentina, along with Bangladesh, Nepal, Chile, China, Hungary, India, Mexico, Rumania, Taiwan, Vietnam and the USA, is one of the countries with the most important health problems associated with As consumption (via water or food) [23]. Therefore, the results of this study are useful for pollution control and risk management of metals, mainly As, not only in Argentina but also in similar areas around the world.

2. Materials and methods

2.1. Study site

SRL is located in the Punilla valley, limited by the Sierras Chicas (east), Sierras Grandes (west), Province of Córdoba (Argentina), at 643 m above sea level (31°22′41″S - 64°28′10″W) (Fig. 1). It is an artificial lake with an area of 25 km^2, with a maximum depth of 35.3 m and a mean depth of 14.1 m. The Cosquín and the San Antonio Rivers represent their main tributaries; it also has two minor tributaries: Los Chorrillos Brook and Las Mojarras Stream.

LML is located in the Calamuchita valley (31°43′30″S y 64°32′20″ W) (Fig. 1), limited by the Sierras Chicas (east) and Sierras Grandes (west). The reservoir has a mean depth of 16 m, a maximum depth of 52 m, an area of 21.1 km2 at spillway level, and a maximum volume of 400 hm^3. Its retention time has been estimated in 451 days. Its main tributaries are: San Pedro River, Los Espinillos River, del Medio River and Los Reartes River. Its only effluent is Los Molinos River (see Fig. 1). The watershed of Los Molinos Reservoir extends over an area of 978 km2.

ERT is located in the Calamuchita valley (south) near the Sierras Chicas (32°11′S, 64°25′W). This reservoir represents the largest artificial water body in Cordoba with an area of 46 km^2, mean depth of 12 m, a maximum depth of 45 m, a maximum volume of 560 hm3, and a residence time of 292 days. Its main tributaries are: Santa Rosa River, Grande River, Amboy River, Quillinzo River and de la Cruz (Fig. 1).

The rainfall regime of the lakes mentioned above is characterized by two well defined seasons, the dry season occurs between June and November, with frequent rains in the remaining months (wet season) [24].

2.2. Sample collection and analysis

Samples were collected in the abovementioned lakes (Fig. 1). Two sampling campaigns were carried out during 2014–2015. Sampling dates were selected taking into account the seasonality and dimensions that characterize the lakes, besides thermal variation. Therefore, we selected August 2015 as the dry season (DS), and Abril 2014 as the wet season (WS). ^{107}Ag, ^{27}Al, ^{75}As, ^{111}Cd, ^{52}Cr, ^{63}Cu, ^{56}Fe, ^{202}Hg, ^{55}Mn, ^{95}Mo, ^{60}Ni, ^{208}Pb, ^{82}Se, ^{88}Sr, ^{51}V and ^{66}Zn were measured in muscle of silverside.

O. bonariensis (average length in SRL: April 2014 14.9 ± 1.1 cm, and August 2015 14.8 ± 3.2 cm; in LML: April 2014 18.3 ± 1.6 cm, and August 2015 20.7 ± 4.4 cm; and in ERT: April 2014 16.2 ± 2.5 cm, and August 2015 16.7 ± 0.8 cm) were captured by rod fishing. After capture, fish were sacrificed, ice-cooled, and transported to the laboratory, where they were dissected, separating the muscle. Only metals concentration in fish muscle (edible portion) was evaluated, since in Argentina this portion is the only part of this fish species that people habitually consume. The samples were dried in an oven at 40 °C to a constant weight before being ground and homogenized with a mortar and pestle. Fish samples were mineralized using teflon tubes. First, approximately 25 mg of muscle sample was weighed and digested with 8 mL of HNO_3 (sub boiling grade) and 1 mL of 30% H_2O_2 (ultrapure), in closed Teflon tubes on heating plates set to 220 °C, during 8 h. Mineralized

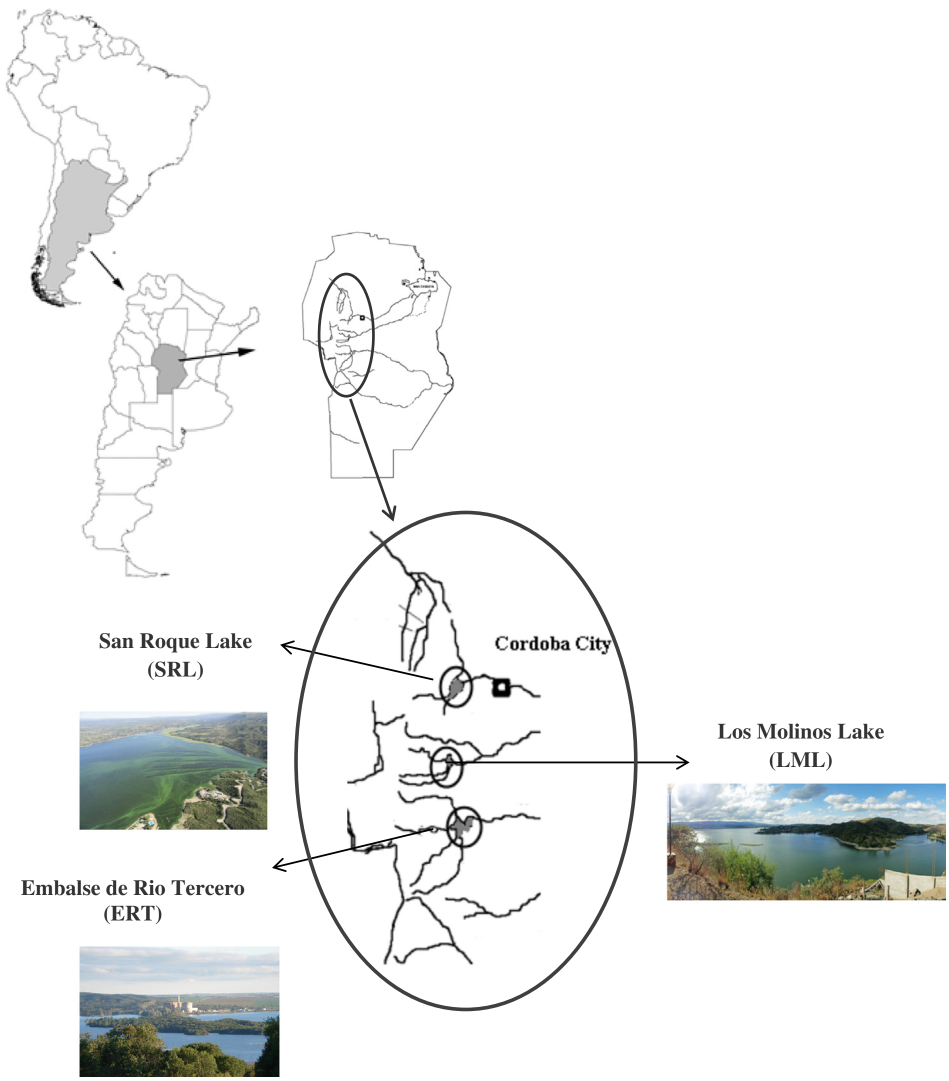

Fig. 1. Map of the Province of Córdoba - Argentina with indication of the studied area.

samples were quantitatively transferred to 10 mL volumetric flasks, completing the volume with HNO_3 2%, followed by filtration using 0.45 μm filters. This process was done in duplicate for all samples.

The concentration of metals, As and Se in samples solutions were measured using an Agilent 7500cx Inductively Coupled Plasma Mass Spectrometer (ICP-MS) (Agilent Technologies, California), equipped with an ASX-100 autosampler (CETAC Technologies, Omaha, NE). The sample introduction system consisted of a microflow concentric nebulizer, a Peltier cooled spray chamber (2 °C), and a 1.5 mm i.d. fixed injector torch. The RF forward power was 1500 W for all of the experiments, and the interface was fitted with Ni sampling and skimmer cones designed for low polyatomic formation. Two operation modes were used: with and without collision cell technology (CCT). CCT mode measurements were performed for Al, V, Cr, Mn, Zn, Fe, Ni, Cu, As, Se, Sr and Mo. The collision cell was flushed with He (high-purity). The elements Ag, Cd, Hg and Pb were measured without operation of the collision cell with gas and, thus, full sensitivity was obtained. The oxide ratio and double-charged species were maintained below 1% in both modes of operation. All of the Q-ICPMS measurements were performed using Sc, Ge, In and Re as internal standards. All of the muscle fish samples were diluted 10-fold using a HNO3 2%before Q-ICPMS measurements. Standards and blanks were prepared using the same HNO3 2%. Instrumental and procedural blanks were determined together with samples, and the mean of three runs was obtained for each sample. Full quantitative analysis was performed against calibration standards for each element. All samples were analyzed in duplicate.

2.3. Quality assurance and quality control

All samples were digested in triplicate. Concentrations of elements were determined in triplicate; the repeatability of ICP-MS measurements was generally ≥97%. Quality assurance (QA) and quality control (QC) of elements analysis were performed using certified reference material (CRM): NIST 8414 (Bovine Muscle Powder). Spiked samples were also prepared. Variable amounts of mixed standard solutions, containing all elements analyzed, were added to 0.02–0.04 g of fish sample (dried muscle) prior to sample digestion, to double the starting concentration for each element. The rest of the procedure was the same as used for non-spiked samples. Replicate analysis of the Reference materials and spike samples showed good accuracy, recoveries from both analyzed samples are showed in Table 1.

2.4. Health risk assessment

2.4.1. Estimated daily intake of metal

The estimated daily intake (EDI) of the elements depends on both, the metal concentrations in fish and the consuming rate. The EDI (μg/kg/day)

Table 1
Trace element concentrations determined in one certified reference materials (all data as means ± SD) A) RM 8414 (Bovine Muscle Powder) μg g^{-1} dry weight. B) Spike samples μg g^{-1} dry weight.

A			
Element	NIST 8414		% recovery
	Certified	Found	
Al	1.7 ± 1.4	1.9 ± 0.2	111,8
As	0.009 ± 0.003	0.008 ± 0.001	88,9
Cd	0.013 ± 0.011	0.0138 ± 0.0009	106,2
Cr	0.071 ± 0.038	0.068 ± 0.006	95,8
Cu	2.84 ± 0.45	2.97 ± 0.11	104,6
Fe	71.2 ± 9.2	75 ± 4	105,3
Hg	0.005 ± 0.003	0.0057 ± 0.0003	114,0
Mn	0.37 ± 0.09	0.35 ± 0.03	94,6
Mo	0.08 ± 0.06	0.086 ± 0.009	107,5
Ni	0.05 ± 0.04	0.047 ± 0.005	94,0
Pb	0.38 ± 0.24	0.41 ± 0.05	107,9
Se	0.076 ± 0.010	0.082 ± 0.009	107,9
Sr	0.052 ± 0.015	0.048 ± 0.012	92,3
Zn	142 ± 14	138 ± 12	97,2

B			
Element	Spike samples		% recovery
	Theoretical μg g^{-1}	Found	
^{107}Ag	6.3 ± 0.5	5.1 ± 0.2	81,4
^{27}Al	6.3 ± 0.5	5.9 ± 0.5	93,9
^{75}As	6.3 ± 0.5	5.3 ± 0.4	83,9
^{111}Cd	6.3 ± 0.5	5.1 ± 0.5	81,8
^{52}Cr	6.3 ± 0.5	6.0 ± 0.5	95,4
^{63}Cu	6.3 ± 0.5	6.5 ± 0.6	103,2
^{56}Fe	6.3 ± 0.5	6.7 ± 0.6	106,4
^{202}Hg	0.85 ± 0.07	0.92 ± 0.08	107,3
^{55}Mn	6.3 ± 0.5	6.4 ± 0.4	101,6
^{98}Mo	3.15 ± 0.32	3.4 ± 0.3	107,0
^{60}Ni	6.3 ± 0.5	5.2 ± 0.5	83,0
^{208}Pb	6.3 ± 0.5	5.8 ± 0.4	93,2
^{82}Se	6.3 ± 0.5	5.4 ± 0.2	86,8
^{88}Sr	6.3 ± 0.5	6.5 ± 0.6	104,5
^{51}V	6.3 ± 0.5	5.1 ± 0.4	81,2
^{66}Zn	6.3 ± 0.5	5.7 ± 0.6	91,1

value for an adults and children were calculated by using the following formula [25]:

$$EDI = (Mc \times \text{Consumption rate})/\text{body weight}$$

where

Mc is the metal concentration in muscle of fish.
Consumption rate 150 and 75 g/day, for adults and children respectively.
Body weight 70 kg for adults and 20 kg for seven-year-old children (US-EPA 2000).

The oral reference dose (RfDo) values (mg/kg/day) used in this study were as follows: Al: 1; V: 0.005; Mn: 0.1; Fe: 0.7; Ag: 0.005; Sr: 0.6; Ni: 0.02; Mo: 0.005; Hg: 0.0001; Cu: 0.04; Cr: 0.003; Zn: 0.3; As: 0.0003; Se: 0.005; Cd: 0.001, provided by the USEPA's regional screening level (USEPA 2015). An RfDo value for Pb does not exist because there is no evidence of a threshold below which a non-harmful intake could be allowed [26] that is why values provided by [27] were used. C is the metals concentration in fish [mg/kg, dry weight (dw)]. Additionally, based on the US-EPA Guidance (1989), we assumed that the ingestion dose is equal to the adsorbed contaminant dose, and that cooking has no effect on the contaminants.

2.4.2. Non-carcinogenic and carcinogenic risk

Health risk assessment to silverside consumer (fisherman and general population) was also performed based on the target hazard quotient (THQ). The THQ is a ratio of determined dose of a pollutant to a reference dose level. If the ratio is <1, the exposed population is unlikely to experience obvious adverse effects. We assumed that the ingestion dose is equal to the adsorbed contaminant dose, and that cooking has no effect on the contaminants according to [25]. The method of estimating risk using THQ was developed by the United States Environmental Protection Agency [25] and it is described by the following equation:

$$THQ = \frac{EFr \times EDtot \times FIR \times C}{RfDo \times BWa \times ATn} \times 10^{-3}$$

where EFr is the exposure frequency; EDtot is the exposure duration (70 years) equivalent to the average lifetime [28]; FIR is the food ingestion rate (150 g/day); C is the concentration (μg g^{-1}); RfDo is the oral reference dose (mg/kg/day) based on [21], the values used are the same used in EDI calculation, which indicates the quantity of the compound per kilogram weight that a human being could ingest per day without risk; Bwa is the body weight (adult 70 kg); ATn is the averaging time for non-carcinogens (365 days/year × number of exposure years), assuming 70 years. The RfD values (mg/kg/day) used for each element are the same as used to calculate the estimated daily intake.

Since the RfD value for Pb had been declined by the European Protection Agency (EPA) [26], the THQ for Pb was calculated using the following equation [5]:

$$THQ = \frac{C}{MRL}$$

C: metals concentration in fish muscle (μg g^{-1} dry weight); MRL (Maximum Residue Limit: 0.3 μg g^{-1}) set by the Regulation (EC) No 1881/2006 [29].

Health risks for fishermen and the general population were considered separately since the frequency of fish consumption is different. For fishermen, an exposure frequency of 48 days/year, once a week was set, while for the general population, it was 12 days/year, once per month.

It has been reported that exposure to two or more pollutants may result in additive and/or interactive effects [30]. For the risk assessment of multiple metals, metalloids and Se containing in fish, a total THQ (TTHQ) was employed by summing of the individual metal THQ values as described [4]:

$$\text{Total THQ (TTHQ)} = \text{THQ (element 1)} + \text{THQ (element 2)} + \text{THQ (element 3)}\ldots$$

Lifetime cancer risk (CR) for As was estimated by using the CSFo, the oral carcinogenic slope factor from the Integrated Risk Information System [31] database, which was 1.5 (mg/kg/day). Carcinogenic risk (CR) for As was calculated using the following equation:

$$CR = \frac{EFr \times EDtot \times FIR \times CSFo}{BWa \times ATn} \times 10^{-3}$$

If CR risk is above the acceptable lifetime risk – ARL – of 10^{-4}, value considered by the [10], and applied in this study, it indicates a probability >1 chance over 10,000 of an individual of developing cancer.

The allowable number of fish meals for adults and children of a specific meal size that may be consumed over a given period of time was also evaluated. For non-carcinogenic effects, we obtained the maximum allowable fish consumption rate meals/month (CRmm) [10] that would not be expected to cause any chronic systemic effects. On the assumption that no other sources of Al, V, Cr, Mn, Zn, Fe, Ni, Cu, As, Se, Sr, Mo, Ag, Cd, Hg and Pb exist in the diet of the consumers, the allowable monthly consumption limits for fish for which no adverse health effects are expected are determined as follows:

$$CRmm = \frac{RfD \times 7 \times 4 \times BW}{C}$$

where CRmm is the maximum safe monthly consumption rate of fish (meals per month); RfD is the reference dose for each trace metal (mg/kg/day); 7 is to calculate the RfD per week; 4 to estimate the RfD per month; BW is the average consumer body weight (in kg); and C is the concentration of chemicals in the edible portion of fish (μg g^{-1}).

2.5. Statistical analysis

Differences among concentration of metals, As and Se in muscle of silverside among different seasons were determined by a one-way analysis of variance (ANOVA), followed by a multiple comparison test (Tukey). When parametric assumptions were not fulfilled, Kruskal–Wallis followed by multi-comparison Dunn's tests was used. Significance level was set at $p < 0.05$. Infostat (Version2013p, [32]) was used for all statistical analyses.

3. Results and discussion

3.1. Digestion process

A simple, digestion method for the mineralization of silverside muscle was optimized for the determination of metals, As and Se by ICP-MS. The reference material NIST 8414 (Bovine Muscle Powder) has been analyzed and the results were in agreement with the certified values, spiked samples using silverside muscle also showed good quantification extraction efficiency (Table 1). The advantage of using this digestion technique is that a small amount of sample (mg) is needed and less volumes of acid and H_2O_2 are used in compare with others techniques [15, 33]. According to these results the digestion method optimized in this work can be consider as an alternative method to the existing ones.

3.2. Metals, As and Se concentrations in muscle fish

Concentrations of Al, V, Cr, Fe, Mn, Ni, Cu, Zn, Se, Hg, Sr, Mo, Ag, Cd, As and Pb were analyzed in muscle of silverside from SRL, LML and ERT during the WS and DS (Table 2).

Pb, Hg, Ag, Se, As, Cu and Ni were statistically higher during the DS (August) compared to the WS (April) in muscle of silverside from the three sampled lakes. This may be so because during the DS inorganic contaminants are concentrated in water due to a decrease in lake levels, leading to increased concentrations of these elements for the exposed fish. Another possible explanation is that, in the southern hemisphere, August is the reproductive period of this fish species, leading to an increase in the metabolic demand during this phase [34], which may facilitate the absorption of some essential and non-essential metals, being their accumulation higher during August (WS) than in April (DS), although Zn, Mn and Sr concentrations in fish muscle show higher values during the WS compared to the DS. On the other hand, V, Fe and Cr concentrations in fish muscle show no difference between sampling seasons, and no clear trend between the DS or WS was observed in Al concentration. For example, in SRL, higher concentrations of Al were observed during DS; while in LML, the highest concentration was observed during the WS; and in ERT, Al concentration showed no difference between sampling seasons. So far, our results could help interpreting the intraspecific differences in elements concentrations between both studied seasons.

Accumulation of metals in fish is a complex process, which is controlled mainly by exogenous and endogenous factors. Among the exogenous factors environmental parameters such as bioavailability of each particular metal, temperature and alkalinity of the environment are the most important, while endogenous factors include the species (physiological requirements of the organisms), type of food, habitat [35].

Several studies have shown that metals enter fish via three main routes, from surface contact with the water, from breathing, and via the food chain, being able to register in their tissues metals concentrations even higher than those in the environment [36].

Table 2
Concentrations of metals measured in fish muscle (μg g^{-1} dry weight-DW) of the SRL, LML and ERT. Values are expressed as means ± SD. <LOD (below detection limit); LODs: Mo- 0.005 μg g^{-1}; Ag- 0.006 μg g^{-1}; Cd- 0.05 μg g^{-1}. LOQs: Cu- 0.15 μg g^{-1}; Pb- 0.03 μg g^{-1}. Different letters indicate significantly different values during the wet and dry seasons in each lake (DMRT, $p \le 0.05$).

	Season	San Roque	Los Molinos	Embalse
^{107}Ag	Dry	0.19 ± 0.12^{b} (0–0.42)	0.07 ± 0.09^{b} (0–0.26)	<LOD
	Wet	0.03 ± 0.002^{a} (0.03–0.004)	0.02 ± 0.02^{a} (0–0.05)	0.02 ± 0.02^{a} (0–0.05)
^{27}Al	Dry	6.5 ± 4.9^{b} (1.6–19.0)	2.4 ± 1.1^{a} (0.8–4.0)	5.1 ± 2.3^{a} (2.3–8.9)
	Wet	3.4 ± 1.1^{a} (2.3–6.1)	5.0 ± 2.1^{b} (3.4–10.1)	4.9 ± 8.4^{a} (0 − 20)
^{75}As	Dry	2.6 ± 0.4^{b} (2.12–3.63)	2.5 ± 0.4^{a} (1.9–3.4)	2.8 ± 0.8^{b} (2.3–4.8)
	Wet	2.0 ± 0.6^{a} (1.1–2.7)	4.0 ± 1.7^{b} (2.1–6.8)	0.58 ± 0.09^{a} (0.45–0.67)
^{111}Cd	Dry	<LOD	<LOD	<LOD
	Wet	<LOD	<LOD	0.065 ± 0.041^{a}
^{52}Cr	Dry	0.24 ± 0.16^{a} (0.11–0.63)	0.14 ± 0.04^{a} (0.06–0.22)	0.21 ± 0.06^{a} (0.11–0.34)
	Wet	0.24 ± 0.08^{a} (0.07–0.32)	0.16 ± 0.09^{a} (0.07–0.37)	0.17 ± 0.07^{a} (0.09–0.26)
^{63}Cu	Dry	0.66 ± 0.187^{a} (0.43–0.96)	0.57 ± 0.15^{a} (0.38–0.93)	0.72 ± 0.20^{c} (0.45–0.99)
	Wet	<LOQ	<LOQ	<LOQ
^{56}Fe	Dry	18 ± 7^{a} (11–35)	12 ± 3^{a} (8–19)	16 ± 4^{a} (10 − 21)
	Wet	19 ± 3^{a} (14–26)	18 ± 2^{a} (15–21)	20 ± 6^{a} (7–25)
^{202}Hg	Dry	1.38 ± 0.41^{b} (0.85–2.52)	1.70 ± 0.43^{b} (1.11–2.90)	0.88 ± 0.43^{b} (0.54–1.97)
	Wet	0.51 ± 0.39^{a}	0.46 ± 0.15^{a}	0.31 ± 0.41^{a}
^{55}Mn	Dry	1.34 ± 0.47^{a} (0.75–2.73)	0.89 ± 0.28^{a} (0.56–1.5)	2.49 ± 1.27^{a} (1.24–4.73)
	Wet	2.1 ± 0.9^{b} (1.2–4.7)	2.2 ± 0.6^{b} (1.6–3.2)	3.91 ± 1.4^{a} (2.2–6.3)
^{95}Mo	Dry	<LOD	<LOD	<LOD
	Wet	<LOD	<LOD	<LOD
^{60}Ni	Dry	0.33 ± 0.09^{b} (0.17-0.49)	0.18 ± 0.04^{b} (0.12-0.30)	0.20 ± 0.05^{a} (0.12-0.27)
	Wet	0.13 ± 0.05^{a} (0.08–0.24)	0.15 ± 0.04^{a} (0.10–0.22)	0.16 ± 0.14^{a} (0–0.44)
^{208}Pb	Dry	0.16 ± 0.08^{a} (0.05–0.33)	0.09 ± 0.08^{a} (0.04–0.25)	0.08 ± 0.03^{a} (0.04–0.11)
	Wet	<LOQ	<LOQ	<LOQ
^{82}Se	Dry	1.3 ± 0.2^{b} (0.9–1.6)	1.0 ± 0.2^{b} (0.7–1.5)	1.3 ± 0.2^{b} (0.9–1.6)
	Wet	0.9 ± 0.1^{a} (0.8–1.0)	0.7 ± 0.1^{a} (0.6–0.8)	0.9 ± 0.4^{a} (0–1.3)
^{88}Sr	Dry	8 ± 3^{a} (3 − 13)	6 ± 3^{a} (3 − 11)	7 ± 3^{a} (3-13)
	Wet	15 ± 3^{b} (9–20)	14 ± 5^{b} (6–20)	11 ± 5^{b} (6–16)
^{51}V	Dry	0.09 ± 0.05^{a} (0.03–0.27)	0.07 ± 0.04^{a} (0.04–0.17)	0.08 ± 0.02^{a} (0.05–0.11)
	Wet	0.08 ± 0.03^{a} (0.06–0.14)	0.08 ± 0.02^{a} (0.06–0.10)	0.09 ± 0.05^{a} (0.04–0.19)
^{66}Zn	Dry	25 ± 5^{a} (17–36)	22 ± 5^{a} (17–35)	26 ± 4^{a} (20 − 33)
	Wet	43 ± 7^{b} (28–53)	48 ± 5^{b} (38–54)	64 ± 15^{b} (38–74)

Kalay et al. [37] indicate that contaminants accumulate in fish muscle after exceeding the body's defense barriers. Therefore, the muscle is not a target organ for the accumulation of substances during acute exposure, but it is a good indicator of chronic exposure to them [38].

The concentration of metals in the muscle of an edible fish like Silverside has a direct implication on individuals who consume [39]. People are more exposed to most of the studied elements by the consumption of fish during winter (August) than autumn (April).

Table 3
Estimated daily intake (EDI) of fish consumption for adults. Pb[1] Chronic renal diseases: 0.63 μg/kg bw/day. Pb[2] Effects on the systolic blood pressure: 1.50 μg/kg bw/day.

	Season	Elements																
		^{107}Ag	^{27}Al	^{75}As	^{111}Cd	^{52}Cr	^{63}Cu	^{56}Fe	^{202}Hg	^{55}Mn	^{95}Mo	^{60}Ni	^{208}Pb1	^{208}Pb2	^{82}Se	^{88}Sr	^{51}V	^{66}Zn
Daily allowed ingest for a 70 kg adult (mg)		0,35	70	0,021	0,07	0,21	2,8	49	0,007	7	0,35	1,4	0,044	0,105	0,35	42	0,35	21
San Roque	Dry	0,029	0,97	**0,40**	0	0,04	0,10	2,7	**0,207**	0,20	0	0,05	0,023	0,023	0,20	1,2	0,01	3,8
	Wet	0,005	0,51	**0,29**	0	0,04	0,00	2,9	**0,076**	0,31	0	0,02	0	0	0,13	2,2	0,01	6,5
Los Molinos	Dry	0,011	0,35	**0,37**	0	0,02	0,09	1,8	**0,255**	0,13	0	0,03	0,014	0,014	0,15	0,9	0,01	3,4
	Wet	0,003	0,75	**0,60**	0,0001	0,02	0,00	2,7	**0,069**	0,33	0	0,02	0	0	0,11	2,0	0,01	7,3
Embalse	Dry	0	0,77	**0,42**	0	0,03	0,11	2,4	**0,121**	0,37	0	0,03	0,011	0,011	0,19	1,1	0,01	3,9
	Wet	0	0,74	**0,09**	0,0088	0,02	0,00	3,1	**0,047**	0,59	0	0,02	0	0	0,15	1,7	0,01	9,6

Bold numbers exceed the acceptable daily ingest for a 70 Kg adult (mg) for the corresponding element.

3.3. Health risk assessment

Silverside is a very important aquatic product in the regions, it is necessary to evaluate the health risks caused by the consumption of this kind of fish in the studied lakes.

The estimated daily intake (EDI) values of metal from fish consumption by the local inhabitants (adults and children) are shown in Tables 3 and 4. Considering the average value for metals, Se and As in muscle of *O. bonariensis* (Table 2), and assuming a 70 kg adult eating 150 g fish muscle per day, the calculation reveals no risk for consumption of most of the elements studied, except for Hg and As in the three lakes during the DS and WS. This situation is obviously worse for children (Table 4) or people with less body weight, and assuming a 20 kg child eating 75 g fish muscle per day, it reveals a risk of As and Hg consumption in the three lakes during both seasons, and Pb consumption for children who eat muscle of silverside from SRL during the DS. It is interesting to mention that the same tendency in muscle of silverside from SRL during the dry, wet and intermediate season has already been demonstrated [6], although fish from that previous report were collected during 2012, so it can be said that accumulation of these toxic compounds in edible part of fish is chronic or constant over time.

The values of estimated daily intake (EDI) of metal per fish consumption were confirmed by the specific calculations rate of meals/month (CR mm). CRmm in adult and children was >8 meals/month for all analyzed metals, except for As and Hg. CRmm for children showed the lowest level of fish meals suggested. The specific consumption limits obtained indicate that it would be appropriate to minimize the monthly meals of the analyzed fish species to avoid chronic systemic effects due to As and Hg content. Fig. 2 shows that CRmm for As and Hg is higher for children and adults during the WS in the three lakes studied, with the exception of As in LML. Especially for children, the consumption limits calculated suggest reducing the monthly meals intake to 0.4 for LML to minimize risk of Hg consumption (Fig. 2). These results are correlated with the lower As and Hg concentrations found in muscle fish during this season.

The target hazard quotients (THQ) estimated for an individual metal through fish consumption by the general population and fishermen are presented in Table 5. The THQ for most metals was <1, which indicates that consumers may experience minor health effects by these metals consumption, except for As and Hg. Arsenic , had THQ values between 1 and 5 for fishermen in the DS in the three lakes sampled, which indicates that consumers are already experiencing adverse health effects to some extent [40] and even a worse situation is seen for fishermen in the WS in LM, with THQ for As is >5, which indicates that consumers may experience major health risks. Hg showed values between 1 and 5 for fishermen in DS and WS in the three lakes, and for the general population during the DS in LM, which indicates that consumers are already experiencing adverse health effects to some extent. The total metal THQ value for fishermen was higher than 1 in all seasons in the three lakes, and for general population in WS in LML, being TTHQ from LML the highest one, indicating potential health risks to people who consume silverside from this lake (Fig. 3A and B).

Comparison of TTHQ reported for fishermen and for the general population during both season studied (Fig. 3A and B) show that the first group presents values about 3.5 times higher than that for the general population suggesting that they could experience adverse health effects, mainly associated with Hg and As. The risk of consuming contaminated fish increases during the DS, where we observed the highest concentrations of As and Hg in fish muscle.

The carcinogenic risk (CR) caused by exposure of this fish species to As is listed in Table 6. CR values obtained for As were higher than the acceptable guideline value of 10^{-4} [41]; general population: 1.41 E 10^{-4}, fishermen: 5.63 E 10^{-4}. This indicates that excessive fish consumption over a long time period from the main lakes in the province of Córdoba might cause carcinogenic effect. This is not just a local problem since these lakes areas receive a great number of tourists worldwide during the summer time.

Arsenic (As) is a metalloid that has been widely reported to have adverse health effects on humans. The problem of water contamination with arsenic is of global importance, 226 million persons are exposed to it. Argentina, Bangladesh, Chile, China, Hungary, India, Mexico, Nepal, Rumania, Taiwan, USA and Taiwan have the highest concentrations and accordingly, the most important health problems [23]. Many reports have demonstrated that chronic exposure to As has been associated with a variety of human health problems mainly several types of cancer (skin, lung, bladder, kidney), and other diseases (neurological, cardiovascular, perinatal conditions and others benign) [42]. Low doses and long term exposures to As lead to a range of medical complications termed as “Arsenicosis” [43]. In Argentina, a case series of patients with arsenicosis showed that the 88% develop skin cancer [42].

Table 4
Estimated daily intake (EDI) of fish consumption for children. Pb[1] Effects on neuro-developmental effects in children: 50 μg/kg bw/day.

	Season	Elements															
		^{107}Ag	^{27}Al	^{75}As	^{111}Cd	^{52}Cr	^{63}Cu	^{56}Fe	^{202}Hg	^{55}Mn	^{95}Mo	^{60}Ni	^{208}Pb1	^{82}Se	^{88}Sr	^{51}V	^{66}Zn
Daily allowed ingest for a 20 kg child (mg)		0,1	20	0,006	0,02	0,06	0,8	14	0,002	2	0,1	0,4	0,006	0,1	12	0,1	6
San Roque	Dry	0,01	0,49	**0,20**	0	0,02	0,05	1,36	**0,10**	0,10	0	0,02	**0,012**	0,10	0,62	0,01	1,88
	Wet	0	0,26	**0,15**	0	0,02	0	1,45	**0,04**	0,15	0	0,01	0	0,07	1,10	0,01	3,25
Los Molinos	Dry	0,01	0,18	**0,19**	0	0,01	0,04	0,90	**0,13**	0,07	0	0,01	**0,007**	0,08	0,45	0,01	1,69
	Wet	0	0,38	**0,30**	0	0,01	0	1,37	**0,03**	0,17	0	0,01	0	0,05	1,00	0,01	3,63
Embalse	Dry	0	0,38	**0,21**	0	0,02	0,05	1,19	**0,06**	0,19	0	0,02	0,005	0,09	0,54	0,01	1,95
	Wet	0	0,37	**0,04**	0	0,01	0	1,56	**0,02**	0,29	0	0,01	0	0,07	0,83	0,01	4,82

Bold numbers exceed the acceptable daily ingest for a 20 Kg child (mg) for the corresponding element.

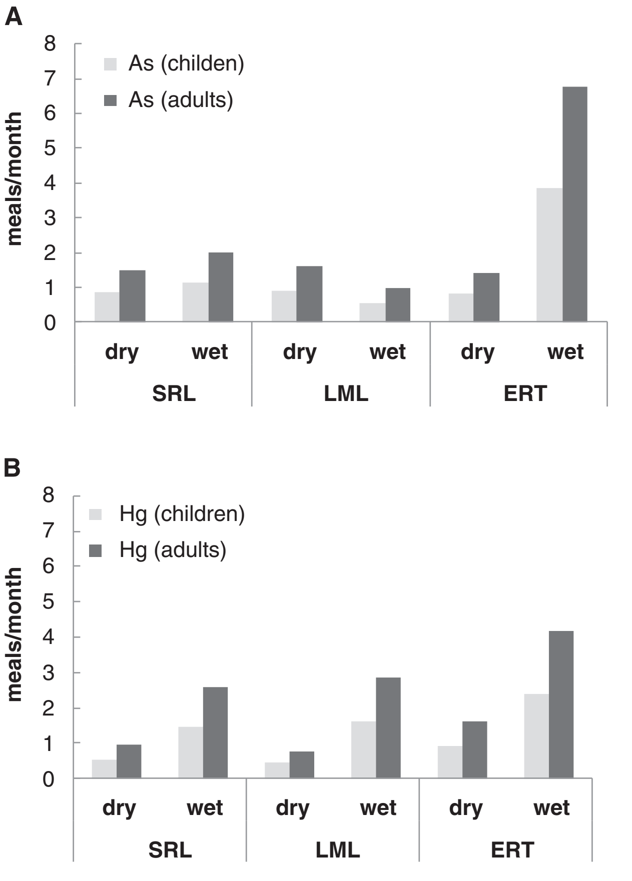

Fig. 2. Maximum allowable fish consumption rate meals/month (CRmm) in children (meal = 75 g) and adults (meal = 150 g) for As (A) and Hg (B).

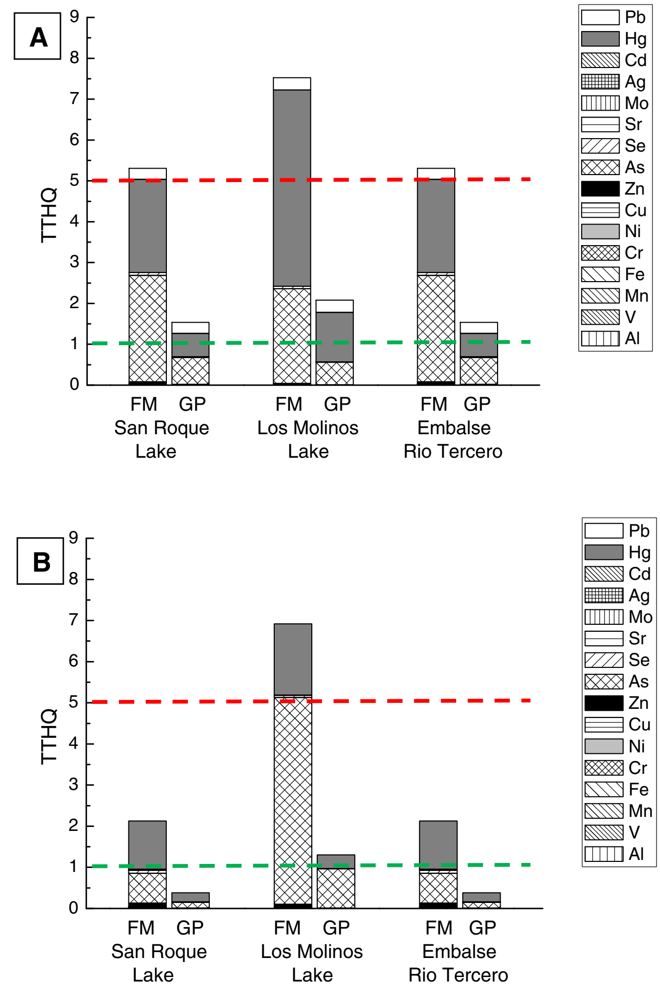

Fig. 3. Estimated total target hazard quotients (TTHQ) from fish consumption by the general population (GP) and fishermen (FM) in three lakes studied during dry season (A) and wet season (B). TTHQ <1: minor health risk. TTHQ 1–5: concerning level. TTHQ >5: mayor health risk.

According to epidemiological studies an increased mortality from bladder cancer, laryngeal cancer, liver cancer, and chronic renal disease in adults are markedly related to As exposure in the early life [44], while perinatal As exposures were associated with increases in late fetal, neonatal, and post neonatal mortality [45].

On the other hand, Mercury (Hg) is a highly toxic element that can be released into the global environment through a number of natural or anthropogenic processes. It has been demonstrated in many reports that the trophic transfer, from lower to higher trophic levels, is a predominant way of Hg accumulation in aquatic environments [46,47]. Hg is found in all fish species and fish-eating animals. In humans, major exposure to Hg occurs via food, being fish and fish products the major sources of Hg consumption [48]. Hg compounds are absorbed through the gastrointestinal tract and affect other systems via this route [21] established a RfDo value of 0.0001 mg/kg of body weight/day, considering the mean Hg concentrations obtained in muscle of silverside from the three lakes sampled during the wet and dry seasons. For an adult of 70 kg of body weight who consumes 150 g of fish/day, the limit established by USEPA would be exceeded, implying a risk to their health by Hg consumption. This element has long been recognized as a neurotoxin for humans, due to the ability of this element to cross through the blood-brain barrier, reaching the brain where it exerts

Table 5
Estimated target hazard quotients (THQ) for individual metals and total THQ (TTHQ) from fish consumption by the general population and fishermen in SRL, LML and ERT.

Sampling	Exposure group		Elements																
			^{107}Ag	^{27}Al	^{75}As	^{111}Cd	^{52}Cr	^{63}Cu	^{56}Fe	^{202}Hg	^{55}Mn	^{95}Mo	^{60}Ni	^{208}Pb	^{82}Se	^{88}Sr	^{51}V	^{66}Zn	TTHQ
San Roque	Fishermen	Dry	ND	0,001	2,608	ND	0,020	0,005	0,006	2,280	0,007	ND	0,003	0,265	0,071	0,003	0,005	0,024	5,299
		Wet	ND	0,001	0,727	0,022	0,021	ND	0,011	1,174	0,015	ND	0,003	ND	0,074	0,007	0,005	0,081	2,142
	General population	Dry	ND	ND	0,657	ND	0,005	0,001	0,002	0,574	0,002	ND	0,001	0,265	0,018	0,001	0,001	0,006	1,532
		Wet	ND	ND	0,137	0,004	0,004	ND	0,002	0,222	0,003	ND	0,001	ND	0,014	0,001	0,001	0,015	0,405
Los Molinos	Fishermen	Dry	0,004	0,001	2,320	ND	0,013	0,004	0,005	4,801	0,003	ND	0,003	0,300	0,058	0,003	0,004	0,021	7,538
		Wet	0,002	0,001	5,029	ND	0,021	ND	0,010	1,733	0,008	ND	0,003	ND	0,054	0,008	0,004	0,061	6,933
	General population	Dry	0,001	ND	0,584	ND	0,003	0,001	0,001	1,209	0,001	ND	0,001	0,300	0,015	0,001	0,001	0,005	2,122
		Wet	ND	ND	0,950	ND	0,004	ND	0,002	0,327	0,002	ND	0,001	ND	0,010	0,002	0,001	0,011	1,309
Embalse	Fishermen	Dry	ND	0,001	2,608	ND	0,020	0,005	0,006	2,280	0,007	ND	0,003	0,266	0,071	0,003	0,005	0,024	5,300
		Wet	ND	0,001	0,727	0,022	0,021	ND	0,011	1,174	0,015	ND	0,003	ND	0,074	0,007	0,005	0,081	2,142
	General population	Dry	ND	ND	0,657	ND	0,005	0,001	0,002	0,574	0,002	ND	0,001	0,266	0,018	0,001	0,001	0,006	1,533
		Wet	ND	ND	0,137	0,004	0,004	ND	0,002	0,222	0,003	ND	0,001	ND	0,014	0,001	0,001	0,015	0,405

Table 6
Estimated carcinogenic risk (CR) of ^{75}As from fish consumption by the general population and fishermen in SRL, LML and ERT.

Sampling	Exposure group	CR
		As
SRL	Fishermen	4.23E−04
	General population	1.07E−04
LML	Fishermen	4.23E−04
	General population	1.07E−04
ERT	Fishermen	4.23E−04
	General population	1.07E−04

toxicity. The brain of adults and, in particular, of developing fetuses, is very sensitive to the neurotoxic effects of Hg [49]. The proposed role of Hg in oxidative stress propagation has led to the community to have serious concerns due to its potentially harmful effects on cardiovascular system. Some epidemiological studies have indeed found a positive correlation between levels of Hg in the body and risk of CVD [50].

Lead (Pb) is a toxic heavy metal with unknown biological function that accumulates in the human body and can pose a serious risk to public health [5]. In the human body, this element is mainly distributed in soft tissues such as blood, liver and kidneys, and also in mineralizing systems (bones and teeth). Increased blood Pb levels in children are related with an impact on their intelligence (reduced IQ). A PTWI (Tolerably Week Intake) value of 0.025 mg/kg bw for Pb for children was established by [51]. With new available data that a PTWI of 0.025 mg of body weight could be responsible for a drop of 3 points in the IQ (Intelligence quotient) in children, the JECFA acknowledged that the established PTWI value was not sufficiently protective, however, they were unable to establish a new health-based guidance value [27]. The European Food Safety Authority (EFSA) [52] concluded that the central nervous system of young children and the cardiovascular system of adults, are the places where Pb has the most harmful effects. The EFSA identified three reference dietary intake values, 0.63 μg/kg bw/day for nephrotoxic effects in adults, 1.50 μg/kg bw/day for cardiovascular effects in adults, and 0.50 μg/kg bw/day for neuro-developmental effects in children [52]. Based on the obtained data (Table 4), children who consume fish from SRL during the dry season are exposed to Pb levels than can affect their IQ. According to these results, it will be necessary to set up regulatory norms for the dietary intake of this fish species.

While it is true that reducing As, Pb or Hg exposure may decrease health risks, elevated rates of cancer may persist for many years after a high-dose exposure [53]. The severity and degree of diseases are very dependent on several factors such as levels of As or Hg in fish, local climate, duration of exposure, age and body weight.

Fish is an important source of nutrients for humans. It is an excellent source of proteins, vitamin D, Se and, especially, long-chain ω3 fatty acids, eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA) and docosahexaenoic acid (DHA). However, fish can also contain harmful substances such as As, Pb and Hg. Based on our results, consumption of silverside from the three Lakes studied represents a considerable human health risks, and the sources of metals and As pollution in fish should clearly be controlled.

4. Conclusions

This study provides data on bioaccumulation of metals, As and Se in muscle of silverside from three lakes with anthropic impact, and on the health risk assessments that could arise from their consumption.

From the human health perspective, potential health risk assessments based on the amount of fish required to reach the prescribed CRmm values, EDI, THQ and CR indicated that health risks associated with metals, As and Se exposure via consumption of the silverside muscles were insignificant to humans for most elements studied, except for As, Pb and Hg. These elements in fish from the lakes studied represent a potential health risk for people who frequently consume these fish species. According to the results presented in this work and in order to expand our studies, a monitoring program on the actual consumption rates of this fish species in the local community (children and adults; male and female/pregnant women), and studies on speciation of some elements found in the muscle of silverside (Cr^{+3} or Cr^{+6}, inorganic form of Hg or As, among others) should be done.

Fish is a significant source of food, especially for fishermen family, and should not be omitted as component of a well-balanced diet. Human health risks associated with silverside consumption is not an issue to ignore According to these results, consumption of silverside from the mains lakes from Cordoba city would pose a carcinogenic risk, thus indicating that this type of food should be limited to avoid potential harmful exposure to these metals, especially As.

Fish consumption advisories for these fish species from SRL, LML and ERT should be established by Argentina governmental health agencies. Moreover, these results are useful tools to construct preventive and palliative policies, particularly for Hg, As and Pb, to protect the health of susceptible populations such as young children and pregnant or childbearing-age women.

Conflict of interest

The authors declare that there are no conflicts of interest.

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