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Heavy metals in fishes from the Tyrrhenian Sea and risk assessment

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ABSTRACT

The heavy metals are persistent pollutants that can bioaccumulate in marine animals such as fish, posing a risk to the marine ecosystem and human health accordingly. Therefore, the present study investigated the levels of eleven heavy metals such as arsenic (As), barium (Ba), cadmium (Cd), chromium (Cr), copper (Cu), mercury (Hg), manganese (Mn), nickel (Ni), lead (Pb) antimony (Sb), and vanadium (V) in two fish species (*Mugil cephalus* and *Diplodus annularis*) caught in the Tyrrhenian Sea along the Campania coast and assessed the risk arising from fish consumption. The analysis of heavy metals in fish edible parts was performed by Q-ICP-MS and the risk assessment was estimated by the Hazard Quotient (HQ) and the Incremental Lifetime Cancer Risk (ILCR). There were statistical differences between two fish species for three heavy metals such as Cd, As, and Hg in muscle samples which were higher in *Diplodus annularis*. Nevertheless, no samples exceeded the legal limits set for Pb, Cd, and Hg. The HQs and ILCRs showed potential risks for exposure to As, Cd, and Hg concentrations above the median. However, the no speciation of As overestimated the risk probably. Overall, the ecological features of *Diplodus annularis* could lead to greater bioaccumulation of heavy metals than *Mugil cephalus*, underscoring the need for continued assessment of different species to address potential risks.

1. Introduction

The marine ecosystem is constantly under fire from anthropic pollutants despite socio-political commitment to this issue. Heavy metals are one of the biggest environmental contaminants due to their prevalence, persistence, and toxicity (Sadighara et al., 2023). They can lead to both systemic and organ-specific adverse effects through the production of reactive oxygen species (ROS) and element-dependent mechanisms (Azeh Engwa et al., 2019). Some of them such as cadmium (Cd), vanadium (V), chromium (Cr), nickel (Ni), arsenic (As), antimony (Sb), and lead (Pb) are classified as known or probable human carcinogens due to their potential to affect DNA and its regulatory mechanisms (IARC). Others such as mercury (Hg), copper (Cu), manganese (Mn), and barium (Ba) can cause neurological, cardiovascular, hepatic, renal, respiratory, and metabolic damage (Choudhury et al., 2001; O'Neal and Zheng, 2015; Anant et al., 2018). However, some heavy metals [(Cu, Mn, Cr, zinc (Zn), selenium (Se), and cobalt (Co)] are essential for organisms and toxic in high doses. They are natural components of the soil and can be released because of volcanic aerosols and forest fires. However human activities are the main cause of their spread in the soil and in the air up to the water (Srivastava et al., 2018). Smelting, mining, fossil fuel combustion, agricultural and chemical industrial activities, vehicles, domestic heating, and human waste are the main anthropogenic sources (Rehman et al., 2018; Zwolak et al., 2019). The marine environment can be a repository for these elements, as seawater is at the end of the pollution pathway. As a matter of fact, heavy metals sink in sediment, which acts both as a reservoir and a source and hence, they can bioaccumulate in fish and other biota and biomagnify in the food chain (Ansari et al., 2003; Keshavarzi et al., 2018; Adegbola et al., 2021; Hoang et al., 2021; Wahiduzzaman et al., 2022). Bioaccumulation could depend on characteristics of marine animals such as habitats, trophic guild, and metabolism (Fernandes et al., 2007; Hosseini et al., 2013; Feng et al., 2021). Furthermore, water parameters such as the pH, hardness, salinity, alkalinity, and occurrence of organic and inorganic ions can affect the chemical forms of heavy metals (Tian et al., 2020; de Paiva Magalhães et al., 2015). As a result, their chemical speciation determines the bioavailability and toxicity in biota. However, some heavy metals (e.g. Hg) are most present in marine organisms in the most

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toxic form (Bosch et al., 2016). Therefore, the quality of marine animals including fish can depend on marine environmental pollution at different steps. On the other hand, the consumption of fish is highly recommended due to its nutritional profile (amino acids, omega-3 fatty acids, vitamins, and minerals). According to EFSA, consuming about 1–4 serving/week of seafood during pregnancy offers benefits for the functional outcomes of children's neurodevelopment and on cardiovascular diseases in adults. However, in a scientific report addressing the risks associated with methyl-Hg, they stated consuming fish species with a high contaminant content should be limited to a few servings (<1–2) in order not to exceed the Tolerable Daily intake (TWI), which may be attained before the Dietary Reference Value (DRV) for omega-3 Long--Chain Polyunsaturated Fatty Acid (LCPUFA) (EFSA, 2015). Therefore, fish can be a relevant exposure pathway for heavy metals and its contamination needs to be constantly assessed due to the potential risks associated with its consumption. For this reason, the occurrence of potentially toxic elements in fish needs to be constantly assessed. Additionally, the potential risks associated with consuming them need to be addressed as well, especially in intense urban and industrial activities such as the coast of Campania (Southern Italy). Tyrrhenian fish is widely appreciated and marketed and represents an important source of food and income. However, this fishing area can be affected by anthropogenic activity as well as historically by significant geologically activity determined by an active volcano (Vesuvius) surrounding this body of water. Recently, two studies investigated the levels of some elements in marine animals for consumption from the coast of Campania (Ariano et al., 2019; Fasano et al., 2018). Fasano et al. (2018) found no concentrations above regulatory limits in both fish and mussels, unlike Ariano et al. (2019) who reported Pb concentrations above the threshold of 300 μg/Kg in Octopus vulgaris. However, for the reasons outlined above, the risk varies depending on the fish species and the geographical areas where they are caught. Therefore, the present study provides a more comprehensive characterization of heavy metals (As, Ba, Cd, Cr, Cu, Hg, Mn, Ni, Pb, Sb, V) in the edible parts of two commercial fish species: *Mugil cephalus* (flathead grey mullet) and *Diplodus annularis* (annular sea bream). The goal of this work is to assess and compare the heavy metals contamination in these two fish species caught along the coast of Campania (Southern Italy) and assess the risk for consumers by a deterministic method.

2. Materials and methods

2.1. Sampling

Adult fish of each species (*Mugil cephalus* and *Diplodus annularis*) were caught by authorized local fishermen in July, September, December 2020, and February 2021. The species were identified at department of Veterinary Medicine and Animal Production. These species are stationary and commercially available. Both species with median weight were collected equally at each sampling site. The average length was 30 - 40 cm for *Mugil cephalus*, and 10 - 20 cm for *Diplodus annularis.* Fish that did not meet these requirements were discarded for the investigation. Overall, thirty fish (*Mugil cephalus* = 15 and *Diplodus annularis* = 15) were analysed. Sampling sites were carried out along the Campania coast (Tyrrhenian Sea) in three macro-areas characterized by intense fishing activity: Domizia, Felgrea, and Castellammare di Stabia.

2.2. Chemical and instrumental analysis

The samples were homogenised, and 1 g aliquots were mixed with 5 mL HNO_3 (65% w/w) and 2 mL of H_2O_2 (30% w/w). Then, the samples were wet mineralised in a microwave (Milestone) at 190 °C for 30 min. The digested samples were cooled and transferred to flasks with the addition of MilliQ water until a volume of 25.0 mL was reached (Agah et al., 2009). Q-ICP-MS (Thermo Scientific™ ICAP™ RQ inductively coupled plasma mass spectrometer) with a Burgener Mira-Mist nebulizer, a quartz cyclonic spray chamber, cooled to 2.7 °C, and skimmer cones was used for the heavy metals detection and quantification. All samples were analysed in duplicate, and each sample was measured in triplicate by Q-ICP-MS detection. The instrument was coupled to Thermo Scientific™ Qtegra™ Intelligent Scientific Data Solution™ (ISDS) Software. The operating conditions of the Q-ICP-MS equipment were optimised using a tuning solution (Ba, Bi, Ce, Co, In, Li, U 1.00 μg/L, Thermo Scientific) on masses ^{115}In, ^{7}Li, ^{59}Co, ^{238}U, ^{209}Bi, and ^{140}Ce was used for oxide and doubly charged interference checks. The analysis was performed in KED (Kinetic Energy Discrimination) mode using Helium as collision gas. The settings used were: plasma gas flow (Ar): 14,8 mL/min; auxiliary gas flow: 0.85 L/min; nebulizer gas flow: 0.98 L/min; cell gas flow for He: 4.8 mL/min; ICP RF Power: 1550 W; CeO/Ce = 0.0057 (Triassi et al., 2023).

Solutions were prepared with water (18.2 MΩ cm resistivity) purified using the Millipore Mill-Q® purification system, concentrated nitric acid (HNO_3 65% m/m, Suprapur®, Merck, Germany) and hydrogen peroxide (H_2O_2 30% w/w, Suprapur®, Merck). An HNO_3 1% v/v (Suprapur®, Merck, Ultrapure) solution was used to clean the Q-ICP-MS apparatus between quantifications.

HNO_3 and H_2O_2 (as mentioned earlier) were added to digest both the samples and the standard solutions. Calibration standards were prepared with multielement standard solution CertiPUR® (Merck, Darmstadt, Germany) 1000 mg L^{-1} at concentrations: 0.5, 1.0, 2.5, 5.0, and 10.0 μg L^{-1}. An internal standard mixture containing 50 μg L^{-1} Ge, 25 μg L^{-1} Y, 10 μg L^{-1} In, and 5 μg L^{-1} Ir was introduced online with an internal standard mixing kit. The internal standard elements were matched to analyte elements accordingly. The Limit of Detection (LOD) in the final sample was 0.15 μg/kg for As, Cd, Cr, Mn, Pb, Sb, V, 6 μg/kg for Ni, Ba, and Cu, and 0.03 μg/kg for Hg. Calibration curves were set by concentration ranges between 0.1 and 10 μg/L for Hg (R^2: 0.999) and 0.3 and 50 μg/L for the other heavy metals ($R^2 > 0.987$). Two blank samples were included for the reagents and digestion method and underwent all the necessary preparation steps. Instrumental calibration was verified by running two control standards for every 20 samples.

2.3. Risk assessment

The risk assessment due to exposure to heavy metals from fish consumption was based on the hazard quotient (HQ) and the incremental lifetime cancer risk (ILCR) for non-carcinogenic and carcinogenic risk, respectively.

HQs were calculated by using the estimated daily intake (EDI, μg/kg_{bw}-day) (Eq. 1) and thresholds (RfD) for each metal (m), as shown in Eq. 2. A ratio above 1 indicates a non-carcinogenic risk. Fish consumption data were obtained from the EFSA database (EFSA, 2022) for the adult population (median: 57.50 g/kg, 95th percentile: 167.20 g/kg). Hence, two risk scenarios were estimated: median and worst case. Body weight was set at 69.7 kg_{bw} according to Leclercq et al. (2009). An exposure to contaminants for 350 days/year in 70 years was supposed.

$$EDI_m = \frac{C_m \times IR \times EF \times TE}{BW \times AT} \tag{1}$$

$$HQ_m = \frac{EDI_m}{RfD_m} \tag{2}$$

C_m: concentration of each heavy metal detected in the samples (μg/kg); IR: Intake Rate of fish (kg/day); BW: Body Weight (kg_{bw}); EF: Exposure frequency (350 g/year); TE: total exposure (70 years); AT: Average lifetime (TE x 365 day/year); RfD_m: Reference dose for each heavy metal (μg/kg_{bw}/day) according to USEPA(a,*b*,c).

Multiple exposure to heavy metals was estimated by a cumulative risk assessment based on the hazard index (HI). This index is calculated by summing the individual HQ (Eq. 3). A HI above 1 points out a non-carcinogenic risk.

$$HI = \sum_{m=1}^{n} HQ_m \qquad (3)$$

The ILCR for exposure to carcinogenic heavy metals was evaluated using Eq. 4.

$$ILCR_m = EDI_m \times CSF_m \qquad (4)$$

CSF_m: Cancer Slope Factor $(\mu g/kg_{bw}/day)^{-1}$ for each carcinogenic heavy metal according to Gebeyehu and Bayissa (2020), Nduka et al. (2019), Real et al. (2017), USEPA(c).

The estimation of the risk due to exposure to multiple carcinogenic elements was determined by summing the individual ILCRs (Eq. 5)

$$ILCR_{tot} = \sum_{m=1}^{n} LTCR_m \qquad (5)$$

According to the USEPA (2011), an ILCR value greater than 1×10^{-4} indicates a high risk of developing cancer over a human lifetime, whereas values between 1×10^{-6} and 1×10^{-4} are considered an acceptable range for cancer risk. Health Canada instead suggests a lower value (1×10^{-5}) as the maximum safety threshold for cancer risk (Health Canada, 2010).

2.4. Statistical analysis

Statistical analysis was carried out using GraphPad Prism version 9 software (GraphPad Software Inc, La Jolla, CA, USA). The Kolmogorov-Smirnov test and the Shapiro-Wilk test were used to test the normality of the data. Since our data set is not normally distributed, we applied a non-parametric test (Kruskal-Wallis test) to assess the significance of the differences between the heavy metal concentrations in the two different matrices analysed. Data analysis and graph processing were performed using R Software version 3.6.0 and the following packages: ggplot2 (Team, 2009). An upper-bound approach was used, assuming concentrations below the LOD equal to the LOD. The risk assessment was performed for heavy metals that reported a central distribution above the LOD.

3. Results and discussion

3.1. Occurrence of heavy metals

The concentrations (mean ± SD, median, min, and max) of each heavy metal in both fish species are listed in Table S1. Statistically significant differences between the two fish species emerged for Cd (p-value<0.05), As, and Hg (p-value<0.01). *Diplodus annularis* showed the highest median values (median, min – max μg/kg w.w.) for all the three heavy metals (As: 81.11, 32.02 – 579.10; Cd: 4.41, <LOD – 24.10; Hg: 101.00, 4.02 – 450.50) than *Mugil cephalus* (As: 22.90, 13.11 – 110.29; Cd: <LOD, <LOD – 24.10; Hg: 7.59, <LOD – 445.01) as depicted in Fig. 1. Both species reported median values <LOD for Ba, Cr, Cu, Mn, Ni, Pb, Sb, and V.

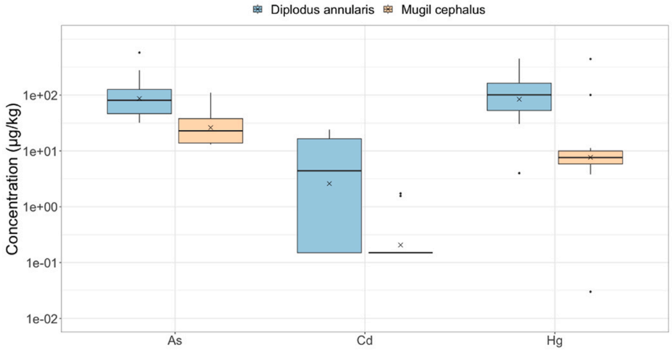

Fig. 1. Concentration (μg/kg w.w.) of As, Cd, and Hg detected in *Diplodus annularis* and *Mugil cephalus* fish samples.

Diplodus annularis demonstrated to be more prone to bioaccumulate heavy metals than *Mugil cephalus*. This trend could be ascribable to biological and/or ecological factors of these two species. Indeed, *Diplodus annularis* and *Mugil cephalus* are omnivorous species belonging to the benthopelagic and pelagic domains, respectively. This behavior suggests that fish closer to the sediment bioaccumulate more heavy metals settling on the bottom (Ansari et al., 2003). As a result, heavy metals levels in fish could depend on their habitat rather than size (see paragraph 2.1), although other factors such as metabolic rate could take part in bioaccumulation phenomena. Likewise, other studies reported a major attitude of benthopelagic species of bioaccumulation Hg (Hilgendag et al., 2022), Cd (Jiang et al., 2018), and As (Saei-Dehkordi et al., 2010) than pelagic one. However, there seems to be a lack of research in the literature addressing the comparison of heavy metals bioaccumulation between Diplodus annularis and Mugil cephalus.

Previous studies determined the bioaccumulation of some heavy metals in these two fish species in Italy. Squadrone et al. (2013) investigated the levels of Pb, Cd, and Hg in *Mugil cephalus* from the Ligurian Sea (northern Italy). They reported higher values (median, min – max μg/kg) than we did for Pb (50, <LOQ (40) – 240) but similar values for Cd (10, <LOQ (10) – 10). The concentrations of Hg were reported as below the LOQ (100 μg/kg), On the contrary, Bonsignore et al. (2013) reported higher levels (mean ± SD μg/g) of Hg (557 ± 303) in *Diplodus annularis* from Augusta Bay (southern Italy). The urban and industrial activity, environmental parameters, and seasonality are potential factors that can affect the levels of contaminants in the sea water (Tian et al., 2020; Rajeshkumar et al., 2018). In addition, geological features of a volcanic area (as in the present study) may contribute to releasing heavy metals into the environment influencing their bioaccumulation in biota (Varrica et al., 2000).

Recently, some studies assessed the levels of heavy metals in the Campania coast area in other marine animals. Ariano et al. (2019) showed mean concentrations of Pb varying between 537 μg/kg in Castellammare di Stabia and 46 μg/kg in Naples in octopus' muscle.

Esposito et al. (2020) detected higher levels of As in sea turtles muscle, with a median values ranging from 200 to 154500 μg/kg. In contrast, they reported levels of Cd and Hg below the LOQ (5 and 89 μg/kg, respectively).

The European Commission has set maximum levels for heavy metals in fish muscle (Commission Regulation (EC) No, 1881/2006). The legal limits for Pb, Cd, and Hg are 300, 50 and 500 μg/kg w.w., respectively. In view of this, no samples of either species exceeded the maximum permissible levels. Therefore, contamination of heavy metal in these fish species caught along the coast of Campania in the Tyrrhenian Sea was within the legally acceptable limits for safe consumption.

3.2. Health risk assessment

The median EDI (Table S2) derived by chronic exposure to As, Cd, And Hg were below the corresponding RfD (HQ<1).

EDI_{Hg} was 0.025 and 0.072 μg/kg/day in the median scenario and worst scenario, providing the highest contribution to the maximum daily exposure (25.03% and 72.08% rspectively). However, the HQ_{Hg} was above 1 for heavy metals concentrations above approximately the 75° percentile (median scenario) and median (worst scenario) (Fig. 2).

The median HQ_{As} was 0.12 (EDI_{As}: 0.036 μg/kg/day) and 0.34 (EDI_{As}: 0.104 μg/kg/day) in the median case and worst case, although rarely exceeded the threshold value.

On the other hand, the HI from cumulative exposure was above 1 in the worst scenario.

The median ILCR based on exposure to the Cd was below the thresholds value in median (4.51e-08) and worst (1.31e-07) scenario, although in the letter the index exceed 1e-05 (Health Canada threshold) for higher heavy metal concentration (Fig. 3). The median ILCR from As

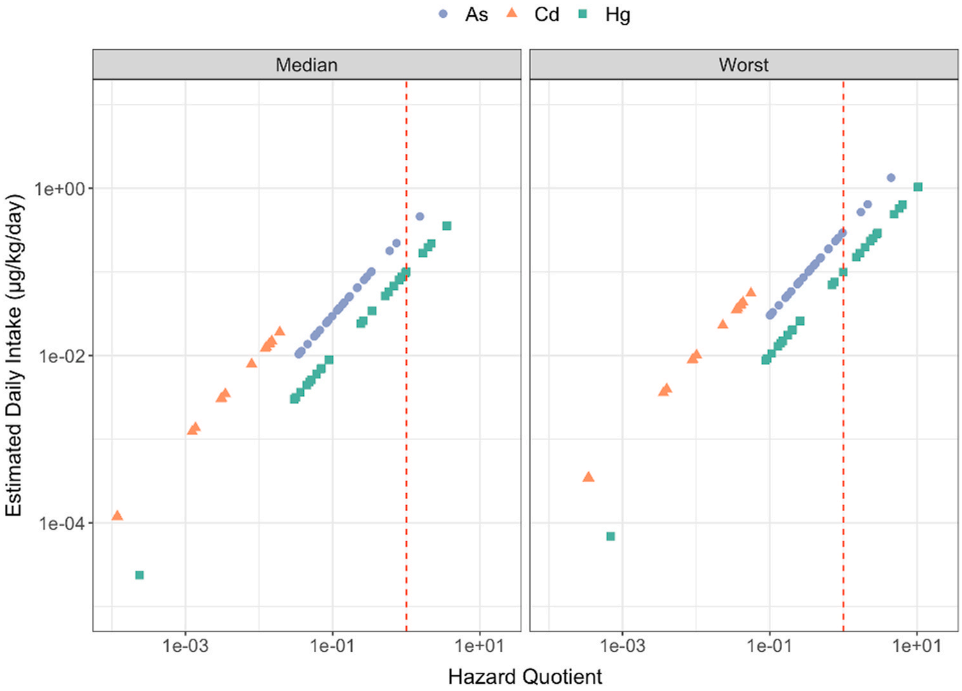

Fig. 2. Hazard Quotient (HQ) and the corresponding threshold values (red line) from As, Cd, and Hg exposure in a median and 95th percentile (worst) consumption scenario.

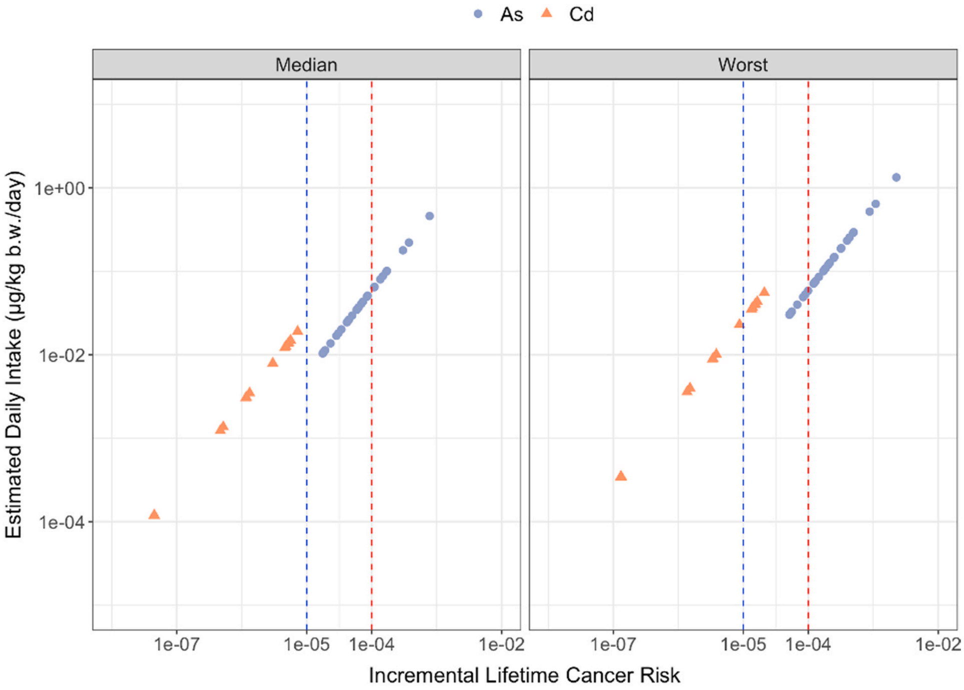

Fig. 3. Incremental lifetime cancer risk (ILCR) from carcinogenic heavy metals exposure in a median and 95th percentile (worst) consumption scenario. The red y-intercepts at 1e-04 according to USEPA (2011) and the blue y-intercept at 1e-05 according to Health Canada (2010) indicate the threshold values for a negligible cancer risk.

exposure exceeded the Health Canada and USEPA threshold values in median (5.89e-05) and worst (1.17e-04) scenario respectively. Consequently, the sum of ILCRs was above at least one threshold value in both scenarios Therefore, the risk of developing cancer by fish consumption was estimated to be over 1:100000 people. However, these estimations do not take into account the speciation of heavy metals. Especially, the RfD_{As} and CSF_{As} are based on evidence from human exposure to inorganic arsenic. On the other hand, the no-toxic organic form (e.i. arsenobetaine) is dominant in marine animals (Zhang et al., 2016) and it could account for almost all the arsenic in fish (Krishnakumar et al., 2016; Lorenzana et al., 2009; Donohue and Abernathy, 1999; Francesconi and Edmonds, 1996). Secondly, according to Lischka et al. (2013), arsenolipids, a toxic organic arsenic specie may be predominant (62%) in fatty fish such as Clupea harengus. Overall, human risk assessment should be estimated on an inorganic As species analysis according to USEPA (2000). Therefore, the risk assessment for As exposure should consider the limitation of the present study that could overestimate the risk. Otherwise, Cd and Hg are typically found in the toxic forms (EFSA, 2015; 2009).

4. Conclusions

Eleven heavy metals were assessed in the muscles of *Mugil cephalus* and *Diplodus annularis* in the Gulf of Naples (Italy) and three heavy metals (Cd, As, and Hg) reported statistical differences between species. *Diplodus annularis* showed greater bioaccumulation of heavy metals probably due to its habitat. However, both species do not exceed the legal limits set for Pb, Cd, and Hg. Potential concerns from risk assessment usually emerged from exposure to heavy metals concentrations above the central distribution in both median and 95th percentile consumption scenarios. However, the no speciation could lead to a likely overestimation of the risk from As exposure. Overall, this study provides the first data on heavy metals in these two fish in waters near metropolitan and industrial areas of Naples, and further evidence on different bioaccumulation of contaminants depending on specie features was given.

CRediT authorship contribution statement

Marcello Scivicco: Methodology, Formal analysis, Investigation, Data curation, Writing - Original draft preparation. **Nunzio Antonio Cacciola:** Methodology, Formal analysis, Data curation, Writing - Original draft preparation, Writing - Review & Editing, Visualization; **Francesco Esposito:** Methodology, Formal analysis, Investigation, Writing - Original draft preparation, Validation, Data curation, Writing-Original draft preparation, Writing - Review & Editing, Supervision; **Jonathan Squillante:** Investigation, Formal analysis, Data curation, Writing- Original draft preparation, Writing - Review & Editing, Visualization; **Andrea Ariano:** Conceptualization, Formal analysis, Investigation; **Lucrezia Borriello:** Data curation, Writing - Original draft preparation, Writing - Review & Editing; **Teresa Cirillo:** Supervision, Writing - Review & Editing. **Lorella Severino:** Conceptualization, Writing - Review & Editing, Resources, Supervision, Project administration.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jfca.2024.106027.

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