



# Mercury–Selenium Accumulation Patterns in Muscle Tissue of Two Freshwater Fish Species, Eurasian Perch (*Perca fluviatilis*) and Vendace (*Coregonus albula*)

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**Abstract** Mercury (Hg) in the form of highly toxic methyl mercury (MeHg) accumulates in aquatic food webs to an extent where it may threaten fish health in many freshwaters. Selenium (Se) mitigates the toxicity of accumulated Hg by forming strong bonds with it, a drawback being diversion of Se from biosynthetic pathways of essential selenoenzymes. We measured Se and Hg in muscle tissue of Eurasian perch (*Perca fluviatilis*) and vendace (*Coregonus albula*). For the

perch, Se and Hg correlated positively. For the vendace, a positive relationship was seen when the effect of fish size was accounted for. All fish displayed surplus Se ( $\text{mol Se} - \text{mol Hg} > 0$ ). For both fish species, the Se molar surplus ( $(\text{nmol Se} - \text{nmol Hg})/\text{g ww}$ ) decreased with fish weight. It was higher in the perch than in the vendace and showed the least variation among the small perch (4–34 g). For the large perch (79–434 g), the Se molar surplus decreased with increasing Hg below  $0.5 \mu\text{g Hg}$  but then increased with further Hg increment despite Hg being a negative term in the Se molar surplus. In case the Se molar surplus reflected the weight-specific Se requirement, the latter clearly decreased with increasing fish size for the vendace. This was less clear for the perch because of the strong correlation between Hg and weight. Together, these Se–Hg relationships suggest that Se accumulation was at least partly subject to homeostatic control and responded to the Hg body burden and the Se requirement.

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## 1 Introduction

Virtually, all mercury (Hg) in fish muscle is in the form of highly toxic methyl mercury (MeHg) (Bloom, 1992). Fish Hg levels prompting fish consumption advisories are frequently found in piscivorous fish

(Stahl et al., 2009), even far from point sources of Hg pollution (Braaten et al., 2019). Toxic reference values (TRVs) for fish tend to be set at lower Hg levels than those set for fish consumption advisories (Fuchsman et al., 2016), suggesting that fish health is also at risk.

It has been known since the 1960s that selenium (Se) can alleviate MeHg toxicity (Parizek & Ostádalová, 1967). Yet, fish consumption advisories and TRVs do not take Se into account, probably because knowledge is still lacking with regard to the evaluation and quantification of Se effects on MeHg toxicity (Gerson et al., 2020). The formation of stable Se and MeHg compounds is a double-edged process that lowers the reactivity and toxicity of MeHg (Bjørklund et al., 2017) but causes a withdrawal of Se from the biosynthesis of vital selenoenzymes (Manceau, Azemard, et al., 2021; Ralston & Raymond, 2010; Spiller, 2018). In a study of brown trout (*Salmo trutta*), thyroid hormone imbalance was linked to Se:Hg molar ratios < 1. The authors proposed that Hg, through its binding of Se, interferes with the production of the selenoenzymes iodothyronine deiodinases (Mulder et al., 2012).

Fish typically have larger selenoproteomes than other vertebrates (Lobanov et al., 2009), suggesting that the ability to efficiently accumulate selenium is critical to the health of fish populations. Atmospheric depositions have a significant effect on both Hg and Se inputs to lakes (Watras et al., 2019; Wiklund et al., 2020). Both elements have shown declining atmospheric deposition during the recent decades (Donner et al., 2019; Zhang et al., 2015). Thus, despite declining lake fish Hg levels (Braaten et al., 2019), negative effects of Hg on lake fish populations could persist if the fish cannot accumulate sufficient Se to uphold a functional selenoenzyme production.

Little is known about the mechanisms of Se uptake in fish and whether fish can upregulate their Se accumulation when needed to uphold a sufficient selenoprotein production. A study of selenite uptake by rainbow trout enterocytes and hepatocytes implicated the involvement of anion membrane transporters. A further finding was that selenite uptake was enhanced by the presence of thiols, possibly through the conversion of selenite to reduced Se species for which high-affinity transport systems may be involved (Misra et al., 2012).

Positive relationships between Hg and Se have been reported for marine mammals (Koeman et al., 1973) and for fish (Azad et al., 2019; Økelsrud et al., 2016). These are consistent with, yet provide no proof of, an ability to increase Se accumulation in response to increased Hg loads. In contrast, negative relationships between fish Hg and fish Se have been reported for high-Se waters (Belzile et al., 2009; Mailman et al., 2014; Paulsson & Lundbergh, 1989; Southworth et al., 1994). Feeding experiments have shown that Se-enriched food reduces MeHg accumulation in fish (Bjerregaard et al., 2011; Deng et al., 2008; Wang & Wang, 2017). Thus, there may be two processes with opposite effects on the relationship between Se and Hg in fish, where one or the other is the strongest depending on the Se and Hg exposure.

No published study seems to have addressed the question whether fish regulate their Se accumulation to handle Hg stress. Our analyses of relationships between Se and Hg in muscle tissue of Eurasian perch (*Perca fluviatilis*) and vendace (*Coregonus albula*) suggest that these fish do respond to increasing Hg loads by increasing their Se accumulation. This tentative conclusion should encourage efforts to prove or disprove that fish can use Se as a remedy against Hg toxicity.

## 2 Material and Methods

### 2.1 Study Site

The study lake Bengtsbrohöljen (lake area: 1.1 km<sup>2</sup>, mean depth 12 m, maximum depth 32 m) is an oligotrophic, low dissolved organic carbon (5 mg L<sup>-1</sup>), circumneutral boreal lake situated in southwestern Sweden 30 km east of the Norwegian border (Fig. S1). It was severely Hg-polluted by a chlor-alkali factory (closed in 1925).

### 2.2 Sampling

Perch (3.6–433.9 g,  $n=49$ ) and vendace (27–60 g,  $n=30$ ) were collected using gill nets in different parts of the lake (Fig. S1). Prior to analyses of Se–Hg relationships, the perch were divided into “small” (3.6–34.5 g,  $n=29$ ) and “large” (78.6–433.9 g,  $n=20$ ) individuals to allow comparison between similar-sized perch and vendace with similar diet and

to separate piscivorous from non-piscivorous perch. The large perch were all caught in August 2019 and all the vendace in November 2019. The small perch were caught on both these occasions. It is likely that the small perch fed mostly on zooplankton and invertebrates and that the large perch were partly piscivorous (Mittelbach & Persson, 1998). A change in diet to piscivory is known to dramatically increase the exposure to MeHg (e.g., MacCrimmon et al., 1983). Vendace of all sizes feeds on zooplankton (Hamrin, 1983). The fish were stored frozen until analysis.

The sediment samples were collected using a gravity corer (Limnos, Ø 93 mm, with a built-in 60 cm slicing system, 1 cm resolution, Poland). The samples were stored frozen until analysis.

The surface water samples (grab samples from the central part of the lake) were collected using long gloves and acid-washed Teflon bottles. The samples were immediately shipped to the laboratory where half of them were filtered (<0.45 µm) directly on arrival and then preserved together with the unfiltered samples by adding hydrochloric acid (0.5%).

### 2.3 Chemical Analyses

Total Hg in water samples was oxidized by adding BrCl and let stand for 12 h.  $\text{NH}_2\text{OH}\cdot\text{HCl}$  was then added prior to reduction of all Hg species to  $\text{Hg}^0$  using  $\text{SnCl}_2$ .  $\text{Hg}^0$  was driven off with nitrogen gas and collected on gold traps, followed by thermal desorption and quantification using a Tekran 2500 cold vapor atomic fluorescence spectrophotometer (CV-AFS) (Tekran Instruments Corporation, ON, Canada). Limit of detection (LOD) was  $0.04 \text{ ng L}^{-1}$  and limit of quantification (LOQ)  $0.1 \text{ ng L}^{-1}$ . Prior to reduction of Hg, 0.3–0.5 g solid samples (fish muscle, sediment) were wet oxidized using  $\text{HNO}_3/\text{H}_2\text{O}_2$  (final volume 50 mL). The vessels (Quarts Inserts) were placed in a microwave oven (Milestones Ethos PU, Italy) under temperature and pressure control. Digested samples were analyzed following the same protocol as for the water samples (LOD:  $0.03 \text{ ng g}^{-1}$ , LOQ:  $0.1 \text{ ng g}^{-1}$ ).

MeHg was separated from water and sediment samples by a distillation procedure. After aqueous-phase ethylation, separation by isothermal gas chromatography, and pyrolysis, MeHg was quantified using an atomic fluorescence detector (Brooks Rand model III and software Mercury Guru, WA, USA).

Standards were made from stock solutions purchased from Brooks Rand and Alfa Aesar, USA (LOD and LOQ:  $0.02 \text{ ng L}^{-1}$  and  $0.06 \text{ ng L}^{-1}$ , respectively).

Total Se in water samples was quantified using an Inductively Coupled Plasma–Quadrupole Mass Spectrophotometer (ICP-QMS) (Thermo Scientific, Model iCAP Q, Germany), and interference elimination using a collision cell containing helium. LOD was  $0.005 \text{ µg L}^{-1}$  and uncertainty of measurement was 20%. The same digested samples as for the total Hg determination were used to determine total Se in fish muscle. After dilution to a specified volume, the samples were analyzed using ICP-QMS. LOD was  $0.1 \text{ µg g}^{-1}$  and uncertainty of measurement was 25%.

Results from analyses of certified reference material (total Hg, MeHg, and Se in solid samples) are provided in the Supplementary Information.

The muscle fat content was determined in five separate individuals of perch and vendace, respectively. The samples were homogenized and mixed with silica gel and anhydrous sulfate (1:1). The mixtures were then transferred to extraction thimbles and extracted with dichloromethane:hexane (1:1) in soxhlet extractors for at least 16 h. Most of the solvents were then removed in a rotary evaporator and the rest in an oven at  $105 \text{ °C}$ . Thereafter, the fat content was determined gravimetrically.

### 2.4 Data Analyses

Data analyses were performed using R free software version 4.0.3 (R Core Team, 2021).

To investigate whether differences between means were statistically significant ( $P < 0.05$ ), the Mann–Whitney and Kruskal–Wallis tests were performed. The Spearman rank correlation test was used to investigate relationships between two variables. Multiple linear regression (MLR) on Se vs. Hg for vendace was performed adjusting for weight in base R using “lm” and “residuals” functions with the following formula:  $\text{Se} \sim \text{Hg} + \text{Weight}$ . The normality of residuals was investigated visually by reviewing diagnostic plots, such as Q–Q plots, residuals vs. fitted, and histograms of residuals (Fig. S2). The diagnostic plots did not indicate severe violation of normality assumption of residuals in the MLR model used. Relationships between Hg and Se, and Hg and the Se molar surplus (see definition below) were analyzed in a generalized linear model. The

presence of a breakpoint along Hg concentrations was identified using Davies' test, with the likelihood ratio test for significance in the package "segmented" (Mueggo, 2008). Outliers were identified using Grubbs' test for one outlier. Frequency distributions before and after the exclusion of one outlier are provided in Figure S3.

The Se molar surplus was defined as nmol Se – nmol Hg per gram wet weight. We also calculated Se:Hg molar ratios (mol Se mol Hg<sup>-1</sup>). To investigate how the relationship between these two metrics is affected by the Hg concentration, we used the equation

$$\text{Se/Hg} = 1 + (\text{Se} - \text{Hg})/\text{Hg} \quad (1)$$

where Se/Hg is the Se:Hg molar ratio and Se – Hg is the molar difference between Se and Hg, the latter which per unit weight is equal to the Se molar surplus as defined above.

Assuming that the Se molar surplus is constant (*k*), we get

$$\text{Se/Hg} = 1 + k/\text{Hg} \quad (2)$$

By fitting the fish Se and Hg data to Eq. 2, a value of *k* is obtained. By regressing the calculated values of the Se:Hg molar ratio (using the determined value of *k* in Eq. 2) against the measured Se:Hg molar ratios, an *r*<sup>2</sup>-value is obtained that reflects the degree to which the Se molar surplus is constant over the measured Hg range. Graphically, it is possible to see at what fish Hg values the Se molar surplus diverges the most from the value of *k*.

### 3 Results

#### 3.1 Total Hg and MeHg in the Sediment

The surface sediment (0–2 cm) total Hg levels in the littoral zone (measured in 2019) averaged 3.7 μg Hg g<sup>-1</sup> dw (range: 2.1–6.5, *n*=22), which is 20–30 times higher than the regional background levels (Table S1). There was no clear concentration gradient away from the historical pollution source (Fig. S1). The mean MeHg level for the same samples was 15.5 ng g<sup>-1</sup> dw (range: 1.1–53, *n*=22) (Table S1).

At two accumulation sites in the central and southern part of the lake, the total Hg concentrations in the 0–2 cm surface layers were 2.3 and 1.9 μg Hg g<sup>-1</sup> dw, respectively (Fig. S1). However, in the most contaminated layers, 11–12 cm (central location) and 8–9 cm (southern location), total Hg reached 72.2 and 49.6 μg Hg g<sup>-1</sup> dw, respectively.

#### 3.2 Total Hg, MeHg, and Total Se in the Surface Water

Total Hg ranged between 1.1 and 1.6 ng L<sup>-1</sup> in unfiltered water and between 0.8 and 1.1 ng L<sup>-1</sup> in filtered water (<0.45 μm), whereas MeHg was below detection (<0.06 ng L<sup>-1</sup>). As opposed to the sediment, the Hg levels in the water were not clearly elevated relative to other Scandinavian lakes (Table S1). The total Se levels ranged between 92 and 120 ng L<sup>-1</sup> in unfiltered water and between 91 and 120 ng L<sup>-1</sup> in filtered water (<0.45 μm) and were at the higher end of those measured in other Scandinavian lakes (Table S1).

#### 3.3 Total Hg and Total Se in the Fish

All fish data are provided in Table S2. The Hg levels were somewhat higher and the Se levels similar to those found in the same fish species in other Scandinavian forest lakes (Table S1). Hg showed significantly higher levels in the vendace than in the small perch (Mann–Whitney, *P*<0.001). In contrast, Se showed significantly higher levels in the small perch than in the vendace (*P*<0.005). Both the Hg and Se levels were significantly higher in the large perch than in the small perch and the vendace (Kruskal–Wallis test, *P*<0.001). Box plots are provided in Figure S4.

#### 3.4 Relationships Between Se, Hg, and Weight

Hg increased with weight in both the perch (*ρ*=0.94, *P*<0.0001; both size classes combined) and the vendace (*ρ*=0.54, *P*<0.005). Se increased with weight in the perch (*ρ*=0.72, *P*<0.0001) but not in the vendace (*ρ*=–0.23, *P*=0.22) (Fig. S5). The relationship between Hg and weight was much stronger for the small perch (*ρ*=0.83, *P*<0.0001) than for the large perch (*ρ*=0.57, *P*<0.05). This was also the case for Se, which did not significantly

increase with weight for any of the two size classes of perch (small perch:  $\rho=0.30$ ,  $P=0.12$ ; large perch:  $\rho=0.07$ ,  $P=0.75$ ) (Fig. S6).

There was a positive correlation between Se and Hg for the perch ( $\rho=0.77$ ,  $P<0.0001$ ), but not for the vendace ( $\rho=0.17$ ,  $P=0.45$ ) (Fig. 1).

For the vendace, the multicollinearity between Hg and weight was sufficiently low (variance inflation factor for weight and Hg: 2.3) to allow us to model Se ( $\text{ng g}^{-1}$  ww) in terms of Hg ( $\text{ng g}^{-1}$  ww) and wet weight (g) using MLR. This model ( $\text{Se}=0.263*\text{Hg}-2.272*\text{Weight}+260$ ,  $r^2=0.22$ ) revealed a positive relationship between Se and Hg ( $P=0.079$ ), and a negative relationship between Se and weight ( $P<0.01$ ). Substituting length (mm) for wet weight resulted in a somewhat better MLR model ( $\text{Se}=0.382*\text{Hg}-2.066*\text{Length}+493$ ,  $r^2=0.33$ ) where both Hg and length had a significant influence on Se ( $P<0.05$  and  $P<0.005$  respectively).

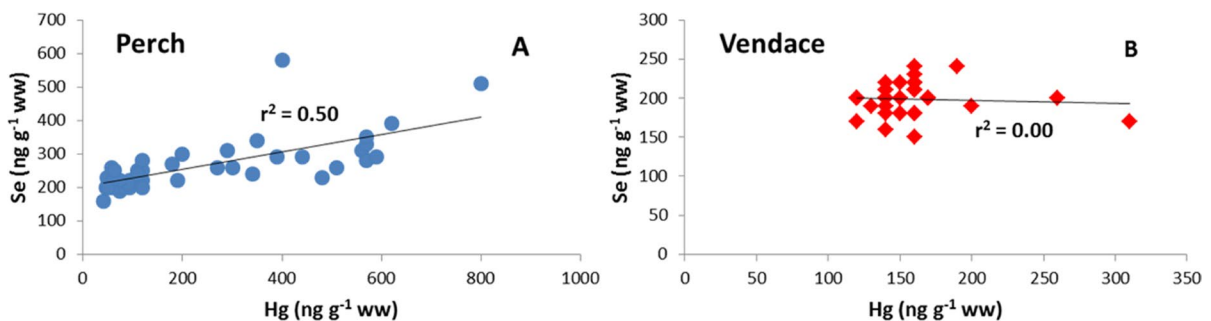
### 3.5 Se Molar Surpluses Versus Hg

For the small perch, the Se molar surplus varied independently of Hg, while it decreased with Hg for the vendace, though not significantly ( $P>0.05$ ) (Fig. 2A and B). There was an outlier (Grubbs' test for one outlier) among the large perch with respect to both the Se molar surplus ( $P<0.01$ ) (Fig. 2C) and Se ( $P<0.01$ ) (Fig. 2D), but not with respect to Hg ( $P=0.2$ ). Repeating the Grubbs' test for one outlier, one Se outlier remained ( $P<0.01$ ) but no Se molar surplus outlier ( $P=0.7$ ). We have no reason to believe that the determinations of Se or Hg in the outlier perch were incorrect. Excluding the individual which was an outlier with respect to both

Se and the Se molar surplus, the Davies test identified a significant break point at  $0.5 \mu\text{g Hg g ww}^{-1}$  ( $P<0.001$ ) for the generalized linear model of both Se molar surplus vs. Hg and Se vs. Hg for the large perch (Fig. 2C and D). For the perch with Hg concentrations at or above the break point concentration ( $n=9$ ) (red-encircled), the Spearman rank correlation test showed a positive correlation between Se and Hg ( $\rho=0.81$ ,  $P<0.05$ ) (Fig. 2D) and a close to significant positive relationship between the Se molar surplus and Hg ( $\rho=0.68$ ,  $P=0.055$ ) (Fig. 2C), despite Hg being a negative term in the Se molar surplus. Excluding the second outlier with respect to Se, although it conforms well with the general pattern, as opposed to the first outlier (Fig. 2C and D; Fig. 3A), the correlation between Se and Hg was still close to being significant ( $\rho=0.74$ ,  $P=0.0528$ ).

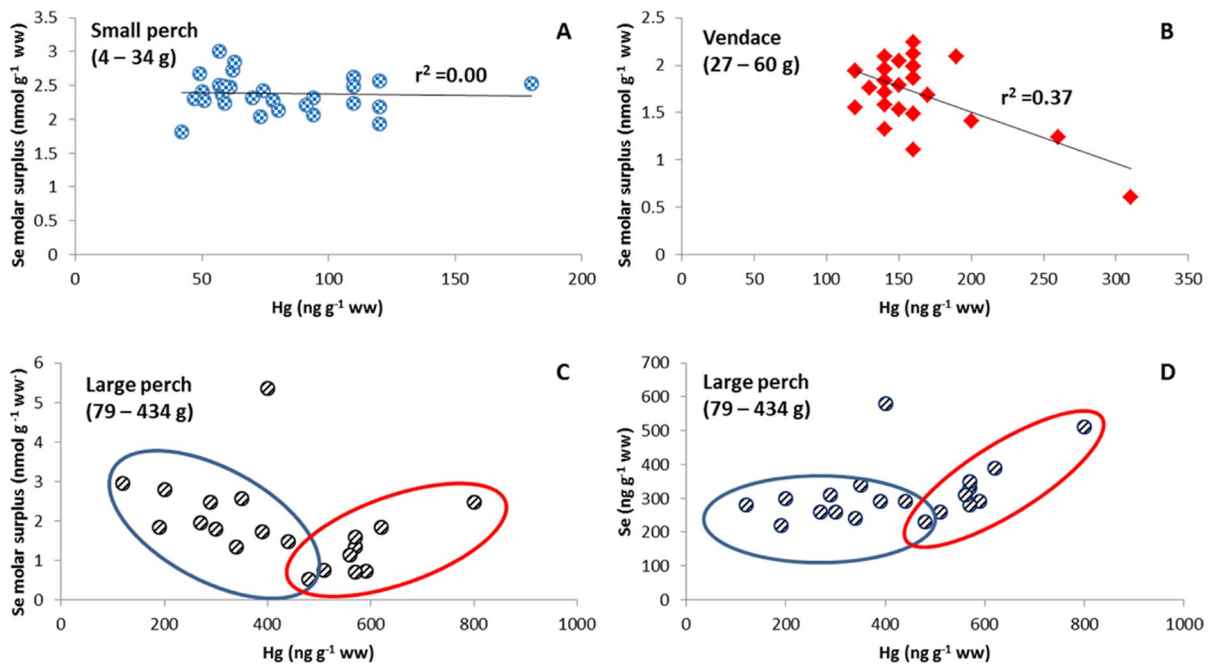
### 3.6 Stability and Level of the Se Molar Surplus Values for the Perch and Vendace

Assuming a constant Se molar surplus ( $k$ ) and fitting  $k$  in Eq. 2 to the Hg and Se data by minimizing the sum of squared errors (SSE) leads to  $k_{\text{perch}}=2.38 \text{ nmol g}^{-1} \text{ ww}$  ( $r^2=0.95$ ,  $n=49$ ) and  $k_{\text{vendace}}=1.77 \text{ nmol g}^{-1} \text{ ww}$  ( $r^2=0.70$ ,  $n=30$ ) (Fig. 3). It thus appears that the assumption that the Se molar surplus is constant better holds for the perch than for the vendace. Also, the perch overall displayed higher Se molar surplus values than the vendace.



**Fig. 1** Relationships (best fit regression lines) between total selenium (Se) (in  $\text{ng g}^{-1}$  ww) and total mercury (Hg) (in  $\text{ng g}^{-1}$  ww) for **A** perch ( $n=49$ ) and **B** vendace ( $n=30$ ) from the study lake Bengtsbrohöljen. Several vendace data points coincide





**Fig. 2** Se molar surplus (in  $\text{nmol g}^{-1} \text{ ww}$ ) versus Hg (in  $\text{ng g}^{-1} \text{ ww}$ ) for **A** the small perch ( $n=29$ ), **B** the vendace ( $n=30$ ), **C** the large perch ( $n=20$ ), and **D** Se (in  $\text{ng g}^{-1} \text{ ww}$ ) vs. Hg (in  $\text{ng g}^{-1} \text{ ww}$ ) for the large perch from the study lake Bengts-

brohöljen. Several vendace data points coincide. Data points for the large perch are encircled to show the different trends. The data point which is not encircled was a significant outlier (Grubbs' test)

### 3.7 Se Molar Surpluses and Se:Hg Molar Ratios vs. Weight

For the small perch, as opposed to the vendace, the Se molar surplus was stable and seemingly independent of weight, whereas the Se:Hg molar ratio decreased with weight for both fish categories. The negative correlation between the Se molar surplus and weight displayed by the vendace was significant ( $\rho = -0.44$ ,  $P < 0.05$ ). There was a negative correlation (though not significant) between the Se molar surplus and weight for the large perch ( $\rho = -0.44$ ,  $P = 0.06$ ) (Fig. 4). For the small and large perch combined, there was a significant negative correlation between the Se molar surplus and weight (outlier included:  $\rho = -0.47$ ,  $P < 0.005$ , outlier excluded:  $\rho = -0.51$ ,  $P < 0.001$ ).

### 3.8 Fat Content of Perch and Vendace

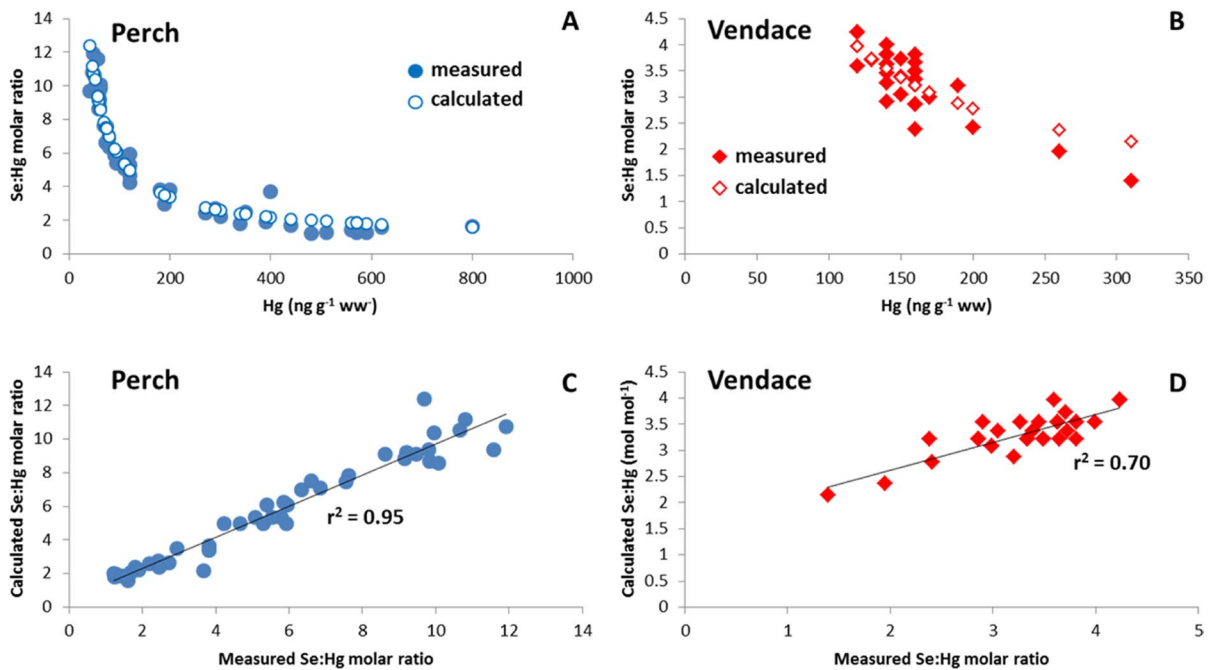
Fat content was measured in the muscle tissue of five additional perch and vendace. In perch, the fat content varied between 0.64 and 0.9% (wet weight basis), and

in vendace, between 1.65 and 2.01%. The fat content decreased with weight for the perch and increased with weight for the vendace, though not significantly in either case ( $\rho = -0.9$ ,  $P > 0.05$ ) and ( $\rho = 0.9$ ,  $P > 0.05$ ) (Fig. S7).

## 4 Discussion

### 4.1 Implications of the Observed Se–Hg Relationships

In this study, we found that (i) Se increased significantly with Hg for the perch (Fig. 1), (ii) Se was positively correlated with Hg for the vendace ( $P < 0.05$ ) when the effect of length (negatively related to Se) was accounted for, (iii) there was no correlation between the Se molar surplus and Hg for the small perch (Fig. 2A), despite Hg being a negative term in the Se molar surplus, (iv) there was a significant positive correlation between Se and Hg for the large perch with Hg levels at or above the break point ( $0.5 \mu\text{g Hg g ww}^{-1}$ ) (Fig. 2D), and (v)



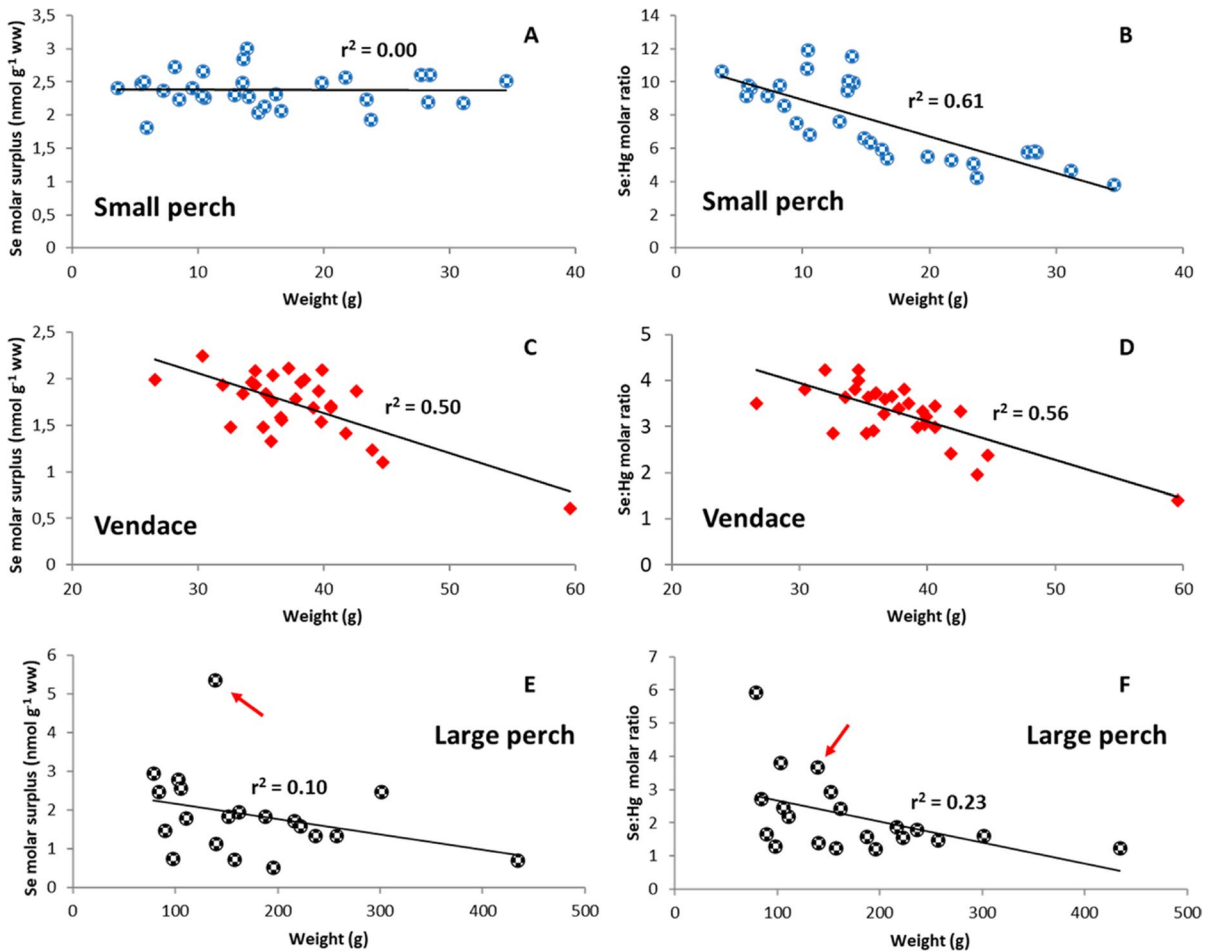
**Fig. 3** Calculated and measured Se:Hg molar ratios versus Hg for **A** the perch and **B** the vendace from the study lake Bengtsbrohöljen. Calculated values were obtained assuming (i) a constant Se molar surplus for each fish species and (ii) choosing Se molar surplus values that resulted in the least

sum of squared errors ( $2.38 \text{ nmol g}^{-1} \text{ ww}$  for the perch and  $1.77 \text{ nmol g}^{-1} \text{ ww}$  for the vendace). **C, D** Calculated versus measured Se molar ratios for the perch ( $n=49$ ) and the vendace ( $n=30$ ). Best fit regression lines are shown

for the latter perch, there was a marginally significant positive correlation ( $0.05 < P < 0.06$ ) between the Se molar surplus and Hg, despite Hg being a negative term in the Se molar surplus (Fig. 2C).

An interesting possibility is that the positive relationships between Se and Hg shown by both fish species in this study were caused by an increased uptake of Se in response to physiological disturbance caused by Hg. An increasing number of researchers have proposed that an important aspect of MeHg toxicity is the disruption of selenoenzyme production (e.g., Dolgova et al., 2019; Mulder et al., 2012; Ralston & Raymond, 2010; Spiller, 2018). MeHg and Se are known to react and form various Hg–Se compounds (Manceau, Azemard, et al., 2021), suggesting that MeHg exposure can divert Se from biochemical pathways of selenoenzyme production, in effect that MeHg causes a shortage of Se. Furthermore, physiological damage caused by MeHg, such as increased oxidative stress (Birnie-Gauvin et al., 2017; Morcillo et al., 2017), may increase the requirement for selenoenzymes known

to provide antioxidant defense such as glutathione peroxidases and thioredoxin reductases (Grim et al., 2011; Pacitti et al., 2014). It is also possible that Se serves to displace MeHg and/or inorganic Hg from sensitive thiol and selenol sites (Madabeni et al., 2020). In fish, but also in other organisms, the binding of MeHg by selenocysteine apparently leads to the demethylation of MeHg and subsequent storage of inorganic Hg bound to selenocysteine and selenide (Manceau, Bourdineaud, et al., 2021). Possibly, the change in the relationship between Hg and Se shown by the large perch (Fig. 2C and D) was explained by elevated requirements for selenoenzymes once Hg exposure increased. A food switch when reaching a certain size could have explained the change in the relationship between these variables. However, the correlation between Hg and weight was weak for the large perch (Fig. S6; Fig. S8). It seems unlikely, but cannot be entirely excluded, that some of the perch, irrespective of size, preferred prey items that happened to have a high Hg and an even higher Se content. It is of note that the vendace displayed a less stable Se molar



**Fig. 4** Se molar surplus (in  $\text{nmol g}^{-1}$  ww) versus wet weight (in grams) for the small perch (A), the vendace (C), and the large perch (E) from the study lake Bengtsbrohöljen, and Se:Hg molar ratio versus wet weight for the small perch (B),

the vendace (D), and the large perch (F). Best fit regression lines are shown. The identified outlier perch with respect to both Se and the Se molar surplus is marked with an arrow. It was included in both regressions

surplus than the perch (Fig. 3), despite a more variable diet of perch than of vendace (vendace being obligate planktivores). This is opposite to what would be expected if the Se and Hg levels of these fish had simply reflected those of their food items.

We have been unable to find any published articles discussing the possibility that organisms increase their Se uptake in response to Hg exposure, even though positive relationships between Se and Hg have been observed for several organisms, including fish (Azad et al., 2019; Økelsrud et al., 2016). Alternative explanations to positive relationships between Se and Hg are that (i) both MeHg and Se are subject to biomagnification (Økelsrud et al., 2016), (ii)

the high affinity between Se and Hg leads to their co-accumulation (Deng et al., 2008), and (iii) both Hg and Se are bound in proteins, leading to dilution of both elements by stored fat (Charette et al., 2021). However, neither of these alternative explanations entirely fit our data. If explanation (i) were important, we would expect both Hg and Se to increase with fish size. This was the case for the perch, but not for the small perch and the large perch when studied separately. For both the small and the large perch, as well as for the vendace, Hg but not Se was positively correlated with size (Fig S4; Fig. S5). If explanation (ii) were important, we would not expect a highly variable relationship between Se and Hg, as the one



displayed by the large perch (Fig. 2C and D), or the lack of relationship between Se and Hg displayed by the vendace when weight or length was not included in the regression (Fig. 1). Explanation (iii) would be important only if the lipid content of the fish showed large variation, which was not the case for either the perch ( $n=5$ ) or the vendace ( $n=5$ ). Also, the lipid contents of the muscle tissue of both fish species were too low to cause any significant dilution of Hg and Se (Fig. S7).

A relocation of Se between different tissues can occur under Se deficiency (Burk & Hill, 2015). Considering that muscle tissue constitutes most of the fish weight, any transfer of Se from other tissues had to be substantial to explain more than a minor part of the variation in Se we observed in fish muscle. It has been shown that MeHg in fish muscle tissue is bound mainly to sulfhydryl groups of cysteine (Harris et al., 2003; Manceau, Bourdineaud, et al., 2021). However, in other fish tissues such as the liver, kidney, and brain, a substantial part of the Hg has been shown to be inorganic and bound to Se (Barst et al., 2013; Manceau, Bourdineaud, et al., 2021), potentially resulting in Se deficiencies that trigger increased Se accumulation. Also, as noted above, physiological damage caused by Hg may lead to an elevated need for selenoenzymes.

The small perch exhibited higher Se and lower Hg levels than the vendace (Fig. S4). This is consistent with (but not necessarily a result of) Se causing reduced Hg accumulation (e.g., Belzile et al., 2009; Deng et al., 2008; Peterson et al., 2009). The positive relationships between Se and Hg obtained when perch and vendace were studied separately do not preclude a reducing effect of Se on Hg accumulation in the studied fish, since this effect could be eclipsed by the accumulation of Se in response to an increased Hg load.

#### 4.2 Se Requirements Versus Fish Size

The negative correlation between fish weight and Se molar surplus for both fish species may suggest that the weight-specific requirement for Se decreases with fish size and/or age. For vendace, the increase in Hg with weight was not the cause of this relationship, because there was no significant correlation between the Se molar surplus and Hg (Fig. 2B), but a significant negative correlation between the Se molar

surplus and weight (Fig. 4C). Furthermore, MLR showed that not only the Se molar surplus but also Se decreased with increasing vendace size. Smaller and younger fish have higher specific metabolic rates and may thus require higher levels of antioxidant selenoenzymes than older and larger fish (Metcalf & Alonso-Alvarez, 2010). Also, the selenoenzymes iodothyronine deiodinases are known to play important roles during the development and maturation of fish (Power et al., 2001). A study of Hg and Se in different developmental stages of yellow perch found decreasing Se levels and increasing MeHg levels going from newly hatched larvae to juveniles (Khadra et al., 2019).

The initial lack of increase in Se with Hg for the large perch (Fig. 2D) was probably not a size effect, because there was only a weak correlation between Hg and weight for these perch (Fig. S8). Rather, their Hg levels were too low to initiate an increase in Se accumulation. The stable Se molar surplus displayed by the small perch (Figs. 2A and 4A) may result when the effects of Hg and size/age on Se requirements balance out or are small. For these perch, Hg and weight were strongly correlated (Fig. S6).

Together, these Se–Hg–weight relationships suggest that weight-specific Se requirements for both the perch and the vendace increased with Hg and decreased with increasing size. Different Se–Hg relationships between different fish species/categories could be the result of species-specific traits, prey choice, and variable relationships between size and Hg level. Definite conclusions about the ability of fish to increase their Se accumulation in response to increased Hg exposure require demonstration of the ability of fish to regulate their Se uptake/excretion, and more and deeper analyses of Hg–Se–size relationships.

#### 4.3 Se Molar Surpluses Versus Se:Hg Molar Ratios as Indicators of Resistance to Hg Toxicity

It can be inferred from Fig. 3A (left side of the graph) that the Se:Hg ratio decreased with increasing Hg for the small perch. This is hardly surprising, given that Hg is the denominator. However, the Se molar surplus of the small perch remained stable and was seemingly independent of both Hg and weight (Figs. 2A and 4A), despite Hg being a negative term in the Se molar surplus.

Similarly, a study of pilot whales demonstrated that the Se:Hg molar ratio in the brains decreased with increasing age and Hg, whereas the Se molar surplus did not (Gajdosechova et al., 2016). These observations suggest that the Se molar surplus better than the Se:Hg molar ratio reflects the ability of an organism to maintain a healthy Se status despite its Hg load. Furthermore, it makes greater sense to uphold a stable Se molar surplus than a stable Se:Hg molar ratio to counteract harmful effects on selenoenzyme production caused by the endogenous Se–Hg binding.

A near 1:1 Se:Hg molar ratio has been observed in tissues of marine mammals and marine fish (Cuvin-Aralar & Furness, 1991; Dietz et al., 2000; Koeman et al., 1973; Sakamoto et al., 2015) and in coastal and inland otters (Haines et al., 2010), seemingly implying that the Se:Hg ratio is kept close to 1:1 to avert Hg toxicity. It is of note that a stable Se molar surplus is consistent with a 1:1 Se:Hg molar ratio when Hg is high (as in the studies referred to above). Equation 2 shows that the Se:Hg molar ratio will approach 1:1 when Hg increases and the Se molar surplus is stable. For low Hg levels, Eq. 2 implies that the Se:Hg molar ratio will vary considerably with Hg even when the Se molar surplus is stable, as illustrated by the small perch in our study (Fig. 4A and B).

The Se molar surplus values calculated here for fish muscle should be viewed as relative rather than absolute measures of the availability of Se for selenoenzyme production within a fish. As already noted, MeHg in fish muscle has been shown to be bound mainly to cysteine moieties (Harris et al., 2003; Manceau, Bourdineaud, et al., 2021). Also, metallothionein (a cysteine-rich low molecular weight protein produced partly to detoxify heavy metals ions/complexes) including Hg(II) and MeHg complexes may alleviate the scavenging of Se by MeHg (Sørmo et al., 2011). On the other hand, the binding between Se and Hg has been shown to involve more than one Se atom per Hg atom (Gajdosechova et al., 2016; Manceau, Azemard, et al., 2021). The large perch data suggest that the requirement for selenoenzymes increases with the Hg body burden, leading to the suspicion that the Se status of a fish population cannot be evaluated simply by calculating Se molar surplus values.

## 5 Conclusions

Se and Hg were positively correlated in the muscle tissue of both perch and vendace, for the latter species after correction for size. The data did not comply with both elements being biomagnified, or with co-accumulation of Se and Hg because of the high affinity between these elements, or with variable muscle fat causing significant variability in the concentrations of Se and Hg. A remaining possibility is that the studied fish increased their Se accumulation in response to Hg exposure, perhaps to ensure a sufficient Se molar surplus to produce vital selenoenzymes. That the Se molar surplus (excess Se per unit weight) decreased significantly with increasing size for both fish species but not with increasing Hg for the vendace may suggest that the requirement for Se decreases with increasing size or age. However, this tendency could be weakened or even reversed when there is a strong correlation between Hg and size. The perch displayed a higher and more stable Se molar surplus than the vendace, perhaps because perch has better ability than vendace to accumulate Se or because vendace has lower Se requirements than perch. We conclude that different fish species, each over a wide size range, should be monitored with respect to both Hg and Se. Such data would inform about changes in MeHg exposure and Se bioavailability that could be related to altered food web structures, water chemistry, atmospheric deposition, and soil retention of Se and Hg. Using Eq. 2, population-specific Se molar surplus values could be calculated by which the Se–Hg status of different fish populations could be compared (Fig. 3). In addition, omics (e.g., scanning of transcriptomes for transcripts of genes encoding selenoproteins) and fish Hg–Se speciation studies (e.g., utilizing the advancement of spectroscopic methods) could deepen our understanding of how and to what extent the Se–Hg status affects fish health.

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**Data Availability** The raw data is provided in the appendix “Supplementary information” (SI).

## Declarations

**Competing Interests** The authors declare no competing interests.

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