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HEAVY METAL CONCENTRATIONS IN FEMALE WILD MINK (*NEOVISON VISON*) IN SWEDEN: SOURCES OF VARIATION AND ASSOCIATIONS WITH INTERNAL ORGAN WEIGHTS

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Abstract: The American mink is an invasive species in Sweden, and it is legally hunted all year. Therefore, the mink is well suited as a sentinel species for environmental monitoring. In the present study female mink ($n = 91$) from 6 different areas in Sweden were analyzed for the concentrations of silver, cadmium, mercury and lead in liver tissue using inductively coupled plasma mass spectrometry. The wet concentrations in liver tissue were 42.6 ± 52.7 ng/g for silver, 99.5 ± 100 ng/g for cadmium, 652 ± 537 ng/g for mercury, and 196 ± 401 ng/g for lead (expressed as mean $\pm$ standard deviation). There were associations between the sample area and the concentrations of silver, lead, and mercury. The concentrations of lead and cadmium varied with season of capture and lead, cadmium, and mercury were positively associated with increasing age. Relative liver weight was positively associated with concentrations of mercury and negatively associated with lead and cadmium. Relative kidney weight was negatively associated with lead concentrations. In summary, it is of importance to take age and season of capture into account when assessing levels of heavy metals in wild mink. Also, liver and kidneys seem to be potential targets for heavy metal toxicity in wild female mink in Sweden. *Environ Toxicol Chem* 2017;36:2030–2035. © 2016 The Authors. Environmental Toxicology and Chemistry Published by Wiley Periodicals, Inc. on behalf of SETAC

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INTRODUCTION

The heavy metals mercury (Hg), cadmium (Cd), and lead (Pb) are known to interfere with a large range of biological processes and can cause a numerous abnormalities in exposed organisms.

Mercury can be widely distributed from a point source as vapor of the metallic form, which can then be oxidized and subsequently methylated to methylmercury (MeHg). Methylmercury has high oral bioavailability and is magnified in the food chain, resulting in high levels in fish [1]. Metallic and organic mercury are mainly considered to be neurotoxicants, and inorganic Hg is considered a nephrotoxicant [1]. Furthermore, there are indications that organic Hg can affect reproductive performance [2]. Also, Hg seems to be estrogenic [3] and to affect reproductive cyclicity [4]. In a Swedish context, levels of Hg in freshwater fish species have been demonstrated to decline until recently, when a more complex picture has emerged that indicates that different areas differ in their temporal variation of Hg burdens [5].

There are acute toxic effects after exposure to high concentrations of Cd, and the effects on kidneys, and to some extent on bone, are major concerns with chronic exposure to this metal [1]. Cadmium can also be a reproductive toxicant [6] and affect offspring in utero [7]. Cadmium has estrogenic effects on the uterus [8] and accumulates in the ovary, causing inhibited growth of ovarian follicles [4]. In Sweden it has been estimated that there is still an increase in the amount of Cd in soil, despite reductions in its use over the last 20 yr [9].

Acute Pb poisoning as a result of ingestion of shotgun pellets is a cause of mortality in wildlife, such as mallards [10], and birds of prey also can accumulate high concentrations from their diet [11]. Lead is a potent neurotoxicant [1], and acute exposure causes renal damage, hematopoietic dysfunction, and infertility [12]. Additionally, Pb exposure in rats may cause hepatic damage as indicated by elevated levels of liver-specific enzymes [13]. Silver (Ag) has not been widely studied in the environment, and the fate and effects of Ag in the environment are still largely unknown.

Mercury, Cd, and Pb are known environmental pollutants and may biomagnify. It is therefore of value to monitor these elements in wildlife. Furthermore, the environmental fate of Ag is currently poorly known. This warrants investigations of Ag concentrations in wildlife. The mink has been suggested as a useful species for the monitoring and evaluation of exposure to toxic anthropogenic chemicals in wildlife [14,15]. The mink is well suited as a sentinel organism because it feeds on a high trophic level—mainly fish and crayfish, but also mammals, birds, and frogs [16]. Additionally, the mink resides within a small home territory, indicating that the levels of toxic chemicals can be assumed to represent the exposure from a defined area [17,18]. Furthermore, there are data on the effects on the organ systems caused by different toxic chemicals [19–21] and field studies where associations between organ measurements and concentrations of pollutants have been found [22].

The aim of the present study was to describe the presence of heavy metals, using mink as a sentinel species. Additionally, associations between the concentrations of metals and gross morphological traits were investigated. The objectives were to describe the concentrations of Hg, Cd, Pb, and Ag in liver from free-ranging mink from 6 different areas in Sweden and to

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characterize variation in concentrations in relation to age and sample season. Because of the toxic properties of these metals, a second objective was to examine associations between metal concentrations and relative organ weights.

MATERIALS AND METHODS

Sampling and postmortem procedure

Mink carcasses were collected from hunters in Sweden during 2004 to 2009, from August to the end of April. All mink were killed for fauna protection measures during regular hunting activities (not initiated by the study itself), and thus ethical approval was not needed according to Swedish legislation. In total, 91 female mink were collected in 6 different areas. A map of sample area locations can be found in Supplemental Data, Figure S1. The Gävle/Söderhamn area (G; $n = 21$) is located at the Baltic coast near 2 towns (70 000 and 12 000 inhabitants), fairly large industries, and the mouths of the Dalälven and Ljusnan Rivers. The Koster Islands in Skagerrak (K; $n = 46$) is an archipelago of small islands about 8 km off the Swedish west coast in the North Sea, close to the Norwegian border. The Märsta area (M; $n = 12$) is an area with high anthropogenic impact by industrial and agricultural activities located next to a town with 25 000 inhabitants. In addition, smaller sample sizes of mink came from the stream Lina älv near the town Gällivare in the north of Sweden (E; $n = 4$); from small lakes around the small town of Linghed near Falun in the middle of Sweden (F; $n = 4$); and from around the Rovakkajärvi lake, north of Övertorneå in the northeast of Sweden (O; $n = 4$). The last 3 areas are characterized by coniferous forests.

The hunters were instructed to freeze the carcasses as soon as possible, at approximately –20 °C. The carcasses were transported frozen and thawed just before necropsy. The decomposition of the carcasses was assessed using a scoring system: 1 = mild, for fresh specimens with no or few signs of decomposition; 2 = moderate, with clear signs of decomposition; 3 = substantial, for more advanced decomposition; and 4 = rotten. The subcutaneous fat pad between the hind legs was dissected and weighed using a precision balance (accuracy class II) with a repeatability of ±0.002 g. The weights of the ovaries, uterus, kidneys, adrenals, and spleen were recorded, as was the anogenital distance (the distance between the genitals and the anal opening). Liver tissue was removed for future analysis and refrozen. Aging was determined by cementum analysis of the mandibular canine tooth by Matson's laboratory. As the mink kits often are born in the beginning of May [23], a birth date of 1 May was assumed.

Metal analysis

All chemicals were of analytical or supra-pure grade, and solutions were diluted with Milli-Q purified water. Concentrated nitric acid (65%; Merck), which was further purified by sub-boil distillation, and hydrogen peroxide (30%; Merck) were used for acid digestion of the liver samples. Multielement calibration standards for evaluation of the acid-digested samples were prepared by dilution of stock solutions (Teknolab; Referensmaterial; BDH Chemicals) and nitric acid. A NexION Setup Solution, containing 1 ppb Be, Ce, Fe, In, Li, Mg, Pb, and U (Perkin Elmer), was used for the daily optimization procedures.

For acid digestion approximately 0.4 g of each liver sample, cut at slightly frozen condition with a ceramic knife, was weighed into quartz tubes, followed by addition of 4.0 mL concentrated nitric acid and 1.0 mL hydrogen peroxide. The quartz tubes were put into steel bombs and sealed with a Teflon lid, closed with a force of 23 Nm, and then heated for 4 h at 160 °C in an oven. After cooling to room temperature, the solutions were quantitatively transferred to 15-mL tubes (Falcon, BD) with subsequent rinsing of the quartz tubes with 3 small portions of Milli-Q, diluted to 10.0 mL with Milli-Q, followed by addition of 1 mL 10 ppb thallium (Tl) standard. Two blank samples were prepared in the same way for each run.

A NexION 300D ICP-MS (Perkin Elmer) was used for measurement of Ag, Cd, Hg, Pb, and Tl with operating conditions given in Table 1. At the start of each analysis session the instrument ran for 45 min to stabilize the plasma before optimization of the system using the SmartTune™ function in the software. The daily optimization procedure optimized parameters such as torch position, nebulizer gas flow, and the AutoLens. The method developed used 60 sweeps of the analyte masses (Table 2) with 3 replicates, and the Tl signal was used as an internal standard. The duration and speed of the sample flush and wash steps (Table 3) were set to minimize carryover effects. Measurements of Milli-Q with 1% HNO_3 were done after each 12th measured sample to assess possible memory effects, and an elemental standard solution was measured after each 24th sample as an additional verification of system stability.

Statistical analysis

Two mink were identified as extreme outliers (according to Cook's *D*) and excluded from the statistical analyses; 1 mink from F area with 5900 ng Hg/g liver weight and another mink from G area with 16 000 ng Pb/g liver weight. Correlations between the contaminant concentrations were investigated using the Pearson correlation test of the SAS CORR procedure (SAS Institute, version 9.3).

For calculating the influence of area on metal concentrations (Ag, Cd, Pb, and Hg), the general linear model procedure (proc GLM) in SAS was used. Metal concentration was used as an independent variable. Dependent variables were sampling season (categorical; winter, spring, summer, autumn, according to previous studies [24]), age (continuous, 0–4 yr old), body condition (continuous; the weight of the subcutaneous fat pad between the hind legs [grams] divided by body weight [kilograms]), and area (categorical; 6 areas, see the section *Sampling and postmortem procedure*). Interactions between the dependent variables were tested but found to be insignificant ($p > 0.05$). Metal concentrations were log-transformed to improve normality of the residuals. Comparisons of least square means (i.e., within-group means adjusted for the other effects in the model) were calculated by *t* tests.

For calculating the influence of sampling season, age, and body condition on the concentrations of metals, the generalized linear mixed model was used (Mixed procedure of SAS). Because the sample sizes for areas O, E, and F were small

Table 1. Inductively coupled plasma mass spectrometric operating conditions

Parameter	Setting
Nebulizer gas flow	1.00 L/min
Auxiliary gas flow	1.20 L/min
Plasma gas flow	15.00 L/min
ICP radiofrequency power	1600 W
Nebulizer	Meinhard Concentric
Spray chamber	Cyclonic
Tubing	Factory standard

Table 2. Analytes and measurement parameters

Analyte	Mass	Scan mode	Dwell time per atomic mass unit (ms)	Integration time (ms)
Ag	106.905	Peak hopping	75	4500
Cd	110.904	Peak hopping	75	4500
Hg	201.971	Peak hopping	75	4500
Pb	207.977	Peak hopping	75	4500
Tl	204.975	Peak hopping	75	4500

($n = 2$–4), the analyses were made with mink from areas M, K, and G only. Area was used as a random factor. Sampling season (categorical), age (categorical; juvenile [$n = 36$], 1 yr old [$n = 28$], and 2 yr old or older [$n = 14$]), and body condition were added as fixed factors. Using the diagnostic plots of the residuals generated by the Mixed procedure, normality, heteroscedasticity, and linear relationships between the dependent and independent variables were examined. Cook's *D* was calculated to investigate the influence of individual observations. The Satterthwaite denominator degrees of freedom method was used. Interactions between the fixed effects were tested but found to be insignificant.

Similarly, generalized linear mixed models were used for calculating associations between the weight-adjusted organ variables (anogenital distance; weights of ovaries, uterus, kidneys, and spleen; and body condition) and the metal concentration variables. Again, the analyses were made with mink from areas M, K, and G only. As independent fixed factors, sampling season, age (continuous), and body condition were included (the latter was excluded in the body condition model) as well as the 4 metal concentrations (log-transformed). Area was used as a random factor. The effect of decomposition was tested but was not kept in the models because of insignificance. In the model for uterus weight, 2 moderate outliers (elevated Pb concentrations) were removed to solve a problem with nonpositive definite matrix of the random effect. These exclusions did not essentially alter the outcome of the analysis (still nonsignificant *p* values). In addition, 6 mink with fetuses were excluded from all models except the model for anogenital distance. In the models where a significant influence ($p < 0.05$) of a metal concentration was found (i.e., those for relative kidney and liver weight), interactions were tested but not found to be significant.

RESULTS

The correlations between metal concentrations were low, with Pearson correlation coefficients ranging from –0.02 to 0.3 ($n = 91$).

There was an overall effect of sampling area on the concentrations of metals ($p < 0.001$). Mink from the west coast area (K) had significantly higher concentrations of Ag ($p < 0.0001$ to $p = 0.002$) than all other areas ($p < 0.001$ to $p = 0.02$). Mink from the inland Märsta area (M) had significantly ($p < 0.01$) lower concentrations of Hg than mink from areas F, G, K, and O (but not area E). Mink from the inland areas in the north of Sweden (areas E and O) had lower concentrations of Pb than those from all other areas (all $p < 0.01$). Detailed results can be found in Supplemental Data, Table S1.

Cadmium and Pb varied significantly with sampling season ($p = 0.008$ and 0.009, respectively). Concentrations of Pb were significantly higher during summer than during other seasons ($p = 0.002$ to $p = 0.03$; Figure 1). In contrast, Cd concentrations in the summer were significantly lower than those in all other sample seasons ($p = 0.0002$ to $p = 0.02$).

Age of the mink influenced the Pb concentrations ($p = 0.01$), and pairwise comparisons of age classes (Figure 2) revealed that the concentrations were significantly higher in livers from the oldest mink compared with the juveniles ($p = 0.003$). Juveniles had significantly lower Hg concentrations than the 1-yr-old mink and the 2-yr-old or older mink ($p = 0.02$ and $p = 0.04$, respectively). Concentrations of Cd also increased with age, with significantly different concentrations between all age classes when comparing least square means ($p < 0.0001$ to $p = 0.03$). Silver concentrations were not influenced by sampling season, age, or body condition (Table 4).

Results from the model investigating relationships between relative organ weights and metal concentrations are found in Table 5. Relative kidney weight was significantly and negatively associated with Pb concentrations. Liver weight was negatively associated with Pb and Cd concentrations but positively associated with Hg concentrations. Body condition was not associated with the concentration of any of the analyzed metals. Likewise, the relative ovary, uterus, adrenal gland, and spleen weights as well as the anogenital distance were not significantly associated with any of the analyzed metals. However, there was a tendency ($p < 0.1$) for a positive association between the concentration of Hg and the weight of the ovaries and a tendency for a positive association between the concentration of Hg and the weight of the uterus. In addition, there was a tendency for a negative relationship between relative spleen weight and the concentration of Cd.

DISCUSSION

We have presented new data on the accumulation of 4 metals in wild mink. For Cd, Pb, and Hg there are previous studies from North America and Norway [25,26], whereas few data are available for Ag. The mink is widely prevalent in Sweden and has previously been used as a sentinel animal in environmental

Table 3. Time and pumping speed for each step of the analysis method

Step	Time (s)	Speed (rpm)
Sample flush	50	24
Read delay	18	20
Analysis	68	20
Wash	75	48

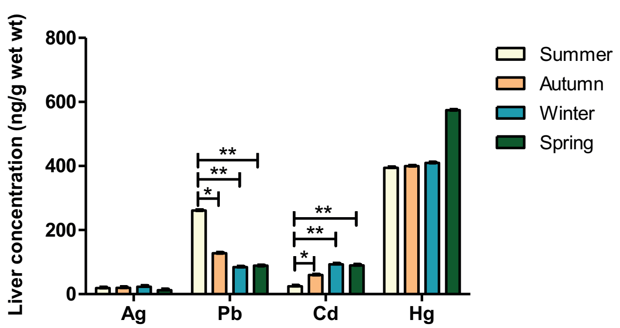

Figure 1. Seasonal variation in metal concentrations. Anti-logarithm of least square mean of metal concentrations (means adjusted for the other terms in the model; see *Materials and Methods* section), standard error, and pairwise comparisons between sample seasons. Bars with * are significantly different on the 5% level and bars with ** on the 1% level.

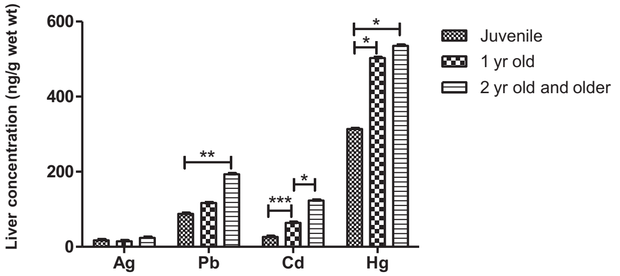

Figure 2. Age variation in metal concentrations. Anti-logarithm of least square mean of metal concentrations (means adjusted for the other terms in the model, see *Materials and Methods* section), standard error, and pairwise comparisons between age classes of mink for each metal. Bars with * are significantly different on the 5% level, bars with ** on the 1% level and bars with *** on the 0.01% level.

monitoring [15]. Mink in Sweden feed on a variety of prey including arthropods (crayfish and insects), amphibians, fish, birds, and mammals. The exact diet composition depends on the availability of different prey, which in turn depends on location and season [16].

Concentrations of Hg, Cd, Pb, and Ag

Mean concentrations of Pb and Cd in the present study were generally in a similar range as in North America, as reviewed by Martin et al. [25]. Only 1 previous study on Ag concentrations in mink was found in the literature, in which the highest concentration recorded in mink from South Carolina (USA) in the 1980s was much higher (up to 4960 ng/g wet wt) than that in the present study (maximum 280 ng/g wet wt) [27].

Previously, concentrations of heavy metals in mink livers have been examined in Norway and North America. Although the exact levels may not be comparable, because of different methodology, the concentrations of Hg were slightly higher in Norwegian mink [26]. The Hg concentrations in liver varied among North American studies, studies in which the animals had been collected in different places, and were higher than [17,18,28], similar to [29], or lower than [30] levels in the present study where wet weight was reported. One female mink found dead, diagnosed with Hg poisoning, had a concentration of 58.2 μg/g, which is several orders of magnitude higher than in the present samples [31]. Comparing the total Hg levels found in the present study with experimental studies [32,33], the levels are low and clinical effects of Hg poisoning cannot be expected.

Variation attributable to sampling area

It can be assumed that the lower concentrations of Pb in livers of mink from the sampled inland areas are related to the lower density of the human population, resulting in less industry and waste production. In addition, the lower density of the human population can result in lower historical emissions of Pb from petrol. The differences in Ag concentrations in mink liver,

Table 4. Liver concentrations of metals in 91 wild female mink from Sweden (ng/g wet wt)

	Mean	Standard deviation	Median	Range
Ag	43.0	52.9	30.3	Not detected–280
Cd	101	100	72.1	3.47–540
Hg	715	770	535	27.5–5950
Pb	30.3	1740	90.9	12–16 400

Table 5. Type 3 tests of fixed effect of contaminant concentrations[a] on relative organ weight measurements in wild female mink from Sweden

		Contaminant concentration[b]			
Dependent variable[c]	*n*	Cd[d]	Hg[d]	Pb[d]	Ag
Liver	65	0.0005 ↘	0.030 ↗	<0.0001 ↘	
Kidney	67			0.0137 ↘	
Spleen	66	0.0682 ↘			
Ovary	66		0.0934 ↗		
Uterus	67		0.0552 ↗		
Adrenal gland	65				
Anogenital distance	74				
Body condition[e]	68				

[a]Concentrations in liver tissue (wet wt).
[b]Independent variables. For description of the models, see *Materials and Methods* section.
[c]All organs are adjusted for body weight.
[d]Data represent *p* values (<0.1) for the contaminant concentration variables. Arrows (↗,↘) symbolize positive and negative relationships, respectively, with the dependent variable.
[e]Weight of subcutaneous fat pad between hind limbs divided by body weight.

with higher concentrations in mink from the saltwater environment of the Swedish west coast, cannot be explained. There appears to be a paucity of data regarding the concentrations of Ag in Swedish inland waters, but concentrations of Ag in European seawater have been measured to be in the picograms per liter range [34]. Mercury levels were lower in livers of mink caught in the area with the most agriculture and the highest density of the human population. This is not in line with the data available from pike and environmental exposure, where fish from the same area have higher concentrations of Hg than fish from the forested areas of the northern parts of Sweden [35].

Variation attributable to sample season and age

The variations seen in metal concentrations that were associated with season of collection of the mink can be explained to some extent by the mobilization of Pb from skeletal depots, which may occur during pregnancy and lactation [36]. However, the lower levels of Cd are more difficult to explain. Cadmium has a long half-life [37], so short-term changes in diet cannot explain seasonal variation.

Cadmium, Pb, and Hg all increased with increasing age; this is to be expected for compounds with long half-lives and continuous exposure. Accumulation with increasing age has also been found in many field studies on heavy metal concentrations in mink and/or otter [25,38,39]. In contrast, no age-related accumulation was found for Ag concentrations in the present study. In pinnipeds, Ag seems to accumulate mainly in the liver and the concentration seems to increase with age (or body length as a measurement of age) [40–42]. The concentrations recorded in pinnipeds were somewhat higher (30–1040 ng/g wet wt) [42] than the concentrations in mink (0.4–280 ng/g wet wt), which could to some extent explain the lack of age dependence in the present study. It can be speculated that Ag is at steady state (elimination match intake); however, because we found no studies on the toxicokinetics of Ag in mammals, no further conclusions can be drawn.

Associations with organ weights

A common finding in experimental studies on rats is that Pb seems to cause an increase in kidney weight [43–47]; however, there are also some studies reporting no effect on kidney weight [46,47]. This contrasts with our findings, where mink with high concentrations of Pb had a lower kidney weight. In a field study, Ma [49] found that an increased relative kidney weight indicated poisoning by Pb in voles and shrews at a shooting range. The concentrations of Pb in voles and shrews were higher than those found in mink in the present study, which may be a reason for the contradictory results. In addition, Aleutian mink disease virus has been found to be common in the Swedish mink population [50]. This infection could possibly also affect the weight of the kidneys [50,51] as both Aleutian mink disease and chronic Pb nephropathy consist of interstitial fibrosis and progressive nephron loss [52,53].

In the present study, a significant positive association between liver weight and concentration of Hg was found. As discussed in a review by Dietz et al. [54], liver weight could possibly serve as a preliminary indicator for persistent organic pollutants and Hg exposure because of the ability to cause oxidative stress in cell membranes and subsequent enlargement of the liver. An accumulation of lipid in the liver has been observed in both mink [33] and ferrets [55] after administration of MeHg.

Another positive association, although not significant, was found between Hg and the reproductive organs of female mink in the present study. This tendency is interesting as both Cd and Hg have been found to increase uterine weight in rats [56] and in a study with subchronic exposure metal mixtures that included Hg and Cd [57].

A negative association between liver weight and concentrations of Pb and Cd was found in the present study. Interestingly, the same results were found in wood mice in a study with an exemplary large sample size [58]. These associations may be considered plausible as relative liver weight was reported to be reduced after Cd or Pb exposure in rats [48,59–61]. Considering the high doses in the latter studies, the concentrations in rats were presumably higher than those found in mink in the present study. On the other hand, studies on effects of metal mixtures have found that additive or more than additive interactions may occur and that the duration of exposure to low levels of metal mixtures is important to consider [62]. In addition, it should be considered that other environmental pollutants have been found in mink in the studied areas [63,64]. This highlights the complexity of studying real-life mixture effects of environmental pollutants but also underlines the need for epidemiological studies on wildlife in order to understand the long-term effects of (low-dose) mixtures.

The present study suggests that there are differences in the concentrations of Pb in free-living mink from different regions in Sweden. These differences may be explained by a lower level of human activity in the less populated forested areas of northern Sweden. For Hg and Ag the observed differences are more difficult to explain. It can be concluded that when assessing heavy metal concentrations in wild mink in Sweden, care should be taken to control for age and sample season. Associations between metal concentrations and relative kidney and liver weights were found. However, there were no significant associations between metal concentrations and biometric parameters of the reproductive tract of female mink. These results emphasize the need for more detailed studies of liver and kidney morphology in wild mink, to elucidate the toxicological implications. The associations between organ weights and increased body burden of heavy metals may be an alert to the fact that chronic exposure to anthropogenic pollution of the environment can cause biological effects that can be difficult to identify in laboratory settings and emphasize the need for further research on effects of pollutants on mammalian wildlife.

Supplemental Data—The Supplemental Data are available on the Wiley Online Library at DOI: 10.1002/etc.3717.

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Data Availability—Data are available through contact with the corresponding author (sara.persson@slu.se).

Disclaimer—The authors declare they have no conflicts of interest.

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