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Citation for the original published paper (version of record):

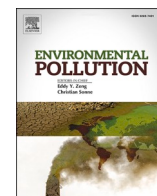
Berger, M L., Shaw, S D., Rolsky, C B., Chen, D., Sun, J. et al. (2023)
Alternative and legacy flame retardants in marine mammals from three northern ocean
regions
Environmental Pollution, 335: 122255-122255
<https://doi.org/10.1016/j.envpol.2023.122255>

Access to the published version may require subscription.

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Alternative and legacy flame retardants in marine mammals from three northern ocean regions[☆]

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ARTICLE INFO

Keywords:

Novel flame retardants
Pinnipeds
Cetaceans
Tissue distribution
Regional comparison
Inter-species comparison

ABSTRACT

Flame retardants are globally distributed contaminants that have been linked to negative health effects in humans and wildlife. As top predators, marine mammals bioaccumulate flame retardants and other contaminants in their tissues which is one of many human-imposed factors threatening population health. While some flame retardants, such as the polybrominated diphenyl ethers (PBDE), have been banned because of known toxicity and environmental persistence, limited data exist on the presence and distribution of current-use alternative flame retardants in marine mammals from many industrialized and remote regions of the world. Therefore, this study measured 44 legacy and alternative flame retardants in nine marine mammal species from three ocean regions: the Northwest Atlantic, the Arctic, and the Baltic allowing for regional, species, age, body condition, temporal, and tissue comparisons to help understand global patterns. PBDE concentrations were 100–1000 times higher than the alternative brominated flame retardants (altBFRs) and Dechloranes. 2,2',4,5,5'-pentabromobiphenyl (BB-101) and hexabromobenzene (HBBZ) were the predominant altBFRs, while Dechlorane-602 was the predominant Dechlorane. This manuscript also reports only the second detection of hexachlorocyclopentadienyl-dibromocyclooctane (HCBBCO) in marine mammals. The NW Atlantic had the highest PBDE concentrations followed by the Baltic and Arctic which reflects greater historical use of PBDEs in North America compared to Europe and greater industrialization of North America and Baltic countries compared to the Arctic. Regional patterns for other compounds were more complicated, and there were significant interactions among species, regions, body condition and age class. Lipid-normalized PBDE concentrations in harbor seal liver and blubber were similar, but HBBZ and many Dechloranes had higher concentrations in liver, indicating factors other than lipid dynamics affect the distribution of these compounds. The health implications of contamination by this mixture of compounds are of concern and require further research.

1. Introduction

It is predicted that nearly 40% of all marine mammal species face extinction by 2050, especially polar species undergoing drastic, climate-

related habitat change (Schipper et al., 2008). Climate change will result in the loss of pack ice, which is mandatory for ice-breeding seals, and lead to shifts in prey availability toward the poles (Kovacs and Lydersen, 2008; Laidre et al., 2008; Peters et al., 2022). Marine mammals also face

[☆] This paper has been recommended for acceptance by Maria Cristina Fossi.

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¹ In memory of Susan Shaw.

several other threats including hunting, bycatch, ecotourism, underwater noise, habitat destruction, and environmental pollution, which act synergistically to threaten future population health (Roman et al., 2013; Avila et al., 2018).

As top predators in marine food webs, marine mammals are particularly susceptible to bioaccumulation of toxic contaminants (Ross, 2006; de Wit et al., 2020; Sonne et al., 2020). Studies from around the world have documented high concentrations of a wide range of environmental contaminants in marine mammals, including banned persistent compounds such as polychlorinated biphenyls (PCBs) and dichlorodiphenyltrichloroethane (DDT), as well as many current-use chemicals such as flame retardants, pesticides, heavy metals, petroleum, and per- and polyfluoroalkyl substances (PFAS) (Shaw et al., 2009; Houde et al., 2011; Law et al., 2014; Shaw et al., 2014; Letcher et al., 2018; Sonne et al., 2020). These chemicals, individually and in combination, likely have detrimental effects on marine mammal immune systems (De Swart et al., 1994; Ross et al., 1996; Levin et al., 2005; Kakuschke and Prange, 2007; Desforges et al., 2017; White et al., 2017), endocrine systems (Jenssen, 2006; Ross, 2006; Tabuchi et al., 2006; Schwacke et al., 2012; Vanden Berghe et al., 2013; Villanger et al., 2013), reproduction (Dietz et al., 2015; Kellar et al., 2017), first year survival (Hall et al., 2009), and cancer rates (Dietz et al., 2015; Randhawa et al., 2015; Gulland et al., 2020).

Flame retardants, the halogenated or phosphate-based organic chemicals added to many products to increase their resistance to fire (Alaee et al., 2003; Birnbaum and Staskal, 2004), have become global contaminants found in air, water, sediments, and aquatic and terrestrial biota at all trophic levels (Hites, 2004; Law et al., 2006; Tanabe et al., 2008; Shaw and Kannan, 2009; Guigueno and Fernie, 2017). Additionally, many of these flame retardants have been linked to adverse health effects in wildlife and humans, including endocrine disruption (Costa and Giordano, 2007; Darnerud, 2008; Legler, 2008; Kim et al., 2014; Guigueno and Fernie, 2017), genotoxicity (Barón et al., 2016; Pereira et al., 2016), neurotoxicity (Viberg and Eriksson, 2011; Sun et al., 2016; Dong et al., 2021), and immunotoxicity (Martin et al., 2007; Watanabe et al., 2008; Lv et al., 2015).

Because of their widespread distribution, persistence in the environment, and demonstrated health effects, some flame retardants, such as the polybrominated diphenyl ethers (PBDEs), have been banned in many countries (Shaw et al., 2010; Covaci et al., 2011; Vorkamp and Rigét, 2014). However, banning PBDEs has led to increased production of previously low-volume chemicals and the development of numerous “novel” or “alternative” flame retardants. These alternative flame retardants are now also being found in wildlife around the world (Vorkamp et al., 2015; Ali et al., 2017; Houde et al., 2017; Vorkamp et al., 2018; Xiong et al., 2019; de Wit et al., 2020; Zafar et al., 2020) and evidence of their negative health effects on laboratory animals is accumulating (Xiong et al., 2019; Lu et al., 2020; Marteinson et al., 2020; Dong et al., 2021), but little is known about their presence in and impact on marine mammals.

Previous studies of flame retardant contamination in marine mammals have generally focused on one geographic region or a limited number of species, thus making the understanding of global patterns more difficult. Therefore, this study measured concentrations of 44 flame retardants, including legacy PBDE congeners, Decchlorane-related compounds, and alternative brominated flame retardants, in the blubber of nine marine mammal species from three northern ocean regions: the Northwest Atlantic represented by samples from the northeast U.S. coast, the Arctic represented by samples from Greenland and Iceland, and the Baltic represented by samples from Sweden. Both the Northwest Atlantic and the Baltic are surrounded by industrialized countries and have a long history of environmental contamination (Jensen et al., 1969; Bergek et al., 1992; Thompson, 2010; Shaw et al., 2011; Roos et al., 2012; Airaksinen et al., 2014; Sonne et al., 2020). The remote Arctic waters were selected as a comparative region with expected lower levels of contamination. Also, all three regions are among areas predicted to

experience the most extreme shifts in marine biomass due to climate change over the next 100 years, and therefore represent important areas for monitoring of sentinel marine species (Bryndum-Buchholz et al., 2019).

This study also compared contaminant concentrations in two different tissues by analyzing both liver and blubber samples that were available from some Northwest Atlantic and Baltic harbor seals (*Phoca vitulina*). Blubber acts as a major reservoir for lipophilic compounds and integrates lifetime accumulation of pollution (Ellisor et al., 2013), while the liver, which is metabolically active and blood-perfused, may be a better indicator of recent exposure and potential toxicity (Raach et al., 2011). Tissue comparisons facilitate understanding the bioaccumulation dynamics of different chemicals and provide a more complete measure of contamination status. This comprehensive study enabled the evaluation of spatial trends, age and species differences, temporal trends, tissue partitioning, and addresses the lack of available information regarding the toxicological implications of current levels of flame retardant contamination within three vulnerable regions.

2. Materials and methods

2.1. Samples

Blubber samples were collected from nine species of marine mammals: harbor seals, grey seals (*Halichoerus grypus*), ringed seals (*Pusa hispida*), harbor porpoises (*Phocoena phocoena*), white-sided dolphins (*Lagenorhynchus acutus*), white-beaked dolphins (*Lagenorhynchus albirostris*), long-finned pilot whales (*Globicephala melas*), minke whales (*Balaenoptera acutorostrata*), and humpback whales (*Megaptera novaeangliae*). Each species was sampled from at least two of the three regions: the Northwest (NW) Atlantic (U.S.), the Baltic (Sweden), and the Arctic (Iceland and Greenland) (Fig. S1, Table 1). While some samples from Iceland and Greenland originated from latitudes south of the Arctic Circle and are technically from the Subarctic Zone (Fig. S1), the label “Arctic” is used for this group of samples for simplicity and to differentiate them from samples from the northern part of the Baltic which is also in the Subarctic Zone (Love, 1970). Tissue differences in contaminant concentrations were analyzed in a subset of the harbor seals from the NW Atlantic and Baltic with matched liver and blubber samples collected from the same individual.

2.2. Sampling methods

NW Atlantic (U.S.): Stranded marine mammals from Long Island, New York, to northern Maine in fresh or fair condition (Code 2 or 3) (Geraci and Lounsbury, 2005) were sampled between 1999 and 2016. For seals, weight, axillary girth, and standard length were measured during necropsy. Age category was estimated from body size and stranding date. For cetaceans, weight and length were measured when possible. Samples were archived in chemically clean glass jars in a

Table 1
Number of blubber samples by age (adult males and juveniles), species, and region.

Species	NW Atlantic		Baltic		Arctic	
	Adult M	Juv	Adult M	Juv	Adult M	Juv
Harbor Seal	9	63	11	73	3	8
Grey Seal	4	2	5	5	5	5
Ringed Seal			5	5	11	12
White-sided Dolphin	9					
White-beaked Dolphin					15	
Harbor Porpoise	9					
Pilot Whale	3				9	
Minke Whale	2				5	
Humpback Whale	1				13	

freezer at -40°C (blubber) or -80°C (liver) until analysis.

The Baltic (Sweden): Seals that were stranded, bycaught, or shot during the legal, annual subsistence hunt were sampled between 2000 and 2016. Weight, axillary girth, and length were measured during necropsy. Age was determined by counting annual growth layers in the cementum of a tooth. All tissue samples were stored in aluminum foil and polyethylene bags in freezers at -20°C in the Environmental Specimen Bank (ESB) at the Swedish Museum of Natural History.

Arctic (Greenland): Marine mammals that were stranded or killed during the legal annual subsistence hunts were sampled between 2010 and 2016. Samples were archived at the Greenland Institute of Natural Resources in freezers at -20°C .

Arctic (Iceland): Stranded or bycaught seals were sampled between 2008 and 2010. Weight and standard length were measured during necropsy. Age category was determined from the body size, and in some cases, through dental examination. Samples were archived in polyethylene bags at -18°C at the Icelandic Seal Center.

Because some samples originated from dead stranded animals which may have been ill and poorly nourished at the time of death, while others originated from animals that were shot while presumably healthy, a condition index (weight (kg)/length (cm)) (Hall et al., 2003) was calculated for every animal with both length and weight measurements. This index was incorporated into the analysis of contaminant concentrations.

2.3. Chemical analysis

The extraction methods for both blubber and liver and instrumental analysis are reported in detail elsewhere (Sun et al., 2022a,b). Briefly, approximately 0.5 g of wet blubber or liver was ground with diatomaceous earth (Fisher Scientific, U.S.) and spiked with surrogate standards. The mixture was subjected to accelerated solvent extraction (Dionex ASE 350, Sunnyvale, USA) and subsequently purified by gel permeation chromatography (GPC) using a mixed solution of hexane:DCM (1:1, v/v). The extraction was further cleaned-up on silica-based solid-phase extraction (SPE; 2 g, Biotage, USA) with hexane:DCM (6:4, v/v), concentrated to 200 μL , and spiked with an internal standard (3'-fluoro-2,2',4,4',5,6'-hexabromodiphenyl ether; F-BDE 154). Instrument analysis was carried out on an Agilent 7890B gas chromatograph (GC) coupled to an Agilent 5977A mass spectrometer (Agilent Technologies, USA) operated in electron capture negative ionization (ECNI) mode.

Quality assurance and control (QA/QC) procedures included spiking tests, blank control, and surrogate standard recoveries. Known amounts of target analytes along with surrogate standards were spiked with pork liver purchased from a local supermarket and processed with the aforementioned methods. The mean (\pm standard deviation; SD) recoveries of spiked FRs ranged from $77.4 \pm 11.2\%$ to $108 \pm 7.1\%$. A procedural blank was processed along with every 10 samples. Only BDE 47, BDE 209 and HBBZ were detectable in procedural blanks, with the levels generally below their limits of detection (LODs). The LOD of an analyte without detection in procedural blanks was defined as its instrumental response plus five times the SD of the noise; otherwise, it was determined as the average level in procedural blanks plus three times the SD of blank contamination.

2.4. Statistical analysis

Chemical concentrations below the LOD were replaced with half of the LOD for compounds that were detected in at least one sample from a species within a region. Individual compounds that were not detected in any samples from a species within a region were replaced with zero. All concentrations are reported on a lipid weight (lw) basis.

For compounds with at least 50% detection in all samples, Generalized Linear Models (GLM) were used to explore the effect of age class (adult M vs juvenile), region (NW Atlantic, Baltic, Arctic), species (harbor, grey, ringed seals), stranding year, and condition index on

contaminant concentrations in blubber. Dummy variables were included for categorical factors with age = adult male, region = NW Atlantic, and species = harbor seal coded as the base for comparison. Since the distribution of contaminant concentrations was approximately log-normal, both Gaussian and Gamma models with a log link were evaluated for best fit, which was determined with Pearson residuals plotted against fitted values, normal probability plots of residuals, and Akaike Information Criteria (AIC) (Zuur and Ieno, 2016). Only pinniped species were included in the GLM analysis because their sample sizes were robust, and all three regions were represented. Cetacean samples were only available from two regions and their sample sizes were smaller, so analysis of their contamination was more qualitative, but still valuable for comparative purposes.

Wilcoxon matched-pairs signed-rank tests were used to compare blubber and liver tissues in harbor seals from the NW Atlantic and Baltic, and Kruskal-Wallis with Dunn's post hoc tests or Wilcoxon Rank Sum tests were used to compare independent groups. All statistical analysis was conducted with StataIC ver. 15.1. An alpha level of 0.05 was used to determine significance of all statistical tests.

Unlike the PBDEs which were marketed as products containing mixtures of congeners and are often reported in the literature as Σ PBDE concentrations, the Dechloranes and the alternative brominated flame retardants (altBFRs) are generally marketed as separate products or mixtures containing a limited number of compounds (Table S1). There is little consistency in the literature as to which compounds are included in analyses of Dechlorane or altBFR concentrations in the environment. Therefore, to make the results of this study comparable to previous research, Dechloranes and altBFRs, as groups, were used for descriptive and organizational purposes. Compounds from these groups that were detected frequently were statistically analyzed as individual compounds rather than as group sums. Compounds that were detected rarely were presented in summary tables and included in qualitative discussions.

3. Results and discussion

3.1. Compounds detected

Of all 44 analyzed chemicals including 21 PBDEs, 9 Dechloranes, and 14 altBFRs, only BDEs-206, -207, and -208, Dechlorane-601, PBBZ and PBBA were not detected in any sample. All other compounds were detected in at least one sample, but there was significant variability among the species and regions. In general, PBDE concentrations were 2–3 orders of magnitude higher than Dechlorane concentrations and 1–2 orders of magnitude higher than the altBFRs.

PBDEs: The tri-hexa PBDE congeners BDE-28, -47, -49, -99, -100, -153, and -154 were detected in the majority (80–100%) of samples from the NW Atlantic and Baltic species (Tables S2 and S3). BDE-17, -66, and -85 were detected rarely at very low concentrations. BDE-47 was detected in 100% of the samples originating from the Arctic, but the detection of other tri-hexa congeners varied greatly among species from this region (Table S4).

Of the higher brominated congeners, BDE-183 was detected in 100% of the NW Atlantic cetacean samples, but only 72–88% of the pinniped samples. Other higher brominated congeners were detected in 0–67% of samples from different species. In samples from the Baltic, all higher brominated congeners were detected variably in 0–64% of samples. In seals from the Arctic, no higher brominated congeners above BDE-183 were detected, but a few higher congeners were detected in two cetacean species. BDE-209 was detected in 1–25% of harbor seals and grey seals from the NW Atlantic and Baltic and 11% of the pilot whales from the NW Atlantic, but was not detected in any other species from any region.

Alternative BFRs: BB-101 and HBBZ were the predominant altBFRs in terms of detection frequency and concentration (Tables S2–S4). Other compounds that were regularly detected, particularly in NW Atlantic samples, include TBBZ, PBEB, BEH-TBP, BTBPE, and PBT. Overall, the

alternative BFRs had highly variable rates of detection among the species from the different regions.

Dechloranes: Dechlorane-602 was the only Dechlorane compound detected in all species from all regions, although rates varied from 62 to 100% of samples from different species (Tables S2–S4). The NW Atlantic species and harbor seals from the Baltic had the greatest diversity of Dechlorane-related compounds in their blubber. All of the analyzed Dechlorane-related compounds, except for Dec-601, were detected in the NW Atlantic species and all but Dec-601 and Dec-604 were detected in harbor seals from Sweden. Dechlorane-603 and Anti-DP were also detected in two grey seal samples from the Baltic. In samples from the Arctic, Dec-603, Dec-604CB, Cl11-DP, Syn- and Anti-DP were detected in a few individuals in addition to the Dec-602 that was found in all Arctic species.

Due to their high detection rates in all species and regions, ΣPBDEs, BB-101, HBBZ, and Dec-602 were included in statistical analyses. Summary results for all compounds are presented in Tables S2–S4.

3.2. PBDE concentrations and composition

Including all species, mean \pm SD total PBDE concentrations in blubber were 2060 ± 4620 ng/g lw, 103 ± 102 ng/g lw, and 83.2 ± 113 ng/g lw from the NW Atlantic, Baltic, and Arctic, respectively. These concentrations are within the range of previous studies of PBDEs in harbor seals between 2000 and 2005 (mean: 1385 and 3646 ng/g lw in adult males and pups, respectively) (Shaw et al., 2008), and white-sided dolphins between 1993 and 2000 (means: 1820 and 2410 ng/g wet

weight in adult males and juveniles, respectively) (Tuerk et al., 2005) from the NW Atlantic. Previous studies of ringed seals from the Baltic between 2001 and 2015 (Range of annual means: 50–200 ng/g lw) (Bjurlied et al., 2018) and Greenland between 1994 and 2008 (mean: 24.4 and 27.4 ng/g lw in juveniles and adults, respectively) (Vorkamp et al., 2011) were also very similar to the ringed seal results from the current study.

In all species and regions, tetra-brominated BDE-47 was the most abundant congener accounting for 50–87% of the PBDE burden (Fig. 1). However, BDE-47 made up a greater proportion of the total PBDE burden in the pinnipeds (mean \pm SD of all individuals: $75 \pm 11\%$) than cetaceans ($58 \pm 11\%$) (t -test, $t_{294} = 11.5$, $p < 0.001$). Conversely, cetaceans had a greater proportion of the hexa- and hepta-brominated congeners BDE-154 ($11 \pm 9.4\%$), and BDE-183 ($2.1 \pm 2.3\%$) than the pinnipeds (BDE-154: $3.0 \pm 3.5\%$, BDE-183: $0.43 \pm 0.93\%$) (t -test, BDE-154: $t_{294} = 10.2$, $p < 0.001$; BDE-183: $t_{294} = 8.7$, $p < 0.001$) (Fig. 1). This difference between seals and cetaceans was also observed in harbor seals and harbor porpoises from the North Sea (Weijs et al., 2009) and in marine mammals from Japanese waters (Nomiya et al., 2014). It may stem from dietary or metabolic differences between cetaceans and seals as previous research has found that cetaceans have a reduced ability to metabolize some non-planar contaminants due to lower CYP2B enzyme activity compared to pinnipeds (Bennett et al., 2009; Pangallo and Reddy, 2010).

While BDE-209 often dominates PBDE composition in marine sediments (Zegers et al., 2003; Morales-Caselles et al., 2017), low detection and low concentrations of BDE-209 in high trophic level marine

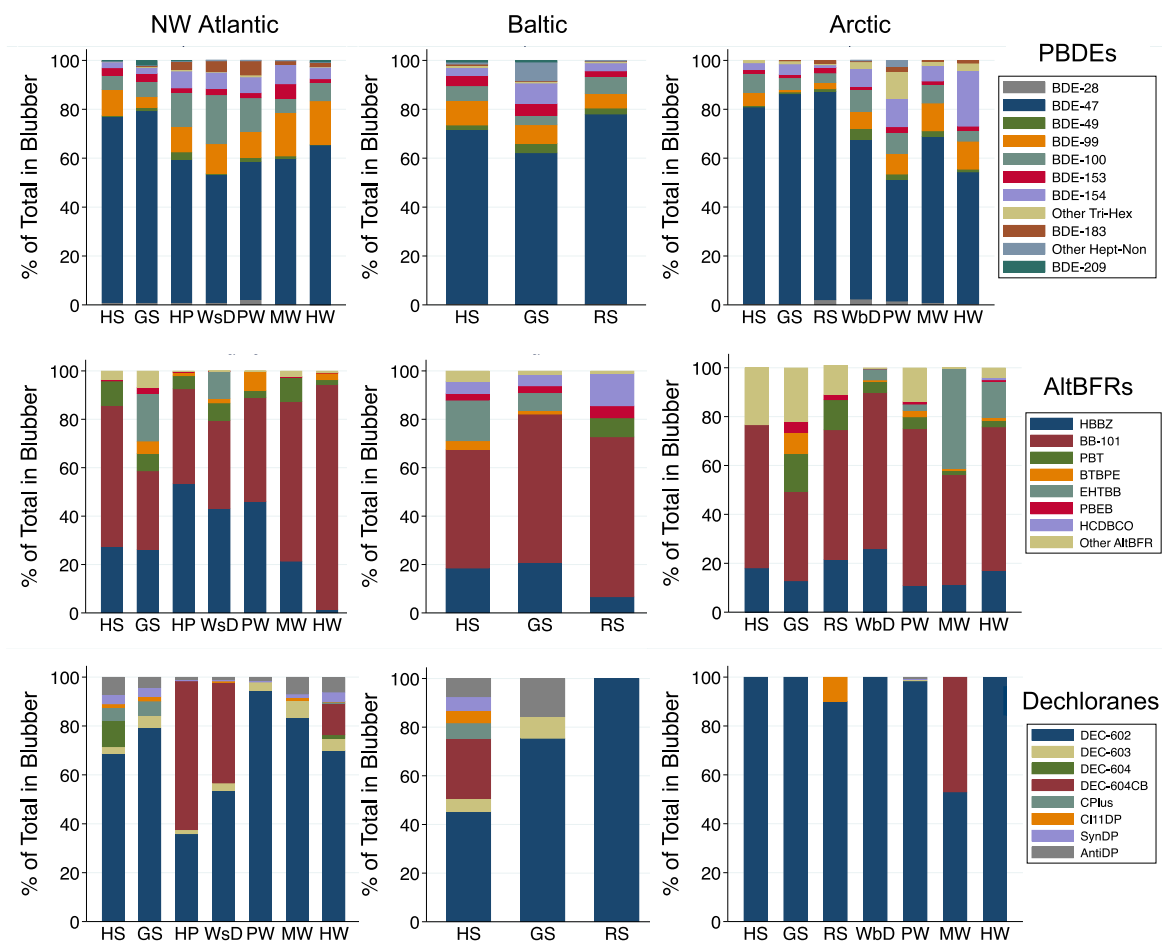


Fig. 1. PBDE, AltBFR, and Dechlorane composition in harbor seals (HS), grey seals (GS), ringed seals (RS), harbor porpoises (HP), white-sided dolphins (WbD), pilot whales (PW), minke whales (MW), and humpback whales (HW) from the NW Atlantic, Baltic, and Arctic.

mammals have been frequently reported (Johnson-Restrepo et al., 2005; Kajiwarra et al., 2008; Tomy et al., 2008). Bioaccumulation of this congener is limited because it tends to bind to particles in air or water and is often debrominated or biotransformed into lighter, more bio-accumulative congeners by lower trophic level organisms (Stapleton et al., 2004; Ross et al., 2009).

For all Generalized Linear Models used to explore the influence of region, species, age class, year, and condition on PBDE concentrations, the Gamma distribution with a log link had a better fit to the data than the Gaussian distribution with a log link as indicated by lower AIC values. However, some model assumptions were violated with either distribution. Heteroscedasticity was apparent in the plots of residuals against fitted values and the residuals were not normally distributed. Therefore, the GLM was used to help interpret complex potential influences on contaminant concentrations, but no attempt was made to predict concentrations using the model coefficients.

After removing one extreme outlier point to improve model fit (a NW Atlantic harbor seal juvenile, Σ PBDE = 44,000 ng/g lw), coefficients for region (Baltic and Arctic vs. NW Atlantic), stranding year, and age class (Juvenile vs. Adult M) were significant and condition index was marginally significant (Table S5). Inclusion of a region*species interaction term improved the AIC slightly and resulted in significant coefficients for region (Baltic: $\beta = -2.37$ [95%CI = -2.85 to -1.88], $p < 0.001$; Arctic: $\beta = -4.21$ [95%CI = -4.92 to -3.49], $p < 0.001$), stranding year ($\beta = -0.053$ [95%CI = -0.099 to -0.0075], $p < 0.05$), age class ($\beta = -1.27$ [95%CI = -2.11 to -0.42], $p < 0.01$), condition index ($\beta = -1.97$ [95%CI = -3.78 to -0.17], $p < 0.05$) and the interaction terms for Baltic*grey seal ($\beta = 1.38$ [95%CI = 0.15 – 2.62], $p < 0.05$) and Arctic*grey seal ($\beta = 2.31$ [95%CI = 1.05 – 3.56], $p < 0.001$). Unfortunately, no length or weight information was available for the ringed seals from Greenland, so when condition index was included in the model, these samples were excluded. If condition index was removed, then the best model resulted in significant coefficients for region (Baltic: $\beta = -2.44$ [95%CI = -2.79 to -2.09], $p < 0.001$; Arctic: $\beta = -4.15$ [95%CI = -4.82 to -3.48], $p < 0.001$), stranding year ($\beta = -0.075$ [95%CI = -0.11 to -0.039], $p < 0.001$), grey seal species ($\beta = -1.62$ [95%CI = -2.50 to -0.74], $p < 0.001$) and the region*grey seal interaction (Baltic: $\beta = 1.81$ [95%CI = 0.71 – 2.90], $p < 0.01$; Arctic: $\beta = 2.24$ [95%CI = 1.03 – 3.45], $p < 0.001$) (Table S5).

The consistent significant coefficients for regional effects on PBDE concentrations likely result from two factors. First, historically, the U.S. and Canada had much greater usage of PBDEs than Europe resulting in greater PBDE contamination of human tissues, wildlife, dust, and food from North America than Europe (Hites, 2004; Costa et al., 2008; Shaw and Kannan, 2009). Additionally, industrialized Europe, and particularly the historically polluted Baltic waters, are generally more contaminated than the remote Arctic (Law et al., 2014; de Wit et al., 2020). Second, condition index was a significant predictor of PBDE concentration, and it was closely tied to regional differences. The juvenile harbor seals from the Swedish waters and the Arctic were older, longer, and in significantly better body condition than the juvenile harbor seals from the NW Atlantic which were mostly recently weaned pups (Kruskal-Wallis test, $X^2 = 68.3$, $p < 0.001$) (Fig. S2). Since contaminant concentrations in blubber can increase during periods of weight loss due to illness and can decrease via dilution when health and feeding are resumed (Hall et al., 2008), the difference in condition between harbor seals from different regions likely has an influence on PBDE concentration differences. Interestingly, there is no significant difference in condition among regions for grey seals or ringed seals (Fig. S2).

The significant negative coefficients for stranding year are consistent with previous analyses of PBDE contamination in harbor seals from Maine and Sweden (Sun et al., 2022a), and ringed seals from the Baltic (Bjurlid et al., 2018), and Arctic (Dam et al., 2011; Vorkamp et al., 2011). PBDE contamination in the Baltic and Arctic peaked in the early 2000s and then consistently declined in most species (Sellström et al.,

1993; Dam et al., 2011; Vorkamp et al., 2011; Brown et al., 2018). PBDE decline starting in the early part of this century likely reflects bans of penta- and octaBDE commercial products that were implemented in the U.S. and Europe around that time (Shaw et al., 2010; Covaci et al., 2011). However, continued use of decaBDE in the United States until its recent ban in 2021 (U.S. Environmental Protection Agency, 2021) means that PBDE contamination is likely to remain a concern for many years in U.S. coastal environments.

Age class also had a significant coefficient in the best model of PBDE contamination that included the condition index. There were no adult female seals in this study and a preliminary analysis of PBDE concentrations in juvenile harbor seals from the Baltic and the NW Atlantic found no difference between young males and females. Therefore, all juveniles were grouped together and compared with adult males. Like many lipophilic contaminants, PBDEs are passed from mothers to pups *in utero* or through lactation leaving the youngest pups with high concentrations (Weijs et al., 2009; Vanden Bergh et al., 2012; Wang et al., 2012). However, the majority of a seal's body burden is acquired through their seafood diet and concentrations often increase with age after the first year of life in males (Addison et al., 2020), although shifts in diet with age can sometimes alter this pattern (Aguilar et al., 1999). When adult male and juvenile harbor seals, grey seals, and ringed seals were analyzed separately from each region, there was a trend for adult males to have higher PBDE concentrations than juveniles for all seals except harbor seals from the Baltic where juveniles (mean \pm SD, median: 108 ± 91.0 , 72.3 ng/g lw) were significantly more contaminated than adult males (43.9 ± 33.5 , 35.8 ng/g lw) (Wilcoxon rank-sum test, $z = -2.92$, $p < 0.01$) (Fig. 2). The reason for the different age-related pattern in the harbor seals from Swedish waters is unclear.

The significant interaction between region and species for grey seals was also noteworthy. For the seals from the NW Atlantic, grey seals had lower PBDE concentrations than harbor seals. However, from the Baltic and Arctic, grey seals had comparable or even slightly higher levels of PBDE contamination than the harbor seals (Fig. 2). Along the Swedish coastline, grey and ringed seal populations are concentrated on the east coast in the Baltic proper and the northern Bothnian Bay region, while harbor seals are more concentrated along the west coast in Skagerrak and Kattegat (Svensson, 2012; Scharff-Olsen et al., 2019). There is some population overlap between grey and harbor seals in the southwest Baltic and the Kattegat–Skagerrak region (Svensson, 2012). Historically, contaminant levels in fish have been higher in the Baltic proper than along the Atlantic coast of western Sweden (Olsson et al., 1994; Bignert et al., 1998). The historical geographic differences in contamination coupled with limited population overlap likely explain differences in contamination among the Baltic seal species. In contrast, the harbor seal and grey seal populations from the northwest Atlantic have significant overlap in habitat (NMFS, 2021; 2022). Therefore, the difference in contamination between the two species likely results from dietary differences or microhabitat use.

3.3. AltBFR concentrations and composition

Total altBFR concentrations from each region were (mean \pm SD) 23.6 ± 49.2 ng/g lw, 4.68 ± 4.98 ng/g lw, and 13.7 ± 15.5 ng/g lw for all samples from the NW Atlantic, Baltic, and Arctic, respectively. BB-101 and HBBZ contributed the most to altBFR contamination ($54 \pm 16\%$ and $23 \pm 14\%$ of total altBFRs, respectively). A similar predominance of BB-101 and HBBZ among the alternative BFRs was previously described in ringed seals from the Canadian Arctic (Houde et al., 2017). These were followed by EHTBB ($8.0 \pm 12\%$) and PBT ($5.5 \pm 6.8\%$) (Fig. 1).

HBBZ and BB-101 were previously analyzed in harp (*Pagophilus groenlandicus*) and hooded seals (*Cystophora cristata*) from the Gulf of Maine in the NW Atlantic (Montie et al., 2010). HBBZ was not detected in either species, but BB-101 was detected in hooded seals (Range: nd – 4.4 ng/g lw). These concentrations were similar to the NW Atlantic grey

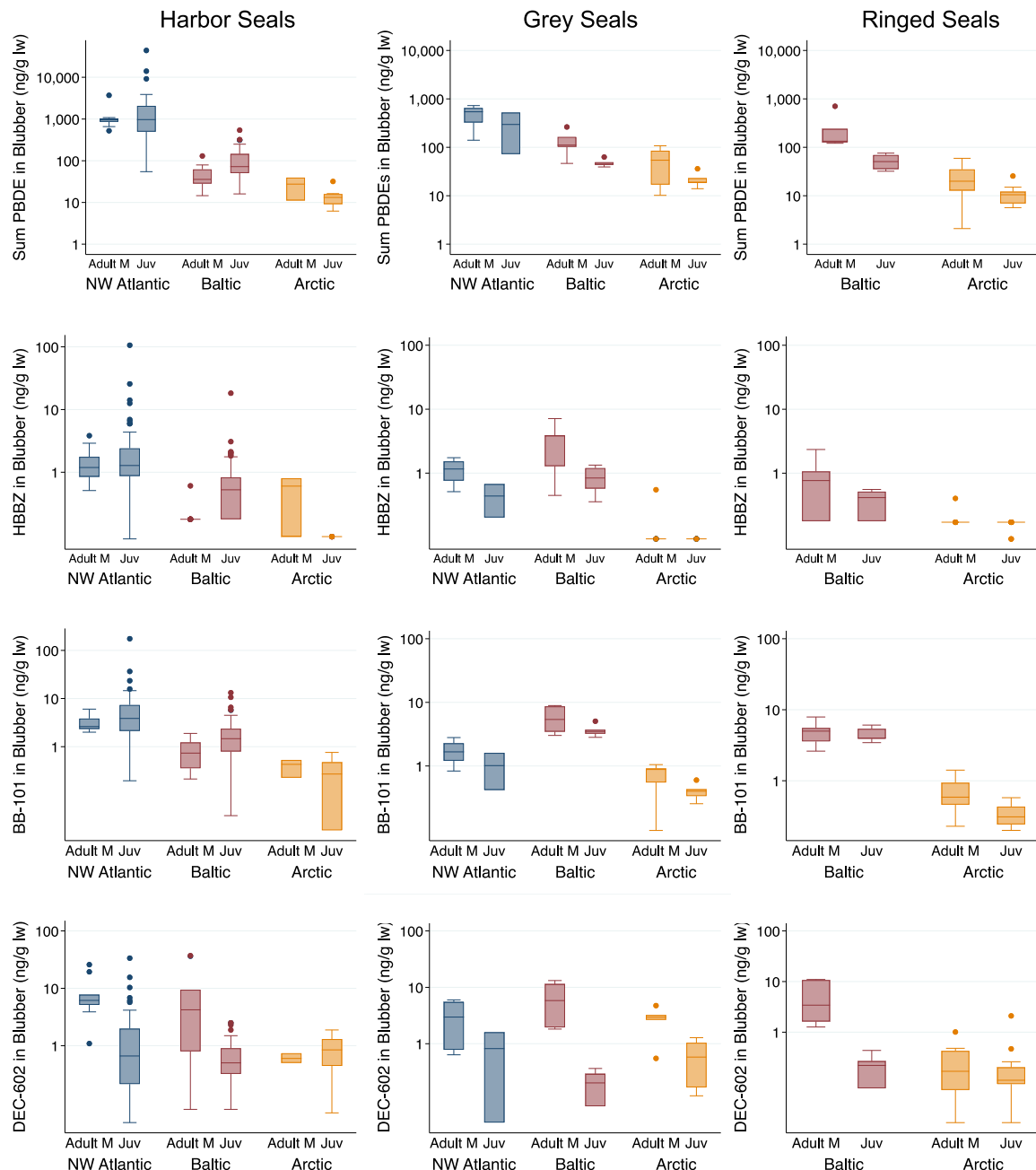


Fig. 2. Concentrations of sum PBDEs, HBBZ, BB-101 and Dec-602 in harbor seals, grey seals, and ringed seals from the NW Atlantic, Baltic, and Arctic by age class. Boxplots indicate median (middle bar), 75th and 25th percentiles (top and bottom of boxes), and 95th and 5th percentiles (whiskers).

seals in the current study, but lower than the harbor seals. In Canadian Arctic ringed seals, concentrations ranged from nd to 2.2 ng/g lw and nd to 0.29 ng/g lw for HBBZ and BB-101, respectively (Houde et al., 2017). In the current study, concentrations and detection rates of BB-101 were higher in the ringed seals from both the Baltic and Greenland/Iceland region of the Arctic than the Canadian Arctic, but the HBBZ results were similar.

The Baltic was unique in that HCDBCO accounted for means of 4.8–14% of the altBFR contamination among the three seal species, but this compound was otherwise only detected in two humpback whales from the Arctic. This compound was previously reported in fish from the Baltic (Rjabova et al., 2016), but to our knowledge, this is only the second report of the presence of this flame retardant chemical in marine mammal tissues. Law et al. (2013) reported DBHCTD, another

abbreviation for hexachlorocyclopentadienyl-dibromocyclooctane, in blubber of harbor porpoises from U.K. waters at concentrations ranging from (0.57–3.8 ng/g lw). The reason for the regional difference in this study is unclear since little information about the global usage of HCDBCO or DBHCTD is available. Previous studies have detected HCDBCO in a herring gull liver (Gentes et al., 2012), peregrine falcon eggs (Guerra et al., 2012), and human serum and breast milk (Zhou et al., 2014) from eastern Canada. Therefore, this compound is clearly present in the northern part of the Northwest Atlantic region bordered by Canada, but it was not found in marine mammals from the nearby U. S. coast of the Gulf of Maine in this study.

For the GLM analysis of both HBBZ and BB-101, the same juvenile harbor seal from the NW Atlantic had concentrations that were extreme outliers (106 ng/g and 175 ng/g lw, respectively), so this individual was

removed to improve model fit. For HBBZ concentrations, the best model that included condition index resulted in significant coefficients for region (Arctic: $\beta = -2.49$ [95%CI = -3.51 to -1.48], $p < 0.001$), age class ($\beta = -1.66$ [95%CI = -3.00 to -0.32], $p < 0.05$), and condition ($\beta = -3.33$ [95%CI = -6.39 to -0.26], $p < 0.05$) (Table S6). No interaction coefficients were significant, so they were not retained in the model. Without condition index, the only significant coefficients in the best model were for region (Baltic: $\beta = -1.02$ [95%CI = -1.61 to -0.43], $p < 0.01$; Arctic: $\beta = -2.43$ [95%CI = -3.65 to -1.21], $p < 0.001$), and the region*species interaction (Baltic*grey seal: $\beta = 2.08$ [95%CI = 0.16 – 4.01], $p < 0.05$) (Table S6).

For BB-101, the best model that included condition index resulted in significant coefficients for region (Baltic: $\beta = -0.78$ [95%CI = -1.30 to -0.28], $p < 0.01$; Arctic: $\beta = -2.63$ [95%CI = -3.39 to -1.88], $p < 0.001$), and the region*species interaction (Baltic*grey seal: $\beta = 2.14$ [95%CI = 0.86 – 3.42], $p < 0.01$; Arctic*grey seal: $\beta = 1.87$ [95%CI = 0.54 – 3.19], $p < 0.01$) (Table S7). Without condition index, region (Baltic: $\beta = -0.81$ [95%CI = -1.14 to -0.49], $p < 0.001$; Arctic: $\beta = -2.53$ [95%CI = -3.15 to -1.92], $p < 0.001$), species (GS: $\beta = -1.29$ [95%CI = -2.06 to -0.51], $p < 0.01$), stranding year ($\beta = -0.45$ [95%CI = -0.079 to -0.010], $p < 0.05$), and the region*species interaction (Baltic*grey seal: $\beta = 2.47$ [95%CI = 1.46 – 3.49], $p < 0.001$; Arctic*grey seal: $\beta = 1.80$ [95%CI = 0.69 – 2.91], $p < 0.01$) coefficients were significant (Table S7).

Many of the significant factors influencing HBBZ and BB-101 concentrations were very similar to those influencing PBDE concentrations discussed above. In general, concentrations from the NW Atlantic were higher than the Baltic and the Arctic although the significant region*species interactions indicate that the regional differences were not consistent across the three seal species. Among harbor seals, the NW Atlantic region had the highest concentrations of these altBFRs (Fig. 2). However, among grey seals, concentrations in the Baltic tended to be the highest. The seals from the Arctic consistently had the lowest concentrations in all three species.

Like the model for PBDEs, the GLM analysis of the factors that affected HBBZ and BB-101 concentrations resulted in a significant coefficient for body condition for HBBZ, but not BB-101 concentrations. Additionally, there was a significant negative coefficient for stranding year on BB-101 concentrations, but not HBBZ. There are few studies of temporal trends of alternative BFRs in marine mammal tissues. The significant decreasing trend for BB-101 is consistent with a previous analysis of these compounds in harbor seals from Sweden, but there was no trend in seals from Maine (Sun et al., 2022a). Simond et al. (2017) report a decreasing trend in HBBZ concentrations in beluga whales from the Canadian Arctic between 1997 and 2013, but that study did not analyze BB-101. Given the wide variety of alternative brominated flame retardants currently being used, additional research is needed to understand their temporal patterns in marine mammals and other wildlife.

3.4. Dechlorane concentrations and composition

Total Dechlorane concentrations from each region were (mean \pm SD) 3.59 ± 6.41 ng/g lw, 2.93 ± 6.42 ng/g lw, and 0.91 ± 1.22 ng/g lw for all samples from the NW Atlantic, Baltic, and Arctic, respectively. Dec-602 accounted for the majority of the Dechlorane contamination in all species ($70 \pm 27\%$). Concentrations of the other compounds were highly variable among species from different regions (Fig. 1).

Most previous studies of Dechlorane-related compounds in marine mammals focused on the *syn*- and *anti*-Dechlorane Plus isomers, although those studies that included Dec-602 usually detected it (Barón et al., 2015; Simond et al., 2017; Sutton et al., 2019). There are no other studies of Dechlorane compounds in marine mammals from the U.S. coast of the NW Atlantic. However, compared to harbor seals from the Pacific coast of the U.S. (Sutton et al., 2019), the harbor seals from the current study had similar detection rates and concentrations of *syn*- and *anti*-DP but lower concentrations of Dec-602 (Median: 2.2 vs. 0.86 ng/g

lw in Pacific vs Atlantic, respectively). For the Baltic, de Wit et al. (2020) reported concentrations of *syn*- and *anti*-DP in grey seals (mean: 6.0 and 26 ng/g, *syn*- and *anti*-DP, respectively) that were one to two orders of magnitude higher than the grey seals in the current study but concentrations in harbor seals (mean: 0.046 and 0.040 ng/g, *syn*- and *anti*-DP respectively) were similar. *Syn*- and *anti*-DP were not detected in Arctic ringed seals in the current study, but they were previously reported at low concentrations in ringed seals from east and west Greenland (Vorkamp et al., 2015).

For the GLM on Dec-602 concentrations, the Gamma model with a log link had the best fit of all available models, but the plots of fitted values vs. residuals included more heteroscedasticity than for the brominated compounds. Therefore, more data is required to clearly understand Dec-602 dynamics in marine mammals. Unlike the PBDEs and the altBFRs, there were no extreme outlier points for Dec-602 concentrations. For models including condition index, the best model resulted in significant coefficients for region (Baltic: $\beta = -1.02$ [95%CI = -1.64 to -0.39], $p < 0.01$; Arctic: $\beta = -0.89$ [95%CI = -1.75 to -0.023], $p < 0.05$) and age class ($\beta = -2.16$ [95%CI = -3.20 to -1.12], $p < 0.001$) (Table S8). None of the interaction effects were significant so they were not retained in the model. Without condition index, the best model had significant coefficients for region (Arctic: $\beta = -1.58$ [95%CI = -2.75 to -0.41], $p < 0.01$), species (ringed seal: $\beta = -1.28$ [95%CI = -1.99 to -0.58], $p < 0.001$), age class ($\beta = -1.32$ [95%CI = -2.20 to -0.44], $p < 0.01$) and the region*age interaction (Baltic*juvenile: $\beta = -1.50$ [95%CI = -2.68 to -0.32], $p < 0.05$) (Table S8).

Unlike the PBDEs and altBFRs, concentrations of Dec-602 were very similar in the NW Atlantic and Baltic regions. The Arctic had somewhat lower concentrations among adult male harbor and ringed seals than the other two regions, but concentrations among juveniles were similar for all three regions and species (Fig. 2). There was a clear trend for higher Dec-602 concentrations in adult males than juveniles for all three species from the NW Atlantic and Baltic which may result from low rates of *in utero* maternal transfer of this compound as was found in some sharks (Marler et al., 2018) and sperm whales (Zaccaroni et al., 2018). In the Arctic, the harbor seal and ringed seal adult males had very similar concentrations to the juveniles (Fig. 2). The reason for the variable patterns in age effects in the three regions is unclear but may be related to the relatively small sample sizes of adults and juvenile harbor seals from the Arctic compared to the other regions.

3.5. Pinniped and cetacean comparisons

Samples from six cetacean species were available from the NW Atlantic and from the Arctic, but small sample sizes prevented analysis by all of the demographic factors considered for the pinnipeds (Table 1). Therefore, for baseline environmental monitoring purposes on some poorly-studied species, qualitative comparisons of contaminant concentrations were made. Overall, there is a pattern that the highest PBDE and altBFR concentrations were found in the small toothed whales (white-sided dolphins, white-beaked dolphins, and pilot whales), followed by the baleen whales (minke and humpback), and the seals (Fig. 3). The other small odontocete sampled from the NW Atlantic, the harbor porpoise, had contaminant concentrations similar to the baleen whales and somewhat lower than the white-sided dolphins and pilot whales. For PBDEs, the NW Atlantic harbor seals had elevated concentrations similar to the harbor porpoise, but harbor seals were less contaminated than the cetaceans for the two altBFRs. There was little difference among the species for Dec-602 concentrations, although in both regions, pilot whales had somewhat higher concentrations than the other species (Fig. 3).

Many halogenated chemicals have been shown to biomagnify in marine food webs such that there are positive relationships between trophic level and contaminant concentration (Tomy et al., 2008; de Wit et al., 2010; Liu et al., 2021) although trophic level relationships for PBDEs have shown mixed patterns due to species-specific metabolic

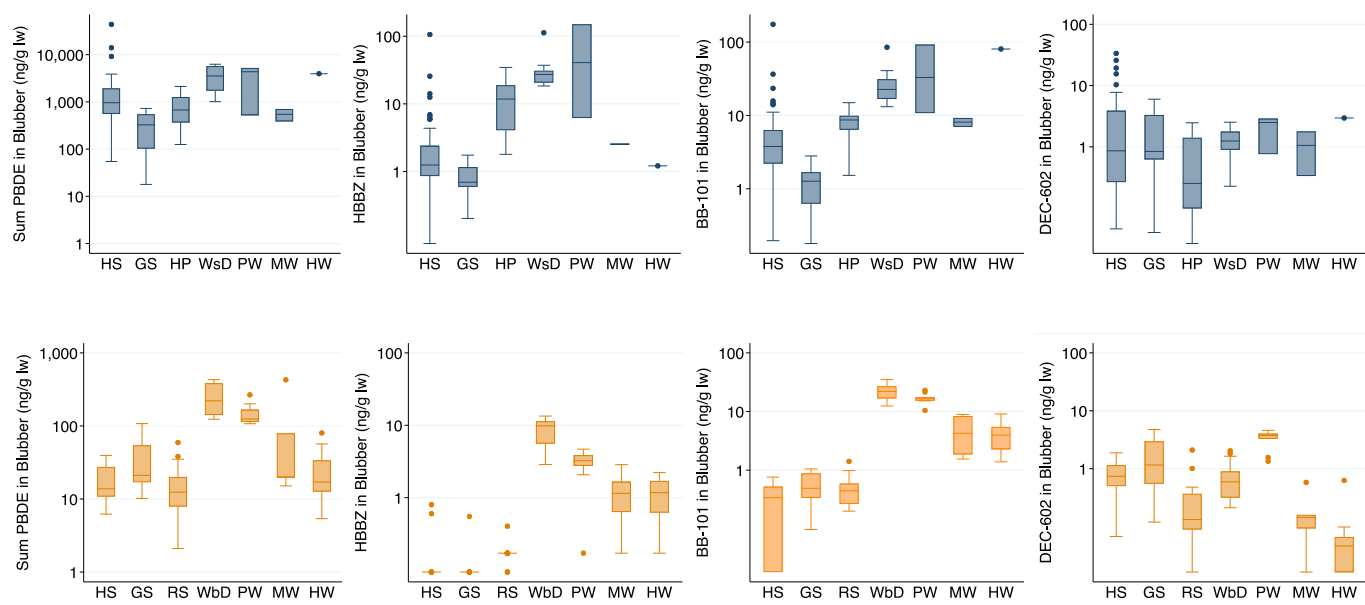


Fig. 3. Concentrations of sum PBDEs, HBBZ, BB-101, and Dec-602 in marine mammals from the NW Atlantic (blue), and the Arctic (orange). Boxplots indicate median (middle bar), 75th and 25th percentiles (top and bottom of boxes), and 95th and 5th percentiles (whiskers). Species abbreviations: harbor seals (HS), grey seals (GS), ringed seals (RS), harbor porpoises (HP), white-sided dolphins (WsD), white-beaked dolphins (WbD), pilot whales (PW), minke whales (MW), and humpback whales (HW). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

differences (de Wit et al., 2010) or dietary specialization (Pinzone et al., 2015). The marine mammals in this study are all high trophic level predators, but on average, there are some differences in their trophic level. From a broad diet-based analysis, Pauly et al. (1998) estimated a trophic level of 3.4 and 3.6 for the baleen minke and humpback whales, respectively. The three seal species have estimated trophic levels ranging from 3.8 to 4.0 and the four toothed whales range from 4.1 to 4.4 (Pauly et al., 1998). Therefore, it is possible that broad trophic differences among the species explain some of the variability in flame retardant contamination, but it is likely that age composition, time trends, and regional dietary differences also play significant roles. More research is needed to understand the dynamics of contamination in these cetacean species.

3.6. Tissue comparisons

PBDE concentrations in matched liver and blubber samples from Baltic and NW Atlantic harbor seals showed inconsistent patterns in the two regions (Tables S9 and S10). Some of the tri-hexa PBDEs had higher concentrations in blubber than liver in the Baltic seals (BDE-49, -100, and -153) while BDE-138 had higher concentrations in liver. In the NW Atlantic, BDE-47, -153, -154 had higher concentrations in liver while BDE-66 was higher in blubber. In both regions, higher-brominated PBDEs were either not significantly different between tissues or not comparable due to low detection in one or both tissues. For total PBDEs, liver concentrations were higher in the NW Atlantic, but there was no difference between the tissues in the seals from the Baltic.

Many previous studies found that tri-hexa PBDE concentrations were closely tied to the lipid content of the tissues and the ratios of lipid-normalized concentrations were generally equal to one (Yordy et al., 2010; Raach et al., 2011). However, Moon et al. (2010) reported greater PBDE concentrations in blubber than liver in minke whales and common dolphins from Korea. Therefore, the inconsistent patterns in the harbor seals from the NW Atlantic and Baltic may be a result of chance, an artifact of a relatively small sample size, or some aspect of dietary differences between the two regions.

In both regions, total altBFR and HBBZ concentrations were higher in liver than blubber (Tables S9 and S10). In the Baltic samples, TBBZ and

HCDBCO concentrations were higher in blubber, but detection rates were low for both compounds (3.3–50%). Studies of tissue partitioning for the alternative brominated flame retardants, particularly between liver and blubber of marine mammals, are very rare. Berger et al. (2023) found concentrations of some alternative BFRs including β - and γ -hexabromocyclododecane (HBCD), TBB, and decabromodiphenyl ethane (DBDPE) were higher in liver than blubber of harbor seal pups. Andvik et al. (2021) measured concentrations of a suite of legacy and emerging contaminants, including HBBZ, in blubber and muscle tissues of killer whales from Norway. On a lipid-weight basis, HBBZ concentrations were higher in muscle than blubber for five individuals with matched tissues samples. It was also higher in liver than blubber in one neonate. These studies provide some evidence that the bioaccumulation of HBBZ, as well as some other alternative BFRs, may not be entirely related to the lipid content of the tissue. There may be an affinity for blood-perfused tissues such as muscle or liver, but the mechanism for this dynamic is unclear.

Dechlorane concentrations were consistently higher in liver than blubber from both regions (Tables S9 and S10). In the NW Atlantic, there were significant tissue differences for Dec-602, -604, and anti-DP, while in the samples from the Baltic, there were differences for Dec-602, -603, syn-DP and anti-DP. There were no Dechlorane compounds with significantly higher concentrations in blubber. Although Dechlorane compounds are highly lipophilic (LogK_{ow} range: 8.1–11.3) (Peng et al., 2014) and their wet weight concentrations are strongly correlated with the lipid content of the tissues (Yin et al., 2020), others have found that lipid-adjusted ratios between tissues were greater or less than one indicating that factors other than lipid content influence the distribution of these compounds (Yin et al., 2020). In human tissues, the lipid-adjusted partitioning ratios of syn-DP and anti-DP between breast milk and maternal serum were 0.43 and 0.47, respectively (Ben et al., 2013) and between adipose tissue and maternal serum were 0.36 and 0.35, respectively (Yin et al., 2020). These authors suggest that DP may interact with certain serum macromolecules that have a greater impact on the tissue partitioning than just the lipid content. Since liver is a highly blood-perfused tissue compared to blubber, a similar mechanism might be acting in these marine mammal tissues.

3.7. Health implications

Numerous studies have linked PBDEs to a range of health effects in marine mammals and humans (Shaw et al., 2010; Linares et al., 2015; Bartalini et al., 2022). However, since it is nearly impossible to perform controlled studies on live marine mammals, understanding the health effects of contaminant exposure stems from the “weight of evidence” (Ross, 2006). This includes evidence from correlative observational studies (Hall et al., 2003, 2009; Gabrielsen et al., 2015; Hoydal et al., 2016), extrapolation from laboratory animal response (Lema et al., 2007; Viberg and Eriksson, 2011; Kodavanti et al., 2015), and the use of *in vitro* cell lines for dose-response studies (Frouin et al., 2010; McKinney et al., 2011; Ishibashi et al., 2018; Rajput et al., 2021). Derivation of a threshold level of PBDE contamination in blubber that is likely to have significant health effects, as has been proposed and often cited for PCBs (Kannan et al., 2000; Murphy et al., 2015; Jepson et al., 2016), has proven challenging. The only PBDE threshold regularly cited for marine mammals, which was derived from young grey seals, is 1500 ng/g lw in blubber as a level that likely indicates endocrine disruption (Hall et al., 2003). In the current study, only marine mammals from the NW Atlantic exceeded this level of PBDE contamination (35% harbor seals, 78% white-sided dolphins, 22% harbor porpoises, 67% pilot whales, and the one humpback whale).

Some laboratory studies have indicated that the dose-response curve for PBDE congeners is more likely to be non-linear, or hormetic, where response is enhanced at low doses and inhibited at middle or higher doses (Calabrese and Baldwin, 2003; Hall et al., 2003). Therefore, although convenient, a threshold model based on one species’ response may not be the most appropriate tool for evaluating health effects of PBDEs in many marine mammal species.

For less-studied compounds such as many of the altBFRs and Dechloranes, the understanding of potential health effects in marine mammals is very poor. Additionally, as has been demonstrated in this study, marine mammals are never exposed to just one chemical at a time. They are simultaneously exposed to a cocktail of chemicals that may be synergistic or antagonistic in their effects (Cullon et al., 2005; Ross, 2006; Dietz et al., 2015). So, while it can be confidently stated that contaminant exposure poses a significant challenge to the health and well-being of marine mammal populations, further research is required to understand the exact nature and extent of these effects.

3.8. Study limitations

This study has some limitations. Marine mammal samples are difficult to obtain, particularly from some of the cetacean species. Therefore, the ideal study design with large sample sizes that are evenly distributed among species, age classes and regions was not possible. Having uneven, smaller sample sizes reduced power and limited some of the potential for robust statistical methods. However, this limitation applies to almost every marine mammal study, so it is important for scientists to synthesize patterns observed in many studies to understand the environmental and ecological factors affecting these species. Additionally, the mixture of samples from stranded, bycaught, and hunted animals added another complication to the analysis. The inclusion of a condition index in the GLM analysis accounted for some of the variability introduced by the different sample sources, but since length and weight measurements were not available for all seals, this was an imperfect solution. However, even with these limitations, this study provides extensive baseline and comparative data for many species and poorly studied contaminants from a broad geographic area.

4. Conclusions

This multi-regional and multi-species study of flame retardant contamination established that all analyzed species from every region carried body burdens of a complex mixture of legacy and alternative

brominated and chlorinated flame retardants. Although concentrations of most chemicals were higher near the industrialized U.S. and Sweden than in the Arctic, the detection of these chemicals in Arctic species, at least at low levels, demonstrates their potential for long-range atmospheric and aquatic distribution. Contaminant concentrations were also influenced by age, species metabolism and diet, body condition, and time trends, often in complex combinations. While most marine mammal contaminant studies rely on blubber tissue because of the ease of collection and greater availability of sample material, some chemicals tend to interact with proteins or other macromolecules in blood rather than the lipids in blubber making them more likely to be detected in liver tissue than blubber. Inclusion of multiple tissue types in studies of contamination allows for better estimation of body burdens. Additional research is needed to understand the health implications of these chemical body burdens.

Credit author statement

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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.

Acknowledgements

The present study was made possible by funding from the National Natural Science Foundation of China (no. 42007287) and the National Key Research and Development Program of China (no. 2019YFC1803402). We would like to thank the Greenlandic subsistence hunters for providing samples from their hunts and for allowing employees from the GINR to enter the flensing area to sample the large whales. We would like to thank Tenna K Boye, Else Ostermann and Peter Hegelund at the Greenland Institute of Natural Resources for help sampling marine mammals in Greenland. We would also like to thank all the fishermen and general public in Iceland and Sweden for collecting seals for this study. Eric dos Santos at the Marine and Freshwater Research Institute and other staff at BioPol helped sub-sample blubber samples from seals in Iceland. We are grateful to Annika Strömberg who subsampled seals from the Swedish Environmental Specimen Bank. Age determination of the seals from Sweden was done by Annika Strömberg and other staff in the laboratory at the museum. The long-term investigation of seal health and sample collection in the Baltic was funded by the National Environmental Monitoring Program commissioned by the Swedish Environmental Protection Agency and the Swedish Museum of Natural History. We would also like to thank the National Marine Fisheries Service (NMFS) and members of the Greater Atlantic Region Marine Mammal Stranding Network: Allied Whale/College of the

Atlantic, Marine Mammals of Maine, New England Aquarium, International Fund for Animal Welfare, and the New York Marine Rescue Center for providing tissue samples from the Northwest Atlantic coast of the U.S. Tissues were collected under NMFS scientific research permit number 22272 and letter of authorization number 19091. Shaw Institute would like to thank Molly McEntee for assistance with tissue preparation and geospatial analysis.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envpol.2023.122255>.

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