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Dietary Exposure to a Group of Naturally Produced Organohalogens (Halogenated Dimethyl Bipyrroles) via Consumption of Fish and Seafood

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Concentrations of four naturally produced halogenated dimethyl bipyrroles (HDBPs) were quantitated in marine fish ($n = 10$), freshwater fish ($n = 10$), canned fish ($n = 10$), and shrimp composites ($n = 10$) collected from 1992 to 2002 for the Canadian Total Diet Study. Canned fish composites composed of epipelagic higher trophic level species contained the highest concentration of HDBPs (ΣHDBP geometric mean ± standard error = 880 ± 690 pg/g of wet weight, $n = 10$), which was significantly higher than that found in the other three composites. There were no significant temporal trends of HDBP concentrations observed for any of the four composites. The estimated daily intake of HDBPs via consumption of fish and seafood was determined to be 53 pg/kg of body mass/day and 0.10 pg of TEQ/kg of body mass/day when transformed to 2,3,7,8-tetrachlorodibenzodioxin equivalents (TEQs). In the canned fish and shrimp composites collected in 1998, HDBPs accounted for approximately 98 and 19%, respectively, of the total quantitated TEQ (which included polychlorinated biphenyls, dioxins, and furans). The results of this study provide the first estimate of human exposure to naturally produced bioaccumulating organohalogens.

KEYWORDS: Bioaccumulative; contaminants; human exposure; biogenic; TEQ

INTRODUCTION

Humans are exposed to a myriad of persistent hydrophobic organohalogens. Due to the physical properties and environmental behavior of these compounds, food is an important route of human exposure. Market basket surveys and duplicate diet studies are often used to measure concentrations of organohalogens in foods to help assess exposure to these compounds and eventually evaluate potential risks to consumers. The majority of organohalogen analytes routinely monitored in food are anthropogenic in origin, such as organochlorine pesticides, polychlorinated biphenyls (PCBs), and polychlorinated dibenzodioxins (PCDDs). In some instances biotransformation products of anthropogenic organohalogens [for example, 1,1-dichloro-2,2-bis(4-chlorophenyl)ethylene (*p*,*p*′-DDE), a metabolite of 1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane (*p*,*p*′-DDT)] are also monitored (*1*−*3*). No studies have examined concentrations of biogenic organohalogens in food or estimated human exposure to these naturally produced compounds.

Recent work has described the environmental existence of persistent bioaccumulative organohalogens that have a natural origin—specifically the occurrence, bioaccumulation, and biomagnification of naturally produced bipyrroles. The first studies dealt with a family of halogenated dimethyl 2,2′-bipyrroles (HDBPs) (*4*−*6*). The molecular structures of the four HDBP congeners observed in environmental samples are shown in

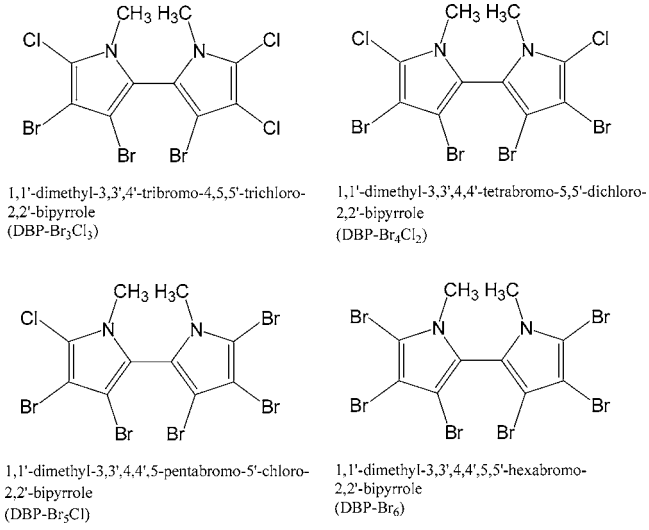

Figure 1. Molecular structures of the four environmentally relevant halogenated dimethyl bipyrroles (HDBPs).

Figure 1 and are very similar to the structure of another marine natural product, hexabromo-2,2′-bipyrrole (*7*). The environmental occurrence of another structurally similar compound—heptachlorinated 1,2′-bipyrrole—has also been examined recently (*8*, *9*). Specific sources of these compounds have not been identified, but radiocarbon analysis strongly suggests that HDBPs are synthesized using a relatively recent source of

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Table 1. Fish and Seafood Items Used To Prepare Total Diet Study Composites[a]

year and city	marine fish	freshwater fish	canned fish	shrimp
1992, Toronto	cod, 3 halibut, 1	lake trout, 1 rainbow trout, 1 whitefish, 2	salmon (in oil), 4 tuna (in oil), 4	precooked, 3 raw, 1
1993, Montreal	cod, 4	trout, 3	salmon (in water), 4 tuna (in water), 4	not analyzed
1994, Winnipeg	cod, 4	trout, 1 pickerel, 3	salmon (in water), 4 tuna (in oil), 4	raw, 2
1995 (winter), Vancouver	cod, 4	trout, 1 whitefish, 3	salmon (in water), 4 tuna (in oil), 4	not analyzed
1995 (summer), Ottawa	cod, 3 haddock, 1	trout, 1 rainbow trout, 2 whitefish, 1	salmon (in water), 4 tuna (in oil), 4	precooked, 4
1998, Whitehorse	cod, 1 haddock, 1	smelt, 1 perch, 1	salmon (in water), 3 tuna (in oil), 3	precooked, 3
1999, Calgary	cod, 4	rainbow trout, 4	salmon (in water), 4 tuna (in oil), 4	raw, 4
2000, Ottawa	cod, 4 haddock, 4 sole, 4	lake trout, 1 trout, 1 rainbow trout, 2	salmon (in water), 4 tuna (in water), 8	raw, 3 precooked, 1
2001, St. John's	cod, 4 haddock, 4 sole, 4	rainbow trout, 6	salmon (in water), 4 tuna (in water), 8	raw, 8
2002, Vancouver	cod, 4 halibut, 4 sole, 4	rainbow trout, 4	salmon (in water), 4 tuna (in water), 4	raw, 4

[a] Values listed refer to the number of different markets from which items were purchased (marine fish, freshwater fish, shrimp) or the number of different brands and/or products used (canned fish). Equal portions of marine fish, freshwater fish, and shrimp obtained from each unique market were combined after preparation and homogenization. Canned fish composites were prepared by combining tuna and salmon homogenates (prepared with equal portions of unique brands or products) in a 3:1 weight ratio.

carbon and thus likely have a biogenic origin, as opposed to most industrially produced organohalogens (*10*, *11*).

Studies have shown HDBPs to be persistent, bioaccumulative, and globally distributed in marine environments. Due to similarities in physical properties and persistence, their environmental behavior has somewhat paralleled the behavior of persistent anthropogenic organohalogens such as the higher chlorinated PCB congeners. HDBPs have been detected in biota sampled from locations around the world and are thought to undergo long-range transport (*6*). They biomagnify to an extent similar to that of persistent anthropogenic organohalogens (e.g., CB-153) but appear to be metabolized by ringed seals (*5*). On occasion, HDBPs have also been measured at concentrations similar to CB-153 in seabird egg and marine mammal blubber samples collected from the northern Pacific Ocean (*4*, *6*). However, the geographical distribution of HDBPs does not mimic the distribution of the higher chlorinated PCBs; the highest concentrations of HDBPs have been observed in biota sampled from the northern Pacific Ocean, as opposed to near industrialized areas (*6*).

Less is known about the toxicity of HDBPs. One in vitro assay has shown that HDBPs bind to the aryl hydrocarbon receptor (AhR) and induce cytochrome P450 1A (CYP1A), measured as ethoxyresorufin-*O*-deethylase activity, in chick embryo hepatocytes (*12*). Induction of CYP1A by individual congeners and HDBP mixtures was similar to that observed by mono-ortho PCBs (*13*). Binding of DBP−Br_6 to the AhR was ∼0.000017 times the affinity of 2,3,7,8-tetrachlorodibenzodioxin (TCDD). However, no significant negative effects on reproduction or morphological characteristics of adults or fledglings were observed during an HDBP feeding study involving captive American kestrels (*Falco sparverius*) (*14*).

This study examined the dietary exposure of Canadians to the four environmentally relevant HDBP congeners. Marine fish, freshwater fish, canned fish, and shrimp composites collected over the past decade for the Canadian Total Diet Study were analyzed for HDBPs. The results of this study provide the first estimate of human exposure to naturally produced bioaccumulating organohalogens.

MATERIALS AND METHODS

Samples. Fish and seafood samples were initially collected and prepared as part of the Canadian Total Diet Study (*15*). The Canadian Total Diet Study is a market basket survey that was conducted biannually from 1992 to 1995 and annually from 1998 to the present. For each Canadian Total Diet Study, foods comprising >1% of the average Canadian's diet are purchased and prepared according to standardized protocols. Food items are purchased from up to four different markets within a selected Canadian city, ensuring a variety of items are obtained from various producers. The foods are prepared and cooked as for consumption, and the replicate food items are combined and homogenized to form composite samples. Four fish and seafood composites are routinely prepared as part of the Canadian Total Diet Study: marine fish (predominantly cod and haddock), freshwater fish (predominantly trout), canned fish (salmon and tuna), and shrimp. **Table 1** provides some detailed information on the items used to prepare the composite samples. The marine and freshwater fish are baked at 230 °C for ∼10 min, or until the fish flakes easily with a fork. The skin and bones are removed, and the fish are homogenized in a food processor. Shrimp are boiled in tap water until cooked and drained, and the inedible parts are removed prior to homogenization. Canned fish are drained and homogenized. After homogenization, the composites are placed in precleaned glass jars with polypropylene caps and poly(tetrafluoroethylene) liners and stored at −20 °C until analysis. Composites from 10 different Canadian Total Diet Studies (1992−1994 summer studies, 1995 summer and winter studies, and 1998−2002 studies) were analyzed.

HDBP Analysis. Approximately 10 g of thawed composite was spiked with a mixture of $^{13}C_{12}$-labeled PCBs ($^{13}C_{12}$-CB118, $^{13}C_{12}$-CB153, $^{13}C_{12}$-CB180, and $^{13}C_{12}$-CB194; ∼20 ng of each congener) as a surrogate standard. Past method development work has shown that method recoveries of $^{13}C_{12}$-labeled PCBs are not significantly different from those obtained for HDBPs. Diatomaceous earth (∼5 g) was added to the composite and mixed thoroughly until a free-flowing mixture was obtained. The mixture was loosely packed into a precleaned 33 mL stainless steel cell that was precleaned with acetone and hexane.

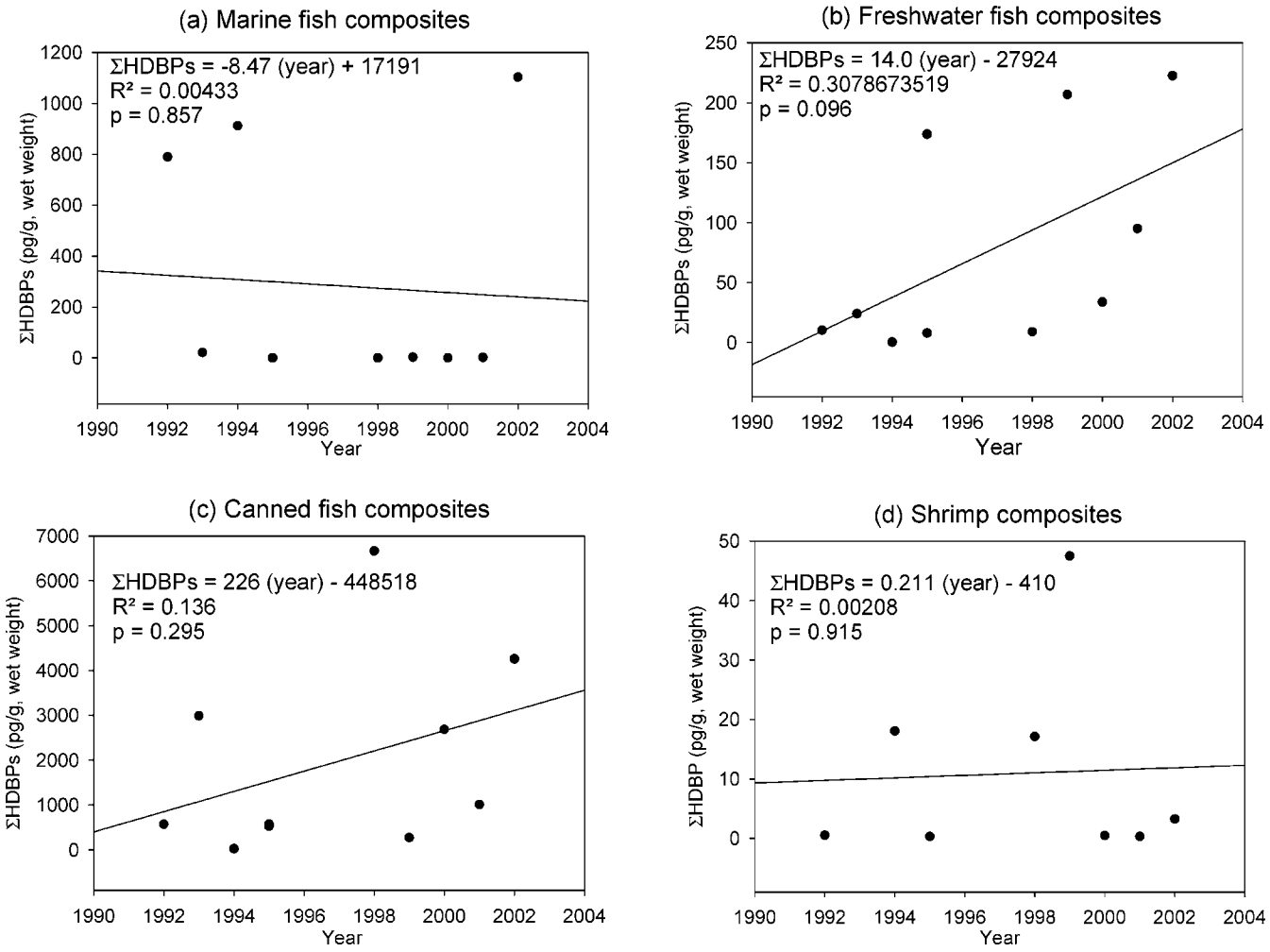

Figure 2. Temporal variation of total halogenated dimethyl bipyrrole (ΣHDBP) concentrations in (**a**) marine fish, (**b**) freshwater fish, (**c**) canned fish, and (**d**) shrimp composites from 1992 to 2002.

The mixture then underwent pressurized liquid extraction using a Dionex ASE 200 instrument (Sunnyvale, CA). A mixture of hexane and acetone [1:2 (v/v)] was used as the extraction solvent. The instrumental conditions for the extractions were as follows: oven temperature, 100 °C; thermal equilibrium time, 5 min; pressure, 2000 psi; static extraction time, 10 min; 100% rinse volume; and purge time of 60 s. The extraction of each sample proceeded over two cycles. One method blank containing only diatomaceous earth was processed with each set of six composite samples.

The extracts were washed in a separatory funnel with water to remove precipitate that had formed during extraction. The organic layer was dried by draining through a bed of anhydrous Na_2SO_4 and reduced in volume on a rotary evaporator. Lipids were determined gravimetrically and subsequently separated from the organohalogens using gel permeation and Florisil column chromatography as described by Tittlemier et al. (*5*).

Samples were analyzed for 1,1′-dimethyl-3,3′,4-tribromo-4,5,5′-trichloro-2,2′-bipyrrole (DBP-Br_3Cl_3), 1,1′-dimethyl-3,3′,4,4′-tetrabromo-5,5′-dichloro-2,2′-bipyrrole (DBP-Br_4Cl_2), 1,1′-dimethyl-3,3′,4,4′,5-pentabromo-5′-chloro-2,2′-bipyrrole (DBP-Br_5Cl), 1,1′-dimethyl-3,3′,4,4′,-5,5′-hexabromo-2,2′-bipyrrole (DBP-Br_6), and $^{13}C_{12}$-PCB congeners using gas chromatography−electron capture negative ionization−mass spectrometry in the selected ion monitoring mode. Samples were introduced into the Agilent 6890 (Palo Alto, CA) gas chromatograph using cool on-column injection (2 μL injection volume) automated by an Agilent 7683 automatic liquid sampler. The gas chromatograph was fitted with a retention gap (deactivated fused silica, 1 m × 0.530 mm) and a DB-5MS analytical column (30 m × 0.25 mm, 250 μm film thickness; J&W Scientific, Mississauga, ON). Ultrapure helium was used as a carrier gas (0.9 mL/min), and methane (99.97%) was used as the moderating gas in the Agilent 5973N mass spectrometer source. The most abundant ions of the molecular ion isotope clusters were used for quantitation; the second most abundant ions in the cluster were qualifying ions. Temperature program details are given in Tittlemier et al. (*5*). External standards were used to quantitate the HDBPs and $^{13}C_{12}$-PCBs.

Statistical analyses were performed using SigmaStat version 2.03 (SPSS Inc., Chicago, IL).

RESULTS

HDBP Concentrations. Recoveries of the $^{13}C_{12}$-PCB standards averaged 92 ± 14% for all of the samples and blanks. All concentration data were recovery corrected using the average recovery of the $^{13}C_{12}$-PCB congeners for each particular analysis.

For all four fish and seafood composites, ΣHDBP concentrations (calculated as the sum of DBP-Br_3Cl_3, DBP-Br_4Cl_2, DBP-Br_5Cl, and DBP-Br_6 concentrations) varied by as much as 2 orders of magnitude from 1992 to 2002. However, there were no statistically significant trends of ΣHDBP concentrations over time (**Figure 2**). Therefore, recovery-corrected HDBP concentration data from the various years were combined and used to calculate mean concentrations for each composite (**Table 2**).

Canned fish composites contained ΣHDBP concentrations that were significantly higher (one-way ANOVA on log transformed ΣHDBP concentrations, $p < 0.05$) than those of the other composites. Of the remaining three composites, freshwater and marine fish appeared to contain higher levels of HDBPs than shrimp, but the differences were not significant.

Table 2. Geometric Mean ± Standard Error (Range) of Lipid Contents and Halogenated Dimethyl Bipyrrole Congener (DBP) Concentrations (Picograms per Gram of Wet Weight) of Total Diet Study Fish Composites Collected from 1992 to 2002[a]

composite (*n*)	lipid %	DBP-Br_3Cl_3	DBP-Br_4Cl_2	DBP-Br_5Cl	DBP-Br_6	ΣHDBP
marine fish (10)	0.95 ± 0.70	12 ± 6	33 ± 120	3 ± 8	2 ± 4	8 ± 140
	(0.28–7.34)	(<12.1[b]– 63.9)	(<15.0–952)	(<1.76–68.2)	(<0.60–36.2)	(<0.60–1100)
freshwater fish (10)	5.7 ± 0.8	8 ± 2	32 ± 23	2.0 ± 1.6	3.5 ± 3.1	26 ± 28
	(2.17–9.71)	(<11.8–28.3)	(7.95–198)	(<0.58–31.8)	(<0.58–31.8)	(<0.58–223)
canned fish (10)	3.3 ± 0.5	55 ± 30	740 ± 640	40 ± 23	16 ± 10	880 ± 690
	(1.89–5.65)	(<12.2–276)	(20.7–6190)	(1.44–206)	(1.12–85.6)	(25–6664)
shrimp (10)	0.84 ± 0.09	<12.1	8 ± 1	2 ± 1	2 ± 3	2 ± 6
	(0.53–1.24)		(2.17–13.7)	(<1.82–8.54)	(<0.60–25.2)	(<0.60–47.5)

[a] Concentrations below the method detection limit (MDL) were assigned values of half the MDL during the calculation of the geometric mean and standard errors. [b] MDL; calculated as the lowest concentration of analyte in sample that would produce a signal 3 times greater than surrounding noise.

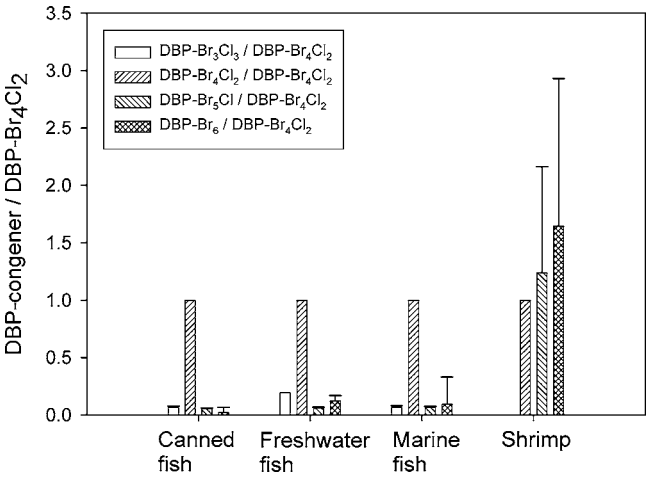

Figure 3. Geometric mean (± standard error) of halogenated dimethyl bipyrrole (HDBP) congener concentrations relative to DBP-Br_4Cl_2.

Table 3. Estimated Daily Intakes of Halogenated Dimethyl Bipyrroles (ΣHDBPs) and HDBP-Derived 2,3,7,8-Tetrachlorodibenzodioxin Equivalents (TEQs) per Kilogram of Body Mass

total diet study composite	ΣHDBP estimated daily intake (pg/kg of body mass/day)	ΣHDBP TEQ estimated daily intake (pg of TEQ/kg of body mass/day)
marine fish	0.47	0.0076
freshwater fish	0.50	0.0014
canned fish	52	0.093
shrimp	0.067	0.00046
total intake from fish and shrimp	53	0.10

HDBP Congener Patterns. The abundances of individual HDBP congeners relative to DBP-Br_4Cl_2 in each composite are shown in **Figure 3**. The geometric mean relative abundances were calculated using only data that were greater than the method detection limits, as opposed to assigning nondetects a value of half the detection limit. This gave a better representation of the HDBP congener pattern that was actually present in the composites.

HDBP EDIs and EDI_{TEQ}s. Table 3 lists the estimated daily intakes (EDIs) of HDBPs and HDBP-derived 2,3,7,8-tetrachlorodibenzodioxin equivalents (TEQs). The EDIs were calculated using the average Canadian daily intake of food composites determined by the 24 h recall section of the Nutrition Canada Survey (*16*), the geometric mean HDBP congener concentrations in fish composites collected from 1992 to 2002 (**Table 2**), and an average body mass of 60 kg. The EDI_{TEQ}s were determined in the same manner and used cytochrome P450 1A induction equivalency factors (IEFs) derived from an in vitro chick embryo hepatocyte assay that monitored ethoxyresorufin-*O*-deethylase activity (DBP-Br_3Cl_3 IEF = 0.001, DBP-Br_4Cl_2 IEF = 0.002, DBP-Br_5Cl IEF = 0.0004, DBP-Br_6 IEF = 0.0005) (*12*).

HDBP Contributions to TEQs. Table 4 lists the HDBP TEQs estimated for the four fish and seafood composites from the 1998 Canadian Total Diet Study, the most recent Total Diet Study for which associated PCDD, polychlorinated dibenzofuran (PCDF), and PCB data are available for these composites. The HDBP TEQs were estimated using the IEFs described above. Calculated TEQs for PCDDs, PCDFs, and mono- and non-ortho PCBs are also listed in **Table 4** to show the relative contribution of HDBPs to total TEQs in each composite. The TEQs of the anthropogenic organochlorines were calculated using World Health Organization toxic equivalency factors for humans (*17*).

DISCUSSION

Occurrence of HDBPs in Dietary Items. HDBPs were measured above the method detection limit in 100% of the canned fish, in 90% of the freshwater fish, in 60% of the marine fish, and in 40% of the shrimp composites analyzed. The occurrence of HDBPs in freshwater fish composites is likely due to the incorporation of farmed fish into the composites, rather than a presence of HDBPs in freshwater environments. Past studies have shown that HDBPs are either nonexistent or present at very low concentrations in higher trophic level freshwater biota (*4*, *6*). Thus, the route of HDBP exposure for farmed fish is most likely via use of fish feed containing fishmeal or fish oil derived from marine species. Herring (*Clupea harengus*) and menhaden (*Brevoortia tyrannus*) are two species of fish that are commonly used to make fishmeal in Canada (Julie Dawson, Canadian Food Inspection Agency, personal communication), and both inhabit the marine environment.

Differences in HDBP concentrations among the composites reflect ecological differences of the fish and seafood items in the composites. Even though the concentrations in **Table 2** are listed on a wet weight basis, normalizing mean ΣHDBP values to lipid content does not change the relative ranking or statistical differences among composites.

Highest amounts of HDBPs were found in canned fish composites for two main reasons. First, the main species present in these composites [skipjack (*Katsuwonus pelamis*), yellowfin (*Thunnus albacares*), and albacore tuna (*Thunnus alalunga* or *Thunnus germo*) and sockeye salmon (*Oncorhynchus nerka*)] are epipelagic and tend to feed on micronekton, including squid and other fish (*18*−*20*). They are thus at relatively high trophic levels and are exposed to higher concentrations of HDBPs than lower trophic level organisms in the other composites, such as shrimp, due to biomagnification. In addition, these fish are mainly distributed in the Pacific Ocean, an area where the

Table 4. Halogenated Dimethyl Bipyrrole (HDBP), Non- and Mono-ortho Polychlorinated Biphenyl (PCB), Polychlorinated Dibenzodioxin (PCDD), and Polychlorinated Dibenzofuran (PCDF) Concentrations (Picograms per Gram of Wet Weight) and Calculated 2,3,7,8-Tetrachlorodibenzodioxin Equivalents (TEQs, Picograms per Gram of Wet Weight) in Total Diet Study Fish Composites, 1998

	concentration				calcd TEQ			
compound class	marine fish	freshwater fish	canned fish	shrimp	marine fish	freshwater fish	canned fish	shrimp
PCDDs[a]	0.031	0.574	0.152	0.643	0.007	0.080	0.047	0.025
PCDFs[b]	0.262	0.479	0.399	0.200	0.022	0.073	0.087	0.020
non-ortho PCBs[c]	7.37	17.1	20.0	4.70	0.122	0.264	0.093	0.057
mono-ortho PCBs[d]	393	689	543	122	0.017	0.030	0.020	0.0046
HDBPs[e]	nd[f]	8.95	6664	17.1	0	0.0045	13	0.026

[a] Data are from J. J. Ryan, unpublished data. PCDD class includes 2,3,7,8-TCDD, 1,2,3,7,8-PnCDD, 1,2,3,4,7,8-HxCDD, 1,2,3,6,7,8-HxCDD, 1,2,3,7,8,9-HxCDD, 1,2,3,4,6,7,8-HpCDD, and OCDD. [b] Data are from J. J. Ryan, unpublished data. PCDF class includes 2,3,7,8-TCDF, 1,2,3,7,8-PnCDF, 2,3,4,7,8-PnCDF, 1,2,3,4,7,8-HxCDF, 1,2,3,6,7,8-HxCDF, 2,3,4,6,7,8-HxCDF, 1,2,3,7,8,9-HxCDF, 1,2,3,4,6,7,8-HpCDF, 1,2,3,4,7,8,9-HpCDF, and OCDF. [c] Data are from J. J. Ryan, unpublished data. Non-ortho PCB class includes CB-77, CB-81, CB-126, and CB-169. [d] Data are from W. H. Newsome and J. Doucet, unpublished data. Mono-ortho PCB class includes CB-105, CB-118, CB-156, CB-157, and CB-189. [e] Data are from this study. HDBP class includes DBP-Br_3Cl_3, DBP-Br_4Cl_2, DBP-Br_5Cl, and DBP-Br_6. [f] Not detected.

highest levels of HDBPs have been observed in biota (*4*, *6*). Atlantic cod (*Gadus morhua*) and haddock (*Melanogrammus aeglefinus*), the principal species in the marine fish composite, inhabit the northern Atlantic Ocean. Past studies have shown that seabird eggs and marine mammal blubber obtained from the northern Atlantic Ocean contain lower amounts of HDBPs than samples obtained from ecologically similar species in the northern Pacific Ocean environment (*4*, *6*).

Concentrations of HDBPs in each composite varied with time in a random fashion. As opposed to anthropogenic organohalogens such as PCBs (*1*) (W. H. Newsome and J. Doucet, unpublished data), there were no significant trends of ΣHDBP concentrations with time in any of the composites. The random variation of composite HDBP concentrations over the decade is consistent with a nonindustrially produced chemical and likely reflects the concentration variability in the items used to create the composites.

The HDBP concentration variability is not due to preparation of the composites, because the processing protocols have not changed over the decade covered in this study. As shown in **Table 1**, the shopping protocols and subsequent composite constitution have somewhat changed to reflect changes in fish and seafood product availability and consumption. However, these changes do not appear to correlate with changes in HDBP concentrations. For example, the 2000−2002 marine fish samples are composed of the same species and proportions of fish, yet the HDBP concentrations in these three samples vary over ∼3 orders of magnitude (**Figure 2**).

It is possible that the variations in HDBP concentrations are due to the different sources of fish. It is plausible that marine and freshwater fish available in stores and markets reflect local stocks (e.g., Atlantic cod in Eastern Canada as opposed to Pacific cod in British Columbia) and thus reflect the geographical variations in HDBP concentrations observed in other biota (*4*, *6*). Unfortunately, this detailed information is not collected for the Canadian Total Diet Studies.

HDBP Congener Patterns. As with ΣHDBP concentrations, ecological differences among species also influenced the HDBP congener patterns observed in each composite. The three fish composites display patterns similar to the "pelagic" HDBP congener pattern observed for biota from the northern Pacific Ocean (*6*). The shrimp composite HDBP congener pattern is enriched with the higher brominated congeners DBP-Br_5Cl and DBP-Br_6. This is similar to the "benthic" pattern previously observed for sediment and benthic organisms (*5*).

HDBP Estimated Daily Intakes. The occurrence of HDBPs is primarily a marine phenomenon, so it is expected that human exposure to HDBPs would occur mainly via consumption of foods with a marine origin. Thus, the four fish and seafood Total Diet Study composites analyzed likely represent the main sources of HDBPs for the general Canadian population. The EDIs given in **Table 3** are an attempt to estimate dietary exposure to HDBPs. It is not apparent how accurate these values are, however, because the food intake data used to calculate the EDIs were generated in 1972 (the most recent Canadian food intake data available), and intake of fish and seafood products has likely changed over the past three decades. The EDIs generated by this study also do not take into account consumption of other seafood (such as mussels, scallops, and oysters) or food items containing fish meal or fish oil derived from marine organisms.

The HDBP EDIs listed in **Table 3** are lower than those for other organohalogens measured in Total Diet Study composites from the same time period. For example, EDIs of total PCBs are ∼100 times higher (*1*). This large difference occurs because PCBs are present in a wider variety of Total Diet Study food composites than HDBPs.

HDBP Contributions to TEQ. Because HDBPs have been shown to bind to the AhR and induce CYP1A in a similar manner in vitro as TCDD (*12*), HDBP EDIs were transformed into EDI_{TEQ}s to estimate the contribution of HDBPs to dietary exposure of dioxin-like compounds. It should be noted that even though HDBP EDI_{TEQ}s can be estimated, dietary exposure to HDBPs may not necessarily result in dioxin-like effects because the significance of CYP1A induction on toxicity is not clear. However, some work suggests CYP1A-inducing compounds may elicit effects concerning oxidative DNA damage (*21*). Also, evidence exists for a relationship between the ability to induce CYP1A and the ability to cause toxic effects in vivo (*22*).

In 1998 Total Diet Study samples, the PCDD/F and non-ortho PCB EDI_{TEQ} was ∼0.75 pg/kg/day (*23*)—about 7 times higher than the HDBP EDI_{TEQ}. However, the HDBP EDI_{TEQ} of 0.10 pg of TEQ/kg/day is 4 times larger than for PCDD/PCDF/non-ortho PCB EDI_{TEQ} when only the four fish and seafood composites are considered. This value is similar to the total non-coplanar PCB EDI_{TEQ} of 0.11 pg of TEQ/kg/day determined from meat, dairy, fish, and fast food composites collected from 1992 to 1996 (*1*). Both of the HDBP and PCB EDI_{TEQ}s are 2 orders of magnitude lower than the tolerable daily intake of 10 pg of TEQ/kg of body mass/day adopted by Canada in 1990 (www.ec.gc.ca/substances/ese/eng/psap/PSL1_dioxins.cfm).

The HDBP relative contributions to total TEQs in the fish and seafood composites were significant only to the canned fish and shrimp composites. In these two composites, HDBPs comprised approximately 98 and 19% of the total TEQ of

quantitated organohalogens. Overall, non-ortho PCBs were the class of compounds to consistently make the largest contribution to total TEQs. It is conceivable, though, that if PCDD/F and PCB concentrations decrease over time, the relative contribution and significance of HDBPs to total TEQs will increase because HDBP concentrations did not display any significant temporal trends.

Conclusions. Humans are exposed to HDBPs, a group of naturally produced organohalogens, via consumption of fish and seafood. The major contributing food item is canned fish, mainly tuna and salmon, because these are higher trophic level epipelagic species that inhabit the northern Pacific Ocean. This is an area where other biota have been found to contain higher amounts of HDBPs. When the average human diet is considered, HDBP EDIs are insignificant compared to other classes of organohalogen contaminants. However, exposure to HDBPs will be larger for populations that consume an above average amount of fish. HDBPs also make a large contribution to canned fish and shrimp total TEQs. The relative contribution of HDBPs is expected to increase with respect to PCDD/Fs and PCBs as environmental concentrations of these organochlorines decrease over time.

The risk of HDBP exposure to human health is unclear at this time because little is known about the biological activity of HDBPs. In addition, the metabolic capability of humans toward HDBPs needs to be examined, especially in light of other studies that suggest HDBPs may be metabolized (*6*, *14*). Studies are currently underway to determine human body burdens and abilities to metabolize HDBPs.

ACKNOWLEDGMENT

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