Polybrominated Dibenzo-*p*-dioxins, Dibenzofurans, and Diphenyl Ethers in Japanese Human Adipose Tissue

JAE-WON CHOI,*,† SUSUMU FUJIMAKI,† KIMIYOSHI KITAMURA,‡ SHUNJI HASHIMOTO,† HIROYASU ITO,† NORIYUKI SUZUKI,† SHIN-ICHI SAKAI,‡ AND MASATOSHI MORITA‡

National Institute for Environmental Studies, 16-2 Onogawa, Tsukuba-Shi, Ibaraki 305-8506, Japan, and Analytical Instrument Division, JEOL Ltd., 1-2 Musashino, Akishima, Tokyo 196-8558, Japan

Human adipose samples collected in Tokyo, Japan in 1970 and 2000 were analyzed for the presence of polybrominated dibenzo-*p*-dioxins (PBDDs), dibenzofurans (PBDFs), and diphenyl ethers (PBDEs), and the concentrations in the two groups were compared. As far as we know, the concentrations of the PBDD/Fs in adipose tissue from the general Japanese population are reported for the first time. Three PBDD/F congeners were found in the following adipose tissues: 2,3,7,8-TeBDD, 2,3,7,8-TeBDF, and 2,3,4,7,8-PeBDF. The median concentrations (ranges) of three PBDD/Fs in 1970 and 2000 were 5.1 (3.4−8.3) and 3.4 (1.9−5.3) pg/g lipid wt (l.w.), respectively. For PBDEs, seven PBDE congeners were determined in the following samples: 2,4,4′-tribromodiphenyl ether (BDE-28), 2,2′,4,4′-tetrabromodiphenyl ether (BDE-47), 2,2′,4,4′,5-pentabromodiphenyl ether (BDE-99), 2,2′,4,4′,6-pentabromodiphenyl ether (BDE-100), 2,2′,4,4′,5,5′-hexabromodiphenyl ether (BDE-153), 2,2′,4,4′,5′,6-hexabromodiphenyl ether (BDE-154), and 2,2′,3,4,4′,5′,6-heptabromodiphenyl ether (BDE-183). Median concentrations (ranges) of PBDEs showed a significant increase from 29.2 (6.8−78.4) pg/g l.w. in 1970 to 1288 (466−2,753) pg/g l.w. in 2000. BDE-47, the major congener of PBDEs, was 56.2% and 35.6% of the total in 1970 and 2000, respectively, whereas the BDE-153 was <1% and 29.7% of the total in 1970 and 2000, respectively. This may indicate that the source of PBDEs had changed during this period. Further analysis of archived human samples from 1970 to 2000 is needed to describe the details of the contamination trends of PBDD/Fs and PBDEs in the Japanese population. Furthermore, PBDD/F monitoring, particularly 2,3,7,8-TeBDD and 2,3,7,8-TeBDF, may give more toxicological information based on TeCDD toxic equivalents (TEQs).

Introduction

Brominated flame retardants (BFRs) comprised 25% of the worldwide production of flame retardants in 1992 (*1*). Polybrominated diphenyl ethers (PBDEs) and tetrabromobisphenol A (TBBPA) are the main types of BFRs. PBDEs are widely used in plastics, textiles, and paints and in electronic appliances including computers, televisions, and other electronic household equipment. The annual worldwide consumption of PBDEs was estimated to be 40 000 tons in 1992 (*2*). In Japan the domestic demand on BFRs increased 3.4-fold from 20 000 tons in 1986 to 67 250 tons in 2000 (*3, 4*). The domestic production of TBBPA, a major BFR in Japan, was 32 300 tons in 2000 and decabromodiphenyl ether (DeBDE) comprised less than 5% of domestic BFR production in 2000 (*5*).

PBDEs can be released into the environment during their production, use, and disposal and from dismantling plants during recycling of PBDE containing materials (*6*). Because of their high lipophilicity, commonly log K_{ow} > 6, and resistance to degradation in the environment, PBDEs are expected to bioaccumulate in the food chain (*7*). Toxicological studies of limited PBDEs indicate that they have weak dioxin-like toxicity through Ah receptor-mediated effects and both agonist and antagonist activities for binding to transthyretin in vitro (*8, 9*). Hydroxylated PBDEs can disrupt normal thyroid hormone functions (*10*). With in vivo tests, toxicological indicators from enzyme induction (cytochrome P-450) to behavioral aberrations including learning and memory functions were observed for some congeners (*11, 12*).

During recent years, much research has been focused on the levels of PBDEs, in both environmental and human samples (*13*). Particularly, since the report of a drastic increase in PBDE concentrations in human milk from 1972 to 1997 in Sweden (*14*), temporal trends in PBDE concentrations have been monitored in other countries. Results from Germany (*15*), Norway (*16*), and Canada (*17*) confirm the increases in the concentrations of these compounds in the human body, during 1972−1999.

Heating of PBDEs, TBBPA, and other BFR-containing materials may lead to the formation of polybrominated dibenzo-*p*-dioxins (PBDDs) and dibenzofurans (PBDFs) (*18, 19*). PBDD/F congeners have been identified during thermal degradation of BFRs including PBDEs and are found in flue gas, fly ash, and residues from municipal solid waste incinerators (MSWI) and in vehicle exhaust (*18, 20−22*). Toxicological studies show that 2,3,7,8-TeBDD and 2,3,7,8-TeBDF have a variety of toxic effects from waste syndrome and liver toxicity to death in experimental animals, and their toxic potencies are comparable to those of 2,3,7,8-TeCDD and 2,3,7,8-TeCDF (*23*). From the results of DR-CALUX and Micro-EROD based bioassays, some 2,3,7,8-substituted PBDD/F congeners (these compounds are still not included in the WHO-TEFs because they are not presently available) have been assigned TEFs based on their equivalent potencies relative to that of 2,3,7,8-TeCDD (TEF = 1.0) (*24*). Therefore, analysis of PBDD/Fs in human tissues would provide more information on the magnitude of their toxicities, estimated as 2,3,7,8-TeCDD toxic equivalents (TEQs). However, there is only limited information on the environmental concentrations of and human exposure to PBDD/F. TeBDD/Fs–HxBDD/Fs were below the detection limits in carp (*Cyprinus carpio*) collected from the Buffalo River in New York (*25*). PBDD/Fs were also not found in soil and sediments collected at a former chlor-alkali plant in Georgia in the United States (*26*). To our knowledge, few cases of human exposure to PBDD/F have been reported. Blood lipids from workers in a plant manufacturing polymers which contained octabro-

* Corresponding author phone: +81 298 50 2914; fax: +81 298 50 2902; e-mail: choi.jae.won@nies.go.jp.
† Analytical Instrument Division, JEOL Ltd.
‡ National Institute for Environmental Studies.

10.1021/es025878o CCC: $25.00
Published on Web 01/25/2003

modiphenyl ether (OBDE) or DeBDE were analyzed, and measurable quantities of 2,3,7,8-TeBDD and 2,3,7,8-TeBDF were found (*27*). The concentration in the blood of a chemist who synthesized TeCDD and TeBDD in the 1950s was reported to be 625 pg/g fresh weight in 1990−1991 (*28*). No PBDD/F congeners were found in 48 composite samples of the general United States population analyzed in 1990 (*29*). Salmon, osprey, and human milk sampled in the early 1990s were analyzed for PBDD/F, but no measurable amounts were found (*30*).

The present study was undertaken to determine and compare the concentrations of PBDD/F and PBDE congeners in adipose tissue collected from the general Japanese population in 1970 and 2000. We also investigated whether the concentrations of PBDD/Fs in human tissue were related to PBDE levels.

Material and Methods

Reference Standards and Chemicals for Cleanup. Seven $^{13}C_{12}$ and $^{12}C_{12}$-PBDE congeners [BDE-28 (2,4,4′-tribromodiphenyl ether), BDE-47 (2,2′4,4′-tetrabromodiphenyl ether), BDE-99 (2,2′,4,4′,5-pentabromodiphenyl ether), BDE-100 (2,2′,4,4′,6-pentabromodiphenyl ether), BDE-153 (2,2′,4,4′,5,5′-hexabromodiphenyl ether), BDE-154 (2,2′,4,4′,5′,6-hexabromodiphenyl ether), and BDE-183 (2,2′,3,4,4′,5′,6-heptabromodiphenyl ether)] in nonane solution were obtained from Wellington Laboratories, Ontario, Canada. Five $^{13}C_{12}$ and $^{12}C_{12}$-PBDD/F congeners [2,3,7,8-TeBDD, 1,2,3,7,8-PeBDD, 2,3,7,8-TeBDF, 1,2,3,7,8-PeBDF, and 2,3,4,7,8-PeBDF] in nonane solution were purchased from Cambridge Isotope Laboratories, Inc. (U.S.A.).

All chemicals used for cleanup were of analytical grade. Silica gel impregnated with 44% sulfuric acid (20 g) (Wako, Japan) was mixed with sodium sulfate (40 g) (Kanto, Japan) and packed into a glass column. Florisil (Kanto, Japan) was heated for 3 h at 150 °C and deactivated with 1% water, prior to column chromatography.

Sample Cleanup. Adipose tissues from persons living in the Tokyo area were collected from hospitals in 1970 (n = 10) and 2000 (n = 10). Women in their forties or fifties were selected. Samples were stored at −20 °C. Fat samples were homogenized with sodium sulfate and extracted for 6 h with dichloromethane in a Soxhlet apparatus. The extract was rotary evaporated, and the extractable lipids were weighed and redissolved in hexane (15−20 mL). Lipid contents of the samples ranged from 72% to 95%. $^{13}C_{12}$-labeled internal standards for PBDD/Fs and PBDEs were added as follows: 200 pg of $^{13}C_{12}$-labeled 2,3,7,8-TeBDD, 2,3,7,8-TeBDF, 1,2,3,7,8-PeBDD, and 2,3,4,7,8-PeBDF and 1 ng of $^{13}C_{12}$-labeled BDE-28, BDE-47, BDE-99, BDE-153, BDE-154, and BDE-183.

Extracted lipids (1−3 g) dissolved in hexane (15−20 mL) were loaded and cleaned up on a large volume sulfuric acid-impregnated silica gel column (column length: 200 mm, 50 mm I.D.). The column was packed with 44% H_2SO_4 and Na_2SO_4 (20 g:40 g).

This simple cleanup does not require the use of a sulfuric acid treatment in a funnel. With this method, almost all of the target compounds are eluted by 250 mL of hexane without clogging. The column was covered with aluminum foil during the experiment.

PBDEs and PBDD/Fs were separated in a column containing Florisil (5 g). The PBDEs were eluted with n-hexane (100 mL), and the PBDD/Fs were eluted subsequently with n-hexane/dichloromethane (40:60, v/v). Each fraction was evaporated, and the samples were further concentrated to 100 μL (PBDEs) and 50 μL (PBDD/Fs) under a gentle stream of N_2. For instrument calibration, $^{13}C_{12}$-2,2′,4,4′,6-PeBDE (BDE-100) and 1,2,3,7,8-PeBDF were added in the final step.

Chemical Analysis. Analyses of PBDEs and PBDD/Fs were performed with a high-resolution gas chromatograph (HRGC)−high-resolution mass spectrometer (HRMS) using an HP6890 gas chromatograph connected to a mass spectrometer (JMS-700K, JEOL, Japan) in selected ion monitoring (SIM) mode. The HRMS was operated in electron impact ionization mode at a resolution of R > 10 000−12 000 (10% valley). A fused silica column DB5-HT (15 m × 0.25 mm I.D., 0.1 μm film thickness) (J&W Scientific, U.S.A.) was used. The temperature program consisted of the following: the injector at 260 °C, the transfer line at 260 °C, an initial oven temperature of 140 °C held for 1.0 min, and heating to 200 °C at 20 °C/min and then to 280 °C at 5 °C/min. Helium was used as the carrier gas, and the flow rate was 1.0 mL/min. The injection volume was 2 μL of each sample and of the calibration standards. A laboratory blank for the human adipose samples was from the Soxhlet extraction step. The only interference found in the laboratory blank was BDE-47. The value from the blank was deducted. Calibration standards for PBDEs and PBDD/Fs at four different concentrations were run with the samples. PBDE and PBDD/F congeners were identified by ion ratios within the correct threshold ranges (±15%) and by comparing the retention times of corresponding standards. Table 1 shows an example of the ions monitored for the identification of PBDDs and PBDFs. Masses for PBDE congeners were also added into the channels since fragments of PBDEs are a potential interference in the identification of PBDFs. PBDEs including tri-BDE to hepta-BDE and PBDD/Fs were quantified using the masses of [M + 2] and [M + 4] for TriBDE, TeBDE, and TeBDD/F, [M + 4] and [M + 6] for PeBDE, HxBDE, and PeBDD/F, and [M + 6] and [M + 8] for HpBDE.

The limits of quantification (LOQ) on a lipid weight basis defined as signal-to-noise (S/N) > 10, were 0.8 pg/g for TeBDD, 0.5 pg/g for TeBDF, 1.3 pg/g for PeBDD, and 0.8 pg/g for PeBDF. The LOQ for each PBDE congener was 1 pg/g for TrBDE, 1.3 pg/g for TeBDE, 2.5 pg/g for PeBDE, and 6.3 pg/g for HxBDE and HpBDE. Mean recoveries of the $^{12}C_{12}$-PBDD/Fs were between 57% and 95% and between 51% and 96% for $^{13}C_{12}$-PBDEs. After injection, identification and quantification of target compounds were done by an isotope dilution method using the XMS data acquisition system and the DioK data processing system (JEOL, Japan). Statistical analysis and correlations were performed using SPSS version 10.0 for Windows.

Results

Three PBDD/Fs (2,3,7,8-TeBDD, 2,3,7,8-TeBDF, and 2,3,4,7,8-PeBDF) and seven PBDEs (BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, BDE-154, and BDE-183) were identified and quantified in the human adipose samples we analyzed. The median and range of concentrations in picograms per gram of extracted lipid are presented in Table 2.

2,3,7,8-TeBDF was detected in all the samples from 1970 and 2000. 2,3,7,8-TeBDD above the LOQ was found in only two cases in the 2000 samples, while it was found in most of the 1970 samples analyzed. Some of 2,3,7,8-TeBDD and 2,3,4,7,8-PeBDF in the samples from 1970 and 2000 were below the LOQ, but when it give rise to peaks above the limit of detection (LOD), defined as a signal-to-noise (S/N) greater than three, the peaks were quantified. 1,2,3,7,8-PeBDD was below the LOD in all the samples. Representative chromatograms of 2,3,7,8-TeBDD and 2,3,7,8-TeBDF from 1970 samples are shown in Figure 1. In this study, a short capillary column (15 m, DB5-HT) was used not only for high sensitivity but also for quick retention times of PBDD/Fs (unpublished data). Target congeners were separated clearly and at unknown peaks/interferences having different retention times and at small amounts in human fat tissue (see TeBDD in Figure 1).

The concentrations of PBDE in the samples from 2000 were much higher than the samples from 1970 (p < 0.001).

TABLE 1. Mass and Relative Ion Abundance for HRMS of PBDDs and PBDFs

channel	m/z	relative abundance	compound	channel	m/z	relative abundance	compound
			Group 1				
1	497.6923	67.8	TeBDD-1G	1	479.6996	17.3	TeBDF-1G
2	499.6903	100	TeBDD-1G	2	481.6975	67.8	TeBDF-1G
3	504.9697	-	PFK lock mass	3	483.6955	100	TeBDF-1G
4	504.9697		check lock	4	492.9697		PFK lock mass
5	509.7326	67.8	13C-TeBDD-1G	5	492.9697		check lock
6	511.7306	100	13C-TeBDD-1G	6	495.7357	100	13C-TeBDF-1G
				7	563.6220	100	PeBDE-1G
				8	565.6200	98.4	PeBDE-1G
				9	575.6620	100	13C-PeBDE-1G
				10	641.5322	76.4	HxBDE-1G
				11	643.5300	100	HxBDE-1G
				12	655.5700	100	13C-HxBDE-1G
			Group 2				
1	577.6008	100	PeBDD-2G	1	577.6099	10.4	PeBDF-2G
2	579.5988	98.5	PeBDD-2G	2	561.6058	100	PeBDF-2G
3	580.9633		PFK Lock Mass	3	563.6039	98.4	PeBDF-2G
4	580.9633		check lock	4	566.9665	-	PFK lock mass
5	589.5411	100	13C-PeBDD-2G	5	566.9665	-	check lock
6	591.6391	98.5	13C-PeBDD-2G	6	573.6462	100	13C-PeBDF-2G
				7	641.5320	76.4	HxBDE-2G
				8	643.5300	100	HxBDE-2G
				9	655.5703	100	13C-HxBDE-2G
				10	721.4405	100	HpBDE-2G
				11	723.4385	98.3	HpBDE-2G
				12	733.4808	100	13C-HpBDE-2G

TABLE 2. Median and Range of Concentrations of Four PBDD/F Congeners, Total PBDD/Fs, Seven PBDE congeners, and Total PBDEs in pg/g Lipid Weight from Japanese Human Adipose Tissue in 1970 and 2000

	1970 ($n = 10$)		2000 ($n = 10$)		
compound	medium	range	median	range	p^b
2,3,7,8-TeBDD	1.7	<0.8–4.2	0.61[a]	0.1–2.0[a]	<0.005
1,2,3,7,8-PeBDD	<1.3	<1.3	<1.3	<1.3	
2,3,7,8-TeBDF	3.3	1.6–4.3	2.8	1.7–4.2	>0.2
2,3,4,7,8-PeBDF	0.31[a]	0.28–0.60[a]	0.99	<0.8–1.9	0.07
PBDD/Fs	5.1	3.4–8.3	3.4	1.9–5.3	0.02
BDE-28 (2,4,4')	2.3	<1.0–7.6	76	47–487	<0.001
BDE-47 (2,2',4,4')	17.0	4.4–60.4	459	109–979	<0.001
BDE-100 (2,2',4,4',6	2.1	<2.5–6.1	250	41–527	<0.001
BDE-99 (2,2',4,4',5)	3.9	<2.5–13.9	116	42–362	<0.001
BDE-154 (2,2',4,4',5,6)	<6.3	<6.3	60	14–104	<0.001
BDE-153 (2,2',4,4',5,5')	<6.3	<6.3	382	122–631	<0.001
BDE-183 (2,2',3,4,4',5',6)	<6.3	<6.3	47	20–177	<0.001
PBDEs	29.2	6.8–78.4	1288	465–2753	<0.001

[a] Below the limit of quantification (LOQ), above the limit of detection (LOD). [b] Level of significance derived from Mann-Whitney U-test.

BDE-47 (2,2',4,4'-TeBDE) was the most abundant congener of the sum PBDEs in both the 1970 and 2000 samples. Mean concentrations of other PBDE congeners (BDE-28, 99, 100, 153, 154, and 183) in the 1970 samples were below 5pg/g l.w.; however, increased contributions of PeBDEs–HpBDE compared to that of TeBDE (BDE-47) were observed in the 2000 samples.

Discussion

To the best of our knowledge, this is the first report of the presence of the PBDD/F congener in adipose tissue samples taken from the general Japanese population. Human exposure to PBDD/F has only been reported for workers or chemists dealing directly with brominated flame retardants (BFRs) or brominated dioxins (*27, 28*). In the present study, 2,3,7,8-TeBDF was detected above the LOQ in all the samples from 1970 and 2000, and the concentration range was the same in both sets of samples. The concentrations of TeBDD and total PBDD/Fs in the 1970 samples were significantly higher than in the 2000 samples, even though the sample sizes were small.

To discuss the trends in concentrations of brominated dioxins and the corresponding chlorinated compounds, the ratios between the concentration of 2,3,7,8-TeBDD/F and the concentration of 2,3,7,8-TeCDD/F in the samples from 1970 and 2000 were compared using the 2,3,7,8-TeCDD/F data for the same samples published previously (*31*) and illustrated in Figure 2. The ratio in the samples from 2000 ranged from 2.0 to 9.2, while that for the 1970 samples varied from 0.6 to 1.5. The differences might be due to the fact that the mean concentrations of TeCDD and TeCDF decreased significantly during the 30 years (*31*). This may also means that relative toxic potencies of TeCDD and TeCDF were decreased compare to those of TeBDD and TeBDF. However, a conclusive remark on this discussion is still not available. More data including environmental temporal trends of PBDD/Fs are needed.

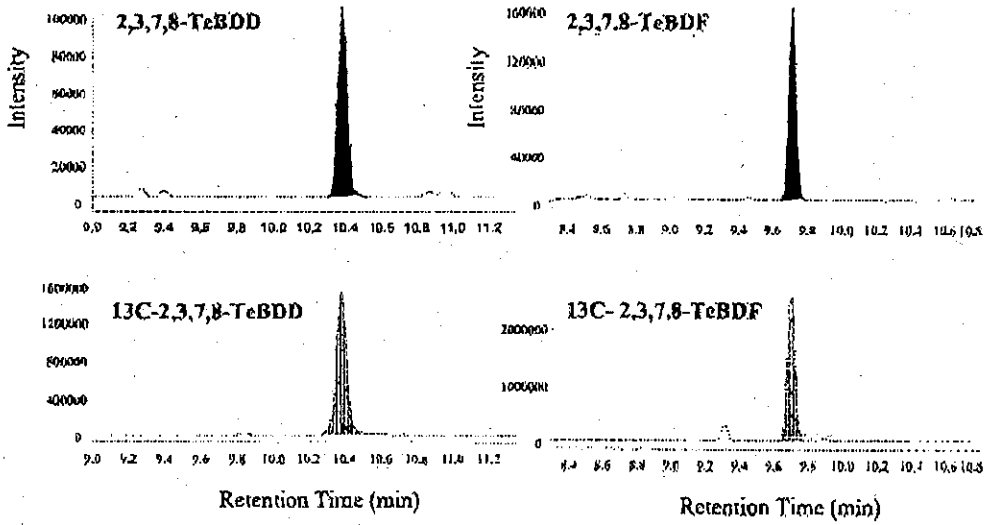

FIGURE 1. Typical SIM chromatograms of 2,3,7,8-TeBDD and 2,3,7,8-TeBDF in Japanese human adipose tissue.

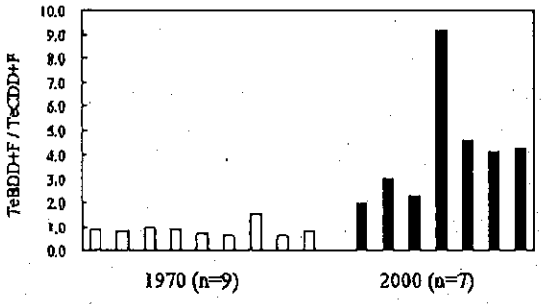

FIGURE 2. Ratios of total TeBDD/F to total TeCDD/F in Japanese human adipose tissue between 1970 and 2000.

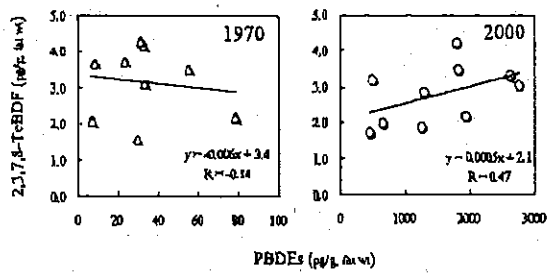

FIGURE 3. Correlations between 2,3,7,8-TeBDF and total PBDEs between the two groups.

The correlations between PBDD/F and PBDE levels in the two groups were compared, and an example is illustrated in Figure 3. Correlations between total PBDEs and 2,3,7,8-TeBDF in the samples from 1970 ($p > 0.5$) and those from 2000 ($p > 0.1$) seemed to show different trends even though both correlations were not statistically significant. The other correlations between each congeners and the sum of PBDD/Fs and PBDEs were also not significant. PBDD/F congeners are formed in the process of manufacturing, pyrolysis, or incineration of BFRs, including PBDEs, TBBPA, and BFR-containing materials (*18, 19, 21*), but we still do not have an explanation for occurrence of PBDD/Fs in humans. Therefore, it seems that increased domestic use of BFRs in Japan during the last 30 years is not directly related to the temporal trends of PBDD/F in human tissue. This may suggest that there are different environmental fates of 2,3,7,8-PBDD/Fs and 2,3,7,8-PCDD/Fs. For example, 1,2,3,7,8-PeBDD was below the detection limits with all samples analyzed, while the mean concentration of 1,2,3,7,8-PeCDD from the same samples was 9.7 pg/g-fat in 1970 and 4.4 pg/g-fat in 2000 (*31*). Similarly, PBDD/Fs in carp (*Cyprinus carpio*) collected from the Buffalo River in New York were below the detection limits of 2–8 pg/g for TeBDD/Fs–HxBDD/Fs, while PCDDs and PCDFs were 27–146 and 22–99 pg/g fresh wt (*25*). PBDD/Fs were also not found in samples of human tissue and human milk, salmon, and osprey surveyed in the United States and Sweden (*29, 30*).

The median PBDE concentrations in 1970 and 2000 were 29.2 and 1288 pg/g l.w., respectively. This may indicate that human exposure to PBDE in Japan increased during the last 30 years. Total PBDEs in the samples collected in 2000 ranged from 466 to 2753 pg/g l.w., which is similar to the concentrations of six PBDE congeners in Japanese human milk collected in 2000 (*32*), which ranged from 668 to 2840 pg/g l.w. The concentration range in the samples from 2000 was also comparable to that in human milk from Finland collected during 1994–1998 (*33*). However, the concentration was lower than in human blood and human milk from Germany and the United States collected during 1992–1999 (*15, 34*).

Of the seven PBDE congeners, BDE-47 (2,2′,4,4′-TeBDE) was the dominant component accounting for > 56% of the total PBDEs in the 1970 samples, whereas the elevated concentrations of BDE-100 (2,2′,4,4′,6-PeBDE, 19.4%) and BDE-153 (2,2′,4,4′,5,5′-HxBDE, 29.7%) were comparable to that of BDE-47 (35.6%) in the samples from 2000 (Figure 4). Furthermore, BDE-183 (2,2′,3,4,4′,5′,6-HpBDE) was found at a mean concentration of 76 pg/g l.w. only in the samples from 2000. This implies a change in the domestic demands particularly on the highly brominated diphenyl ethers during 1970–2000. For example, the contribution of DeBDE to the total domestic PBDE products changed from 67% in 1986 to 100% in 2000 (*3, 4*).

One of the major issues concerning human exposure to BFRs is to verify the ongoing temporal increasing of PBDE concentrations in human tissue. Concentrations in human milk from Sweden increased from 0.07 ng/g l.w. in 1972 to 4.0 ng/g l.w. in 1997 compared to a decrease in organochlorine compounds in the same period (*14*). Gradual increases in PBDE concentrations from 2864 pg/g l.w. to 4871 pg/g l.w. in German blood samples were observed during the period

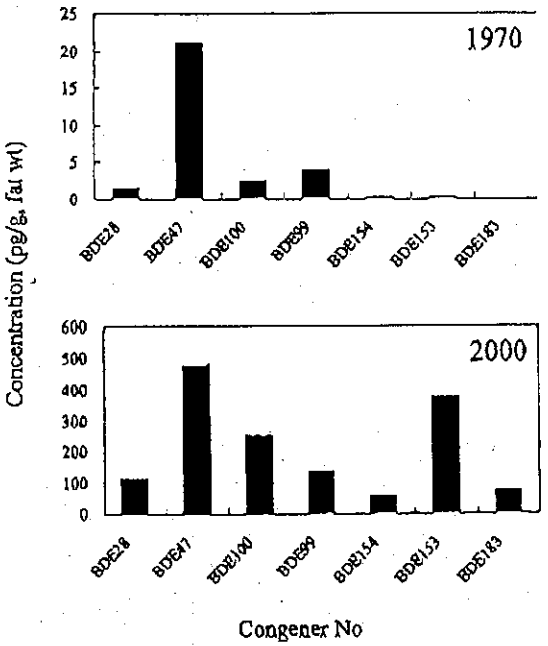

FIGURE 4. Congener profiles of PBDEs in Japanese human adipose tissue in the two groups.

of 1985 to 1999 (*16*). A survey of Canadian human milk in 1992 demonstrated that PBDE concentrations were 2 orders of magnitude higher than those of samples collected in 1981–1982 (*17*). Results with Norwegian archived serum samples collected from 1977 to 1999 also indicated that the six PBDEs increased gradually from 0.44 ng/g l.w. to 3.3 ng/g l.w. (*16*).

The concentrations in lipids of the coplanar PCBs (sum of non-*ortho* PCBs and mono-*ortho* PCBs) in Japanese from the same period during 1970–2000 showed a decrease of 68% from 92.9 ng/g fat in 1970 to 29.8 ng/g fat in 2000. The levels of PCDD/Fs in the samples also decreased 96.5% during 1970–2000 (*31*). However, PBDE concentrations in the same samples measured in the present study showed a significant 44-fold increase (despite the small sample size). The results presented here on the temporal trend of PBDE concentrations between 1970 and 2000 are comparable to other studies of human exposure mentioned above. The preliminary results in present study suggest the need for further analysis of archived human adipose samples to provide more details about the time-dependent increases in PBDE concentrations in the Japanese population. In addition, selective PBDD/F congeners were found for the first time in the general Japanese population, mainly 2,3,7,8-TeBDD and 2,3,7,8-TeBDF. These congeners (particularly 2,3,7,8-TeBDD) cause typical 2,3,7,8-TeCDD-like effects, including wasting syndrome, thymus atrophy, and liver toxicity in laboratory mammals (*23*). Therefore, monitoring these compounds may give more toxicological information based on toxic equivalents (TEQs).

Literature Cited

(1) Selected brominated flame retardants. Risk reduction Monograph 3: Organisation for Economic Cooperation and Development (OECD), Environment Directorate: Paris, France, 1994.

(2) Environmental Health Criteria 162. Brominated Diphenyl Ethers; International Program on Chemical Safety, World Health Organization: Geneva, Switzerland, 1994.

(3) Kagaku Kogyo Nenkan. Flame Retardants; Kagaku Kogyo Nippo: Tokyo, Japan, June 2001; pp 367–369.

(4) Tatsukawa, R.; Watanabe, I. *Pollut. Countermeasure* 1990, *26*, 658–668.

(5) Nikkei Ecology. Special Issue on Dioxins; Nikkei Business Publications: Tokyo, Japan, July 2001; pp 40–41.

(6) Sjodin, A.; Carlsson, H.; Thuresson, K.; Sjodin, S.; Bergman, A.; Ostman, C. *Environ. Sci. Technol.* 2001, *35*, 448–454.

(7) Boolj, K.; Zegers, B. N.; Boon, J. P. *Organohalogen Compd.* 2000, *47*, 89–92.

(8) Murk, A. J.; Leonards, P. E. G.; van Hattum, B.; Luit, R.; vander Weiden, M. E. J.; Smit, M. *Environ. Toxicol. Pharmacol.* 1998, *6*, 91–102.

(9) Meerts, I. A. T. M.; Luijks, E. A. C.; Marsh, G.; Jakobsson, E.; Bergman, Å.; Brouwer, A. *Organohalogen Compd.* 1998a, *37*, 147–150.

(10) Meerts, I. A. T. M.; Marsh, G.; van Leeuwen-Bol, I.; Luijks, E. A. C.; Jakobsson, E.; Bergman, Å.; Brouwer, A. *Organohalogen Compd.* 1998b, *37*, 309–312.

(11) von Meyerinck, L.; Hufnagel, B.; Schmoldt, A.; Benthe, H. F. *Toxicology* 1990, *61*, 259–274.

(12) Eriksson, P.; Viberg, H.; Jakobsson, E.; Orn, U.; Fredriksson, A. *Organohalogen Compd.* 1999, *40*, 333–336.

(13) De Wit, C. A. *Chemosphere* 2002, *46*, 583–624.

(14) Noren, K.; Meironyte, D. *Chemosphere* 2000, *40*, 1111–1123.

(15) Schroter-Kermani, C.; Helm, D.; Herrmann, T.; Papke, O. *Organohalogen Compd.* 2000, *47*, 49–52.

(16) Thomsen, C.; Lundanes, E.; Becher, G. *Environ. Sci. Technol.* 2002, *36*, 1414–1418.

(17) Ryan, J. J.; Patry, B. *Organohalogen Compd.* 2000, *47*, 57–60.

(18) Sakai, S.; Watanabe, J.; Honda, Y.; Takatsuki, H.; Aoki, I.; Futamatsu, M.; Shiozaki, K. *Chemosphere* 2001, *42*, 519–531.

(19) Thoma, H.; Rist, S.; Hauschulz, G.; Hutzinger, O. *Chemosphere* 1986, *15*, 2111–2113.

(20) Luijk, R.; Wever, H.; Olie, K.; Govers, H. A. J.; Boon, J. J. *Chemosphere* 1991, *8–10*, 1173–1183.

(21) Buser, H. R. *Environ. Sci. Technol.* 1986, *20*, 404–408.

(22) Haglund, P.; Egeback, K. E.; Jansson, B. *Chemosphere* 1988, *11*, 2129–2140.

(23) Environmental Health Criteria 205. Polybrominated Dibenzo-*p*-dioxins and Dibenzofurans: International Program on Chemical Safety, World Health Organization: Geneva, Switzerland, 1998.

(24) Behnisch, P. A.; Hosoe, K.; Brouwer, A.; Sakai, S. *Organohalogen Compd.* 2001, *52*, 49–52.

(25) Loganathan, B. G.; Kannan, K.; Watanabe, I.; Kawano, M.; Irvine, K.; Kumar, S.; Sikka, H. C. *Environ. Sci. Technol.* 1995, *29*, 1832–1838.

(26) Kannan, K.; Watanabe, I.; Giesy, J. P. *Environ. Toxicol. Chem.* 1998, *67*, 135–146.

(27) Zober, M. A.; Ott, M. G.; Papke, O.; Senft, K., Germann, C. *Brit. J. Ind. Med.* 1992, *49*, 532–544.

(28) Schecter, A.; Ryan, J. J. *J. Occup. Med.* 1992, *34*, 707–707.

(29) Cramer, P. H.; Ayling, R. E.; Thornburg, K. R.; Stanley, J. S. *Chemosphere* 1990, *7–9*, 821–827.

(30) Wiberg, K.; Rappe, C.; Haglund, P. *Chemosphere* 1992, *10*, 1431–1439.

(31) Choi, J. W.; Miyabara, Y.; Hashimoto, S.; Morita, M. *Chemosphere* 2002, *47*, 591–597.

(32) Ohta, S.; Ishizuka, D.; Nishimura, H.; Nakao, T.; Aozasa, O.; Shimidzu, Y.; Ochiai, F.; Kida, T.; Nishi, M.; Miyata, H. *Chemosphere* 2002, *46*, 689–696.

(33) Strandman, T.; Koistinen, J.; Vartiainen, T. *Organohalogen Compd.* 2000, *47*, 61–64.

(34) She, J.; Winkler, J.; Visita, P.; McKinney, M.; Petreas, M. *Organohalogen Compd.* 2000, *47*, 53–56.

Received for review June 14, 2002. Revised manuscript received November 30, 2002. Accepted December 5, 2002.

ES0258780