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Screening of polybrominated dibenzo-*p* dioxins and furans (PBDD/Fs) in blood from the Nordic population

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Abstract

In a previous study, also performed by MTM and commissioned by the Swedish EPA, the presence of polybrominated dibenzo-*p* dioxins and furans (PBDD/Fs) were detected in human adipose tissue from the Swedish population for the first time. However, no PBDD/Fs were detected in blood samples taken from the same individuals as the adipose tissue. In this current study the presence of PBDD/Fs in the Nordic population was investigated further. Blood samples from three different groups were analysed for tetra- to octa substituted PBDD/Fs. In the first sample set blood samples from seventeen Norwegians with reportedly high concentrations of PBDEs were analysed. In the second sample set five individuals, possibly suffering from occupational exposure, were analysed together with blood samples from six individuals representing the general Swedish population. In the last sample set, sample volumes were increased by up to three times to facilitate a positive identification of PBDD/Fs. Ten additional adipose tissue samples were also included in the initial research assignment. However, delayed sampling of specimens has put these samples on hold.

PBDD/Fs could not be detected above the limit of quantification in the different blood and serum samples. Traces that corresponded to 2,3,7,8-TeBDF, 1,2,3,7,8-PeBDF and 2,3,4,7,8-PeBDF were seen during one analytical run in several of the Norwegian samples but the detection limit could not be improved to verify the presence of PBDD/Fs in these samples. Traces of 2,3,7,8-TeBDF were also seen in three of the Swedish samples, both in serum from individuals with and without occupational exposure. Since the sample volumes were significantly increased for the latter sample sets these results indicate that levels of PBDD/Fs cannot be monitored in human blood until detection limits have been significantly improved or the levels in this matrix have increased.

1. Introduction

In a previous study we could for the first time detect polybrominated dibenzo-*p* furans in all ten adipose tissue samples analysed, all originating from individuals representing the Swedish general population and with no known occupational exposure [1]. In the same study, blood samples from the same individuals were analysed but the levels were too low to positively identify any PBDD/Fs. In this study, blood samples from different groups tentatively representing different types of exposure were analysed. Attempts to increase the sample volumes were done to facilitate a positive identification of PBDD/Fs. Seventeen samples from Norwegians with reportedly high levels of PBDEs resulting from a high consumption of fish from Lake Mjösa [2] were analysed to explore if high levels of PBDEs may result in detectable levels of PBDD/Fs in human blood. Serum from individuals working at an electronic dismantling facility in Örebro, Sweden, were analysed and compared with serum from six individuals without any known occupational exposure and considered to represent the general Swedish population.

Toxicologically PBDD/Fs are considered to exhibit similar toxicity as PCDD/Fs, as shown for cell lines of both human and mammalian species [3-4]. However, steric hindrance originating from the larger size of the bromine atom could possibly alter the level of toxicity for some of the congeners when comparing PBDD/Fs and PCDD/Fs [4-5]. The presence of PBDD/Fs have been identified in a large variety of matrices that could result in human exposure including; ambient air in large cities such as Kyoto [6], Osaka [7-8], Shanghai [9] and different locations in Taiwan [10], at electronic waste dismantling areas in China [11], flue gases [12-13] and sediments [8, 14-15]. PBDD/Fs are also found in diet samples [16-17], shellfish [18-19] and fish [19]. However, only a limited number of reports have been published on PBDD/Fs in human samples. Initially PBDD/Fs were only found in blood from occupationally exposed individuals [20-21] but more recently they have been detected in adipose tissue from Japan [22], and in mother's milk from several countries [23].

The origin and spreading of PBDD/Fs are most certainly due to the large scale use of brominated flame retardants (BFRs). During incineration of bromine containing waste PBDD/Fs as well as PBCDD/Fs and PCDD/Fs are formed in different distributions [12]. In areas without industries intensively producing or consuming BFRs the PBDD/F levels correlate with PCDD/Fs which might imply that they originate from the same sources, such as incineration, traffic emissions and metallurgic industry [9-10]. PBDD/Fs exhibit a structural similarity with the chlorinated dibenzo-*p* dioxins and furans (PCDD/Fs) but because of the larger size of the bromine atom as well as difference in electro negativity between the chlorine and bromine atom the physicochemical properties are somewhat different between the brominated and chlorinated analogues. PBDD/Fs have higher molecular weights, higher melting points, lower water solubilities and lower vapour pressure. The PBDD/Fs are believed to bio accumulate as the chlorinated homologues but appear to be less persistent in the environment and more sensitive towards UV degradation as well as thermal degradation [3]. These differences also have implications for the analysis of PBDD/Fs, which are more sensitive towards thermal degradation

during extraction, clean up, injection and separation [24]. Normally the clean up procedures applied are very similar to clean up procedures used for PCDD/Fs although performed under "cut off UV" conditions. During analysis, columns with thin phases (10 µm) are used preferable in combination with softer injection techniques as on-column injection or programmable temperature vaporizing (PTV) injection.

2. Materials and Methods

2.1 Samples

The Norwegian blood samples were collected by the Norwegian Institute of Public Health during the period October 2004 to May 2005. Venous blood was frozen in tubes of polypropylene (Sarstedt, Nümbrecht, Germany). In all, 66 samples were collected and subsamples of these were analysed for polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane by the Norwegian Institute of Public Health. The results from the Norwegian study showed that the median dietary intake of sum 7 PBDEs for the study participants, eating fish from Lake Mjösa, were the highest reported and that some of the participants had very high serum levels of PBDEs [2]. For this study 17 out of 66 samples were analysed. Eleven of the samples with highest PBDE levels documented and five of the samples with lowest PBDE levels were chosen for this study.

Blood samples from Swedish individuals working with electronic waste dismantling and individuals without any known occupational exposure were collected by a visiting nurse. The blood was drawn into heparin tubes and was left to cool and coagulate before centrifugation at 3500 rpm at 10 min. The serum was collected in polypropylene containers (Nalgene, USA). All samples were stored dark and at -20ºC until analysis. Blood samples from ID 26 and ID 27 were pooled to obtain a larger sample in order to investigate if a larger sample volume would make a positive identification of PBDD/Fs in human blood possible. These samples were chosen since they were from two male individuals in the same age. The pooled sample is referred to ID 26 in the following text and tables. Age, gender, occupation and number of children nursed by female participations are presented in Table 1.

Table 1. Participants in the inventory of PBDD/F levels in blood from Swedes with and without possible occupational exposure

Sample I.D.	Age (years)	Gender	Occupation	Children[a]
ID 21	62	Female	Office worker	Two, 36 and 33 years old
ID 22	51	Female	Office worker	Two, 17 and 15 years old
ID 23	53	Male	Office worker	
ID 24	36	Male	Office worker	
ID 25	31	Male	Physician	
ID 26[b]	54	Male	Chemist	

ID 27[b]	52	Male	Biologist
ID 28	56	Male	E-waste dismantler
ID 29	48	Male	E-waste dismantler
ID 30	50	Male	E-waste dismantler
ID 31	35	Male	E-waste dismantler
ID 32	40	Male	E-waste dismantler

[a] Only given for women who have been nursing children
[b]These samples were pooled to investigate if a larger sample size would facilitate positive identification of PBDD/Fs in human blood.

2.2. Chemicals

The blood samples were spiked with two different mixtures of labelled compounds. The first set analysed, the Norwegian blood samples, were spiked with ^{13}C-labelled 2,3,7,8-TeBDF, 1,2,3,7,8-PeBDF, 2,3,4,7,8-PeBDF, 1,2,3,4,7,8-HxBDF and 1,2,3,7,8-PeBDD all from Cambridge Isotope Laboratories Inc., Andover, MA, USA. As recovery standard, ^{13}C-labelled 2,3,7,8-TeBDD was used.
For the two other samples sets, the groups with and without occupational exposure, a recently commercialized internal standard mixture (EDF-5408; CIL, Andover, USA) was added containing PBDD/Fs of each substitution level, including; ^{13}C-labeled 2,3,7,8-TeBDD, 1,2,3,7,8-PeBDD, 1,2,3,4,7,8-HxBDD, 1,2,3,6,7,8-HxBDD, 1,2,3,4,6,7,8-HpBDD, OBDD, 2,3,7,8-TeBDF, 2,3,4,7,8-PeBDF, 1,2,3,4,7,8-HxBDF, 1,2,3,4,6,7,8-HpBDF and OBDF was used. As recovery standard the EDF-5409 mixture from CIL, Andover, USA including 1,2,3,7,8,9-HxBDD and 1,2,3,7,8-PeBDF was used.
The same congeners were also present in the native standard mixture.

Organic solvents used were of pesticide grade and purchased from Riedel de Haën (methanol, *n*-hexane, dichloromethane, and toluene). Ethanol was purchased from Kemetyl.

2.3 Sample preparation

2.3.1 Whole blood and serum
Whole blood and serum samples were ground with anhydrous sodium sulphate. Open column chromatography was applied for approximately 20 gram of whole blood (Norwegian samples) or 25 gram of serum (Swedish samples). First, the homogenate to be extracted were spiked ^{13}C-labelled internal standard and then the lipid fraction was extracted by a mixture of *n*-hexane: dichloromethane (1:1) using open column chromatography. Secondly, sample clean-up was done on three open columns (multilayer silica, AlOx and active carbon). The multilayer silica columns contained KOH silica, neutral activated silica, 40% H_2SO_4 silica gel, 20% H_2SO_4 silica gel, neutral activated silica gel and Na_2SO_4 and was eluted with *n*-hexane. This column was followed by an AlOx column eluted with *n*-hexane/ dichloromethane. Additional clean up and fractionation was done on an active carbon column, containing Carbopack C dispersed on Celite 545, which was eluted with 10 ml of *n*-hexane for non-planar compounds and then 80 ml of toluene to elute the planar fraction containing PBDD/Fs. Addition of a ^{13}C-labelled recovery standard was done prior to instrumental analysis. Throughout the

sample preparation the samples were kept shielded from UV light to avoid photo degradation.

2.4 Instrumental analysis

2.4.1 HRGC/HRMS

HRGC/HRMS analysis was performed on a Micromass Autospec Ultima operating at 10 000 resolution using EI ionization at 35 eV. All measurements were performed in the selective ion recording mode (SIR), monitoring the two most abundant ions of the molecular bromine cluster. Quantification was performed using the internal standard method. Two different chromatographic columns were used for quantification and verification, a 25 m (0.25 mm i.d, 10 µm) BPX 5 column (SGE; Ringwood, Australia) and a 15 m (0.25 mm i.d, 10 µm) DB-5MS columns (J&W Scientific; Folsom, CA, USA). On-column injection in track-oven mode was applied to inject 1 µl of the final extract on the GC column. GC temperature programs were used to optimize the response (and minimize the degradation in both the injector and on the column) depending on column length and GC performance. Detection levels were calculated at a S/N ratio of 3, corrected for recovery of the internal standard. Unfortunately, it was impossible to achieve stable conditions for analysing octa brominated dioxins and furans. Even though short and thin phased columns were used in combination with on-column injection the degradation of octa substituted congeners were too extensive.

2.5 Quality assurance

Method performance was controlled by extracting ^{13}C-labelled internal standards allowing recovery values between 50-150 %. With every batch of samples extracted an extraction blank was also prepared and analyzed. The MTM laboratory participates on a regular basis in international intercalibration studies. In studies organized by AMAP, QUASIMEME and the Norwegian Institute of Public Health the MTM laboratory shows qualified results.

3. Results and Discussion

In all, 28 whole blood or serum samples were analysed for PBDD/Fs in this study. Up to date, PBDD/Fs have only been detected in human blood and serum from individuals exposed to extreme concentrations of PBDD/Fs [20, 25]. The recovery varied between 50 -120% for all samples analysed.

3.1 The Norwegian samples

PBDD/Fs were not detected in the Norwegian samples, see Table 2. The available sample volumes were only approximately 20 ml of whole blood resulting in very small lipid weights and consequently very low PBDD/F concentrations. However, in several of the

samples traces corresponding to 2,3,7,8-TeBDF, 1,2,3,7,8- and 2,3,4,7,8-PeBDF were seen during the analysis on the 25 m thin phased (0.10 µm) column. Unfortunately, it was not possible to establish as sensitive conditions during a run on the 15 m column to further improve the detection limits and the identity and concentration of these peaks could not be verified and established. The detected traces corresponded both by retention time match with the labelled compounds and by isotope ratio but the levels were slightly below the detection limit. Furthermore, small peaks possibly corresponding to unidentified hexa and hepta substituted furans were seen in some of the samples with traces corresponding to tetra and penta substituted PBDFs. They had corresponding isotope ratio to brominated furans but since these samples did not contain labelled hexa- and hepta-substituted congeners the possible identity could not be established. The concentrations for these peaks were also close to, but below the determined detection limits.

The observed traces of TeBDF and PeBDF could point towards an increased presence of PBDD/Fs in blood samples with elevated concentrations of PBDEs. However, larger sample volumes and/or improved detection limits are needed to further investigate this and to fully rule out that the possible presence of PBDD/Fs in the blood samples are not resulting from thermal degradation from PBDEs during analysis.

Table 2. Levels (pg/g lipid) in blood from Norwegians with reportedly high levels of PBDEs.

	ID 1	ID 2	ID 3	ID 4	ID 5	ID 6	ID 7	ID 8	ID 9	ID 10	ID 11	ID 12	ID 13	ID 14	ID 15	ID 16	ID 17
Furans																	
2,3,7,8-TeBDF	<4.2	<2.7	<4.1	<3.60	<1.6	<3.5	<2.5	<5.0	<2.3	<4.1	<3.6	<3.9	<3.5	<1.2	<4.5	<4.1	<4.2
1,2,3,7,8-PeBDF	<9.1	<5.9	<8.8	<7.8	<3.5	<7.6	<5.4	<11	<5.0	<8.8	<7.8	<8.5	<7.6	<2.5	<9.7	<8.8	<9.1
2,3,4,7,8-PeBDF	<6.5	<4.2	<6.3	<5.6	<2.5	<5.4	<3.9	<7.8	<3.6	<6.3	<5.6	<6.1	<5.4	<1.8	<7.0	<6.3	<6.5
1,2,3,4,7,8-HxBDF	<60	<39	<58	<52	<24	<50	<36	<72	<34	<58	<52	<57	<50	<17	<65	<58	<60
1,2,3,4,6,7,8-HpBDF	<68	<55	<67	<63	<45	<62	<53	<76	<51	<67	<63	<66	<62	<40	<71	<67	<68
OBDF	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Dioxins																	
2,3,7,8-TeBDD	<4.2	<2.7	<4.1	<3.6	<1.6	<3.5	<2.5	<5.0	<2.3	<4.1	<3.6	<3.9	<3.5	<1.2	<4.5	<4.1	<4.2
1,2,3,7,8-PeBDD	<7.3	<4.7	<7.0	<6.2	<2.8	<6.1	<4.4	<8.7	<4.0	<7.0	<6.2	<6.8	<6.1	<2.0	<7.8	<7.0	<7.3
1,2,3,4,7,8-HxBDD	<11	<7.2	<11	<9.5	<4.3	<9.3	<6.7	<13	<6.2	<11	<9.5	<10	<9.3	<3.1	<12	<11	<11
1,2,3,6,7,8-HxBDD	<18	<11	<17	<15	<6.9	<15	<11	<21	<9.8	<17	<15	<17	<15	<4.8	<19	<17	<18
1,2,3,7,8,9-HxBDD	<12	<7.9	<12	<10	<4.7	<10	<7.3	<15	<6.7	<12	<10	<11	<10	<3.3	<13	<12	<12
1,2,3,4,6,7,8-HpBDD	<34	<26	<33	<31	<19.4	<30	<24	<39	<23	<33	<31	<33	<30	<16.6	<36	<33	<34
OBDD	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

n.a.= not analysed since it was not possible to achieve stable conditions for analysing OBDD and OBDF.

3.2 The Swedish samples

Larger sample volumes were applied in the Swedish samples. Serum volumes of approximately 25-35 ml corresponding to 50-70 ml of whole blood were extracted. Despite the significantly increased sample volumes no PBDD/Fs were detected in the samples from the electronic waste dismantlers or the samples from the individuals corresponding to the general Swedish population, see Table 3. In three samples, from both groups, traces corresponding to 2,3,7,8-TeBDF were seen but at a concentration below the established detection limit. As mentioned above, the detection limit could not be improved when using a shorter column and it was possible to verify any presence of PBDD/Fs.

In the pooled sample, were over 50 ml of serum were extracted, no traces of PBDD/Fs were seen. These results indicate that levels in blood and/or serum from humans without extreme exposure to PBDD/Fs are not possible to monitor during prevailing detection limits.

Table 3. Levels of PBDD/Fs in serum (pg/g lipids) from individuals with and without occupational exposure. Gender (F or M) and age are given in the table heading.

	ID 21	**ID 22**	**ID 23**	**ID 24**	**ID 25**	**ID 26**	**ID 28**	**ID 29**	**ID 30**	**ID 31**	**ID 32**
Furans	**F 62**	**F 51**	**M 53**	**M 36**	**M 31**	**Pooled sample**	**M 56**	**M 48**	**M 50**	**M 35**	**M 40**
2,3,7,8-TeBDF	<0.81	<0.91	<1.2	<1.3	<1.3	<0.50	<3.0	<1.1	<1.5	<0.84	<1.3
1,2,3,7,8-PeBDF	<4.0	<4.5	<4.0	<4.0	<3.9	<1.9	<5.5	<3.2	<3.5	<3.9	<3.8
2,3,4,7,8-PeBDF	<2.0	<2.1	<2.0	<2.0	<2.0	<0.98	<2.8	<1.6	<1.8	<2.0	<1.9
1,2,3,4,7,8-HxBDF	<19	<21	<19	<19	<18	<9.1	<26	<15	<16	<19	<18
1,2,3,4,6,7,8-HpBDF	<12	<13	<12	<12	<12	<5.8	<16	<9.6	<10	<12	<11
OBDF	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Dioxins											
2,3,7,8-TeBDD	<0.69	<0.77	<0.69	<0.69	<0.67	<0.33	<0.94	<0.56	<0.60	<0.68	<0.65
1,2,3,7,8-PeBDD	<2.5	<2.8	<2.5	<2.5	<2.4	<1.2	<3.4	<2.0	<2.2	<2.5	<2.4
1,2,3,4,7,8-HxBDD	<3.5	<3.9	<3.5	<3.5	<3.4	<1.7	<4.8	<2.8	<3.0	<3.4	<3.3
1,2,3,6,7,8-HxBDD	<5.5	<6.1	<5.5	<5.5	<5.4	<2.7	<7.5	<4.4	<4.8	<5.4	<5.2
1,2,3,7,8,9-HxBDD	<3.8	<4.2	<3.8	<3.8	<3.7	<1.8	<5.2	<3.1	<3.3	<3.7	<3.6
1,2,3,4,6,7,8-HpBDD	<7.5	<8.4	<7.5	<7.5	<7.3	<3.6	<10	<6.1	<6.5	<7.4	<7.1
OBDD	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.

n.a.= not analysed since it was not possible to achieve stable conditions for analysing OBDD and OBDF.

4. Conclusions

PBDD/Fs could not be detected in any of the blood or serum samples. The high PBDE concentrations in the Norwegian sample did not result in detectable levels of PBDD/Fs at the actual level of quantification in this study. Moreover, the significantly increased sample volumes for the samples sampled in Sweden did not result in detectable levels of PBDD/Fs. Noteworthy is that traces possibly matching 2,3,7,8-TeBDF, 1,2,3,7,8-PeBDF and 2,3,4,7,8-PeBDF were seen in some of the samples.
To further investigate the Norwegian samples larger sample volumes are needed and/ or improved detection limits. The results from the Swedish samples, where the sample volumes were significantly enlarged, indicate that the levels are still too low in human blood and serum and that detection limits are still too high to continue with further analysis of this sample matrix.

5. References

1. Ericson Jogsten, I., J. Hagberg, G. Lindstrom, and B. van Bavel, Analysis of POPs in human samples reveal a contribution of brominated dioxin of up to 15% of the total dioxin TEQ. Chemosphere, 2010. 78: p. 113–120.
2. Thomsen, C., H. Knutson, V. Liane, M. Froshaug, H. Kvalem, M. Haugen, H. Meltzer, J. Alexander, and G. Becher, Consumption of fish from a contaminated lake strongly affects the concentrations of polybrominated diphenyl ethers and hexabromocyclododecane in serum. Molecular Nutrition & Food Research, 2008. 52: p. 228 – 237.
3. Birnbaum, L.S., D.F. Staskal, and J.J. Diliberto, Health effects of polybrominated dibenzo-p-dioxins (PBDDs) and dibenzofurans (PBDFs). Environment International, 2003. 29(6): p. 855-860.
4. Olsman, H., M. Engwall, U. Kammann, M. Klempt, J. Otte, B. van Bavel, and H. Hollert, Relative differences in aryl hydrocarbon receptor-mediated response for 18 polybrominated and mixed halogenated dibenzo-p-dioxins and -furans in cell lines from four different species. Environmental Toxicology and Chemistry, 2007. 26(11): p. 2448-2454.
5. Samara, F., B.K. Gullett, R.O. Harrison, A. Chu, and G.C. Clark, Determination of relative assay response factors for toxic chlorinated and brominated dioxins/furans using an enzyme immunoassay (EIA) and a chemically-activated luciferase gene expression cell bioassay (CALUX). Environment International, 2009. 35(3): p. 588-593.
6. Hayakawa, K., H. Takatsuki, I. Watanabe, and S. Sakai, Polybrominated diphenyl ethers (PBDEs), polybrominated dibenzo-*p*-dioxins/dibenzofurans (PBDD/Fs) and monobromo-polychlorinated dibenzo-*p*-dioxins/dibenzofurans (MoBPXDD/Fs) in the atmosphere and bulk deposition in Kyoto, Japan. Chemosphere, 2004. 57(5): p. 343-356.

7. Ohta, S., T. Nakao, H. Nishimura, T. Okumura, O. Aozasa, and H. Miyata, Contamination levels of PBDEs, TBBPA, PCDDs/DFs and PXDDs/DFs in the environment of Japan. Organohalogen Compounds, 2002. 57: p. 57-60.
8. Watanabe, I., M. Kawano, and R. Tatsukawa, Polybrominated and mixed polybromo/chlorinated dibenzo-*p*-dioxins and -dibenzofurans in the Japanese environment. Organohalogen Compounds, 1995. 24: p. 337-340.
9. Li, H.R., H.L. Feng, G.Y. Sheng, S.L. Lu, J.M. Fu, P.A. Peng, and R. Man, The PCDD/F and PBDD/F pollution in the ambient atmosphere of Shanghai, China. Chemosphere, 2008. 70: p. 576-583.
10. Wang, L.C., C.H. Tsai, G.P. Chang-Chien, and C.H. Hung, Characterization of polybrominated dibenzo-*p*-dioxins and dibenzofurans in different atmospheric environments. Environmental Science & Technology, 2008. 42(1): p. 75-80.
11. Li, H.W., L. Yu, G. Sheng, J. Fu, and P. Peng, Severe PCDD/F and PBDD/F pollution in air around an electronic waste dismantling area in China. Environmental Science &. Technology, 2007. 41: p. 5641-5646.
12. Wang, L.C. and G.P. Chang-Chien, Characterizing the emissions of polybrominated dibenzo-p-dioxins and dibenzofurans from municipal and industrial waste incinerators. Environmental Science & Technology, 2007. 41(4): p. 1159-1165.
13. Schuler, D. and J. Jager, Formation of chlorinated and brominated dioxins and other organohalogen compounds at the pilot incineration plant VERONA. Chemosphere, 2004. 54(1): p. 49-59.
14. Choi, J.W., J. Onodera, K. Kitamura, S. Hashimoto, H. Ito, N. Suzuki, S. Sakai, and M. Morita, Modified clean-up for PBDD, PBDF and PBDE with an active carbon column - its application to sediments. Chemosphere, 2003. 53(6): p. 637-643.
15. Hagberg, J., E. Grahn, B. van Bavel, and G. Lindström, Occurence and levels of PCDD/Fs and PBDD/Fs in two swedish lake sediments. Organohalogen Compounds, 2005.
16. Nomura, T., T. Tanagi, E. Fukuzawa, Y. Kono, K. Komatsu, and M. Morita, Brominated dioxins and PBDEs in diet samples collected frpm FY2002 and FY2005 in Japan. Organohalogen Compounds, 2007. 69: p. 2773-2776.
17. Fernandes, A.R., C. Tlustos, F. Smith, M. Carr, R. Petch, and M. Rose, Polybrominated diphenylethers (PBDEs) and brominated dioxins (PBDD/Fs) in Irish food of animal origin. Food Additives & Contaminants Part B - Surveillance, 2009. 2(1): p. 86-94.
18. Fernandes, A., P. Dicks, D. Mortimer, M. Gem, F. Smith, M.D. Ield, S. White, and M. Rose, Brominated and chlorinated dioxins, PCBs and brominated flame retardants in Scottish shellfish: Methodology, occurrence and human dietary exposure. Molecular Nutrition & Food Research, 2008. 52(2): p. 238-249.
19. Ashizuka, Y., R. Nakagawa, T. Hori, D. Yasutake, K. Tobiishi, and K. Sasaki, Determination of brominated flame retardants and brominated dioxins in fish collected from three regions of Japan. Molecular Nutrition & Food Research, 2008. 52(2): p. 273-283.

20. Zober, M.A., M.G. Ott, O. Papke, K. Senft, and C. Germann, Morbidity Study Of Extruder Personnel With Potential Exposure To Brominated Dioxins And Furans. 1. Results Of Blood Monitoring And Immunological Tests. British Journal Of Industrial Medicine, 1992. 49(8): p. 532-544.
21. Schecter, A. and J.J. Ryan, Persistent brominated and chlorinated dioxin blood-levels in a chemist - 35 years after dioxin exposure. Journal of Occupational and Environmental Medicine, 1992. 34(7): p. 702-707.
22. Choi, J.W., S. Fujimaki, K. Kitamura, S. Hashimoto, H. Ito, N. Suzuki, S. Sakai, and M. Morita, Polybrominated dibenzo-p-dioxins, dibenzofurans, and diphenyl ethers in Japanese human adipose tissue. Environmental Science & Technology, 2003. 37(5): p. 817-821.
23. Kotz, A., Bestimmung von bromierten und gemischt bromiert-chlorierten unweltkontaminanten in biologischen matrizes mit HRGC-HRMS. 2006, University of Basel. Dissertation.
24. Hagberg, J., Analysis of brominated dioxins and furans by high resolution gas chromatography/high resolution mass spectrometry. Journal Of Chromatography A, 2009. 1216(3): p. 376-384.
25. Schecter, A. and J.J. Ryan, Brominated And Chlorinated Dioxin Blood-Levels In A Chemist 34 Years After Exposure To 2,3,7,8-Tetrachlorodibenzodioxin And 2,3,7,8-Tetrabromodibenzodioxin. Chemosphere, 1991. 23(11-12): p. 1921-1924.

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