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Screening of polybrominated dibenzo-*p* dioxins and furans (PBDD/Fs) in adipose tissue from the Swedish population

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Abstract

In a screening study during 2007-2008, also performed by MTM and commissioned by the Swedish EPA, the presence of polybrominated dibenzo-*p* furans (PBDFs) were detected in human adipose tissue from the Swedish population for the first time. In this study ten additional adipose samples were analysed for polybrominated dibenzo-*p* dioxins and furans, PBDD/Fs. In all samples, 2,3,7,8-TeBDF was present in levels ranging from 0.23 to 0.54 pg g^{-1} lipid and pentabrominated furans were present in nine out of ten samples. The levels of 2,3,7,8-TeBDF, 1,2,3,7,8- and 2,3,4,7,8-PeBDF were similar to those reported in the previous screening study [1].

By lowering the detection limits by using larger injection volumes by employing the PTV injection technique, 2,3,7,8-TeBDD, 1,2,3,4,7,8-/1,2,3,6,7,8-HxBDD, 1,2,3,4,6,7,8-HpBDD, 1,2,3,4,7,8-HxBDF and 1,2,3,4,6,7,8-HpBDF were detected for the first time in human adipose tissue samples from Sweden. 2,3,7,8-TeBDD was detected in five out of ten samples in the range of 0.03-0.05 pg g^{-1} lipid. 2,3,7,8-TeBDD has been detected in samples with human origin earlier but not in samples from Sweden and levels of 1,2,3,4,7,8-HxBDF has previously been detected in human milk samples from several countries, including Sweden. However, the detection of 1,2,3,4,7,8-/1,2,3,6,7,8-HxBDD, 1,2,3,4,6,7,8-HpBDD and 1,2,3,4,6,7,8-HpBDF in human tissue is to our knowledge reported for the first time.

To summarize, results from nineteen samples (the present and previous study) demonstrate the presence of brominated furans in the general Swedish population. Additionally, the individuals having the highest PBDD/F concentrations had also the highest levels of PCDD/Fs (pg TEQ g^{-1}). This might support the general assumption that brominated and chlorinated dioxins have the same sources and exposure routes.

1. Introduction

Polybrominated *p*-dibenzo dioxins and furans (PBDD/Fs) are considered to exhibit similar toxicity as PCDD/Fs, as shown for cell lines of both human and mammalian species [2-3]. 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 [3-4]. During the last decade the number of scientific papers concerning the analysis of PBDD/Fs in different matrices has increased. 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 [5], Osaka [6-7], Shanghai [8] and different locations in Taiwan [9], at electronic waste dismantling areas in China [10], house dust from e-waste dismantling and urban areas[11-13], flue gases [14-15] and sediments [7, 16-18]. PBDD/Fs are also found in diet samples [19-21], shellfish [22-23] and fish [23]. However, only a limited number of publications report human levels of PBDD/Fs. Initially PBDD/Fs were only found in blood from occupationally exposed individuals [24-25] but more recently they have been detected in adipose tissue from Japan [26] and Sweden [1], and in mother's milk from several countries [18, 27].

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 [14]. 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 [8-9]. 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 [2].

In a previous study we could for the first time detect polybrominated dibenzo-*p* furans in all nine adipose tissue samples analysed, all originating from individuals representing the Swedish general population and with no known occupational exposure [1]. In this study ten additional adipose samples, also representing the general Swedish population, have been analysed for PBDD/Fs.

2. Materials and methods

2.1 Samples

Human adipose tissue samples were collected during the autumn of 2009 at the Örebro University hospital from ten persons undergoing surgery. Sample sizes ranged from 3 to 9 grams of adipose tissue. None of the participants had suffered any weight loss before giving samples. Age and gender of the study participants are given in Table 1. Samples were stored in amber glass bottles at - 20°C prior to extraction and analysis.

Table 1. Age and gender of the study participants.

Sample I.D.	Age (years)	Gender
ID 1	43	Male (M)
ID 2	50	Male (M)
ID 3	41	Female (F)
ID 4	44	Female (F)
ID 5	55	Female (F)
ID 6	23	Female (F)
ID 7	33	Female (F)
ID 8	55	Male (M)
ID 9	47	Female (F)
ID 10	47	Female (F)

2.2. Chemicals

Samples were spiked with ^{13}C-labelled internal standard mixture EDF-5408 (CIL, Andover, USA), including ^{13}C-labelled 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 before extraction. 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.

For chlorinated dioxin analysis ^{13}C-labelled internal PCDD/F standard including ^{13}C-2,3,7,8-TCDD, 2,3,7,8-TCDF, 1,2,3,7,8-PeCDD, 2,3,4,7,8-PeCDF, 1,2,3,4,7,8-HxCDD, 1,2,3,6,7,8-HxCDD, 1,2,3,4,7,8-HxCDF, 1,2,3,6,7,8-HxCDF, 2,3,4,6,7,8-HxCDF, 1,2,3,4,6,7,8-HpCDD, 1,2,3,4,6,7,8-HpCDF, OCDD and OCDF was added to the sample prior to analysis. As recovery standards ^{13}C-labelled 1,3,7,8-TCDD and 1,2,3,7,8,9-HxCDD were used. The quantification standard included 2,3,7,8-TCDD, 2,3,7,8-TCDF, 1,2,3,7,8-PeCDD, 1,2,3,7,8-PeCDF, 2,3,4,7,8-PeCDF, 1,2,3,4,7,8-HxCDD, 1,2,3,6,7,8-HxCDD, 1,2,3,6,7,9-HxCDD, 1,2,3,4,7,8-HxCDF, 1,2,3,6,7,8-HxCDF, 1,2,3,4,7,8,9-HxCDF, 2,3,4,6,7,8-HxCDF, 1,2,3,4,6,7,8-HpCDD, 1,2,3,4,6,7,8-HpCDF, 1,2,3,4,7,8,9-HpCDF, OCDD and OCDF. All PCDD/F standards were purchased from Wellington Laboratories Inc., Guelph, Canada.

Organic solvents used were of pesticide grade and purchased from Fluka (methanol, *n*-hexane, dichloromethane, and toluene). Ethanol was purchased from Sharlau.

2.3 Sample preparation

2.3.1 Adipose tissue

Adipose tissue samples were ground with anhydrous sodium sulphate (in the ratio 1 to 5). Open column chromatography was applied for approximately 5 gram of adipose tissue. First, the homogenate to be extracted was spiked ^{13}C-labelled internal standards 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 extract the planar fraction containing PBDD/Fs. Addition of ^{13}C-labelled recovery standards was done prior to instrumental analysis. Throughout the sample preparation the samples were kept shielded from UV light to avoid photo degradation. Toxic equivalents (TEQs) were calculated using World Health Organization toxic equivalency factors (TEFs) for PCDD/Fs [28].

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 or chlorine cluster. Quantification was performed using the internal standard method. Two different chromatographic columns were used for quantification and verification of PBDD/Fs, 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-1 columns (J&W Scientific; Folsom, CA, USA). For PBDD/Fs analysis, programmable temperature vaporizing (PTV) injection was applied to inject 8 µl of the final extract on the GC column. PCDD/Fs were analysed by injecting 2 µl of extract using splitless injection on a 30 m BPX 5 (0.25 mm id, 25 µm) column (SGE; Ringwood, Australia). GC temperature programs were used to optimize the response (and minimize the degradation in 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. The criteria for positive peak identification were isotope ratio within ±15% of the theoretical value and retention time match with that of the corresponding labelled compound.

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 show qualified results for chlorinated dioxins and furans.

3. Results and discussion

In all, 10 adipose tissue samples were analysed for PBDD/Fs and PCDD/Fs. The recovery varied between 51 -118 % for all congeners and samples analysed except for OBDD and OBDF. The recoveries for OBDF were approximately 30% and somewhat lower for OBDD. The low recoveries are due to thermal degradation of the octa-substituted congeners during both injection and the chromatographic separation.

3.1. Levels of PBDD/Fs

The result from the PBDD/F analysis is presented in Table 2. For the first time PBDD/Fs of higher substitution levels, i.e. hexa and hepta, are found in human adipose tissue. This is due to improved detection limits by injecting larger sample volumes, i.e. 8 µl, using the PTV injection technique.

In all samples, the brominated furans are overrepresented reflecting the general PBDD/Fs distribution in environmental and food samples [21, 29]. 2,3,7,8-TeBDF was found in the range of 0.23-0.54 pg g^{-1} lipid in all samples analysed. This is similar to what we reported in the earlier screening study performed by our group [1], but the levels reported here are somewhat lower possibly due to a more precise calibration of the lower span of the calibration curve. Both or one of the 1,2,3,7,8- and 2,3,4,7,8-PeBDF congeners were found in nine out of ten samples. The levels of 2,3,4,7,8-PeBDF were higher than the levels of 1,2,3,7,8-PeBDF in all samples where they were present simultaneously. This distribution between the pentabrominated furans is also seen in various other sample types reflecting possible routes of human exposure, i.e. in avian, bovine, ovine, porcine fat and liver samples as well as in eggs and cow´s milk from Ireland [21] and ambient air [8-9]. Levels of 2,3,7,8-TeBDF and 2,3,4,7,8-PeBDF have been reported in human milk from Sweden and Japan among other countries [18, 27]. In the Japanese study human milk from both primiparae and multiparae were analysed for PBDD/Fs and low levels of 1,2,3,7,8-PeBDF were only detected in the primiparae samples while the levels for 1,2,3,7,8-PeBDF were below the detection limit in the Swedish sample [27]. 1,2,3,4,7,8-HxBDF and 1,2,3,4,6,7,8-HpBDF were found in some of the samples and to our knowledge reported for the first time in human adipose tissue. However, 1,2,3,4,7,8-HxBDF have previously been detected in human milk from Sweden, Finland, and Italy [27].

Incineration is considered to be one of the major sources of PBDD/Fs and 1,2,3,4,7,8-HxBDF and 1,2,3,4,6,7,8-HpBDF are next after OBDF the most abundant PBDD/F congeners present in stack flue gases [30]. Unfortunately, data on hexa, hepta and octa brominated congeners are often missing due to difficulties in analysing these substances and because labelled standards for these compounds became available just a few years ago. However, the presence of 1,2,3,4,7,8-HxBDF, 1,2,3,4,6,7,8-HpDBF and OBDF is also overrepresented in samples (house dust, soil, dust, residues) from contaminated e-waste recycling sites in China and Vietnam [31-32] and when plastics from TV casings are subjected to sunlight [33]. The use of products containing brominated flame retardants could tentatively be a human exposure route for brominated furans.

Table 2. Levels (pg g^{-1} lipid) of PBDD/Fs in ten Swedish human adipose tissue samples.

Furans	**ID 1 M 43**	**ID 2 M 50**	**ID 3 F 41**	**ID 4 F 44**	**ID 5 F 55**	**ID 6 F 23**	**ID 7 F 33**	**ID 8 M 55**	**ID 9 F 47**	**ID 10 F 47**
2,3,7,8-TeBDF	**0.31**	**0.33**	**0.23**	**0.40**	**0.40**	**0.45**	**0.54**	**0.35**	**0.46**	**0.29**
1,2,3,7,8-PeBDF	**0.08**	<0.01	**0.08**	**0.16**	<0.007	**0.09**	**0.24**	<0.02	**0.01**	**0.03**
2,3,4,7,8-PeBDF	**0.14**	<0.01	**0.18**	**0.35**	**0.51**	**0.24**	<0.009	**0.64**	**0.20**	**0.15**
1,2,3,4,7,8-HxBDF	<0.08	<0.11	<0.10	<0.07	**0.33**	<0.06	<0.05	<0.07	<0.12	<0.07
1,2,3,4,6,7,8-HpBDF	<0.05	<0.07	<0.07	<0.05	**1.6**	**0.25**	<0.03	**0.92**	<0.08	<0.04
OBDF	<62	<87	<78	<55	<42	<48	<37	<52	<92	<51
Dioxins										
2,3,7,8-TeBDD	<0.005	<0.006	**0.03**	<0.004	**0.03**	**0.03**	<0.003	<0.004	**0.05**	**0.04**
1,2,3,7,8-PeBDD	<0.06	<0.09	<0.08	<0.05	<0.04	<0.05	<0.04	<0.05	<0.09	<0.05
1,2,3,4,7,8-/1,2,3,6,7,8-HxBDD	<0.06	<0.08	<0.08	<0.05	**0.19**	<0.05	<0.04	**0.26**	**0.04**	<0.05
1,2,3,7,8,9-HxBDD	<0.10	<0.14	<0.13	<0.09	<0.07	<0.08	<0.06	<0.9	<0.15	<0.08
1,2,3,4,6,7,8-HpBDD	<0.25	<0.34	<0.30	<0.21	**0.89**	<0.19	<0.14	<0.20	<0.36	<0.20
OBDD	<11	<15	<14	<9.7	<7.3	<8.5	<6.5	<9.2	<16	<8.9
Sum PBDD/Fs pg g^{-1}	**0.53**	**0.33**	**0.52**	**0.91**	**3.9**	**1.1**	**0.78**	**2.2**	**0.76**	**0.51**

F: female, M: male, XX: age at time of sampling.

In five out of ten samples 2,3,7,8-TeBDD was detected in concentrations ranging from 0.03-0.05 pg g^{-1} lipid, see chromatogram in Figure 1. Human levels of 2,3,7,8-TeBDD have previously been reported in adipose tissue samples from Japan and in human milk from Ireland, Italy, Russia, Slovakia and Spain [26-27]. The reported levels of both 2,3,7,8-TeBDD and 2,3,7,8-TeBDF from Japan were about ten times higher than the levels reported in this study tentatively indicating a higher degree of exposure in Japan. Surprisingly, 1,2,3,4,7,8-/1,2,3,6,7,8-HxBDD and 1,2,3,4,6,7,8-HpBDD were detected in a few samples of adipose tissue. There are to our knowledge no publications on HxBDDs and HpBDDs in humans. However, the occurrence of 1,2,3,4,7,8-, 1,3,4,6,7,8-HxBDD, 1,2,3,4,6,7,8-HpBDD and OBDD in fly and bottom ash and in stack flue gases are more prominent than the lower brominated congeners [30], found in these samples, indicating that they ought to exist in the environment and possibly accumulate in the food chain.

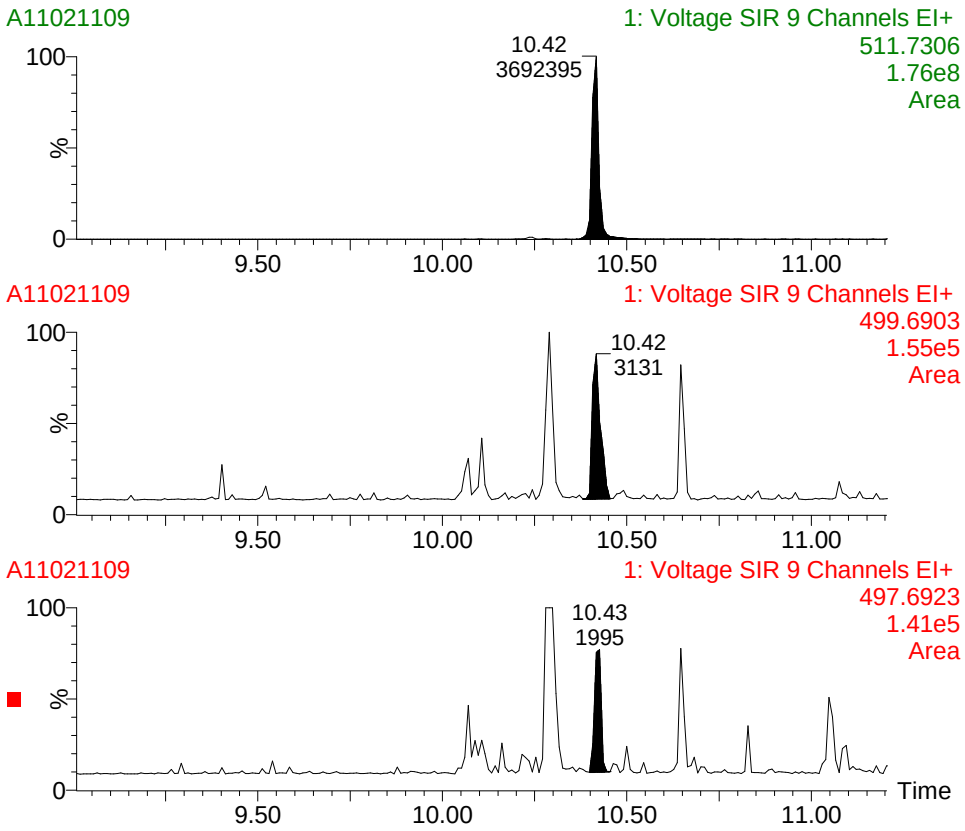

Figure 1. Chromatogram of 2,3,7,8-TeBDD in human adipose tissue. The upper trace belongs to ^{13}C-labelled 2,3,7,8-TeBDD, whereas the two lower traces belong to native 2,3,7,8-TeBDD present in the sample. The isotope ratio for the native isotopes (i.e. 63.7 %) was within ±15% of the theoretical value (67.8 %). The peak shape of the native 2,3,7,8-TeBDD was somewhat distorted due to the low amount present in the sample.

3.2. Levels of PCDD/Fs

The levels of PCDD/Fs were analysed as reference for the ten adipose tissue samples included in this screening and are presented in Table 3. The PCDD/F levels are similar to those reported earlier for adipose tissue samples collected in Sweden [1], Spain [34] and Japan [35].

Table 3. Levels (pgTEQ g^{-1} lipid; WHO 1998) of PCDD/Fs in ten Swedish human adipose tissue samples.

	ID 1	**ID 2**	**ID 3**	**ID 4**	**ID 5**	**ID 6**	**ID 7**	**ID 8**	**ID 9**	**ID 10**
Furans	**M 43**	**M 50**	**F 41**	**F 44**	**F 55**	**F 23**	**F 33**	**M 55**	**F 47**	**F 47**
2,3,7,8-TeCDF	0.03	0.02	0.03	0.03	0.03	0.07	0.02	0.11	0.05	0.06
1,2,3,7,8-PeCDF	0.004	0.005	0.007	0.003	<0.001	0.03	0.008	0.03	0.04	0.01
2,3,4,7,8-PeCDF	2.1	3.4	1.3	3.4	4.7	2.8	1.7	6.0	2.4	2.8
1,2,3,4,7,8-HxCDF	0.10	0.22	0.10	0.19	0.17	0.31	0.12	0.28	0.34	0.17
1,2,3,6,7,8-HxCDF	0.13	0.22	0.08	0.13	0.16	0.22	0.15	0.32	0.24	0.14
2,3,4,6,7,8-HxCDF	0.04	0.12	0.05	0.04	0.01	0.09	0.09	0.11	0.21	0.10
1,2,3,7,8,9-HxCDF	0.07	0.13	0.01	0.04	<0.002	0.01	<0.002	0.02	0.12	0.05
1,2,3,4,6,7,8-HpCDF	0.01	0.02	0.02	0.01	0.01	0.03	0.02	0.05	0.05	0.02
1,2,3,4,7,8,9-HpCDF	<0.0001	<0.0001	0.002	<0.0001	<0.0001	0.001	0.001	0.003	0.003	0.002
OCDF	<0.0001	0.0002	0.0003	0.00007	0.0001	0.0001	<0.0001	0.00007	<0.0001	<0.0001
Dioxins										
2,3,7,8-TeCDD	0.36	0.96	0.30	0.87	1.07	0.49	0.36	1.19	0.46	0.71
1,2,3,7,8-PeCDD	1.4	2.1	0.86	2.4	3.4	1.2	1.3	5.3	1.6	1.8
1,2,3,4,7,8-HxCDD	0.05	0.17	0.06	0.19	0.07	0.06	0.07	0.07	0.11	0.08
1,2,3,6,7,8-HxCDD	0.58	0.70	0.24	1.0	1.4	0.23	0.61	1.8	0.47	0.65
1,2,3,7,8,9-HxCDD	0.10	0.10	0.04	0.19	0.28	0.07	0.21	0.17	0.05	0.08
1,2,3,4,6,7,8-HpCDD	0.05	0.06	0.06	0.11	0.04	0.05	0.22	0.05	0.06	0.19
OCDD	0.008	0.008	0.007	0.02	0.01	0.004	0.01	0.006	0.008	0.01
Sum pgTEQ g^{-1}	**5.0**	**8.3**	**3.2**	**8.7**	**11.3**	**5.6**	**4.8**	**15.6**	**6.2**	**7.0**
Sum UB pg g^{-1}	**106**	**115**	**81**	**217**	**148**	**77**	**163**	**129**	**118**	**162**
Sum LB pg g^{-1}	**106**	**115**	**81**	**217**	**148**	**77**	**163**	**129**	**118**	**162**

UB: upper bound concentration, including <-values, LB: lower bound concentration, excluding <-values, F: female, M: male, XX: age at time of sampling.

4. Conclusions

In all samples, 2,3,7,8-TeBDF was present in levels ranging from 0.23 to 0.54 pg g^{-1} lipid and pentabrominated furans were present in nine out of ten samples. The levels of 2,3,7,8-TeBDF, 1,2,3,7,8- and 2,3,4,7,8-PeBDF were similar to those reported in a previous screening study performed by our research group [1]. In all, results from nineteen samples demonstrate the presence of brominated furans in the general Swedish population.

More interestingly, by lowering the detection limits by using larger injection volumes by employing PTV injection, 2,3,7,8-TeBDD, 1,2,3,4,7,8-/1,2,3,6,7,8-HxBDD, 1,2,3,4,6,7,8-HpBDD, 1,2,3,4,7,8-HxBDF and 1,2,3,4,6,7,8-HpBDF were detected for the first time in human adipose tissue from Sweden. 2,3,7,8-TeBDD was detected in five out of ten samples in the range of 0.03-0.05 pg g^{-1} lipid. 2,3,7,8-TeBDD has been detected in samples with human origin earlier but not in samples from Sweden. Levels of 1,2,3,4,7,8-HxBDF has previously been detected in human milk samples from several countries, including Sweden. The detection of 1,2,3,4,7,8-/1,2,3,6,7,8-HxBDD, 1,2,3,4,6,7,8-HpBDD and 1,2,3,4,6,7,8-HpBDF in human adipose tissue is to our knowledge reported for the first time.

The individuals having the highest PBDD/F concentrations had also the highest levels of pg TEQ g^{-1} of PCDD/Fs, i.e. individuals 5 and 8. This might support the general assumption that brominated and chlorinated dioxins have the same sources and exposure routes. Still, the analysis of PBDD/Fs suffers from difficulties in analysing the higher brominated dioxins and furans, which can be seen by the higher LODs for these compounds.

5. References

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