CONCENTRATION AND DISTRIBUTION OF DIOXINS AND RELATED COMPOUNDS IN VARIOUS HUMAN ORGANS

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Introduction

Polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and non-*ortho* coplanar polychlorinated biphenyls (Non-Co-PCBs) and mono-*ortho* coplanar polychlorinated biphenyls (Mono-Co-PCBs) accumulate in the human body due to their highly lipophilic properties. In recent years, there has been some concern about the potential health effects of dioxins and related chemicals for the general population of humans.

Although there exists an enormous amount of data on this subject, most of it is from breast milk and blood, due to ease of collection; information concerning concentrations and distribution in various human organs hardly exists. Therefore, new data concerning various human tissues is required to evaluate the pathophysiological significance of dioxins and related compounds in humans.

The aim of this study was to investigate the concentration levels and distribution of dioxins and related compounds in various human organ tissues.

We previously reported on the concentration levels in the human liver and adipose tissues from 28 donors[1].

In this paper, we determined the concentrations of dioxin-like isomers in 8 organs, including blood, lungs, liver, bile, spleen, pancreas, kidney and mesentery fat from 20 donors.

Materials and Methods

The human organ samples were collected from twenty patients who had died at School of Medicine, Keio University in 1999-2001. The families of the donors gave their informed consent. The collected organs were blood, lungs, liver, bile, spleen, pancreas, kidney and mesentery fat. The samples were stored at -20 degrees for later analysis. Donor ages ranged from 27 to 90 years; the average age was 65 years.

Each sample was extracted by an accelerated solvent extractor (ASE-200, Dionex, Sunnyvale, CA), weighed to 5 g accuracy, and mixed with 4 g Isolute (International Sorbent Technology Ltd., Hengoed, Mid Glamorgen, UK). After the mixed sample was loaded into the extraction cell, ^{13}C-labeled-PCDDs, ^{13}C-labeled-PCDFs, and ^{13}C-labeled-PCBs, as internal standards, were added. Acetone and n-hexane (1:4, v/v) were used as extraction solvents. The lipid obtained was dissolved in n-hexane and treated with concentrated sulfuric acid. The separated hexane layer was applied to a silver nitrate/silica gel column (0.5 g) and eluted with 15 ml of n-hexane. The eluted solution was loaded into an active carbon column (0.5 g) after being evaporated to 1 ml and separated into two fractions. The first fraction, containing Mono-Co-PCBs, was eluted with 10 ml of 10% (v/v) dichloromethane /n-hexane. PCDDs, PCDFs, and Non -Co-PCBs were eluted with 25 ml of toluene as the second fraction. The method employed here requires only a reduced amount of blood collected from patients compared with the conventional method[2,3]. The column packing (silver nitrate silica gel, active carbon column, and anhydrous sodium sulfate) used in this experiment was washed in order to reduce blank materials by ASE-200 under the same conditions as the lipid extraction with n-hexane or toluene. Concentrations of the PCDDs, PCDFs, Non-Co-PCBs and Mono-Co-PCBs were measured using HRGC/HRMS (Autospec Ultima E, MicroMass Ltd., Manchester, UK) equipped with an SCLV (SGE International, Victoria, Australia) injection system. The column used for solvent-cut was a BPX-5 fused silica pre-capillary column (0.25 mm i.d.×6 m, 0.25 μm film thickness), and for the analytical column was a BPX-5 fused silica capillary column (0.15 mm i.d.×30 m, 0.15 μm film thickness), (SGE International, Victoria, Australia), respectively.

Results and Discussions

Concentration of dioxins in various organs: Table 1 shows the mean concentrations of PCDDs, PCDFs, Non-Co-PCBs and Mono-Co- PCBs in eight organs. The mean TEQ concentrations in blood, lung, liver, bile, spleen, pancreas, kidney and

mesentery fat were 119, 178, 228, 50, 113, 163, 138 and 139 pg-TEQ/g lipid, respectively. Parallel levels were seen in the blood, spleen, kidney and mesentery fat; in the lungs and pancreas, levels were somewhat higher. Among the organ tissues sampled, the highest concentration was observed in the liver and the lowest in the bile. Mean total-TEQ concentration of the liver was about 4.5 times higher than that of bile.

The prevalent congener among PCDDs was OCDD, ranging from 923 to 6837 pg/g lipid; among PCDFs, it was 2,3,4,7,8-PeCDF except for in the liver sample. In the mesentery fat sample, the mean TEQ concentration was 108 pg-TEQ/g lipid (except for Mono-Co-PCBs). This value was 1.9 times higher than that of our previous data[1] of 56 pg/g lipid for mean age of 56 years old. Age-related increases in dioxin concentrations in human samples have been reported[4,5]; however, whether our observations have a pathophysiological significance or show the effects of age cannot be decided at present.

Contribution of each isomer to the total TEQ: Figure 1 shows the toxic contribution of each congener for 8 organs to the total TEQ.

The average toxic contribution of PCDDs, PCDFs, Non -Co-PCBs, and Mono-Co-PCBs in tissue samples was 32 ± 6%, 25 ±7 %, 24 ± 6% and 19 ± 4% to the total TEQ value, respectively. In the liver and spleen sample, the contribution rate of PCDFs was higher (30%) than in other organs (20%). The contribution rate varied slightly among organs, with the rate of Non -Co-PCBs in spleen falling as low as 13%.

Correlations of concentration of dioxins in various organs: We estimated concentrations of the correlations of toxic congeners among 8 tissues determined in this study using linear regression analysis. The data on TEQ are summarized in Table 2. The TEQ concentration in the liver correlated well with that in mesentery fat, blood, kidney, spleen, pancreas and lung; however, the bile did not correlate with the liver. A positive correlation among almost all the congeners was observed in tissues; however, levels of highly chlorinated PCDDs and PCDFs such as HpCDDs/DFs and OCDD/OCDF did not correlate with the levels of the other congeners.

Table 1 Mean concentrations of dioxins and related compounds in various human samples

Congeners	Blood (n=18)	Lung (n=18)	Liver (n=20)	Bile (n=15)	Spleen (n=18)	Pancreas (n=18)	Kidney (n=20)	Mesentery fat (n=20)
2,3,7,8-TCDD	4.9	8.2	7.8	2.7	5.0	5.8	5.7	5.4
1,2,3,7,8-PeCDD	21	38	35	12	27	25	26	23
1,2,3,4,7,8-HxCDD	8.6	18	17	2.9	21	12	18	8.5
1,2,3,6,7,8-HxCDD	67	112	96	30	92	90	97	73
1,2,3,7,8,9-HxCDD	12	15	20	7.3	12	10	13	10
1,2,3,4,6,7,8-HpCDD	48	101	167	28	145	55	129	32
OCDD	1344	2173	6837	1128	1961	1158	2152	923
2,3,7,8-TCDF	1.9	3.0	10	ND	ND	2.9	2.0	2.6
1,2,3,7,8-PeCDF	1.8	2.3	9.2	1.2	1.3	2.1	2.3	2.1
2,3,4,7,8-PeCDF	43	67	119	19	58	51	55	42
1,2,3,4,7,8-HxCDF	15	23	81	7.9	24	13	21	12
1,2,3,6,7,8-HxCDF	21	27	128	8.7	22	16	21	15
2,3,4,6,7,8-HxCDF	6.8	14	30	2.2	22	6.1	16	4.7
1,2,3,7,8,9-HxCDF	5.3	ND	3.6	ND	ND	ND	ND	ND
1,2,3,4,6,7,8-HpCDF	14	13	119	4.6	20	7.9	16	8.6
1,2,3,4,7,8,9-HpCDF	ND	ND	11	ND	2.4	ND	ND	ND
OCDF	ND	4.3	14	ND	ND	ND	ND	ND
3,4,4',5-TCB (#81)	20	19	24	6.1	ND	24	14	21
3,3',4,4'-TCB (#77)	109	29	50	33	8.4	25	19	20
3,3',4,4',5-PenCB (#126)	309	367	545	91	133	472	276	422
3,3',4,4',5,5'-HxCB (169)	217	249	242	76	162	317	189	301
2',3,4,4',5-PenCB (#123)	955	931	1211	361	373	1203	626	1458
2,3,4,4',5-PenCB (#118)	52116	42611	58955	20505	18215	44238	33899	64235
2,3,4,4',5-PenCB (#114)	3997	3425	4546	1840	1606	4509	2817	5289
2,3,3',4,4'-PenCB (#105)	11022	9472	12743	4987	4671	10901	7649	14986
2,3,4,4',5,5'-HexCB (#167)	7715	6309	10458	2660	2729	8089	4469	11644
2,3,3',4,4',5-HexCB (#156)	24300	19446	27367	10077	10068	23902	14509	33700
2,3,3',4,4',5'-HexCB (#157)	5349	4431	5662	2550	2223	5367	3219	6784
2,3,3',4,4',5,5'-HpCB (#189)	2486	2359	3067	991	1336	2779	1659	3766
TotalPCDD	1505	2465	7180	1210	2262	1357	2441	1074
TotalPCDF	113	157	524	49	154	103	139	92
TotalNon-*ortho* PCBs	654	663	862	206	308	838	498	764
TotalMono-*ortho* PCBs	107939	88984	124009	43971	41220	100989	68846	141861
PCDDs-TEQ	35	62	58	19	46	43	46	38
PCDFs-TEQ	27	41	86	12	36	29	34	25
Non-*ortho* PCBs-TEQ	33	39	57	10	15	50	30	45
Mono-*ortho* PCBs-TEQ	24	36	26	10	16	40	28	31
TotalTEQ	119	178	228	50	113	163	138	139

Table 2 Correlations of concentration of TEQ in various human samples

	Blood	Lung	Liver	Bile	Spleen	Pancreas	Kidney	Mesenteric fat
Blood								
Lung	0.8190*							
Liver	0.6328	0.8505*						
Bile	0.4137	0.8344*	0.3287					
Spleen	0.4816	0.8707*	0.8396*	0.5868				
Pancreas	0.8183*	0.9938*	0.8117*	0.7727*	0.9015*			
Kidney	0.7818*	0.9788*	0.8854*	0.4579	0.9252*	0.9678*		
Mesentery fat	0.8133*	0.9781*	0.7969*	0.8337*	0.8209*	0.9934*	0.9468*	

*$p<0.01$

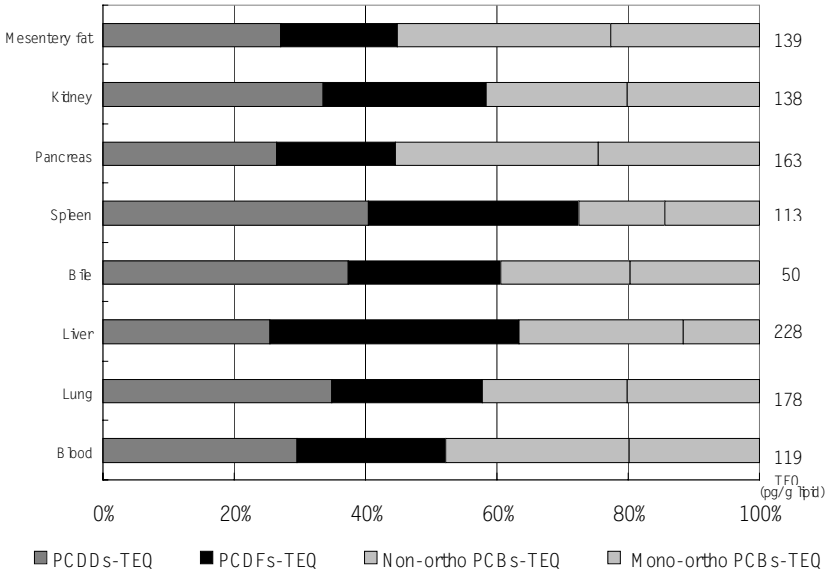

Fig.1 Percent distribution of TEQs in various human

Conclusions

We determined the concentrations of dioxin-like isomers in 8 human organs from 20 donors. The lipid-adjusted mean TEQ levels were from 50 to 228 pg/g. Positive correlations were observed among concentrations of dioxins in various tissues. We have a plan to evaluate the relationship between the accumulation levels of dioxins and their pathophysiological significance. However, it is needed to collect data from a more extensive group of human samples.

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