Tissue Concentrations of PCDDs and PCDFs in Rats

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ABSTRACT

Two defined mixtures of polychlorinated dibenzo-*p*-dioxins (PCDDs) or dibenzofurans (PCDFs) were administered subcutaneously 16 times (every third day) to two groups of 10 male Wistar rats, controls were treated with the vehicle. Each dose of the PCDD-mixture contained the following 2,3,7,8-substituted congeners: 70 ng/kg Cl5DD, 180 ng/kg Cl6DDs, 370 ng/kg Cl7DD and 300 ng/kg Cl8DD (Cl4DD was not present in the mixture). The PCDF-mixture contained 22 ng/kg Cl4DF, 106 ng/kg Cl5DFs, 189 ng/kg Cl6DFs, 490 ng/kg Cl7DFs and 94 ng/kg Cl8DF. Concentrations of the congeners were determinated in hepatic and adipose tissue one day after the 3rd, 8th and 16th injection as well as 13 and 34 days after the last treatment in two rats of each group.

Concentrations of the PCDD and PCDF congeners in the liver were considerably higher compared to concentrations in the adipose tissue. However, the liver/adipose tissue concentration ratios increased with the degree of chlorination. For the 2,3,7,8-substituted PCDDs we calculated ratios between 6 and 11 for Cl5DD and between 11 and 60 for Cl8DD, the concentration ratios for Cl6DDs and Cl7DD were between these extreme values. In the PCDF treated group the ratios for the 2,3,7,8-substituted congeners were between 1 and 4 for Cl4DF and between 24 and 60 for Cl8DF. The concentration ratios for Cl5DFs, Cl6DFs and Cl7DFs were between these values.

KEYWORDS

Polychlorinated dibenzo-*p*-dioxins (PCDDs); Polychlorinated dibenzofurans (PCDFs); Wistar rats; Tissue concentrations

ABBREVIATIONS

PCDDs = Polychlorinated dibenzo-*p*-dioxins
PCDFs = Polychlorinated dibenzofurans
Cl4DD;Cl4DF = Tetrachlorodibenzo-*p*-dioxin; Tetrachlorodibenzofuran
Cl5DD;Cl5DF = Pentachlorodibenzo-*p*-dioxin; Pentachlorodibenzofuran
Cl6DD;Cl6DF = Hexachlorodibenzo-*p*-dioxin; Hexachlorodibenzofuran
Cl7DD;Cl7DF = Heptachlorodibenzo-*p*-dioxin; Heptachlorodibenzofuran
Cl8DD;Cl8DF = Octachlorodibenzo-*p*-dioxin; Octachlorodibenzofuran

INTRODUCTION

Polychlorinated dibenzodioxins (PCDDs) and dibenzofurans (PCDFs) are formed, for example, as by-products of combustion processes. Since these chemicals are persistent in the environment, the human population is also exposed to a *mixture* of these substances, and exposure against a single defined compound is a very rare event. On the other hand, most of the toxicological and kinetic data available have been established with single congeners.

In this paper we present some data on studies on the tissue distribution of PCDD and PCDF congeners after repeated application of a defined PCDD- or a PCDF-mixture in rats. We compared concentrations achieved in liver tissue with concentrations in the adipose tissue.

MATERIAL and METHODS

Two groups of 10 male Wistar rats were treated 16 times (every third day) subcutaneously with 0.1 ml/kg body wt of a PCDD or PCDF-mixture diluted in a toluene/DMSO-solution. The composition of both mixtures is shown in Table 1. These mixtures were synthesized by copper-catalyzed dechlorination/hydrogenation as described by Hagenmaier et al. (1). 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (Cl4DD) was not present in the mixtures. Concentrations of all congeners in hepatic and adipose tissue were determined by GC-MS several times during the treatment period (one day after the 3rd, 8th and 16th injection) as well as 13 and 34 days after the last treatment. Details of the determination of different congeners by GC-MS are described elsewhere (2).

RESULTS and DISCUSSION

The composition of the administered PCDD- and PCDF-mixture is shown in Table 1. Tissue concentrations of several 2,3,7,8-substituted PCDDs and PCDFs in liver and adipose tissue during and after the treatment period are given in Table 2. On the 13th and 34th day after the last treatment concentrations of 2,3,7,8-Cl4DF were under the limit of detection in both tissues, the concentration of 1,2,3,7,8,9-Cl6DF in adipose tissue was under the limit of detection at all times (see: Material and Methods). The levels of all other 2,3,7,8-substituted congeners were higher in liver than in adipose tissue. Furthermore, the ratio between the concentrations in these two compartments increased with the degree of chlorination. At the indicated times in the PCDD treated group we calculated liver/adipose tissue ratios of 11, 7, 7, 6, 7 for Cl5DD and 11, 60, 54, 39 and 43 for Cl8DD (mean values of two animals at each point). The ratios for Cl6DDs and Cl7DD were between these extreme values.

Similar results were obtained in the PCDF treated group: ratios of 3, 4, 6, 1 and 2 for 1,2,3,7,8-Cl5DF and of 36, 52, 55, 46 and 41 for Cl8DF were calculated, the ratios for 2,3,4,7,8-Cl5DF, Cl6DFs and Cl7DFs were between these values. The very low ratios of 2,3,7,8-Cl4DF and 1,2,3,7,8-Cl5DF are striking in contrast to the high ratios for 2,3,4,7,8-Cl5DF (16, 27, 43, 40).

Although the doses of the non-2,3,7,8-substituted congeners administered with this mixture were considerably higher than those of the 2,3,7,8-substituted dioxins and furans, only some of them were found in relatively low concentrations during the treatment period, and only some of the higher chlorinated congeners could be detected after treatment.

REFERENCES

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Table 1: Composition of the administered PCDD- and PCDF-mixture.

PCDDs	Dose (ng/kg body wt)	PCDFs	Dose (ng/kg body wt)
Cl_4DD		**Cl_4DF**	
2,3,7,8	**0**	**2,3,7,8**	**22**
non-2,3,7,8-sub. *	*440*	*non-2,3,7,8-sub.* *	*1880*
Cl_5DD		**Cl_5DF**	
1,2,3,7,8	**70**	**1,2,3,7,8**	**89**
		2,3,4,7,8	**17**
non-2,3,7,8-sub. *	*940*	*non-2,3,7,8-sub.* *	*1540*
Cl_6DD		**Cl_6DF**	
2,3,7,8-sub.*	**180**	**1,2,3,4,7,8**	**86**
		1,2,3,6,7,8	**87**
		1,2,3,7,8,9	**3**
		2,3,4,6,7,8	**13**
non-2,3,7,8-sub. *	*1050*	*non-2,3,7,8-sub.* *	*700*
Cl_7DD		**Cl_7DF**	
2,3,7,8-sub.*	**370**	**1,2,3,4,6,7,8**	**470**
		1,2,3,4,7,8,9	**20**
non-2,3,7,8-sub. *	*600*	*non-2,3,7,8-sub.* *	*90*
Cl_8DD	**300**	**Cl_8DF**	**94**
Sum PCDDs:	**3,950**	**Sum PCDFs:**	**5,111**
2,3,7,8-sub.	**920**	**2,3,7,8-sub.**	**900**
non 2,3,7,8-sub.	3030	non 2,3,7,8-sub.	4210

* - sum of all congeners of this group of homologues

Table 2: Concentrations of 2,3,7,8-substituted PCDDs and PCDFs in liver and adipose tissue during and after the treatment period.

At each time indicated two rats were sacrificed and individual data are given;
n.d. = concentration below the limit of detection.

	Tissue concentration of 2,3,7,8-substituted PCDDs and PCDFs (ng/g)									
	Number of injections (days after last injection)									
	3 (1)		8 (1)		16 (1)		16 (13)		16 (34)	
Congener	liver	adip. tiss.	liver	adip. tiss.	liver	adip. tiss.	liver	adip. tiss.	liver	adip. tiss.
(A) PCDDs:										
Cl5DD	1.91	0.19	9.08	1.43	14.43	2.03	10.35	1.61	8.17	0.70
	2.99	0.24	7.72	1.12	18.69	2.91	8.65	1.83	4.72	1.45
Cl6DDs										
123478	0.54	0.02	6.52	0.23	9.98	0.35	9.12	0.20	3.82	0.15
	0.61	0.03	4.70	0.13	12.95	0.46	7.65	0.32	3.03	0.26
123678	0.99	0.04	10.97	0.36	20.12	0.63	21.27	0.38	13.70	0.33
	1.35	0.04	7.53	0.25	23.44	0.77	20.07	0.57	11.85	0.59
123789	0.14	0.01	1.72	0.09	2.47	0.12	2.20	0.06	0.99	0.03
	0.22	0.01	1.48	0.06	3.20	0.17	1.93	0.08	0.73	0.06
Cl7DD	1.34	0.11	14.24	0.29	26.28	0.55	25.94	0.58	18.00	0.46
	1.93	0.06	11.72	0.18	31.91	0.63	28.10	0.71	17.18	0.59
Cl8DD	0.64	0.13	7.98	0.16	13.03	0.28	12.13	0.35	9.02	0.18
	1.03	0.07	5.11	0.07	17.57	0.29	15.77	0.37	9.79	0.27
(B) PCDFs:										
Cl4DF	0.11	0.07	0.11	0.03	0.18	n.d.	n.d.	n.d.	n.d.	n.d.
	0.22	0.13	0.14	0.04	0.16	n.d.	n.d.	n.d.	n.d.	n.d.
Cl5DFs										
12378	1.01	0.34	1.23	0.42	2.40	0.36	0.12	0.21	0.06	0.04
	2.28	0.75	1.64	0.46	1.60	0.36	0.15	0.24	0.07	0.04
23478	1.11	0.06	3.08	0.12	7.03	0.17	4.85	0.17	5.46	0.13
	1.25	0.09	3.75	0.13	7.05	0.16	5.55	0.19	4.99	0.14
Cl6DFs										
123478	5.92	0.31	15.83	0.75	36.25	1.04	39.84	1.30	39.98	1.53
	5.50	0.17	20.37	0.81	35.40	1.28	34.23	1.40	30.68	1.28
123678	6.87	0.34	20.41	0.72	42.99	1.08	48.40	1.23	46.07	1.37
	6.40	0.21	23.24	0.85	39.46	1.32	39.24	1.40	32.69	1.12
123789	0.05	n.d.	0.12	n.d.	0.21	n.d.	0.05	n.d.	0.08	n.d.
	0.13	n.d.	0.14	n.d.	0.23	n.d.	0.06	n.d.	0.03	n.d.
234678	1.34	0.06	3.58	0.14	8.06	0.21	6.36	0.21	8.05	0.24
	1.51	n.d.	4.72	0.15	8.29	0.23	7.06	0.24	5.70	0.19
Cl7DFs										
1234678	20.18	0.60	76.30	1.63	155.3	3.13	140.8	2.81	122.2	3.65
	19.85	0.46	82.12	1.93	140.1	3.56	133.8	3.12	105.2	3.03
1234789	0.97	n.d.	2.71	0.07	6.70	0.13	5.80	0.14	6.72	0.21
	1.04	n.d.	4.21	0.07	7.68	0.16	6.46	0.15	5.97	0.15
Cl8DF	3.62	0.15	13.18	0.24	24.77	0.41	14.57	0.35	20.45	0.51
	3.78	0.08	12.87	0.27	25.46	0.52	21.18	0.43	18.09	0.43