Comparison of the kinetics of chlorinated and brominated dioxins and furans in the rat.

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ABSTRACT

When using TCDD-toxicity-equivalencies the differences in the kinetics for various congeners have to be taken into consideration. The toxicokinetic properties of two chlorinated dibenzofurans [(2,3,7,8-tetrachlorodibenzofuran (Cl_4DF) and 2,3,4,7,8-pentachlorodibenzofuran (Cl_5DF)] and of one dibenzo-p-dioxin [1,2,3,7,8-pentachlorodibenzo-*p*-dioxin (Cl_5DD)] were compared with the toxicokinetics of the corresponding brominated congeners (2,3,7,8-Br_4DF, 2,3,4,7,8-Br_5DF and 1,2,3,7,8-Br_5DD). Female Wistar rats were injected subcutaneously with a mixture of the compounds. After the treatment tissue concentrations of each congener were measured at different times (3 - 95 days).
For Cl_4DF and Br_4DF considerable differences were observed in the rate of elimination from liver and adipose tissue. As observed before, the Cl_4DF concentration decreased rapidly (half-lives of 2.6 days in the liver and 5.6 days in adipose tissue) during the first two weeks after administration. In contrast, Br_4DF concentrations rather increased during this time period in both tissues, probably due to slow absorption.
For the other chlorinated substances (Cl_5DF and Cl_5DD), the time-course of the concentrations was comparable with the brominated compounds. However, the decreases of the concentrations in the liver were faster for the dioxins (t/2 of 24 for Cl_5DD and 21 for Br_5DD) when compared to the furans (t/2 of 60 for Cl_5DF and 99 for Br_5DF). A similar change was found in the adipose tissue. The data suggest that with respect to kinetic variables, the TE-factors for the penta-chlorinated and penta-brominated congeners studied would not have to be adjusted. For the TE-factors of Br_4DF the kinetic behaviour is of great importance.

TOX

KEYWORDS

Polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDDs and PCDFs); Polybrominated dibenzo-*p*-dioxins and dibenzofurans (PBrDDs and PBrDFs); Tissue concentrations; Toxicokinetics; Elimination; Half-life

ABBREVIATIONS

Cl4DF = 2,3,7,8-tetrachlorodibenzofuran
Cl5DF = 2,3,4,7,8-pentachlorodibenzofuran
Cl5DD = 1,2,3,7,8-pentachlorodibenzo-*p*-dioxin
Br4DF = 2,3,7,8-tetrabromodibenzofuran
Br5DF = 2,3,4,7,8-pentabromodibenzofuran
Br5DD = 1,2,3,7,8-pentabromodibenzo-*p*-dioxin

INTRODUCTION

In this paper we present some data from studies on the tissue distribution in rats of some polychlorinated dibenzodioxins (PCDDs) and dibenzofurans (PCDFs) in comparison to the corresponding polybrominated congeners. Concentrations achieved in liver and in adipose tissue were measured and the eliminations half-lives were calculated.

MATERIAL and METHODS

Female Wistar rats weighing 220-260 g were treated subcutaneously with a mixture containing Cl4DF, Cl5DF, Cl5DD, Br4DF, Br5DF and Br5DD. The substances were dissolved in toluene/DMSO (1+2; v/v) and injected at following doses (calculated as nmol/kg body wt): 0.8 Cl4DF, 1.0 Cl5DF, 1.8 Cl5DD, 1.7 Br4DF, 1.1 Br5DF and 2.2 Br5DD. Concentrations of all congeners in hepatic and adipose tissue were determined by GC-MS at different times (3, 7, 14, 35, 56 and 95 days) after treatment.

RESULTS and DISCUSSION

Concentration time-courses of the congeners in liver and adipose tissue are shown in Figure 1. The data were calculated as percent of the injected dose per gram tissue (%/g) due to different concentrations of the congeners in the mixture. Considerable differences in the kinetics were found between Cl4DF and Br4DF. During the first two weeks after administration the concentration of Cl4DF revealed a rapid decrease with an elimination half-life (t/2) of 2.6 days in the liver and 5.6 days in the adipose tissue. In contrast, Br4DF concentration rather increased during this time period in both tissues. This may be due to a slow absorption and a low rate of elimination. At the following times (35, 56 and 95 days after treatment), the concentration of Cl4DF in the adipose tissue was below the limit of detection. However, the time-course of the Cl4DF concentration in the liver changed from day 14, the elimination being considerably slower (t/2 of 16 days).

For the penta-substituted chlorinated substances (Cl5DF and Cl5DD) the time-course of the concentration was comparable with that of the brominated compounds. However, differences were found in the elimination of dioxins as compared with furans (Table 1).
The elimination half-lives in the liver calculated from data obtained between day 35 and 95 after treatment were much shorter for the dioxins (24 days for Cl5DD and 21 days for Br5DD) than for the furans (60 days for Cl5DF and 99 days for Br5DF). A similar behaviour was also observed with respect to the concentrations in the adipose tissue.

Table 1 Elimination half-lives of some chlorinated or brominated dioxins and furans in liver and adipose tissue. Half-lives were calculated from tissue concentrations measured between 35 and 95 days after the treatment.

Congener	Hepatic tissue		Adipose tissue	
	t/2 (days)	95% conf. interval (days)	t/2 (days)	95% conf. interval (days)
Cl4DF(A)	**2.6**	2.1 - 3.4	**5.6**	4.4 - 7.5
Cl4DF(B)	**15.6**	10.1 - 34.2	---	--- - ---
Br4DF	**20**	17 - 25	**30**	26 - 36
Cl5DF	**60**	42 - 104	**115**	71 - 303
Br5DF	**99**	59 - 302	**80**	49 - 220
Cl5DD	**24**	20 - 30	**42**	35 - 53
Br5DD	**21**	17 - 27	**55**	39 - 97

(A) = calculated for the time period 3-14 days after injection
(B) = calculated for the time period 14-56 days after injection

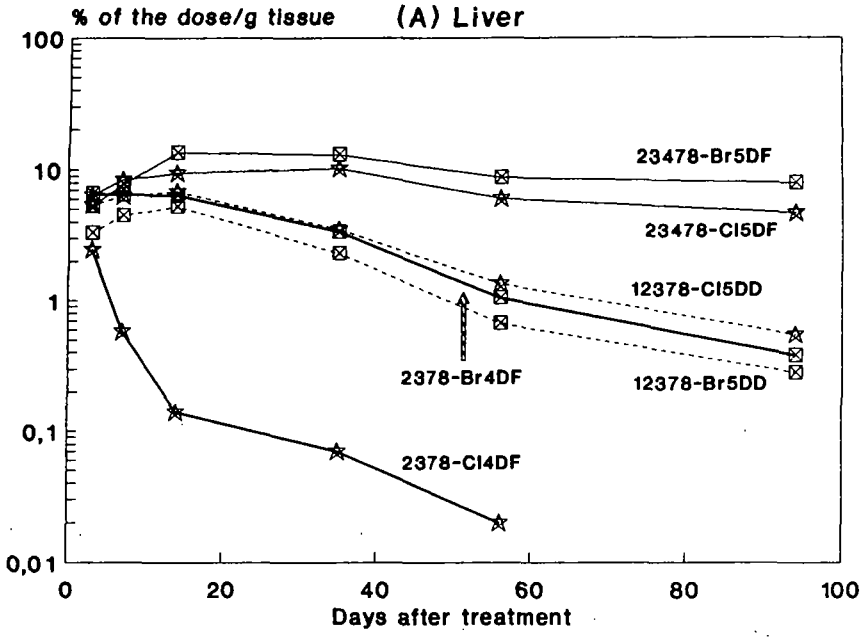

Figure 1: Concentrations of some congeners in the liver (A) and in the adipose tissue (B) after a single s.c. injection. ***(The data were calculated as percent of the injected dose per gram tissue)***