Tissue distribution of octachlorodibenzo-p-dioxin in rats after intravenous injection.

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ABSTRACT

The toxicokinetics of OCDD were investigated in female Wistar rats. Tissue concentrations of this congener were determined in liver and adipose tissue at different times after a single intravenous (i. v.) injection of 0.8 μg ^{14}C-OCDD/kg body wt.
Three days after treatment 55.6 ± 6.8 % of the applied dose was found in the liver, corresponding to a tissue concentration of 17.3 ± 1.1 ng/g. A biphasic elimination kinetics was found in the liver. During the first two weeks after treatment, the concentrations decreased to mean values of 7.1 ± 2.6 ng/g; the calculated elimination half-life (t/2) for this time period was 7 days. However, from day 14 a slower decrease of the concentrations with a t/2 of about 73 days was observed.
In contrast, the concentrations in adipose tissue increased continously during the investigation period from 0.43 ± 0.07 ng/g (day 3) to 0.91 ± 0.20 ng/g (day 70).

KEYWORDS

Polychlorinated dibenzo-*p*-dioxins and dibenzfurans (PCDDs and PCDFs); Octachlorodibenzo-p-dioxin (OCDD); Tissue concentrations; Toxicokinetics; Elimination; Half-life

INTRODUCTION

Among various chlorinated dibenzo-p-dioxins, octachlorodibenzo-p-dioxin is considered to be one of the least toxic substances. However, it is present in the environment and in human tissue at concentrations 100 - 1000 times higher than tetrachlorodibenzo-p-dioxin (TCDD). We investigated the kinetic properties of OCDD because they may be of great importance, when attempting a risk assessment of this compound.

MATERIALS and METHODS

Female Wistar rats weighing 160 - 215 g were treated intravenously with a single dose of 0.8 μg ^{14}C-OCDD/kg body wt (^{14}C-OCDD has a specific activity of 120 mCi/mmol). OCDD was suspended in a mixture of peanut oil/ 0.9% NaCl (1+9, v/v). At different intervals after injection (3 days, 1, 2, 3, 4, and 10 weeks), groups of four animals were sacrificed and samples of liver and adipose tissue were taken for the determination of the tissue concentrations by liquid scintillation counting.

RESULTS and DISCUSSION

Results of the time course of tissue concentrations in liver and adipose tissue are shown in Figure 1.
Three days after administration 55.6 % of the applied dose were found in the whole liver (9.7 % per gram tissue) corresponding to concentrations of 17.3 ± 1.1 ng/g (n=4). During the first two weeks after administration the concentration of OCDD in the liver revealed a rapid decrease to values of 7.1 ± 2.6 ng/g (n=4). The rate of elimination (t/2) in this time period was 7 days (95% confidence interval: 5.9 - 8.5 days). However, the time-course of the OCDD liver concentrations changed from day 14 and the elimination was considerably slower (t/2 of 73 days; 95% confidence interval: 49 - 141 days).
In contrast, the concentrations in the adipose tissue increased continously during the entire investigation period from 0.43 ± 0.07 ng/g (day 3) to 0.9 ± 0.2 ng/g (10 weeks). Calculated as percentage of dose per gram adipose tissue these values correspond to 0.24 ± 0.04 %/g (day 3) and 0.5 ± 0.1 %/g (10 weeks).
Our findings are in good accordance to previous reports from Birnbaum et al., 1988. After injection of a lower dose of OCDD (0.8 μg vs 50 g/kg body wt) we found comparable percentages of the applied dose in the liver and adipose tissue. The elimination half-life of OCDD in the liver during our study (73 days) was also in agreement with previous results (84 days).

However, two new aspects arise from our investigations. In contrast to the previous studies an initial rapid decrease of the OCDD concentration in the liver with an elimination half-life of 7 days was observed. And secondly, the OCDD concentrations in adipose tissue revealed a continous increase during an observation period up to 10 weeks.
These new findings are apparently due to pronounced redistribution phenomena, but they also could be due to the different doses, different vehicles or the different strains of rats used. To clarify these problems further long-term studies with i.v. administration of OCDD are necessary.

REFERENCES

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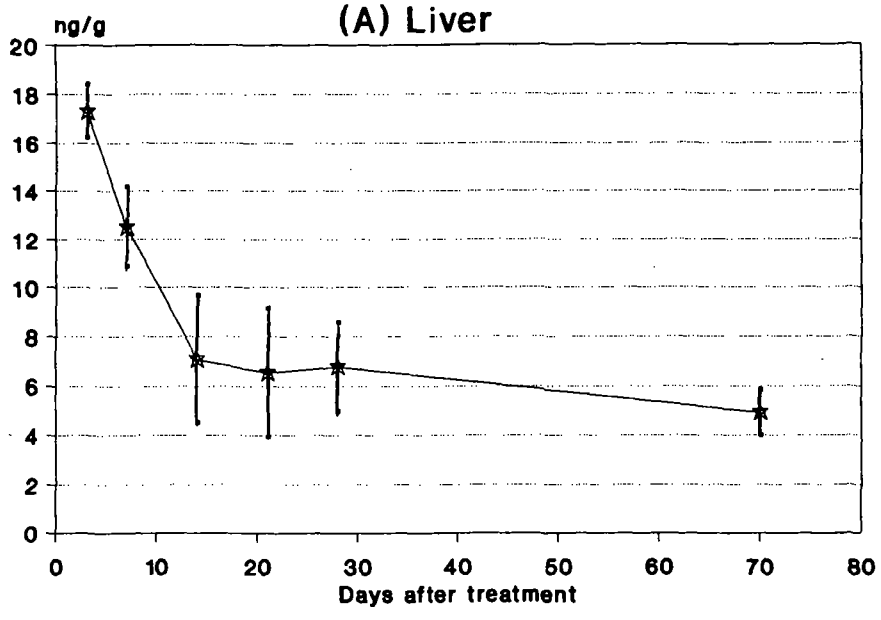

Figure 1: Tissue concentrations of OCDD in the liver (A) and in the adipose tissue (B) after a single i.v. injection of 0.8 µg ^{14}OCDD/kg body wt.