Hydroxylated PCDF metabolites in blood of rats dosed with PCDFs mixture

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Hydroxylation is a major metabolic pathway of halogenated aromatic compounds such as PCBs, PCDFs and PCDDs even though these are persistent environmental contaminants. In many PCB metabolism studies, determination of hydroxylated PCBs (OH-PCBs) in mainly faeces has been reported. The OH-PCBs are considered to be normally excreted in faeces and urine in contrast to PCB methyl sulphones, another type of PCB metabolite , which have been detected in biota. Quite recently we have demonstrated that the OH-PCBs are selectively retained in blood of rats dosed with Aroclor 1254 but also in blood from the Baltic grey seals and from human[1]. The retention of OH-PCBs in blood is probably due to a binding to a thyroxin transporting proteins (e.g. transthyretin, TTR)[2]. The metabolism of PCDFs has been shown to give rise to a large number of OH-PCDF metabolites, excreted in faeces (32 % of the dose was excreted in faeces within 5 days), after administration to rats of a PCDFs mixture (mainly 14 % 1,2,7,8-tetraCDF, 35 % 2,3,7,8-tetraCDF and 48 % 1,2,3,7,8-pentaCDF)[3]. The binding assay in vitro of synthesized OH-PCDFs to TTR showed a similarity in structure requirements for TTR binding between OH-PCBs and OH-PCDFs[4].

In the present study, rats were dosed with the PCDFs mixture mentioned above in order to study potential retention of OH-PCDF metabolites in blood. The PCDFs mixture was prepared by chlorination of dibenzofuran[3]. 12 Wistar male rats (200 g) were dosed orally with PCDFs mixture (5 mg/kg b.w.) for three subsequent days. Three rats were killed 24h, 7 days, 15 days and 21 days after the last dosage, respectively. Blood(serum), lung, kidney and adipose tissue were collected from the rats for analyses of PCDFs and OH-PCDF metabolites. OH-PCDFs, after methylation, were analyzed by GC(ECD), GC/MS(EI and NICI) and identification was done by comparison to synthesized reference compounds.

One OH-PCDF was detected in the serum (24 h) and identified as 3-OH-2,4,7,8-tetraCDF, a metabolite formed after NIH shift of 2,3,7,8-tetraCDF(cf Figure 1). In PCDFs fraction, 2,3,7,8-tetra- and 1,2,3,7,8-pentaCDF were determined in rat serum (24h) whereas 1,2,7,8-tetraCDF was not detected (cf Figure 1). Concentrations of 3-OH-2,4,7,8-tetraCDF, 2,3,7,8-tetraCDF and 1,2,3,7,8-pentaCDF in rat serum (24 h) were 15.3 - 56.0, 3.8 - 8.2 and 20.3 - 57.7 ng/g serum, respectively. The ratio of 2,3,7,8-tetraCDF and 3-OH-2,4,7,8-tetraCDF was in the range 0.1 - 0.4, indicating the strong retention of OH-PCDF with two chlorine substitution adjacent to the OH-group in the serum.

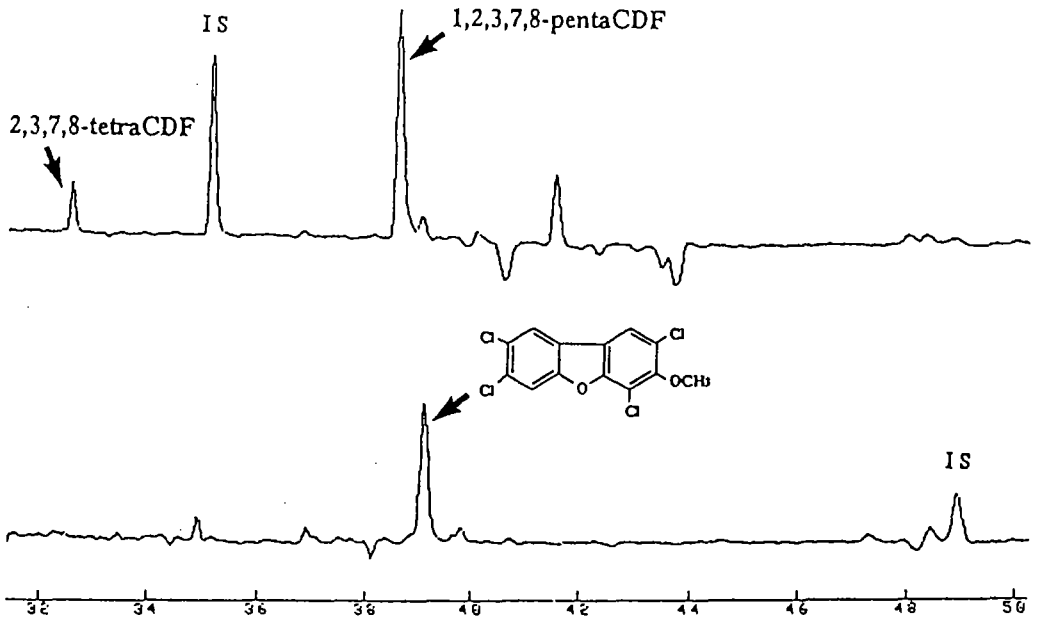

Figure 1. Gas chromatograms of hydroxylated PCDFs as methylated derivatives (lower) and PCDFs (upper) in the rat serum (24 h).
IS for hydroxylated PCDFs; 4-OH-2,3,5,6,3',4',5'-heptaCB
IS for PCDFs; 6-CH_3-2,3,4,8-tetraCDF

References

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