SELECTIVE RETENTION OF HYDROXYLATED PCBs IN BLOOD

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Although polychlorinated biphenyls (PCBs) are persistent environmental contaminants, most of the PCB congeners are metabolized by mammals even though the metabolism rate varies. During the metabolism, mediated by cytochrome P-450 enzymes, arene oxides are formed that are further metabolized to hydroxylated and sulphur containing metabolites, e.g. PCB methyl sulphones. Several aryl methyl suplhones have been shown to exhibit specific tissue binding properties in mammals[1]. More recently, hydroxylated PCBs have been determined to be retained in blood but also accumulation in mouse fetus has been reported[2,3]. The retention in serum was shown to be due to binding of a hydroxylated metabolite of 3,3',4,4'-tetraCB (I-77) to a thyroxin transporting protein (transthyretin, TTR)[3]. The metabolite was identified as 4-OH-3,3',4',5-tetraCB[4]. The relative binding *in vitro* of a number of synthesized hydroxylated chlorinated biphenyls (CBs) showed that the 4-OH-3,3',4',5-tetraCB had higher affinity for the TTR than thyroxin, the endogenous ligand[4]. In a recent study, the metabolism in mice of 2,3,3',4,4'-pentaCB (I-105) was shown to give rise to a high concentration in the serum (0.3 µg/g serum) of a hydroxylated metabolite - 4-OH-2',3,3',4',5-pentaCB (unpublished, cf poster by L. Lindberg *et al*).

In the present study, rats were dosed with Aroclor 1254 in order to study if also other PCBs can be transformed to metabolites with selective retention in the serum. The rats (3 groups of 3 male Wistar rats, 170 g) were dosed orally for three subsequent days with 25 mg Aroclor 1254/ kg bw. The rats were killed after 24 h, 7 days and 14 days after dosage, respectively. Blood, lung, kidney, liver and adipose tissue were analyzed for PCB and OH-PCB. After extraction, isolation and methylation of the OH-PCBs, identification and quantification by comparison to synthesized reference compounds were done by GC(EC) and GC/MS. The study also includes samples with relevance to the environmental situation; blood samples from Baltic Grey seals and human serum samples.

In the ratblood 12 hydroxylated PCBs were determined by GC/MS and the major peak (cf chromatogram) was identified as 4-OH-2',3,3',4',5-pentaCB - a metabolite of 2,3,3',4,4'-pentaCB (I-105). Also hydroxylated metabolites of the PCB congeners I-118 (2,3',4,4',5-pentaCB) and I-156 (2,3,3',4,4',5-hexaCB) were identified. The other minor peaks corresponded to other mono-hydroxylated PCBs of pentaCBs and hexaCBs, but also dihydroxylated metabolites of pentaCBS and hexaCBs were indicated by GC/MS. In the ratlung and ratlung hydroxylated PCBs were also determined whereas no hydroxylated PCBs could be detected in the adipose tissue. Also in seal-blood, 4-OH-2',3,3',4',5-pentaCB has

been identifed as the major compound and a hydroxy-hexaCB, so far not identified, was indicated by GC/MS. In the preliminary results of human serum samples, in addition to the I-105 metabolite (4-OH-2',3,3',4',5-pentaCB), 4-OH-2',3,3',4',5,5'-hexaCB (metabolite of I-156) has been identified.

Acknowledgement: This study has been supported by grants from the Swedish EPA.

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