METABOLISM OF 2,3,3',4,4'-PENTACHLORO-BIPHENYL IN MINK AND MOUSE

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Biological effects may be caused by persistent environmental contaminants, their reactive intermediates formed during metabolism or any of their metabolites. The mechanism behind the effects observed may be irreversible binding to macromolecules or non-covalent binding to proteins (receptors). PCB, as present in the environment, and individual chlorinated biphenyls (CBs) are known as toxicological important compounds. In order to understand biological responses to xenobiotics, e.g. of PCB, it is of importance to know the metabolism of the compounds. More thourough metabolism studies, especially in mammals shown to be sensitive to exposure to certain chemicals, are thus needed. The most sensitive species to PCB toxicity are mammals such as seals, otter and mink, all species reported to have impaired reproductive success as observed in populations of these animals in e.g. the Baltic or in the inland waters in Sweden[1,2,3]. Mink has been used as an experimental animal in studies of PCBs reproductive toxicity[4]. The results of these studies show that mink are very sensitive to PCB. However, there are no studies on the metabolism of PCB in mink. The present study was performed to give information on metabolism of one PCB congener - 2,3,3',4,4'-pentachlorobiphenyl (peCB, I-105) - in the mink and, for comparison, the metabolism of this compound was also studied in mice. PeCB was chosen because it is a 1-*ortho* substituted PCB and considered to be of toxicological significance[5]. PeCB is present in fairly high concentration both in technical PCB and in environmental samples[6,7].

In the present study, mink (4 females, 1,2 kg) and mice (16 females, C57Bl, 20 g) were dosed orally with ^{14}C-labelled peCB (1.0 mCi/mmol, 10 mg/kg bw). The animals were kept in metabolism cages and urine and feces were collected daily for five days. On day 5 after dosage, the animals were sacrificed and liver, adipose tissue and blood were taken out for analysis of peCB metabolites. The tissues and feces were extracted and metabolites isolated as described elsewhere[8] and analyzed by GC/MS.

Both mink and mice excreted the radiolabelled peCB and its metabolites mainly via feces. As determined by radioactivity, approximately 60% of the peCB dose for mice and approx 7% of the dose for mink were excreted within the 5 days and only 1% of the dose was excreted in urine by both species. In the mouse, all the radiolabelled compounds in feces were lipophilic - unmetabolized peCB and several hydroxylated metabolites (*ortho*-, *meta*- and *para*-substituted OH-peCBs) were identified by GC/MS and, in addition, peCB metabolites bound to lipids (lipid adducts) were indicated. The relative amount of lipid adducts increased with time after dosage and was approx. 20 % of the total radioactivity in feces on the third day after dosage. In the mink, ca 50% of the radiolabelled compounds were water soluble and were, after acidic hydrolysis, identified as hydroxylated peCBs, thus indicating the presence

of peCB conjugates. The lipophilic compounds, fractionated by GPC, were peCB, hydroxylated metabolites (*meta-* and *para-* OH-peCBs) but also lipid adducts of peCB were present in the feces (ca 40% of the extractable radioctivity on day 3 after dosage). No mercapturic acid pathway metabolites were detected in either species.

In adipose tissue from both mink and mouse, only unmetabolized peCB was found. In both the mouse and the mink liver, the major compound was the unmetabolized peCB and only small amounts of 4-OH-2',3,3',4',5-pentaCB were detected. In the mouse liver, traces of 5-OH-peCB were also detected, whereas the 2-OH-2',3,3',4,4'-pentaCB was determined in the mink liver. Approx. 20% of the total radioactivity content was covalently bound in livers from both species. A high concentration (ca 300 ng/g serum) of one hydroxylated metabolite - 4-OH-2',3,3',4',5-pentaCB was detected in mouse blood. The ratio was determined to be 15 between the 4-OH-2',3,3',4',5-pentaCB and the peCB in the mouse serum. The corresponding ratio in mink blood was 1 with a concentration of approximately 100 ng compound/g serum. The high concentration of 4-OH-2',3,3',4',5-pentaCB in the mouse serum should be correlated with the specific binding of certain hydroxylated PCBs to a thyroxin-binding transportprotein in the serum (TTR) that has been reported[9].

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