Methyl sulphone metabolites of PCB and DDE in human adipose tissue and liver

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1. Introduction

In the biotransformation of lipophilic substances usually polar metabolites are formed, which are more easily excreted from the body than the parent compounds. However, certain metabolites have lipophilic character, e.g., methyl sulphone metabolites of chlorinated biphenyls ($MeSO_2$-CBs) and DDE ($MeSO_2$-DDE)[1-3] or have specific protein binding properties, e.g., hydroxy-CBs[4], $MeSO_2$-CBs[5] and $MeSO_2$-DDE[6] and thus are retained in the body. In the environment $MeSO_2$-CBs and $MeSO_2$-DDE were first identified in seal blubber from the Baltic[1]. Since then such metabolites have been found in several species of animals[2-3] an in man[7]. Recently, $MeSO_2$-CBs and $MeSO_2$-DDE were determined in Swedish mother's milk[8] and $MeSO_2$-CBs in blood plasma from potentially exposed workers and controls[9]. The profiles of $MeSO_2$-CBs in the swedish samples differed from those in a Japanese investigation[7]. $MeSO_2$-DDE has been shown to be a potent toxicant for the adrenal cortex[6]. The toxicological significance of $MeSO_2$-CBs has not yet been elucidated but recently it was reported that certain 3-$MeSO_2$-CBs are potent inducers of several heptic microsomal drug metabolizing enzymes while the 4-$MeSO_2$-CBs tested were inactive[10-11].

In order to get a more complete knowledge of the degree of metabolism and accumulation in humans the concentrations of $MeSO_2$-CBs and $MeSO_2$-DDE together with CBs and DDE are determined in liver and adipose tissue from the same individual. Preliminary results from one subject are presented.

2. Experimental

Adipose tissue and liver samples were obtained during autopsy of a 68-year-old male individual (Swedish).

Internal standards, 2,2',3,3',4,5,5',6-octachlorobiphenyl (CB-198) and 3-methylsulphonyl-4-methyl-2',3',4',5,5'-pentachlorobiphenyl ($MeSO_2$-IS) were added to the sample. It was homogenized with an Ultra Turrax homogenizer, extracted twice with hexane/2-propanol (3:2, by vol.) and once with hexane. After evaporation of solvents lipids and lipophilic compounds were transferred to the lipophilic gel Lipidex by a liquid-gel partitioning technique previously described[12]. The gel with incorporated lipophilic compounds was washed with aqueous methanol before organochlorine compounds and some lipids were eluted with acetonitrile. Remaining lipids were eluted with chloroform/methanol/hexane (1:1:1, by vol.). The two fractions containing lipids were taken to near dryness under reduced pressure and dried to constant weight in a desiccator with silica gel. The sum of the weights of the residues in the two fractions defined the amount of lipids in the sample. The residue from the acetonitrile eluate was fractionated on partly deactivated aluminium oxide for purification and for separation of $MeSO_2$-CBs and $MeSO_2$-DDE from other organochlorine compounds. After

further separation on a silica gel column PCB and p,p´–DDE were detemined by gas chromatogaphy with electron capture detection. $MeSO_2$–CBs and $MeSO_2$–DDE were separated from coeluting lipids by gel permeation chromatography and were determined by GC–MS. Identification and quantification of $MeSO_2$–CBs and 3–$MeSO_2$–DDE were made by comparison to identical reference compounds. The compounds were gifts from Prof. Åke Bergman. The reference compound 3–$MeSO_2$–DDE was also used to quantify 2–$MeSO_2$–DDE. GC–MS analyses were performed using electron ionization (EI) at an electron energy of 30 eV. The resolution at m/z 293 was 5000. The MS was operated in the selected ion recording mode.

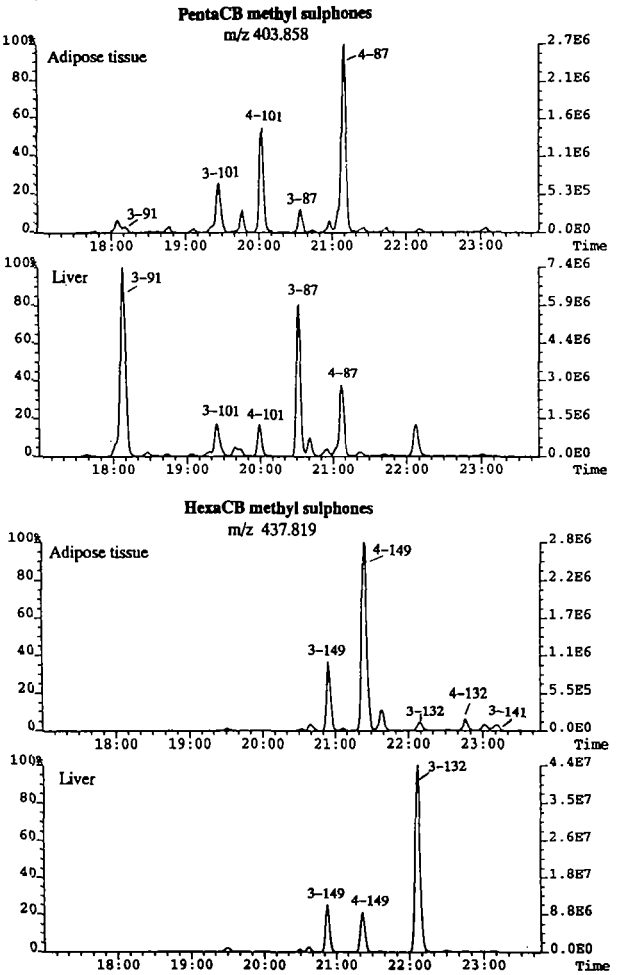

Figure 1. Selected ion current chromatograms of $MeSO_2$–CBs in human adipose tissue and liver.

3. Results and discussion

The recoveries of $MeSO_2$–IS and CB–198 added to the liver and adipose tissue samples before extraction ranged from 70 to 101%. The study included the compounds given in Table 1. The detection limits of $MeSO_2$–CBs and $MeSO_2$–DDE using GC–MS were 0.01–0.03 ng/g lipids. Selected ion current chromatograms of $MeSO_2$–pentaCBs and $MeSO_2$–hexaCBs in adipose tissue and liver are shown in Figure 1.

Table 1. $MeSO_2$-CBs and $MeSO_2$-DDE in human adipose tissue and liver (one subject).

Structures	Abbrevations[a]	Concentrations (ng/g lipids) Adipose tissue	Liver
3-$MeSO_2$-2,2',4',5-tetraCB	3-49	0.05	0.15
4-$MeSO_2$-2,2',4',5-tetraCB	4-49	0.20	0.19
3-$MeSO_2$-2,2',5,5'-tetraCB	3-52	<0.01	<0.01
4-$MeSO_2$-2,2',5,5'-tetraCB	4-52	<0.01	<0.01
3-$MeSO_2$-2,4',5,6-tetraCB	3-64	0.03	0.08
4-$MeSO_2$-2,3,4',6-tetraCB	4-64	0.03	0.02
3-$MeSO_2$-2,3',4',5-tetraCB	3-70	0.06	0.14
4-$MeSO_2$-2,3',4',5-tetraCB	4-70	0.02	0.04
3-$MeSO_2$-2,2',3',4',5-pentaCB	3-87	0.09	2.6
4-$MeSO_2$-2,2',3',4',5-pentaCB	4-87	1.9	2.6
3-$MeSO_2$-2,2',4',5,6-pentaCB	3-91	0.03	4.0
4-$MeSO_2$-2,2',3,4',6-pentaCB	4-91	<0.02	<0.02
3-$MeSO_2$-2,2',4',5,5'-pentaCB	3-101	0.24	0.62
4-$MeSO_2$-2,2',4',5,5'-pentaCB	4-101	0.54	0.54
3-$MeSO_2$-2,3',4',5,6-pentaCB	3-110	<0.02	<0.02
4-$MeSO_2$-2,3,3',4'6-pentaCB	4-110	<0.02	<0.02
3-$MeSO_2$-2,2',3',4',5,6-hexaCB	3-132	0.07	37.0
4-$MeSO_2$-2,2',3,3',4',6-hexaCB	4-132	0.10	0.12
3-$MeSO_2$-2,2',3',4',5,5'-hexaCB	3-141	0.07	0.09
4-$MeSO_2$-2,2',3',4',5,5'-hexaCB	4-141	0.50	0.49
3-$MeSO_2$-2,2',4',5,5',6-hexaCB	3-149	0.40	5.8
4-$MeSO_2$-2,2',3,4',5',6-hexaCB	4-149	1.8	6.8
3-$MeSO_2$-2,2',3',4',5,5',6-heptaCB	3-174	<0.03	0.9
3-$MeSO_2$-2,2',3,3',4',5',6-heptaCB	4-174	<0.03	<0.03
2-$MeSO_2$-DDE		0.06	7.2
3-$MeSO_2$-DDE		1.8	22.8
Total $MeSO_2$-CBs		6.1	62.2
Total $MeSO_2$-DDE		1.9	30.0
Total CBs (the sum of 20 congeners)		1551	1241
p,p'-DDE		707	925
CB-153		536	416
Ratio total $MeSO_2$-CBs/total CBs		0.004	0.05
Ratio total $MeSO_2$-DDE/p,p'-DDE		0.003	0.03

[a] Based on IUPAC numbering of precursor PCB congener.

Concentrations of the compounds are given in Table 1. In adipose tissue $MeSO_2$-pentaCBs and $MeSO_2$-hexaCBs were found in similar amounts and in liger amounts than the tetra- and heptachlorinated congeners. In liver the concentration of $MeSO_2$-hexaCBs were higher than the tetra-, penta- and hepta chlorinated compounds with congener 3-132 being the most dominating compound. The concentration of this compound in the adipose tissue was low, indicating a strong selective retention of congener 3-132 in liver. Also the other 3-$MeSO_2$-CBs seem to be selectively retained in liver (Table 1). Of the 4-$MeSO_2$-CBs only congener 4-149 was found in higher concentration in the liver than in the adipose tissue. In adipose tissue congeners 4-87 and 4-149 were found at highest

concentrations. These were also the dominating congeners in Swedish mother's milk[8] and blood plasma[9]. In a Japanese investigation of adipose, lung and liver tissue from a Yusho patient and a control, different profiles were reported with 4-$MeSO_2$-4,4',5-CB and 4-$MeSO_2$-2,3',5-CB being the major compounds in adipose tissue and liver, respectively[7]. The concentration ratios of the sum of $MeSO_2$-CBs to CB-153 were in the adipose and liver samples 0.01 and 0.15, respectively. The ratio in the adipose tissue was similar to the ratios in mother's milk (0.02-0.04) and blood plasma (0.002-0.03).

The sum of the concentrations of 2-$MeSO_2$-DDE and 3-$MeSO_2$-DDE were higher in liver than in adipose tissue. The isomer 2-$MeSO_2$-DDE was found in about 3 times lower concentration than 3-$MeSO_2$-DDE. The ratio of the sum of 3-$MeSO_2$-DDE and 2-$MeSO_2$-DDE to p,p'-DDE was in the adipose tissue and liver samples 0.003 and 0.03, respectively. The ratio in the adipose tissue was similar to that in mother's milk (0.002)[8]. In Japanese human samples (liver, adipose, lung) the ratios were slightly higher and similar in the different tissues (0.007-0.009)[13].

4. Acknowledgements
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5. References

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