Distribution of Methyl Sulfone Metabolites of Polychlorinated Biphenyls and *p,p′*-DDE in Human Tissues

Shaogang Chu,[1] Adrian Covaci,[1] Werner Jacobs,[2] Koichi Haraguchi,[3] and Paul Schepens[1]

[1]Toxicological Center, University of Antwerp, Wilrijk, Belgium; [2]Department of Forensic Pathology, University Hospital of Antwerp, Edegem, Belgium; [3]Daiichi College of Pharmaceutical Sciences, Fukuoka, Japan

We determined methylsulfonyl metabolites of chlorinated biphenyls ($MeSO_2$-CBs) and 1,1-bis(4-chlorophenyl)-2,2-dichloroethene (*p,p′*-DDE) in human adipose, liver, brain, and lung tissues obtained from 11 Belgian individuals (9–62 years of age). The total concentration of $MeSO_2$-CBs (lipid weight basis) decreased in the following order: liver (mean, 9.30 ng/g; range, 1.68–27.03 ng/g lipid) > lung [mean, 2.72 ng/g; range, not detected (ND) to 11.54 ng/g lipid] > adipose tissue (mean, 1.57 ng/g; range, 0.33–4.33 ng/g lipid) > brain (mean, 0.24 ng/g; range, ND–0.56 ng/g lipid). The profiles of $MeSO_2$-CBs and $MeSO_2$-DDE in each tissue were similar for all 11 subjects. In adipose, brain, and lung tissues, 4′-$MeSO_2$-CB87, 4′-$MeSO_2$-CB101, and 3-$MeSO_2$-CB149 (except brain) occurred at higher concentrations than did other $MeSO_2$-CBs. However, 3′-$MeSO_2$-CB132 was by far the most abundant congener in liver, contributing on average to approximately 60% of the sum of $MeSO_2$-CBs. The concentrations of 3-$MeSO_2$-DDE in different tissues were at the same or lower levels than the total concentrations of $MeSO_2$-CBs. This study suggests that the distribution patterns of $MeSO_2$-CBs and $MeSO_2$-DDE in humans differ between liver and other tissues. Moreover, these profiles differ from those found in other mammals, such as polar bears, porpoises, and otters. *Key words:* **adipose tissue, brain, DDE, humans, liver, lung, methyl sulfone, PCBs.** *Environ Health Perspect* **111:1222–1227 (2003). doi:10.1289/ehp.6141 available via *http://dx.doi.org/* [Online 6 March 2003]**

Polychlorinated biphenyls (PCBs) and 1,1-bis (4-chlorophenyl)-2,2-dichloroethene (*p,p′*-DDE) are well-known pollutants that have been found in many environmental matrices and in humans (Kimbrough and Jensen 1989; Turusov et al. 2002). Despite their persistence in the environment, PCBs and *p,p′*-DDE are susceptible to enzyme-mediated biotransformation in biota. Generally, an initial step in the PCB metabolism is the generation of an arene oxide intermediate. Further, two main metabolic pathways in mammals have been reported: the mercapturic acid pathway to give methyl sulfone ($MeSO_2$) metabolites and hydroxylation to yield biphenylols (Letcher et al. 2000a). Although the major metabolic route is hydroxylation generally followed by excretion, significant amounts of methylsulfonyl metabolites of chlorinated biphenyls ($MeSO_2$-CBs) and of DDE ($MeSO_2$-DDE) may be accumulated in tissues because of their lipophilic character and specific protein-binding properties (Jönsson et al. 1994; Lund et al. 1985, 1988). $MeSO_2$-CBs and $MeSO_2$-*p,p′*-DDE have been mostly quantified in fat and liver tissues (Letcher et al. 2000a, 2000b), whereas hydroxylated PCBs were mostly determined in blood (Letcher et al. 2000a).

$MeSO_2$-CBs and $MeSO_2$-DDE were detected in several wildlife species (Bergman et al. 1994; Haraguchi et al. 1988; Jensen and Jansson 1976; Stapleton et al. 2001) and in human breast milk (Norén and Meironyté 2000; Yoshida and Nakamura 1977), blood (Norén et al. 1996, 1999; Weistrand et al. 1997), and other tissues (Ellerichmann et al. 1998; Haraguchi et al. 1986; Weistrand and Norén 1997, 1998).

The biologic activities and toxicologic significance of methylsulfonyl metabolites have been recently reviewed (Letcher et al. 2000a). It has been shown that 3′-$MeSO_2$-CB87 and 3′-$MeSO_2$-CB101, but not their corresponding 4-$MeSO_2$-metabolites, induced hepatic CYP2-family protein levels and related catalytic activities in rats (Letcher et al. 2000a). Moreover, the potential of persistent $MeSO_2$-CBs to influence endocrine-related processes has been demonstrated (Letcher et al. 2000a). 3′-$MeSO_2$-CB132, 3′-$MeSO_2$-CB141, 3-$MeSO_2$-CB149, and 4-$MeSO_2$-CB149 reduced thyroid hormone levels in blood and increased thyroid weight and hepatic CYP protein levels in rats (Kato et al. 2000).

It was previously shown that the distribution of methylsulfonyl metabolites depends on both the congener structure and the species-specific metabolic capacity (Letcher et al. 1998; Stapleton et al. 2001). In experimental animals, it was demonstrated that $MeSO_2$-CBs might also have specific protein-binding properties reflected by specific retention in the body, such as adrenal, lung, kidney tissues, and uterine fluid (Bergman et al. 1979; Brandt and Bergman 1987; Jönsson et al. 1994; Lund et al. 1985, 1988). Although specific accumulation in selected organs has been demonstrated in experimental animals dosed for a short period (no more then few weeks) (Brandt et al. 1982; Jönsson et al. 1992), it is difficult to relate it to the distribution of methylsulfonyl metabolites in humans. Although several $MeSO_2$-CBs have been recently observed to be selectively and strongly retained in human liver (Norén et al. 1999; Weistrand and Norén 1997), the knowledge of accumulation and distribution of methylsulfonyl metabolites in other human tissues is still scarce.

The occurrence of $MeSO_2$-CBs and $MeSO_2$-DDE in wildlife and human samples and the demonstrated accumulation of certain $MeSO_2$-CBs and $MeSO_2$-DDE in specific tissues of mammals have made the investigation of these compounds in the environment important. In the present study, we have determined $MeSO_2$-CB and $MeSO_2$-DDE levels, together with PCBs and *p,p′*-DDE in different human tissues from Belgian individuals, to investigate their congener distribution and correlation between metabolites and parent compounds.

Materials and Methods

Samples. Human tissues, including adipose, liver, lung, and brain, were collected in the first half of 2002 from 11 subjects during medicolegal autopsy. The subjects (8 men and 3 women) died suddenly from causes unrelated to environmental contamination, and the age of subjects ranged from 9 to 62 years (mean, 34 years; median, 30 years). The body weight ranged from 30 to 100 kg (mean, 71 kg; median, 75 kg). No information was available on the subjects' diets or professions. Detailed information of the subjects is presented in Table 1. All of the samples were stored at –20°C until analysis.

Reagents and standards. All 26 individual standards of $MeSO_2$-CBs and 3-$MeSO_2$-DDE, together with 3-$MeSO_{2-4}$-methyl-2,2′,3′,4′,5′-pentachlorbiphenyl (3-$MeSO_2$-4-Me-CB), which was used as internal standard, were prepared at the Daiichi College of Pharmaceutical Sciences (Fukuoka, Japan) as described by Haraguchi et al. (1987). The chemical names of $MeSO_2$-CB congeners were simplified on the basis of the International Union of Pure and Applied Chemistry (IUPAC)-derived numbering system of the parent PCBs (Letcher et al. 2000a). All 29 individual PCB congeners and 3

Address correspondence to A. Covaci, Toxicological Center, University of Antwerp, Universiteitsplein, 1, Bldg. S, 6th Floor, 2610 Wilrijk, Belgium. Telephone: 0032-3-820-2704. Fax: 0032-3-820-2722. E-mail: covaci@uia.ua.ac.be

The authors declare they have no conflict of interest.

Received 2 December 2002; accepted 6 March 2003.

organochlorine pesticides [*p,p′*-DDE, *p,p′*-DDD (dichlorodiphenyldichloroethane), and *p,p′*-DDT (dichlorodiphenyltrichloroethane)] were purchased from Dr. Ehrenstorfer (Augsburg, Germany).

All solvents [hexane, acetone, methanol, isooctane, and dichloromethane (DCM)] were of pesticide grade (Merck, Darmstadt, Germany). Concentrated sulfuric acid (H_2SO_4; 95–97%), potassium hydroxide (KOH), and silica gel 60 (70–230 mesh) were obtained from Merck. Before use, anhydrous sodium sulfate (Na_2SO_4; Merck) was heated at 600°C for 6 hr in a muffle furnace. Florisil (60–100 mesh) (Supelco, Bornem, Belgium) was activated at 130°C overnight and then deactivated with 2% (wt/wt) water. Silica gel impregnated with KOH (33% KOH, wt/wt) was prepared by dissolving KOH in methanol and adding it to dry silica gel. The solvent was then evaporated at 60°C, and the resulting silica gel was heated at 150–170°C before use. The acid silica (45%, wt/wt) was prepared by dropwise addition of concentrated H_2SO_4 to dry silica gel under continuous stirring.

Table 1. Details of the investigated human subjects (n = 11).

Subject no.	Sex	Age (years)	Weight (kg)
1	Male	9	30
2	Male	12	30
3	Male	22	70
4	Male	25	65
5	Male	25	100
6	Male	30	100
7	Male	32	75
8	Female	51	75
9	Female	51	75
10	Male	57	90
11	Female	62	75
Mean ± SD		34 ± 18	71 ± 23

Extraction and cleanup. The sample preparation and analysis of $MeSO_2$ metabolites were as reported elsewhere (Chu et al. 2002) and are briefly described here. The tissue samples (0.5 g adipose tissue or 5 g of other tissues) were thawed, quantitatively weighed, and dehydrated by grinding with anhydrous Na_2SO_4 until a free-flowing powder was obtained. The samples were spiked with 100 µL × 10 pg/µL 3-$MeSO_2$-4-Me-CB as internal standard for $MeSO_2$-CBs and $MeSO_2$-DDE, and 100 µL × 100 pg/µL 2,2′,3,6′-tetra-CB (CB46) and 2,2′,3,4,5,6′-hexa-CB (CB143) as internal standards for PCBs and organochlorine pesticides. A Soxhlet system (B-811; BUCHI, Brussels, Belgium) was used in hot extraction mode for 4 hr with 100 mL hexane/acetone (3/1, vol/vol). After the extract was concentrated to approximately 10 mL and transferred to a centrifuge tube, an accurate portion (~10%) was removed for the gravimetric determination of lipid concentration. The remaining extract was concentrated, and the solvent was exchanged to hexane and reduced to a volume of 2 mL.

$MeSO_2$-CBs and $MeSO_2$-DDE were separated from other organochlorine compounds by liquid–liquid partitioning with concentrated H_2SO_4. The hexane solution was extracted twice with 2 mL concentrated H_2SO_4, and the acid phase was separated by centrifugation (4,000 rpm). The acid phases were combined and used for the determination of $MeSO_2$-CBs and $MeSO_2$-DDE, and the remaining hexane layer was used for the determination of PCBs and organochlorine pesticides.

For the determination of $MeSO_2$-CBs and $MeSO_2$-DDE, the combined sulfuric acid phase (~4 mL) was diluted with 4 mL cold distilled water. The solution was cooled, and the analytes were twice back-extracted with 2 mL hexane. The resulting organic layer was separated and washed with 2 mL NaCl solution (10%, wt/wt). The organic phase containing $MeSO_2$-CBs and $MeSO_2$-DDE was concentrated and loaded on a column packed with 1 g basic silica (33% KOH) and 5 g anhydrous Na_2SO_4 and eluted with 10 mL DCM. The solvent was exchanged to hexane, concentrated to approximately 1 mL, and applied to a column (30 cm × 1 cm) filled with 8 g Florisil. The column was first eluted with 40 mL DCM/hexane (1:1, vol/vol), and 10 mL DCM, which were discarded. The $MeSO_2$ metabolites were eluted with 40 mL DCM, and this fraction was collected and concentrated to approximately 2 mL. The purified extract was evaporated to dryness by a gentle stream of nitrogen at ambient room temperature. The residue was dissolved in 100 µL isooctane and then transferred to an injection vial.

Table 2. Levels of $MeSO_2$-CBs and $MeSO_2$-DDE (ng/g lipid weight) in Belgian human tissues.

Compound	Chlorine substitution	LOD	Adipose		Liver		Brain		Lung	
			Range	Mean	Range	Mean	Range	Mean	Range	Mean
Lipid (%)			65.0–87.7	79.5	2.8–14.0	7.3	5.0 – 9.0	7.4	0.8–2.8	1.5
3-$MeSO_2$-CB31	2,5-4′	0.06	ND	ND	ND	ND	ND	ND	ND	ND
4-$MeSO_2$-CB31	2,5-4′	0.06	ND–0.18	ND	ND–0.25	ND	ND	ND	ND	ND
3′-$MeSO_2$-CB49	2,4-2′,5′	0.06	ND–0.16	ND	ND–0.09	ND	ND	ND	ND	ND
4′-$MeSO_2$-CB49	2,4-2′,5′	0.07	ND–0.57	0.11	ND–0.23	ND	ND	ND	ND–0.78	ND
3-$MeSO_2$-CB52	2,5-2′,5′	0.06	ND	ND	ND	ND	ND–0.08	ND	ND	ND
4-$MeSO_2$-CB52	2,5-2′,5′	0.06	ND–0.07	ND	ND–1.00	0.13	ND	ND	ND	ND
3-$MeSO_2$-CB64	2,5,6-4′	0.06	ND	ND	ND	ND	ND	ND	ND	ND
4-$MeSO_2$-CB64	2,5,6-4′	0.06	ND–0.09	ND	ND	ND	ND	ND	ND	ND
3-$MeSO_2$-CB70	2,5-3′,4′	0.06	ND–0.19	ND	ND–0.12	ND	ND	ND	ND	ND
4-$MeSO_2$-CB70	2,5-3′,4′	0.06	ND–1.15	0.13	ND–0.14	ND	ND	ND	ND	ND
3′-$MeSO_2$-CB87	2,3,4-2′,5′	0.07	ND–0.20	ND	ND–0.82	0.34	ND	ND	ND–0.71	0.11
4′-$MeSO_2$-CB87	2,3,4-2′,5′	0.06	0.13–0.98	0.33	ND–0.87	0.35	ND–0.20	0.10	ND–1.06	0.55
3-$MeSO_2$-CB91	2,5,6-2′,4′	0.06	ND–0.15	ND	ND–2.21	0.82	ND	ND	ND–0.67	ND
4-$MeSO_2$-CB91	2,5,6-2′,4′	0.06	ND–0.15	ND	ND–0.09	ND	ND	ND	ND	ND
3′-$MeSO_2$-CB101	2,4,5-2′,5′	0.06	ND–0.32	0.08	ND–0.52	0.15	ND–0.10	ND	ND	ND
4′-$MeSO_2$-CB101	2,4,5-2′,5′	0.06	0.12–0.93	0.27	ND–1.04	0.27	ND–0.23	0.10	ND–1.18	0.46
3-$MeSO_2$-CB110	2,5,6-3′,4′	0.06	ND	ND	ND–0.12	ND	ND	ND	ND–0.89	0.08
4-$MeSO_2$-CB110	2,5,6-3′,4′	0.06	ND–0.17	ND	ND–0.30	0.07	ND–0.10	ND	ND–0.89	0.15
3′-$MeSO_2$-CB132	2,3,4-2′,5′,6′	0.06	ND–0.15	ND	1.58–16.16	5.42	ND	ND	ND–2.16	0.37
4′-$MeSO_2$-CB132	2,3,4-2′,5′,6′	0.06	ND–0.19	ND	ND–0.20	ND	ND	ND	ND–0.89	0.08
3′-$MeSO_2$-CB141	2,3,4,5-2′,5′	0.06	ND–0.09	ND	ND–0.09	ND	ND	ND	ND–0.71	ND
4′-$MeSO_2$-CB141	2,3,4,5-2′,5′	0.06	ND–0.25	ND	ND–0.30	0.07	ND	ND	ND–0.89	0.08
3-$MeSO_2$-CB149	2,5,6-2′,4′,5′	0.06	ND–0.48	0.18	ND–4.42	1.15	ND–0.14	ND	ND–1.57	0.42
4-$MeSO_2$-CB149	2,5,6-2′,4′,5′	0.07	ND–0.17	0.08	ND–0.42	0.10	ND	ND	ND–0.89	0.08
3′-$MeSO_2$-CB174	2,3,4,5-2′,5′,6′	0.07	ND	ND	ND–0.40	0.19	ND	ND	ND–0.71	ND
4′-$MeSO_2$-CB174	2,3,4,5-2′,5′,6′	0.07	ND	ND	ND	ND	ND	ND	ND–0.89	0.08
Sum $MeSO_2$-CBs			0.33–4.33	1.57	1.68–27.03	9.30	ND–0.56	0.24	ND–11.54	2.72
3-$MeSO_2$-DDE		0.10	ND–4.68	1.15	1.00–21.85	4.69	ND–1.57	0.22	ND–2.75	0.50

PCBs and organochlorine pesticides were determined as previously described (Covaci et al. 2002). The remaining hexane phase from the partitioning with concentrated H_2SO_4 was further cleaned on a column filled with 10 g acid silica gel (45%, wt/wt), and the analytes were eluted with 30 mL hexane. After evaporation to dryness, the residue was dissolved in 100 µL isooctane and transferred to vials for gas chromatography/electron-capture detection (GC-ECD) and gas chromatography/mass spectroscopy (GC/MS) analysis.

Determination of $MeSO_2$-CBs and $MeSO_2$-DDE by GC/electron-capture negative ionization MS. An Agilent 6890 gas chromatograph (Agilent, Palo Alto, CA, USA) equipped with a 5973 quadrupole MS detector was used for the determination of $MeSO_2$-CBs and $MeSO_2$-DDE. The GC column was an AT-5MS capillary column 50 m × 0.18 mm internal diameter with a film thickness of 0.25 µm (Alltech, Lokeren, Belgium). Helium was used as carrier gas at a constant flow of 0.5 mL/min. Extract (2 µL) was injected in solvent vent mode. The injector temperature was held at 90°C for 0.3 min, heated at 600°C/min to 300°C, and then held for 20 min. The vent flow was 100 mL/min, and vent and purge times were 0.2 and 2 min, respectively. The oven temperature was programmed as follows: 80°C, held for 2.5 min, then at 20°C/min to 250°C, then at 5°C/min to 290°C, and finally held for 40 min. The transfer line and quadrupole temperatures were 250°C and 150°C, respectively. Ionization was performed in electron-capture negative ionization (ECNI) mode, using methane as reagent gas.

The fraction containing $MeSO_2$-CBs and $MeSO_2$-DDE was analyzed in the selected ion-monitoring mode, and the identification of analytes was based on their retention times and the ratios of monitored ions (Chu et al. 2002). Three most intense ions from M^- and/or $[M\text{-}Me]^-$ clusters were monitored (Chu et al. 2002). Twenty-six $MeSO_2$-CB congeners and $MeSO_2$-DDE, representing the majority of $MeSO_2$ metabolites identified so far in biota (Letcher et al. 2000a), were chosen for the method validation. Quantitative determination was done using a five-level calibration curve spanning the range of the analyte concentrations in real samples.

Determination of PCBs and organochlorine pesticides by GC-ECD and GC/MS. An Agilent 6890 GC with µ-cell ECD was used for the determination of PCBs and pesticides. The separation was performed on an HT-8 capillary column (25 m × 0.22 mm, 0.25 µm film thickness) from SGE (Darmstadt, Germany). The carrier and make-up gas were helium (1 mL/min) and argon/methane 95%/5% (40 mL/min), respectively. The oven temperature was programmed as follows: 90°C, held for 1 min, then to 180°C at 15°C/min, held for 1 min, to 250°C at 3°C/min, and then to 290°C at 15°C/min, held for 6 min. The injector and detector temperatures were 270°C and 320°C, respectively. One microliter of the extract was injected in pulsed splitless mode, and the purge time was 1 min. The identification was based on the retention time of individual standard congeners, and a multicalibration curve was used for quantitative determination.

For confirmation, all samples were analyzed by GC/MS with electron ionization source and selected ion-monitoring mode. An HP-1MS capillary column (30 m × 0.25 mm, 0.25 µm film thickness) was used for the separation of analytes. The oven temperature was programmed as follows: 90°C, held for 2 min, then to 200°C at 3°C/min, then to 290°C at 3°C/min, held for 20 min. The injector temperature was 300°C. One microliter of extract was injected in splitless mode, and the purge time was 1 min. Although GC/MS (electron ionization) analysis can give additional information concerning the analyte identification, its sensitivity was lower than that of GC-ECD. Therefore, the quantitative results were based on the ECD determination, except for a few pairs of PCB congeners and pesticides (e.g.,

Table 3. Levels of PCBs and organochlorine pesticides (ng/g lipid weight) in Belgian human tissues.

		Adipose		Liver		Brain		Lung	
Compound	LOD	Range	Mean	Range	Mean	Range	Mean	Range	Mean
CB18	17.1	ND	ND	ND	ND	ND	ND	ND	ND
CB28	24.6	ND	ND	ND	ND	ND	ND	ND	ND
CB31	21.8	ND	ND	ND	ND	ND	ND	ND	ND
CB44	2.5	ND–3.8	ND	ND–4.2	ND	ND	ND	ND–13.7	6.0
CB52	2.5	ND–4.7	3.0	ND–12.4	4.5	ND–5.1	2.6	5.1–23.8	14.0
CB74	2.2	2.8–17.2	8.2	ND–33.1	8.3	ND–5.1	ND	2.8–51.2	12.8
CB87	1.0	ND	ND	ND	ND	ND	ND	ND–68.5	14.5
CB95	5.7	ND	ND	ND–11.5	ND	ND	ND	7.0–38.7	20.2
CB99	4.2	5.7–25.9	12.1	ND–25.4	8.7	ND–5.1	ND	4.9–85.5	19.2
CB101	1.0	1.2–7.0	3.6	1.8–6.7	4.3	ND–4.7	2.5	5.4 – 42.0	18.9
CB105	3.6	ND–16.1	5.6	3.6–13.4	6.8	ND–5.7	ND	6.7–47.9	21.4
CB110	2.2	ND–6.4	3.6	ND–14.1	7.6	ND–10.0	4.3	6.1–67.8	25.9
CB118	2.5	7.5–61.3	20.3	5.5–56.2	17.4	ND–9.7	4.3	7.1–145.1	35.2
CB128	0.7	0.9–7.0	2.3	ND–4.4	2.4	ND–2.2	0.8	ND–17.2	7.4
CB132	1.7	ND–33.1	10.6	ND–26.0	8.5	ND–3.8	1.9	3.7–98.1	18.3
CB138	3.0	21.0–135.9	56.4	5.4–114.3	34.6	ND–14.3	5.9	10.7–384.9	65.3
CB149	3.0	ND–5.2	3.0	ND–10.4	4.9	ND–5.6	ND	4.9–39.3	18.4
CB153	3.0	40.3–251.0	108.6	10.6–240.3	77.6	6.3–29.9	13.3	18.9–797.7	123.4
CB156	6.0	ND–33.1	13.7	ND–27.6	8.5	ND	ND	ND–99.5	14.1
CB163	4.8	14.5–78.1	38.8	ND–58.3	25.4	ND–8.3	ND	6.2–221.0	37.3
CB167	4.3	ND–9.7	ND	ND–9.5	ND	ND	ND	ND–29.5	10.0
CB170	1.2	10.0–59.1	29.9	2.4–52.8	21.1	ND–6.7	1.7	5.7–190.8	31.7
CB177	0.5	2.6–18.4	7.1	0.8–17.5	6.7	ND–2.0	0.9	1.3–64.7	9.9
CB180	2.6	29.3–161.8	81.9	5.4–142.9	54.7	ND–16.3	7.1	11.4–485.4	76.0
CB183	0.8	4.5–24.1	10.1	1.3–20.1	6.7	ND–2.4	0.9	3.0–70.5	11.8
CB187	0.8	7.6–56.9	23.6	2.4–54.6	18.2	1.0–6.8	3.1	6.8–184.1	30.2
CB194	0.4	5.0–36.5	16.1	2.2–32.3	12.0	ND–3.2	0.8	3.3–88.6	17.3
CB196	0.6	3.1–22.5	10.1	1.0–16.7	7.1	ND–2.2	0.7	2.2–54.1	10.5
CB199	0.2	2.3–20.4	8.9	0.8–15.2	5.8	ND–2.2	0.5	2.3–41.4	9.3
Sum PCBs		185.7–1058.2	479.6	79.9–931.6	358.9	23.5–121.8	59.7	197.7–3215.0	796.4
p,p´-DDE	20.0	84.1–1782.1	484.3	100.4–1196.7	468.9	55.3–213.4	116.9	ND–7807.3	1041.8
p,p´-DDD	20.0	ND	ND	ND–120.0	27.6	ND	ND	ND–90.9	ND
p,p´-DDT	20.0	ND–50.6	ND	ND–22.0	ND	ND	ND	ND–99.9	ND

CB132 and *p,p′*-DDD) coeluting on the column used on GC-ECD.

Quality control. The limit of detection (LOD) was defined as 3 times the standard deviation of measured values for samples (n = 7) spiked with the analyte amount that produced a signal approximately equal with three times the noise response in a blank sample. For $MeSO_2$-CB and $MeSO_2$-DDE determination, the limits of detection ranged from 0.06 to 0.10 ng/g lipid weight. Average recoveries of individual $MeSO_2$-CB congeners and $MeSO_2$-DDE from vegetable oil spiked with standards (1 ng) ranged between 84% and 99%, with a mean value of 89%. For PCB and organochlorine pesticide determination, the LOD ranged from 0.40 ng/g (CB149) to 24.6 ng/g (CB28), and the recovery ranged from 84 to 111%. The recoveries of internal standards (CB46 and CB143) in the samples ranged from 60 to 97%. No recovery corrections were applied to the final results. Quality control was ensured by regular analysis of procedural blanks and of certified reference material (CRM 350, PCBs in mackerel oil; Bureau of Community Research, Geel, Belgium), for which all measurements were within the range of certified values.

All statistical analyses were completed with STATISTICA for Windows, version 5.1, from StatSoft. Inc. (Tulsa, OK, USA). Concentrations of pollutants in tissues are summarized using arithmetic means along with minimum and maximal values (Tables 2 and 3).

Results

The individual concentrations of 26 $MeSO_2$-CB congeners and 3-$MeSO_2$-DDE, together with the sum of $MeSO_2$-CBs, measured in four different tissues from 11 Belgian subjects are presented in Table 2. Individual and total concentrations of 29 PCB congeners, together with concentrations of selected organochlorine pesticides (*p,p′*-DDE, *p,p′*-DDD, and *p,p′*-DDT), are shown in Table 3. All concentrations listed in Tables 2 and 3 are expressed in nanograms per gram lipid weight, to conveniently compare them with previously reported data. Concentrations of CB18, CB28, and CB31 were below the LOD in all samples and are omitted from Table 3.

The sum of determined PCBs and *p,p′*-DDE (expressed per lipid weight) was similar in adipose tissue and liver from the same subject. However, higher concentrations of $MeSO_2$-CBs, ranging from 1.68 to 27.03 ng/g lipid weight, were found in liver compared with other tissues (Table 2). The ratios between the sum of $MeSO_2$-CBs and the sum of PCBs and between $MeSO_2$-DDE and *p,p′*-DDE, as calculated from the individual values, were 4–28 and 2–11 times higher in liver than in adipose tissue, respectively. When comparing levels of contaminants (expressed on wet weight basis) between the tissues from the same subject, the highest concentrations were found in adipose tissue. The total concentration of $MeSO_2$-CBs decreased in the following order: adipose (mean, 1.30 ng/g wet weight; range, 0.25–3.62 ng/g) > liver (mean, 0.79 ng/g; range, 0.14–3.78 ng/g) > lung [mean, 0.03 ng/g; range, not detected (ND) to 0.14 ng/g] ≈ brain (mean, 0.02 ng/g; range, ND–0.05 ng/g) tissue.

The data on chemical residues were not normally distributed (Liliefors test), and therefore, all data were log-transformed before statistical analysis. Values below the LOD were set to zero. Pearson's correlation coefficients between the sum of $MeSO_2$-CBs or $MeSO_2$-DDE and the sum of PCBs or DDE were not high (Tables 4 and 5) and sometimes not statistically significant, whereas they were very low for most individual $MeSO_2$-CBs and their corresponding PCB precursors. Significant correlation ($p < 0.05$) was found between age and sum of PCBs in lung, adipose tissue, and liver, whereas age was correlated only with sum of $MeSO_2$-CBs in adipose tissue (Table 4).

The investigated tissues had characteristic profiles for the $MeSO_2$ metabolites. In adipose, brain, and lung tissues, 4′-$MeSO_2$-CB87 and 4′-$MeSO_2$-CB101 occurred at higher concentrations than did other $MeSO_2$-CBs. These two congeners contributed together, on average, 55, 67, and 50% to the sum of $MeSO_2$-CBs in adipose, brain, and lung, respectively. In adipose tissue, the concentration of 3′-$MeSO_2$-CB132 was below the LOD or < 10% of the sum of $MeSO_2$-CBs. In contrast, 3′-$MeSO_2$-CB132 was the most abundant $MeSO_2$-CB congener in liver, contributing on average 59% to the sum of $MeSO_2$-CBs. In liver, the concentration of the sum of 3-$MeSO_2$-CBs was higher than for the sum of 4-$MeSO_2$-CBs, whereas in other tissues a reversed condition was observed. The ratio between the concentrations of the sum of 3-$MeSO_2$-CBs and the sum of 4-$MeSO_2$-CBs was 9.3, 0.3, 0.1, and 0.5 in liver, adipose, brain, and lung, respectively.

Discussion

The concentrations of $MeSO_2$-CB congeners and $MeSO_2$-DDE varied in various tissues from the subjects. Most of the lower chlorinated $MeSO_2$-CB congeners were not detected in human tissues, probably because of a reduced abundance of lower chlorinated PCBs in the tissues (Table 3). In contrast, congeners with four to six chlorine atoms predominated in accordance with the longer biologic half-lives of the higher chlorinated $MeSO_2$ metabolites (Letcher et al 2000a).

Weistrand and Norén (1997) have reported that the concentration of $MeSO_2$-CBs in Swedish subjects ranged from 2.0 to 9.0 ng/g lipid weight in adipose tissue and from 11.8 to 358 ng/g lipid weight in liver. The concentrations of $MeSO_2$-CBs are similar for adipose tissue in the Swedish and the present study, whereas the concentrations of $MeSO_2$-CBs in Swedish liver are higher than the levels determined in the Belgian subjects, resulting from the wider concentration range determined in the Swedish liver samples. A possible explanation might be the difference in the age of subjects in both studies (34 years for Belgian subjects and 68 years for Swedish individuals), although only low correlation coefficients between $MeSO_2$-CBs and age could be computed (Table 4). The difference in the diet might have an impact, as well. In addition, the PCB and *p,p′*-DDE levels in the Belgian subjects investigated in this study were lower than in the Swedish samples collected in the 1990s, probably in accordance with the decrease in PCB contamination during the last 10 years (Norén and Meironyté 2000).

Ellerichmann et al. (1998) determined the enantiomers of eight $MeSO_2$-CBs atropisomers in human liver and lung and found that the concentration of $MeSO_2$-CBs present in

Table 4. Pearson's correlation coefficients for certain individual and total concentrations of methyl sulfones of PCBs and DDE versus individual and total concentrations of PCBs and *p,p′*-DDE in different tissues from 11 subjects.

	Pearson's correlation coefficient (r)		
	Liver	Adipose tissue	Lung
$MeSO_2$-CB101 vs. PCB101	0.28 (p = 0.41)	0.55 (p = 0.08)	NC
$MeSO_2$-CB132 vs. PCB132	0.73**	NC	NC
$MeSO_2$-CB149 vs. PCB149	–0.02 (p = 0.95)	–0.16 (p = 0.63)	NC
Sum $MeSO_2$-CBs vs. sum PCBs	0.52 (p = 0.10)	0.79**	0.36 (p = 0.28)
$MeSO_2$-DDE vs. *p,p′*-DDE	0.69*	0.67*	NC
Sum $MeSO_2$-CBs vs. age	0.32 (p = 0.34)	0.65*	0.31 (p = 0.35)
Sum PCBs vs. age	0.75**	0.81**	0.58*

NC, not computed because most values were below the LOD. $MeSO_2$-CB is the sum of corresponding 3-$MeSO_2$-CB and 4-$MeSO_2$-CB. All data were log-transformed before statistical analysis. *$p < 0.05$. **$p < 0.01$.

lung was substantially lower than in liver tissue. This result is in accordance with the present study, where $MeSO_2$-CBs and $MeSO_2$-DDE are also preferentially stored in the liver relative to other tissues. Calculated on a wet-weight basis, the concentrations of $MeSO_2$-CBs in the lung were 1–2 orders of magnitude lower than those in adipose or liver, because of a much lower lipid percentage (Ellerichmann et al. 1998). In an early investigation (Haraguchi et al. 1986), $MeSO_2$-CBs concentrations in lung and adipose tissue from a patient who died from causes unrelated to the Yusho accident are similar to those found in the present study. However, in the Yusho patient, the highest concentration of $MeSO_2$-CBs was found in lung (15.9 ng/g wet weight). The Yusho patient had ingested rice oil contaminated with a large quantity of Kanechlor 400 (a PCB mixture) in a short period (Haraguchi et al. 1986), whereas the normal exposure to PCBs (as in the present study) is through the daily intake of foods with low levels of contamination.

There are no previously reported data for $MeSO_2$-CB or $MeSO_2$-DDE residues in the human brain. In the present investigation, only a few $MeSO_2$-CB congeners (Table 2) could be quantitatively determined from brain tissues, although the lipid concentration in brain is similar to that in liver. Phospholipids, the dominating lipids in brain (Aguilar 1985; Tilbury et al. 1997), are less able to dissolve lipophilic compounds compared with triglycerides, which are present only in a small percentage (3–5%) (Kawai et al. 1988). However, the distribution of $MeSO_2$-CBs in biota tissues can not be totally explained by a simple physical partition theory, and in this case, protein binding may play an important role in the tissue-specific retention (Letcher et al. 2000a).

For monitoring of $MeSO_2$-CB residues in humans, blood and milk were more often investigated (Newsome and Davies 1996; Norén et al. 1996). It was reported that the mean concentration for the sum of $MeSO_2$-CBs was 1.7 ng/g lipid in Canadian human milk, and the major congeners were 3′-$MeSO_2$-CB101, 4′-$MeSO_2$-CB87, and 4′-$MeSO_2$-CB151 (Newsome and Davies 1996). In Swedish human milk, the concentration of $MeSO_2$-CBs decreased from 9 to 2 ng/g lipids between 1972 and 1992, and the concentrations of 4-$MeSO_2$-CBs were higher than the corresponding 3-$MeSO_2$-CBs, with the major congeners being 4′-$MeSO_2$-CB87 and 4-$MeSO_2$-CB149 (Norén et al. 1996). Norén et al. (1999) reported that the concentration of the sum of $MeSO_2$-CBs in Swedish human plasma ranged from 1 to 5 ng/g lipids, and that 4-$MeSO_2$-CB149, 4′-$MeSO_2$-CB87, and 4′-$MeSO_2$-CB101 were the dominant congeners. These congener profiles seem to be similar to those in the adipose tissue investigated in the present study, although we did not determine the presence of 4′-$MeSO_2$-CB151.

3′-$MeSO_2$-CB132 is the most abundant $MeSO_2$-CB congener we found in liver, contributing an average of 59% to the sum of $MeSO_2$-CBs (Figure 1). Similar results were found in previous investigations (Weistrand and Norén 1997, 1998), where 3′-$MeSO_2$-CB132 was present in higher concentration than other $MeSO_2$ metabolites in Swedish human liver, whereas 4′-$MeSO_2$-CB87 and 4-$MeSO_2$-CB149 were the predominant $MeSO_2$-CBs in adipose samples. In the present study, the concentration of the sum of 3-$MeSO_2$-CBs in liver was higher than the sum of 4-$MeSO_2$-CBs, whereas in other tissues a reversed condition was observed. A specific affinity for 3-$MeSO_2$-CBs in the liver has been observed in gray seals and otters (Bergman et al. 1994), whereas a specific retention of 4-$MeSO_2$-CBs has been observed in the lungs of rats and mice (Bergman et al. 1979; Haraguchi et al. 1999). This phenomenon indicates a different binding affinity (probably also species dependent) of 3-$MeSO_2$-CB and 4-$MeSO_2$-CB metabolites in various tissues (Haraguchi et al. 1999).

The profiles of $MeSO_2$-CB congeners in human tissues differ from those obtained from wild animals (Bergman et al. 1994). In muscle or blubber of wildlife (otter, mink, and gray seal) from Sweden, 3′-$MeSO_2$-CB101 was the predominant $MeSO_2$-CB congener, although 4′-$MeSO_2$-CB101 was also found at high concentrations (Bergman et al. 1994). Letcher et al. (1995a, 1995b) reported that the concentration of total $MeSO_2$-CBs in polar bear liver was 4–8-fold higher than in fat, with 3′- and 4′-$MeSO_2$-CB87, 3′- and 4′-$MeSO_2$-CB101, and 4-$MeSO_2$-CB149 congeners accounting for approximately 53% of the sum of $MeSO_2$-CBs. Both 3′- and 4′-$MeSO_2$-CB101 were found at the highest concentrations in blubber of harbor porpoises, followed by 3′- and 4′-$MeSO_2$-CB49, 3′- and 4′-$MeSO_2$-CB87, and 3- and 4-$MeSO_2$-CB149 (Karlson et al. 2000). It seems that in these species, the bioaccumulation/bioformation efficiency is less selective for 3- and 4-$MeSO_2$ metabolites.

In the present study, it is not possible to clearly determine the relative roles of bioaccumulation versus bioformation of $MeSO_2$ metabolites, but it is useful to indicate that

Table 5. Pearson's correlation coefficients for methyl sulfones of PCBs and DDE versus total concentrations of PCBs and *p,p′*-DDE in different tissues from 11 subjects.

	Pearson's correlation coefficient (*r*)
$MeSO_2$-DDE (liver) vs. $MeSO_2$-DDE (adipose)	0.82**
p,p′-DDE (liver) vs. *p,p′*-DDE (adipose)	0.90**
Sum $MeSO_2$-CBs (liver) vs. sum $MeSO_2$-CBs (adipose)	0.74*
Sum PCBs (liver) vs. sum PCBs (adipose)	0.93**
Sum $MeSO_2$-CBs (lung) vs. sum $MeSO_2$-CBs (adipose)	0.81**
Sum PCBs (lung) vs. sum PCBs (adipose)	0.71*

$MeSO_2$-CB is the sum of corresponding 3-$MeSO_2$-CB and 4-$MeSO_2$-CB. All data were log-transformed before statistical analysis.
*$p < 0.05$. **$p < 0.01$.

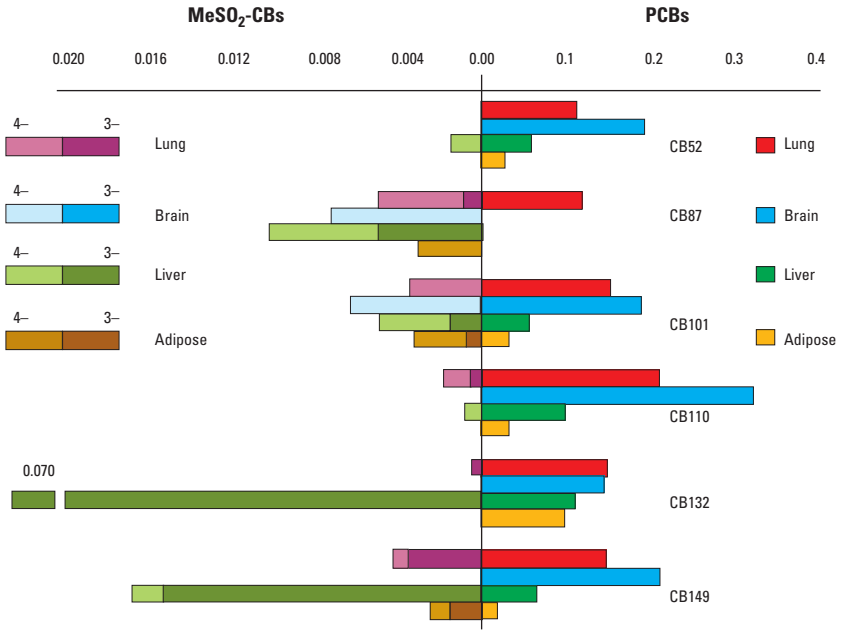

Figure 1. Mean ratios of $MeSO_2$-CBs and their corresponding precursor compounds to CB153 in human tissues.

both may contribute. This could be part of the reason why there is such poor or no correlation between individual $MeSO_2$-CBs and their precursors (Table 4). Letcher et al. (1998) have reported a clear indication of formation of 3′- and 4′-$MeSO_2$-CB87, 3- and 4-$MeSO_2$-CB91, and 3′- and 4′-$MeSO_2$-CB141 and 4′-$MeSO_2$-CB49 in polar bears. The bears bioaccumulated all of the $MeSO_2$-CB132 because the precursor was absent in the diet (seal). Most of the remaining congeners (3- and 4-$MeSO_2$-CB31, 3′- and 4′-$MeSO_2$-CB49, 3- and 4-$MeSO_2$-CB64, 3- and 4-$MeSO_2$-CB70, 3′- and 4′-$MeSO_2$-CB101, and 3- and 4-$MeSO_2$-CB110 and 3-$MeSO_2$-CB149) were likely bioaccumulated. The reason why patterns of $MeSO_2$-CBs differ between wildlife and humans could be because the relative importance of bioaccumulation may be higher in some wildlife species and because of a very different diet.

$MeSO_2$-CBs, $MeSO_2$-DDE, and their precursor compounds (PCBs and *p,p′*-DDE) are all lipophilic contaminants, but their bioaccumulation efficiency is not similar. $MeSO_2$-CBs and $MeSO_2$-DDE are selectively retained in liver tissues because of specific protein binding (Brandt and Bergman 1987). This phenomenon was also observed in the present study. In paired samples of human adipose tissue and liver, the concentrations of PCBs and DDE were similar on the lipid weight basis, but the concentrations of methylsulfonyl metabolites were different. The average ratios of the sum $MeSO_2$-CBs to the sum PCBs were 1/306 and 1/39 in adipose tissue and liver, respectively. In this study, only 3-$MeSO_2$-DDE was determined, because other $MeSO_2$-DDE standards were unavailable. The ratios of 3-$MeSO_2$-DDE to *p,p′*-DDE, calculated from average values, were 1/421 and 1/100 in adipose tissue and liver, respectively.

For the precursor compounds of the investigated $MeSO_2$-CBs, only low levels of CB52, CB87, CB101, and CB110 were found in the tissues. To minimize the variations among individual subjects, the concentration of $MeSO_2$-CBs and their precursors was normalized to the concentration of CB153 in individual tissues (Figure 1). It is well known that CB153 is resistant to biotransformation in many organisms, and it is assumed that CB153 represents the maximum bioaccumulation potential for slowly metabolized lipophilic compounds (Boon et al. 1992, 1997; Tanabe et al. 1994). A different distribution of metabolites was observed between the tissues (Figure 1). The ratios between $MeSO_2$-CB and the parent CB decreased in the following order: liver > brain ~ lung > adipose tissue. The highest normalized concentration of $MeSO_2$-CBs and the highest ratio of $MeSO_2$-CB congener concentration versus its corresponding precursor CB congener were found for 3′-$MeSO_2$-CB132 in liver. The reasons for these ratio variations are complex and depend not only on the congener metabolism but also on the preferential affinity of the metabolite for tissues.

In conclusion, the present results show that $MeSO_2$-CB congeners have a different distribution, both as concentration and as profiles, in human tissues. Further studies are needed to reveal details of their mechanisms and their selective protein-binding affinity in different tissues.

References

Aguilar A. 1985. Compartmentation and reliability of sampling procedures in organochlorine pollution surveys of cetaceans. Residue Rev 95:91–114.

Bergman A, Brandt I, Jansson B. 1979. Accumulation of methylsulfonyl derivatives of some bronchial-seeking polychlorinated biphenyls in the respiratory tract of mice. Toxicol Appl Pharmacol 48:213–220.

Bergman A, Norstrom RJ, Haraguchi K, Kuroki H, Beland P. 1994. PCB and DDE methyl sulfones in mammals from Canada and Sweden. Environ Toxicol Chem 13:121–128.

Boon JP, Van Arnhem E, Jansen S, Kannan N, Petrick G, Schulz D, et al. 1992. The toxicokinetics of PCBs in marine mammals with sepecial reference to possible interactions of individual congeners with the cytochrome P450-dependent monooxygenase system: an overview. In: Persistent Pollutants in Marine Ecosystems (Walker CH, Livingstone DR, eds). Oxford, UK:Pergamon Press, 119–160.

Boon JP, Van der Meer J, Allchin CR, Klungsoyr J, Leonards PEG, Spliid H, et al. 1997. Concentration-dependent changes of PCB patterns in fish-eating mammals: structural evidence for induction of cytochrome P450. Arch Environ Contam Toxicol 33:298–311.

Brandt I, Bergman A. 1987. PCB methyl sulfones and related compounds: identification of target cells and tissues in different species. Chemosphere 16:1671–1676.

Brandt I, Klasson-Wehler E, Rafter J, Bergman A. 1982. Metabolism of 2,4′,5-trichlorobiphenyl: tissue concentrations of methylsulphonyl-2,4′,5-trichlorobiphenyl in germ-free and conventional mice. Toxicol Lett 12:273–280.

Chu SG, Covaci A, Haraguchi K, Schepens P. 2002. Optimized separation and determination of methyl sulfone metabolites of polychlorinated biphenyls (PCBs) and *p,p′*-DDE in biota samples. Analyst 127:1621–1626.

Covaci A, de Boer J, Ryan JJ, Voorspoels S, Schepens P. 2002. Distribution of organobrominated and organochlorinated pollutants in Belgian human adipose tissue. Environ Res 88:210–218.

Ellerichmann T, Bergman A, Franke S, Huhnerfuss H, Jakobsson E, Konig WA. 1998. Gas chromatographic enantiomer separations of chiral PCB methyl sulfones and identification of selective retained enantiomer in human liver. Fresenius Environ Bull 7:244–257.

Haraguchi K, Kato Y, Kimura R, Masuda Y. 1999. Tissue distribution of methylsulfonyl metabolites derived from 2,2′,4,5,5′-penta- and 2,2′,3,4′,5′,6-hexachlorobiphenyls in rats. Arch Environ Contam Toxicol 37:135–142.

Haraguchi K, Kuroki H, Masuda Y. 1986. Capillary gas chromatographic analysis of methylsulfone metabolites of polychlorinated biphenyls retained in human tissues. J Chromatogr 361:239–252.

———. 1987. Synthesis and characterization of tissue-retainable methylsulfonyl polychlorinated biphenyl isomers. J Agric Food Chem 35:178–182.

———. 1988. Occurrence and distribution of chlorinated aromatic methylsulfones in biological samples. Chemosphere 19:487–492.

Jensen S, Jansson B. 1976. Anthropogenic substances in seal from the Baltic: methyl sulfone metabolites of PCB and DDE. Ambio 5:257–260.

Jönsson CJ, Lund BO. 1994. In vitro bioactivation of the environmental pollutant 3-methylsulphonyl-2,2-bis (4-chlorophenyl)-1,1-dichloroethene in the human adrenal gland. Toxicol Lett 71:169–175.

Jönsson CJ, Lund BO, Bergman A, Brandt I. 1992. Adrenocortical toxicity of 3-methylsulphonyl-DDE. 3: Studies in fetal and suckling mice. Reprod Toxicol 6:233–240.

Karlson K, Ishaq R, Becker G, Berggren P, Broman D, Colmosjo A. 2000. PCBs, DDTs and methyl sulfone metabolites in various tissues of harbour porpoises from Swedish waters. Environ Pollut 110:29–46.

Kato Y, Haraguchi K, Shibahara T, Yumoto S, Masuda Y, Kimura R. 2000. Reduction of serum thyroxine concentrations by methylsulfonyl metabolites of tetra-, penta- and hexachlorinated biphenyls in male Sprague-Dawley rats. Chemosphere 40:1233–1240.

Kawai S, Fukushima M, Miyazaki N, Tatsukawa R. 1988. Relationship between lipid composition and organochlorine levels in the tissues of striped dolphins. Mar Pollut Bull 19:129–133.

Kimbrough RD, Jensen AA. 1989. Halogenated Biphenyls, Terphenyls, Naphthalenes, Dibenzodioxins and Related Products. 2nd ed. Amsterdam:Elsevier.

Letcher RJ, Klasson-Wehler E, Bergman A. 2000a. Methyl sulfone and hydroxylated metabolites of polychlorinated biphenyls. In: New Types of Persistent Halogenated Compounds (Paasivirta J, ed). Berlin:Springer-Verlag, 315–360.

Letcher RJ, Norstrom RJ, Bergman A. 1995a. An integrated analytical method for determination of polychlorinated aryl methyl sulfone metabolites and polychlorinated hydrocarbon contaminants in biological matrices. Anal Chem 67:4155–4163.

———. 1995b. Geographical distribution and identification of methyl sulfone PCB and DDE metabolites in pooled polar bear (*Ursus maritimus*) adipose tissue from western hemisphere Arctic and Subarctic regions. Sci Total Environ 160/161:409–420.

Letcher RJ, Norstrom RJ, Muir DCG. 1998. Biotransformation versus bioaccumulation: source of methyl sulfone PCB and 4,4′-DDE metabolites in the polar bear food chain. Environ Sci Technol 32:1656–1661.

Letcher RJ, Norstrom RJ, Muir DCG, Sandau CD, Koczanski K, Michaud R, et al. 2000b. Methylsulfone polychlorinated biphenyl and 2,2-bis(chlorophenyl)-1,1-dichloroethylene metabolites in beluga whale (*Delphinapterus leucas*) from the St. Lawrence River estuary and western Hudson Bay, Canada. Environ Toxicol Chem 19:1378–1388.

Lund BO, Bergman A, Brandt I. 1988. Metabolic activation and toxicity of a DDT-metabolite, 3-methylsulphonyl-DDE, in the adrenal zona-fasciculata in mice. Chem Biol Interact 65:25–40.

Lund J, Brandt I, Poellinger L, Bergman A, Klasson-Wehler E, Gustafsson JA. 1985. Target calls for the polychlorinated biphenyl metabolite 4,4′-bis(methylsulfonyl)-2,2′,5,5′-tetrachlorobiphenyl—characterization of high affinity binding in rat and mouse lung cytosol. Mol Pharmacol 27:314–323.

Newsome WH, Davies D. 1996. Determination of PCB metabolites in Canadian human milk. Chemosphere 33:559–565.

Norén K, Lundén A, Pettersson E, Bergman A. 1996. Methylsulfonyl metabolites of PCBs and DDE in human milk in Sweden 1972–1992. Environ Health Perspect 104:766–772.

Norén K, Meironyté D. 2000. Certain organochlorine and organobromine contaminants in Swedish human milk in perspective of past 20–30 years. Chemosphere 40:1111–1123.

Norén K, Weistrand C, Karpe F. 1999. Distribution of PCB congeners, DDE, hexachlorobenzene, and methylsulfonyl metabolites of PCB and DDE among various fractions of human blood plasma. Arch Environ Contam Toxicol 37:408–414.

Stapleton H, Letcher RJ, Baker JE. 2001. Metabolism of PCBs by the deepwater sculpin (*Myoxocephalus thompsoni*). Environ Sci Technol 35:4747–4752.

Tanabe S, Iwata H, Tatsukawa R. 1994. Global contamination by persistent organochlorines and their ecotoxicological impact on marine mammals. Sci Total Environ 154:163–177.

Tilbury KL, Stein JE, Meador JP, Krone CA, Chan SL. 1997. Chemical contaminants in harbour porpoises (*Phocoena phocoena*) from the north Atlantic coast; tissue concentrations and intra- and inter-organ distribution. Chemosphere 34:2159–2181.

Turusov V, Rakitsky V, Tomatis L. 2002. Dichlorodiphenyltrichloroethane (DDT): ubiquity, persistence, and risks. Environ Health Perspect 110:125–128.

Weistrand C, Norén K. 1997. Methylsulfonyl metabolites of PCBs and DDE in human tissues. Environ Health Perspect 105:644–649.

———. 1998. Polychlorinated naphthalenes and other organochlorine contaminants in human adipose and liver tissue. J Toxicol Environ Health A 53:293–311.

Weistrand C, Norén K, Nilsson A. 1997. Occupational exposure—organochlorine compounds in blood plasma from potentially exposed workers. Environ Sci Pollut Res 4:2–9.

Yoshida S, Nakamura A. 1977. Studies on a metabolite of PCB (methylsulfone PCB) in mother milk. J Food Hyg Soc Jpn 18:387–388.