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Maternal and cord serum exposure to PCB and DDE methyl sulfone metabolites in eastern Slovakia

Linda Linderholm^{1,*}, June-Soo Park², Anton Kocan³, Tomas Trnovec³, Maria Athanasiadou¹, Åke Bergman¹, and Irva Hertz-Picciotto²

¹ Department of Environmental Chemistry, Stockholm University, SE-106 91 Stockholm, Sweden

² Department of Public Health Science, University of California Davis, Davis CA 95616, USA

³ Department of Toxic Organic Pollutants, Slovak Medical University, SK-833 03 Bratislava, Slovak Republic

Abstract

Polychlorinated biphenyls (PCBs) were commercially produced between 1959 and 1984 in eastern Slovakia. Improper handling led to a highly contaminated local environment and high levels of PCBs in humans and wildlife in the Michalovce area. The aim of this study was to analyse serum for methylsulfonyl metabolites of PCB (MeSO₂-PCBs) and DDE (3-MeSO₂-DDE) in serum samples from pregnant women and in a selected number of paired cord blood samples to assess maternal sulfone levels and patterns, and transplacental transfer of these metabolites. The donating women were from two districts in eastern Slovakia. A liquid-liquid extraction method together with separation of substance groups and further clean up on silica gel columns were applied prior to analysis by gas chromatography/mass spectrometry. 3-MeSO₂-DDE was the major methyl sulfone in most of the samples followed by a yet not identified MeSO₂-hexaCB, 4'-MeSO₂-CB101, 4'-MeSO₂-CB87 and 4-MeSO₂-CB149. The women from the contaminated area had three times higher concentrations of the MeSO₂-PCBs than women from the reference area. This is the first report on methyl sulfone metabolites of PCB and DDE in human cord serum. It is shown that these metabolites are transported through the placenta. The levels of MeSO₂-PCBs in the maternal serum were about 1.5 times higher than in the corresponding cord serum on a lipid weight basis. For 3-MeSO₂-DDE, the levels were about the same in maternal and cord serum. The difference in the maternal:cord ratio, comparing MeSO₂-PCBs with 3-MeSO₂-DDE might be due to differences in transport through the placenta caused by their different affinities for lipoproteins and plasma proteins.

Keywords

Human exposure; PCB methyl sulfone; DDE methyl sulfone; PCB metabolites; Michalovce; PCB

Introduction

Between 1959 and 1984, 22,000 tons of polychlorinated biphenyls (PCBs) were produced at Chemco Inc., a chemical plant located in the district of Michalovce in eastern Slovakia. The waste water from the plant was discharged untreated, contaminating the surroundings and the nearby Laborec River and Srava Lake. High concentrations of PCBs have been found in air,

*Corresponding author: Phone: +46-8-163995, Fax: +46-8-163979, E-mail: E-mail: linda.linderholm@mk.su.se.

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soil, water, fish, meat and human blood in the area (Kocan et al., 1994; Kocan et al., 2001; Kocan et al., 2004; Hovander et al., 2006) making this one of the world's hot-spots for contamination of PCBs.

PCBs have been known as environmental contaminants since 1966 (Anonymous, 1966; Jensen, 1972). Ten years later, PCBs were shown to be metabolized to PCB methyl sulfones (MeSO₂-PCBs) (Jensen and Jansson, 1976). The *meta*-substituted methylsulfonyl metabolite of 2,2-bis(4-chlorophenyl)-1,1-dichloroethene (3-MeSO₂-DDE) was also identified at this time. The metabolic pathway leading to aryl methyl sulfones was clarified in the early 1980's (Bakke et al., 1982). A pathway via cytochrome P-450 mediated formation of an arene oxide, and reaction with glutathione to the mercapturic acid pathway (MAP). The cysteine conjugate formed through MAP is cleaved at the cysteine C-S bond by the intestinal microflora. The thiol formed is methylated and oxidized to the corresponding methyl sulfone metabolite (Letcher et al., 2000). By far, most methylsulfonyl metabolites of PCB in biota have a 2,5; 2,3,6 or a 2,5,6 chlorine substitution pattern in the phenyl ring carrying the sulfone group. The chlorines next to the epoxide group have a stabilising effect of the epoxide.

MeSO₂-PCBs were first found in blubber from grey seals (Jensen and Jansson, 1976) but since then, they have been reported in numerous mammalian species as recently tabulated by Norström (Norström, 2006). Methylsulfonyl metabolites of PCBs and DDE have also been analysed in human blood, milk, adipose tissue, lung, liver and brain (Haraguchi et al., 1986b; Weistrand and Norén, 1997; Norén et al., 1999; Chu et al., 2003; Hovander et al., 2006). The MeSO₂-PCBs and MeSO₂-DDE are highly lipophilic leading to their accumulation in adipose tissue. However they may also bind to specific proteins, leading to strong retention in certain tissues. For example, some *para* MeSO₂-PCB congeners bind to the secretory protein (uteroglobin) present in the Clara cells in the lung of e.g. mice (Brandt and Bergman, 1981; Brandt and Bergman, 1987; Stripp et al., 1996). The function of this protein is uncertain, but it has been shown to bind progesterone (Lund et al., 1985). The MeSO₂-binding protein is also present in human lungs (Haraguchi et al., 1986a; Haraguchi et al., 1986b). One symptom among Yusho patients was respiratory distress, related to the accumulation of sulfones in the lung (Shigematsu et al., 1978; Haraguchi et al., 1986a; Haraguchi et al., 1986b), a link that has not been proven to exist.

MeSO₂-PCBs have also been found in uterine fluid bound to uteroglobin in animal studies (Brandt et al., 1982) and in seals and dolphins (Brandt et al., 1982; Troisi et al., 2001). In experiments in rats, MeSO₂-PCB causes reduction of thyroid hormone levels in serum and induction of drug metabolizing enzymes in the liver (Kato et al., 1998). Anti-estrogenic effects of some MeSO₂-PCB congeners have also been seen *in vitro* (Letcher et al., 2002). MeSO₂-DDE accumulates in fat but it also binds irreversibly to the cell constituents in *zona fasciculata* of the adrenal cortex in mice and humans after a metabolic activation of the DDE metabolite (Lund et al., 1988; Jönsson et al., 1994; Jönsson and Lund, 1994).

The present study is part of a large birth cohort study of PCBs, their metabolites, and early child development conducted in the contaminated Michalovce district and in Svidník, an area with lower PCB contamination that is located 70 km to the north. Pregnant women were recruited when they were admitted to the hospital for delivery. Maternal blood, cord blood and breast milk, as well as blood specimens from the children at 6 and 16 months, were collected (Hertz-Picciotto et al., 2003). The aim of this part of the project was to assess the most abundant MeSO₂-PCBs and 3-MeSO₂-DDE in 50 maternal serum samples and 10 cord serum samples from the two districts, to determine maternal sulfone patterns and concentrations. Further, we sought to assess transplacental transfer of the MeSO₂-PCBs and -DDE.

Materials and Methods

Samples

1103 maternal and 483 cord serum samples were collected from pregnant women living in the Michalovce (n=762) and Svidnik (background) (n=341) districts in eastern Slovakia during 2002–2004 (Hertz-Picciotto et al., 2003). Whole blood samples were collected in tubes without anticoagulants from the mothers at delivery. The samples were allowed to clot and were then centrifuged to isolate the serum. The samples were stored in glass tubes at -80°C until analysis. Based on PCB concentrations in the women, 200 of their serum samples and 100 cord serum samples were selected for OH-PCB analysis (Park et al., 2006a) and 50 out of the 200 maternal serum samples were also analysed for MeSO₂-PCB (43 from Michalovce and 7 from Svidnik). The selection of samples for these laboratory analyses was based on a stratified sample designed to represent the full range of PCB exposures, but with greater representation of the higher PCB concentrations. Cord serum samples corresponding to the 10 maternal serum samples with the highest concentrations of PCB methyl sulfones were also analysed for MeSO₂-PCB and MeSO₂-DDE metabolites.

Chemicals

The following PCB methyl sulfones were used as analytical standards: 4-MeSO₂-2,2',5,5'-tetraCB (4-MeSO₂-CB52), 3-MeSO₂-2,2',3',4',5-pentaCB (3'-MeSO₂-CB87), 4-MeSO₂-2,2',3',4',5-pentaCB (4'-MeSO₂-CB87), 4-MeSO₂-2,2',4',5,5'-pentaCB (4'-MeSO₂-CB101), 4-MeSO₂-2,2',3,4',5',6-hexaCB (4-MeSO₂-CB149), 4-MeSO₂-2,2',3,3',4',5',6-heptaCB (4-MeSO₂-CB174), 4-Me-3-MeSO₂-2',3',4',5,5'-pentaCB (4'-Me-5'-MeSO₂-CB106) and 3-MeSO₂-4,4'-DDE. The abbreviation of the PCB methyl sulfones is applied according to Norström (Norström, 2006). All analytical standards were purchased from Cambridge Isotope Laboratories, except for 4'-MeSO₂-CB87, which was synthesized in house (Bergman and Wachtmeister, 1978; Haraguchi et al., 1987). All solvents, acids and salts were of highest quality available. Silica gel, 200–400 mesh, 60Å, was purchased from Aldrich, USA.

Clean-up procedure

The method used for the extraction of PCB and PCB metabolites is described elsewhere (Hovander et al., 2000). In the present study, 2 ng of 4'-Me-5'-MeSO₂-CB106 was added as a surrogate standard (SS) to 5 g of serum. The proteins were denatured with hydrochloric acid and 2-propanol and the analytes were extracted with a mixture of n-hexane:MTBE (1:1). After re-extraction of the serum, the combined organic phases were washed with a 1% potassium chloride solution. A neutral and a phenolic fraction were received through partitioning with potassium hydroxide (0.5 M) in 50% ethanol. The neutrals (dissolved in 4 ml n-hexane) were partitioned with dried DMSO (1 ml) to isolate methylsulfonyl metabolites of PCBs and DDE from their parent compounds since aryl methyl sulfones partition into the DMSO phase as previously described (Bergman et al., 1992; Bergman et al., 1994b; Hovander et al., 2006). After separation, the DMSO phase was re-extracted with n-hexane (3 ml) and the organic phases containing neutral analytes, except for compounds with Lewis base characteristic, were combined. By addition of water (1.5 ml) and n-hexane (4 ml) to the DMSO phase, the methylsulfonyl substituted analytes were extracted from the DMSO/water phase. The DMSO/water phase was re-extracted with n-hexane (3 ml) and the combined organic phases were further cleaned up on a multilayered silica gel column. The column was packed with activated silica gel (0.1 g) in the bottom, followed by potassium hydroxide (1M):activated silica gel (1:2; 0.3 g) and, 90%^{w/w} sulfuric acid: activated silica gel (1:2; 0.8 g) on top. The silica gel was baked at 550°C overnight to activate the silica and eliminate impurities that could interfere with the analytes. The first fraction of the mobile phase, n-hexane:dichloromethane (DCM) (1:1; 7 ml), was discarded. A second fraction, with DCM (30 ml) as the mobile phase, containing methylsulfonyl metabolites of PCBs and DDE, was collected. The volume of the

second fraction from the column was reduced almost completely and the solvent was changed to n-hexane. 4'-MeSO₂-CB174 (3.4 ng) was added as an injection standard (IS) and solvent volume was reduced to 50 µl before instrumental analysis.

Instrumental analysis

The analysis was performed by gas chromatography/mass spectrometry (GC/MS) utilising a Finnigan SSQ 710 instrument (ThermoFinnigan, Bremen, Germany) connected to a Varian 3400 gas chromatograph equipped with a CTC A200S autosampler. The transfer line temperature was set to 270°C and the ion source temperature to 150°C. Automated sample injections (1 µl) were made via a split/splitless injector operated in the splitless mode for 1 minute at a temperature of 260°C. A DB-5 MS capillary column (30 m × 0.25 mm i.d., 0.25 µm film thickness; J&W Scientific) with helium as the carrier gas with a head pressure of 11 psi was used for the chromatographic separation. The column oven was programmed from 80°C (2 min), 20°C/min, to 230°C, 3°C/min, to 300°C (5 min). The instrument was operated in the electron capture negative ionization (ECNI) mode with methane (methane 5.5, AGA, Sweden) as the electron thermalisation gas at 5600 mTorr. Selected ion monitoring (SIM) was performed for the [M]⁻ and [M+2]⁻ for the methylsulfonyl PCBs with four to seven chlorines (*m/z*=367.9, 369.9; 401.8, 403.8; 435.8, 437.8; 469.7, 471.7), the 3-MeSO₂-4,4'-DDE (*m/z* 393.9, 395.9) and for the surrogate standard (SS) 3-MeSO₂-4-Me-2',3',4',5,5'-pentaCB (*m/z* 415.9, 417.9). All chromatographic data were collected, analyzed, and quantified using the proprietary ICIS2 software from Thermofinnigan. A calibration curve was run to check the linearity and the samples were then calculated in relation to one point in the calibration curve. The concentrations were corrected for the recovery of the surrogate standard.

QA/QC

Human serum was purchased from the Center for Blood Research, Sacramento (California, USA) to be used for quality control of the analysis. Relevant methylsulfonyl standards were added and the control samples were used to determine the recoveries of the analytes. One spiked control sample and one solvent blank sample were included in each batch of 10 samples.

The limit of detection (LOD) was set to three times the baseline noise. The limit of quantification (LOQ) was calculated from the lowest point of the calibration curve (0.08 pg/µl) by extrapolation until the signal for each congener was 10 times the baseline noise. The LOQs were 0.048, 0.030, 0.023, 0.040 and 0.064 pg for 3'-MeSO₂-CB87, 4'-MeSO₂-CB87, 4'-MeSO₂-CB101, 4-MeSO₂-CB149 and 3-MeSO₂-DDE, respectively, in 50 µl final volume and 1 µl injection volume. The mean recovery of the surrogate standard was 79% (SD 12.0).

Statistics

Basic statistics were calculated. Due to the skewed sampling for sulfone analysis it is not possible to present the true median concentration of MeSO₂-PCBs in the full material sampled. Hence, an estimated median was calculated based on the known median concentration of CB153 for all 1103 individuals analysed and related to the graph obtained for the maternal levels of CB153 versus ΣMeSO₂-PCBs (see Figure 3). The CB153 median was 130 ng/g fat as obtained for the 1103 samples.

Results

Median and the min-max concentrations of five MeSO₂-PCB congeners and of 3-MeSO₂-4,4'-DDE determined in Slovakian women from Michalovce and Stropkov/Svidnik districts are presented in Table 1. 3-MeSO₂-DDE was the major sulfone metabolite in 63% of the maternal serum. The dominating MeSO₂-PCB metabolite was a hitherto unidentified MeSO₂-hexaCB, with the next most abundant ones being 4'-MeSO₂-CB101, 4'-MeSO₂-CB87 and 4-MeSO₂-

CB149, respectively. The unidentified compound was quantified using the response factor of 4-MeSO₂-CB149. The mean lipid content in the maternal samples was 1.1%.

Analysis of PCB and DDE metabolites in the cord samples corresponding to the ten maternal samples with the highest concentrations of methylsulfonyl PCBs showed in seven out of 10 samples that the unknown MeSO₂-hexaCB was the most abundant PCB methyl sulfone metabolite (Table 1). However, in two cord specimens, the 3-MeSO₂-DDE was the major metabolite; and in one, 4'-MeSO₂-CB101 predominated. The same patterns were seen in the ten corresponding maternal samples. All concentration data of MeSO₂-PCB and 3-MeSO₂-DDE for the paired maternal and cord serum are given in Table 1. The mean lipid weight in the cord serum was 0.22%, one fifth of the lipid content in maternal serum. A comparison of the concentrations of MeSO₂-PCB and -DDE and CB153 and DDE in cord and maternal serum is shown in two box-and-whisker plots (Figure 1). There seems to be individual differences in the maternal/cord ratio. In six out of ten cases the ΣMeSO₂-PCBs are higher in the maternal serum compared to the cord serum but in four cases the concentration is the same or even higher in the cord sample. Data on an individual maternal/cord paired basis are illustrated in Figure 2.

Discussion

The human population in eastern Slovakia is unique due to their exposure pattern and concentrations of PCBs. This is a result of exposure to the technical PCB product, Delor, formerly produced in the area. The high levels of PCB make it rather easy to measure their methylsulfonyl metabolites in both maternal and cord blood. PCB methyl sulfones are assessed and reported for the first time in cord blood within the frame of this study. The levels of MeSO₂-PCBs in blood are partitioned to and dissolved in the blood lipids at quite low concentrations. The major sulfone metabolite in most maternal samples analysed in this study is 3-MeSO₂-DDE, followed by an as yet not identified MeSO₂-hexaCB. The median ΣMeSO₂-PCB (4 congeners) for the 50 selected maternal samples was 2.5 ng/g fat, ranging from 0.42–35 ng/g fat. Since the samples for MeSO₂-PCB analysis in the present study were not randomly selected (the higher end of the PCB distribution is over-represented in the 50 samples selected for methyl sulfone analysis) the median concentration of MeSO₂-PCBs is in reality lower. A median value reflecting the whole group of women can be estimated by linear regression analysis. In Figure 3, ΣMeSO₂-PCBs in maternal and cord serum is plotted relative to CB153 to enable us to present a more reliable median for ΣMeSO₂-PCBs in the mothers analysed (c.f. Statistics above). On the assumption that the relationship is linear, the median CB153 value in all 1103 maternal samples (130 ng/g fat) would correspond to a median ΣMeSO₂-PCB value of 1.0 ng/g fat in the whole group of pregnant women. This is clearly lower than the median (2.5 ng/g fat) obtained if the median value is calculated only on the 50 samples analysed herein.

When the maternal samples are divided into two groups, women from the contaminated Michalovce district and women from the background district Svidnik, the levels of the MeSO₂-PCBs in the Michalovce women are almost three times higher than the levels in Svidnik women. But this comparison is based on only 7 samples from Svidnik compared to 43 samples from Michalovce. A similar difference between the two groups was seen for the CB153 concentration (250 and 100 ng/g fat in Michalovce and Svidnik respectively). The observed difference is similar to what has been reported previously (Hovander et al., 2006). There is a difference in the concentration of 3-MeSO₂-DDE between the two groups as well, but the difference is less pronounced than for the MeSO₂-PCBs (Table 1). This difference is suggested to reflect the differences in agriculture in the two districts and also the proximity to Ukraine, where DDT has been frequently used (Li et al., 2006).

Methylsulfonyl metabolites of both PCB and DDE were also found in the cord samples, proving that these metabolites are transferred from the mother to the foetus through the placenta. Since the intestinal microflora and enterohepatic circulation are involved in the metabolism of PCBs to MeSO₂-PCB metabolites it is not likely that this metabolism occurs in the foetus. In wildlife, analysis of mother/foetus pairs of beluga whale blubber resulted in good correlation between the levels of methylsulfonyl metabolites in the mother and foetus suggesting transplacental transfer of the MeSO₂-PCBs (Herman et al., 2001). PCBs are known to cross the placenta, and their hydroxylated metabolites (OH-PCBs) are also found in cord blood in humans (Sandau et al., 2002; Meironyté Guvenius et al., 2003; Soechitram et al., 2004; Park et al., 2006b) but these compounds are primarily bound to proteins (Lans et al., 1993; Bergman et al., 1994a). The OH-PCBs in cord blood are probably the result of metabolism in the mother and transfer through the placenta, but metabolism in the foetus itself cannot be excluded.

The results presented herein are comparable to those from a previous study in Slovakia in which PCB and hydroxylated and methylsulfonyl metabolites were analysed in 300 adults 2003–2004 (Trnovec et al., 2004; Hovander et al., 2006). The levels of MeSO₂-PCBs in that study were higher and had a slightly different pattern than in the present study: the sum of MeSO₂-PCBs were 4.2 (0.41–100) ng/g fat and 1.5 ng/g fat (0.34–11) in Michalovce and Svidnik respectively compared to 2.6 ng/g fat (0.42–35) and 0.90 ng/g fat (0.43–2.4) in the present study. This difference is likely due to the characteristics of the study populations. The earlier study population consisted of both men and women 20–59 years of age, while the current study was comprised of a much more homogeneous group of young pregnant women. In the earlier study there was a significant difference in the PCB concentration between men and women, but not for MeSO₂-PCB. Both PCB and MeSO₂-PCB correlated with age. The relationship in concentrations between the two districts, Michalovce and Svidnik, was similar in both studies (e.g. almost three times higher in Michalovce than in Svidnik, c.f. above). In a Swedish study of potentially exposed workers and controls, median total MeSO₂-PCB concentration (17 congeners) in blood plasma was 2.3 ng/g fat, ranging between 0.8 and 5.6 ng/g fat (Weistrand et al., 1997). 4'-MeSO₂-87 was the major congener in the Swedish study, followed by 4-MeSO₂-149 and 4'-MeSO₂-101, which is different from the pattern in the present study. The difference in the composition of the major congeners might be due to the usage of different technical PCB products in the two countries. In a time trend study on organohalogen compounds performed on Swedish mothers milk from 1972 to 1992 (Norén and Meironyté, 2000), the concentrations of the sum of MeSO₂-PCBs were decreasing, from 9.24 ng/g fat in 1972, to 1.57 ng/g fat in 1992. The overall half life of MeSO₂-PCBs in humans was estimated to be 9 years. The half life for CB153 was calculated to 17 years and for DDE and 3-MeSO₂-DDE, 6 years in both cases.

In humans, the highest concentrations of MeSO₂-PCBs are found in liver followed by lung and adipose tissue (Weistrand and Norén, 1997; Chu et al., 2003). The levels of ΣMeSO₂-PCBs in human adipose and liver tissue were about 3 and 30 ng/g fat respectively in seven Swedish subjects (Weistrand and Norén, 1997). In previous studies in human tissues, *para*-MeSO₂-PCBs are more abundant than the corresponding *meta*-MeSO₂-PCBs in all tissues (e.g. adipose, lung, milk and blood) except from liver where *meta*-MeSO₂-PCBs are dominating. In liver, 5'-MeSO₂-CB132 is by far the most abundant congener, a metabolite that is found in very low concentrations in other tissues (Norén et al., 1996; Weistrand and Norén, 1997; Chu et al., 2003). This particular MeSO₂-PCB congener was not possible to quantify in the present study. Moreover, MeSO₂-CB132 and MeSO₂-CB149 are chiral and a highly enantioselective retention have been seen in human liver (Ellerichmann et al., 1998). No further studies were performed on this material to characterize chirality. Similar to the occupational exposed Swedish workers, the present study in pregnant women also identified *para*-MeSO₂-PCBs as dominant in blood compared to *meta*-MeSO₂-PCBs. In a recent study, patterns and levels of MeSO₂-PCBs in human samples from Sweden, Slovakia and Faroe Islands were discussed

(Athanasiadou et al., 2006). In contrast to the present study, analysis of samples from the Faroe Islands showed higher levels of the *meta*-MeSO₂-PCBs than the *para*-MeSO₂-PCBs and a time-trend study of Swedish samples from 1988 to 2002 showed a higher proportion of the *meta* metabolite with time. The Faroese have the highest levels of MeSO₂-PCBs, with most of their methyl sulfones probably originating from their diet of pilot whale blubber, whereas the PCB methyl sulfones in the Swedish subjects probably originate from PCBs in the diet and subsequent internal PCB metabolism. In Slovakia, the MeSO₂-PCBs may be a result of a more direct PCB exposure with internal metabolism playing a key role; hence it is difficult to explain the difference in MeSO₂-PCB patterns between Sweden and the Slovak populations in particular.

MeSO₂-PCBs and 3-MeSO₂-DDE are retained in the body not only because of their lipophilicity but also due to their capacity to bind to specific proteins. This leads to selective binding of different congeners to certain organs (e.g. liver, lung, adrenal cortex and uterus). Norén and co-workers examined MeSO₂-PCBs and 3-MeSO₂-DDE in various fractions of human plasma and found that these metabolites were, to a higher extent than the parent PCB and DDE compounds, associated with the protein rich fraction of the blood rather than with the lipoproteins (Norén et al., 1999). Comparing maternal with the corresponding paired cord samples, concentrations of MeSO₂-PCB were about 1.5 times higher in the mothers than in their cord blood on a lipid weight basis (Figure 1). This is in contrast to CB153 where the levels in maternal and cord samples are almost the same. The 3-MeSO₂-DDE concentration in the paired maternal and cord samples differ from the MeSO₂-PCB pattern since the levels of 3-MeSO₂-DDE are quite similar in maternal and cord samples: in five out of ten samples the concentration of 3-MeSO₂-DDE is even higher in the cord sample than in the maternal sample. A similar pattern is seen for the precursor, DDE. The difference between MeSO₂-PCB and PCB compared to 3-MeSO₂-DDE and DDE in maternal versus cord serum might be due to some difference in the transport over the placenta or to the different affinity to plasma proteins and lipoproteins. It is presently not possible to point out the mechanisms of retention more precisely.

The precursors of the methylsulfonyl PCBs are found in very low concentrations in the environment since the occurrence in the technical products are low and since they are metabolized due to their vicinal hydrogen atoms. For this reason, 3-MeSO₂-PCB metabolites can be more stable than their precursors. The technical PCB mixture produced at Chemko, Delors 103–106, consisted of 0.2–1% CB87, 0.3–5% CB101 and 0.05–8% CB149. Delor's content of CB153, the major PCB congener found in the environment, was 0.1–17% (Taniyasu et al., 2003). We examined MeSO₂-PCB congeners in relation to the CB153 concentration since CB153 is known to correlate well with other PCB congeners and ΣPCB. The concentrations of MeSO₂-PCBs correlated well with the CB153 concentration in both maternal and cord samples (Figure 3). The ratio between methylsulfonyl metabolites and CB153 varied from 0.05% for 3'-MeSO₂-CB87 to 1% for the unknown MeSO₂-hexaCB. Similar ratios of ΣMeSO₂-PCBs and CB153 were seen in Michalovce and Svidník (0.14 and 0.11%). The mean 3-MeSO₂-DDE/DDE ratio for the 50 maternal samples was 0.4% (0.06–2%). The correlation between 3-MeSO₂-DDE and DDE or DDT is low (not shown).

In summary, a limited number of studies on methylsulfonyl metabolites of PCBs and DDE in humans have been conducted. The present study is the first to report on MeSO₂-PCBs and 3-MeSO₂-DDE in human cord samples, showing that these metabolites are able to pass the placenta. The concentration of MeSO₂-PCBs was 1.5 times higher in maternal plasma compared to the cord samples, whilst the CB153 concentrations were about the same. For 3-MeSO₂-DDE and DDE, the levels were similar in maternal and cord serum, indicating a higher placental transfer of 3-MeSO₂-DDE than for MeSO₂-PCBs.

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Figure 1.

Box plot of data from 10 paired maternal and cord serum samples in delivering women from eastern Slovakia. Median, 25th and 75th percentile, and min-max concentrations of methylsulfonyl-PCB and -DDE are compared to CB153 and DDE levels (ng/g fat).

Figure 2.
The sum concentrations (ng/g fat) of MeSO₂-PCBs in ten maternal and their ten corresponding cord serum samples, obtained from women in Michalovce.

Figure 3.

Estimate of median levels (ng/g fat) of $\Sigma\text{MeSO}_2\text{-PCBs}$ in maternal serum (n=50) based on comparison to the median obtained for CB153 in all samples analysed (1103). The procedure is described under material and methods.

Table 1

Median and min-max concentrations (ng/g fat) of five MeSO₂-PCBs, among which one congener is not yet structurally identified, and of 3-MeSO₂-DDE in maternal serum from women living in two areas of eastern Slovakia, Michalovce and Svidnik, respectively. Maternal and cord serum concentrations are presented in ten paired samples in the lower part of the table.

Sampled 2002–2004	3'-MeSO ₂ -CB87 Median (min-max)	4'-MeSO ₂ -CB87 Median (min-max)	4'-MeSO ₂ -CB101 Median (min-max)	4-MeSO ₂ -CB149 Median (min-max)	MeSO ₂ -hexaCB Median (min-max)	ΣMeSO ₂ -PCBs Median (min-max)	3-MeSO ₂ -DDE Median (min-max)
Maternal							
Michalovce n=43	<LOQ (<LOD-1.0)	0.45 (0.08–7.1)	0.54 (0.09–6.8)	0.29 (0.04–5.6)	1.3 (0.19–21)	2.6 (0.42–35)	1.8 (0.29–9.4)
Svidnik n=7	<LOD (<LOD-<LOQ)	0.17 (0.07–0.27)	0.20 (0.09–0.81)	0.11 (0.07–0.36)	0.47 (0.17–1.2)	0.90 (0.43–2.4)	1.3 (0.25–3.3)
Cord n=10	0.26 (<LOD-0.63)	1.3 (0.10–5.5)	1.3 (0.40–2.9)	0.84 (<LOD-3.3)	4.8 (0.40–16)	10 (1.0–26)	1.7 (0.70–17)
Maternal n=10	0.41 (<LOQ-1.0)	2.0 (0.11–7.1)	2.0 (0.43–6.8)	2.3 (0.34–5.6)	7.7 (0.80–21)	17 (1.8–36)	1.7 (0.57–9.3)

^a LOQ=limit of quantification.

^b LOD=limit of detection.