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Hydroxylated polychlorinated biphenyls in human sera from adolescents and their mothers living in two U.S. Midwestern communities

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HIGHLIGHTS

- Fifty-eight OH-PCBs were assessed in serum of 85 adolescents and 74 their mothers.
- Lower-chlorinated OH-PCBs were rarely detected in serum.
- Mothers had significantly higher total OH-PCB concentrations than their children.
- 4-OH-PCB 107 and 4-OH-PCB 187 changed significantly within subject across 3 years.
- OH-PCBs did not differ between subjects from the urban vs. the rural community.

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ABSTRACT

Hydroxylated polychlorinated biphenyls (OH-PCBs) have been detected in human specimens and some are suspected as being more toxic than their parent compounds. We compared 58 OH-PCB congeners (in 51 chromatographic peaks) in serum samples from participants in the AESOP Study, a longitudinal cohort study of adolescents and their mothers living in urban and rural areas in the United States. We hypothesized that adolescents would have lower levels of OH-PCBs than their mothers and that serum concentration of OH-PCBs would be stable over a 3-year period. We found statistically significant differences in total OH-PCBs between age groups in both East Chicago ($p = 0.001$) and Columbus Junction ($p < 0.001$), with adolescents having lower concentrations than their mothers. We observed that lower-chlorinated OH-PCBs were rarely detected, suggesting that they are not retained in serum and/or rapidly biotransformed into other forms. Twelve OH-PCBs, including several that are rarely reported (4,4′-diOH-PCB 202, 4′−OH−PCB 208, and 4-OH-PCB 163) were detected in over 60% of participants. Lastly, from repeated measures within subject serum for three OH-PCBs, concentrations of 4-OH-PCB 107 and 4-OH-PCB 187 changed significantly over three years of the study.

1. Introduction

Hydroxylated polychlorinated biphenyls (OH-PCBs), the major metabolites of PCBs in humans, have been detected in human tissues and fluids (Guvenius et al., 2002; Nomiyama et al., 2010; Fangstrom et al., 2002, 2005; Hovander et al., 2002, 2006; Sandanger et al., 2004; Weiss et al., 2006; Park et al., 2007, 2009; Hisada et al., 2013; Marek et al., 2013b, 2014). Recent studies also found OH-PCBs in sediments (Marek et al., 2013a) and human waste has been proposed as a source to surface waters (Ueno et al., 2007). Our group previously demonstrated that OH-PCBs are important metabolic products of PCB 11 and PCB 3 in rats and are excreted in urine and feces (Hu et al., 2013, 2014; Dhakal et al.,

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2014). OH-PCBs were present in the original Aroclors and this may have contributed OH-PCBs to sediments (Marek et al., 2013a). Thus, OH-PCBs are both metabolic products and environmental contaminants.

Some of the OH-PCB congeners mimic endogenous thyroxine (T4) and bind strongly to transthyretin (TTR) resulting in the alteration of thyroid hormone homeostasis (Rickenbacher et al., 1986; Darnerud et al., 1996; Meerts et al., 2002). OH-PCB congeners bearing a *para*-substituted hydroxyl group and adjacent chlorine on the *meta* or *ortho* position of the biphenyl rings are more likely to cause alteration of thyroid hormone levels (Quinete et al., 2014; Tehrani and Van Aken, 2014). Some OH-PCBs decrease serum retinol transport (Brouwer and Vandenberg, 1986) and are potential endocrine disruptors (Meerts et al., 2004) and neurotoxicants (Shimokawa et al., 2006; Londono et al., 2010; Lesmana et al., 2014; Kimura-Kuroda et al., 2007).

We measured these potentially toxic compounds in a large cohort of individuals as part of the Airborne Exposure to Semivolatile Organic Pollutants (AESOP) Study (Ampleman et al., 2015). Blood samples have been collected annually since 2008 from participants, most of whom are mother-child dyads. Several households have more than one enrolled child. Participants live in East Chicago, Indiana or within Columbus Community School District, Iowa. East Chicago is a highly industrialized urban area with known high PCB contamination. Each year, about 7.5 kg PCBs volatilize from the Indiana Harbor and Ship Canal in East Chicago (Martinez et al., 2010). In contrast, the Columbus Community School District is rural with no industrial PCB contamination.

We hypothesized that many OH-PCBs are detectable in serum and that adolescents have lower concentrations than their mothers. We tested our hypothesis using an analytical method that allowed for detection of a much larger suite of OH-PCBs than has been previously examined. Most prior studies of OH-PCBs in humans have reported only a few OH-PCB congeners (Soechitram et al., 2004; Fangstrom et al., 2005; Hovander et al., 2006; Weiss et al., 2006; Park et al., 2008) including our laboratory (Marek et al., 2013b, 2014). Two exceptions are a study that measured 90 OH-PCB congeners and detected 35 in serum of Japanese women (Nomiyama et al., 2010) and another that identified 38 OH-PCBs in plasma (Hovander et al., 2002). The significant improvement of this study compared to our previous studies is our current methodology enables us to identify as many as 64 OH-PCB congeners in human serum. To our knowledge, this is the first report to compare a large number of OH-PCB congeners in adolescents and their mothers from both urban and rural areas. Several studies have investigated a specific population such as mothers, pregnant women, or residents in highly contaminated areas (Fangstrom et al., 2002; Hovander et al., 2006; Park et al., 2009; Nomiyama et al., 2010; Hisada et al., 2013). Our study advances understanding of the distribution and levels of OH-PCBs in two communities (urban vs. rural), with each community having two age groups (adolescents and their mothers). We are also able to evaluate changes in serum levels of three OH-PCB congeners over three sequential years.

2. Materials and methods

2.1. Sample collection

Serum samples collected between April 1, 2010 and March 31, 2011 from 97 adolescents (ages 14–18 years) and 86 mothers (ages 29–58 years) were available from East Chicago and Columbus Community School District. Sixteen instances of poor surrogate standard recovery resulted in the exclusion of 12 households from this analysis (25 participants). We report OH-PCB data from the remaining 33 adolescents and 30 mothers from East Chicago and 52 adolescents and 44 mothers from Columbus Junction (N = 159).

Bilingual AESOP staff from each community collected blood samples at the subjects' homes. Blood was drawn into six 5 mL Vacutainer glass tubes and allowed to clot for 30 min while capped before centrifuging to isolate serum. Samples were stored in glass vials with Teflon caps at −25 °C. Questionnaires were administered by field staff in English or Spanish as previously described (Ampleman et al., 2015). All protocols were approved by our Institutional Review Board. Written consent and assent were obtained in English or in Spanish from all participants.

2.2. Chemicals

Sixty-four calibration standards were purchased from AccuStandard (New Haven, CT) and Wellington Laboratories (Guelph, ON). 4′−OH−2,3,3′,4,5,5′-hexachlorobiphenyl (4′−OH−PCB 159) was used as a surrogate standard and 2,4,6-trichlorobiphenyl (PCB 30) and 2,2′,3,4,4′,5,6,6′-octachlorobiphenyl (PCB 204) as internal standards. Diazomethane was provided by Dr. Hans-Joachim Lehmler (The University of Iowa). All solvents used in this study were pesticide grade.

2.3. Analytical

OH-PCBs in human sera were extracted and separated from PCBs using a method described previously (Hovander et al., 2000; Marek et al., 2013b, 2014). Four grams of serum from each participant were spiked with 0.65 ng of ^{13}C-labeled PCB surrogate standards and 10 ng of 4′−OH−PCB 159 just before extraction. Extraction and separation of OH-PCBs are described in Supplementary Material (SM). PCB fractions were spiked with 0.6 ng of ^{13}C-labeled PCB surrogate standards and internal standards were added before instrument analysis. Samples were analyzed using gas chromatography-tandem mass spectrometry (GC-MS/MS) (Marek et al., 2013a).

2.4. Instrument

Methods for instrumental analysis of PCBs and OH-PCBs were previously published (Marek et al., 2013b, 2014). Briefly, PCBs and OH-PCBs (as MeO-PCBs) were analyzed and quantified using an Agilent 7000 GC-MS/MS under multiple reaction monitoring mode (MRM). Sixty-four OH-PCB standards were quantified as single or co-eluting MeO-PCBs in 57 chromatographic peaks eluting on an SPB-Octyl column. A full MeO-PCB chromatogram (Fig. S1) and full details of the precursor and product ions (Table S1) and retention times (Table S2) are presented in SM. Congener identity was confirmed using DB-5 and DB-1701 columns in a subset of 20 pooled samples.

2.5. Quality control

A quality control protocol was used during extraction and analysis. A method blank (4 mL 1% KCl) was included in each batch of 10 serum samples and underwent the same extraction, analysis and quantification processes as the serum samples. Method blanks had significantly lower levels of $\sum$OH-PCBs than samples ($p < 0.001$) and each OH-PCB congener in the blank was consistently low (mean 0.0023 ± 0.0031 ng). A limit of quantification (LOQ) for each congener was generated based on the method blank mean plus twice the standard deviation. A list of the LOQ values for the analyzed congeners is provided in SM (Table S3). Each congener mass in a sample was assigned a value of 0 if the detected mass was <LOQ. Recovery of the surrogate standard (72% ± 13%) was used to adjust for extraction efficiency.