Environment International 63 (2014) 130–136

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Polybrominated diphenyl ethers in UK human milk: Implications for infant exposure and relationship to external exposure

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ARTICLE INFO

Article history:
Received 12 August 2013
Accepted 6 November 2013
Available online 28 November 2013

Keywords:
PBDEs
Human milk
Infant exposure
BDE 209

ABSTRACT

Fourteen tri-deca polybrominated diphenyl ethers (PBDEs) were investigated in 35 human milk samples from Birmingham, UK. While none of the hepta–nona BDEs (the main components of the octaBDE technical mixture) was above the limit of quantitation (LOQ); BDE-47 (average concentration = 3.3 ng g^{-1} lipid weight (lw)) was quantified in all samples contributing 34–74% to Σtri-hexa BDEs (the principal constituents of the pentaBDE commercial formulation). BDE-209 (the main congener in the decaBDE formulation) was present above the LOQ in 69% of samples (average concentration = 0.31 ng g^{-1} lw). Concentrations of Σtri-hexa BDEs ranged from 0.2 to 26 ng g^{-1} lw with concentrations of BDE-47 > BDE-153 > BDE-99. While concentrations of Σtri-hexa BDEs in this study (average = 5.95 ng g^{-1} lw) were at the high end of those reported from other European countries, concentrations of BDE-209 were lower than those reported in human milk from other countries. The average exposure of a UK nursing infant to Σtri-hexa BDEs (35 ng (kg bw)$^{-1}$ day^{-1}) via breast milk exceeded the upper-bound dietary intakes of both UK adults and toddlers. Using a simple one compartment pharmacokinetic model, PBDE intakes of UK adults via inhalation, diet and dust ingestion were converted to predicted body burdens. Predictions compared well with those observed for Σtri-hexa BDEs and BDE-209 in breast milk.

1. Introduction

Polybrominated diphenyl ethers (PBDEs) have been extensively used as flame retardants for a wide range of consumer products including furniture, carpets, mattresses and casings for electronic equipment (BSEF, 2013). Three technical PBDE formulations were commercially available: Penta (consisting primarily of BDE-47 and BDE-99 — 38–49% each, alongside smaller amounts of other tri- to hepta-BDEs), octa (a mixture of hexa- to deca-BDEs — the exact congener composition varying substantially between the two principal formulations marketed) and deca (92–97% decabromodiphenyl ether – BDE 209 – plus nona- (principally) and octa-BDEs) (La Guardia et al., 2006). DecaBDE has dominated worldwide production with a global market demand of 56,100 t in 2001, compared to 7500 and 3790 t for pentaBDE and octaBDE formulations respectively (BSEF, 2013). Despite their utility, the persistence and bioaccumulative characters of these compounds have resulted in increasing concern over their potential adverse effects to human health (Frederiksen et al., 2009; Harrad et al., 2010). Animal studies have shown PBDEs to pose potential health risks including: endocrine disruption, neurodevelopmental and behavioral outcomes, hepatic abnormality and possibly cancer (Birnbaum and Staskal, 2004; Darnerud, 2008; Hakk, 2010; Wikoff and Birnbaum, 2011). The few data available from human epidemiological studies imply effects on: male reproductive hormones (Johnson et al., 2013; Palace et al., 2010), semen quality (Akutsu et al., 2008), thyroid hormone homeostasis (Turyk et al., 2008), cryptorchidism (Main et al., 2007), behavioral factors in pregnant women (Buttke et al., 2013), as well as lower birth weight and length (Chao et al., 2007; Lignell et al., 2013). Such evidence has contributed to complete EU bans for penta and octaBDE, and restrictions on the use of decaBDE in addition to other restrictions within several jurisdictions on the manufacture and new use of the three commercial PBDE formulations across the world (Harrad et al., 2010). Moreover, PBDEs associated with penta and octaBDE have been listed under the UNEP Stockholm Convention on POPs, while DecaBDE is currently under consideration for listing under Annexes A, B and/or C to the convention (Stockholm convention on POPs, 2009). Despite such restrictions, human exposure to PBDEs is likely to continue for the foreseeable future, given their persistence and ubiquity of flame-retarded consumer materials (Harrad and Diamond, 2006).

Several studies have reported different levels of PBDEs in various human tissues including the serum, placenta, liver, adipose tissue and breast milk from different European, Asian and North American countries in the last few years (Cui et al., 2012; Frederiksen et al., 2009). These biomonitoring data provide a direct measurement of the human body burden of BFRs resulting from various external exposure pathways (e.g. inhalation, ingestion of dust, diet and water) and contribute to the risk assessment of such compounds. However, the only available

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http://dx.doi.org/10.1016/j.envint.2013.11.009

information on BFRs in UK human samples is for tri- to hexa-BDEs (major components of the pentaBDE commercial product) where the median concentrations for Σtri-to hexa-BDEs in human milk and serum samples collected in 2003 were 6.3 and 4.18 ng g^{-1} lipid weight (lw) respectively (Kalantzi et al., 2004). In addition, BDE-209 was detected in 11 out of 153 serum samples at concentrations from 0.015 to 0.240 ng g^{-1} lw (Thomas et al., 2006).

Current understanding is that non-occupational human exposure to PBDEs occurs mainly via a combination of diet, air and indoor dust (either via ingestion or dermal contact) (Frederiksen et al., 2009; Lorber, 2008; Trudel et al., 2011). However, the extent to which the known contamination of indoor environments with PBDEs influences human body burdens remains unclear. While some studies have managed to establish significant positive correlations between the levels of PBDEs in food or indoor dust and their concentrations in human milk or serum (Dunn et al., 2010; Thomsen et al., 2008; Wu et al., 2007); such correlations could not be established in other studies (Roosens et al., 2009; Wang et al., 2013). An alternative approach involved application of a simple pharmacokinetic model to predict the body burdens of PBDEs in American adults using intake data from different exposure pathways. The predicted body burdens were then compared to the reported levels of PBDEs in human matrices and the relationship between external and internal exposure of American adults to PBDEs was discussed (Lorber, 2008).

To address this paucity of UK human biomonitoring data for PBDEs, this study reports concentrations of Σtri-hexa BDEs and *for the first time* BDE-209 in 35 human milk samples from Birmingham, UK. These data are then used to estimate the dietary exposure of UK nursing infants under different exposure scenarios. Finally, a simple, one-compartment pharmacokinetic model is applied to predict the body burdens of the studied PBDEs in UK adults (using indoor air and dust levels reported elsewhere by our research group for Birmingham, UK) (Abdallah and Harrad, 2010; Harrad and Abdallah, 2011; Harrad et al., 2006; Harrad et al., 2008a). The model predictions are then compared to the concentrations of target compounds measured in the analyzed human milk samples (used as an indicator of adult female body burdens) for further understanding of the relationship between external and internal human exposure to PBDEs in UK adults.

2. Materials and methods

2.1. Sample collection

Breast milk samples (each comprising ~50 mL) were obtained from 35 adult (aged 22–35), healthy, primiparous volunteers via Birmingham Women's Hospital Milk Bank after the study protocol was approved by Warwickshire Research Ethics Committee and the R&D Department in Birmingham Women's NHS Foundation Trust. Informed consent was obtained from all the participants before sample collection. Samples collected in January–February 2010, were kept in clean screw-capped glass containers and transferred from the Milk Bank to the laboratory in special ice boxes then stored at −20 °C until the time of analysis. Due to ethical regulations, the samples were collected in a completely anonymous fashion with all participant information kept strictly confidential. For the purpose of this study, only 1 milk sample was collected from each mother during her first 3 months of lactation. Further details on the sample collection protocol are provided in the Supplementary data section.

2.2. Sample extraction

Accurately weighted aliquots of the freeze-dried samples (~2 g) were loaded into pre-cleaned 66 mL Accelerated Solvent Extraction (ASE 300, Dionex Inc., UK) cells containing 1.5 g florisil, 3 g alumina, 5 g anhydrous Na_2SO_4 and hydromatrix (Varian Inc., UK) to fill the void volume of the cells, spiked with 25 ng of each of the ^{13}C-labeled BDE-47, BDE-99, BDE-153, BDE-183, and BDE-209 (Wellington Lab., Guelph, ON, Canada) as internal (surrogate) standards. The ASE cells were extracted with hexane:dichloromethane (1:9, v/v) at 90 °C and 1500 psi. The heating time was 5 min, static time 4 min, purge time 90 s, and flush volume 50%, with three static cycles. The lipid weight of the studied samples was determined gravimetrically on separate aliquots using a standard procedure (The European Standard EN 1528-2, 1996; see Supplementary data for more details).

2.3. Sample clean-up

The crude extracts were concentrated to 0.5 mL using a Zymark Turbovap® II (Hopkinton, MA, USA) then washed with 3 mL of 98% sulfuric acid. After phase separation, the hexane layer was transferred onto a florisil column topped with sodium sulfate and eluted with 25 mL of hexane:dichloromethane (1:1, v/v). The eluate was evaporated to dryness under a gentle stream of N_2 and the dried extract reconstituted in 200 μL of ^{13}C-BDE-100 (25 pg μL^{-1} in methanol) used as a recovery determination (or syringe) standard to determine the recoveries of internal standards for QA/QC purposes.

2.4. LC–APPI–MS/MS analysis

Sample analysis was carried out using an LC–MS/MS system composed of a dual pump Shimadzu LC-20AB Prominence liquid chromatograph equipped with an SIL-20A autosampler, a DGU-20A3 vacuum degasser coupled to a Sciex API 2000 triple quadrupole mass spectrometer. Details of the multi-residue analytical methodology used for separation and quantification of the studied PBDEs (28, 47, 85, 99, 100, 153, 154, 183, 196, 197, 203, 206, 207, 208 and 209) can be found elsewhere (Abdallah et al., 2009) (a brief description is given in the Supplementary data section).

2.5. Comparison of PBDE intake to human body burdens

We have previously estimated UK adult intake of the target PBDEs via inhalation, dust ingestion and diet (Harrad and Abdallah, 2011; Harrad et al., 2006, 2008a,b) (a summary of the assumptions on which these estimations are based is provided as Supplementary data). To examine the relationship between these estimated intakes and the body burdens indicated via human milk samples, a simple one-compartment, first order pharmacokinetic (PK) model was used. The studied PBDEs were hypothesized to accumulate in lipids (the single compartment in the model). Therefore, the change in PBDE lipid concentration over time can be expressed by Eq. (1) (Lorber, 2008).

$$\frac{\delta C_{PBDE}}{\delta t} = \frac{I_{PBDE}(t) \times AF_{PBDE}}{BL(t) - K_{PBDE} \times C_{PBDE}(t)} \quad (1)$$

where C_{PBDE} is the compound specific concentration in lipids (ng g^{-1} lw); I_{PBDE} is the daily intake of the target BFR (ng day^{-1}); AF_{PBDE} is the absorption fraction (unitless); BL is body lipid mass (g) and K_{PBDE} is the compound specific first order dissipation rate (day^{-1}).

If K_{PBDE} is assumed to be constant over time then Eq. (1) can be solved into:

$$C_{PBDE}(t) = C_{PBDE}(0) \times e^{(-K_{PBDE} \cdot t)} + \left[\frac{(I_{PBDE}(t) \times AF_{PBDE})}{BL(t)}\right] \times \left[\frac{\left(1 - e^{(-K_{PBDE} \cdot t)}\right)}{K_{PBDE}}\right] \quad (2)$$

where C_{PBDE} (0) is the studied PBDE body lipid concentration at time 0 (initial concentration before intake).

Assuming a constant dose over time at constant body lipid mass, the steady state PBDE lipid concentration can be calculated from Eq. (3). It is