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Regional variation and possible sources of brominated contaminants in breast milk from Japan

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ABSTRACT

This study focuses on the regional trends and possible sources of brominated organic contaminants accumulated in breast milk from mothers in southeastern (Okinawa) and northwestern (Hokkaido) areas of Japan. For persistent brominated flame retardants, polybrominated diphenyl ethers (PBDEs; major components, BDE-47 and BDE-153) were distributed at higher levels in mothers from Okinawa (mean, 2.1 ng/g lipid), while hexabromobenzene (HeBB) and its metabolite 1,2,4,5-tetrabromobenzene were more abundantly detected in mothers from Hokkaido (0.86 and 2.6 ng/g lipid), suggesting that there are regional differences in their exposure in Japan. We also detected naturally produced brominated compounds, one of which was identified as 2′-methoxy-2,3′,4,5′-tetrabromodiphenyl ether (2′-MeO-BDE68) at higher levels in mothers from Okinawa (0.39 ng/g lipid), while the other was identified as 3,3′,4,4′-tetrabromo-5,5′-dichloro-2,2′-dimethyl-1,1′-bipyrrole in mothers from Hokkaido (0.45 ng/g lipid). The regional variation may be caused by source differences, i.e. southern seafood for MeO-PBDEs and northern biota for halogenated bipyrroles in the Japanese coastal water.

1. Introduction

Persistent organic pollutants (POPs) are biomagnified in the food chain (Borgå et al., 2001). Irrespective of the nature of their source, they are widespread and probably undergo extensive transport and fates that are governed by their physicochemical properties such as vapor pressure, aqueous solubility, Henry's Law constant and octanol/water partition coefficient (K_{ow}) (Hackenberg et al., 2003; Tittlemier et al., 2004; Vetter et al., 2004). As a result, their residues accumulate in the human body by way of dietary intake or inhalation throughout a person's lifetime. Therefore, regular monitoring of POP contamination in human milk can help to identify specific sources of pollutants, exposure trends and potential risks of exposure to mothers and infants.

It seems likely that bioaccumulative brominated flame retardants (BFRs), such as polybrominated diphenyl ethers (PBDEs), hexabromocyclododecane and hexabromobenzene (HeBB) are globally spreading throughout the marine biosphere. Some of these compounds have been reported to transfer via the placenta and breast milk from mothers to offspring in humans and exhibit endocrine-disrupting effects (Kawashiro et al., 2008) or developmental neurotoxic effects (Costa and Giordano, 2007). In Japan, PBDEs have been used to prevent combustion in consumer products, such as electronics, construction materials and textiles (Ueno et al., 2004), but have leveled off in recent years after voluntary phasing out of penta- and octa-PBDE formulations in the 1990s (Ueno et al., 2010). The residue levels of PBDEs have recently been reported in human milk (Eslami et al., 2006; Haraguchi et al., 2009c) and blood (Kawashiro et al., 2008) as well as in seafood from Japanese coastal water (Ueno et al., 2004). The sources are probably house dust and/or electric waste (Fromme et al., 2009; Thomsen et al., 2010) as well as seafood (Ueno et al., 2004). Although the temporal trends in human exposure to PBDEs are steadily decreasing in Japan, the current status of BFR use seems to differ from region to region and from country to country (Watanabe and Sakai, 2003). Similar to PBDEs, HeBB has been used as an additive flame retardant for paper, plastic and electronic goods and is still used at low volumes in Japan (350 tons per year between 1994 and 2001) (Watanabe and Sakai, 2003). Thus far, the levels of HeBB in adipose tissues of Japanese people have been reported (Yamaguchi et al., 1988), but no recent trends for HeBB levels in breast milk are available.

Regarding related organobromine residues, methoxylated PBDEs (MeO-PBDEs) and halogenated bipyrroles of natural origin have been found in biota from Japanese coastal water (Haraguchi et al., 2009b; Marsh et al., 2005). MeO-PBDEs can biomagnify in higher-trophic

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organisms via the food chain from the Pacific Ocean (Haraguchi et al., 2010; Vetter et al., 2009). A series of mixed halogenated bipyrroles, i.e. 1,1′-dimethyl-3,3′,4,4′-tetrabromo-5,5′-dichloro-2,2′-bipyrrole (DBP-Br_4Cl_2) and 2,3,3′,4,4′,5,5′-heptachloro-1′-methyl-1,2′-bipyrrole (MBP-Cl_7), have also been found to biomagnify at higher-trophic levels via the food chain to similar extents to recalcitrant POPs. In fact, these two bipyrroles have been found in fish, seabirds and marine mammals from the North Pacific (Gribble et al., 1999; Tittlemier et al., 2002; Tittlemier, 2004) and Oceania (Vetter et al., 2001, 2009), owing to their similar physical properties to PBDEs (Hackenberg et al., 2003; Tittlemier et al. 2004; Vetter et al., 2004). Therefore, human exposure to these brominated compounds is of concern for the health of mothers and infants, because DBP-Br_4Cl_2, for example, has displayed some *in vitro* dioxin-like ability (Tittlemier et al., 2003). However, the regional trends in the contamination status of MeO-PBDEs and halogenated bipyrroles in human breast milk are poorly understood.

The aim of this study was to investigate the trends and sources of anthropogenic PBDEs and HeBB, as well as naturally occurring MeO-PBDEs and halogenated bipyrroles, in human breast milk from Japan. To investigate the regional trends in these brominated contaminants, we selected human milk samples from the most northeast area (Hokkaido) and the most southwest area (Okinawa) of Japan (Fig. 1).

2. Materials and methods

2.1. Sample collection

Human milk samples were obtained from the Kyoto University Human Specimen Bank using a standardized protocol (Koizumi et al., 2005, 2009). A total of 40 samples were collected during 2005–2006 from volunteers living in Hokkaido ($n = 20$) and Okinawa ($n = 20$) as shown in Table 1. Milk samples (30–50 mL) were collected manually during breastfeeding at 4–8 weeks after childbirth, either by the subjects themselves or with the assistance of midwifes. The breast milk was kept frozen (−20 °C) prior to analysis. The Ethics Committee of Kyoto University approved the protocol of the present study (E25) and appropriate written informed consent was obtained from all the participants.

Table 1
Information regarding the participants and lipid contents of milk samples from Hokkaido and Okinawa.

Region	Location		Year	*n*	Mean age	Lipid (%)
	Latitude	Longitude				
Hokkaido	42–90′N	140–99′E	2005	20	30.5	2.30
Okinawa	26–20′N	127–69′E	2005–2006	20	30.3	2.63
All				40	30.4	2.45

2.2. Chemicals

Two standards, 4′-methoxy-2,3′,4,5′,6-pentachlorodiphenyl ether (4′-MeO-BDE121), as an internal standard for the determination of all brominated contaminants, and 2,2′-dimethoxy-3,3′,4,4′-tetrabromobiphenyl (2,2′-diMeO-BB80) were donated by Dr. G. Marsh (Stockholm University). Native BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, BDE-154, hexabromobenzene (HeBB), 1,2,4,5-tetrabromobenzene (TeBB), 2′-hydroxy-2,3′,4,5′-tetrabromodiphenyl ether (2′-MeO-BDE68) and 6-methoxy-2,2′,4,4′-tetrabromodiphenyl ether (6-MeO-BDE-47) were purchased from Cambridge Isotope Laboratories (Andover, MA, USA). Two bipyrrole standards, 1,1′-dimethyl-3,3′,4,4′-tetrabromo-5,5′-dichloro-2,2′-bipyrrole (DBP-Br_4Cl_2) and 2,3,3′,4,4′,5,5′-heptachloro-1′-methyl-1,2′-bipyrrole (MBP-Cl_7), were synthesized according to the methods outlined in Gribble et al. (1999) and Wu et al. (2002), respectively. The purities of the compounds were >99% by gas chromatography. The standards were used for the calibration, recovery and quantification of target compounds. All solvents of pesticide grade quality were purchased

Fig. 1. Sampling sites of breast milk in Japan (Hokkaido and Okinawa Prefecture).