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SOURCES AND HUMAN EXPOSURE TO POLYBROMINATED DIPHENYL ETHERS

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ABSTRACT

Polybrominated diphenyl ethers (PBDEs) are a class of widely used flame retardants that are incorporated into a wide range of consumer products such as household appliances, plastics, textiles and computers, to prevent fire. They were first introduced in the environment in the 1970s and their concentrations have been increasing ever since. Their persistence in the environment, widespread distribution and bioaccumulation in humans and wildlife has rendered them chemicals of concern.

The main route of entry of these chemicals into the human body is via the food web, but occupational exposure may also occur in the workplace during handling, repair and dismantling of flame retarded goods. Inhalation of indoor air and dermal uptake may also be another important route of entry of PBDEs into humans.

PBDEs structural similarities to better known and studied chemicals like PCBs, are causes for concern. Individual PBDE congeners have been associated with neurotoxic effects following neonatal exposure in animals and effects on thyroid hormone function. PBDEs have also been associated with non-Hodgkin's lymphoma in humans, teratogenicity and fetal toxicity. There are still many toxicity gaps, including their carcinogenic potential and human health effects.

This paper reviews the sources and exposure of humans to PBDEs, highlighting recent scientific data.

KEYWORDS: polybrominated diphenyl ethers, environmental levels, human exposure, sources.

1. INTRODUCTION

PBDEs belong to a larger family of chemicals known as persistent organic pollutants (POPs), which have low water solubilities, high lipophilicity and tend to bioaccumulate in fatty tissues and persist in the environment. PBDEs are the most widely used additive flame retardants. They are blended with the polymeric material, which makes them more likely to leach out and volatilise into the environment (McDonald, 2002). PBDEs are mainly used in polyurethane foams, television sets, computers, radios, textiles, paints and plastics to reduce fire risk. Their mechanism of action is decomposition before the matrix of the polymer following heat application, achieving the prohibition of flammable gas formation (Rahman *et al*., 2001). PBDEs were first detected in biota in fish from Sweden (Andersson and Blomkvist, 1981) and their concentrations have been shown to increase in the environment during the 1980s, 90s and 00s (Meironyté *et al*., 1999).

PBDEs are structurally similar to PCBs and consist of two diphenyl rings joined with an oxygen atom. Like PCBs, there are 209 BDE congeners, produced by brominating diphenyl ether in the presence of a catalyst (Om *et al*., 1996). They have low vapour pressures and water solubility (both inversely proportional to the degree of bromination), high lipophilicity and are persistent in the environment (de Wit, 2002). Over the last two decades there have been indications of increased environmental PBDE concentrations, although their levels are still generally lower than those of PCBs, due to different usage volumes (De Wit, 2002).

Exposure to PBDEs gives rise to adverse effects in experimental in vivo models, such as developmental neurotoxicity, altered thyroid hormone homeostasis, foetal toxicity/teratogenicity in rats and rabbits and morphological effects in the thyroid, liver and kidney of adult animals. Little is known about the human effects and toxicokinetics of PBDEs, as well as their carcinogenicity (Darnerud, 2003).

PBDE metabolism studies have concentrated on experimental rodents (rats and mice) aquatic organisms (fish, mussels and bacteria) and human liver microsomes. Oxidative metabolism of PBDEs is likely to be taking place, as indicated by the presence of detectable residues of OH-PBDEs in the blood of PBDE exposed wildlife (Burreau *et al*., 2000). Thyroid hormone-like OH-PBDE congeners have been shown to bind competitively with human transthyretin (TTR), a transport protein for thyroid hormones (Brouwer *et al*., 1998). In rats and fish oxidative debromination of BDE-209 and/or BDE-99 is also occurring (Hakk and Letcher, 2003). Photolytic debromination has been observed in experimental conditions (Soderstrom *et al*., 2004), and more recently in biota (LaGuardia *et al*., 2007), indicating that it may be occurring in the environment.

2. PRODUCTION AND USE

PBDEs were first manufactured and used in the early 1970s. They are produced at three different degrees of bromination: penta- (penta-BDE), octa- (octa-BDE) and decabromodiphenyl ether (deca-BDE). Deca-BDE is mainly used in polymers such as polycarbonates, polyester resins, polyolefins, polyvinyl chloride and rubber, octa-BDE in ABS resins and penta-BDE in polyurethane foam and textiles (Alaee *et al*., 2003).

Commercial penta-BDE consists of 50-62% penta-BDE, 24-38% tetra-BDE and 4-8% hexa-BDE, whereas the commercial octa-BDE consists of 43-44% hepta-BDE, 31-35% octa-BDE, 10-12% hexa-BDE and 9-11% nona-BDE. Commercial deca-BDE is typically composed of 97-98% deca-BDE and 0-1% octa-BDE (WHO, 1994). In terms of individual congeners, more than 70% of penta-BDE is composed of BDEs 47 and 99, with BDEs 28, 100, 153 and 154 contributing smaller amounts (Alaee *et al*., 2003). BDE-183 is the major congener found in the octa-BDE formulation and deca-BDE consists almost entirely of BDE-209 (Alaee *et al*., 2003).

Deca-BDE is by far the most widely used PBDE in Europe and the rest of the world. In Asia and the Americas 23,000 tonnes of deca-BDE are consumed annually, whereas in Europe 7,500 tonnes. Octa-BDE and penta-BDE are mostly used in Asia and the Americas, followed by Europe. Asia accounts for 56.2% of global PBDE production, the Americas for 29% and Europe for 15%, 10% of which is consumed in the United Kingdom (BSEF, 2000).

DecaBDE may be the most commonly used PBDE mixture, but it is poorly absorbed and does not significantly bioaccumulate in wildlife. However, it can be photolytically decomposed to lower brominated congeners, such as BDE-47. The latter is the most commonly occurring congener in the environment and an important constituent of the penta-BDE mixture, mostly used in flame-retarding polyurethane foam in furniture. In the European Union, both penta- and octa-BDE have been banned under Directive 76/769 on restrictions of marketing and use (European Union, 2004). 10 US States have also banned the penta- and octa-products.

3. ENVIRONMENTAL LEVELS

Environmental release of PBDEs may occur at any time during the manufacture, use, recycling, disposal or incineration of flame-retarded products. Unfortunately, little information is available from the industry on PBDE emissions, so any attempts to quantify releases into the environment are difficult (Alcock *et al*., 2003; Sakai *et al*., 2006). Since they are not chemically bound to the products they are used in, PBDEs are prone to leaching out and volatilising in the environment. Once released, they can be transported by air to such remote and far away from point sources regions like the Arctic and the Antarctic (Ikonomou *et al*., 2002; Corsolini *et al*., 2006).

The environmental distribution and partitioning of PBDEs varies according to their individual physicochemical properties. More brominated and heavier congeners such as BDE-209 tend to stay in soil, sediments and sewage sludge, whereas the lighter and less brominated congeners such as BDE-47 are deposited in plants and can re-volatilise and bioaccumulate up the foodchain. Congener composition varies in different matrices. In biota BDEs 47, 99, 100, 153 and 154 usually make up about 75% of the total PBDE levels, whereas in indoor air and sediments BDE-209 is the predominant congener. The higher up the foodchain, the larger the % certain congeners make up in an organism due to biomagnification.

PBDEs were first detected in the environment in sewage sludge (DeCarlo, 1979) and since then they have been found in virtually every part of the environment: in air (Lee *et al*., 2004), water (Oros *et al*., 2005), terrestrial mammals and birds (Sellström *et al*., 1993), marine mammals (Haglund *et al*., 1997), fish (Hale *et al*., 2001), sediments (Covaci *et al*., 2005) and humans (Kalantzi *et al*., 2009; Thomas *et al*., 2006). The number of individual PBDEs found in the environment is much lower than that for PCBs, because the three commercial mixtures contain only a limited number of congeners, compared to PCBs (Hooper and McDonald, 2000).

Time trend studies in humans have been performed using serum (Thomsen *et al*., 2002; Sjödin *et al*., 2004) and breast milk (Meironyté *et al*., 1999; Akutsu *et al*., 2003; Fängström *et al*., 2008), and have all shown an increase over the years, until the 1990s. In humans typical mean ΣPBDE concentrations range from 1.74 ng g^{-1} lipid in serum from Japan (Inoue *et al*., 2006) and 6.38 in breast adipose from Belgium (Naert *et al*., 2006) to 77.5 ng g^{-1} lipid in breast adipose from California, USA (She *et al*., 2004) . A summary of PBDE concentrations in non-occupationally exposed adults is presented in Table 1. It is interesting to note that levels in North America are much higher than those in Europe and Asia, probably due to the use of the penta-BDE product, which has been banned in Europe.

Table 1. Concentrations (in ng g^{-1} fat) of ΣPBDEs in non-occupationally exposed humans

Tissue	Location	Year	n	mean	Reference
Adipose	USA (California)	1995-8	152	134	Petreas *et al*., 2011
Adipose	Belgium	2000	20	4.75	Covaci *et al*., 2002
Adipose	Belgium	2001-3	53	6.38*	Naert *et al*., 2006
Adipose	Spain	2003	20	3.85	Fernandez *et al*., 2007
Adipose	Brazil	2004	32	1.89	Kalantzi *et al*., 2009
Adipose	Italy	2005-6	12	11	Schiavone *et al*., 2010
Adipose	Czech Republic	N/A	98	3.1*	Pulkrabová *et al*., 2009
Breast milk	Russia	2000-2	37	0.47/0.71	Polder *et al*., 2008
Breast milk	Italy	2000-1	4 (pools of 40)	2.75	Ingelido *et al*., 2004
Breast milk	Sweden	2000-1	15	2.14*	Guvenius *et al*., 2003
Breast milk	Norway	2000-2	29	4.1*	Polder *et al*., 2008
Breast milk	Canada	2001-2	98	22	Pereg *et al*., 2003
Breast milk	Germany	2001-3	93	2.23	Vieth *et al*., 2004
Breast milk	UK	2001-3	54	8.9	Kalantzi *et al*., 2004
Breast milk	Indonesia	2001-3	30	2.2	Sudaryanto *et al*., 2008a
Breast milk	Spain	2002	15	2.41	Schuhmacher *et al*., 2004
Breast milk	Hong Kong	2002-3	238 (10 pools)	3.4	Hedley *et al*., 2010
Breast milk	Australia	2002-3	157 (17 pools)	10.2	Toms *et al*., 2007
Breast milk	Mexico	2003	7	4.4	López *et al*., 2004
Breast milk	USA (California)	2004	16	77.5	She *et al*., 2004
Breast milk	Norway	2003-9	393	2.1*	Thomsen *et al*., 2010
Breast milk	China	2004	19	2.5	Sudaryanto *et al*., 2008b
Breast milk	USA	2004-6	331	51*	Daniels *et al*., 2010
Breast milk	Japan	2005	89	1.56	Inoue *et al*., 2006
Breast milk	China	2005	205 (23 pools)	1.2	Li *et al*., 2008
Breast milk	Germany	2005	42	1.9	Raab *et al*., 2008
Breast milk	USA (New Hampshire)	2005-6	40	35.5	Dunn *et al*., 2010
Breast milk	China	2006	80 (pooled)	2.83	Zhu *et al*., 2009
Breast milk	China	2006-7	158	2.24-4.16	Sun *et al*., 2010

*median; N/A: not available

Table 1. Concentrations (in ng g^{-1} fat) of ΣPBDEs in non-occupationally exposed humans (continued)

Tissue	Location	Year	n	mean	Reference
Breast milk	USA (Texas)	2007	30	57.6	Schecter et al., 2010a
Breast milk	Taiwan	2007	20	2.65	Horng *et al., 2010*
Breast milk	Taiwan	2007-8	46	3.59	Chao *et al*., 2010
Breast milk	China	N/A	27	3.5*	Bi *et al*., 2006
Breast milk	Korea	N/A	17	130	Kang *et al*., 2010
Serum	Norway	1999	29	3.34	Thomsen *et al*., 2002
Serum	Faroe Islands	1999	2 (pools of 10)	8-8.4*	Fängström *et al*., 2005
Serum	USA (California)	1999-2000	270	26.5*	Chevrier *et al*., 2010
Serum	Netherlands	2001-2	78	10.7	Weiss *et al*., 2004
Serum	USA (New York, New Jersey)	2001-3	93	24.6	Morland *et al*., 2005
Serum	New Zealand	2001	23	7.17	Harrad and Porter, 2007
Serum	UK	2003	154	5.6*	Thomas *et al*., 2006
Plasma	Mexico	2003	5	29.1	López *et al*., 2004
Serum	USA	2003-4	2062	291	Sjödin *et al*., 2008
Maternal Serum	Spain	2003-4	113	9.7-12*	Gómara *et al*., 2007
Paternal Serum	Spain	2003-4	104	12*	Gómara *et al*., 2007
Maternal serum	Spain	2003-5	174	14	Vizcaino *et al*., 2011
Serum	Romania	2005	1 (pool of 192)	1.04	Dirtu *et al*., 2006
Serum	Japan	2005	89	2.89	Inoue *et al*., 2006
Serum	China	2006	156 (12 pools)	613	Zhu *et al*., 2009
Serum	Belgium	2007	19	1.9*	Roosens *et al*., 2009
Serum	Greece	2007	31	0.96*	Kalantzi *et al*., 2011
Serum	China	N/A	21	4.4*	Bi *et al*., 2006

*median; N/A: not available

4. ROUTES OF EXPOSURE

PBDEs may enter the human body through a variety of routes: indoor air, indoor dust, dermal uptake and food. The latter is considered the main route of entry, particularly through the consumption of contaminated fish (Törnkvist *et al*., 2011) and sea food. High serum and human breast milk levels of PBDEs were correlated to a high consumption of fatty fish in Sweden and Japan (Sjödin *et al*., 2000; Ohta *et al*., 2002). Market basket studies have estimated a total daily intake of PBDEs by food to be 97 ng day^{-1} in Spain (Bocio *et al*., 2003), 51 ng day^{-1} in Sweden (Darnerud *et al*., 2006), 44 ng day^{-1} in Canada (Ryan and Patry, 2001), 35 ng day^{-1} in Belgium (Voorspoels *et al*., 2007) and 50 ng day^{-1} in the United States (Schecter *et al*., 2010b). PBDEs have also been detected in other food products such as fish, meat, eggs, dairy products, but at relatively lower concentrations than fish (Ohta *et al*., 2002; Schecter *et al*., 2006). The fact that PBDE levels are not correlated PCB levels in most studies, further indicates that their sources are different (which in the case of PCBs is primarily via food) and points towards other sources of exposure in humans.

Since most flame-retarded goods are made for indoor applications (at home, in the workplace, or in vehicles) and humans spend a great deal of their daily lives indoors, inhalation of contaminated air and dust from flame retarded products could play a key role in human exposure. Recent studies have found a positive relationship between PBDE concentrations in human plasma (Karlsson *et al*., 2006), breast milk (Wu *et al*., 2007) and household dust, supporting the hypothesis that indoor air dust plays an important role in the exposure of humans to PBDEs. Another study investigated the role of indoor air by means of analysing dust and dryer lint from homes and found lower levels of PBDEs than in dust from the same houses, but no correlation between total PBDEs in dryer lint and total PBDEs in house dust (Stapleton *et al*., 2005). A more recent study studied the air in passenger cars and observed that BDE-209 was the dominating congener (Mandalakis *et al*., 2008). PBDEs in car air were highest in newer models, as observed by a significant positive correlation between log-normalized ∑PBDE concentrations and the year of manufacture.

In general, PBDE concentrations in the air of homes seem to be an order of magnitude higher in North America, than in Europe and Asia (Harrad *et al*., 2006; Wilford *et al*., 2004), with BDE-209 again being the dominant congener. Air exposure to PBDEs can be through inhalation of compounds in the gas or particle phase. There can also be a direct exposure via dermal absorption by direct contact with flame-retarded goods, or by contact with house dust (Johnson-Restrepo and Kannan, 2009). Dermal contact can be responsible for up to 35% of the total PBDE exposure (Webster et al., 2005). A study which examined the dermal uptake of PBDEs to the hands from everyday routine behaviour, concluded that hand to mouth transfer may provide additional exposure at rates comparable to dietary sources (Stapleton *et al*., 2007).

Occupational exposure during handling, repairing and dismantling of flame-retarded products is also considered an important route of uptake of PBDEs in the body of exposed workers. A Swedish study observed that computer technicians have higher PBDE levels in their blood than computer clerks and hospital cleaners (Jakobsson *et al*., 2002), which indicates that PBDEs used in computers and electronics contaminate the working environment and accumulate in workers. The same study observed a correlation between some higher brominated PBDE congeners and the duration of computer work, which makes it reasonable to assume that more work with computers leads to higher PBDE exposure. PBDEs have also been found in dust fractions from an electronics dismantling facility in Sweden, with the highest concentrations in the inhalable fraction (Julander *et al*., 2005) and also in hair of individuals working in electronic waste recycling facilities in China (Ma *et al*., 2011). PBDEs have also been detected in electronic waste (e-waste) from recycling plants (Morf *et al*., 2005), autoshredder waste (Petreas *et al*., 2005) and in air and dust in electronic waste storage facilities (Muenhor *et al*., 2010). Other groups of people with higher burdens of PBDEs because of their occupation are foam recyclers and carpet installers (Stapleton *et al*., 2008) and aircraft cabin personnel (Christiansson *et al*., 2008).

Despite being a large and unstable molecule with a relatively short half-life, BDE-209 has been measured in human breast milk and serum, which indicates that humans are exposed to it via food and indoor air and dust inhalation. Amongst exposed individuals, children are more at risk due to their increased contact with dusty surfaces and their frequent hand-to-mouth behaviours. A study of a family of four in California found the highest PBDE concentrations in the youngest child (Fischer *et al*., 2007). BDE-209 levels in the child were comparable to levels found in occupationally exposed workers in Sweden (Thuresson *et al*., 2005). Infants are also at greater risk of exposure from their mothers. A study investigating maternal and foetal blood from umbilical cords observed similar PBDE levels, implying that these chemicals can be transferred from mother to baby across the placenta (Mazdai *et al*., 2003).

5. CONCLUDING REMARKS

Despite PBDEs' protective use against fires, their increasing levels, persistence, bioaccumulation in the environment and toxicity potential has raised concerns. Humans come into contact with these chemicals in their everyday life from a variety of consumer products and studies have indicated that exposure via indoor air and dust may be of particular significance, in addition to dietary intake. More data is needed on the possible sources and emissions of PBDEs, as well as on the toxicity of individual PBDE congeners and human exposure.

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