Polybrominated Diphenyl Ethers
(PBDEs)

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Introduction

Polybrominated diphenyl ethers are a group of commercially produced substances that are used as flame retardants in a wide range of consumer products including television sets, computers, printers, fax machines, carpets, and upholstery. They are structurally related to PCBs and, like PCBs, are produced commercially as mixtures of various chemical configurations, or congeners. Different congeners contain various degrees of bromination, which in turn influence their bioavailability, bioaccumulation potential, persistence, and toxicological properties.

Although PBDEs contain structural similarities to PCBs, they have been far less studied from a toxicological perspective and are released into the environment in a very different manner. Research has shown that PBDE mixtures are released from consumer products as these products deteriorate with age[1]. Since PBDEs are used only as additives in other materials, they may leach out of products or volatilize into the environment over many years[2].

The human health effects of exposure to PBDEs have not been well studied. It is not known whether PBDEs cause adverse health effects in humans at environmentally relevant levels.

Exposure to PBDEs

Exposure may occur through a number of different pathways. Diet is likely one major source of human exposure, with the consumption of contaminated fatty animal foods, such as meat, fish, and dairy products providing the largest source of dietary exposure[3]. PBDEs accumulate in the fat tissues of animals and enter the food chain when animal products are consumed.

It has also been suggested that humans may be exposed to PBDEs through ingestion of dust, or by inhalation of some PBDE congeners at home or at a job in the electronics and computer industries. PBDEs have been detected in indoor dust, giving rise to the possibility of transfer via inhalation of the particulate matter in indoor air and the ingestion of dust[4]. Recently, the indoor environment has been shown to play a prominent role in human exposure to PBDEs[5]. The results of recent studies suggest that ingestion of house dust is a large contributor to exposure for children and adults[5-7].

The presence of low levels of PBDEs in human breast milk and blood indicates that people are being exposed to PBDEs. Developing fetuses and infants may be exposed through transfer of maternal PBDEs, which are able to cross the placenta and enter into fetal circulation. Infants may be exposed through contaminated breast milk.

Temporal trend in PBDE levels

Levels of PBDEs in milk and blood serum have been increasing rapidly throughout industrialized countries. Positive significant correlations with year of sample collection show that the concentrations are rising in human serum samples in the United States[8]. Examination of Swedish human milk samples from 1972 to 1997 showed an exponential increase in PBDE levels with a doubling rate of about 5 years[9]. Levels of PBDEs in human milk samples from Canadian women appear to follow this upward trend (Table I). Further, results from individual milk samples collected in the Vancouver, British Columbia area show an increase of more than an order of magnitude over 10 years[10]. Several authors have reported a greater individual variation with levels of PBDEs in breast milk compared to other persistent organic pollutants. The widely varying levels in humans suggest that diet is not the only route of exposure.

Table 1. *Total PBDEs in human milk samples from Canada (ng/g lipid)*[10]

Year	Sample size	Median	Range
1982	P; n=200	<0.2	---
1986	P; n=100	0.6	---
1992	I; n=72	3.0	0.6-580
2001-2002	I; n=98	22.0	0.8-956

P: pooled samples, I: individual samples

Table 2. *Total PBDEs in human milk from the Nunavik region of Quebec (ng/g lipid)*[10]

Year	Sample size	Median	Range
1989-1991	I; n=20	1.7	*ND-14
1996-2000	I; n=20	6.8	0.2-318

*non-detectable

Absorption, distribution, metabolism, and excretion

The toxicokinetics of PBDEs vary with the congener in question. In rodents, deca-BDE, the major commercial product, is poorly absorbed from the gastrointestinal tract and rapidly eliminated, mainly through the feces. The extent to which deca-BDE is metabolized in humans is not known. In contrast, the lower brominated congeners, such as penta-BDE and octa-BDE, are readily absorbed and only slowly eliminated in rodents. Half-lives of lower brominated congeners are long in rodents, suggesting that the lower BDEs may also persist in humans. All PBDEs appear to undergo metabolism, producing hydroxylated and methoxylated metabolites. The extent of metabolism depends on the degree of bromination, as well as the route of exposure[11].

Toxicity

Due to the structural similarities between PBDEs and PCBs, PBDEs likely share certain neurotoxic and endocrine disrupting properties with PCBs[12]. Reported endocrine disrupting activity includes effects on thyroid function *in vivo*, observed as induction of thyroid hyperplasia or induction of thyroid production[8]. Certain PBDE congeners are able to displace thyroxine (T_4) from transthyretin *in vitro* after conversion to metabolites[12]. PBDE metabolites may also have estrogenic activity. Hydroxylated PBDE metabolites are able to induce the estrogen receptor signal transduction pathway *in vitro*, using a human breast cancer cell line[12]. It is difficult to isolate the effects of PBDEs in humans, as different persistent organic pollutants may share similar mechanisms for toxicity; however, preliminary data has suggested that levels of thyroid hormones in human serum may be affected by PBDE exposure.

PBDEs can cross the placenta and may also have developmental toxicity upon maternal exposure. At doses 6-29x higher than the highest levels reported in human breast adipose tissue, exposure of female rats to PBDE-99 during gestation caused hyperactivity in the offspring. Exposure to low doses during development also caused reduced sperm and spermatid counts in male offspring[13]. Doses that produced neurobehavioural differences in offspring were below those that caused detectable maternal toxicity. A correlation has been shown between maternal blood PBDE levels and fetal blood levels at birth (r^2=0.986)[14]. It is likely, due to the lipophilic nature of PBDEs, that these contaminants are moved into fetal circulation along with maternal lipids. The effects of the increased circulation of maternal lipids during the third trimester, a critical period of fetal brain development, are not known.

Minimizing PBDE exposure

There are several ways in which PBDE exposure might be reduced. For example, before purchasing new products, consumers can ask retailers about PBDEs in the products. Electronics and furniture manufacturers are able to produce products free of PBDEs. As older products break down, PBDEs are released and can accumulate in house dust; houses should therefore be cleaned regularly. To reduce

hand-to-mouth exposure, people should regularly wash their hands. Also, since PBDEs are stored in fatty tissues, PBDE exposure through ingestion might be reduced by choosing meat and dairy products that are low in fat[15]. PBDEs are found in many consumer products, and this may be a source of avoidable exposure.

Regulations

The proposed regulations for PBDEs were published in the December 16, 2006 issue of the Canada Gazette[16]. The official regulations were registered on June 19, 2008 and were published in the July 9, 2008 issue of the Canada Gazette[17]. The purpose of these regulations is to protect Canada's environment from the risks posed by the use and emission of PBDEs.

The official regulations prohibit the manufacture of PBDEs (tetra-, penta-, hexa-, hepta-, octa-, nona-, and deca-BDE congeners). The use, sale, offer for sale, and import of tetra-, penta-, hexa- mixtures, polymers, and resins containing these substances are also prohibited[16].

Conclusion

Temporal trends indicate that concentrations of PBDEs are increasing in the environment and in humans. At this time though there have been no studies linking adverse health effects with existing PBDE levels in humans. However, experimental animal data indicate behavioural, endocrine disrupting, and neurotoxic effects at higher levels of exposure. The transfer of maternal PBDEs to the developing fetus has also been shown to occur. Along with food consumption, ingestion and inhalation of PBDE contaminated air and dust are likely the major routes of PBDE exposure. Indoor PBDEs may originate from use of PBDEs in consumer products.

Human PBDE levels peaked in Sweden in 1997, after which a slight decrease has been observed[18]. This phenomenon may be the result of a voluntary ban on specific PBDE congeners introduced in certain European countries in the early 1990s.

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PBDE Fact Sheet

Introduction

- PBDEs are man-made organic compounds with no known natural sources in the environment.
- PBDEs are used as flame retardants in a wide range of consumer products including television sets, computers, printers, fax machines, carpets, and upholstery.
- PBDE mixtures are noncovalently bound additives that are released from consumer products as products deteriorate with age.
- PBDEs breakdown slowly in the environment.
- Very little is known about human health effects from exposure to PBDEs, but adverse effects have been reported in animals.

Exposure to PBDEs

- The relative importance of different exposure routes remains unknown. Exposure to PBDEs may occur through a number of pathways including:
    - food consumption;
    - dust ingestion;
    - dust and air inhalation.
- Diet is likely an important source of human exposure. PBDEs accumulate in animal fat tissue and may enter the food chain through the consumption of animal products.
- Developing fetuses and infants may be exposed to PBDEs through transfer of maternal PBDEs. Infants may be exposed to PBDEs through contaminated breast milk.
- House dust is another major contributor to PBDE exposure. Ingestion of house dust may be a particularly important exposure route for toddlers and young children.

Temporal trend in PBDE levels

- Levels of PBDEs have been rapidly increasing throughout industrialised countries.
- Levels of PBDEs in human milk samples from Canadian women appear to follow this upward trend.
- Recent results from individual milk samples collected in the Vancouver area show an increase of more than an order of magnitude for PBDEs over 10 years.
- The positive skewing evident in data sets of PBDE levels in human samples indicates that a subset of the population may have much higher levels than their peers.

Absorption, distribution, metabolism, and excretion

- The toxicokinetics of PBDEs vary with the congener in question.
- Deca-BDE, the major commercial product, is poorly absorbed from the gastrointestinal tract and rapidly eliminated in rodents. The major route of excretion is through the feces.
- The lower brominated congeners, such as penta-BDE and octa-BDE, are readily absorbed and only slowly eliminated in rodents. Half-lives of lower brominated congeners are long in rodents, suggesting that the lower BDEs may also persist in humans.
- All PBDEs appear to undergo metabolism, producing hydroxylated and methoxylated metabolites.

Toxicity

- PBDEs likely share certain neurotoxic and endocrine disrupting properties with PCBs.
- Reported endocrine disrupting activity includes:
    - effects on thyroid function *in vivo*, observed as induction of thyroid hyperplasia or induction of thyroid production;
    - displacement of T_4 from transthyretin *in vitro* after conversion to metabolites;
    - induction by metabolites of the estrogen receptor signal transduction pathway *in vitro*, using a human breast cancer cell line.
- Reported developmental effects include:
    - hyperactivity in offspring of female rats exposed during gestation;
    - reduced sperm and spermatid counts in male offspring of female rats exposed during gestation.
- There may be potential for developmental toxicity, since PBDEs are able to cross the placental barrier.
- A high correlation has been shown between maternal blood PBDE levels and fetal blood levels at birth.

Minimizing PBDE exposure

- Choose foods that are low in fat, since PBDEs accumulate in fatty tissues.
- Purchase furniture and electronics from manufacturers that do not use PBDEs in their products.
- Clean houses regularly, as PBDEs can accumulate in dust.
- Wash hands frequently to reduce the ingestion of dust.

PBDE regulations

- Canada is phasing out the manufacture of all PBDEs and the use of many PBDEs.
- This action should result in declining levels of PBDEs in Canadians.

Conclusion

- Temporal trends indicate that the concentrations of PBDEs are increasing in the environment and in humans.
- At this time, there have been no studies linking adverse health effects with existing PBDE levels in humans. Further research is needed into the human health effects of PBDE exposure.
- Toxicity data indicate the potential for endocrine disrupting and neurotoxic effects. The transfer of maternal PBDEs to the developing fetus has also been shown to occur.
- Along with food consumption, ingestion and inhalation of PBDE-contaminated dust from deteriorating consumer products are likely the major routes of PBDE exposure.

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