THE TOXICOLOGY OF THE COMMERCIAL POLYBROMINATED DIPHENYL OXIDE FLAME RETARDANTS: DBDPO, OBDPO, PeBDPO

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Introduction

Brominated flame retardants (BFRs) comprise about 25% of the volume of flame retardants (FR) used on a global scale, and are used in applications requiring high FR performance or in resins needing a FR active in the gas phase. BFRs as a class are structurally diverse and include aromatic diphenyl oxides (a.k.a. ethers), cyclic aliphatics, phenolic derivatives, aliphatics, phthalic anhydride derivatives and others. The bromine portion of the compound is responsible for the molecules flame retardant activity and is unique in its ability to provide flame retardancy in the gas phase. BFR toxicology reviewed in this paper are the commercial polybrominated diphenyl oxides (PBDPO, PBDE): decabromodiphenyl oxide (DBDPO), octabromodiphenyl oxide (OBDPO) and pentabromodiphenyl oxide (PeBDPO).

Composition, production volumes, uses and toxicology of the commercial PBDPO products

The composition, production volumes, uses and toxicology of the three commercial PBDPO flame retardants DBDPO, OBDPO and PeBDPO are distinctly different. DBDPO together with Tetrabromobisphenol A (TBBPA) makes up approximately 50% of all BFR usage globally. The remaining 50% of the global volume of BFRs is composed of a number of different BFR structural types and includes the two other commercial PBDPO flame retardants: OBDPO and PeBDPO. OBDPO and PeBDPO are produced and used in substantially smaller quantities than DBPDO. DBDPO's main use is in high impact polystyrene (HIPS) for electronic enclosures. A comparatively minor, but important, use of DBDPO is to flame retard upholstery fabric where it is applied as a fabric backcoat encapsulated in latex. The composition of the commercial DBPDO product is $\geq$ 97% in purity. OBDPO, a mixture of brominated diphenyl oxide congeners ranging from nona- to tetra-, is used to flame retard business equipment constructed of acrylonitrile-butadiene-styrene (ABS) plastic. PeBDPO, a very highly viscous liquid composed mainly of tetra-, penta- and hexaBDPO congeners, is used to flame retard polyurethane foam used as cushioning in upholstery. 2,2',4,4',5-PeBDPO and 2,2',4,4'-TeBDPO are the predominate isomers in the commercial PeBDPO product.

The potential toxicologic effects of the three commercial PBDPO products vary with their degree of bromination. The greater the degree of bromination on the diphenyl oxide molecule, the lesser the toxicity of the PBDPO. For example, only minimal effects were observed following chronic treatment at high doses with DBDPO in which both aromatic rings are fully brominated. Because of the variation in toxicology associated with the degree of bromination, generalized statements regarding the potential health and environmental effects of the entire class of PBDPOs are inappropriate.

Toxicology of Decabromodiphenyl oxide (DBDPO)

DBDPO is a large molecule with a high molecular weight (959 g/m). DBDPO has undergone a wide range of toxicology tests in mammalian and aquatic species. DBDPO is not acutely toxic to mammalian or aquatic species.[1] DBDPO is not irritating to the skin or eye, is not a sensitizer, and does not induce chloracne or hepatic enzymes.[1] The soot and char combustion products from HIPS/DBDPO/Sb2O3 are also not acutely toxic and are not chloracnegenic.[1] DBDPO is not a reproductive toxicant and is not teratogenic.[1] Pharmacokinetic studies have shown DBPDO is poorly absorbed (<0.3% oral dose), has a short half life (<24 hr), is rapidly eliminated in the feces (>99% in 72 hr), and can be metabolized.[2,3] DBDPO's low long-term toxicity is likely related to its poor absorption and rapid elimination.[2,3] Doses of 10% and 5% of the diet were tolerated by rats and mice with no adverse effects for 14 and 90 days, respectively.[2] Doses of 5% in the diet were tolerated for two years by rats and mice with no effect on body weight or mortality and only minimal evidence of organ effects.[2] Two two year carcinogenicity bioassays have been conducted.[2,4] The first at a top dose level of 1 mg/kg in rats produced no evidence of carcinogenicity.[4] The second conducted at 2.5 and 5% of the diet in rats and mice produced no, equivocal and some evidence of carcinogenicity depending on genus and sex.[2] DBDPO is not acutely toxic to fish or algae[1], does not bioconcentrate in fish[1] and can undergo aqueous photodegradation (at a very slow rate) without production of lower brominated diphenyl oxides[5]. Leaching from polymers is insignificant.[5] DBDPO is not widely distributed in the environment, and where found, is largely confined to sediments near point sources.[1] DBDPO is likely to be highly bound to sediment/soil which will limit its bioavailability and is unlikely to be toxic or accumulated in sediment-dwelling species. DBDPO is not being detected in fish, marine mammals, sea birds or water.[1,6] DBDPO is unlikely to present a toxicologic risk to wildlife, based on its low degree of toxicity in multiple studies in mammals. Although not "readily" biodegradable, DBDPO does not present a bioaccumulation risk based on its physical/chemical properties, and results of laboratory studies and environmental monitoring. DBDPO has negligible water solubility (<0.1 ug/L) and vapor pressure (4.63 x 10-6 Pa).[7] Its measured octanol water partion coefficient is 6.265.[7]

Toxicology of Octabromodiphenyl oxide (OBDPO)

The molecular weight of the OBDPO molecule is 801 g/m. The commercial OBDPO product is a mixture of PBDPO congeners ranging from penta- to nonaBDPO. All studies summarized were performed on the commercial OBDPO product. Like DBDPO, OBDPO is not acutely toxic, is not irritating, is not mutagenic, is not acutely toxic to fish or daphnia, is not chronically toxic to daphnia, and does not bioconcentrate in fish.[1,7] Like DBDPO, OBDPO has negligible water solubility (<1 ug/L) and vapor pressure (6.59 x 10-6 Pa) and has an octanol water partition coefficent of 6.29.[7] OBDPOs mammalian toxicology data demonstrates its properties on repeated exposure are different from that of DBDPO. OBDPO induced liver effects in 14, 28 and 90 day studies (12 mg/kg for 14 days or 100 mg/kg for 28 days) whereas DBDPO did not at significantly higher levels (10% diet for 14 days).[1] OBDPO was also effective in inducing hepatic enzymes whereas DBDPO was not.[1] OBDPO produced teratogenic effects in the rat, but not the rabbit.[1]

Toxicology of Pentabromodiphenyl oxide (PeBDPO).

The molecular weight of the PeBDPO molecule is 564 g/m. The commercial PeBDPO product is

a mixture of PBDPO congeners consisting primarily of 2,2',4,4',5-PeBDPO followed by 2,2',4,4'-TeBDPO. All studies were performed using a commercial product unless otherwise indicated. The water solubility of the commercial PeBDPO product is very low (13.3 ug/L-Sum for Commercial Product) and the individual water solubilities of its major components has been determined (2.4 ug/L-2,2',4,4',5- PeBDPO; 10.9 ug/L-2,2',4,4'-TeBDPO).[7] Its vapor pressure is also extremely low (4.69 x 10-5 Pa) and its measured octanol water partition coefficient is 6.58. [7] Like DBDPO and OBDPO, PeBDPO is not acutely toxic, is not irritating and is not mutagenic.[1] Like OBDPO on repeated exposure, PeBDPOs results are different from that of DBDPO.[1] Liver effects were induced at 100 mg/kg in a 28 day study, and the NOEL in a 90 day study in rats was 2 mg/kg.[1] PeBDPO was effective in inducing rat hepatic enzymes[1], but did not adversely effect the rats immune system[8] nor did its major components compete *in vitro* for binding with thyroxin to a minor plasma protein (transthyretin)[9]. In the rat, 2,2',4,4'-TeBDPO was readily absorbed, poorly metabolized and only slowly eliminated.[10] Less than 0.5% of the oral dose was eliminated in 5 days. 2,2',4,4',5-PeBDPO also was poorly metabolized in the rat, but 43% of the oral dose was excreted within 3 days.[11] No evidence for activation of the AH receptor was found *in vitro* for either 2,2',4,4'-TeBDPO or 2,2',4,4',5-PeBDPO.[12] 2,2',4,4'-TeBDPO did not effect behavior or learning in the neonatal mouse; the no effect level on learning was reported to be between 0.8 and 12 mg/kg for 2,2',4,4',5-PeBDPO.[13] The commercial mixture as a whole was found to bioconcentrate in fish: the major constituent of the product, 2,2',4,4',5-PeBDPO, showed no significant accumulation (BCF=73), but the BCF of 2,2',4,4'-TeBDPO was 35,000.[1] Neither 2,2',4,4'-TeBDPO nor 2,2',4,4',5-PeBDPO induced mortality in fish eggs,[14] and the commercial PeBDPO product when injected into embryos had little or no effects on fish fry liver morphology[15]. Likewise, PeBDPO did not affect fish reproduction when incorporated in the diet.[16] Further, PeBDPO was not acutely toxic to fish or algae.[7] Effects were seen in daphnia below the limits of its water solubility after acute or chronic administration.[17] The no effect concentration in a fish early life stage test was ~ the water solubility of the product. [17] The EC50 on chronic exposure to the sediment organisms Hyalella, Chironmus, and Lumbriculus was >50mg/kg dry wt.[17] PeBDPO was not toxic to earthworms in a 14 day study or to soil nitrification organisms. [17] In 4 of 6 of higher plant species tested, no effect was found at 1000 mg/kg dry wt. In 1 plant species, the no effect level was 125 mg/kg and in another the EC25 was 154 mg/kg.

Summary

Brominated flame retardants (BFRs) are a structurally diverse group of compounds; their major point in common is not their chemical structure but rather that of their use as flame retardants. One class of BFRs is the polybrominated diphenyl oxides (PBDPO) consisting of three commercial PBDPO products: DBDPO, OBDPO and PeBDPO. DBDPO is used to flame retard styrenic resins used in electronic enclosures and upholstery fabric. OBPDO is used to flame reatard ABS resins used in business equipment. PeBDPO is used to flame retard flexible polyurethane foam used in upholstery. OBPDO and PeBDPO are manufactured in substantially smaller quantities than DBPDO.

DBDPO, OBDPO and PeBDPO are high molecular weight compounds ranging from 564 (PeBDPO) to 959 (DBDPO) with negligible vapor pressures and water solubilities. Their water solubilities are <0.1 ug/L (DBDPO), <1 ug/L (OBDPO), and 13 ug/L (sum of major components

PeBDPO product). Their vapor pressures are also extremely low (4.6 x 10-6 Pa for DBPDO, 6.6 x10-6 Pa for OBDPO, 4.7 x10-5 Pa for PeBDPO). Adsorption to soil/sediment is therefore expected to be high. Extraction studies on DBDPO establish that migration from polymers into water is negligible. Thus, DBPDO's potential to move into and in the environment is minimal irrespective of its lack of "ready" biodegradability. DBPDO, OBDPO and the major isomer in the PeBDPO commercial product (2,2',4,4',5-PeBDPO) are not bioconcentrating in fish. The 2,2'4,4'-TeBDPO isomer of the PeBDPO product bioconcentrated in fish. However, little evidence for an acute or chronic effect on aquatic species has been found. DBDPO, OBDPO and PeBDPO are not skin sensitizers and are not mutagenic. DBPDO and PeBDPO are not developmental toxicants in the rat. OBDPO induced developmental effects in the rat but not the rabbit. DBPDO did not effect reproduction in a one generation study, and no evidence of an effect no reproductive organs was found in subchronic or chronic studies at very high dose levels. The NOAEL for DBDPO in subchronic and/or chronic studies in the rat or mouse is ~1000 mg/kg/d. The effect levels of OBDPO and PeBDPO in subchronic studies are lower than DBPDO's NOAEL DBDPO is minimally absorbed from the gastrointestinal tract (<1%), has a short half life (< 24 hrs), and is rapidly eliminated via fecal excretion (>99% in 72 hr). The elimination by the rat of 2,2',4,4'-TeBDPO or 2,2',4,4',5-PeBDPO, the major components in the PeBDPO product, is substantially slower than that of DBPDO. Less than 0.5% of a 2,2',4,4'-TeBDPO oral dose was eliminated by the rat in 5 d. 43% of a 2,2',4,4',5-PeBDPO oral dose was excreted in 72 hr.

In summary, the composition, production volumes, and uses of DBPDO, OBDPO and PeBDPO are distinctly different, and their toxicology is sufficiently different that generalized statements regarding "PBDPOs" are inappropriate.

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