BROMINATED FLAME RETARDANTS – A BURNING ISSUE

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Introduction

The discoveries of several persistent and lipophilic pesticides, in particular DDT and its metabolites, and technically used chemicals with similar characteristics, e.g. PCB, led to legislative measures for their production and use in many countries. In fact the societies reacted within a few years after the chemicals were determined to be bioaccumulating and biomagnifying. The determination of polychlorinated dibenzofurans (PCDFs) and dibenzo-*p*-dioxins (PCDDs) as byproducts from certain technical processes, incineration and from other sources during the latter part of the 70's and during the 80's also led to a range of measures worldwide.

Today, twenty years after the first report on polybrominated diphenyl ethers (PBDEs) in the environment [1] we still are facing a discussion on the properties of these chemicals and their potential of being environmentally unfriendly. The present basis for assessing the environmental threat posed by PBDEs and questions related to their properties must be discussed. Further, the whole area of polybrominated flame retardants (BFRs) should be brought into focus; Which of these chemicals/chemical classes do we need to concentrate more research efforts on in order to assess their potential of being environmentally hazardous and/or a threat to human health.

Brominated flame retardants (BFRs)

BFRs made up approximately 25% of all flame retardants used approximately 10 years ago [2] but unfortunately no recent data on the world production volumes on organic brominated, chlorinated, phosphorous containing flame retardants and inorganic flame retardants are, at least not easily, available. It is however reasonable to believe that the production profile of the flame retardants have not yet undergone any major changes. Tetrabromobispehenol A (TBBPA) and decabromodiphenyl ether (decaBDE) are the dominating commercial BFRs [3,4]. Still though, also verities of other BFRs are produced (examples given in Figure 1). Among these it is possible to find both neutral and lipophilic as well as phenolic substances that are both lipophilic and less lipophilic. PBDE congeners, present in commercial PentaBDE and OctaBDE, are BFRs with high log K_{ow} [3]. Further, chemicals such as bis(2,4,6-tribromophenoxi)ethane (BTBPE), hexabromocyclododecane (HBCDD) and diethylhexyl-3,4,5,6-tetrabromophthalic ester are all highly lipid soluble BFRs. The fate of neutral tetrabromobisphenol A derivatives, such as the bis(2,3-dibromopropyl ether) and bis(allyl ether) have not yet been discussed even though it is clear that these compounds are also lipophilic and potentially bioaccumulating. Among the polybrominated phenolic compounds it is of special interest to look at pentabromophenol and 2,4,6-tribromophenol since these compounds seem to have properties that make them accumulate in e.g. human blood [5].

It is evident that several BFRs are unreactive (persistent) compounds under environmental conditions even though several of the BFRs can undergo photochemical reactions as exemplified by UV irradiation of PBDEs and TBBPA, respectively [6,7]. PBDEs with an intermediate number of bromine substituents are most likely less reactive than the perbrominated decabromodiphenyl ether (BDE-209) under nucleophilic aromatic substitution conditions, similarly to the reactivity of hexachlorobenzene [8]. Studies need to be performed to understand the reactivity of BDE-209 under such conditions, reactivity that may have implications on the fate of BDE-209 in humans and wildlife (c.f. below). The potential for ether cleavage shall not be underestimated leading to the

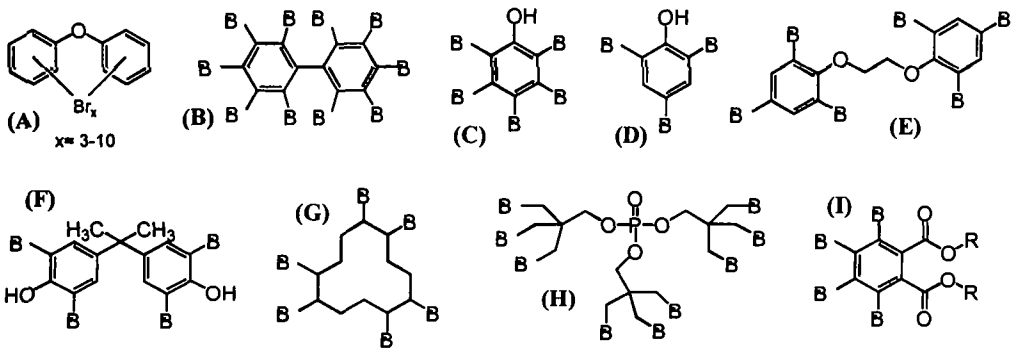

Figure 1. Chemical structures of some of the BFRs that are of environmental concern; (A) polybrominated diphenyl ethers (PBDEs), (B) decabromobiphenyl, (C) pentabromophenol, (D) 2,4,6-tribromophenol, (E) 1,1-bis(2,4,6-tribromophenoxy) ethane (BTBPE), (F) tetrabromobisphenol A (TBBPA), (G) hexabromocyclo-dodecane (HBCDD), (H) tris(tribromoneopentyl)fosfate and (I) brominated phthalate.

formation of pentabromophenol and 2,4,6-tribromophenol products from e.g. BDE-209 and BTBPE, respectively. BFRs may act as direct alkylating agents as in the case of HBCDD that does react with 4-nitrobenzylpyridine through the displacement of a bromine atom (unpublished) and may be taken as an explanation for the HBCDD intercellular recombination effect reported [9]. Similarly, the 2,3-dibromoproyl ether derivative of TBBPA and tris(tribromoneopentyl) phosphate ester may also undergo similar alkylations.

Again, it is fully clear that some of the BFRs are bioaccumulating agents. A vast number of studies have shown that PBDEs, including BDE-209, to bioaccumulate in wildlife and humans. Some representative concentration data are given in Table 1 of a selected number of PBDE congeners in biota from different parts of the world. The compound present at the highest concentrations in the biosphere is 2,2',4,4'-tetrabromodiphenyl ether (BDE-47) even though this PBDE congener is not the major congener produced. It is one of the major constituents of PentaBDE [10] but since this type of PBDE product does not make up more than ca. 10% of the total PBDE production it is tempting to believe that BDE-47 may be formed via debromination of higher brominated PBDE congeners. However, no such conclusive data have so far been published. It may be pointed out that the highest concentrations reported of BDE-47 is up to 25 ppm in fish exposed to PBDE contaminated water from the Swedish West Coast [1] but levels almost as high has been determined in fish from two Virginia/North Carolina rivers [11]. Apart from these reports the concentrations in wildlife are rarely more than a few ppm (mg/kg l.w.) and in human blood the levels are lower (c.f. Table 1).

The human background exposures to PBDEs are also dominated by BDE-47 as observed in mothers milk from Sweden, in men not consuming and in those consuming fat fish from the Baltic Sea [14,15] as well as in women working as cleaners at a hospital in Sweden [16]. The picture is somewhat different in U.S. blood donors with highly variable concentrations of several of the PBDE congeners analyzed for [17]. It is notable that BDE-209 is present in many of the samples even among non-occupationally exposed persons [16, 17]. This compound was recently shown to accumulate in personnel at a plant dismantling electronics [16] but also shown to have a short half-life in humans [18]. The half-life was calculated to 6.8 days indicating that people in general must have more or less a continuos exposure to this compound in order to show the residues reported. It is obvious that even a molecule with as high molar mass as BDE-209 is bioavailable. The fate of this compound in biota is still not clear but it has been shown that BDE-209 is transformed to lower brominated diphenyl ethers in fish [19] and that it seems to be transformed in rats [20]. The identity of any BDE-209 metabolites is not yet known.

Table 1. Selected data on concentrations (ng/g lipid weight) of PBDEs in wildlife and humans

Species	Steelhead trout	Salmon	Grey seal	Human [1]
Year of sampling	1996	1995	1979-85	1991
Location	Lake Michigan, USA	River Dalälven, Sweden	Baltic Sea	Sweden
Tissue	Muscle	Muscle	Blubber	Plasma
Number of samples	6	8	8 homogenate	11
Reference	12	12	13	14
	Mean (*SD*)	**Mean (*SD*)**	**Mean**	**Mean (*SD*)**
2,2',4,4'-tetraBDE (BDE-47)	1700 (*760*)	110 (*34*)	650	3.0 (*4.6*)
2,2',4,4',5-pentaBDE (BDE-99)	600 (*350*)	35 (*6.1*)	40	
2,2',4,4',5,5'-hexaCB (CB-153)	2900 (*850*)	1000 (*250*)	92000	500 (*250*)

[1] Consuming 4-8 meals of fatty Baltic Sea fish per month

Unfortunately much less data are available on the bioavailability and accumulation of the other BFRs. Still we know that HBCDD is bioaccumulating in wildlife but no data has yet been published on this compound in humans. Polybrominated biphenyls (PBBs), mostly known as the agent involved in the contamination of livestock feed in Michigan in 1973 [21] have been shown to accumulate and distribute over a large geographical area in the U.S. In fact, it can not be excluded that the results presented by Patterson et al [17], of high levels of 2,2',4,4',5,5'-hexabromobiphenyl in U.S. blood donors is related to this incident. TBBPA is present in persons highly exposed to this BFR [18] but due to a very short half life it is not detectable in humans exposed to only background levels of TBBPA. Yet other BFRs have been indicated in workplace air and consequently inhaled at these sites. This is true for BTBPE [22]. Also the presence of TBBPA bis(2,3-dibromopropyl ether) has been shown to potentially cause occupational exposures (unpublished).

It is fully clear, as summarized above, that several of the BFRs are persistent and bioaccumulating compounds. In addition to the exposure data there are toxicological data on several of these chemicals, such as reported in the ICPS documents on PBDEs [3], TBBPA [4], and PBBs [23] and in some additional review articles [21,24,25]. Still some more recent toxicological data indicate that at least some of the BFRs have more serious health effects than what we have previously thought they have. The major data set is on the PBDEs. Thus it is clear that PBDE congeners can induce behavioral effects [26], with 2,2',4,4',5-pentaBDE as the most potent PBDE congener studied, so far. PBDEs are metabolized to hydroxylated compounds [27] and as such these polybrominated phenoxyphenols may compete with thyroxine for the binding to the thyroxine transporting protein, transthyretin (TTR) [28]. TBBPA is a very strong competitor for TTR binding as well as pentabromophenol, both with a relative binding potency of over 20 times that of thyroxine [29]. Some PBDE congeners act as agonists but mostly as antagonists in the Ah receptor transduction pathway [30]. Also, very recently Meerts et al [31] have reported on estrogenic activities on PBDEs and hydroxylated PBDEs as determined in the human T47D breast tumor cell line stably transfected with estrogen responsive luciferase reporter gene construct [32]. A commercial Penta-PBDE mixture has been reported to reduce circulating thyroxine and to induce rat liver EROD and PROD activities in the parent animal as well as in the offspring [33]. The data on PBDEs indicate this class of BFRs to be endocrine disruptors. Very few data have been published on any of the other PBDEs. However, it has been shown that HBCDD induces intragenic recombination in mammalian cells [9] indicating this flame retardant to be carcinogenic.

The present toxicological data on some of the BFRs supports the concern raised for the continuos production of these chemicals and call for immediate actions to be taken by the producers, consumers and finally the society. We must be able to show that we have learned a lesson from the past. Even doing so, much more work must be added on the classes of BFRs for which there are poor evidence of exposures and toxicological/ecotoxicological data on their effects.

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