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Transformation of hydroxylated and methoxylated 2,2′,4,4′,5-brominated diphenyl ether (BDE-99) in plants

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ABSTRACT

The occurrence and fate of hydroxylated polybrominated diphenyl ethers (OH-PBDEs) and methoxylated polybrominated diphenyl ethers (MeO-PBDEs) have received significant attention. However, there is limited information on the metabolism relationship between OH-pentaBDEs and MeO-pentaBDEs that were frequently detected with relatively high concentrations in the environment. In this study, the biotransformation between OH-BDE-99 and MeO-BDE-99 was investigated in rice, wheat, and soybean plants. All the three plants can metabolize OH-BDE-99 to corresponding homologous methoxylated metabolites, while the transformation from MeO-BDE-99 to OH-BDE-99 could only be found in soybean. The conversion of parent compounds was the highest in soybean, followed by wheat and rice. Transformation products were found mainly in the roots, with few metabolites being translocated to the shoots and solution after exposure. The results of this study provide valuable information for a better understanding of the accumulation and transformation of OH-PBDEs and MeO-PBDEs in different plants.

Introduction

Polybrominated diphenyl ethers (PBDEs) are manufactured as brominated flame retardants (BFRs) and widely used in a variety of consumer products (de Wit, 2002; Yang et al., 2014; Pang et al., 2014). Over the past few decades, PBDEs have received broad attention due to their persistence, bioaccumulation and toxicity (Wu et al., 2012; Sha et al., 2015; Ma et al., 2016). Recently, focus has transferred to structural analogs of PBDEs, such as hydroxylated PBDEs (OH-PBDEs) and methoxylated PBDEs (MeO-PBDEs), which have been detected in various environmental matrices (Lacorte and Ikonomou, 2009; Malmvarn et al., 2005; Sun et al., 2013a; Ueno et al., 2008; Wan et al., 2009).

For some viewpoint, OH-PBDEs are considered to be more toxic than PBDEs due to their adverse effects on organisms, including the thyroid hormone homeostasis disruption, neurotoxicity, and oxidative phosphorylation disruption (Cantón et al., 2008; Meerts et al., 2001; Mercado-Feliciano and Bigsby, 2008; Morgado et al., 2007; Van Boxtel et al., 2008; Wan et al., 2010a). It is also reported that MeO-PBDEs have a greater effect on mRNA abundance of steroidogenic enzymes in the H295R cell line and could induce DNA damage in organisms (He et al., 2008; Xu et al., 2015).

PentaBDE, a commercial PBDE mixture, was used in polyurethane foam, textiles, and electronic components (Hites, 2004). Although the manufacture and use of pentaBDEs were discontinued in the United States and European Union in 2004

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(European Union Directive, 2002/95/EC), they are still ubiquitous in environment (Li et al., 2014; Sun et al., 2016b). The congener 2,2′,4,4′,5-pentabromodiphenyl ether (BDE-99), among others, is a major congener in the commercial pentaBDE mixture (La Guardia et al., 2006). The occurrence of OH-BDE-99 and MeO-BDE-99 was observed in many environmental samples (Nomiyama et al., 2011; Sun et al., 2013a, 2013b). They were also identified as metabolites of BDE-99 in laboratory exposure studies (Hakk and Letcher, 2003; Marsh et al., 2006; Teuten et al., 2005). Recently, Sun et al. (2014) and Xu et al. (2016) had found the interconversion of OH-tetraBDEs and MeO-tetraBDE in young pumpkins and maize. However, the transformation between OH-pentaBDEs and MeO-pentaBDEs was not studied, which is necessary to gain a thorough view into PBDEs metabolic pathways.

Plants serve as a vital component of the terrestrial ecosystem and play an important role in the metabolism of organic pollutants in environment (Collins et al., 2006). Contamination by BDE-99 in crops has been reported in numerous studies (Du et al., 2013; Mahmood et al., 2015). It is important to explore the relationship between OH-BDE-99 and MeO-BDE-99 in crop plants. In this study, three plants, including rice, wheat and soybean, which are the common crops in the world, were selected as model plants. The main objectives of this study are to (a) reveal the relationships between OH-BDE-99 and MeO-BDE-99 by hydroponic exposure; and (b) investigate the uptake and distribution of these targeted compounds in the selected three plants.

1. Materials and methods

1.1. Chemicals

Chemical standards of two OH-PBDEs (5′-OH-BDE-99 and 6′-OH-BDE-99) and two MeO-PBDEs (5′-MeO-BDE-99 and 6′-MeO-BDE-99) were used as exposure compounds. Standards of all four exposure chemicals were >99% pure. 2,2′,4,5,5′-pentachlorobiphenyl (CB-101) and 4′-OH-CB-101 were used as surrogate standards for neutral and phenolic chemicals, respectively. All the exposure standards and surrogate standards were purchased from AccuStandard (New Haven, CT, USA). Distilled water (18.2 MΩ) was used in all the experiments. Solvents, including acetonitrile (HPLC grade), methyl tert-butyl ether (MTBE) (HPLC grade), acetone (pesticide grade), hexane (pesticide grade), and dichloromethane (DCM) (pesticide grade) were purchased from Fisher Scientific (Pittsburgh, PA, USA). All the other chemicals and reagents used were of analytical reagent grade or higher purity. Anhydrous sodium sulfate (Na_2SO_4) was heated for 6 hr at 660°C. Silica gel (100–200 mesh size) (Merck, Darmstadt, Germany) was activated at 450°C for 7 hr. Acidified silica gel was prepared by combining 70 g of activated silica with 30 g of concentrated H_2SO_4.

1.2. Exposure experiment

Rice (*Oryza sativa* L.), wheat (*Triticum aestivum* L.) and soybean (*Glycine max* L.) were obtained from the Chinese Academy of Agricultural Sciences, Beijing, China. Seeds of different plants were selected and sterilized using 3% (V/V) H_2O_2, and then germinated on a bed of sterilized perlite with distilled water. Uniform seedlings were used for exposure after growing to approximately 10 cm in height. The exposure solutions of each individual compound were obtained by first dissolving the standard solution in acetone, and then gradually diluting with distilled water in bottles wrapped with aluminum foil, resulting in an initial concentration of 20 ng/mL. The volume of acetone in the solutions was less than 1‰ (V/V). Each reactor was wrapped with parafilm to prevent volatilization of the exposure compound and then placed in a controlled environment growth chamber at a light intensity of 250 μmol/m^2/sec for 16 hr/day, a 22 ± 2°C temperature regime and a relative humidity of 80%. The exposure time was 7 days.

Unplanted controls (exposure compounds in the absence of seedlings) were designed and assessed simultaneously for each exposure chemical to monitor any possible loss. Blank controls (seedlings in the absence of exposure compounds) were used to monitor possible cross-contamination (Fig. 1). All the samples were prepared in triplicate in separate containers.

Roots, shoots and solutions were sampled for the subsequent analysis after exposure. The roots of samples were first thoroughly rinsed with distilled water, blotted with tissue paper, weighed at fresh weight, and then freeze-dried for further treatment. The subsequent calculations were based on dry weight.

1.3. Sample pretreatment and instrumental analysis

The extraction, separation, and cleanup procedures for OH-PBDEs and MeO-PBDEs were adapted from previous methods (Sun et al., 2013b). In brief, all the samples were spiked with the surrogate standards (10 ng for each). The solution samples were liquid–liquid extracted with DCM (40 mL). Solid samples (roots and shoots) were homogenized and repeatedly extracted with hexane/MTBE mixture (1:1; V/V) using a TissueLyser (Qiagen, Hilden, Germany). The extract was combined and concentrated to dryness using a rotary evaporator (Heidolph4000, Germany) and redissolved in 30 mL of DCM. Acidified silica gel (10 g) was added, and the mixture was shaken vigorously until the extracts were colorless. Then, an anhydrous Na_2SO_4 column was used to remove the acidified silica gel. DCM (30 mL) was applied to elute the targeted compounds. The eluate was concentrated under a gentle of nitrogen to dryness, and redissolved in 200 μL of hexane. Half the extract (100 μL in hexane) was used for subsequent analysis of MeO-PBDEs by gas chromatography–mass spectrometry (GC/MS). The other half of the extract (100 μL in hexane) was solvent-exchanged to acetonitrile for analysis of OH-PBDEs by liquid chromatography/tandem mass spectrometry (LC/MS/MS).

Quantification of MeO-PBDEs was carried out on a GC/MS instrument (7890B/5977A, Agilent Technologies, Santa Clara, CA, USA) using an electron ionization source. Selected ion monitoring (SIM) mode was used for quantification. DB-5 MS (J&W Scientific, Folsom, CA, USA) capillary column (30 m, 0.25 mm i.d., 0.25 μm film thickness) was employed for the separation. The carrier helium gas was kept at a constant flow of 1.0 mL/min. The GC temperature program was set as follows: initial temperature 90°C and then increased to 210°C at a rate of 10°C/min. The post run was set at 300°C, held for

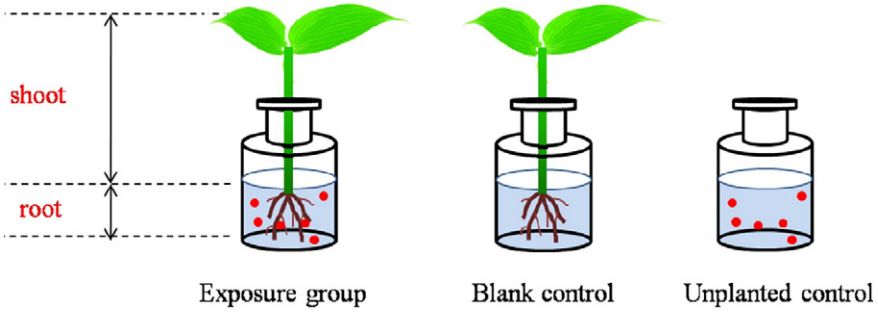

Fig. 1 – Scheme of exposure and control groups and sampling.

3 min. The monitored ions were *m/z* 595.7 and 597.8 for both 5′-MeO-BDE-99 and 6′-MeO-BDE-99. Identification and analysis of OH-PBDEs was performed on a LC/MS/MS instrument (Agilent 1260–6460). Reverse-phase separation was achieved using a C18 column (100 mm × 2.1 mm, 2.2 μm particle size; Thermo Fisher Scientific, Waltham, MA, USA). The mobile phase consisting of acetonitrile (Solvent A) and water (Solvent B) was used with a gradient elution of elution of A:B from 60:40 to 75:25 in 20 min at a flow rate of 0.3 mL/min. The column temperature was set at 40°C. Electro-spray ionization (ESI) source in negative ion multiple-reaction monitoring (MRM) mode was used for mass spectrometric detection. For 5′-OH-BDE-99, the MRM transitions were 578.6 → 498.2 and 578.6 → 78.7. For 6′-OH-BDE-99, the MRM transitions were 578.6 → 80.8 and 578.6 → 78.7.

1.4. Quality assurance and quality control

During the experiment, data quality control and assurance measures were performed strictly. No background interference was observed in the analysis of OH-PBDEs and MeO-PBDEs. Average recoveries of MeO-PBDEs and OH-PBDEs in the spiked samples were 84.1%–94.7% and 82.5%–90.4%, respectively, where the relative standard deviation (RSD) was lower than 15% (n = 3). Recoveries for the surrogate standards were 85.6%–105.4%. The concentrations were not recovery-corrected. Five-point calibration curves were made to quantify the amount of analytes in samples. The method limit of quantification (MLQ) was determined as the quantity of analytes yielding a peak 10 times the noise. For OH-PBDEs, MLQs were from 78 to 95 pg/L in water, and from 55 to 75 pg/g in plants. For MeO-PBDEs, the MLQs were from 66 to 125 pg/L in water, and from 72 to 86 pg/g in plants.

2. Result and discussion

2.1. Control group and purity determination

Previous studies have implied that an important prerequisite for the exposure research is ensuring that exposure chemical and media were free of impurities that could lead to false results (Sun et al., 2013c, 2016a; Wan et al., 2010b; Zhai et al., 2014). In this study, the purity of the four standards was checked and no target MeO-PBDEs or OH-PBDEs were detected. Thus, metabolites measured in plants from the exposure reactors originated from biotransformation of exposed parent chemicals. Mass balance was calculated, and the mean recoveries of 5′-OH-BDE-99, 6′-OH-BED-99, 5′-MeO-BDE-99, and 6′-MeO-BDE-99 were 91.8%, 90.1%, 92.7% and 93.6%, respectively for unplanted controls. No OH-PBDEs or MeO-PBDEs were detected in blank controls, indicating that there was no chemical cross-contamination between the reactors. The formation of metabolites was not detected in unplanted controls and blank controls, indicating that there was no chemical transformation in the reactors. Potential photodegradation of chemicals was eliminated by wrapping the exposure reactors with aluminum foil and further verified by unplanted controls.

2.2. Uptake and translocation of exposure chemicals

The distributions of the four exposure chemicals in different compartments of plants were investigated to elucidate their translocation in plants. The majority of exposure chemicals (over 70% of the initial amount) were accumulated by the roots after 7 days' exposure (Fig. 2). Root concentration factors (RCFs, calculated as the ratio of the concentrations in plant roots to the concentrations in the exposure solutions) were calculated to compare the uptake abilities of the three kinds of plants. The average RCF values followed the order: soybean (32,543 to 23,252) > wheat (20,367 to 26,228) > rice (12,835 to 21,552). The values were higher than those of MeO-tetraBDEs and OH-tetraBDEs in pumpkin (Sun et al., 2014). A reasonable explanation is that the K_{ow} of OH-pentaBDEs and MeO-pentaBDEs was higher than that of OH-tetraBDEs and MeO-tetraBDEs, and renders it more prone to partition from solution to roots(Chiou et al., 2001).

The concentrations of all four parent chemicals in roots of soybean were slightly higher than those in roots of wheat, and much higher than those in roots of rice. The average mass of parent chemicals decreased gradually in the shoots and solution, with <10% of the initial amount of parent chemical being translocated to the shoots. The concentrations of OH-PBDEs were 1.20–1.49, 1.03–1.47, and 1.07–1.21 times higher than the concentrations of MeO-PBDEs in shoots of rice, wheat and soybean, respectively. Different concentrations of all four parent chemicals were observed in shoots of different plants. The concentrations were the highest in shoot of rice, followed by wheat and soybean. Translocation factors (TFs) were calculated as the ratio of the concentrations in shoots to the concentrations in roots. The average TFs were in the following order: rice (0.139 to 0.189) > wheat (0.070 to

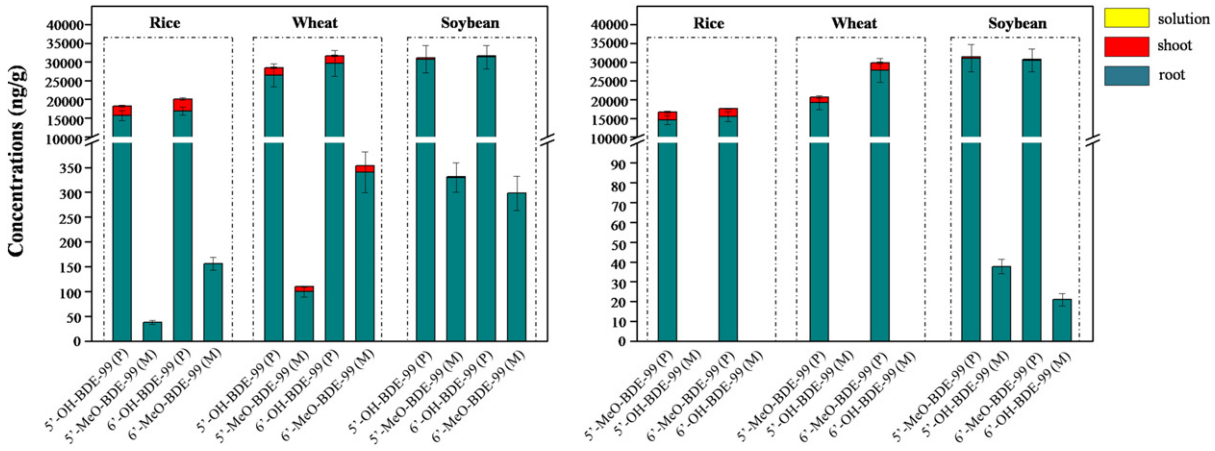

Fig. 2 – Concentrations of the parent compounds (P) and their metabolites (M) after the *in vivo* exposure study.

0.077) > soybean (0.010 to 0.012). It suggested that uptake of the four exposure chemicals was easier in soybean and wheat than in rice. However, all the parent chemicals were more prone to transfer from roots to shoots in rice and wheat than those in soybean.

2.3. Methylation of OH-BDE-99

The metabolite 5′-MeO-BDE-99 was detected in different plants after being exposed to 5′-OH-BDE-99. Likewise, the metabolite 6′-MeO-BDE-99 was detected in different plants after being exposed to 6′-OH-BDE-99. The concentrations of MeO-PBDEs in different compartments of three plants are showed in Fig. 2. Among the three plants, the concentrations of MeO-PBDEs in the roots ranged from 37.7 ng/g to 341 ng/g, which were much higher than those in the shoots and solutions. The results indicated that all the three plants can metabolize 6′-OH-BDE-99 and 5′-OH-BDE-99 into homologous methoxylated metabolites and the transformation occurred mainly in the roots. In rice roots and wheat roots, the concentrations of 6′-MeO-BDE-99 were higher than those of 5′-MeO-BDE-99. However, in soybean roots, the average concentrations of the two compounds were comparable. Overall, the concentrations of MeO-BDE-99 in whole soybean were higher than those in whole rice and wheat.

Conversion rates, from the mass of the metabolites and that of the initial parent chemicals (M/P), are illustrated in Table 1. The M/P values of rice and wheat exposed to 6′-OH-BDE-99 (0.72% and 0.95% respectively) were higher than those exposed to 5′-OH-BDE-99 (0.21% and 0.36% respectively). However, the biotransformation rate from 6′-OH-BDE-99 to 6′-MeO-BDE-99 (M/P = 0.79%) in soybean was comparable with that from 5′-OH-BDE-99 to 5′-MeO-BDE-99 (M/P = 0.87%). The difference in the metabolic profile among rice, wheat and soybean may be the result of species difference in enzyme expression, which remained unclear so far.

Recoveries of chemicals ranged from 84.8% to 87.9% for the exposure reactors, which were lower than those in the unplanted controls. These results indicate that some other metabolites might be produced, whereas, none of them have been identified.

Table 1 – Detection of metabolites after intact plants being exposed for seven days.

Exposure compound	Metabolites	Conversion * (%)		
		Rice	Wheat	Soybean
5′-OH-BDE-99	5′-MeO-BDE-99	0.21 ± 0.10	0.36 ± 0.12	0.87 ± 0.25
5′-MeO-BDE-99	5′-OH-BDE-99	nd **	nd	0.09 ± 0.03
6′-OH-BDE-99	6′-MeO-BDE-99	0.72 ± 0.17	0.95 ± 0.22	0.79 ± 0.24
6′-MeO-BDE-99	6′-OH-BDE-99	nd	nd	0.05 ± 0.02

* Mean ± standard deviation (n = 3).
** Nondetectable.

2.4. Demethylation of MeO-BDE-99

Transformation from MeO-BDE-99 to their corresponding hydroxylated metabolites was observed. Demethylation of MeO-BDE-99 varies in different plant species, which might due to the difference in metabolic enzyme activity and uptake ability of different plant species (Huang et al., 2012). Of all the plants, OH-PBDEs can only be detected in soybean after exposed to individual chemicals for 7 days (Fig. 2). No metabolite was detected in rice and wheat during the exposure period. The average concentrations of 6′-OH-BDE-99 and 5′-OH-BDE-99 in roots of soybean were 20.9 ng/g and 37.7 ng/g, respectively. No metabolite was detected in shoots of soybean, which may be due to the low conversion rate and their higher hydrophobicity. There was no OH-BDE-99 in solution, suggesting that no hydroxylated metabolites exuded from roots into the rhizosphere compartment during the experimental period. Obviously, metabolism of OH-BDE-99 is easier than that of MeO-BDE-99 in plants. This was consistent with the result obtained in pumpkin exposure experiment, in which the methylation of OH-tetraBDE occurred more easily than the demethylation of MeO-tetraBDE (Sun et al., 2014). The concentration percentages between transformation products and the initial exposure chemicals of 6′-MeO-BDE-99 and 5′-MeO-BDE-99 in soybean were 0.05% and 0.09%, respectively. The recoveries of parent chemicals and metabolites ranged from 84.8% to 89.6% for the exposure reactors.

The demethylation of MeO-BDE-99 in this study is more difficult than that of MeO-BDE-47 in the previous report (Sun et al., 2014; Xu et al., 2016). For one hand, the number of Br atom of MeO-BDE-99 is more than that of MeO-BDE-47. On the other hand, the species of plant may be responsible for the differences in demethylation. There were no OH-PBDEs detected in any controls, implying that soybean plants play a key role in the formation OH-PBDEs from MeO-PBDEs.

3. Conclusion

The uptake, translocation and metabolism of 5′-OH-BDE-99, 6′-OH-BDE-99, 5′-MeO-BDE-99, and 6′-MeO-BDE-99 in rice, wheat, and soybean were observed in this study. The accumulation concentrations of the four exposure chemicals were higher in soybean and wheat roots than in rice roots. However, all the parent chemicals were easier translocated within rice and wheat than in soybean. All the three plants can metabolize OH-BDE-99 into homologous MeO-BDE-99 and the transformation occurred mainly in the roots. The demethylation of MeO-BDE-99 only occurred in the roots of soybean, and was more difficult than the methylation of OH-BDE-99. Overall, the largest interconversion rates were observed in soybean, while the lowest were observed in rice. The results of this study provide important information for better understanding the mechanism on plant accumulation and transformation of OH-PBDEs and MeO-PBDEs.

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