BIOAVAILABILITY AND BIOLOGICAL RESPONSE OF PBDES ADMINISTERED TO RATS IN HOUSEHOLD DUST

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Abstract
Household dust has recently been implicated as a source of PBDE exposure. This study investigated the bioavailability of PBDEs in house dust administered through the diet as compared to PBDEs in oil via the diet. PBDEs in household dust were just as bioavailable as PBDEs dissolved in oil. Lower brominated congeners (tri-hexa) accounted for most of the PBDEs in adipose, brain, and carcass, whereas the higher congeners (hepta-deca) accounted for at least 50% of the PBDEs in liver. Hepatic Cyp2b mRNA expression increased at nearly equal amounts in both the high dose dust and oil exposed animals, demonstrating a biological response to dust. This suggests that components other than the PBDEs in the dust (ie. PAHs) are causing the Cyp1a1 induction.

Introduction
Due to the widespread use of PBDEs in household items, non-dietary exposures, specifically household dust inhalation or ingestion, are of major concern and have been implicated as a source of PBDE exposure.[1] With a consensus that children ingest more dust than do adults, dust ingestion by children may be a major PBDE exposure pathway. A recent case study of a U.S. family showed that the children had PBDE levels 2- to 5-fold higher than their parents, suggesting that children could be ingesting more PBDEs than adults.[2] With no existing absorption data on PBDEs in dust, this study compares the bioavailability of PBDEs administered through the diet and the resulting hepatic responses.

Methods
Animals and treatment: Male Harlan Sprague-Dawley rats (215.2 ± 7.43 g) were obtained from Harlan Sprague Dawley Inc. (Indianapolis, IN). Animals (n=4/group) received feed mixed with SRM-2585 NIST dust, or oil prepared with PBDE mixtures (DE 71, DE 79, and DE 83R) to attain congener concentrations similar to those in SRM-2585 NIST dust. Animals were trained to consume all their feed (12 g/day), and were fed for 21 days. Rats were then euthanized and samples were collected. Tissues were weighed and stored at -80°C until use.

	Daily Dose	
Dose Group	ng PBDEs	ng PBDEs/kg body wt
Control	18 (feed only)	84
Low oil	180	840
Low dust	250	1150
High oil	1150	5350
High dust	1460	6700

Chemicals: NIST Standard Reference Material-2585 was obtained from the National Institute of Standards and Technology, Gaithersburg, MD, USA. The commercial BDE mixtures (DE 71, DE 79, and DE 83R) were generously provided by the Great Lakes Chemical Corporation, now "Chemtura", (West Lafayette, IN, USA).
GC/MS Analyses: The adipose tissue (epididymal fat), brains, livers, and carcasses were individually homogenized and aliquots were purified on an automated Fluid Management System Unit utilizing triphasic silica and basic alumina cartridges; PBDEs were quantitated by an isotope-dilution HR-GC/MS method.[3] The amount of the dose that was bioaccumulated was calculated by subtracting the average control rat tissue levels from the dosed levels.
RNA isolation, relative real-time RT-PCR, and data analysis: Total RNA was isolated using the RNeasy Midi Kit with DNase I digestion performed during column purification (Qiagen, Hilden, Germany). Real-time RT-PCR was performed using the ABI Prism 5700 Sequence Detection System (ABI, Foster City, CA). All data are

represented as the mean ± standard deviation. Statistical intergroup comparisons were determined by using one-way analysis of variance (ANOVA). The levels of probability of statistical significance are $p < 0.05$.

Results

Figures 1 and 2 present the relative distribution of PBDE congeners among tissues. When fed to rats, PBDEs from dust were found to be equally as bioavailable as PBDEs in oil. (data not shown) Lower brominated congeners (tri- to hexa-BDEs) accounted for the majority of the PBDEs present in adipose, brain, and carcass; however, higher brominated congeners (hepta- to deca-BDEs) accounted for 50% or more of the PBDEs in liver. Livers from the high oil group contained slightly more of the dose than the high dust group mainly due to higher amounts of nona- and decaBDEs.

Figure 1
Distribution in high dose dust group

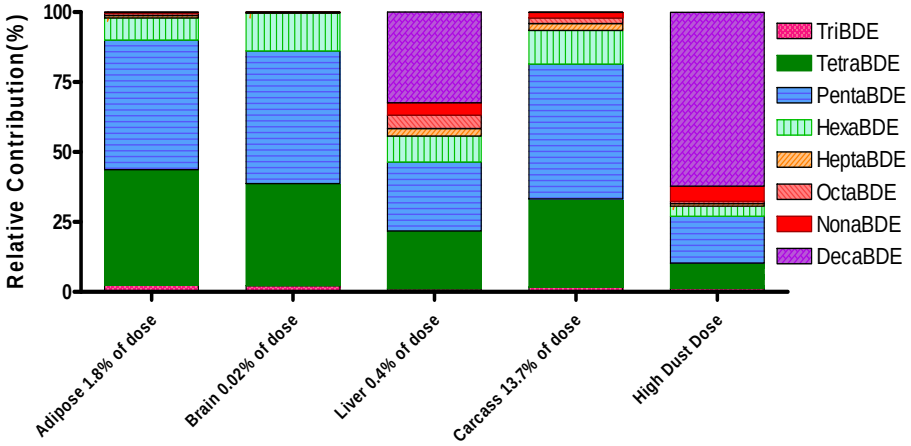
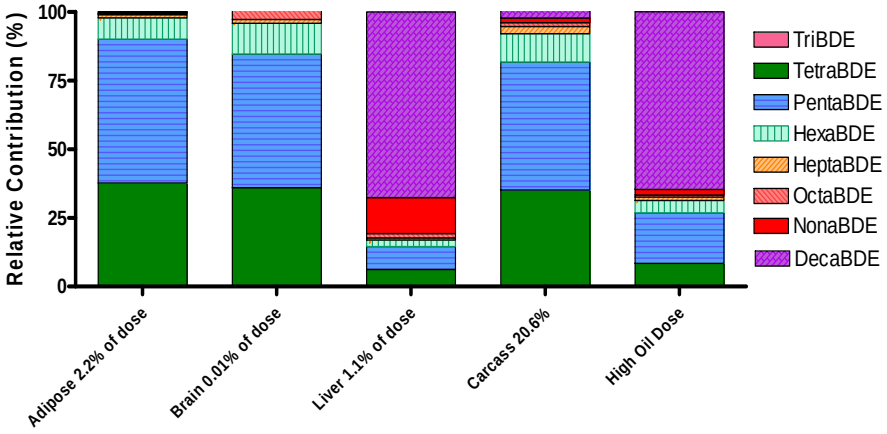


Figure 2
Distribution in high dose oil group



Figures 3 and 4 demonstrate the bioactivation of liver enzyme systems for the different dose groups**.** Hepatic Cyp1a1 mRNA expression in rats receiving the oil PBDE mixture was not significantly different than controls. Expression increased 2.1- and 2.7-fold in the low (250 ng PBDEs/day) and high (1460 ng PBDEs/day) dust exposure groups, respectively. Hepatic Cyp2b1 and Cyp2b2 mRNA expression did not increase significantly with exposure to the low oil and low dust treatments, 180 and 250 ng PBDEs/day, respectively. Increases in hepatic Cyp2b1 and Cyp2b2 mRNA expressions were observed in the exposure groups receiving the high oil (1150 ng PBDEs/day) and high dust treatments (1460 ng PBDEs/day). The inductions were 3.8- and 3.7-fold, respectively (Cyp2b1) and 3.8- and 4.1-fold, respectively (Cyp2b2). (*Statistically significant as compared to control; p <0.05)

Figure 3

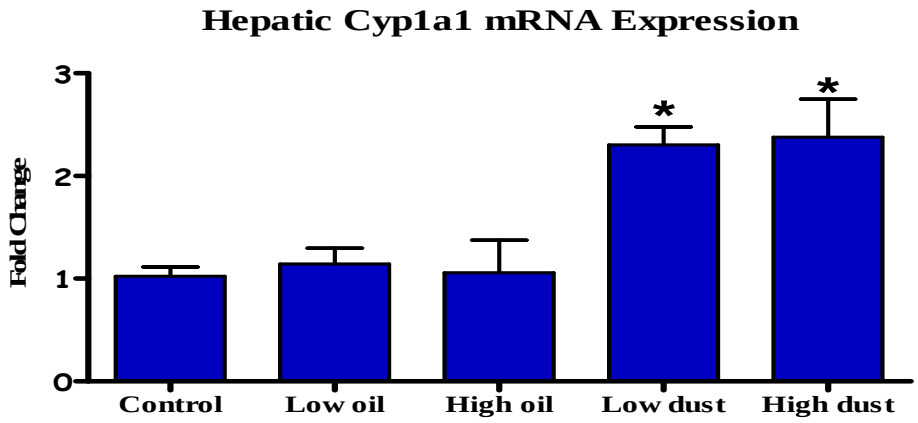
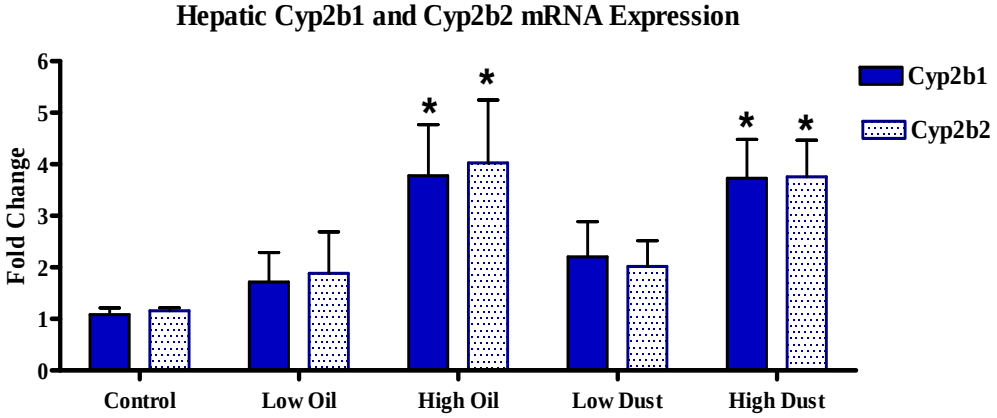


Figure 4



Conclusions

The present report compared the bioavailability, as well as the hepatic response, of PBDEs administered in house dust or in oil. PBDEs found in household dust were equally or more bioavailable than PBDEs dissolved in oil when fed to rats as part of the diet. Uptake and distribution of PBDEs in rats varied depending on the level of bromination and pattern of substitution. BDE-47 concentrated to a higher degree than BDE-99 into adipose, which may explain, at least in part, the generally higher levels of BDE-47, observed in biota. BDE-209 bioaccumulated to a lesser degree in adipose tissue, but was the major congener detected in liver. Tri- to octa-BDEs were found in all tissues. The lower concentration of nona- and deca-BDEs in liver from the high dust group compared to the high oil group is of interest and may be due to alterations in metabolism. Hepatic

Cyp1a1 mRNA expression increased significantly with dust exposure (high and low dust), but did not increase with oil exposures. This suggests that components other than PBDEs caused the induction of Cyp1a1 in dust (ie. PAHs). Cyp1a1 induction could also be the result of halogenated dioxins or furans known to contaminate household dust.[4] The hepatic Cyp1a1 mRNA expression did not correlate with PBDE concentrations found in the liver. This finding coincides with reports showing PBDEs are not inducers of Cyp1a1.[5] This further supports the hypothesis that chemicals in dust other than PBDEs are causing the induction of Cyp1a1 mRNA expression in liver. However, the induction of Cyp2b1/2 mRNA from PBDEs in both house dust and oil supports the biological response to the ingested PBDEs. In summary, dietary exposures to PBDEs in dust were equally as bioavailable as PBDEs in oil. This supports the hypothesis that household dust can be a source of exposure to PBDEs, which may have important implications for young children.

Acknowledgements
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References

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