COMPARISON OF PBDEs IN CAT SERUM TO LEVELS IN CAT FOOD: EVIDENCE OF DECA DEBROMINATION?

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Abstract
Since the introduction of brominated flame retardants (such as the PBDEs), increases in feline hyperthyroidism have been observed. We hypothesized that PBDE exposure was linked to the increased occurrence of hyperthyroidism in cats. Herein, PBDEs in serum of pet cats and levels in cat food were determined. Samples were extracted and analyzed by electron capture negative ionization gas chromatographic mass spectrometry for major PBDE congeners. Data indicated that cats were highly exposed to PBDEs, and that body burden in certain “outliers” was 4 to 7-fold higher than other cats. Using estimates of total serum lipid in cats, lipid adjusted cumulative PBDE serum levels in cats were compared to whole blood levels in U.S. adults. Cats had body burdens that were ≥ 10-fold higher. Data indicated that dry food contained relatively high levels of BDE-209, and that cats consuming dry food had significantly greater serum levels of BDE-209. Furthermore, results suggest that in cats, BDE-207 may represent an important meta-position deca debromination product. Improved understanding of how the purportedly stable BDE-209 compound undergoes metabolism and clearance is an important area of investigation. The debromination pathways suggested for these cats are seemingly in agreement with recent reports in humans and various animal species.

Introduction
Since the introduction and widespread use of brominated flame retardants (such as the PBDEs), parallel increases in feline hyperthyroidism have been observed.1,2 We hypothesized that PBDE exposure was, in some manner, linked to the increased occurrence of hyperthyroidism in cats. To this end, we measured PBDEs in the serum of pet cats and in a variety of cat food products.

Materials and Methods
Serum was obtained during 2005-2006 from pet cats with (n=11) and without (n=12) documented hyperthyroidism. Ages ranged from 1.5 to 18 years. Commercially available dry and canned cat food products were purchased during 2005-2006. Serum and food samples were extracted and analyzed by electron capture negative ionization gas chromatographic mass spectrometry for the major PBDE congeners.

Results and Discussion
Overall, data showed that pet cats were in fact highly exposed to PBDEs, and that PBDE body burden in certain “outliers” were 4 to 7-fold higher than other cats. Using estimates of total serum lipid in cats, lipid adjusted cumulative PBDE serum levels in pet cats were compared to whole blood levels in U.S. adults, as reported by Schecter et al.3 Again, similar to the cats, in certain human individuals, values were 7-8 times higher than the median value of the corresponding sex. Overall, cats appeared to have PBDE body burdens that were ≥ 10-fold higher than that of U.S. adults (Fig. 1).
Furthermore, a spectrum of BDE congeners was detected in all cats, with BDE-47, 99, 207, and 209 predominating. Due to high variability within each group, no differences were detected between cumulative PBDE levels in hyperthyroid cats compared to non-hyperthyroid cats.

We did observe, however, that cats consuming dry food had significantly greater serum levels of BDE-209 as well as BDE-207. Subsequent evaluation of cat food PBDE content revealed that dry food contained relatively high levels of BDE-209, with only minor quantities of BDE-207 or other nona- or octa-brominated congeners (Fig. 2). It is also feasible that in addition to dietary exposure, house dust exposure (via ingestion of dust during grooming) contributes to the increased PBDE body burdens observed in pet cats. This finding may be relevant because risk of developing feline hyperthyroidism is known to be associated with indoor living.¹

**FIGURE 1.** Comparison of PBDE levels in U.S. cats and humans.

**FIGURE 2.** Mean octa- to deca-PBDE congeners in cat serum (stratified by diet) compared to the octa- to deca-PBDE congeners present in different flavors of commercial dry cat food (ng/g wet wt).

*Significantly different than canned food-eating cats.*
Results suggest that in cats, BDE-207 may represent an important meta-position deca debromination product. To further assess potential debromination pathways of BDE-209, we examined correlations between serum concentrations of BDE-209 vs. that of other highly brominated congeners. Significant correlations were observed for 209 vs. 207 ($p = 0.001$; $R = 0.75$), 209 vs. 208 ($p = 0.005$; $R = 0.57$), and 209 vs. 183 ($p = 0.008$; $R = 0.54$); but not with other congeners. Significant correlations were also observed for 207 vs. 208 ($p = 0.001$; $R = 0.74$), 207 vs. 197 ($p = 0.008$; $R = 0.54$), 207 vs. 183 ($p = 0.002$; $R = 0.62$), and 207 vs. 201 ($p = 0.03$; $R = 0.44$). Because no BDE-203, -205, or -206 congeners were detected, it appears that either ortho-position debromination of fully brominated BDE congeners does not readily occur in cats, or alternatively, when it does occur, the resulting compound is rapidly eliminated.

In light of recent studies implicating 5-deiodinase or cytochrome P_{450} enzymes in removal of bromine from meta- (and possibly para-) positions in fish, we propose the following schematic to explain the correlations noted above and the relative levels of hepta-deca BDE congeners detected in cat serum (Fig. 3).

**FIGURE 3.** Possible debromination pathways of BDE-209 in cats.

Lastly, data indicated that serum levels of BDE-183 in hyperthyroid cats were higher than non-hyperthyroid cats ($p = 0.03$). Hence, improved understanding of how the purportedly stable BDE-209 compound undergoes metabolism and clearance is an active area of research. The pathways suggested for these cats are compatible with recent reports in humans, cows, rats, and birds. For example, BDE-207 and 209 can be prominent congeners in people — with 209 accounting for as much as one third of the total PBDEs in serum of women living in Japan. Future studies will be necessary to determine whether PBDE accumulation of the magnitude detected in these hyperthyroid cats may in fact interfere with their thyroid homeostasis. If more definitive associations can be established between PBDE exposure and altered T_{4} levels in cats, data from these “sentinel” cats suggest that chronic (cumulative) low-dose PBDE exposure may be more endocrine disrupting than would be predicted by many short-term or even chronic PBDE studies in laboratory rodents. It will be necessary to elucidate how specific BDE congeners are metabolized in cats, including debromination pathways following exposure to the deca commercial mixture. Evaluation of potential differences in the elimination half-lives of key PBDE...
congeners in cats, as compared to humans, will also be important in order to more completely understand how PBDE exposure may alter thyroid hormone levels in sentinel species — and whether comparable risk may exist for similarly exposed humans.

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References