Interconversion of Hydroxylated and Methoxylated Polybrominated Diphenyl Ethers in Japanese Medaka

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INTRODUCTION

- Polybrominated diphenyl ethers (PBDEs) and structurally related hydroxylated (OH-) and methoxylated (MeO-) PBDEs are ubiquitous in the environment.
- Several origins for OH-PBDEs and MeO-PBDEs have been suggested.
  - Ortho-substituted OH-PBDEs and MeO-PBDEs are formed as naturally occurring compounds in the marine environment.
  - Result from biotransformation of synthetic PBDEs
  - Demethylation of natural MeO-PBDEs is a major contributor of OH-PBDEs.
- We have previously demonstrated, in vitro, that 6-MeO-BDE-47 is a precursor for 6-OH-BDE-47. In this same study no 6-OH-BDE-47 was generated during the microsomal metabolism of BDE-47. Currently no direct evidence of this pathway of OH-PBDE formation.

OBJECTIVES

Objective 1: Establish maternal transfer of BDE-47, 6-MeO-BDE-47 and 6-OH-BDE-47, and metabolites,

- Eggs were collected each morning (days 0-14) during the exposure period.
- Medaka were fed diets of food spiked with BDE-47, 6-OH-BDE-47 or 6-MeO-BDE-47.
- All exposures were performed in duplicate tanks.
- Medaka were fed diets of food spiked with BDE-47, 6-OH-BDE-47 or 6-MeO-BDE-47, or acetone (vehicle control) for 14 days.
- Eggs were collected each morning (days 0-14) during the exposure period.
- On day 16 six female fish were collected from each tank and liver and liver-free carcasses were collected for analysis of target chemical concentrations.

MEDAKA EXPOSURE

- Sexually mature Japanese medaka (Oryzias latipes)(8 females and 4 males) randomly assigned to 10L tanks containing 6L of dechlorinated tap water.
- All exposures were performed in duplicate tanks.
- Medaka were fed diets of food spiked with BDE-47, 6-OH-BDE-47 or 6-MeO-BDE-47, or acetone (vehicle control) for 14 days.
- Eggs were collected each morning (days 0-14) during the exposure period.
- On day 16 six female fish were collected from each tank and liver and liver-free carcasses were collected for analysis of target chemical concentrations.

RESULTS

Purity of Dosing Solutions

Table 1: Concentrations of 6-OH-BDE-47, 6-MeO-BDE-47 and BDE-47 in Spiked Food (ng/g dry weight) and Stock Standard Solutions (ng/ml).

<table>
<thead>
<tr>
<th>Analyzed Chemical</th>
<th>BDE-47</th>
<th>6-MeO-BDE-47</th>
<th>6-OH-BDE-47</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDE-47 Food</td>
<td>&lt; 0.02</td>
<td>0.1</td>
<td>1.6</td>
</tr>
<tr>
<td>6-OH-BDE-47 Food</td>
<td>0.90</td>
<td>0.2</td>
<td>15</td>
</tr>
<tr>
<td>6-MeO-BDE-47 Food</td>
<td>&lt; 0.02</td>
<td>0.2</td>
<td>28.3</td>
</tr>
<tr>
<td>BDE-47 Food</td>
<td>&lt; 0.02</td>
<td>0.2</td>
<td>21,000</td>
</tr>
<tr>
<td>6-OH-BDE-47 Stock</td>
<td>1,500,000</td>
<td>4,300</td>
<td>1,900</td>
</tr>
<tr>
<td>6-MeO-BDE-47 Stock</td>
<td>&lt; 0.8</td>
<td>1,300,000</td>
<td>4,800</td>
</tr>
<tr>
<td>BDE-47 Stock</td>
<td>&lt; 0.8</td>
<td>&lt; 1.0</td>
<td>50,000</td>
</tr>
</tbody>
</table>

- 6-OH-BDE-47 not an impurity in BDE-47 or 6-MeO-BDE-47 food.
- 6-MeO-BDE-47 was detected in the fish food, but did not affect conclusions.
- Purity tests were not reported in previous exposure studies, however the possible contribution of impurities of MeO-PBDEs in commercial rat food containing fish or shrimp cannot be neglected.

CONCLUSIONS

- This study presents direct in vitro evidence of biotransformation of 6-MeO-BDE-47 to 6-OH-BDE-47.
- Biotransformation of 6-OH-BDE-47 to 6-MeO-BDE-47 was demonstrated in vivo, but the conversion was not observed in vitro (liver microsomes).
- The previously hypothesized formation of OH-PBDEs from synthetic BDE-47 did not occur.
- Biotransformation products formed in female medaka were transferred to eggs.

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