Reproductive Toxicology 33 (2012) 118–119

Contents lists available at SciVerse ScienceDirect

Reproductive Toxicology

journal homepage: www.elsevier.com/locate/reprotox

Letter to the Editor

Response to comment on "Characterization of maternal transfer of decabromodiphenyl ether (BDE-209) administered to pregnant Sprague-Dawley rats" by Biesemeier et al.

We appreciate Biesemeier et al.'s comment regarding our publications on the characteristics of maternal transfer of decabromodiphenyl ether (BDE-209) and we welcome the opportunity to respond to their questions below.

The commercial product of decabromodiphenyl ether (BDE-209) is a typical mixture of BDE-209 (≥97%), nonaBDEs (BDE-206, BDE-207, BDE-208, ≤3%) and traces of octa-BDEs [1]. In our study the used BDE-209 product was purchased from Tokyo Kasei (Tokyo, Japan), whose purity is given as >95.0% (GC) on the company's website (available at: http://www.tci-asiapacific.com/catalog/D1388.html). To learn more detailed information of the congener's content in the product, its components in hexane solution were analyzed and quantified by GC/MS during our study. And then the purity of BDE-209 was determined. Our results showed that the commercial product was composed of 98.6% of BDE-209, 0.4% of BDE-208, 0.7% of BDE-207 and 0.3% of BDE-206. Trace of octa-BDEs was also detected but below the quantification detection limit. So in our article the purity of BDE-209 was given as >98% [2]. In addition, we also noted that the purity of >98% BDE-209 in this commercial product has also been reported by other researchers [3,4].

Another concern of Mr. Biesemeier et al. is the photolytically induced debromination of BDE-209 during sample preparation. Since it is expected that the photolysis of BDE-209 might occur in the environment, some precautions were taken for the samples to avoid from light during our experiments. The samples were covered with aluminum foil and kept in the dark place when the samples were temporarily stored. Direct light irradiation to the samples was avoided during the sample treatment. Under these conditions, no significant debrominated congeners of BDE-209 were observed for the quality control samples in which the analytical standard of BDE-209 was added. Only trace of nona-BDEs was found, however, all of them were below the quantification detection limit. In addition, it has been shown that BDE-209 can be metabolized to less brominated BDEs and other metabolites in the organisms [5–7]. nona- and octa-BDEs, hydoxy/methoxy metabolites containing five to seven bromine atoms and hydroxylated octa-BDE were characterized as the metabolites of BDE-209 by rats [8–10]. So, we consider that nona- and octa-BDEs in the dosed rats are from the metabolism rather than from photochemical degradation of BDE-209.

As for the comment that accumulation of more BDE-209 will occur under the repeated exposure conditions, we mean that although the half-life of BDE-209 in rats was estimated to be relatively short, the repeated exposure can still lead to a significant accumulation of BDE-209 in rats. Since the scenarios of repeated exposure to BDE-209 can be found in the realistic environment, the toxicokinetics and its effect under this condition should be considered for the risk assessment of BDE-209. Based on the changes of BDE-209 plasma concentrations, Biesemeier et al. [11] claimed that steady-state plasma concentrations of BDE-209 were achieved within 14 days, however, apparent differences of plasma concentrations can still be observed between their used dosages and sampling intervals. For example, in the case of their used dosage of 100 and 1000 mg/(kg day), BDE-209 plasma concentrations in dams were 2299 ± 759 and 1457 ± 394 ng/ml, respectively, after 8 h after dosing on GD 20 with CO as the vehicle (Supplemental Table S6). For the case of the same dosage, 100 mg/(kg day), for example, an increasing trend can be seen from the plasma concentrations in dams up to 8 h after dosing on GD 20 with CO as the vehicle and the plasma concentrations at 4 and 8 h after dosing were 2011 ± 440 and 2299 ± 759 ng/ml (Supplemental Table S6), respectively. In our study after the dams were exposed for 14 and 18 days the concentrations of BDE-209 in dam's blood were 701 ± 63 and 501 ± 131 μg/g lipid weight, respectively. So, our results were comparable to those of Biesemeier et al. [11]. However, it should be also pointed out that the contents of BDE-209 were expressed as ng/ml plasma in the study of Biesemeier et al. [11] whereas the lipid weight-based concentrations were used in our study. Additionally, although Biesemeier et al. [11] thought that there had a steady state for the repeated exposure to BDE-209, the exact time when the steady state achieved was not given due to only data on GD 20. In our paper the concentrations of BDE-209 were increased from GD 15 to 21 (7–14 days exposure), which maybe reflected the process that BDE-209 was achieving the steady state during pregnancy. So, detailed information on the pharmacokinetics would be required for determining the exact time to achieve the steady state.

We acknowledge that no adverse effects of BDE-209 on neurobehavioural endpoints have also been reported in the literatures [12–14], however, a comprehensive review of the neurotoxicity of BDE-209 is beyond the scope of our paper. The purpose of our paper was to exhibit the presence of BDE-209 and its metabolites in both maternal tissue and fetus whole body, and their change tendency during pregnancy and lactational period. The documents about the adverse effects of BDE-209 were cited as the examples of the biological effects caused by BDE-209, and we want to emphasize the important relationship between these chemical data of maternal transfer of BDE-209 and/or its metabolites and their possible biological effects. Certainly, complete information of toxicoketics and the biological effects (adverse and no adverse evidence) is needed in the health risk assessment of BDE-209. In addition, since a final conclusion has not yet been made on whether BDE-209 is a developmental neurotoxicant, that BDE-209 is transformed in the environment or in the human body to lower brominated PBDE of potentially greater human toxicity (and developmental neurotoxicity) needs to be further investigated [15].

0890-6238/$ – see front matter
doi:10.1016/j.reprotox.2011.10.006

References

[1] Goodman JE. Neurodevelopmental effects of decabromodiphenyl ether (BDE-209) and implications for the reference dose. Regul Toxicol Pharmacol 2009;54:91–104.
[2] Cai Y, Zhang W, Hu J, Sheng G, Chen D, Fu J. Characterization of maternal transfer of decabromodiphenyl ether (BDE-209) administered to pregnant Sprague-Dawley rats. Reprod Toxicol 2011;31(1):106–10.
[3] Deng D, Guo J, Sun G, Chen X, Qiu M, Xu M. Aerobic debromination of deca-BDE: isolation and characterization of an indigenous isolate from a PBDE contaminated sediment. Int Biodeterior Biodegradation 2011;65: 465–9.
[4] Yu S, Zou P, Zhu W, Yang L, Xiao L, Jiang L, et al. Effects of humic acids and microorganisms on decabromodiphenyl ether, 4,4′-dibromodiphenyl ether and anthracene transportation in soil. Sci China Chem 2010;53:950–68.
[5] Stapleton HM, Alaee M, Letcher RJ, Baker JE. Debromination of the flame retardant decabromodiphenyl ether by juvenile carp (*Cyprinus carpio*) following dietary exposure. Environ Sci Technol 2004;38:112–9.
[6] Kierkegaard A, Balk L, Tjarnlund U, De Wit CA, Jansson B. Dietary uptake and biological effects of decabromodiphenyl ether in rainbow trout (*Oncorhynchus mykiss*). Environ Sci Technol 1999;33:1612–7.
[7] La Guardia MJ, Hale RC, Harvey E. Evidence of debromination of decabromodiphenyl ether (BDE-209) in biota from a wastewater receiving stream. Environ Sci Technol 2007;41:6663–70.
[8] Morck A, Hakk H, Orn U, Wehler EK. Decabromodiphenyl ether in the rat: absorption, distribution, metabolism, and excretion. Drug Metab Dispos 2003;31:900–7.
[9] Riu A, Cravedi JP, Debrauwer L, Garcia A, Canlet C, Jouanin I, et al. Disposition and metabolic profiling of [C-14]-decabromodiphenyl ether in pregnant Wistar rats. Environ Int 2008;34:318–29.
[10] Huwe JK, Smith DJ. Accumulation, whole-body depletion, and debromination of decabromodiphenyl ether in male Sprague-Dawley rats following dietary exposure. Environ Sci Technol 2007;41:2371–7.
[11] Biesemeier JA, Beck MJ, Silberberg H, Myers NR, Ariano JM, Bodle ES, et al. Effects of dose, administration route, and/or vehicle on decabromodiphenyl ether concentrations in plasma of maternal, fetal, and neonatal rats and in milk of maternal rats. Drug Metab Dispos 2010;38(10): 1648–54.
[12] Biesemeier JA, Beck MJ, Silberberg H, Myers NR, Ariano JM, Radovsky A, et al. An oral developmental neurotoxicity study of decabromodiphenyl ether (DecaBDE) in rats. Birth Defects Res B Dev Reprod Toxicol 2011;92(1): 17–35.
[13] Hardy ML, Schroeder R, Biesemeier J, Manor O. Prenatal oral (gavage) developmental toxicity study of decabromodiphenyl oxide in rats. Int J Toxicol 2002;21(2):83–91.
[14] Hardy ML, Banasik M, Stedeford T. Toxicology and human health assessment of decabromodiphenyl ether. Crit Rev Toxicol 2009;39(S3):1–44.
[15] Costa LG, Giordano G. Is decabromodiphenyl ether (BDE-209) a developmental neurotoxicant? Neurotoxicology 2011;32:9–24.

Yunmei Cai [a,b]
[a] *State Key Laboratory of Organic Geochemistry, Guangzhou Institute of Geochemistry, Chinese Academy of Sciences, Guangzhou 510640, China*
[b] *Graduate School of the Chinese Academy of Science, Beijing, China*

Wenbing Zhang [*]
State Key Laboratory of Organic Geochemistry, Guangzhou Institute of Geochemistry, Chinese Academy of Sciences, Guangzhou 510640, China

Junjie Hu [a,b]
[a] *State Key Laboratory of Organic Geochemistry, Guangzhou Institute of Geochemistry, Chinese Academy of Sciences, Guangzhou 510640, China*
[b] *Graduate School of the Chinese Academy of Science, Beijing, China*

Guoying Sheng
State Key Laboratory of Organic Geochemistry, Guangzhou Institute of Geochemistry, Chinese Academy of Sciences, Guangzhou 510640, China

Dunjin Chen
The Research Institute of Gynaecology and Obstetrics, Guangzhou Second People's Hospital, Guangzhou 510150, China

Jiamo Fu
State Key Laboratory of Organic Geochemistry, Guangzhou Institute of Geochemistry, Chinese Academy of Sciences, Guangzhou 510640, China

[*] Corresponding author. Tel.: +86 20 85290205; fax: +86 20 85290192.
E-mail address: zhwb@gig.ac.cn (W. Zhang)

14 April 2011
Available online 25 October 2011