Arch. Environ. Contam. Toxicol. 41, 381–385 (2001)
DOI: 10.1007/s002440010263

ARCHIVES OF
Environmental
Contamination
and Toxicology

Hepatic Enzyme Induction and Acute Endocrine Effects of 2,2′,3,3′,4,6′-Hexachlorobiphenyl and 2,2′,3,4′,5′,6-Hexachlorobiphenyl in Prepubertal Female Rats

M.-H. Li,[1] P.-C. Hsu,[2] Y. L. Guo[3]

[1] Department of Geography, National Taiwan University, 1, Section 4, Roosevelt Road, Taipei 106, Taiwan, R.O.C.
[2] Department of Safety, Health and Environmental Engineering, National Kaohsiung First University of Science and Technology, 1 University Road, Yuanchau, Kaohsiung, Taiwan, R.O.C.
[3] Department of Environmental and Occupational Health, National Cheng Kung University Medical College, 61 Shiao Tong Road, Tainan 70428, Taiwan, R.O.C.

Received: 2 January 2001/Accepted: 3 April 2001

Abstract. Polychlorinated biphenyls (PCBs) with the liable 2,3,6-substitution are important components of certain commercial mixtures and frequently detected in biota, but little is known about their enzyme induction abilities and possible endocrine-disrupting effects. CB 132 (2,2′,3,3′,4,6′-hexachlorophenyl) and CB 149 (2,2′3,4′,5′,6-hexachlorophenyl) were investigated in weanling female rats dosed intraperitoneally on days 21 and 22 and killed on day 24 of age. Uterotropic response, serum thyroid hormone, and hepatic enzyme induction were examined in prepubertal female rats treated with these two environmentally relevant 2,3,6-substituted chlorobiphenyl (CB) congeners from 8 mg/kg to 96 mg/kg. The readily metabolized CB 132 did not cause any significant increase in all endpoints measured in the present study. On the other hand, CB 149 was a weak PROD and BROD inducer and a modest depleter of serum thyroxine in prepubertal female rats. The finding of thyroid hormone disruption by CB 149 may lead to biologically significant neurobehavioral and neurochemical changes in developing animals via milk lactation.

Polychlorinated biphenyls (PCBs) are ubiquitous environmental pollutants with 209 congeners possessing different numbers of chlorine atoms substituted on the biphenyl rings. Among 209 possible congeners, a small group of coplanar chlorobiphenyl (CB) congeners resembles 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) in molecular configuration. The toxicities of these coplanar CB congeners are mediated through the aryl hydrocarbon (*Ah*) receptor, and the toxic potencies of these dioxin-like coplanar CB congeners can be predicted based on their induction of hepatic cytochrome P450 1A enzymes as compared to TCDD (Safe 1994). Until now, most of PCB toxicity studies have been extensively focused on the approximately 20 coplanar CB congeners. On the other hand, the majority of CB congeners presented in the environment are noncoplanar. The toxicities of environmentally relevant CB congeners with at least two or more *ortho* chlorine substitutions are still poorly understood (Hansen 1998), although phenobarbital (PB)-type enzyme induction (Denomme *et al.* 1983) and dopamine depletion (Shain *et al.* 1991) for some *ortho*-substituted CB congeners has been described. Moreover, the different types of CB congeners have distinct biological activities and the "toxicity" of PCBs reported is dependent on the endpoints measured and the congeners selected (Hansen 1998).

Among different *ortho*-substituted CB congeners, certain CB congeners with the labile 2,3,6-chlorine pattern on one phenyl ring, such as 2,2′,3,5′,6-pentachlorophenyl (CB 95), 2,3,3′,4′,6-pentachlorophenyl (CB 110), 2,2′,3,3′,4,6′-hexachlorophenyl (CB 132), and 2,2′,3,4′,5′,6-hexachlorophenyl (CB 149), are major components in commercial PCB mixtures (Frame *et al.* 1996). The 2,3,6-substituted ring is rapidly metabolized to methylsulfonyl PCBs (Noren *et al.* 1996), for example, both methylsulfonyl CB 132 and CB 149 metabolites can be detected in human tissues (Weistrand and Noren 1997). Therefore, these congeners are considered to be not persistent and have attracted little attention in PCB toxicity studies. More recently, there is some limited evidence suggesting that 2,3,6-substituted CB congeners possess certain toxicities that were not identified before. For example, CB 95 was found to be a PB-type enzyme inducer (Sajid 1996) and the most potent of several congeners in altering microsomal calcium ion transport by selective interaction with ryanodine receptor of muscle sarcoplasmic reticulum and brain endoplasmic reticulum (Wong and Pessah 1997). CB 110 was found to be weakly uterotopic, a PB-type enzyme inducer and a modest depleter of serum thyroxine (T_4) in prepubertal female rats (Li *et al.* 1998). However, little information is available for other environmentally relevant 2,3,6-substitued CB congeners in terms of their possible toxic properties.

Both CB 132 and CB 149 are conformationally stable chiral CB congeners with the 2,3,6-chlorine pattern on one phenyl

Correspondence to: M.-H. Li; *email:* meihuili@ccms.ntu.edu.tw

ring (Glausch *et al.* 1996). Considering the fact that both CB 132 and CB 149 are major components in Aroclor mixtures (Frame *et al.* 1996) and frequently detected in human milk (Glausch *et al.* 1995; Blanch *et al.* 1999) as well as biota (Jordan and Feeley 1999; Reich *et al.* 1999; Jimenez *et al.* 2000; Serrano *et al.* 2000), it is important to investigate enzyme induction abilities and possible endocrine-disrupting effects of these two congeners. In this study, we used immature Sprague-Dawley female rats as an animal model to examine the uterotropic response, serum thyroid hormone, and enzyme induction of two environmentally relevant 2,3,6-substitued CB congeners, CB 132 and CB 149.

Materials and Methods

Chemicals

Corn oil was purchased from Sigma Chemical Company (St. Louis, MO). CB 132 and CB 149 were obtained from AccuStandard (New Haven, CT; guaranteed $>$ 99% pure). All chemicals and reagents used in enzyme assays were obtained from Sigma Chemical Company. Radioimmunoassay kits for determining serum thyroid hormone were purchased from Diagnostic Systems Laboratories, Inc. (Webster, TX).

Animals and Treatments

Sprague-Dawley rats were obtained from the animal center of National Cheng Kung University Medial College (Tainan, Taiwan, R.O.C.) and were housed in a rodent vivarium. The animals were kept in temperature and humidity controlled rooms (21–22°C, 40–50% humidity), on a 12-h light/dark cycle. Laboratory Rodent Diet 5001 (LabDiet, Richmond, IN) and water were available *ad libitum*. Rats were weaned at 20 days of age. Female pups were injected intraperitoneally with CB 132 or CB 149 dissolved in 0.1 ml corn oil or corn oil alone between 1 and 2 PM on day 21 and day 22. Doses were based on a 50 g rat with half of the dose delivered on each of 2 consecutive days.

Necropsy and Tissue Processing

Rats were decapitated between 9:30 and 11:30 AM on day 24, 44 h after the second dose; blood was collected immediately and allowed to clot. Serum was separated by centrifugation and stored at −20°C until thyroid hormone analysis. The uterus was excised, trimmed of fat, cut at the cervical os, and weighed to the nearest 0.01 mg. Livers were perfused *in situ* with ice-cold 0.05 M Tris–0.15 M KCl buffer (pH 7.4), excised, blotted on tissue paper, and weighed. The livers were then homogenized in the same Tris-KCl buffer. The crude homogenate was centrifuged at 10,000 × *g* for 15 min at 4°C. The pellet from the final centrifugation was resuspended in buffer (0.05 M Tris-HCl, 20% glycerol [v/v], 1 mM EDTA; pH 7.4 at 4°C) and stored at −80°C until assayed.

Enzyme Assays

7-Ethyoxyresorufin O-deethylase (EROD), 7-pentoxyresorufin O-depentylase (PROD), and 7-benzyloxyresorufin O-debenzylase (BROD) were determined by a modification of the method of Pohl and Fouts (1980), as previously described in Li *et al.* (1994). EROD was used as a measurement of cytochrome P450 1A activity, and PROD and BROD were used as a measurement of cytochrome P450 2B activity. UDPGT activity in the microsomal suspension was measured using 4-nitrophenol and phenolphthalein as substrates. UDPGT activities toward 4-nitrophenol and toward phenolphthalein were determined by a modification of the method of Watanaba *et al.* (1986) as described in Seo *et al.* (1995). Microsomal protein was determined by the modification of the Lowry method reported by Guengerich (1982) using bovine serum albumin as a standard. Each sample was measured in duplicate.

Thyroid Hormone Analysis

Serum thyroid stimulating hormone (TSH), total 3,3′,5-triiodothyronin (T_3) and T_4 concentrations were determined using commercially available radioimmunoassay kits (Diagnostic System Laboratories, Inc. Webster, Texas). Due to limited amount of serum obtained from each rat, T_3 and TSH were analyzed only once for each sample. The detection limit of the assay was 0.4 μg/dl for T_4, 4.3 ng/dl for T_3, and 0.03 μlU/ml for TSH.

Data Analysis

All data are expressed as mean ± standard errors. Data were analyzed by one-way analysis of variance (ANOVA) using the Minitab statistical program (Release 13.2) with a significant level of $p \leq 0.05$. If a significant result was found, the Dunnett's *t* test was used to compare treatment groups versus a control group.

Results

Acute Endocrine Response

Both CB 132 and CB 149 did not cause any significant uterine weight increase from 8 mg/kg to 96 mg/kg (Table 1). CB 149 decreased serum total T_4 more than 25% at 32 mg/kg or higher (Figure 1). On the other hand, CB 132 did not cause any significant decrease in serum total T_4 and T_3 from 8 mg/kg to 96 mg/kg. In addition, TSH levels were very low in all treatment groups, and most TSH measurements were below the detection limit (data not shown).

Hepatic Enzyme Activities

EROD, PROD, and BROD activities were not induced by CB 132 from 8 mg/kg to 96 mg/kg (Table 2). CB 149 increased PROD and BROD activity in a dose-dependent manner. At 96 mg/kg, PROD and BROD activities were significantly increased approximately two- and fourfold compared to the control group, respectively (Table 2). In addition, there was no effect on 4-nitrophenol UDPGT or phenolphthalein UDPGT activities by either CB 132 or CB 149 from 8 mg/kg to 96 mg/kg (Table 3).

Discussion

The major differences between CB 132 and CB 149 are rates of metabolism and potency as enzymes inducers. According to a

Table 1. Body weight and uterotropic responses in prepubertal female rats administered CB 132 or CB 149

Treatment	Dose (mg/kg)	n	Body Weight at Day 21 (g)	Body Weight at Day 24 (g)	Uterine Weight (mg)
Control	0	9	39.28 ± 1.89	51.67 ± 1.81	38.00 ± 4.30
Estradiol	0.04	6	39.08 ± 0.93	52.75 ± 0.93	42.20 ± 2.87
CB 132	8	5	37.40 ± 3.45	48.10 ± 2.62	30.90 ± 2.88
	32	5	41.60 ± 3.87	50.08 ± 1.31	28.94 ± 3.31
	96	5	42.60 ± 2.66	51.78 ± 2.34	34.70 ± 4.85
CB 149	8	5	38.50 ± 2.17	52.90 ± 3.26	37.04 ± 9.23
	32	5	38.60 ± 1.33	54.00 ± 2.21	38.46 ± 4.35
	96	5	39.70 ± 1.09	55.80 ± 1.84	38.36 ± 3.80

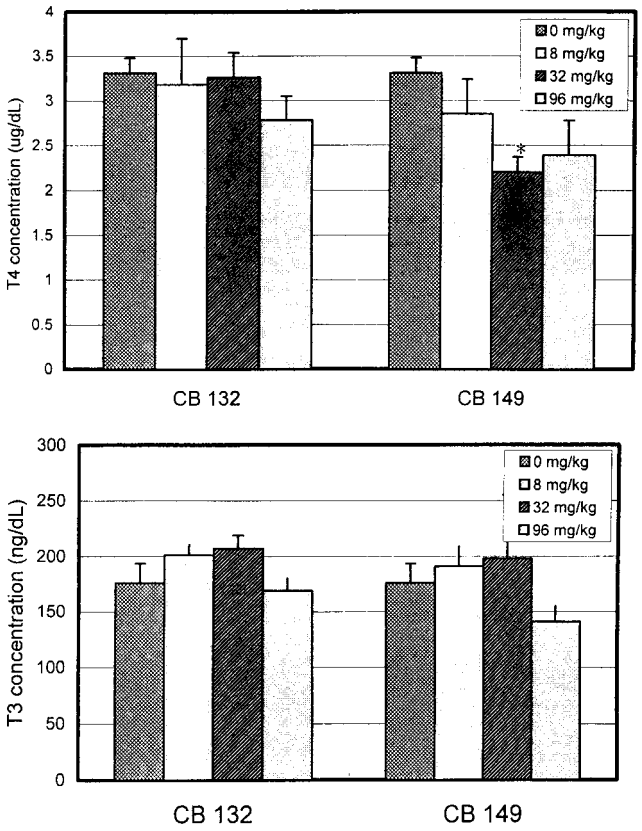

Fig. 1. Thyroid hormones status in prepubertal female rats administered CB 132 or CB149. *Significantly different from controls by Dunnett's *t* test ($p \leq 0.05$)

classification scheme of Kannan *et al.* (1995) on rates of metabolism for different CBs, CB132 belongs to a group of readily metabolizable CB congeners with both vicinal H atoms in both *ortho/meta* and *meta/para* positions, whereas CB 149 is a group of less readily metabolizable CB congeners with vicinal H atoms in only *meta/para* position and is metabolized to less extent compared to CB 132. CB 132 was an ineffective enzyme inducer in the present study. CB 149 increased PROD and BROD activities significantly two- and fourfold at 96 mg/kg, respectively.

There is no clear relationship between metabolic potency and enzyme induction ability in 2,3,6-substituted CB congeners from current available information (Table 4). Among 18 CBs with the labile 2,3,6-chlorine pattern on one phenyl ring, they can be classified into two groups based on the presence/absence and position of vicinal hydrogen atoms in term of their metabolism rates (Table 4). One group (group IV) is CB congeners with both *meta-para* and *ortho-meta* vicinal hydrogen atoms, the other group (group II) is CB congeners with only *meta-para* vicinal hydrogen atoms (Kannan *et al.* 1995). CB 95, CB 136, CB 149, and CB 199 belong to the less readily metabolizable group (group II) and possess PB-type enzyme induction abilities. On the other hand, both CB 110 and CB 132 belong to the readily metabolizable group (group IV) but with different degree of enzyme induction. CB 110 was found to be a PB-type enzyme inducer (Li *et al.* 1998), whereas CB 132 was an ineffective enzyme inducer in the present study. It seems there is no obvious relationship between enzyme induction and metabolic characteristics of 2,3,6-substitued CBs.

Uterotropic activity in immature female rodents is a common endpoint of estrogenic activity but is a relatively insensitive indication. Among CB congeners studied so far, several *ortho*-substituted CB congeners as well as some hydroxylated CB congeners did find some weak uterotropic activity in rodents (Korach *et al.* 1988; Jansen *et al.* 1993; Li *et al.* 1994, 1998). The mechanism for induction of estrogenic effects by CB congeners is still not clear, however, some evidence indicate that hydroxylated metabolites of PCBs play an important role in the estrogenicity of PCBs (Korach *et al.* 1988). In the present study, CB 132 and CB 149 did not produce any significant increase in uterine weight. It may be related to the lack of formation of hydroxylated metabolites which are presumably more reactive with estrogenic receptor (Korach *et al.* 1988) because of weak P450 2B enzyme induction in these two CB congeners observed in this study.

It is known that there are a variety of mechanisms by which both TCDD-like CB congeners and non-TCDD-like CB congeners can exert their effects on thyroid hormone homeostasis (Li and Hansen 1997; Hansen 1998). PCBs can directly cause injury in thyroid glands (Collins and Capen 1980; Byrne *et al.* 1987) or indirectly affect thyroid function via either enhanced thyroid hormone metabolism or by decreased plasma T_4 levels through displacement of T_4 from its carrier protein by hydroxylated PCB metabolites (Li and Hansen 1997). Although there was no increase of UDPGT activities observed in the present study, a possible mechanism of serum total T_4 depletion caused by CB 149 via enhanced T_4 metabolism cannot be completely excluded. A

Table 2. Liver microsomal enzyme activities (mean ± SE; nmol resorufin formed/min/mg protein) in prepubertal female rats administered CB 132 or CB 149

Treatment	Dose (mg/kg)	n	EROD	PROD	BROD
Control	0	9	0.731 ± 0.109	0.087 ± 0.016	0.048 ± 0.011
CB 132	8	5	0.535 ± 0.116	0.095 ± 0.018	0.029 ± 0.009
	32	5	0.570 ± 0.030	0.107 ± 0.017	0.074 ± 0.018
	96	5	0.607 ± 0.115	0.106 ± 0.026	0.071 ± 0.020
CB 149	8	5	0.937 ± 0.145	0.122 ± 0.017	0.087 ± 0.017
	32	5	0.817 ± 0.071	0.160 ± 0.025	0.118 ± 0.018
	96	5	0.868 ± 0.114	0.171 ± 0.028[a]	0.182 ± 0.041[a]

[a] Significantly different from controls by Dunnett's *t* test ($p \leq 0.05$).

Table 3. UDPGT activities (mean ± SE; nmol substrate disappearing/min/mg protein) in prepubertal female rats administered PCB 132 or PCB 149

Treatment	Dose (mg/kg)	n	4-NP UDPGT	PP UDPGT
Control	0	9	5.14 ± 0.70	2.03 ± 0.27
PCB 132	8	5	5.16 ± 1.11	1.77 ± 0.60
	32	5	4.33 ± 1.17	1.68 ± 0.49
	96	5	3.41 ± 0.82	1.32 ± 0.37
PCB 149	8	5	4.36 ± 3.26	1.69 ± 0.07
	32	5	3.89 ± 2.21	1.74 ± 0.30
	96	5	4.96 ± 0.94	1.93 ± 0.27

direct measurement of T_4 glucuronidation will be needed to definitely rule out this mechanism. Kato *et al.* (1998) found that both methylsulfonyl CB 132 and CB 149 metabolites at 20 μmol/kg possess the ability to reduce thyroid hormone levels in male Sprague-Dawley rats. However, it was only found that CB 149, but not CB 132, reduced T_4 levels in the present study. It is likely that the depletion of T_4 by CB 149 may be due to induced P450 2B activities and the generation of more bioactive metabolites, such as methylsulfonyl metabolites. It will be greatly helpful to understand toxicities of different CBs by investigating the mechanism of PB-type enzyme induction and the possible role of metabolites.

In conclusion, neither CB 132 nor CB 149 induced EROD significantly in the present study, confirming that they are poor agonists for the *Ah* receptor. The readily metabolized CB 132 did not cause any significant increase in PROD and BROD activities or decrease in thyroid hormone levels in prepubertal female rats. On the other hand, the less readily metabolized CB 149 was a weak PB-type enzyme inducer and a modest depleter of serum thyroxine in prepubertal female rats. Thyroid hormones are known to play an important role in neurodevelopment events of the developing animals (Dussault and Ruel 1987). Although CB 149 is considered relatively nonpersistent, CB 149 is commonly found at different environmental samples as well as milk samples. The finding of thyroid hormone disruption by CB 149 may lead to biologically significant neurobehavioral and neurochemical changes in developing animals via milk lactation.

Acknowledgments. This study was supported by the National Science Council under grant NSC 89-2320-B-002-024 and NSC-89-2320-B-002-213. We are grateful to Ms. Chow-Yen Chuang for her contribution in this study. We also thank Dr. Larry Hansen (University of Illinois at Urbana) for his suggestion in selections of PCB congeners.

References

Blanch GP, Glausch A, Schuring V (1999) Determination of the enantiomeric ratios of chiral PCB 95 and 149 in human milk samples by multidimensional gas chromatography with ECD and MN (SIM) detection. Eur Food Res Technol 209:294–296

Byrne JJ, Carbone JP, Hanson EA (1987) Hypothyroidism and abnormalities in the kinetics of thyroid hormone metabolism in rats treated chronically with polychlorinated biphenyl and polybrominated biphenyl. Endocrinology 121:520–527

Collins WT, Capen CC (1980) Ultrastructural and functional alterations of the rat thyroid gland produced by polychlorinated biphenyls compared with iodide excess and deficiency, and thyrotropin and thyroxine administration. Virchows Arch B Cell Path 33:213–231

Denomme MA, Bandiera S, Lambert I, Copp L, Safe L, Safe S (1983) Polychlorinated biphenyls as phenobarbitone-type inducers of microsomal enzymes. Biochem Pharmacol 32:2955–2963

Dussault JH, Ruel J (1987) Thyroid hormones and brain development. Ann Rev Physiol 49:321–334

Frame GM, Cochran JW, Bowadt SS (1996) Complete PCB congener distributions for 17 Aroclor mixtures determined by 3 HRGC systems optimized for comprehensive, quantitative, congener-specific analysis. J High Resol Chromatogr 19:657–668

Glausch A, Hahn J, Schurig V (1995) Enantioselective determination of chiral 2,2′,3,3′4,6′-hexachlorobiphenyl (PCB 132) in human milk samples by multidimensional gas chromatography/electron capture detection and by mass spectrometry. Chemosphere 30: 2079–2085

Glausch A, Blanch GP, Schurig V (1996) Enantioselective analysis of chiral polychlorinated biphenyls in sediment samples by multidimensional gas chromatography-electro-capture detection after steam distillation-solvent extract and sulfur removal. J Chromatogr A 723:399–404

Guengerich FP (1982) Microsomal enzymes involved in toxicology-analysis and separation. In: Hayes AW (ed) Principles and methods of toxicology. Raven Press, NY, pp 609–634

Hansen LG (1998) Stepping backward to improve assessment of PCB congener toxicities. Environ Health Perspect 106S:171–189

Jansen HT, Cooke PS, Porcelli J, Liu TC, Hansen LG (1993) Estrogenic and antiestrogenic actions of PCBs in the female rat: *in vitro* and *in vivo* studies. Reprod Toxicol 7:237–248

Table 4. Structure characteristics and environmental occurrences of 2,3,6-substituted CB congeners

IUPAC No.	A Ring	B Ring	Chiral	Metabolic Group[a]	Environmental Occurrences[b]	Enzyme Induction[c]
24	236		No	IV		—
45	236	2	Yes	IV	X	—
59	236	3	No	IV		—
64	236	4	No	IV		—
84	236	23	Yes	IV	X	—
91	236	24	Yes	IV	X	—
95	236	25	No	II	XX	Weak PB
110	236	34	No	IV	X	Weak PB
113	236	35	No	II	—[d]	—
132	236	234	Yes	IV		None[e]
135	236	235	Yes	II		—
136	236	236	Yes	II	X	Weak PB
149	236	245	Yes	II	X	Weak PB[e]
150	236	246	No	II	—[d]	—
164	236	345	No	II		—
174	236	2345	Yes	II	X	—
179	236	2356	No	II	X	—
199	236	23456	No	II	X	PB

[a] Metabolic groups are defined according to a classification scheme of Kannan *et al.* (1995).
[b] Environmental relevance is adapted from Hansen (1998). Important congeners are indicated by X or, especially important, XX.
[c] Enzyme induction is based on Hansen (1998).
[d] PCB congeners are not detected in Aroclor mixtures above 0.01 weight % (Frame *et al.* 1996).
[e] Based on this study.

Jimenez O, Jimenez B, Gonzalez MJ (2000) Isomer-specific polychlorinated biphenyl determination in cetaceans from the Mediterranean Sea: enantioselective occurrence of chiral polychlorinated biphenyl congeners. Environ Toxicol Chem 19:2653–2660

Jordan SA, Feeley MM (1999) PCB congener patterns in rats consuming diets containing Great Lakes salmon: analysis of fish, diets and adipose tissue. Environ Res A 80:S207–S212

Kannan N, Reusch TBH, Schulz-Bull DE, Petrick G, Duinker JC (1995) Chlorobiphenyls: model compounds for metabolism in food chain organisms and their potential use as ecotoxicological stress indicators by application of the metabolic slope concept. Environ Sci Technol 29:1851–1859

Kato Y, Haraguchi K, Shibahara T, Masuda Y, Kimura R (1998) Reduction of thyroid hormone levels by methylsulfonyl metabolites of polychlorinated biphenyl congeners in rats. Arch Toxicol 72:541–544

Korach KS, Sarver P, Chae K, McLachlan JA, Mckinney JD (1988) Estrogen receptor-binding activity of polychlorinated hydroxybiphenyls: conformationally restricted structural probes. Mol Pharmacol 33:120–126

Li M-H, Hansen LG (1997) Consideration of enzyme and endocrine interactions in the risk assessment of PCBs. Rev in Toxicol 1:71–156

Li M-H, Zhao YD, Hansen LG (1994) Multiple dose toxicokinetic influence on the estrogenicity of 2,2′,4,4′,5,5′-hexachlorobiphenyl. Bull Environ Contam Toxicol 53:583–590

Li M-H, Rhine C, Hansen LG (1998) Hepatic enzyme induction and acute endocrine effects of 2,3,3′,4′,6-pentachlorobiphenyl in prepubertal female rats. Arch Envioron Contam Toxicol 35:97–103

Noren K, Lunden A, Pettersson E, Bergman A (1996) Methylsulfony metabolites of PCBs and DDE in human milk in Sweden, 1972–1992. Environ Health Perspect 104:766–773

Pohl RA, Fouts RJ (1980) A rapid method for assaying the metabolism of 7-ethoxyresorufin by microsomal subcellular fractions. Anal Biochem 107:150–155

Reich S, Jimenez B, Marsili L, Hernandez LM, Schurig V, Gonzalez MJ (1999) Congener specific determination and enantiomeric ratios of chiral polychlorinated biphenyls in striped dolphins (*Stenella coeruleoalba*) from the Mediterranean sea. Environ Sci Technol 33:1787–1793

Safe S (1994) Polychlorinated biphenyls (PCBs): environmental impact, biochemical and toxic responses, and implications for risk assessment. Crit Rev Toxicol 24:87–149

Sajid TM (1996) Enzyme induction and acute endocrine effects of PCB 95 and PCB 99 in immature female rats. Masters thesis, University of Illinois at Urbana-Champaign

Seo BY, Li M-H, Hansen LG, Moore RW, Peterson RE, Schantz SL (1995) Effects of gestational and lactational exposure to coplanar PCB congeners or TCDD in thyroid hormone concentrations in weanling rats. Toxicol Lett 78:253–262

Serrano R, Fernandez M, Rabanal R, Hernandez M, Gonzalez MJ (2000) Congener-specific determination of polychlorinated biphenyls in shark and grouper liver from the northwest African Atlantic Ocean. Arch Environ Contam Toxicol 38:217–224

Shain W, Bush B, Seegal R. (1991) Neurotoxicity of polychlorinated biphenyls: structure-activity relationships of individual congeners. Toxicol Appl Pharmacol 111:33–42

Watanaba HK, Hoskind B, Ho IK (1986) Selective inhibitory effect of organophosphates on UDP-glucuronyl transferase activities in rat liver microsomes. Biochem Pharmacol 35:455–460

Weistrand C, Noren K (1997) Methylsulfonyl metabolites of PCBs and DDE in human tissue. Environ Health Perspect 105:644–649

Wong PW, Pessah IN (1997) Noncoplanar PCB 95 alters microsomal calcium transport by an immunophilin FKBP12-dependent mechanism. Mol Pharmacol 51:693–702