DEVELOPMENT OF TOXIC EQUIVALENCY FACTORS FOR POLYCHLORINATED BIPHENYLS (PCBs)

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ABSTRACT

Some of the biochemical and toxic effect elicited by the commercial PCBs are similar to those caused by 2,3,7,8-TCDD and related compounds. The specific congeners associated with these toxic responses include the coplanar PCBs, 3,3',4,4'- and 3,4,4',5-tetra-, 3,3',4,4',5-penta and 3,3',4,4',5,5'-hexachlorobiphenyls and the monoortho coplanar PCBs, 2,3,3',4,4'-penta-, 2,3',4,4',5-penta-, 2,3,4,4',5-penta-, 2',3,4,4'5-penta, 2,3,3',4,4',5-hexa-2',3,3',4,4',5-hexa-, 2,3',4,4',5,5'-hexa- and 2,3,3',4,4',5,5'-heptachlorobiphenyl. The total "2,3,7,8-TCDD-like" toxicity of a mixture of PCBs is the summation of the concentrations of the individual toxic congeners times a relative potency factor for each individual congener. Based on quantitative dose-response data for PCB congeners, the following TEFs (relative to 2,3,7,8-TCDD) have been assigned; 0.1 for 3,3',4,4',5-pentachlorobiphenyl (pentaCB), 0.;05 for 3,3',4,4'5,5'-hexachlorobiphenyl (hexaCB), 0.01 for 3,3',4,4'-tetrachlorobiphenyl (tetraCB) and 0.001 for the monoortho coplanar PCBs.

INTRODUCTION

The development of TEFs for the toxic halogenated aromatics has been necessitated by the identification of complex mixtures of these compounds in almost every compartment of the global ecosystem. Although extensive toxicologic and carcinogenic data are available for one member of this family, namely 2,3,7,8-TCDD, only limited information is available for the remaining congeners. There is good evidence that the toxic halogenated aromatic hydrocarbons elicit common toxic responses through a common receptor-mediated mechanism of action (1-3). Moreover, the SARs observed for the different classes of halogenated aromatics provide support for both the proposed receptor-mediated mechanism

of action and the development of TEFs for this family of chemicals (2,3). The TEF values for the PCDDs and PCDFs have been proposed by several groups (reviewed in 4) and this paper will propose TEFs for specific PCB congeners.

MATERIALS AND METHODS

The data reported in this study have primarily been derived from previous studies (reviewed in 2) or recent work by D. Davis (5) and C. Yao (6) who investigated the structure-dependent effects of PCBs as immunosuppressive agents in C57BL/6 mice and as inducers of aryl hydrocarbon hydroxylase (AHH) and ethoxyresorufin-O-deethylase (EROD) activities in chick embryo hepatocytes.

RESULTS AND DISCUSSION

Tables 1 and 2 summarize the ED_{50}/EC_{50} values for several toxic responses elicited by individual PCB congeners in several species/cells. It was apparent that for each congener there was a range of relative potency values (compared to 2,3,7,8-TCDD) which are summarized in Table 3. Based on the relative priority rating of the individual ED_{50}/EC_{50} values obtained for various responses, single TEF values have been assigned to the coplanar and monoortho coplanar PCB congeners and these are summarized in Table 3. Applications of these TEF values for estimating the toxic potencies of PCB mixtures have shown that there is an excellent correlation between the calculated vs. observed TEFs (4). It should be noted that the TEF approach for toxic halogenated aromatic hydrocarbons provides an estimate of the 2,3,7,8-TCDD-like toxicity of halogenated aromatic mixtures but does not address the relative potencies of other toxic responses which are not Ah receptor-mediated.

Table 1. Comparative Toxic and Biochemical Potencies of Coplanar PCBs (4)

Response	Target Species/Cell	ED_{50}/EC_{50} Values			
		3,3,4,4'-tetraCB	3,3',4,4',5-pentaCB	3,3',4,4',5,5'-hexaCB	2,3,7,8-TCDD
Subchronic Toxicities					
Body weight loss	Rat (μmol/kg)	> 500	3.3	15	0.05
Thymic atrophy	Rat (μmol/kg)	> 500	0.95	8.9	0.09
Bursal lymphoid development	Chick embryo (μg/kg)	50	4	300	
Thymic lymphoid development	Mouse Fetuses (M)	3×10^{-7}	2×10^{-9}	2×10^{-7}	2×10^{-10}
Immunotoxicity	Mice (μmol/kg)				.0024
Teratogenicity	Mice (μmol/kg)			.055-.110 (328)	.011
AHH induction	rat (μmol/kg)	~ 500	0.50	1.10	0.004
AHH induction	H-4-II E cells (M)	3.5×10^{-5}	2.4×10^{-10}	6.0×10^{-8}	7.2×10^{-11}
AHH induction	Chick embryo hepatocytes	2.2×10^{-9}	2.0×10^{-9}	-	2.0×10^{-11}
Receptor binding	Rat cytosol (M)	4.3×10^{-7}	1.2×10^{-7}	insoluble	1.0×10^{-8}

Table 2. Comparative Toxic and Biochemical Potencies of Monoortho Coplanar PCBs (4)

Response	Target Cell/ Species	ED_{50}/EC_{50} Values								
		2,3',4,4',5-pentaCB	2,3,3',4,4'-pentaCB	2',3,4,4',5-pentaCB	2,3,4,4',5 pentaCB	2,3,3',4,4',5-hexaCB	2,3,3',4,4',5'-hexaCB	2,3',4,4',5,5'-hexaCB	2,3,3',4,4',5,5'-heptaCB	2,3,7,8-TCDD
Subchronic Studies										
Body weight loss	Rat (umol/kg)	1450	750	370	180	180	220			0.05
Thymic atrophy	Rat (umol/kg)	1550	1030	2790	200	180	225			0.09
Bursal lymphoid development	Chick embryos (ug/kg)	>6000	<6000			<6000	>6000	>6000		
Immunotoxicity development	Mice (umol/kg)					2				0.0024
Teratogenicity	Mice (umol/kg)					328				0.011
AHH induction	Rat (umol/kg)	165	65	130	30	7	6			0.004
	Rat hepatoma cells (M)	$1.2x10^{-5}$	$8.8x10^{-8}$	$3.9x10^{-6}$	$9.7x10^{-7}$	$2.1x10^{-6}$	$1.1x10^{-5}$	$1.3x10^{-5}$		$7.2x10^{-11}$
	Chick embryo hepatocytes (M)	$5.0x10^{-8}$			$1.0x10^{-7}$	$1.4x10^{-5}$				$2.0x10^{-11}$
Receptor binding	Rat cytosol (M)	$9.1x10^{-5}$	$4.3x10^{-6}$	$1.4x10^{-5}$	$4.7x10^{-6}$	$7.1x10^{-6}$	$5.0x10^{-6}$	$1.6x10^{-5}$		$1.0x10^{-8}$

Table 3. Proposed TEF Values for the Coplanar and Monoortho Coplanar PCB Congeners.

Congener		TEF Values	Relative Potency Ranges
1.	Coplanar PCBs		
	3,3',4,4',5-pentaCB	0.1	0.3-0.0006
	3,3'4,4'5,5'-hexaCB	0.05	0.1-0.0012
	3,3'4,4'-tetraCB	0.01	0.009-0.00008
2.	Monoortho coplanar PCBs	0.001	0.0008-0.0000014

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