INDICATIVE ANALYSIS OF RELATIVE RISKS AND DATA GAPS OF DIOXIN-LIKE COMPOUNDS IN BALTIC SEA FISH, BASED ON BODY BURDEN, BIOKINETIC AND BIOACTIVITY RATIOS

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Introduction

The Baltic Sea is heavily loaded by dioxins, notable e.g. in high TEqs in herring[1-6;7], other fish[2-6] and some humans[9-12;13]. Associated risks are affected not only by dioxin levels, but also by the relative toxicities[14] and toxicokinetics[15-19] of the various compounds. Many substances without TEF values have been found to exert dioxin toxicity or bioactivity and to possess properties which may justify their inclusion in aggregate assessments[20-28]. Despite their lower toxicity and perhaps persistence, they may be present at sufficient levels in target tissues to play a role in overall dioxin toxicity. Substance specific assessments are thus needed to pinpoint the compounds and congeners of most concern and to alleviate limitations in the TEF scheme. To focus further risk assessments of dioxins in the Baltic and especially in its fish, and to identify information gaps, a comparative assessment of dioxin-like substances was done.

Methodology

The approach is based on ratios between published peer-reviewed values for key properties of dioxin-like compounds and those of TCDD, and combining the ratios to indices of relative risks. The properties selected include a) contents in herring and, in more detailed analysis, in salmon (fillet); in human (blood); in the marine mammal with haloaromatic-linked reproductive disorders, ringed seal (blubber); and in herring gull or guillemot (eggs); b) metabolic elimination for these consumers; c) relative dioxin toxicity in these groups approximated by TEFs or Ah-R binding or metabolizing enzyme activation (cf. explanations in Table 1). Thus, the ratio for each property and compound is obtained by dividing the respective value for the compound with that of TCDD; relative risk indices are finally obtained as linear products of these ratios. This is an extension of the TEF approach[14] to address other compounds and properties influencing risks.

Results and discussion

The approach enables systematic and flexible initial analysis and ranking of relative risks associated with dioxin-like compounds. Use of ratios of variables increases compatibility across metrics. However, the analysis is constrained by data and model incompleteness. Of the latter, variation between compounds in absorption and distribution are omitted. Also, consumer body burdens are desirable instead of herring levels to describe risks in those consumers more fully. Yet, most of the risk to humans of the WHO set seemed attributable to 23478-C_5DF which may thus be studied in more depth and function as a proxy[cf. 30]. Also the other C_5DD/Fs are notable, as is CB-126 even without elimination data. The study indicates that congener-specific data are needed especially on a) compounds with no representative and reliable measurements in the Baltic, including bromodioxins and PAHs, and also the WHO set in birds and wild mammals; b) metabolism of many compounds, including some in the WHO set, in target organisms and tissues; c) relative toxicity and its markers *in vivo*; d) basis for extrapolation to other taxa/groups (e.g. fetuses), tissues and settings. Simulations by suited models may substitute for some of these data. The analysis can be supplemented on the basis of the developing Nordic, Baltic Sea and EU work on dioxins/POPs.

Table 1. Relative risks to human and other herring consumers from dioxin-like compounds in the Baltic Sea, based on published body burdens, elimination rates and TEFs or activities on AhR or enzymes in respective vertebrate systems in relation to those for TCDD. All values have been rounded off to 1 digits. In parentheses, extrapolated and particularly uncertain values.

Compound (IUPAC No)	Body burden in Baltic S biota relative to TCDD (fat based)					Body retention relative to TCDD (body T1/2 based)			Potency relative to TCDD, WHO-TEF (or receptor or enzyme activity based)			Indicative order-of-magnitude relative risk of substance to		
	her-ring	sal-mon	hum bloo	seal blub	pred. birds	hum	fish	bird	mam[k]	fish[l]	birds[m]	human/ mammal	salmon	pred. bird
	1	2	9-12	29		15-7	(18)	19	14,20-5	14,22-4,26	14,28			
	c_{fh}	c_{fs}	c_h	c_s	c_b	$t_{1/2h}$	$t_{1/2f}$	$t_{1/2b}$	r_m	r_f	r_b	c_{fh} $t_{1/2x}$ r_x (c_{fh} r_x)		
Polychlorinated dibenzo-p-dioxins and furans														
2378-C_4DD	1		1	a	1	1		1	1	1	1	1	1	1
12378-C_5DD	5		3			2		(0.7)	1	1	1	10		
123478-C_6DD	0.5		0.4			1			10^{-1}	10^{-1}	5.10^{-1}	0.05		
123678-C_6DD	6		10			2		(0.9)	10^{-1}	10^{-1}	10^{-2}	1		
123789-C_6DD	0.6		3			0.7		(0.8)	10^{-1}	10^{-1}	10^{-1}	0.04		
1234678-C_7DD	0.3		5			0.5		(1)	10^{-2}	10^{-3}	<	0.002		
C_8DD	0.3		30			0.9		(3)	10^{-4}	-	-	0.00003		
2378-C_4DF	0.5		4	3/a		1		(0.8)	10^{-1}	5.10^{-2}	1	0.05		
12378-C_5DF	5		0.2	0.1/a		2		(0.7)	5.10^{-2}	5.10^{-2}	10^{-1}	0.5		
23478-C_5DF	40		0.5			3		(0.7)	5.10^{-1}	5.10^{-1}	1	60		
123478-C_6DF	1		1			0.9		(0.7)	10^{-1}	10^{-1}	10^{-1}	0.09		
123678-C_6DF	2		1			0.8		(0.6)	10^{-1}	10^{-1}	10^{-1}	0.2		
123789-C_6DF	0.1		0.06			0.8			10^{-1}	10^{-1}	10^{-1}	0.008		
234678-C_6DF	2		0.4			0.8		(0.6)	10^{-1}	10^{-1}	10^{-1}	0.2		
1234678-C_7DF	0.2		4			0.4		(1)	10^{-2}	10^{-2}	10^{-2}	0.0008		
1234789-C_7DF	0.04		0.01			0.4		(1)	10^{-2}	10^{-2}	10^{-2}	0.00002		
C_8DF	<		3			>		(2)	10^{-4}	10^{-4}	10^{-4}	<		
Polychlorinated biphenyls - WHO TEQ set														
PCB 81									10^{-4}	5.10^{-4}	10^{-1}			
PCB 77	70		(2)			0.003			10^{-4}	10^{-4}	5.10^{-2}	0.0002		
PCB 126	80		4						10^{-1}	5.10^{-3}	10^{-1}	(8)		
PCB 169	40		4			1			10^{-2}	5.10^{-4}	10^{-3}	0.4		
PCB 105	6		300			0.3			10^{-4}	0	10^{-4}	0.0002		
PCB 114	0.4		40						5.10^{-4}	0	10^{-4}	(0.0002)		
PCB118	20		1000			0.7			10^{-4}	0	10^{-5}	0.001		
PCB 123	2								10^{-4}	0	10^{-5}	(0.0002)		
PCB 156	4		1000			0.4			5.10^{-4}	0	10^{-4}	0.0008		
PCB 157	0.8		200						5.10^{-4}	0	10^{-4}	(0.0004)		
PCB 167	0.9		300						10^{-5}	0	10^{-5}	(0.00009)		
PCB 189	0.4								10^{-4}	0	10^{-5}	(0.00004)		
Other PCBs with relevant potency data														
PCB 78									(10^{-3})		(10^{-4})			
PCB 79									(2.10^{-3})		(4.10^{-3})			
PCB 101						0.007			(2.10^{-5})		0			
PCB 122									(8.10^{-5})		(2.10^{-5})			
PCB 127									(10^{-3})		(5.10^{-3})			
PCB 138						4			(8.10^{-6})		(10^{-3})			
PCB 153						7			(6.10^{-6})		0			
PCB 170									(5.10^{-6})		(2.10^{-4})			
PCB 180						3			(6.10^{-6})		(2.10^{-4})			

Table 1. (cont'd)

Compound (IUPAC No)	Body burden in Baltic S biota relative to TCDD (fat based)					Metabolic elimination relative to TCDD (body T1/2 based)			Potency relative to TCDD, WHO-TEF (or receptor or enzyme activity based)			Indicative order-of-magnitude relative risk of substance to c_x $t_{1/2x}$ r_x (c_x r_x)		
	her-ring 1 c_{fh}	sal-mon 2 c_{fs}	hum bloo 9-12 c_h	seal blub 29 c_s	pred. birds c_b	hum 15-7 $t_{1/2h}$	fish (18) $t_{1/2f}$	bird 19 $t_{1/2b}$	mam[k] 14,20-5 r_m	fish[l] 14,22-4,26 r_f	birds[m] 14,28 r_b	human/ mammal	salmon	pred. bird
Polychlorinated azobenzenes and azoxybemzenes														
TCAB														
TCAOB														
Polybrominated, bromo-chlorinated and polyfluorinated dibenzo-p-dioxins and furans														
2378-B_4DD						1				2				
28-C_2-37-B_2-DD										7.10^{-1}				
237-C_3-8-B-DD										7.10^{-1}				
12378-B_5DD										10^{-1}				
1378-B_4DD										10^{-2}				
237-B_3DD										2.10^{-2}				
123478-B_6DD										9.10^{-3}				
2378-B_4DF						0.2				3.10^{-1}				
23478-B_5DF										7.10^{-2}				
12378-B_5DF										4.10^{-2}				
123478-B_6DF										2.10^{-3}				
TFDD														
Polybrominated biphenyls														
33'44'-B_4B											10^{-3}			
33'44'55'-B_6B											10^{-4}			
Polychlorinated naphthalenes														
12367-C_5N									(10^{-4})					
12378-C_5N									(4.10^{-5})					
12456-C_5N									(2.10^{-6})					
123467-C_5N									(10^{-3})					
123567-C_5N									(10^{-3})					
123568-C_6N									(10^{-3})					
123678-C_6N									(10^{-3})					
123456-C_6N									(2.10^{-3})					
123457-C_6N									(2.10^{-5})					
123578-C_6N									(2.10^{-3})					
1234567-C_7N									(10^{-3})					
Polychlorinated dibenzothiophenes, thianthrenes and diphenylsulfides														
2378-TCDT														
2378-TCTA														
33'44'-TCDPS														
Polyaromatic hydrocarbons														
Benzo(k)fluoranthene				1900/a					(5.10^{-3})	(10^{-3})				
Dibenzo(a,i)pyrene									na	(4.10^{-4})				
Dibenz(a,h)anthracene									(2.10^{-3})	(4.10^{-4})				
Benzo(a)pyrene				800/a					(4.10^{-4})	(3.10^{-4})				
Indeno(123-cd)pyr.ene				2600/a					(10^{-3})	(3.10^{-4})				
Benzo(b)fluoranthene									(3.10^{-3})	(2.10^{-4})				
Pentacene									na	(2.10^{-4})				
Benzo(b)anthracene									na	(10^{-4})				
Benzo(b)fluorene									na	(10^{-4})				
Chrysene				17200/a					(2.10^{-4})	(5.10^{-5})				
Benzo(a)anthracene				6700/a					(3.10^{-5})	(4.10^{-5})				
Benzo(e)pyrene				4200/a					na	(3.10^{-5})				
Triphenylene									na	(10^{-5})				

Legend: c_{fh}= (Finnish) mean Baltic herring concentration/that of TCDD; c_{fs}= (Finnish) mean Baltic Sea salmon concentration/that of TCDD; c_h= (Finnish) mean adult human blood (plasma) conc/that of TCDD; c_s= Baltic Sea ringed seal blubber concentration/that of TCDD; c_b= Baltic Sea herring gull or guillemot egg concentration/that of TCDD; $t_{1/2h}$= body elimination half-life in human adult/that of TCDD (in parentheses, in adipose or extrapolated from rodent models); $t_{1/2f}$= same for fish; $t_{1/2b}$= same for birds; r_m= WHO-TEF for mammals (in parentheses, mammalian *in vivo* or *in vitro* Ah-R binding or drug metabolizing enzyme activity/that of TCDD; r_f= same for fish; r_b= same for birds; c_x $t_{1/2x}$ r_x = indicative relative risk of substance to human/mammal, salmon or predatory bird (if no metabolic elimination data is available, computed as c_x r_x).

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