SUPPORTING INFORMATION

Predicting concentrations of organic chemicals in fish based on toxicokinetic models

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1. Experiments data

1.1. Origin of measured internal concentrations

The TOXRES Database yielded seven publications (with 22 different chemicals) for rainbow trout and 16 publications (with 23 different chemicals) for fathead minnow, which fulfilled the criteria listed in main manuscript. Both these species are recommended for toxicity testing (e.g. Fish Full Life Cycle, Fish Partial Life Cycle, acute and bioconcentration tests) by the Organisation for Economic Cooperation and Development (OECD)[1] and the U.S. Environmental Protection Agency[2].

In the Scopus online database, we searched with the following terms: "internal concentration", "body burden", "body residue" and "tissue residue" in combinations with: "rainbow trout", "*Oncorhynchus mykiss*", “*Salmo gairdneri*”, “fathead minnow” and “*Pimephales promelas*”. The above terms were searched for on 18 Mar – 29 Apr 2011 in article titles, abstracts and keywords for all document types and for all available publishing years. One publication for rainbow trout and one publication for fathead minnow were found in addition to those identified in the TOXRES Database.

Table S1. Chemicals for which measured data of internal concentrations were found.

Chemical	References	
	rainbow trout	**fathead minnow**
1,2,3,4-Tetrachlorobenzene	1 concentration[3]	6 concentrations[4]
1,2,3-Trichlorobenzene	1 concentration[3]	—
1,2,4,5-Tetrachlorobenzene	1 concentration[3]	—
1,2,4-Trichlorobenzene	1 concentration[3]	6 concentrations[5]
1,2-Dibromobenzene	4 concentrations[6]	—
1,2-Dichlorobenzene	1 concentration[3] 2 concentrations[6]	—
1,2-Difluorobenzene	2 concentrations[6]	—
1,3,5-Trichlorobenzene	2 concentrations[3]	—
1,3-Dichlorobenzene	—	4 concentrations[4]
1,4-Dibromobenzene	2 concentrations[6]	—
1,4-Dichlorobenzene	1 concentration[3] 2 concentrations[6]	3 concentrations[4]
1,4-Difluorobenzene	2 concentrations[6]	—
2,2',5,5'-Tetrachlorobiphenyl	1 concentration[7]	—
2,3,7,8-Tetrachlorodibenzofuran	2 concentrations[8]	—
2,3,7,8-Tetrachlorodibenzo-p-dioxin	2 concentrations[8]	—
2,4,5-Trichlorophenol	—	1 concentration[9]
2,4-Dinitrophenol	1 concentration[10]	—
4-Nitrophenol	1 concentration[10]	1 concentration[9]
Alachlor	—	2 concentrations[11]
Bromacil	—	1 concentrations[12]
Chlordecone (Kepone)	—	4 concentrations[13]
Chlorpyrifos	—	4 concentrations[14]
Dicofol (Kelthane)	—	2 concentrations[15]
Dieldrin	2 concentrations[16]	—
Dinoseb	—	2 concentrations[11]
Diuron	—	1 concentration[12]
Dodecylbenzene Sulfonate	—	4 concentrations[17]
Endrin	—	2 concentrations[18]
Fenvelerate	3 concentrations[19]	3 concentrations[15]
Flucythrinate (AC 222,705)	—	2 concentrations[20]
Hexachloro-1,3-butadiene	1 concentration[3]	—
Hexachlorobenzene	1 concentration[3]	6 concentrations[4] 1 concentration[21]
Hexachlorocyclopentadiene	—	2 concentrations[22]
Hexachloroethane	1 concentration[3]	—
Octamethylcyclotetrasiloxane	—	1 concentration[23]
Pentachlorobenzene	1 concentration[3]	3 concentrations[4]
Pentachlorophenol	1 concentration[24]	4 concentrations[25]
Permethrin	—	2 concentrations[20]
Phenol	—	1 concentration[9]

Required parameters from experiments were taken from publications found via Tissue Residue database and Scopus online database, and they are presented for rainbow trout and fathead minnow in **Table S2** and **Table S3** respectively.

Table S2. Experimental data required for modelling chemical internal concentrations in rainbow trout

	Name	CAS	$logK_{ow}$[a]	Oxygen conc.[b] (mg/l)	Water temp (°C)	Fish weight (kg)	Exposure Time (d)	Exposure concentr. (µg/l)	measured Cint (µg/g)	Ref.
1	1,2,3,4-Tetrachlorobenzene	634662	4.6	8.87	15	0.25	105	0.026	0.32	3
2	1,2,3-Trichlorobenzene	87616	4.05	8.87	15	0.25	105	0.071	0.21	3
3	1,2,4,5-Tetrachlorobenzene	95943	4.64	8.87	15	0.25	105	0.021	0.32	3
4	1,2,4-Trichlorobenzene	120821	4.02	8.87	15	0.25	105	0.052	0.18	3
5	1,2-Dibromobenzene	583539	3.64	9.7	12	0.056	0.07	26184.9	424.6	6
6	1,2-Dibromobenzene	583539	3.64	9.7	12	0.056	0.15	13446.3	448.2	6
7	1,2-Dibromobenzene	583539	3.64	9.7	12	0.056	0.025	25241.3	134.5	6
8	1,2-Dibromobenzene	583539	3.64	9.7	12	0.056	0.23	17574.55	566.2	6
9	1,2-Dichlorobenzene	95501	3.43	9.7	12	0.056	0.196	6012.3	138.2	6
10	1,2-Dichlorobenzene	95501	3.43	9.7	12	0.056	0.342	2381.4	147	6
11	1,2-Dichlorobenzene	95501	3.43	8.87	15	0.25	105	0.94	0.67	3
12	1,2-Difluorobenzene	367113	2.37	9.7	12	0.056	0.88	21564.9	111.8	6
13	1,2-Difluorobenzene	367113	2.37	9.7	12	0.056	0.88	15061.2	74.2	6
14	1,3,5-Trichlorobenzene	108703	4.19	8.87	15	0.25	105	0.045	0.2	3
15	1,3,5-Trichlorobenzene	108703	4.19	8.87	15	0.25	105	0.69	0.64	3
16	1,4-Dibromobenzene	106376	3.79	9.7	12	0.056	0.058	12832.96	205.2	6
17	1,4-Dibromobenzene	106376	3.79	9.7	12	0.056	0.20	4765.18	184	6
18	1,4-Dichlorobenzene	106467	3.44	9.7	12	0.056	0.05	3748.5	47	6
19	1,4-Dichlorobenzene	106467	3.44	9.7	12	0.056	0.83	933.45	69.1	6
20	1,4-Dichlorobenzene	106467	3.44	8.87	15	0.25	105	0.67	0.54	3
21	1,4-Difluorobenzene	540363	2.13	9.7	12	0.056	0.07	15517.6	43.4	6
22	1,4-Difluorobenzene	540363	2.13	9.7	12	0.056	0.17	7302.4	33.1	6
23	2,2',5,5'-Tetrachlorobiphenyl	35693993	6.09	10.75	11	0.767	2	10	25.34	7
24	2,3,7,8-Tetrachlorodibenzofuran	51207319	6.53	8.55	11	0.00038	28	0.00393	0.0106	8
25	2,3,7,8-Tetrachlorodibenzofuran	51207319	6.53	8.55	11	0.00038	28	0.00041	0.0025	8
26	2,3,7,8-Tetrachlorodibenzo-p-dioxin	1746016	6.8	8.55	11	0.00038	28	0.000176	0.00452	8
27	2,3,7,8-Tetrachlorodibenzo-p-dioxin	1746016	6.8	8.55	11	0.00038	28	0.000038	0.00098	8
28	2,4-Dinitrophenol	51285	1.67	6	12	0.0008	4	1800	16.7	10
29	4-Nitrophenol[c]	100027	1.91	6	12	0.0008	4	6600	270.6	10
30	Dieldrin	60571	5.4	9.6	12.5	0.0028	4	0.99	5.65	16
31	Dieldrin	60571	5.4	9.6	12.5	0.0028	4	0.15	0.548	16
32	Fenvalerate	51630581	6.2	9.6	12	0.000357	70	0.135	1.6	19
33	Fenvalerate	51630581	6.2	9.6	12	0.000357	70	0.08	0.24	19
34	Fenvalerate	51630581	6.2	9.6	12	0.000357	70	0.018	0.07	19
35	Hexachloro-1,3-butadiene	87683	4.78	8.87	15	0.25	105	0.0034	0.063	3
36	Hexachlorobenzene	118741	5.73	8.87	15	0.25	105	0.008	0.16	3
37	Hexachloroethane	67721	4.14	8.87	15	0.25	105	0.0071	0.0071	3
38	Pentachlorobenzene	608935	5.17	8.87	15	0.25	105	0.009	0.22	3
39	Pentachlorophenol	87865	5.12	10.75	11.5	0.735	2	1	0.11	24

[a] - $logK_{ow}$ were taken from EPI Suite: experimental database
[b] - Dissolved oxygen concentration in water
blue colour - chemicals which have been found also for fathead minnow (but from different experiments)

Table S3. Experimental data required for modelling chemical internal concentrations in fathead minnow

	Name	CAS	logKow[a]	Oxygen conc.[c] (mg/l)	Water temp (°C)	Fish weight (kg)	Exposure Time (d)	Exposure concentr. (μg/l)	measured Cint (μg/g)	Ref.
1	1,2,3,4-Tetrachlorobenzene	634662	4.6	7.4	25	0.000057	33	410	1100	4
2	1,2,3,4-Tetrachlorobenzene	634662	4.6	7.4	25	0.000098	33	250	640	4
3	1,2,3,4-Tetrachlorobenzene	634662	4.6	7.4	25	0.000102	33	110	200	4
4	1,2,3,4-Tetrachlorobenzene	634662	4.6	7.4	25	0.000114	33	39	94	4
5	1,2,3,4-Tetrachlorobenzene	634662	4.6	7.4	25	0.000114	33	19	46	4
6	1,2,3,4-Tetrachlorobenzene	634662	4.6	7.4	25	0.000112	33	3	7	4
7	1,2,4-Trichlorobenzene	120821	4.02	8.1	25.7	0.000067	32	920	477.5	5
8	1,2,4-Trichlorobenzene	120821	4.02	8.1	25.7	0.000085	32	500	160	5
9	1,2,4-Trichlorobenzene	120821	4.02	8.1	25.7	0.000085	32	280	127.5	5
10	1,2,4-Trichlorobenzene	120821	4.02	8.1	25.7	0.000089	32	140	67.5	5
11	1,2,4-Trichlorobenzene	120821	4.02	8.1	25.7	0.000092	32	75	31	5
12	1,2,4-Trichlorobenzene	120821	4.02	8.1	25.7	0.000095	32	15	5	5
13	1,3-Dichlorobenzene	541731	3.53	6.9	25	0.000102	32	1000	120	4
14	1,3-Dichlorobenzene	541731	3.53	6.9	25	0.000098	32	560	57	4
15	1,3-Dichlorobenzene	541731	3.53	6.9	25	0.000099	32	300	29	4
16	1,3-Dichlorobenzene	541731	3.53	6.9	25	0.0001	32	20	1.3	4
17	1,4-Dichlorobenzene	106467	3.44	7.3	25	0.000087	32	1000	103	4
18	1,4-Dichlorobenzene	106467	3.44	7.3	25	0.000101	32	570	69.5	4
19	1,4-Dichlorobenzene	106467	3.44	7.3	25	0.000101	32	19	6.8	4
20	2,4,5-Trichlorophenol	95954	3.72	8.22	22	0.000115	28	49.3	100	9
21	4-Nitrophenol[d]	100027	1.91	8.22	21.9	0.000115	28	44.1	25.1	9
22	Alachlor (Technical grade)	15972608	3.52	7.72	24.7	0.000316	64	1100	50.4	11
23	Alachlor (Technical grade)	15972608	3.52	7.72	24.7	0.000423	64	520	23.8	11
24	Bromacil (Technical grade)	314409	2.11	7.72	25	0.000479	17	1000	3	12
25	Chlordecone (Kepone)	143500	5.41	7	22	0.000277	60	3.1	3.8	13
26	Chlordecone (Kepone)	143500	5.41	7	22	0.000277	60	1.2	2.6	13
27	Chlordecone (Kepone)	143500	5.41	7	22	0.000277	60	0.31	0.38	13
28	Chlordecone (Kepone)	143500	5.41	7	22	0.000277	60	0.17	0.17	13
29	Chlorpyrifos	2921882	4.96	7.5	25.1	0.000191	200	2.68	5.11	14
30	Chlorpyrifos	2921882	4.96	7.5	25.1	0.000191	200	1.21	3.03	14
31	Chlorpyrifos	2921882	4.96	7.5	25.1	0.000191	200	0.63	0.95	14
32	Chlorpyrifos	2921882	4.96	7.5	25.1	0.000191	200	0.27	0.47	14
33	Dicofol (Kelthane)	115322	6.06[b]	7.15	25	0.000137	28	8.9	28	15
34	Dicofol (Kelthane)	115322	6.06[b]	7.15	25	0.000137	28	19	81	15
35	Dinoseb (Technical grade)	88857	3.56	7.69	24.7	0.000517	64	48.5	3.05	11
36	Dinoseb (Technical grade)	88857	3.56	7.69	24.7	0.000679	64	14.5	0.91	11
37	Diuron (Technical grade)	330541	2.68	7.51	24.3	0.000563	24	33.4	4.8	12
38	Endrin	72208	5.4	6.95	24.8	0.0003	300	0.25	1.8	18
39	Endrin	72208	5.4	6.95	24.8	0.0003	300	0.14	1	18
40	Fenvalerate	51630581	6.2	7.15	25	0.0002	30	0.14	0.23	15
41	Fenvalerate	51630581	6.2	7.15	25	0.0002	30	0.17	0.45	15
42	Fenvalerate	51630581	6.2	7.15	25	0.0002	30	0.19	0.88	15
43	Flucythrinate (AC 222,705)	70124775	6.2	6.55	25	0.000129	32	0.07	0.17	20
44	Flucythrinate (AC 222,705)	70124775	6.2	6.55	25	0.000128	32	0.03	0.16	20
45	Hexachlorobenzene	118741	5.73	7	25	0.000165	32	4.8	97	4
46	Hexachlorobenzene	118741	5.73	7	25	0.00015	32	2.6	46	4
47	Hexachlorobenzene	118741	5.73	7	25	0.000164	32	1.2	27	4
48	Hexachlorobenzene	118741	5.73	7	25	0.000172	32	0.7	15	4
49	Hexachlorobenzene	118741	5.73	7	25	0.000159	32	0.3	8	4
50	Hexachlorobenzene	118741	5.73	7	25	0.00017	32	0.003	0.3	4
51	Hexachlorobenzene	118741	5.73	9.06	20	0.000068	28	5	46.5	21
52	Hexachlorocyclopentadiene	77474	5.04	7.9	25	0.00013	30	7.3	0.08	22
53	Hexachlorocyclopentadiene	77474	5.04	7.9	25	0.00011	30	3.7	0.04	22
54	Octamethylcyclotetrasiloxane	556672	5.1	7.06	21.5	0.00048	28	0.26	2.83	23
55	Pentachlorobenzene	608935	5.17	7.2	25	0.000099	31	55	380	4
56	Pentachlorobenzene	608935	5.17	7.2	25	0.000107	31	28	270	4

57	Pentachlorobenzene	608935	5.17	7.2	25	0.000104	31	0.6	1.1	4
58	Pentachlorophenol	87865	5.12	7.65	25	0.000081	32	58.2	25.1	25
59	Pentachlorophenol	87865	5.12	7.65	25	0.00009	32	27.6	12.3	25
60	Pentachlorophenol	87865	5.12	7.65	25	0.000102	32	12.7	5.2	25
61	Pentachlorophenol	87865	5.12	7.65	25	0.000103	32	5.6	2.5	25
62	Permethrin	52645531	6.5	6.55	25	0.00011	32	1.4	4.51	20
63	Permethrin	52645531	6.5	6.55	25	0.000093	32	0.66	2.16	20
64	Phenol	108952	1.46	8.22	21.9	0.000115	28	32.7	1584	9
65	Dodecylbenzene Sulfonate	25155-30-0	1.96	8.1	24	0.00019	8	300	0.0157	17
66	Dodecylbenzene Sulfonate	25155-30-0	1.96	8.1	24	0.00019	32	126	0.0121	17
67	Dodecylbenzene Sulfonate	25155-30-0	1.96	8.1	24	0.00019	32	293	0.0232	17
68	Dodecylbenzene Sulfonate	25155-30-0	1.96	8.1	24	0.00019	32	927	0.0606	17

[a] - $\log K_{ow}$ were taken from EPI Suite: experimental database
[b] - $\log K_{ow}$ could not be taken from EPI Suite; value taken from [26]
[c] - Dissolved oxygen concentration in water
blue colour - chemicals which have been found also for rainbow trout (but from different experiments)

2. Models

2.1. One-compartment A model (developed by Arnot and Gobas[27])

Abbreviations and symbols used to describe the one-compartment A model for fish are presented in **Table S4**.

Table S4. Abbreviations and symbols used to describe the one-compartment A model for fish (from [27] if it is not indicated differently)

Abbreviation /symbol	Units	Value	Description
w_w	kg	model input	body wet weight
K_{ow}	—	model input	octanol-water partition coefficient
S	%	model input	dissolved oxygen saturation
T	^oC	model input	water temperature
C_w	$\mu g \cdot L^{-1}$	model input	chemical concentration in water
lipid	kg	model input	lipid weight
β	—	0.035*	sorption capacity constant
d_w	kg	28% of w_w[28]	body dry weight
f_lipid	—	Equation S1	lipid fraction
f_NLOM	—	Equation S2	fraction of non lipid organic matter
f_water	—	Equation S3	water content
K_{bw}	—	Equation S4	fish - water partition coefficient
C_{ox}	$mg\ O_2 \cdot L^{-1}$	Equation S5	dissolved oxygen concentration in water
G_v	$L \cdot d^{-1}$	Equation S6	gill ventilation rate
E_w	—	Equation S7	gill chemical uptake efficiency
k_{in}	$L \cdot kg^{-1} \cdot d^{-1}$	Equation S8	aqueous uptake clearance rate constant
k_{out}	$kg \cdot kg^{-1} \cdot d^{-1}$	Equation S9	gill elimination rate constant
k_G	d^{-1}	Equation S10	growth dilution rate constant
C_{int}	$\mu g \cdot g^{-1}$	Equation S11	chemical internal concentration

* Although Arnot and Gobas[27] set the beta term equal to 0.035, subsequent work has shown that the true value might be closer to 0.05[29]

Model equations:

- Fish lipid fraction in fish

$$f\_lipid = \frac{lipid}{w\_w} \qquad \textbf{(eq. S1)}$$

- Fraction of non lipid organic matter in fish

$$f\_NLOM = \frac{d\_w - lipid}{w\_w} \qquad \textbf{(eq. S2)}$$

- Water fraction in fish

$$f\_water = \frac{w\_w - d\_w}{w\_w} \qquad \textbf{(eq. S3)}$$

- Fish - water partition coefficient

$$K_{bw} = f\_lipid \cdot K_{ow} + f\_NLOM \cdot \beta \cdot K_{ow} + f\_water \qquad \textbf{(eq. S4)}$$

- Dissolved oxygen concentration

$$C_{ox} = (-0.24 \cdot T + 14.04) \cdot \frac{S}{100}, \quad \frac{mg\,O_2}{L} \qquad \textbf{(eq. S5)}$$

- Gill ventilation rate

$$G_v = 1400 \cdot \frac{w\_w^{0.65}}{C_{ox}}, \quad \frac{L}{d} \qquad \textbf{(eq. S6)}$$

- Gill chemical uptake efficiency

$$E_w = \frac{1}{1.85 + \frac{155}{K_{ow}}} \qquad \textbf{(eq. S7)}$$

- Aqueous uptake clearance rate constant

$$k_{in} = \frac{E_w \cdot G_v}{w\_w}, \quad \frac{L}{kg \cdot d} \qquad \textbf{(eq. S8)}$$

- Gill elimination rate constant

$$k_{out} = \frac{k_{in}}{K_{bw}}, \quad \frac{kg}{kg \cdot d} \qquad \textbf{(eq. S9)}$$

- Growth dilution rate constant

$$k_G = 0.0005 \cdot w\_w^{-0.2}, \frac{1}{d} \text{ for temperatures around } 10\ ^{o}C$$

$$k_G = 0.00251 \cdot w\_w^{-0.2}, \frac{1}{d} \text{ for temperatures around } 25\ ^{o}C \qquad \textbf{(eq. S10)}$$

- Chemical internal concentration

$$\frac{d}{dt}C_{int}(t) = \frac{k_{in}}{1000}\cdot C_w(t) - (k_{out} + k_G)\cdot C int(t),\ \frac{\mu g}{g\cdot d} \qquad \textbf{(eq. S11)}$$

2.2. One-compartment B model (developed by Hendriks et al. [30])

Abbreviations and symbols used to describe the one-compartment model B for fish are presented in **Table S5**.

Table S5. Abbreviations and symbols used to describe the one-compartment model B for fish (from [30] if it is not indicated differently)

Abbreviation /symbol	Units	Value	Description
w_w	kg	model input	body wet weight
K_{ow}	—	model input	octanol-water partition coefficient
C_w	$\mu g \cdot L^{-1}$	model input	chemical concentration in water
lipid	kg	model input	lipid weight
i	—	2 (for animals)	trophic level
j	—	0 - from water	type of chemical uptake
κ	—	0.25	rate exponent
$\rho_{CH2,i}$	$d \cdot kg^{-\kappa}$	68 (for animals)	lipid layer permeation resistance
$\rho_{H2O,j}$	$d \cdot kg^{-\kappa}$	$2.8 \cdot 10^{-3}$	water layer diffusion resistance
γ_0	$kg^{-\kappa} \cdot d^{-1}$	200 water breathing	water absorption-excretion coefficient
γ_1	$kg^{-\kappa} \cdot d^{-1}$	0.0006	biomass (re)production coefficient
$q_{T:c}$	$kg \cdot kg^{-1}$	1 (cold-blooded)	temperature correction factor
f_lipid	—	Equation S12	lipid fraction
k_{in}	$L \cdot kg^{-1} \cdot d^{-1}$	Equation S13	substance absorption rate constant
k_{out}	$kg \cdot kg^{-1} \cdot d^{-1}$	Equation S14	substance excretion rate constant
k_G	d^{-1}	Equation S15	growth dilution rate constant
C_{int}	$\mu g \cdot g^{-1}$	Equation S16	chemical internal concentration

- Fish lipid fraction in fish

$$f\_lipid = \frac{lipid}{w\_w} \qquad \textbf{(eq. S12)}$$

- Substance absorption rate constant

$$k_{in} = \frac{w\_w^{-\kappa}}{\rho_{H2O,j} + \frac{\rho_{CH2,i}}{K_{ow}} + \frac{1}{\gamma_0}},\ \frac{L}{kg\cdot d} \qquad \textbf{(eq. S13)}$$

- Substance excretion rate constant

$$k_{out} = \frac{1}{f\_lipid\cdot(K_{ow} - 1) + 1}\cdot k_{in},\ \frac{kg}{kg\cdot d} \qquad \textbf{(eq. S14)}$$

- Growth dilution rate constant

$$k_G = q_{T:c} \cdot \gamma_1 \cdot w\_w^{-\kappa}, \quad \frac{kg}{kg \cdot d} \qquad \textbf{(eq. S15)}$$

- Chemical internal concentration

$$\frac{d}{dt} C_{int}(t) = \frac{k_{in}}{1000} \cdot C_w(t) - (k_{out} + k_G) \cdot C int(t), \quad \frac{\mu g}{g \cdot d} \qquad \textbf{(eq. S16)}$$

2.3. Physiologically Based Toxicokinetic model (based on[31-34])

Abbreviations and symbols used to describe the PBTK model for fish are presented in **Table S6**.

Table S6. Abbreviations and symbols used to describe the PBTK model for fish (from [31-34] if it is not indicated differently)

Abbreviation/ symbol	Units	Value		Description
		rainbow trout	fathead minnow	
w_w	kg	model input		body wet weight
K_{ow}	—	model input		octanol-water partition coefficient
C_w	$\mu g \cdot L^{-1}$	model input		chemical concentration in inspired water
T	^oC	model input		water temperature
C_{ox}	$mg\ O_2 \cdot L^{-1}$	model input		dissolved oxygen concentration in water
lipid	—	model input		lipid content of fish (fraction of body weight)
K	—	for T > 10 ^oC, K = $3.05 \cdot 10^{-4}$ [35]		constant in equation S18
n	—	for T > 10 ^oC, n = 1.855 [35]		constant in equation S18
m	—	for T > 10 ^oC, m = -0.138 [35]		constant in equation S18
α_b	—	0.014 [36]	0.019 [36]	lipid content of blood tissue (fraction of body weight)
α_f	—	0.942 [36]	1.010 [36]	lipid content of fat tissue (fraction of body weight)
α_k	—	0.052 [36]	—	lipid content of kidney tissue (fraction of body weight)
α_l	—	0.045 [36]	0.074 [36]	lipid content of liver tissue (fraction of body weight)
α_m	—	0.030 [36]	0.025 [36]	lipid content of muscle tissue (fraction of body weight)
γ_b	—	0.839 [36]	0.876 [36]	water content of blood tissue, (fraction of body weight)
γ_f	—	0.050 [36]	0.016 [36]	water content of fat tissue, (fraction of body weight)
γ_k	—	0.789 [36]	—	water content of kidney tissue, (fraction of body weight)
γ_l	—	0.746 [36]	0.766 [36]	water content of liver tissue, (fraction of body weight)
γ_m	—	0.769 [36]	0.806 [36]	water content of muscle tissue, (fraction of body weight)
$lipid_l$	—	Equation S20	Equation S21	Lipid content of lean tissue (fraction of body weight)
V_l	L	$0.012 \cdot w\_w$	$0.018 \cdot w\_w$ [37,38]	volume of liver compartment
V_f	L	Equation S22		volume of fat compartment
V_m	L	Equation S23	Equation S24	volume of poorly perfused compartment (mainly white muscle)
V_r	L	$0.063 \cdot w\_w$	$0.072 \cdot w\_w$ [37,38]	volume of richly perfused compartment
V_k	L	$0.009 \cdot w\_w$	—	volume of kidney compartment
Q_c	$L \cdot h^{-1}$	Equation S17 [31]		cardiac output
Q_l	$L \cdot h^{-1}$	$0.029 \cdot Q_c$	$0.024 \cdot Q_c$	blood flow to the liver compartment
Q_f	$L \cdot h^{-1}$	$0.085 \cdot Q_c$	$0.010 \cdot Q_c$	blood flow to the fat compartment
Q_m	$L \cdot h^{-1}$	$0.600 \cdot Q_c$	$0.440 \cdot Q_c$	blood flow to the poorly perfused compartment (mainly white muscle)
Q_r	$L \cdot h^{-1}$	$0.230 \cdot Q_c$	$0.526 \cdot Q_c$	blood flow to the richly perfused compartment
Q_k	$L \cdot h^{-1}$	$0.056 \cdot Q_c$	—	blood flow to the kidney compartment
VO_2	$mg\ O_2 \cdot h^{-1}$	Equation S18 [35]		oxygen consumption rate for 1kg fish
Q_w	$L \cdot h^{-1}$	Equation S19		effective respiratory volume

P_{bw}	—	Equation S25 [36]		chemical blood:water partition coefficient
P_i	—	Equation S26 [36]		liver:blood (P_l), fat:blood (P_f), muscle:blood (P_m) and kidney:blood (P_k) (only for rainbow trout) partition coefficients of a chemical
P_r	—	Equation S27		chemical richly perfused tissue:blood partition coefficient
A_i	μg	Equation S28 [36]		chemical amount in fat (A_f), poorly perfused (A_m) and richly perfused (A_r) compartments
A_l	μg	Equation S29		chemical amount in the liver compartment
A_k	μg	Equation S230	—	chemical amount in the kidney compartment
C_{int}	μg	Equation S31	Equation S32	average concentration of the chemical in the whole organism
C_{art}	$\mu g \cdot L^{-1}$	Equation S33		chemical concentration in arterial blood
C_{ven}	$\mu g \cdot L^{-1}$	Equation S34	Equation S35	chemical concentration in venous blood

- Cardiac output

$$Q_c = (0.23 \cdot T - 0.78) \cdot \left(\frac{1000 \cdot w\_w}{500}\right)^{-0.1} \cdot w\_w^{0.75}, \ \frac{L}{h} \qquad \textbf{(eq. S17)}$$

- Oxygen consumption rate

$$VO_2 = K \cdot \left(32 + T \cdot \frac{9}{5}\right)^n \cdot \left(\frac{w\_w}{0.4536}\right)^m \cdot \frac{10000}{24}, \ \frac{mgO_2}{h} \qquad \textbf{(eq. S18)}$$

- Effective respiratory volume

$$Q_w = \frac{VO_2}{C_{ox} - 0.2 \cdot C_{ox}} \cdot w\_w^{0.75}, \ \frac{L}{h} \qquad \textbf{(eq. S19)}$$

Lipid content of lean tissue was calculated based on the simplification presented by Nichols and colleagues.[39] In their work, it was assumed that the lipid content of lean tissue (which consists of all tissues except of adipose fat) does not depend on the lipid content of whole body. Thus, in our study, lean tissue includes: liver, richly perfused, poorly perfused and kidney (only for rainbow trout) compartments, and its lipid content was calculated based on values from Table S6 (note, that to calculate lipid content of lean tissue, here, the volume of poorly perfused tissues was equal to 0.818·w_w[34] and 0.888·w_w[37] for rainbow trout and fathead minnow, respectively).

- Lipid content of lean tissue – rainbow trout

$$lipid_l = \frac{V_l \cdot a_l + V_r \cdot a_r + V_m \cdot a_m + V_k \cdot a_k}{V_l + V_r + V_m + V_k} \qquad \textbf{(eq. S20)}$$

- Lipid content of lean tissue – fathead minnow

$$lipid_l = \frac{V_l \cdot a_l + V_r \cdot a_r + V_m \cdot a_m}{V_l + V_r + V_m} \qquad \textbf{(eq. S21)}$$

- Volume of fat compartment – rainbow trout

$$V_f = w\_w \cdot \frac{lipid - lipid_l}{\alpha_f - lipid_l}, \ L \qquad \textbf{(eq. S22)}$$

NOTE: This assumption will not work in extreme situations when the lipid content of whole body is lower than lipid content of lean tissue (which is assumed to be independent of whole body lipid content). These conditions could happen e.g. during starvation.

- Volume of poorly perfused compartment (mainly white muscle) – rainbow trout

$$V_m = w\_w - (V_l + V_f + V_k + V_r),\ L \qquad \textbf{(eq. S23)}$$

- Volume of poorly perfused compartment (mainly white muscle) – fathead minnow

$$V_m = w\_w - (V_l + V_f + V_r),\ L \qquad \textbf{(eq. S24)}$$

- Blood:water partition coefficient of a chemical

$$P_{bw} = 10^{0.72*\log K_{ow} + 1.04\cdot\log(\alpha_b) + 0.86} + \gamma_b \qquad \textbf{(eq. S25)}$$

- Liver:blood, fat:blood, muscle:blood, and kidney:blood (only for rainbow trout) partition coefficients of a chemical

$$P_i = \frac{10^{0.72*\log K_{ow} + 1.04\cdot\log(\alpha_i) + 0.86} + \gamma_i}{P_{bw}} \qquad \textbf{(eq. S26)}$$

- Richly perfused tissue:blood partition coefficient of a chemical

$$P_r = P_l \qquad \textbf{(eq. S27)}$$

- Chemical amount in fat, poorly perfused and richly perfused compartments

$$\frac{dA_i(t)}{dt} = Q_i \cdot \left(C_{art}(t) - \frac{A_i(t)}{V_i \cdot P_i} \right),\ \frac{\mu g}{h} \qquad \textbf{(eq. S28)}$$

- Chemical amount in the liver compartment

$$\frac{dA_l(t)}{dt} = Q_r \cdot \frac{A_r(t)}{V_r \cdot P_r} + Q_l \cdot C_{art}(t) - (Q_r + Q_l) \cdot \frac{A_l(t)}{V_l \cdot P_l},\ \frac{\mu g}{h} \qquad \textbf{(eq. S29)}$$

- Chemical amount in the kidney compartment (only for rainbow trout)

$$\frac{dA_k(t)}{dt} = 0.6 \cdot Q_m(t) \cdot \frac{A_m(t)}{V_m \cdot P_m} + Q_k \cdot C_{art}(t) - \left(0.6 \cdot Q_m + Q_k\right) \cdot \frac{A_k(t)}{V_k \cdot P_k},\ \frac{\mu g}{h} \qquad \textbf{(eq. S30)}$$

- Chemical internal concentration in the whole body of rainbow trout

$$C\text{int}(t) = \frac{A_f(t) + A_m(t) + A_r(t) + A_l(t) + A_k(t)}{1000 \cdot w\_w},\ \frac{\mu g}{g} \qquad \textbf{(eq. S31)}$$

- Chemical internal concentration in the whole body of fathead minnow

$$C\text{int}(t) = \frac{A_f(t) + A_m(t) + A_r(t) + A_l(t)}{1000 \cdot w\_w},\ \frac{\mu g}{g} \qquad \textbf{(eq. S32)}$$

- Chemical concentration in arterial blood

$$\text{Cart}(t) = \min(Q_w, Q_c \cdot P_{bw}) \cdot \frac{C_w - \dfrac{C_{ven}(t)}{P_{bw}}}{Q_c} + C_{ven}(t),\ \frac{\mu g}{L} \qquad \textbf{(eq. S33)}$$

- Chemical concentration in venous blood of rainbow trout

$$\mathrm{Cven}(t) = \frac{Q_f \cdot \frac{A_f(t)}{V_f \cdot P_f} + 0.4 \cdot Q_m \cdot \frac{A_m(t)}{V_m \cdot P_m} + (0.6 \cdot Q_m + Q_k) \cdot \frac{A_k(t)}{V_k \cdot P_k} + (Q_r + Q_l) \cdot \frac{A_l(t)}{V_l \cdot P_l}}{Q_c}, \ \frac{\mu g}{L} \qquad \textbf{(eq. S34)}$$

- Chemical concentration in venous blood of fathead minnow

$$\mathrm{Cven}(t) = \frac{Q_f \cdot \frac{A_f(t)}{V_f \cdot P_f} + Q_m \cdot \frac{A_m(t)}{V_m \cdot P_m} + (Q_r + Q_l) \cdot \frac{A_l(t)}{V_l \cdot P_l}}{Q_c}, \ \frac{\mu g}{L} \qquad \textbf{(eq. S35)}$$

2.4. Model runs

All three toxicokinetic models were run in **ModelMaker 4** with the following settings:

a) Run

- start value: 0,
- stop value: last day of exposure,
- repeated run: no.

b) Integration

- random seed: 1,
- integration method: Runge-Kutta,
- output points: user defined (dependent on stop value)
- fixed step: no,
- accuracy: 10^{-6},
- minimum value: 10^{-10},
- approx no of steps: 100,
- error scaling: a constant value (10).

3. Results

3.1. Predicted vs. measured internal concentrations of chemicals

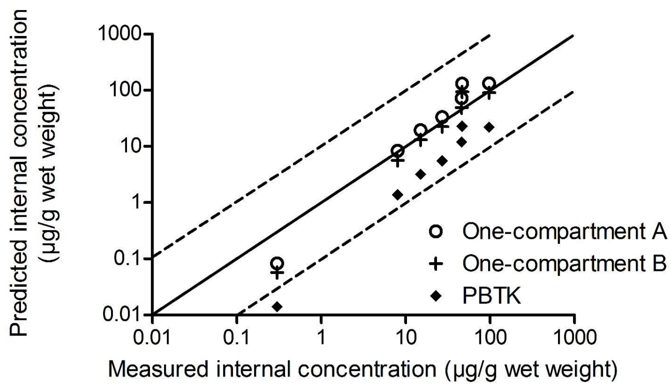

Figure S1. Comparison of predicted internal concentrations of hexachlorobenzene (based on one-compartment A, one-compartment B and PBTK models) and measured internal concentrations in fathead minnows.

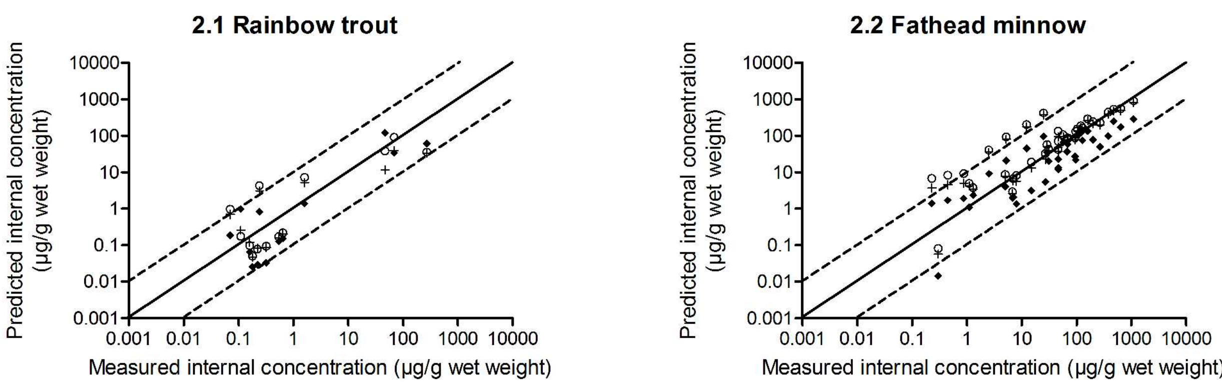

Figure S2. Comparison of TK models: One-compartment A (o), one-compartment B (+) and PBTK (♦), for the same chemicals for 2.1 rainbow trout and 2.2 fathead minnows (8 chemicals, 45 data points).

3.2. Sensitivity analysis

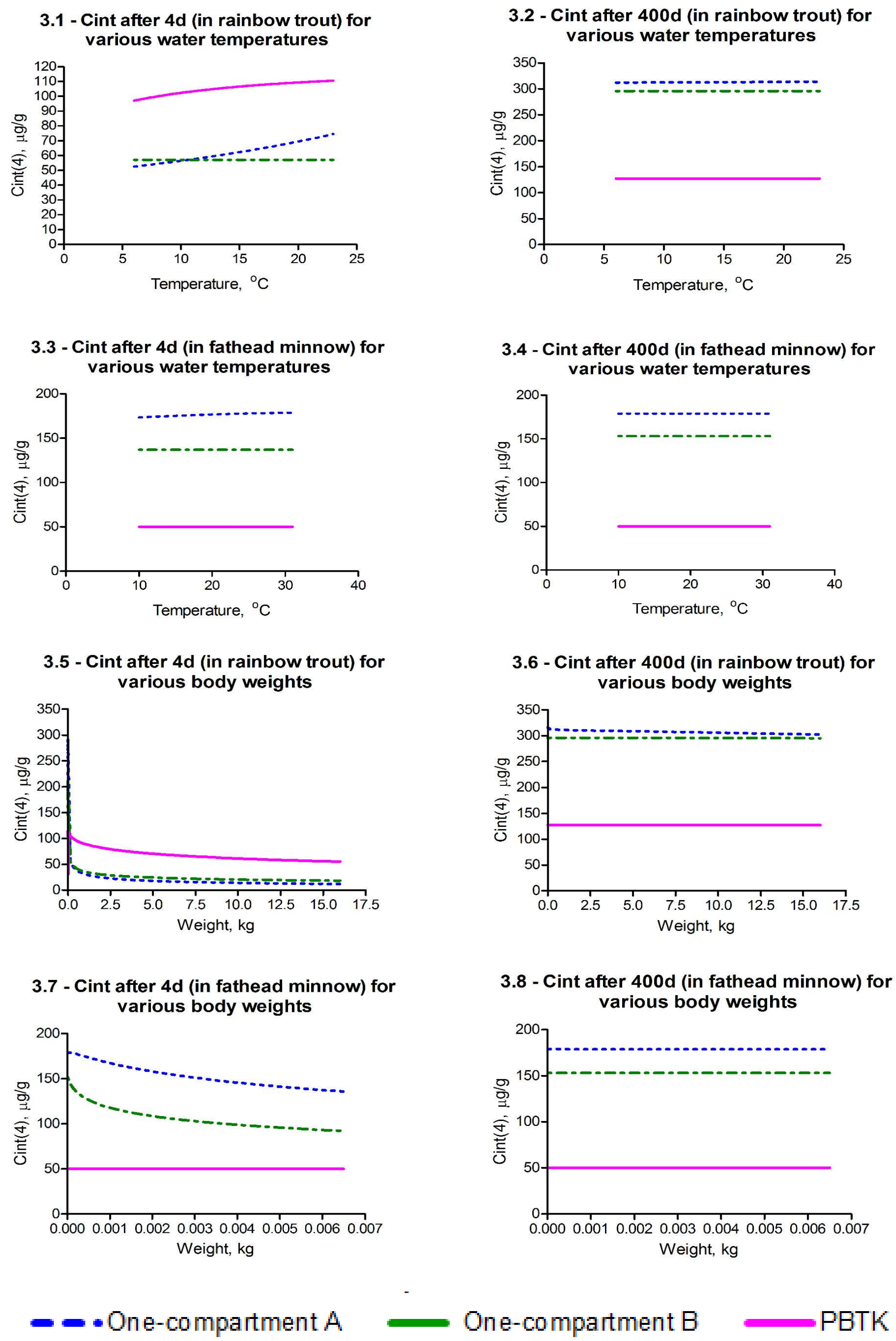

Figure S3. TK model predictions for rainbow trout and fathead minnows: 3.1 – 3.4: sensitivity analysis for water temperature, 3.5 – 3.8: sensitivity analysis for fish weight; experiment parameters for rainbow trout: log K_{OW} = 4.4, fish weight = 0.13 kg, water temperature = 12.8 °C, lipid fraction = 0.12; experiment parameters for fathead minnow: log K_{OW} = 4.4, fish weight = 0.00018 kg, water temperature = 24.8 °C, lipid fraction = 0.05.

Figure S3 shows that fish weight and water temperature have smaller impact on predicted internal concentrations of chemicals than chemical log K_{OW} and fish lipid fraction. In addition, this influence is visible only under non steady state-conditions.

3.3. Predicted Chemical concentrations in various tissues and organs

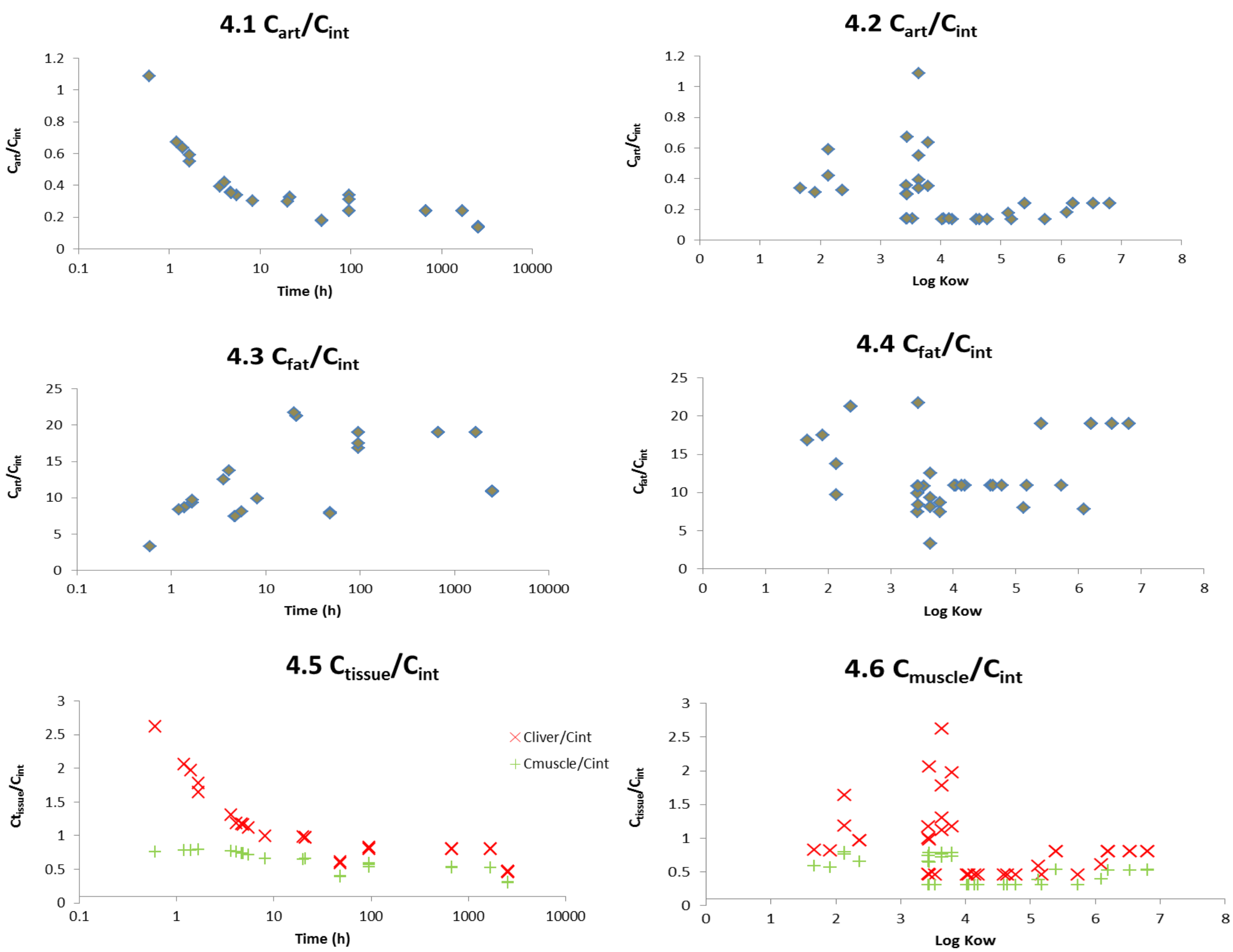

Figure S4. PBTK model predictions of chemical concentrations in rainbow trout tissues in comparison to their concentrations in the whole body (C_{int}): 4.1, 4.3, 4.5: depending on exposure time 4.2, 4.4, 4.6: depending on log K_{OW}. Each point represents a model prediction corresponding to a measured internal concentration in the different experimental studies.

Figure S4 shows that there is a clear relationship between exposure time and chemical concentrations in arterial blood and some tissues while the relationship between log K_{OW} and chemical concentrations is not visible here. The relationship between exposure time and chemical concentrations in fat is not so clear; possibly a result of the fact that most of the chemical concentrates in fat and here steady-state conditions are reached later than in other tissues. It is generally thought that for constant exposure, chemical concentrations in whole body increase in time until steady-state conditions are reached; however, according to Figure S4, the C_{tissue}/C_{int} and C_{art}/C_{int} ratios (except of C_{fat}/C_{int}) decrease in time. This is caused by the small volume of blood, low chemical concentrations in these tissues and high chemical concentration in fat. Thus, chemical concentrations in fat have an impact on the increase of chemical concentration in whole body and the decrease of other C_{tissue}/C_{int} ratios. However, according to

Figure S4, for long time exposure (longer than 100 h), the relationship between chemical concentrations does not change as much as during shorter exposure.

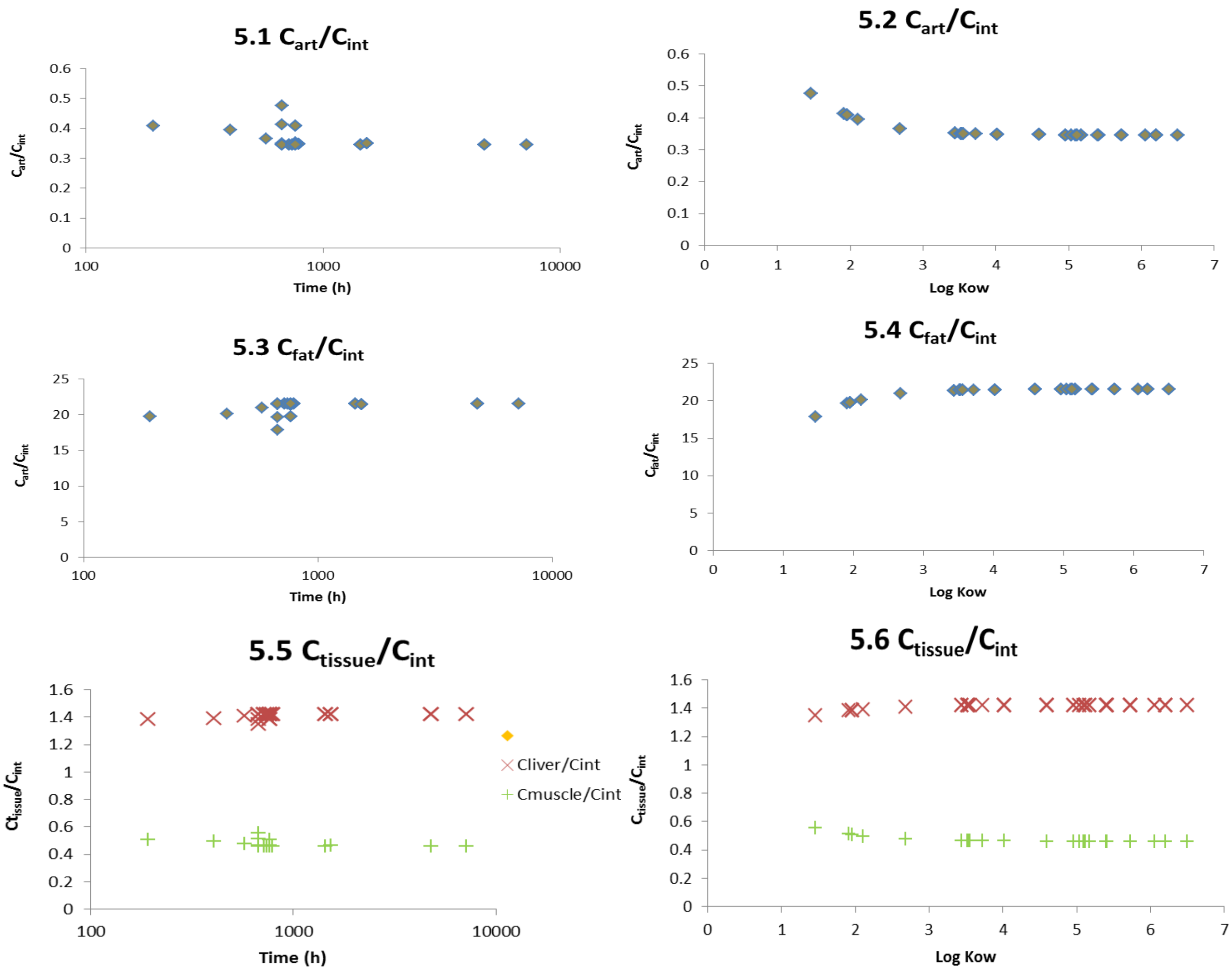

Figure S5. PBTK model predictions of chemical concentrations in fathead minnow tissues in comparison to their concentrations in the whole body (C_{int}): 5.1, 5.3, 5.5: depending on exposure time 5.2, 5.4, 5.6: depending on log K_{OW}. Each point represents a model prediction corresponding to a measured internal concentration in the different experimental studies.

As opposite to Figure S4, Figure S5 shows that there is a relationship between log K_{OW} and chemical concentrations in tissues and no visible relationship between exposure time and chemical concentrations. This is due to different exposure time used in studies for rainbow trout and fathead minnow. As it was noticed for Figure S4, exposure time longer than 100 h did not have a clear impact on the relationship between chemical concentrations in different tissues which probably is caused by reaching steady-state conditions. However, Figure S5 shows, that even during steady-state conditions, the log K_{OW} influents C_{tissue}/C_{int} ratio. Thus, according to Figure S4 and Figure S5, both exposure time and log K_{OW} have an impact on the relationship between chemical concentrations in different tissues.

Note however, that the patterns shown in Figures S4 and S5 depend on the assumption made to parameterize the lipid content in tissues (eqs. S20 – S22). These patterns could change if a different relation between total and organ specific lipid content is assumed, especially for short exposures where steady-state is not approached.

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