

Supporting Information
for
Occurrence of Pharmaceuticals and Personal Care Products in German
Fish Tissue: A National Study

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Total number of pages (including cover page): 17

Page S2: Figure S1

Page S3: Analytes, Surrogates, and Internal Standards

Page S4: Quality Assurance and Quality Control (QAQC)

Page S5: Table S1

Page S6: Table S2

Page S7: Table S3

Page S8: Table S4

Page S9: Table S5

Page S10: Table S6

Page S11 and S12: Table S7

Page S13: Table S8

Page S14: Lipid Determination and Figure S2

Page S15: Influence of WWTPs on PCPs Fish Tissue Concentration

Page S16: Figure S3

Page S17: References

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GESB Sample Locations.



Figure S1. GESB sample locations

Analytes, Surrogates, and Internal Standards. All chemicals were purchased as reagent grade or better from commercial vendors and have been previously described.^{1, 2} The pharmaceuticals measured include: analgesics (acetaminophen, codeine), antihypertensions (atenolol, propranolol, and diltiazem), antibiotics (trimethoprim and sulfamethoxazole), antidepressants (sertraline, fluoxetine, and paroxetine), stimulant (caffeine), antihistamine (diphenhydramine (DPH)), antiseizure (carbamazepine), benzodiazepine (diazepam), antilipemic (gemfibrozil), and select metabolites (norfluoxetine and desmethylsertraline (DMS)). Personal care products include: insect repellent (*m*-tolumide), sunscreen and UV-filters (benzophenone, octocrylene, and 4-methylbenzylidene camphor (4-MBC)), synthetic musk fragrances (galaxolide (HHCB), tonalide (AHTN), celestolide, musk ketone, and musk xylene), surfactant metabolites (*p*-octylphenol and *p*-nonylphenol), and antimicrobial (triclosan). All pharmaceuticals were accompanied with their isotopically labeled compounds as surrogates whereas benzophenone-d₁₀, *p*-nonylphenol-¹³C₆, and pentachloronitrobenzene were used as surrogates for personal care products. Phenanthrene-d₁₀ was used as internal standard for personal care products. N-methyl-N-(trimethylsilyl)-trifluoroacetamide (derivatizing agent) was obtained from VWR Scientifics (Irving, TX, USA).

Quality Assurance and Quality Control (QAQC). Twenty-eight fish tissue composites were grouped into two batches when performing extraction and the analysis. Each batch composed of two blanks (extraction solvent spiked with isotopically labeled analogs only), and duplicate matrix spikes. Two samples (out of 28) were randomly selected for matrix spikes (matrix spike and its duplicate, MS and MSD). Spiking concentrations of unlabeled compounds were equivalent to the CCV concentrations.

Eight reference samples were fortified with analytes at a concentration corresponding to less than ten times the expected method detection limits (MDL). Approximately 1 g and 2.5 g ww of fish tissue samples for pharmaceutical and personal care products were extracted for MDL calculation, respectively. MDL were calculated by multiplying the standard deviation of eight replicates of matrix spike by the one-sided Student *t*-value at $\alpha = 0.01$ and $df = 7$. The MDL for pharmaceuticals analytes ranged from 0.04 to 2.04 ng g⁻¹ ww (Table S1) while from 1.2 to 37.9 ng g⁻¹ ww for personal care products (Table S2).

Continuous Calibration Verification (CCV) was used to evaluate the instrumental performance by the relative percent difference (RPD) between initial concentration of prepared CCV standards and their measured concentration. Two samples (out of 28) were randomly selected to prepare a pair of matrix spikes (matrix spike and its duplicate, MS and MSD) and analytes were spiked at CCV level concentrations. Laboratory blanks were included with each batch of fish tissue samples. Analytes were not detected in blanks and hence, fish tissue concentrations were not blank corrected.

Average pharmaceuticals recoveries for MS and MSD were 89% and 85% for batch I and II, respectively (Table S3 and S4), indicating acceptable accuracy for monitored target analytes in fish samples. RPDs between the pair of matrix spikes were $\pm 12\%$. The average PCPs recoveries for the MS and MSD for batch I and II were 68% and 64%, respectively (Table S5 and S6) and the RPDs between the pair of matrix spikes were within $\pm 22\%$, except for 4-MBC which shows an average RPD of $\pm 31\%$. Average recoveries of HHCB and AHTN for the batch I and II were 64% and 74% with an average RPD of 16% and 15%, respectively. CCVs analyses performed both at the beginning and at the end of batch analysis results into average RPDs of $\pm 20\%$ and $\pm 26\%$ for pharmaceuticals and personal care products, respectively.

Duplicate fish samples were analyzed for PPCPs in all of 14 different GESB sampling locations. The relative standard deviations of measured tissue concentration of HHCB and AHTN for duplicate analysis were $\leq 30\%$; however, relative standard deviations for AHTN at Ulm/Danube and Jochenstein/Danube are 34 and 43%, respectively.

Table S1. Method Detection Limits for Pharmaceuticals Using 100 μ L Injections (ng g^{-1} wet weight)

analytes	lowest cal. pt.	highest cal. pt.	BC1	BC2	BC3	BC4	BC5	BC6	BC7	BC8	mean	STD Dev	RSD %	MDL ³	spiking level	spiking level/MDL
Acetaminophen	0.20	400	3.95	4.37	4.12	4.92	3.94	4.58	4.06	4.22	4.27	0.34	8.0	1.02	4.32	4.2
Atenolol	0.10	200	1.87	1.65	1.61	1.90	1.74	1.49	1.92	1.73	1.74	0.15	8.9	0.46	2.10	4.6
Codeine	0.40	800	10.9	11.3	11.3	12.0	10.8	12.6	12.3	11.8	11.6	0.65	5.6	1.95	10.4	5.3
Caffeine	0.20	400	5.53	5.54	6.32	5.97	7.55	5.96	5.72	5.53	6.02	0.68	11.3	2.04	6.00	2.9
Sulfamethoxazole	0.10	200	4.03	3.93	4.36	3.90	3.89	4.45	3.99	4.39	4.12	0.24	5.9	0.72	4.04	5.6
Trimethoprim	1.00	200	4.14	4.79	4.25	4.96	3.98	4.67	4.75	4.81	4.54	0.36	8.0	1.09	4.90	4.5
DPH	0.01	20.0	0.09	0.07	0.09	0.05	0.07	0.09	0.07	0.09	0.08	0.01	19	0.04	0.10	2.2
Propranolol	0.10	200	2.38	1.91	2.26	1.90	1.90	2.01	2.17	2.27	2.10	0.19	9.2	0.58	1.37	2.4
Diltiazem	0.01	20.0	0.09	0.07	0.10	0.08	0.09	0.12	0.08	0.09	0.09	0.01	15	0.04	0.11	2.8
CBZ	0.10	200	0.65	0.67	0.65	0.55	0.58	0.59	0.73	0.72	0.64	0.06	10	0.19	0.77	4.0
Paroxetine	0.20	400	3.62	3.51	3.44	3.39	3.15	3.54	3.59	3.74	3.50	0.17	5.0	0.52	3.62	6.9
Norfluoxetine	0.20	400	4.19	3.30	3.65	3.87	3.70	4.01	3.70	3.54	3.74	0.28	7.4	0.83	4.14	5.0
Fluoxetine	0.40	800	6.76	6.60	6.53	6.69	7.23	6.91	6.65	6.38	6.72	0.26	3.9	0.78	7.46	9.6
DMS	0.20	400	4.87	5.36	5.59	5.15	5.76	5.06	6.12	5.16	5.38	0.41	7.7	1.24	5.13	4.1
STL	0.20	400	2.67	2.68	2.50	2.42	2.77	2.89	2.71	2.95	2.70	0.18	6.6	0.53	2.90	5.4
Diazepam	0.20	400	5.57	6.22	5.54	5.74	5.57	5.67	6.04	5.50	5.73	0.26	4.6	0.78	5.63	7.2
Gemfibrozil	0.40	800	8.50	9.50	8.89	8.41	8.38	8.10	9.06	8.80	8.70	0.45	5.1	1.34	10.5	7.8

BC = Bream composite; STD Dev = standard deviation; MDL = method detection limit; MDL = STD Dev*2.998 (student t -value at $\alpha = 0.01$ and $df = 7$); RSD = relative standard deviation; DPH = diphenhydramine; CBZ = carbamazepine; DMS = desmethylsertraline; STL = sertraline; cal. pt. = calibration point.

Table S2. Method Detection Limits for PCPs (ng g⁻¹ wet weight)

analytes	lowest cal. pt. (ng g ⁻¹)	highest cal. pt. (ng g ⁻¹)	spiking level (ng g ⁻¹)	BC1	BC2	BC3	BC4	BC5	BC6	BC7	mean	STD Dev	RSD%	MDL ⁴ (ng g ⁻¹)	spiking level/MD L
<i>m</i> -Toluamide	10.0	2000	20.0	19.0	20.3	22.6	23.0	21.4	20.5	21.6	21.2	1.37	6.5	4.3	4.6
Benzophenone	19.2	3840	38.4	22.7	44.7	45.6	41.2	49.0	40.8	21.8	38.0	11.1	29	34.9	1.1
Celestolide	5.60	1080	11.2	5.04	6.88	6.08	5.76	4.40	3.84	7.28	5.61	1.26	23	4.0	2.8
<i>p</i> -Octylphenol	6.00	1200	12.0	20.6	18.2	17.7	19.3	18.0	18.7	19.0	18.8	1.00	5.3	3.1	3.8
HHCB	4.00	803	8.00	4.80	5.84	5.92	6.24	6.16	6.16	6.24	5.91	0.51	8.7	1.6	5.0
AHTN	7.20	1440	14.4	9.04	9.92	11.2	9.52	9.68	9.04	11.4	9.97	0.95	9.6	3.0	4.8
Musk Xylene	110	22000	220	169	198	180	182	161	171	186	178	12.1	6.8	37.9	5.8
<i>p</i> -Nonylphenol	4.00	800	8.00	5.12	5.04	5.20	4.80	4.40	4.24	4.48	4.75	0.38	8.1	1.2	6.6
4-MBC	40.0	8000	80.0	23.4	16.9	18.8	17.4	15.0	18.9	10.5	17.3	3.94	23	12.4	6.5
Musk Ketone	180	36000	360.0	243	228	264	253	248	242	240	245	11.2	4.6	35.2	10
Triclosan	4.80	960	9.60	7.44	9.04	10.4	9.76	8.48	7.52	8.88	8.79	1.09	12	3.4	2.8
Octocrylene ^a	10.0	2000	20.0	11.1	10.6	11.7	11.5	10.6	10.6	10.7	11.0	0.48	4.4	1.5	13

BC = Bream composite (% lipid 2.76); STD Dev = standard deviation; MDL = method detection limit; MDL = STD Dev x 3.143 (student *t*-value at $\alpha = 0.01$ and *df* = 6); ^aspiking level > 10×MDL; RSD = relative standard deviation; HHCB = galaxolide; AHTN = tonalide; 4-MBC = 4-methylbenzylidene camphor; cal. pt. = calibration point.

Table S3. Quality Assurance and Quality Control Summary for 100 μ L Injections for Analysis of Pharmaceuticals-Batch I

analytes	calibration range (ng g ⁻¹)		method blank		continuing calibration verification (CCV) (ng mL ⁻¹)					duplicate matrix spike (ng g ⁻¹ wet weight)					
	lowest cal. pt.	highest cal. pt.	I	II	spiking level	CCV - initial	RPD %	CCV - final	RPD %	spiking level	MS	MSD	mean	RPD %	recovery %
Acetaminophen	0.20	400	ND	ND	100	94.7	5.0	93.7	6.0	100	96.0	101	98.4	4.7	98
Atenolol	0.10	200	ND	ND	50.0	44.2	12	42.0	16	50.0	44.9	43.4	44.1	3.2	88
Codeine	0.40	800	ND	ND	200	175	12	174	13	200	175	172	174	1.9	87
Caffeine	0.20	400	ND	ND	100	85.7	14	89.7	10	100	81.4	89.5	85.5	9.5	85
Sulfamethoxazole	0.10	200	ND	ND	50.0	45.0	10	44.5	11	50.0	43.1	43.4	43.2	0.6	86
Trimethoprim	1.00	200	ND	ND	50.0	44.2	11	43.6	13	50.0	48.6	45.8	47.2	5.9	94
DPH	0.01	20	ND	ND	5.00	4.16	17	4.13	17	5.00	4.55	4.57	4.56	0.4	91
Propranolol	0.10	200	ND	ND	50.0	41.9	16	41.9	16	50.0	43.0	41.6	42.3	3.1	85
Diltiazem	0.01	20	ND	ND	5.00	4.34	13	4.38	12	5.00	4.62	4.41	4.51	4.7	90
CBZ	0.10	200	ND	ND	50.0	44.0	12	43.7	13	50.0	44.1	44.3	44.2	0.5	88
Paroxetine	0.20	400	ND	ND	100	89.2	11	89.8	10	100	95.5	93.3	94.4	2.3	94
Norfluoxetine	0.20	400	ND	ND	100	86.4	14	84.4	16	100	84.7	83.2	83.9	1.7	84
Fluoxetine	0.40	800	ND	ND	200	175	13	176	12	200	179	180	180	0.3	90
DMS	0.20	400	ND	ND	100	85.3	15	83.0	17	100	85.3	84.2	84.7	1.4	85
STL	0.20	400	ND	ND	100	85.7	14	85.3	15	100	86.7	87.2	87.0	0.6	87
Diazepam	0.20	400	ND	ND	100	91.2	9.0	92.5	8.0	100	85.5	89.5	87.5	4.6	88
Gemfibrozil	0.40	800	ND	ND	200	191	5.0	190	5.0	200	185	180	183	3.0	91

ND = non-detected; RPD = relative percentage deviation; DPH = diphenhydramine; CBZ = carbamazepine; DMS = desmethylsertraline; STL = sertraline; cal pt. = calibration point; CCV = continuous calibration verification; MS = matrix spiked; MSD = matrix spiked duplicate; cal. pt. = calibration point.

Table S4. Quality Assurance and Quality Control Summary for 100 μ L Injections for Analysis of Pharmaceuticals-Batch II

analytes	method blank		continuing calibration verification (CCV) (ng mL ⁻¹)					duplicate matrix spike (ng g ⁻¹ wet weight)					
	I	II	spiking level	CCV - initial	RPD%	CCV - final	RPD%	spiking level	MS	MSD	mean	RPD%	recovery%
Acetaminophen	ND	ND	100	94.3	6.0	91.9	8.0	100	86.6	87.6	87.1	1.1	87
Atenolol	ND	ND	50.0	41.8	16	41.5	17	50.0	41.2	40.7	40.9	1.2	82
Codeine	ND	ND	200	168	16	166	17	200	160	160	160	0.2	80
Caffeine	ND	ND	100	81.0	19	81.6	19	100	75.7	83.6	79.6	9.9	80
Sulfamethoxazole	ND	ND	50.0	40.0	20	41.2	18	50.0	41.0	41.6	41.3	1.6	83
Trimethoprim	ND	ND	50.0	40.2	20	40.5	19	50.0	40.1	45.1	42.6	12	85
DPH	ND	ND	5.00	4.02	20	4.03	19	5.00	4.00	4.06	4.03	1.5	81
Propranolol	ND	ND	50.0	40.4	19	40.6	19	50.0	40.1	39.9	40.0	0.6	80
Diltiazem	ND	ND	5.00	4.86	3.0	4.70	6.0	5.00	4.58	4.80	4.69	4.7	94
CBZ	ND	ND	50.0	41.8	16	42.2	16	50.0	40.4	40.0	40.2	1.0	80
Paroxetine	ND	ND	100	93.6	6.0	90.4	10	100	88.5	88.7	88.6	0.3	89
Norfluoxetine	ND	ND	100	90.2	10	87.2	13	100	80.0	84.0	82.0	4.9	82
Fluoxetine	ND	ND	200	187	6.0	189	6.0	200	175	179	177	2.5	89
DMS	ND	ND	100	83.3	17	84.0	16	100	86.3	82.1	84.2	5.0	84
STL	ND	ND	100	85.7	14	83.2	17	100	87.0	85.4	86.2	1.8	86
Diazepam	ND	ND	100	81.0	19	92.0	8.0	100	88.5	89.9	89.2	1.6	89
Gemfibrozil	ND	ND	200	181	10	182	9.0	200	171	180	175	5.1	88

ND = non-detected; RPD = relative percentage deviation; DPH = diphenhydramine; CBZ = carbamazepine; DMS = desmethylsertraline; STL = sertraline; cal pt. = calibration point; CCV = continuous calibration verification; MS = matrix spiked; MSD = matrix spiked duplicate.

Table S5. Quality Control and Quality Assurance Summary for PCPs-Batch I

analytes	method blank data		continuing calibration verification (CCV) (ng μL^{-1})					duplicate matrix spike [†] (ng g ⁻¹ wet weight) ⁴					
	I (ng g ⁻¹)	II (ng g ⁻¹)	spiking Level	CCV initial	RPD %	CCV final	RPD %	spiking level	MS	MSD	average	RPD %	recovery %
<i>m</i> -Toluamide	ND	ND	1.56	1.60	2.3	1.68	7.6	125	100	112	106	11	85
Benzophenone	ND	ND	3.00	2.91	3.0	2.90	3.4	240	166	197	182	17	76
Celestolide	ND	ND	0.84	0.99	17	1.02	21	67.2	35.8	40.4	38.1	12	57
<i>p</i> -Octylphenol	ND	ND	0.94	0.81	14	0.81	14	75.2	53.6	55.3	54.4	3.1	72
HHCB	ND	ND	0.63	0.54	14	0.56	12	50.4	32.9	40.5	36.7	21	73
AHTN	ND	ND	1.13	1.09	3.3	1.14	1.1	90.4	49.0	61.3	55.2	22	61
Musk Xylene	ND	ND	17.2	12.9	25	13.4	22	1375	937	1160	1048	21	76
<i>p</i> -Nonylphenol	ND	ND	0.62	0.56	9.8	0.55	11	49.6	33.2	36.5	34.8	9.4	70
4-MBC	ND	ND	6.25	6.40	2.4	6.16	1.4	500	305	373	339	20	68
Musk Ketone	ND	ND	28.1	20.8	26	24.6	13	2250	1287	1284	1286	0.2	57
Triclosan	ND	ND	0.75	0.57	24	0.56	26	60.0	39.9	39.4	39.6	1.4	66
Octocrylene	ND	ND	1.56	1.09	30	1.25	20	125	71.4	70.2	70.8	1.6	57

ND = not detected; RPD = relative percentage deviation; [†] fish fillet composite; “Bimmen/Rhine” was taken for matrix spiking recovery study; HHCB = galaxolide; AHTN = tonalide; 4-MBC = 4-methylbenzylidene camphor; CCV = continuous calibration verification; MS = matrix spiked; MSD = matrix spiked duplicate.

Table S6. Quality Control and Quality Assurance Summary for PCPs-Batch II

analytes	method blank		continuing calibration verification (CCV) (ng μL^{-1})					duplicate matrix spike [†] (ng g ⁻¹ wet weight)					
	I (ng g ⁻¹)	II (ng g ⁻¹)	spiking level	CCV initial	RPD %	CCV final	RPD %	spiking level	MS	MSD	average	RPD %	recovery %
<i>m</i> -Toluamide	ND	ND	1.56	1.45	7.2	1.62	3.5	125	95.0	100	97.6	5.3	78
Benzophenone	ND	ND	3.00	2.79	7.1	2.98	0.6	240	160	167	163	4.6	68
Celestolide	ND	ND	0.84	0.87	3.5	0.94	12	67.2	62.2	63.8	63.0	2.4	94
<i>p</i> -Octylphenol	ND	ND	0.94	0.69	27	0.67	28	75.2	51.6	54.6	53.1	5.6	71
HHCB	ND	ND	0.63	0.55	13	0.56	12	50.4	26.2	29.3	27.7	11	55
AHTN	ND	ND	1.13	1.34	19	1.36	20	90.4	74.4	80.4	77.4	7.8	86
Musk Xylene	ND	ND	17.2	20.9	22	17.4	1.1	1375	1083	1067	1075	1.5	78
<i>p</i> -Nonylphenol	ND	ND	0.62	0.49	21	0.48	23	49.6	34.6	37.1	35.9	6.9	72
4-MBC	ND	ND	6.25	7.16	15	6.37	1.9	500	124	190	157	42	31
Musk Ketone	ND	ND	28.1	32.7	16	31.5	12	2250	1140	1354	1247	17	55
Triclosan	ND	ND	0.75	0.58	23	0.51	32	60.0	29.8	31.4	30.6	5.2	51
Octocrylene	ND	ND	1.56	1.64	4.9	0.90	42	125	43.4	42.0	42.7	3.4	34

ND = not detected; RPD = relative percentage deviation; [†] fish fillet composite; “Lake Belau” was taken for matrix spiking recovery study; HHCB = galaxolide;

AHTN = tonalide; 4-MBC = 4-methylbenzylidene camphor; CCV = continuous calibration verification; MS = matrix spiked; MSD = matrix spiked duplicate.

Table S7. WWTPs nearby the GESB sampling locations

river	GESB sampling locations	MAF (m ³ s ⁻¹)	WWTPs	PSL	CIE	start up	WWTPs capacity (m ³ d ⁻¹)	additional information
Saar	Gudingen	60	Brebach	0.0	135 000	Mar, 2001	up to 41 000	
			Saargemünd	10.8	61 500	1976, 2005	-	built in 1976, re-newed in 2005
	Rehlingen	80	Saarlouis	6.2	93 000	Nov, 1989	up to 48 000	no information available, small WWTP with capacity < 10 000
			Ensdorf	13.7	58 000	1995	up to 58 000	
			Völklingen	19.7	80 000	1994	up to 40 000	
			Burbach	28.5	200 000	1989	up to 60 000	
	Rhine	Weil	500	Basel	4.4	1 200 000	Sep, 1983	up to 120 000
Chemie Basel				4.4	*	Dec, 1982	up to 9 500	10 600 m ³ s ⁻¹ effluent in the River Rhine
Steith				4.6	**	-	up to 4 200	4 320 m ³ d ⁻¹ effluent in the River Rhine
Iffezheim		-	Rheinmünster	8.5	6 400	1978	-	
			Lichtenau	15.5	-	-	-	no information available, small WWTP
			Straßbourg	34.1	1 000 000	1988	up to 240 000	
			Kehl	35.4	48 000	1981	about 8 000	10 411 m ³ d ⁻¹ effluent in the River Rhine
			Offenburg	50.7	200 000	-	about 28 000	discharge into the River Kinzig distance to the River Kinzig is 14.3 km distance to the River Rhine is 36.4 km
Bimmen		2000	Salmorth	6.9	40 833	1975	up to 76 800	5 524 487 m ³ y ⁻¹ effluent in the River Rhine
			Emmerich	14.0	126 736	1982	up to 67 200	5 331 880 m ³ y ⁻¹ effluent in the River Rhine
			Kalkar-Hönnepel	23.2	38 401	1980	up to 27 744	2 661 626 m ³ y ⁻¹ effluent in the River Rhine (2009)
			Xanten-Vynen	33.8	606	1972	up to 2 400	248 423 m ³ y ⁻¹ effluent in the River Rhine
			Xanten-Lüttingen	41.1	5 753	1982	up to 17 280	1 336 890 m ³ y ⁻¹ effluent in the River Rhine (2009)
	Wesel		50.1	19 900	1980	up to 60 000	6 200 780 m ³ y ⁻¹ effluent in the River Rhine	
Danube	Ulm	100	Erbach	6.1	class 4	-	-	no additional information available
			Ehingen	22.3	class 4	-	-	
			Rottenacker	26.8	class 4	-	-	
			see additional information					8 further plants (class 4) on the next 175 km

			Danubeschingen	181	148 000		up to 86 400		
	Kelheim	400	Saal	6.9	class 4	-	-		
			Staubing	18.6	class 2	-	-		
			Neustadt	29.4	class 4	-	-		
			see additional information						3 further WWTPs of class 3
			Ingolstadt	50.3	275 000	1972	up to 156 000	22 570 000 m ³ y ⁻¹	
	Jochenstein	1000	Obernzell	0.0	class 3	-	-	no further WWTPs were added in this list because of many tributaries upstream Achleiten. There are several WWTPs (classes 1, 2, and 3) at each river.	
			Thyrnau	5.6	class 3	-	-		
			Achleiten	8.0	class 4	-	-		
	Prossen	no data available, the sampling site is located at the Czech border; 23.5 km downstream the city of Decin (50 000 inhabitants), 48 km downstream the city of Usti and Labem (100 000 inhabitants)							
Elbe	Barby	-	Aken	15.6	27 000	1995	about 8 100		
			Calbe	17.7	-	-	-	no information available, discharge in the River Saale (17.0 km), 10 100 inhabitants	
			Dessau	28.3	-	-	about 18 000	3 300 000 m ³ y ⁻¹ effluent in the River Elbe (2008), 87 700 inhabitants	
			Bernburg	34.2	-	-	-	no information available, discharge in the River Saale (33.5 km), 35 900 inhabitants	
			Coswig	50.4	20 000	1995	-		
			Wittenberg	68.9	-	1995	-	no information available, 50 000 inhabitants	
			Halle-Nord	86.8	300 000	Sep, 1998	about 75 000	discharge in the River Saale (86.1 km)	
	Blankenese	800	Köhlbrandhöft/ Dradenau	4.0	2 900 000	1910	up to 1 641 600	450 000 m ³ d ⁻¹ effluent in the River Elbe (2010)	
			Geesthacht Düneberg	42.6	60 000	1970	up to 5 800		
	Saale	Wettin	115	Halle-Nord	15.0	300 000	Sep, 1998	about 75 000	
Leipzig-Rosental				63.7	628 000	-	-	no further information available, discharge in the Elster-Saale-channel	
Mulde	Dessau	64	Bitterfeld-Wolfen	37.2	422 000	1994	-	also WWTP for industrial wastewater	

WWTP: waste water treatment plant, MAF: mean annual flow, PSL: proximity to the sampling locations, CIE: capacity inhabitant equivalent

* WWTP of chemical industry: F. Hoffmann-LaRoche AG, Novartis Pharma AG, Ciba Chemie AG and Syngenta AG, right-hand side of the River Rhine

** WWTP of chemical industry: Clariant, Ciba AG (Huningue) and Novartis Pharma AG (St. Johann), left-hand side of the River Rhine

Class 1: < 1 000, class 2 = 1 000 - 5 000, class 3: 5 000 – 10 000, class 4: 10 000 – 100 000, class 5: > 100 000

Note: Authors acknowledge the fact these WWTPs and the relevant information are not the exhaustive ones; however, represent the maximum information that could be acquired.

Table S8. Pharmaceuticals and Personal Care Products Measured in Fish Fillet Composites from GESB Sites

river	GESB sampling locations	fish tissue concentration								% lipid ^a (n = 4–6)
		pharmaceuticals (ng g ⁻¹ ww)					personal care products (ng g ⁻¹ lw)			
		DPH	DMS	CBZ	diltiazem	atenolol	HHCB	ATHN	triclosan	
Rhine	Weil	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	1110 960	120 127	<MDL <MDL	6.98
	Iffezheim	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	1870 1610	182 129	<MDL <MDL	7.51
	Bimmen	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	1410 1330	68.0 91.0	<MDL <MDL	6.09
Saar	Gudingen	0.04 <MDL	<MDL 1.65	<MDL <MDL	<MDL <MDL	<MDL <MDL	10,100 9250	246 330	<MDL <MDL	3.90
	Rehlingen	0.07 <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	12,000 10,200	316 448	<MDL <MDL	4.02
Danube	Ulm	<MDL <MDL	1.83 4.72	<MDL <MDL	<MDL <MDL	<MDL <MDL	1270 1210	199 121	<MDL <MDL	6.66
	Kelheim	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	1030 663	98.0 <MDL	<MDL <MDL	5.21
	Jochenstein	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	948 662	127 68.0	<MDL <MDL	6.86
Elbe	Prossen	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	1500 1250	<MDL <MDL	<MDL <MDL	1.79
	Barby	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	285 251	<MDL <MDL	<MDL <MDL	2.39
	Blankenese	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	367 438	<MDL <MDL	<MDL <MDL	4.64
Mulde	Dessau	0.06 0.05	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	636 <MDL	<MDL <MDL	<MDL <MDL	2.68
Saale	Wettin	<MDL 0.05	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	1290 1430	112 128	<MDL <MDL	4.50
Lake Belau	Lake Belau	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	<MDL <MDL	1.91

<MDL = below method detection limits; DPH = diphenhydramine; DMS = desmethylsertraline; CBZ = carbamazepine; HHCB = galaxolide; ATHN = tonalide; ^amean data from the German Federal Environmental Agency.

Lipid Determination. The correlation between the percent lipid content and the measured tissue concentration of HHCb and AHTN has been demonstrated (Figure S3). The logarithmic fish tissue concentration of HHCb and AHTN were positively correlated with percent lipid contents in fish tissue composites (HHCb: $r^2 = 0.71$, $p = 0.001$ and AHTN: $r^2 = 0.59$, $p = 0.043$). The HHCb and AHTN concentrations from Saar were not plotted. Potential correlations of pharmaceuticals fish tissue concentration with lipid content could not be investigated due to insufficient data. The pharmaceuticals fish tissue concentrations were not correlated with lipid content from fish collected from the United States.¹ In fact, the bioaccumulation potential depends on the physiological pH,⁵ metabolism, and degree of ionization (pK_a).¹ HHCb and AHTN have lower ionization properties than that of pharmaceuticals which make them more bioaccumulative.

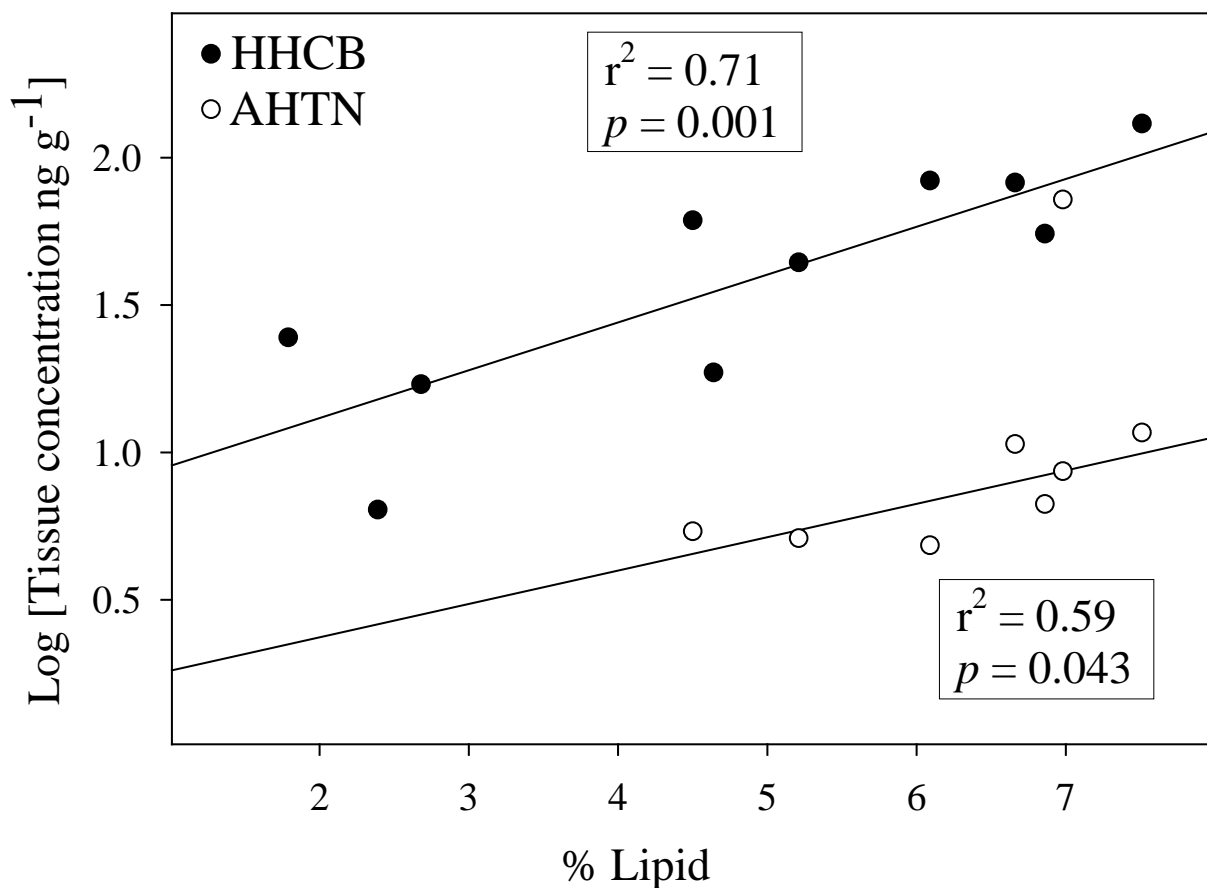


Figure S2. Correlations of HHCb and AHTN fish tissue concentrations with lipid

Influence of WWTPs on PCPs Fish Tissue Concentrations. Excluding CIE, the least significant predictor variable, from the MLR analysis of HHCB and AHTN fish tissue concentrations with PSL and MAF provided r^2 of 0.44 ($p = 0.177$) and 0.56 ($p = 0.131$).

$$\text{HHCB} = 6896 - (445 * \text{PSL}) - (2.88 * \text{MAF}) \quad (r^2 = 0.44, p = 0.177)$$

$$\text{AHTN} = 271.0 - (10.9 * \text{PSL}) - (0.09 * \text{MAF}) \quad (r^2 = 0.56, p = 0.131)$$

Furthermore, excluding largest MAF sampling location (Bimmen/Rhine, $2000 \text{ m}^3 \text{ s}^{-1}$), multiple linear regression of HHCB and AHTN fish tissue concentrations with MAF, PSL, and CIE (<30 km) provided r^2 for HHCB of 0.79 ($p = 0.075$) and AHTN of 0.81 ($p = 0.129$). The following multiple linear regression equations were obtained.

$$\text{HHCB} = 9825 - (635 * \text{PSL}) - (9.91 * \text{MAF}) + (3.51 \times 10^{-4} * \text{CIE}) \quad (r^2 = 0.79, p = 0.075)$$

$$\text{AHTN} = 329.0 - (14.9 * \text{PSL}) - (0.26 * \text{MAF}) + (1.70 \times 10^{-5} * \text{CIE}) \quad (r^2 = 0.81, p = 0.129)$$

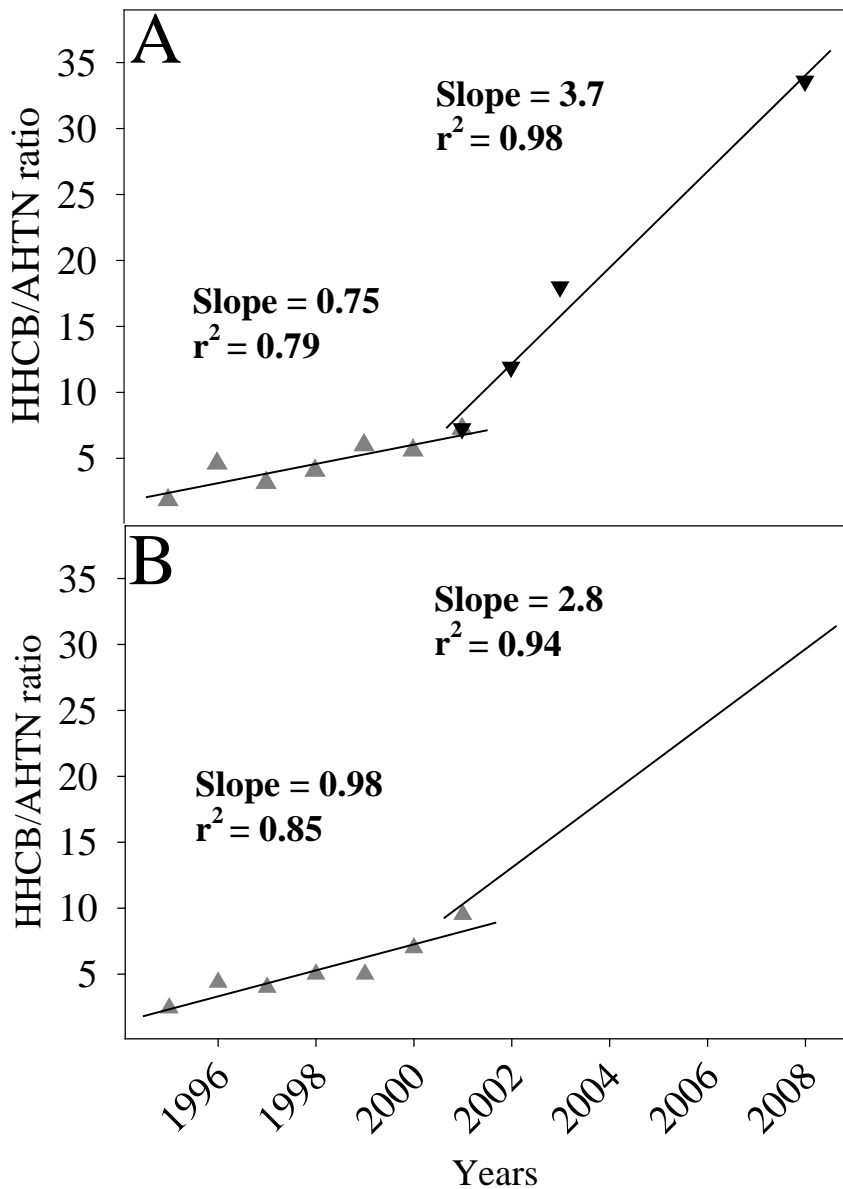


Figure S3. HHCB/AHTN ratio as a function of time: A) Gudingen/Saar and B) Rehlingen/Saar

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