Electronic Supplementary Material (ESI) for Analytical Methods.

Electronic Supplementary Material

An LC-MS/MS method for the determination of 28 environmental contaminants and metabolites in vegetables irrigated with treated municipal wastewater

Christina Riemenschneider[1], Bettina Seiwert[1], Myah Goldstein[2], Marwan Al-Raggad[3], Elias Salameh[3], Benny Chefetz[2], Thorsten Reemtsma[1]

[1] Helmholtz Centre for Environmental Research - UFZ, Department of Analytical Chemistry, Permoserstrasse 15, 04318 Leipzig

[2] The Hebrew University of Jerusalem, Department of Soil and Water Sciences, P.O. Box 12, Rehovot 7610001, Israel

[3] University of Jordan, Water, Energy and Environment Center, Amman 11942, Jordan

* Corresponding author: Thorsten Reemtsma (thorsten.reemtsma@ufz.de)

Chemicals

Acesulfame, acridine, benzotriazole, caffeine, carbamazepine, carbamazepine 10,11-epoxide (EP-CBZ), carbamazepine-d10, diclofenac, gabapentin, hydrochlorothiazide, 4-methyl-1H-benzotraizole, 5-methyl-1H-benzotraizole, oxcarbazepine, sulfamethoxazole and trimethoprim were purchased from Sigma-Aldrich (Munich, Germany). 2-hydroxy carbamazepine (2-OH-CBZ), 3-hydroxy carbamazepine (3-OH-CBZ), 10,11-dihydro-10-hydroxy carbamazepine (10-OH-CBZ), *cis*-10,11-dihydroxy-10,11-dihydrocarbamazepine (*cis*-DiOH-CBZ), rac *trans*-10,11-dihydro-10,11-dihydroxycarbamazepine (*trans*-DiOH-CBZ), lamotrigine and acridone were obtained from Toronto Research Chemicals (Toronto, Canada). Ciprofloxacin was ordered from Bioforsk (Saerheim, Norway), gemfibrozil from ICV-Biomedicals (Eschwege, Germany), mefenamic acid from ABCR (Karlsruhe, Germany) and iohexol from Santa Cruz Biotechnology (Heidelberg, Germany). Iomeprol and metalaxyl were purchased from Dr. Ehrensdorfer (Augsburg, Germany) and iopamidol and iopromide were obtained from EDQM (Straßburg, France). Bondensil-PSA and anhydrous magnesium sulfate were from Agilent Technologies (Santa Clara, US), acetone from AppliChem (Darmstadt, Germany) and sodium chloride from Merck (Darmstadt, Germany).
Methanol, acetonitrile and acetic acid (Biosolve, Valkenswaard, The Netherlands) were of analytical and UPLC grade. All aqueous solutions were prepared by using ultrapure water from a Milli-Q system (Merck, Darmstadt, Germany).

Table S1: Optimized parameters for the QTrap-MS/MS analysis of the target compounds: declustering potential (DP), collision energy (CE) and mean retention time (RT).

compound	ESI polarity	Precursor ion (m/z)	DP (V)	MRM 1	CE 1 (eV)	MRM 2	CE 2 (eV)	RT (min)
Acesulfame	-	162	-50	82	-20	78	-40	4.2
4-/5-Methylbenzotriazole	+	134	71	77	31	78	29	11.3
Benzotriazole	+	120	126	65	29	92	23	8.4
Ciprofloxacine	+	332	106	314	29	231	51	7.3
Caffeine	+	195	80	138	27	110	31	7.7
Diclofenac	-	295	-40	252	-16	250	-16	44.5
Gabapentin	+	172	36	154	19	137	21	6.3
Gemfibrozil	-	249	-60	121	-24	127	-16	45.4
Hydrochlorothiazide	-	295	-110	268	-28	205	-32	5.5
Iohexol	+	821	136	803	27	603	35	3.5
Iomeprol	+	777	76	686	29	558	33	3.9
Iopamidol	+	777	76	558	33	686	29	2.4
Iopromide	+	791	46	572	33	773	27	6.3
Lamotrigine	+	256	91	211	39	109	63	8.2
Mefenamic acid	-	240	-65	196	-24	180	-38	45.3
Metalaxyl	+	280	71	220	19	160	33	30.1
Sulfamethoxazole	+	254	56	156	21	92	35	8.4
Carbamazepine (CBZ)	+	237	106	194	25	193	47	22.4
Acridine	+	180	40	152	47	-	-	9.6
Acridone	+	196	126	167	49	-	-	16.1
carbamazepine 10,11-epoxide (EP-CBZ)	+	253	31	180	41	236	15	12.8
10,11-dihydro-10-hydroxy carbamazepine (10-OH-CBZ)	+	255	51	194	31	237	15	12.8
2-hydroxy carbamazepine (2-OH-CBZ)	+	253	61	210	29	208	35	12.9
3-hydroxy carbamazepine (3-OH-CBZ)	+	253	61	210	27	208	29	15.7
10,11-dihydro-10,11-*cis*-dihydroxycarbamazepine (*cis*-DiOH-CBZ)	+	271	86	180	43	210	21	7.9
Oxcarbazepine	+	253	71	236	19	208	27	15.1
10,11-dihydro-10,11-*trans*-dihydroxy-carbamazepine (*trans*-DiOH-CBZ)	+	271	26	180	49	253	11	11.6

Table S2: Concentration of carbamazepine (CBZ) and its metabolites in treated wastewater (TWW) and the irrigation water of greenhouse experiments (spiked TWW). Analysis was performed by LC-MS/MS.

	concentration in TWW [*µ*g/L] [#]	**concentration in spiked TWW [*µ*g/L]**
		greenhouse experiment
CBZ	1.06	1.99
EP-CBZ	N.A.*	0.07
2-OH-CBZ	N.A.	0.23
3-OH-CBZ	N.A.	0.08
10-OH-CBZ	N.A.	0.76
trans-DiOH-CBZ	N.A.	2.44

[#] M. Goldstein, M. Shenker and B. Chefetz, *Environ. Sci. Technol.*, 2014, **48**, 5593-5600.
* Not analyzed.

Table S3: Physico-chemical properties and application of target analytes

Compound	Molecular weight (g/mol)	Formula	log *D* (pH 7)*	pKa*	Application
Acesulfame	163.15	$C_4H_4KNO_4S$	-3.12	-	artificial sweetener
4-/5-Methylbenzotriazole	133.15	$C_9H_9N_3$	1.67	1.7; 8.5	corrosion inhibitor
Benzotriazole	119.12	$C_6H_5N_3$	1.59	1.2; 8.4	corrosion inhibitor
Ciprofloxacine	331.34	$C_{17}H_{18}FN_3O_3$	-2.47	6.4; 8.7	antibacterial agent
Caffeine	194.19	$C_{15}H_{12}N_2O$	0.42	-	stimulant
Diclofenac	296.15	$C_{14}H_{11}Cl_2NO_2$	1.83	4.2	antirheumatic agent
Gabapentin	171.24	$C_9H_{17}NO_2$	-1.47	4.7; 10.3	anticonvulsant
Gemfibrozil	250.34	$C_{15}H_{22}O_3$	1.86	4.8	pharmaceutical
Hydrochlorothiazide	297.74	$C_7H_8ClN_3O_4S_2$	0.02	9.0; 9.6	diuretic
Iohexol	821.14	$C_{19}H_{26}I_3N_3O_9$	-3.03	>11.3	x-ray contrast agent
Iomeprol	777.09	$C_{17}H_{22}I_3N_3O_8$	-2.55	>11.3	x-ray contrast agent
Iopamidol	777.09	$C_{17}H_{22}I_3N_3O_8$	-2.35	>10.9	x-ray contrast agent
Iopromide	791.11	$C_{18}H_{24}I_3N_3O_8$	-1.98	>10.6	x-ray contrast agent
Lamotrigine	256.10	$C_9H_7Cl_2N_5$	2.32	5.4	anticonvulsant
Mefenamic acid	241.29	$C_{15}H_{15}NO_2$	2.14	3.7	antirheumatic agent
Metalaxyl	279.33	$C_{15}H_{21}NO_4$	1.81	1.4	pesticide
Sulfamethoxazole	253.28	$C_{10}H_{11}N_3O_3S$	-0.30	1.4; 5.8	antibacterial agent
Carbamazepine (CBZ)	236.27	$C_{15}H_{12}N_2O$	2.17	-	anticonvulsant
Acridine	179.22	$C_{13}H_9N$	3.30	5.6	CBZ metabolite
Acridone	195.22	$C_{13}H_9NO$	4.08	-	CBZ metabolite
carbamazepine 10,11-epoxide (EP-CBZ)	252.27	$C_{15}H_{12}N_2O_2$	1.37	-	CBZ metabolite
10,11-dihydro-10-hydroxy carbamazepine (10-OH-CBZ)	254.28	$C_{15}H_{12}N_2O_2$	1.69	-	CBZ metabolite
2-hydroxy carbamazepine (2-OH-CBZ)	252.27	$C_{15}H_{12}N_2O_2$	1.87	10.3	CBZ metabolite
3-hydroxy carbamazepine (3-OH-CBZ)	252.27	$C_{15}H_{12}N_2O_2$	2.22	10.0	CBZ metabolite
10,11-dihydro-10,11-*cis*-dihydroxycarbamazepine (*cis*-DiOH-CBZ)	270.28	$C_{15}H_{14}N_2O_3$	-	-	CBZ metabolite
Oxcarbazepine	252.27	$C_{15}H_{12}N_2O_2$	2.00	-	CBZ metabolite
10,11-dihydro-10,11-*trans*-dihydroxy-carbamazepine (*trans*-DiOH-CBZ)	270.28	$C_{15}H_{14}N_2O_3$	0.71	-	CBZ metabolite

*predicted from ACD/Percepta, 2015

Table S4: Matrix-effects (ME)[#], absolute recovery (RA) and relative standard deviations (RSD, n=3) of solid-liquid extraction (SLE) and QuEChERS method for the extraction of 28 polar pollutants from plant material

	SLE lettuce leaves / cabbage leaves			QuEChERS lettuce leaves / cabbage leaves		
Analyte	ME [%]	RA [%] 50 ng/g	RSD [%] 50 ng/g	ME [%]	RA [%] 50 ng/g	RSD [%] 50 ng/g
Acesulfame	-70 / -46	77.9 / 66.1	6.5 / 5.6	74 / 72	12.6 / 18.1	59.8 / 27.5
4-/5-Methylbenzotriazole	-62 / -33	73.0 / 65.2	2.2 / 11.5	59 / 66	54.9 / 52.0	17.3 / 6.0
Benzotriazole	-55 / -15	70.4 / 58.2	4.7 / 10.1	58 / 45	44.2 / 41.0	17.9 / 10.8
Ciprofloxacine	-153 / -36	98.4 / 91.5	6.2 / 2.5	-63 / -86	2.2 /1.0	86.3 / 35.3
Caffeine	-49 / -5	65.9 / 53.0	4.8 / 16.8	-53 / -49	21.6 / 19.2	17.8 / 7.8
Diclofenac	-32 / -21	65.2 / 56.5	6.1 / 4.0	57 / 75	1.5 / 1.1	23.9 / 5.7
Gabapentin	-74 / -44	72.3 / 65.3	4.5 / 17.8	-79 / -79	3.8 / 3.2	44.8 54.6
Gemfibrozil	-46 / -23	69.4 / 56.2	4.3 / 3.6	35 / 58	7.2 / 4.7	22.2 / 25.3
Hydrochlorothiazide	-46 / -21	69.6 / 57.8	6.6 / 16.9	51 / 53	57.1 / 50.9	20.3 / 7.3
Iohexol	30 / -6	27.1 / 49.7	6.5 / 16.1	-79 / -78	-/ -	-/ -
Iomeprol	26 / -7	28.6 / 45.4	2.6 / 2.3	-74 / -73	-/ -	-/ -
Iopamidol	30 / 54	27.5 / 17.4	17.8 / 13.1	-84 / -83	-/ -	-/ -
Iopromide	-49 / -11	65.1 / 47.5	2.5 / 7.0	-64 / -66	<MQL / -	-/ -
Lamotrigine	-52 / -29	65.6 / 50.7	2.6 / 5.8	-62 / -63	12.4 / 8.4	16.3 / 9.6
Mefenamic acid	-59 / -10	68.1 / 39.2	3.2 / 4.9	42 / 41	1.1 / 0.6	49.0 / 42.4
Metalaxyl	-50 / -49	65.7 / 61.2	2.8 / 1.8	49 / 76	74.8 / 62.1	16.1 / 2.3
Sulfamethoxazole	-60 / -14	62.8 / 50.8	2.0 / 4.2	64 / 57	15.9 / 10.3	21.7 / 2.1
Carbamazepine (CBZ)	-51 / -38	67.9 / 65.1	3.4 / 16.5	51 / 63	71.7 / 59.7	14.8 / 2.1
Acridine	67 / 73	63.9 / 54.2	10.0 / 5.0	-67 / -66	90.8 / 49.0	11.5 / 16.0
Acridone	-54 / -39	70.0 / 61.4	3.6 / 3.3	57 / 68	78.7 / 62.5	13.4 / 4.4
EP-CBZ	-41 / -26	62.4 / 62.9	4.1 / 17.4	44 / 54	65.7 / 54.6	14.6 /3.3
10-OH-CBZ	-45 / -28	63.1 / 61.7	3.0 / 16.3	41 / 54	58.5 / 48.6	13.9 / 1.3
2-OH-CBZ	-49 / -25	67.0 / 62.5	2.1 / 14.8	50 / 59	59.3 / 50.4	12.4 / 4.5
3-OH-CBZ	-57 / -41	71.4 / 61.6	3.6 / 3.2	54 / 71	48.7 / 41.4	13.5 / 17.7
cis-DiOH-CBZ	-32 / -10	62.6 / 52.3	6.6 / 10.9	29 / 34	47.1 / 40.1	13.6 / 8.2
Oxcarbazepine	-7 / 24	52.8 / 35.5	1.2 / 3.2	3 / 10	54.6 / 16.4	15.9 / 5.2
trans-DiOH-CBZ	-52 / -38	67.5 / 65.6	5.1 / 17.4	41 / 55	41.2 / 35.4	14.8 / 15.3

[#]Signal supression (+) and enhancement (-)

Table S5: Method validation parameters for solid-liquid extraction of 28 environmental contaminants from freeze-dried tomato fruits: method detection limit (MDL), method quantitation limit (MQL), matrix-effects (ME)[#], absolute recoveries (RA) and relative standard deviations (RSD, n = 3) at three different spiking concentrations.

Analyte	MDL [ng/g d.w.]	MQL [ng/g d.w.]	ME [%]	Absolute recovery [%] 5 ng/g d.w.	Absolute recovery [%] 25 ng/g d.w.	Absolute recovery [%] 50 ng/g d.w.	Intra-day RSD [%] 5 ng/g d.w.	Intra-day RSD [%] 25 ng/g d.w.	Intra-day RSD [%] 50 ng/g d.w.	Inter-day RSD [%] 5 ng/g d.w.	Inter-day RSD [%] 25 ng/g d.w.	Inter-day RSD [%] 50 ng/g d.w.
4,5-Methylbenzotriazole	0.2	1.0	1	80.4	70.3	73.2	3.0	3.0	3.5	2.0	2.6	3.9
Acesulfame	1.0	2.0	6	78.5	75.5	79.0	13.6	3.4	1.2	2.1	3.3	0.3
Benzotriazole	1.0	2.0	28	43.0	51.4	55.2	20.9	6.5	4.6	8.3	7.0	4.3
Caffeine	1.0	2.0	14	100.3	63.7	68.7	9.2	6.3	11.5	4.4	4.8	2.2
Ciprofloxacine	1.0	2.0	9	40.5	34.6	46.2	8.9	3.3	13.7	16.4	12.0	10.8
Diclofenac	1.0	2.0	31	71.7	63.4	71.9	14.9	5.5	2.5	11.1	3.2	0.8
Gabapentin	1.0	2.0	0	48.8	48.7	76.5	0.9	1.6	4.9	3.9	3.3	5.6
Gemfibrozil	0.2	1.0	20	66.3	61.4	66.5	8.0	1.2	1.8	6.4	2.2	2.5
Hydrochlorothiazide	<0.2	0.2	39	53.6	50.1	54.9	5.7	0.9	3.7	2.2	0.9	3.2
Iohexol	2.0	10.0	60	<MQL	24.9	32.9	-	14.1	3.3	-	10.1	4.5
Iomperol	2.0	10.0	56	<MQL	26.7	39.5	-	3.9	2.8	-	10.3	3.4
Iopamidol	2.0	10.0	74	<MQL	19.8	20.4	-	1.4	16.8	-	10.9	19.8
Iopromide	2.0	10.0	50	<MQL	40.4	44.7	-	7.0	2.8	-	4.1	7.7
Lamotrigine	0.2	1.0	-4	74.0	71.1	79.5	8.0	3.2	3.5	4.9	5.8	1.4
Mefenamic acid	1.0	2.0	19	64.8	53.3	60.1	9.6	2.2	0.9	1.9	2.8	2.0
Metalaxyl	1.0	2.0	7	96.5	93.5	97.9	3.1	4.5	4.5	8.5	1.6	0.9
Sulfamethoxazole	0.2	1.0	23	51.9	51.8	49.8	10.3	5.2	13.2	16.7	7.9	11.5
Carbamazepine (CBZ)	0.2	1.0	5	88.6	87.2	91.0	0.7	2.9	0.0	1.6	2.3	1.3
Acridine	0.2	1.0	-10	82.5	78.3	86.6	3.0	1.2	2.0	7.6	1.3	4.2
Acridone	<0.2	<0.2	0	91.9	89.4	96.1	2.1	2.2	0.7	2.2	0.9	2.0
EP-CBZ	0.2	1.0	13	76.2	77.0	79.7	1.9	4.3	0.7	2.1	3.1	0.7
10-OH-CBZ	0.2	1.0	6	86.8	86.2	89.4	4.0	3.8	2.9	3.1	2.1	2.4
2-OH-CBZ	0.2	1.0	6	82.5	79.1	82.7	2.7	0.9	2.6	4.3	1.9	1.6
3-OH-CBZ	<0.2	0.2	3	89.8	88.0	93.1	2.3	0.8	1.1	1.3	0.8	0.6
cis-DiOH-CBZ	0.2	1.0	31	52.5	53.4	57.4	2.0	4.7	2.0	3.9	3.1	3.6
Oxcarbazepine	0.2	1.0	4	81.4	88.9	92.8	1.3	2.5	0.8	5.1	1.1	1.9
trans-DiOH-CBZ	0.2	1.0	11	72.4	71.5	75.2	4.6	4.3	1.2	6.3	5.3	2.0

[#]Signal supression (+) and enhancement (-)

Table S6: Method validation parameters for solid-liquid extraction of 28 environmental contaminants from freeze-dried tomato leaves: method detection limit (MDL), method quantitation limit (MQL), matrix-effects (ME)[#], absolute recoveries (RA) and relative standard deviations (RSD, n = 3) at three different spiking concentrations.

Analyte	MDL [ng/g d.w.]	MQL [ng/g d.w.]	ME [%]	Absolute Recovery [%] 5 ng/g d.w.	Absolute Recovery [%] 25 ng/g d.w.	Absolute Recovery [%] 50 ng/g d.w.	Intra-day RSD [%] 5 ng/g d.w.	Intra-day RSD [%] 25 ng/g d.w.	Intra-day RSD [%] 50 ng/g d.w.	Inter-day RSD [%] 5 ng/g d.w.	Inter-day RSD [%] 25 ng/g d.w.	Inter-day RSD [%] 50 ng/g d.w.
4,5-Methylbenzotriazole	0.2	2.0	5	72.6	66.6	66.9	4.1	5.2	7.1	3.5	0.6	2.1
Acesulfame	1.0	2.0	26	69.6	64.8	68.0	16.8	3.0	9.5	2.7	1.5	0.3
Benzotriazole	1.0	20.0	37	44.5	46.8	48.9	12.1	9.5	10.6	7.3	1.5	4.0
Caffeine	0.2	1.0	19	118.5	67.0	59.7	10.9	2.8	5.2	6.4	2.0	2.8
Ciprofloxacine	2.0	10.0	-6	<MQL	24.4	60.9	-	7.4	7.1	-	9.5	14.6
Diclofenac	1.0	2.0	35	68.3	48.6	53.8	20.6	3.9	7.9	29.9	5.8	8.6
Gabapentin	1.0	1.0	3	79.1	52.5	73.1	9.3	10.7	14.3	5.6	3.4	4.5
Gemfibrozil	0.2	1.0	40	51.6	39.8	43.5	10.7	2.3	1.5	6.0	1.1	1.7
Hydrochlorothiazide	0.2	1.0	55	42.9	39.3	41.6	5.9	4.3	11.3	6.6	0.8	1.2
Iohexol	2.0	2.0	42	<MQL	27.6	49.5	-	12.8	6.7	-	11.7	4.5
Iomperol	2.0	10.0	60	<MQL	25.8	38.8	-	1.8	6.2	-	5.0	0.9
Iopamidol	2.0	10.0	78	<MQL	19.3	21.9	-	7.0	11.7	-	5.6	4.7
Iopromide	2.0	10.0	63	<MQL	32.3	38.4	-	9.0	9.4	-	7.4	3.9
Lamotrigine	0.2	10.0	18	51.3	58.3	63.9	4.2	2.3	14.6	17.4	3.9	0.6
Mefenamic acid	1.0	2.0	56	33.2	28.9	32.8	2.8	2.0	6.4	7.4	2.4	2.0
Metalaxyl	1.0	1.0	4	91.2	94.5	98.9	4.3	3.7	2.5	2.5	3.1	2.0
Sulfamethoxazole	1.0	2.0	45	28.6	29.4	29.1	9.0	12.2	19.4	16.8	7.9	12.5
Carbamazepine (CBZ)	0.2	1.0	62	35.2	31.9	33.3	3.5	2.8	2.1	3.8	0.5	1.9
Acridine	0.2	2.0	-17	97.2	95.4	95.3	3.8	6.8	10.9	4.7	3.1	2.2
Acridone	<0.2	1.0	4	87.1	85.3	87.7	2.2	5.3	3.9	2.4	1.2	1.3
EP-CBZ	0.2	1.0	11	81.0	75.2	79.0	4.7	5.0	5.5	1.6	2.7	2.2
10-OH-CBZ	0.2	0.2	12	86.5	80.2	83.6	2.8	4.7	5.5	2.8	2.0	2.7
2-OH-CBZ	0.2	1.0	13	76.3	79.8	81.6	5.1	4.0	2.7	6.5	3.9	2.3
3-OH-CBZ	<0.2	1.0	11	81.0	80.8	85.2	3.3	4.1	5.5	2.1	0.5	1.4
cis-DiOH-CBZ	1.0	1.0	38	55.3	47.5	49.3	1.9	11.4	5.1	11.3	4.8	3.2
Oxcarbazepine	0.2	<0.2	13	56.2	58.9	61.6	3.0	8.2	14.0	7.5	7.0	14.1
trans-DiOH-CBZ	0.2	1.0	32	64.5	64.4	66.9	10.0	1.7	7.0	5.8	2.5	1.1

[#]Signal supression (+) and enhancement (-)