Supplementary information

Multi-residue enantioselective determination of emerging drug contaminants in seawater by solid phase extraction and liquid chromatography-tandem mass spectrometry

Katie McKenzie[a], Colin F. Moffat[a,b] Bruce Petrie[a*]

[a]School of Pharmacy and Life Sciences, Robert Gordon University, Aberdeen, AB10 7GJ, UK

[b]Office of the Chief Scientific Advisor Marine, Scottish Government, Marine Laboratory, 375 Victoria Road, Aberdeen, AB11 9DB, UK

*Corresponding author email: b.r.petrie@rgu.ac.uk Tel. +44 (0)1224 262824

The supplementary information contains 19 figures and six tables describing the stability of analytes in collected seawater samples stored under different conditions, chemical properties of studied analytes, MRM transitions, sample locations of the Clyde and Forth estuaries, instrument validation data and metals present in extracted samples.

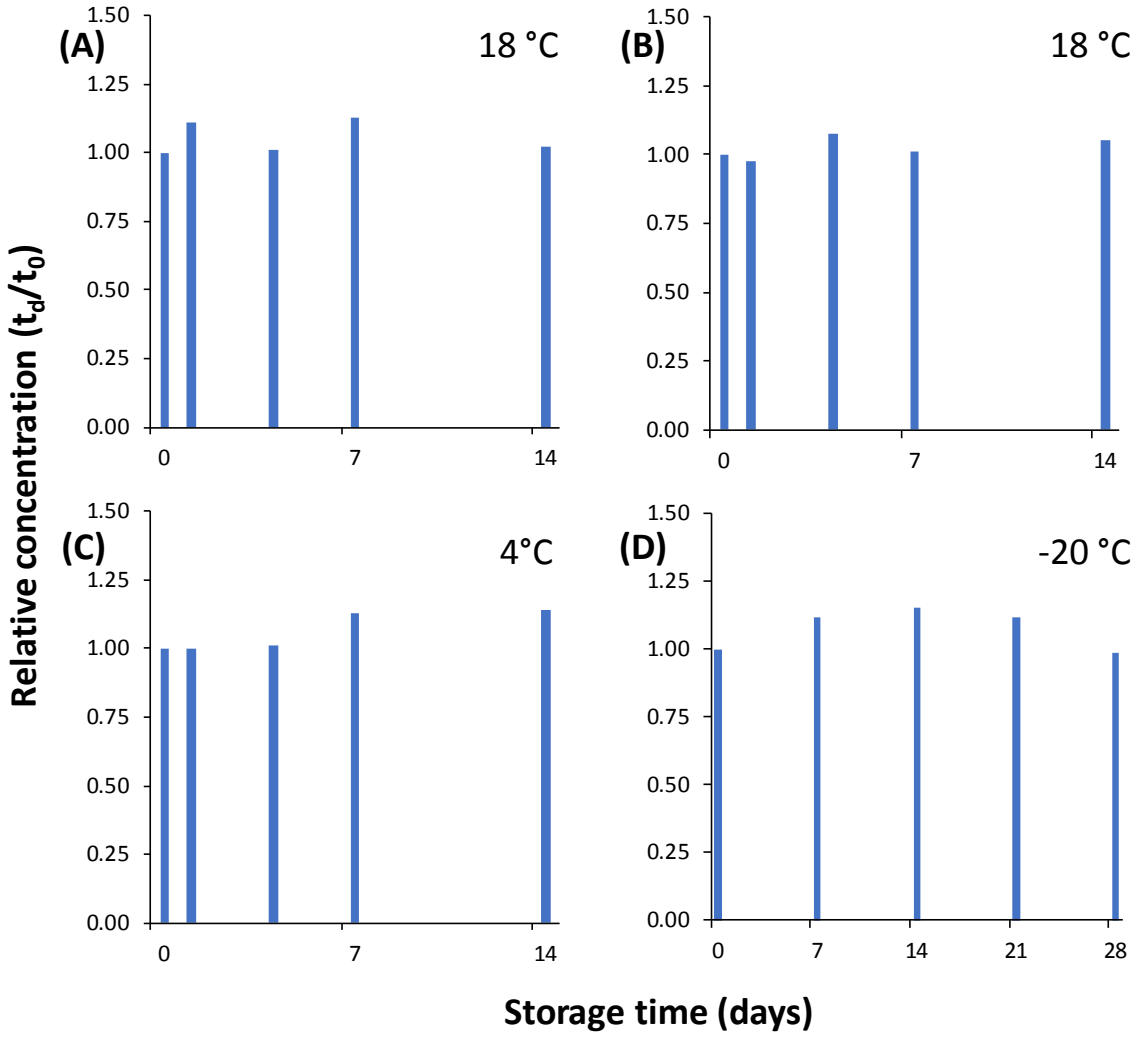


Figure S1. Relative concentration of paracetamol spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

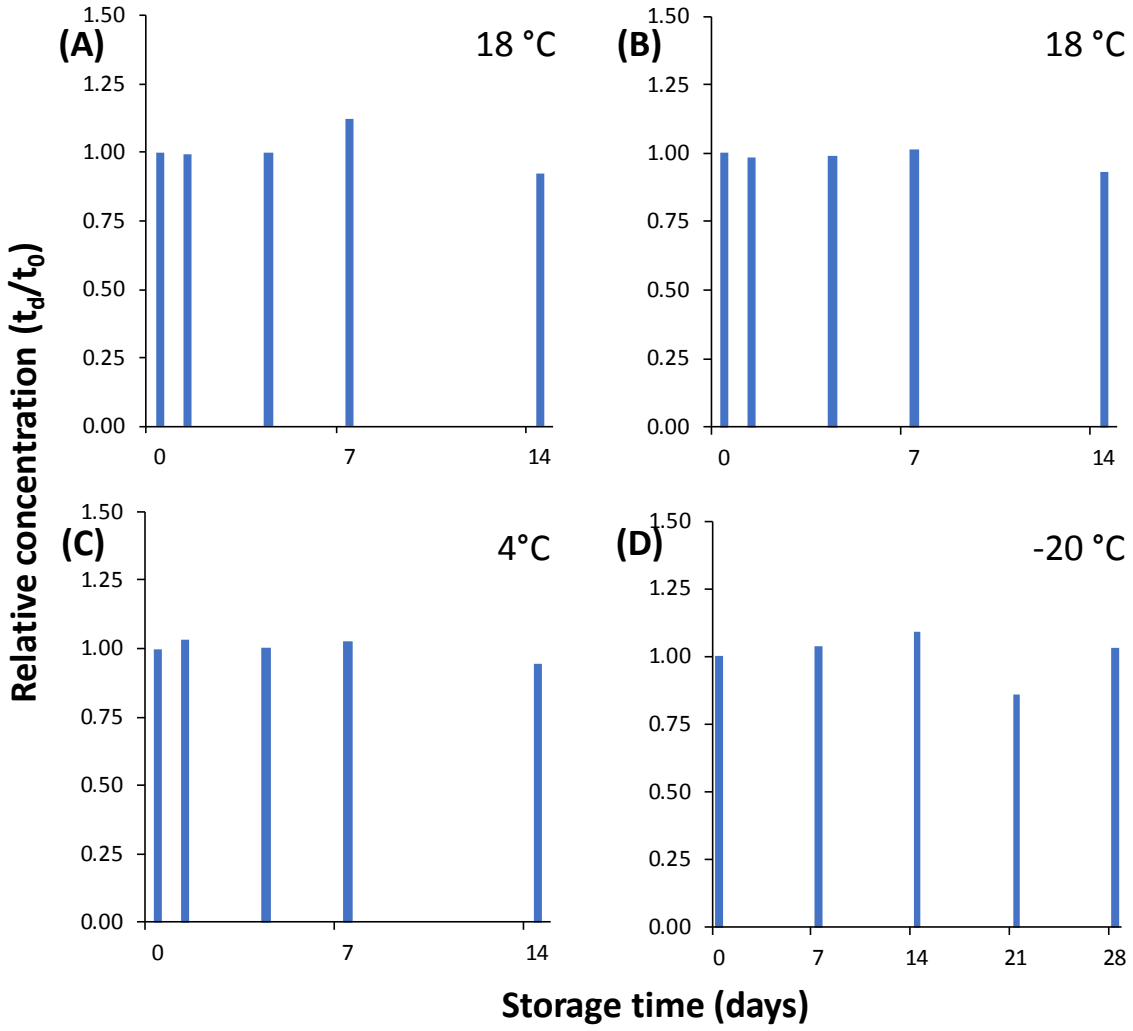


Figure S2. Relative concentration of carbamazepine spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

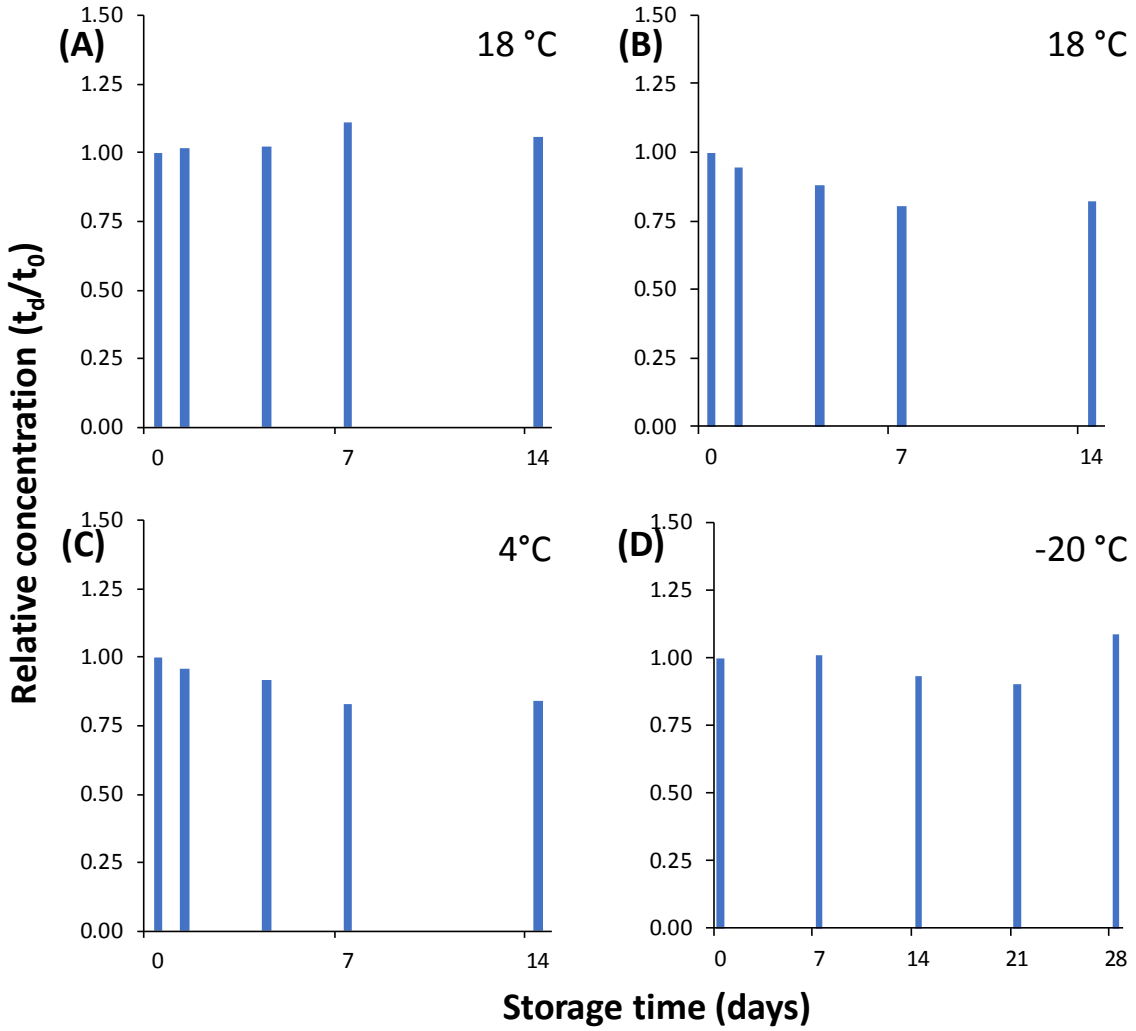


Figure S3. Relative concentration of carbamazepine epoxide spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

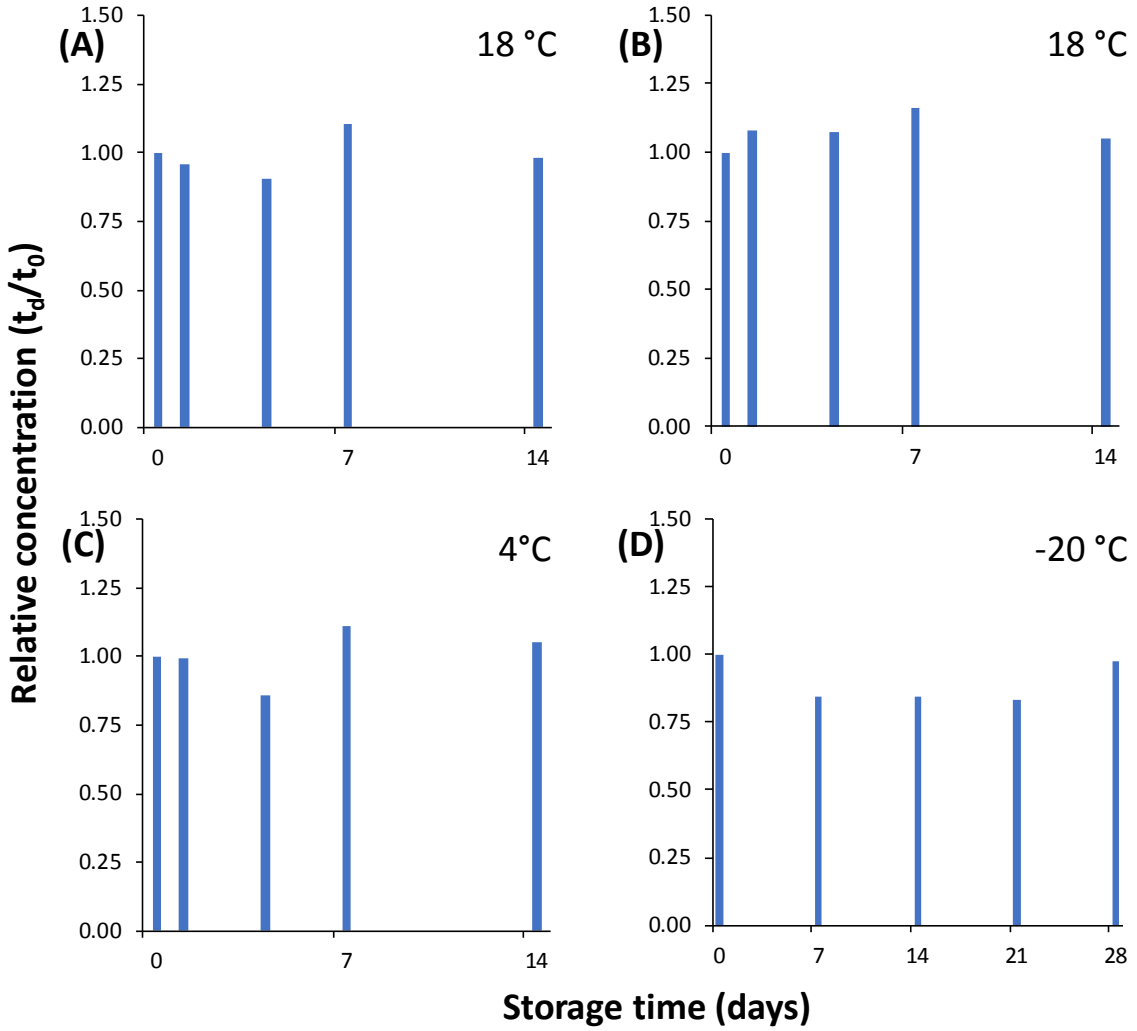


Figure S4. Relative concentration of caffeine spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

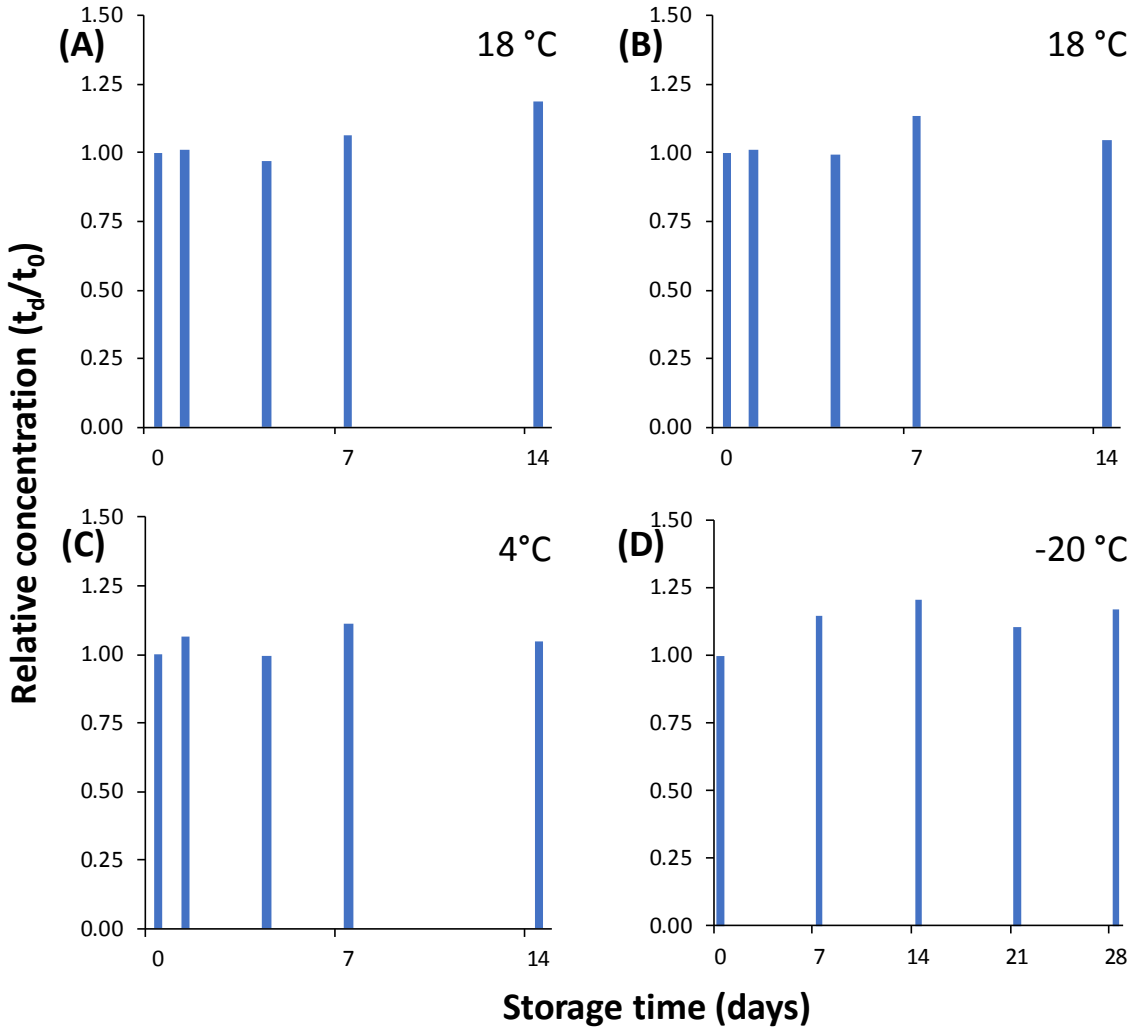


Figure S5. Relative concentration of cotinine spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

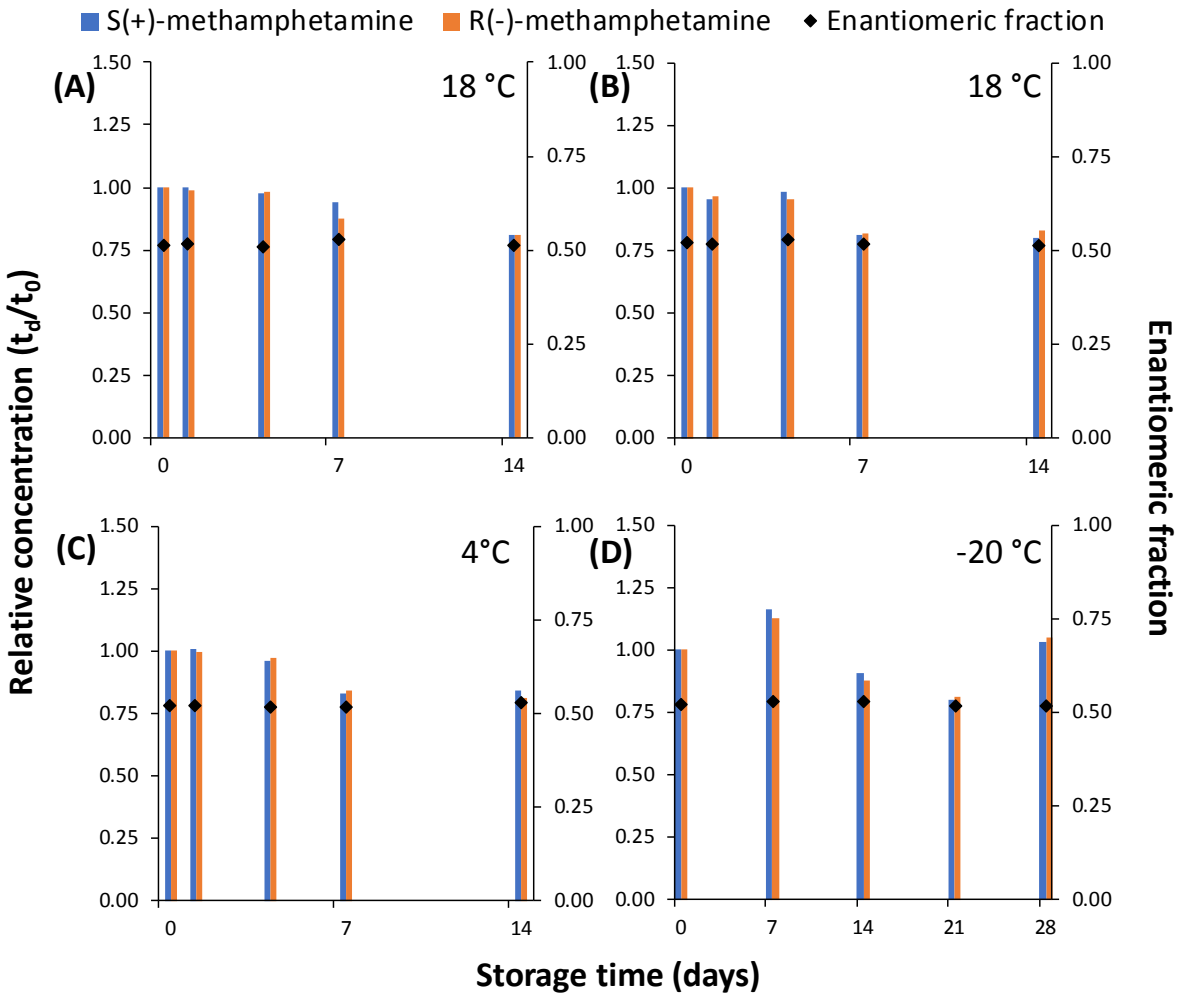


Figure S6. Relative concentration and enantiomeric fraction of *R/S(±)*-methamphetamine spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

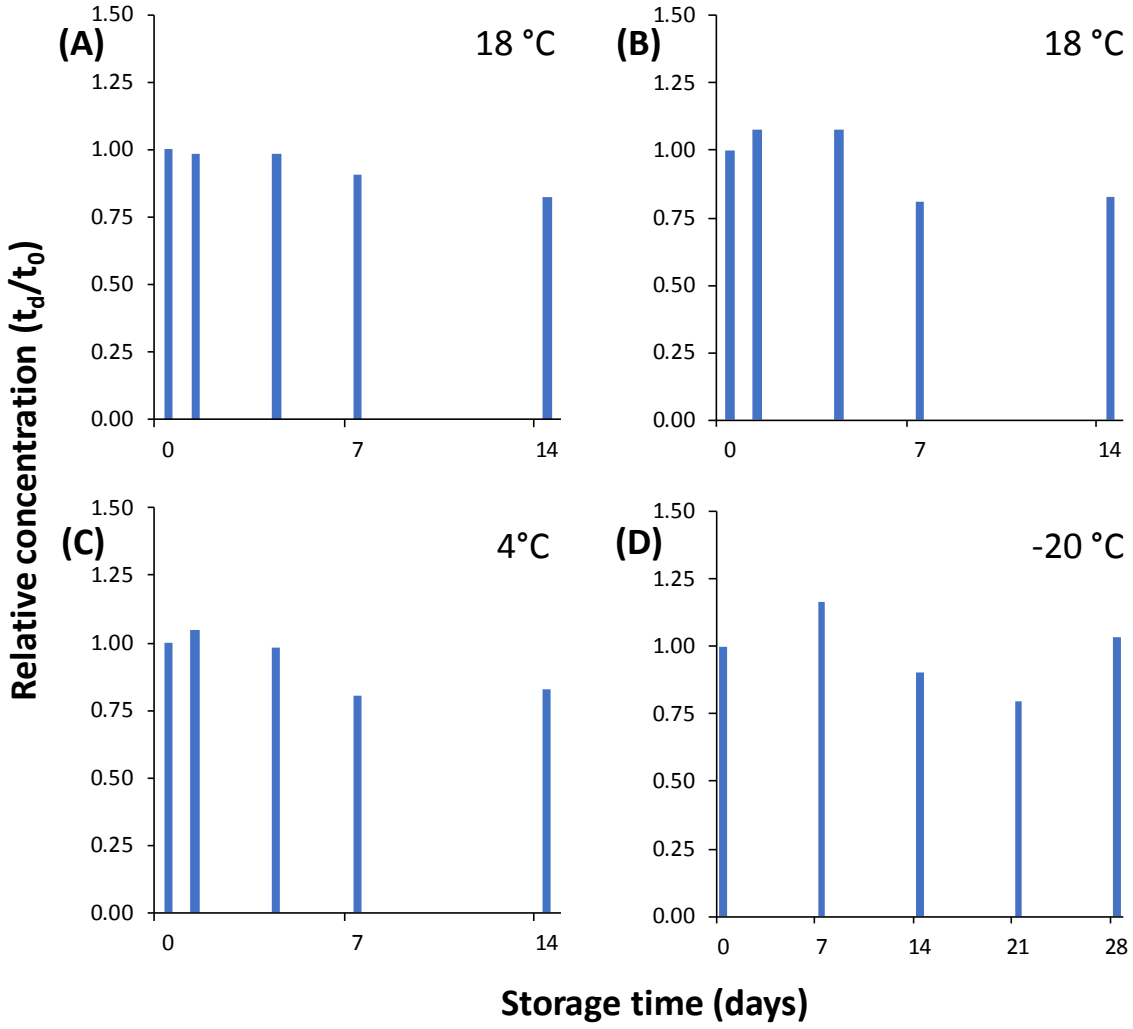


Figure S7. Relative concentration of *R/S(±)*-MDMA spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

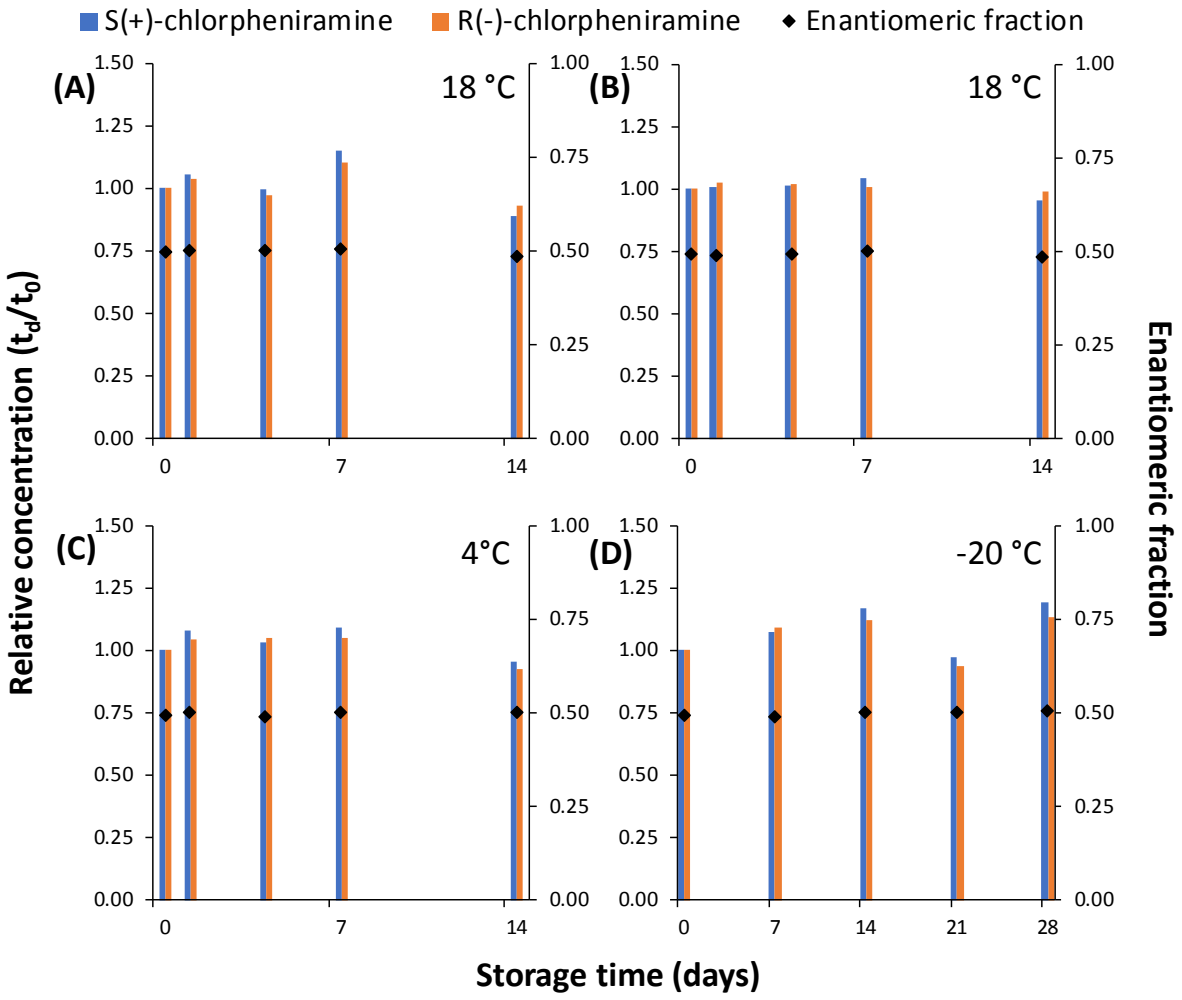


Figure S8. Relative concentration and enantiomeric fraction of *R/S(±)*-chlorpheniramine spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

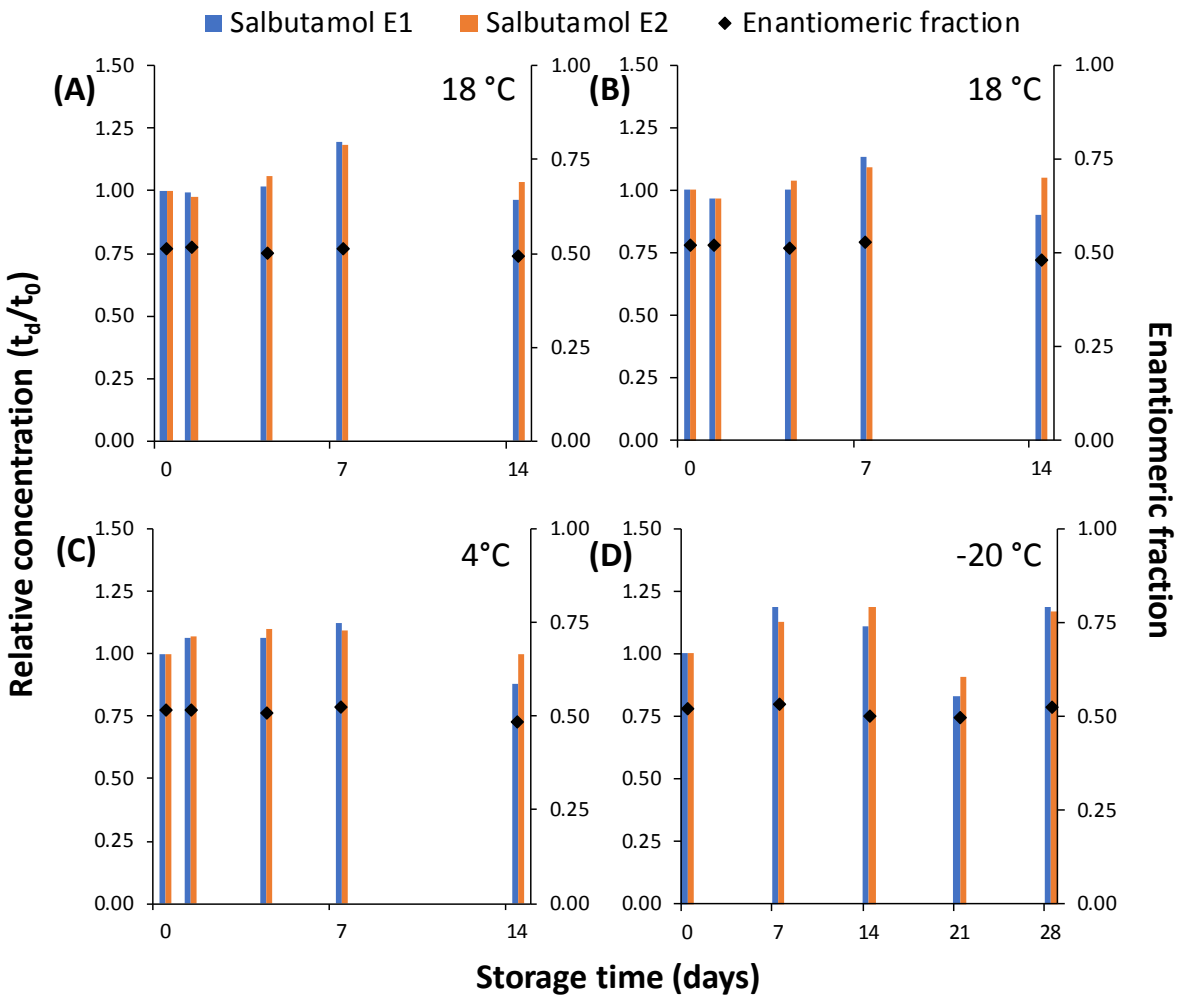


Figure S9. Relative concentration and enantiomeric fraction of *R/S(±)*-salbutamol spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

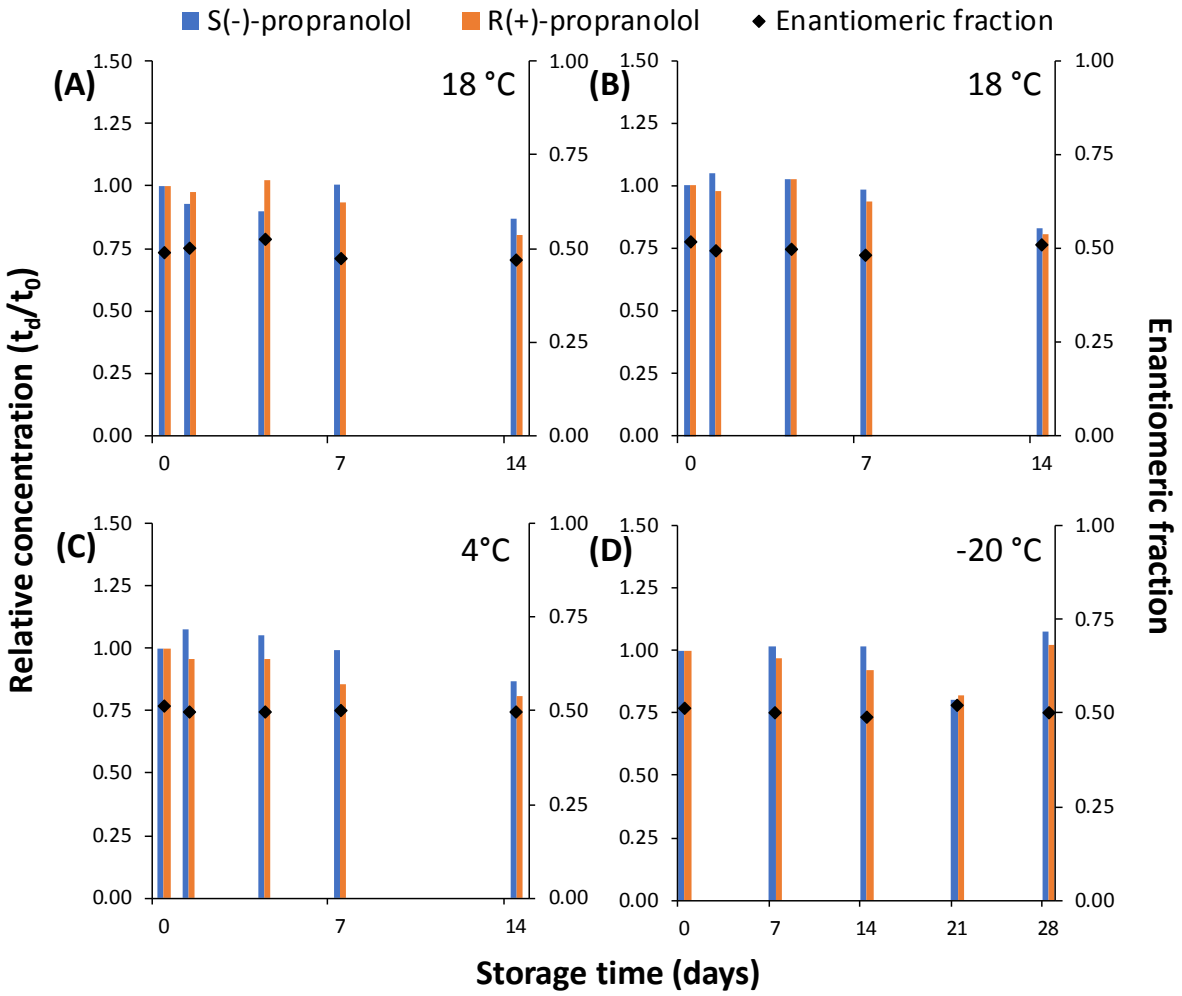


Figure S10. Relative concentration and enantiomeric fraction of *R/S(±)*-propranolol spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

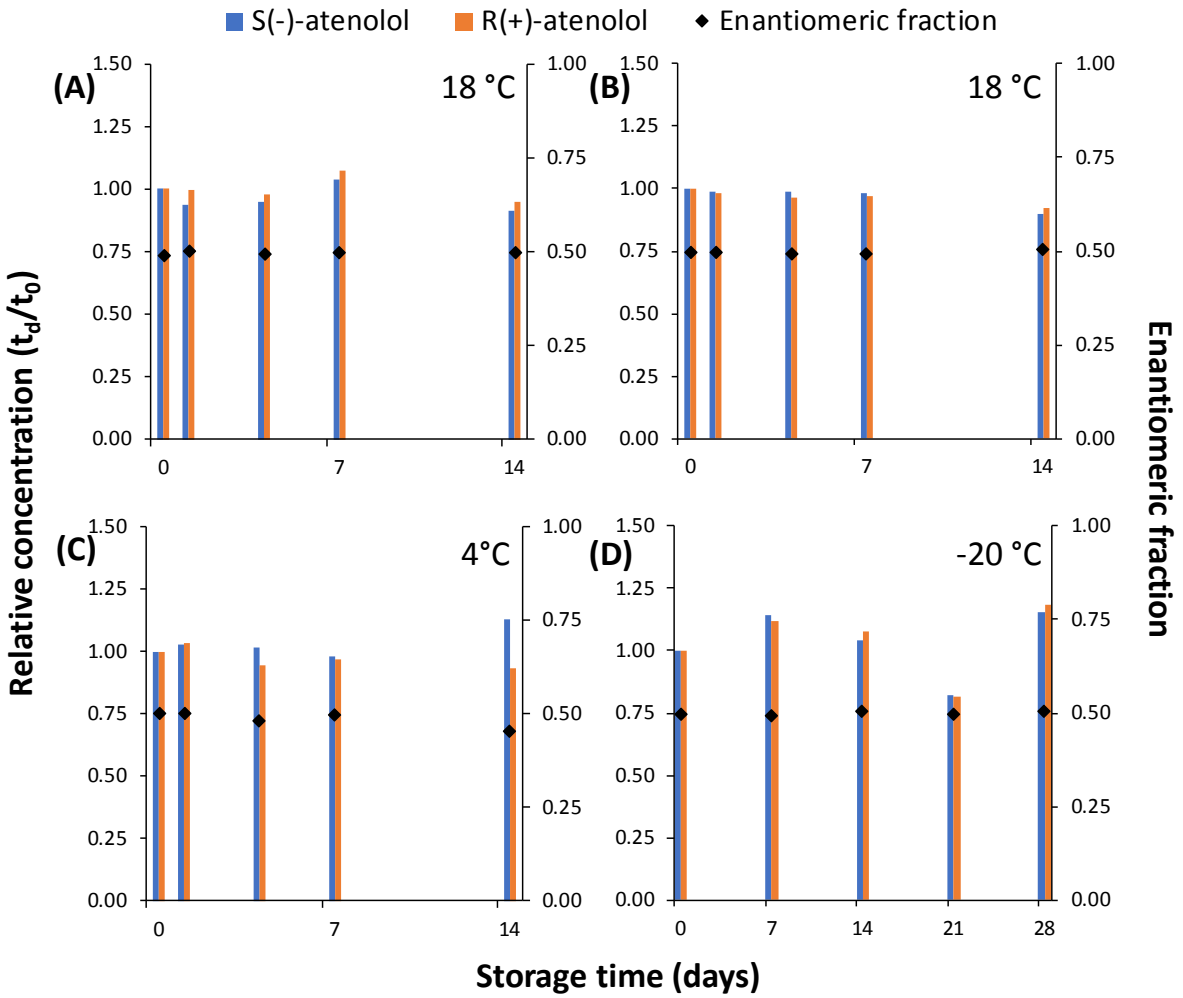


Figure S11. Relative concentration and enantiomeric fraction of *R/S(±)*-atenolol spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

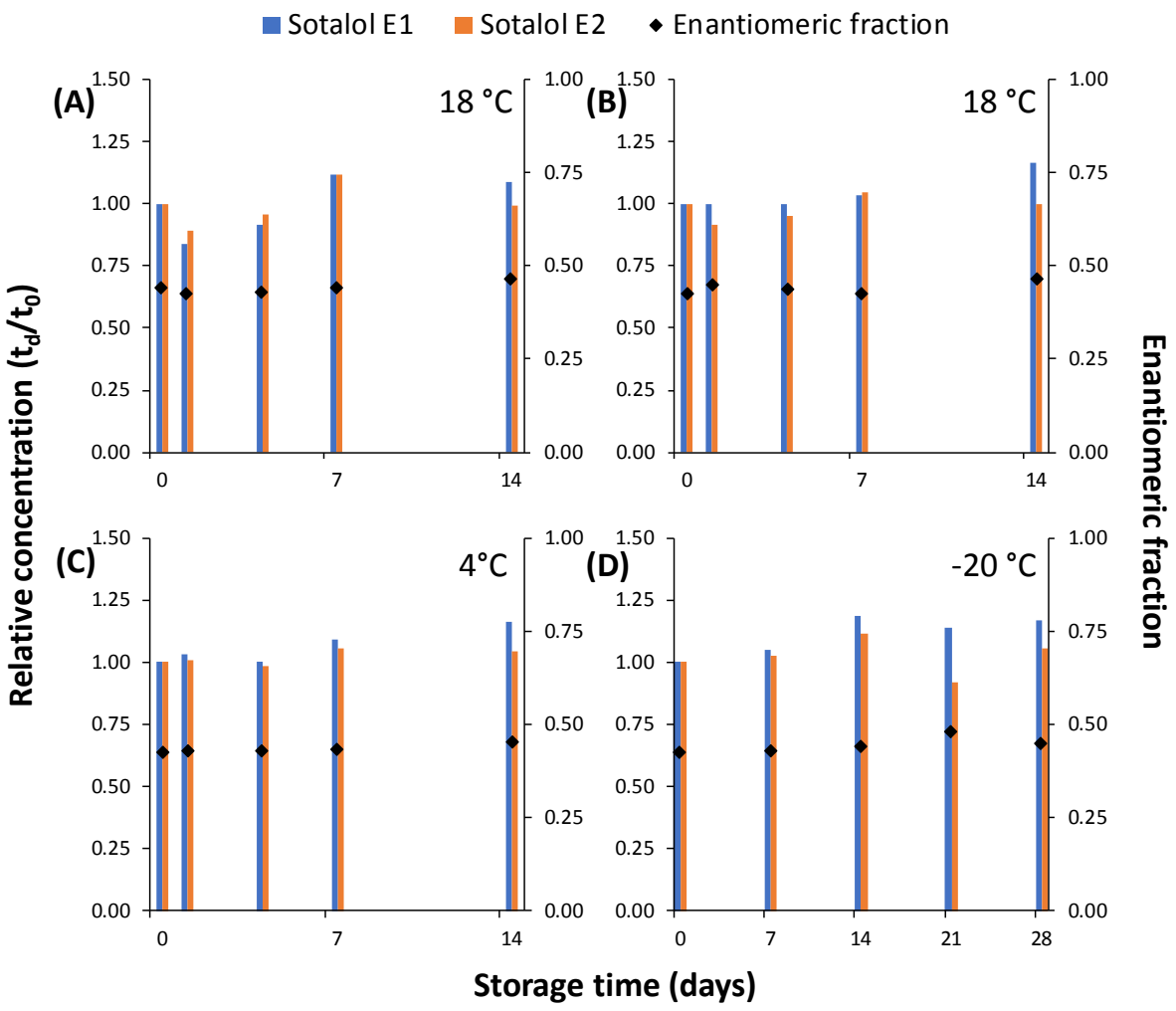


Figure S12. Relative concentration and enantiomeric fraction of *R/S(±)*-sotalol spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

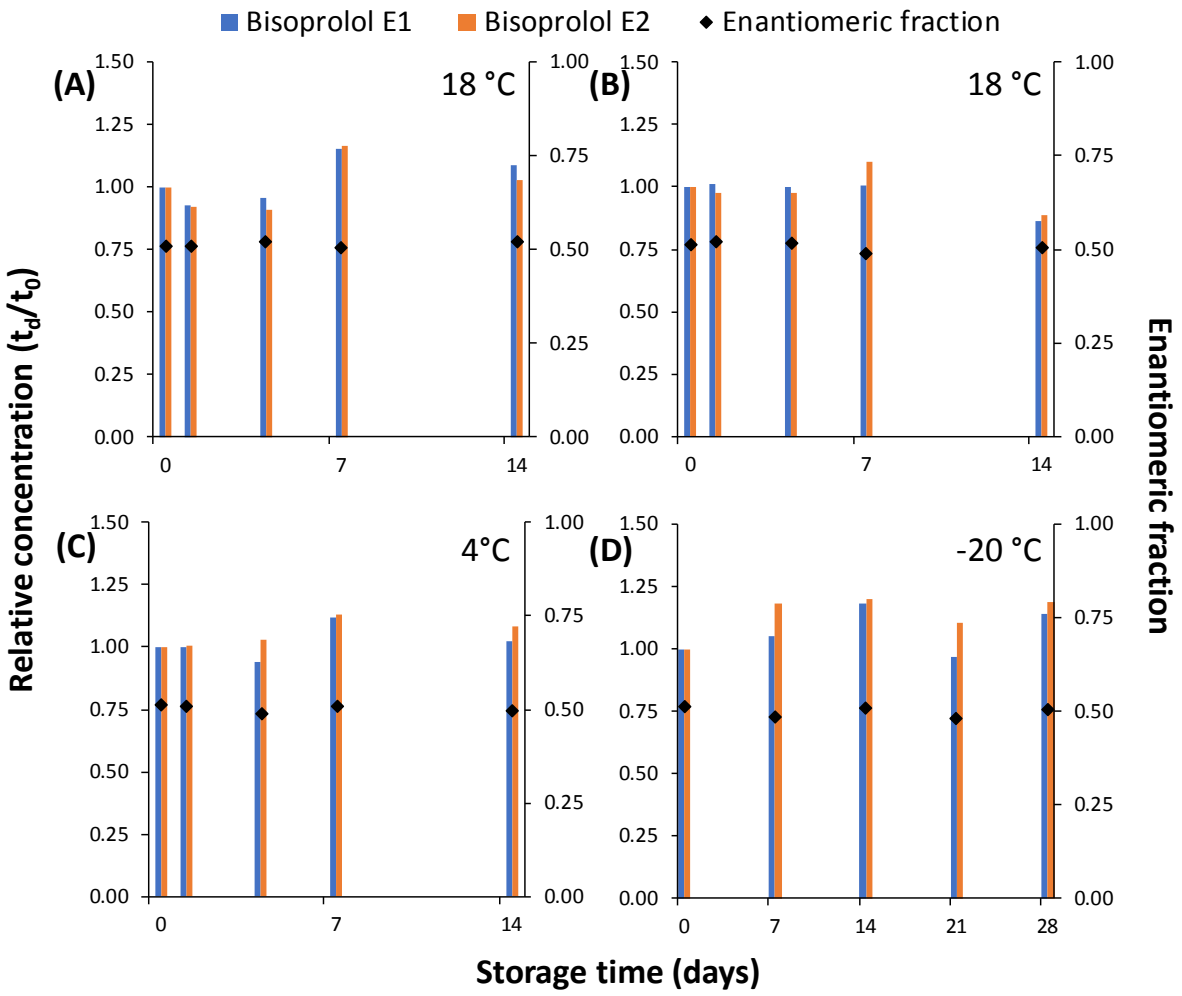


Figure S13. Relative concentration and enantiomeric fraction of *R/S(±)*-bisoprolol spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

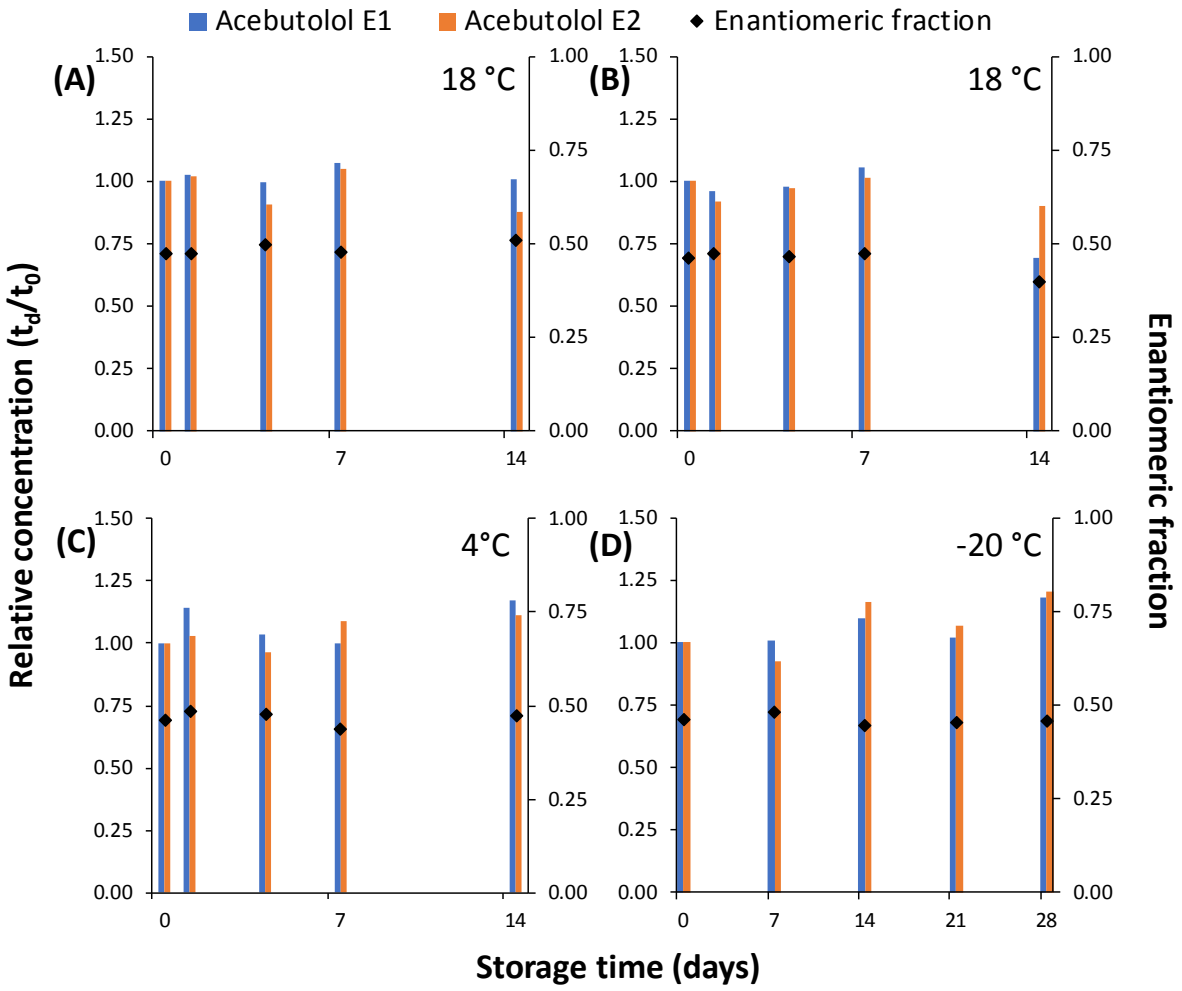


Figure S14. Relative concentration and enantiomeric fraction of *R/S(±)*-acebutolol spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

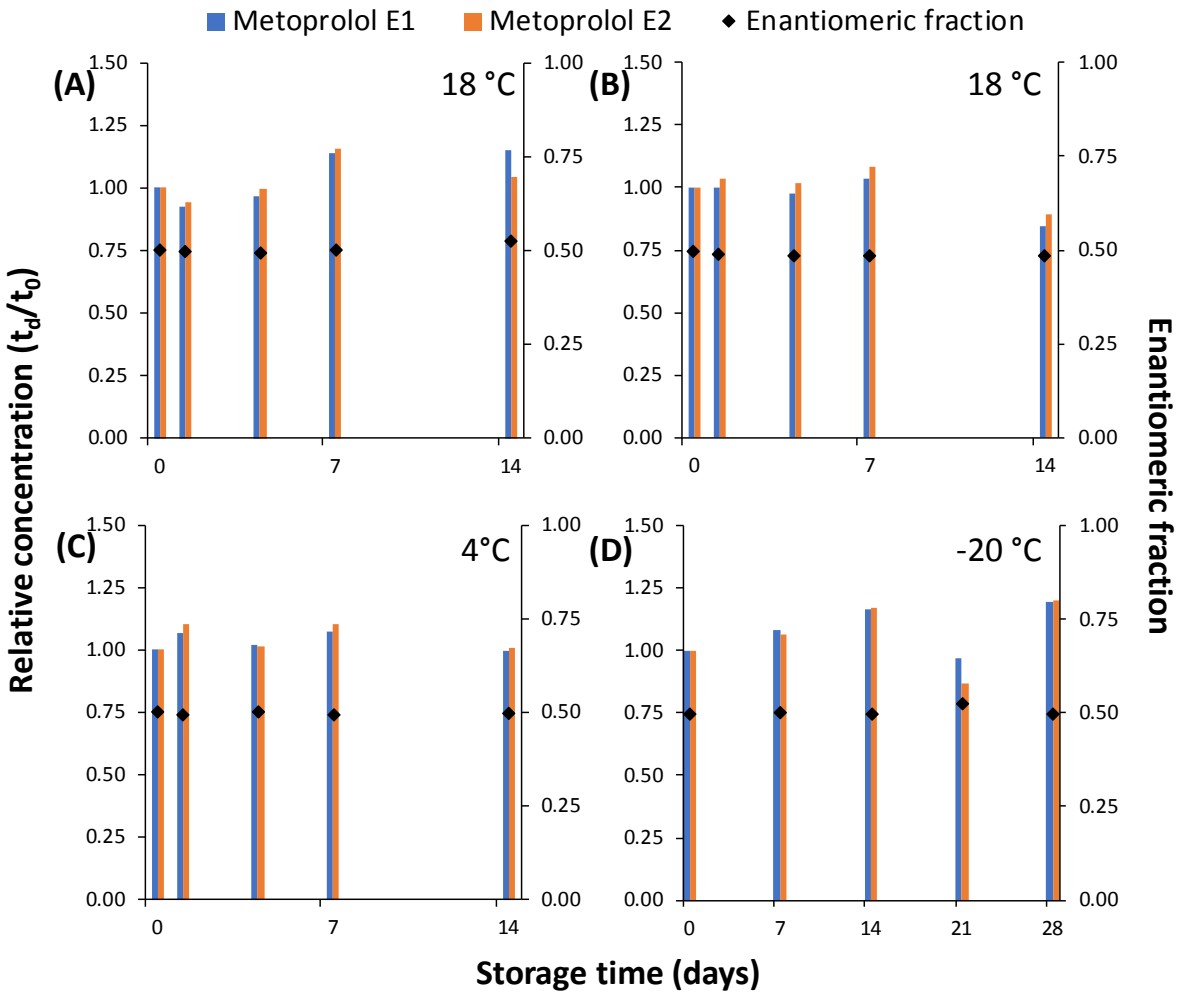


Figure S15. Relative concentration and enantiomeric fraction of *R/S(±)*-metoprolol spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

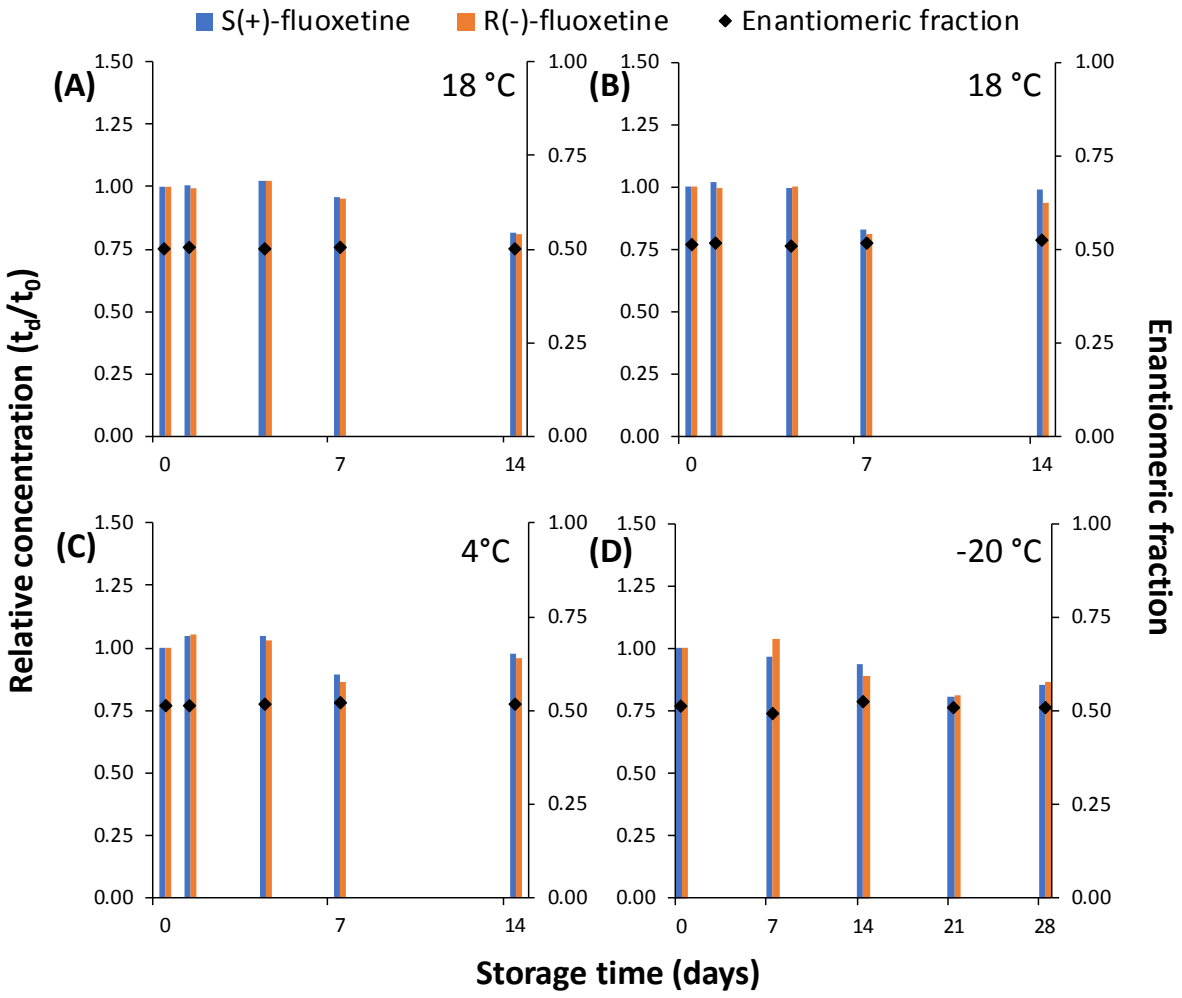


Figure S16. Relative concentration and enantiomeric fraction of *R/S(±)*-fluoxetine spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

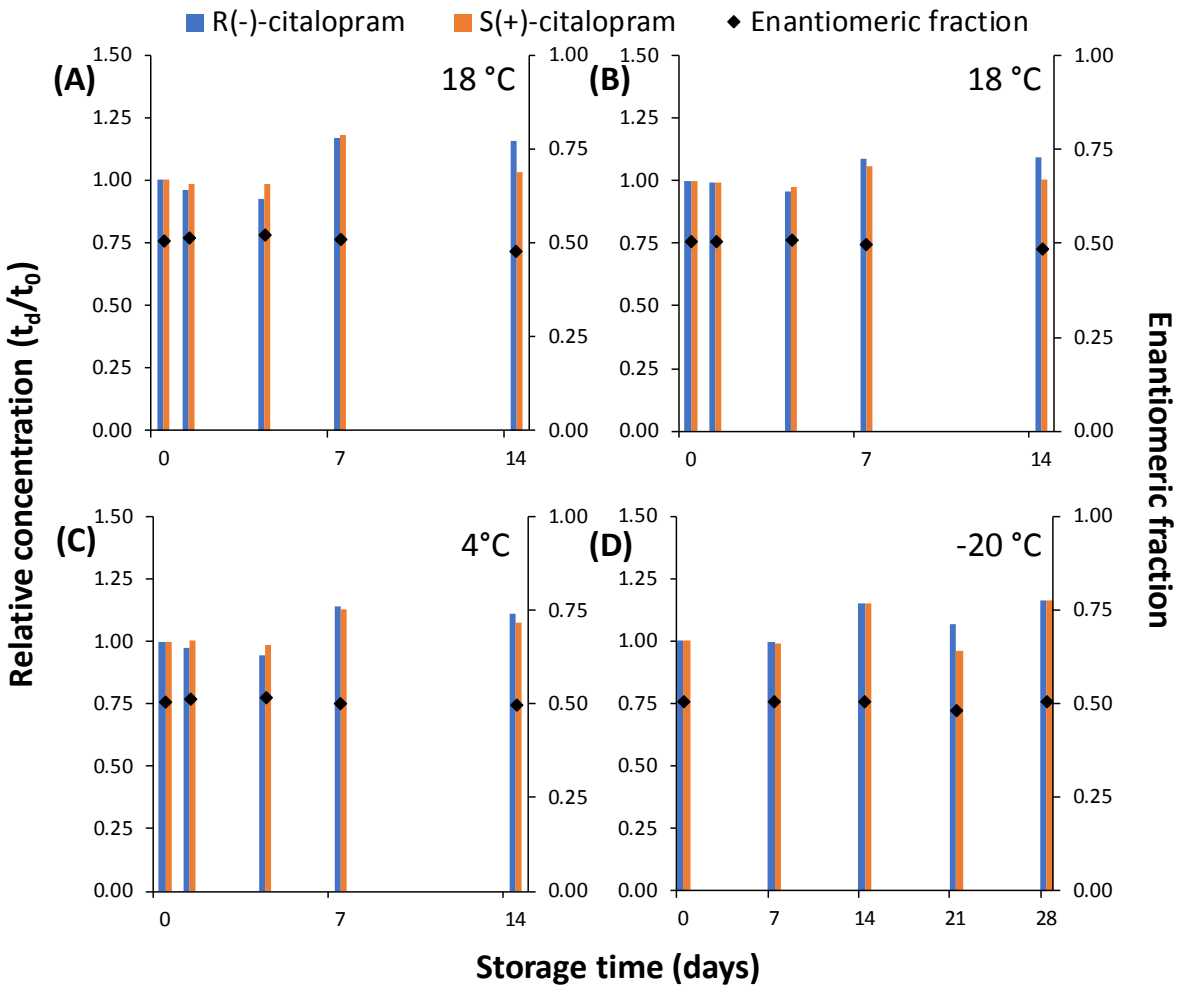


Figure S17. Relative concentration and enantiomeric fraction of *R/S(±)*-citalopram spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

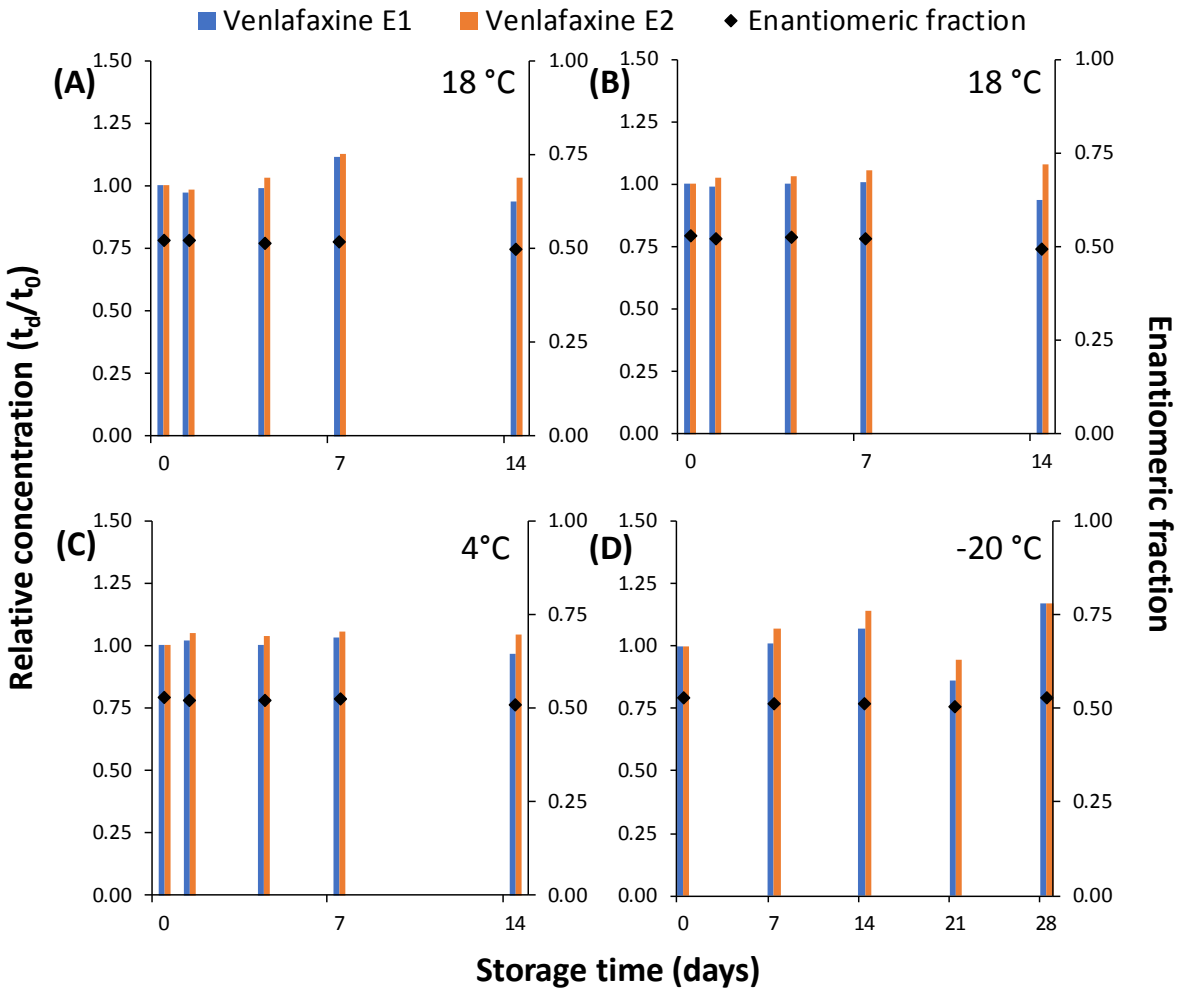


Figure S18. Relative concentration and enantiomeric fraction of *R/S(±)*-venlafaxine spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

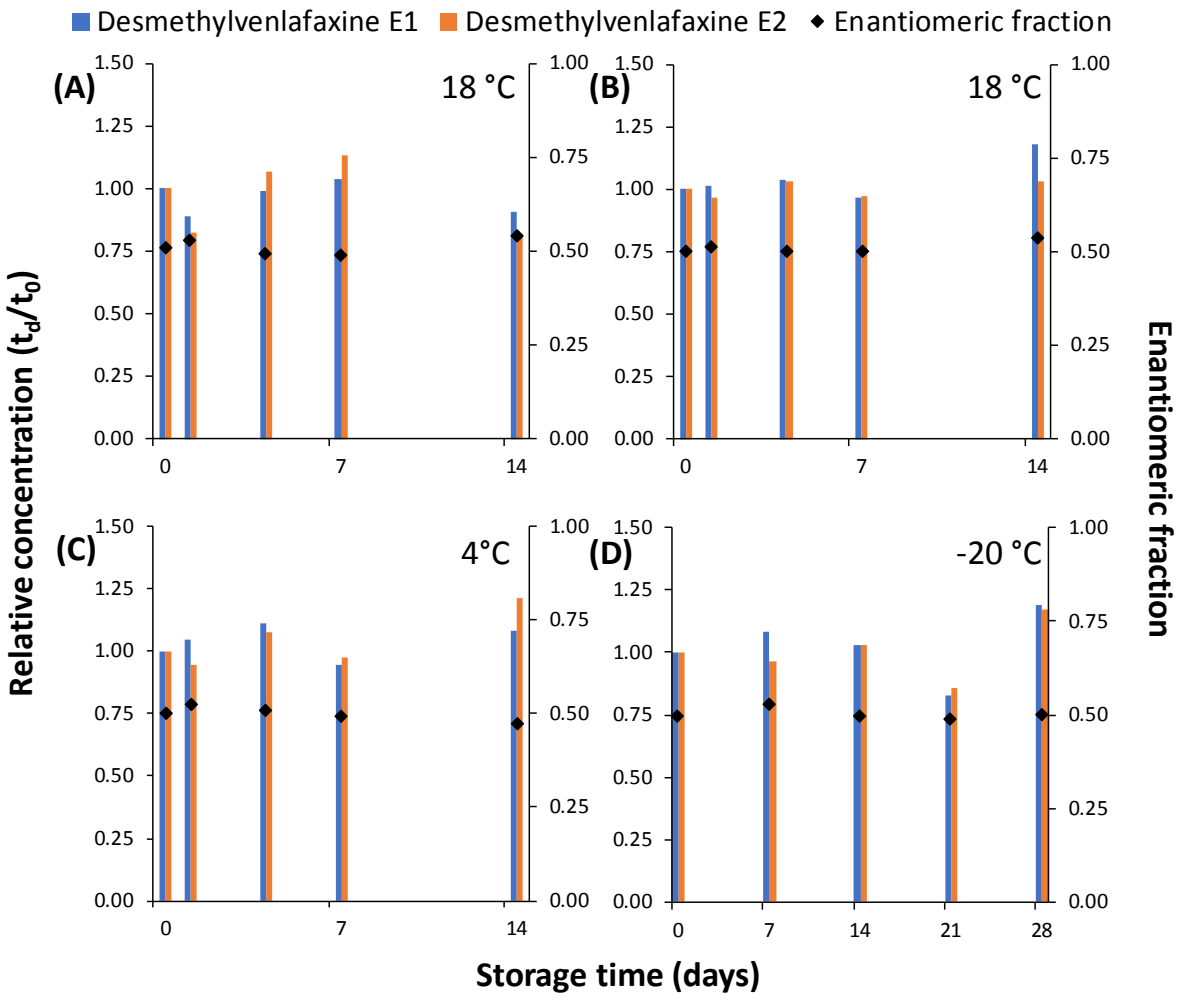
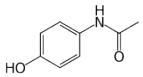
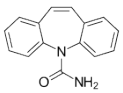
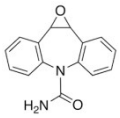
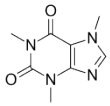
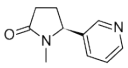
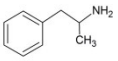
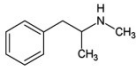
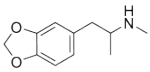
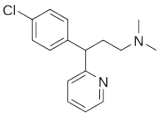
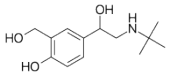
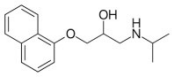
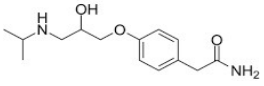
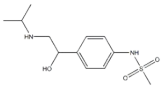
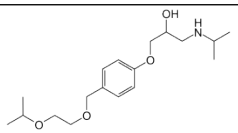
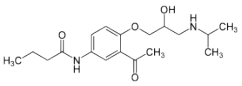
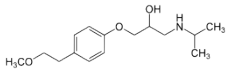
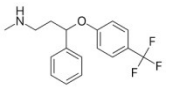
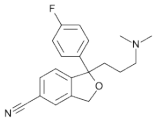
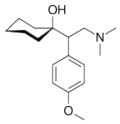
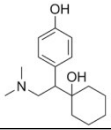


Figure S19. Relative concentration and enantiomeric fraction of *R/S(±)*-desmethylvenlafaxine spiked at 500 ng L^{-1} (n=2) in ultra-pure water at 18 ˚C (A), seawater at 18 ˚C (B), seawater at 4 ˚C (C) and seawater at -20 ˚C (D). Key: t_d, concentration when sample collected; t_0, concentration at 0 days following spiking

Table S1. Chemical properties of studied analytes

Analyte	Structure	Molecular weight (g/mol)	Water solubility (mg/L)	Log K_{OW}	pKa (most acidic)	pKa (most basic)
Paracetamol		151.17	$3.04x10^4$	0.27	9.86	1.72
Carbamazepine		236.28	17.7	2.25	13.94	-0.49
Carbamazepine epoxide		252.27	-	-	13.91	-0.50
Caffeine		194.19	$2.63x10^3$	0.16	-	0.52
Cotinine		176.22	$9.99x10^5$	0.34	-	4.72
R/S(±)-amphetamine		135.21	$2.80x10^4$	1.76	-	9.94
R/S(±)-methamphetamine		149.24	$1.33x10^4$	2.22	-	10.38
R/S(±)-MDMA		193.25	$7.03x10^3$	2.28	-	10.32
R/S(±)-chlorpheniramine		274.79	$5.50x10^3$	3.38	-	9.47
*R/S(±)-s*albutamol		239.31	$1.43x10^4$	0.64	10.12	9.40
R/S(±)-propranolol		259.35	228	2.60	13.84	9.50
R/S(±)-atenolol		266.34	685	-0.03	13.88	9.43
R/S(±)-sotalol		272.36	$5.51x10^3$	0.24	10.07	9.43

R/S(±)-bisoprolol		325.44	2.24 x10^3	1.84	13.86	9.42
R/S(±)-acebutolol		336.43	259	1.71	13.91	9.57
R/S(±)-metoprolol		267.37	4.77x10^3	1.69	13.89	9.43
R/S(±)-fluoxetine		309.33	60.3	4.65	-	10.05
R/S(±)-citalopram		324.4	31.1	3.74	-	9.57
R/S(±)-venlafaxine		277.41	267	3.28	14.84	9.26
R/S(±)-desmethylvenlafaxine		263.38	-	-	10.04	9.33

Key: MDMA, 3,4-methylenedioxymethamphetamine

Table S2. MS/MS transitions of all analytes and deuterated surrogates

Analyte	R_t (minutes)	Precursor (m/z)	Fragmentor (V)	Product 1 (m/z)	CE (eV)	Product 2 (m/z)	CE (eV)
Paracetamol	3.3	151.9	100	110.0	10	65.1	30
Carbamazepine	3.6	236.8	130	193.9	20	178.9	40
Carbamazepine epoxide	3.9	252.8	90	179.9	30	210.0	10
Caffeine	4.2	194.9	90	138.0	18	110.0	20
Cotinine	3.8	176.9	90	80.0	30	98.0	20
R/S(±)-amphetamine	12.3, 14.2	135.8	70	90.9	20	65.0	40
R/S(±)-methamphetamine	16.0, 17.9	150.0	90	91.0	20	65.0	40
R/S(±)-MDMA	18.2	193.9	90	162.8	10	104.8	30
R/S(±)-chlorpheniramine	18.8, 20.7	274.9	90	229.9	10	166.8	40
R/S(±)-*s*albutamol	8.1, 9.2	239.9	90	147.9	10	165.9	10
R/S(±)-propranolol	12.4, 13.9	259.9	110	115.9	10	182.9	10
R/S(±)-atenolol	18.1, 19.7	266.9	100	145.0	30	189.9	20
R/S(±)-sotalol	13.0, 15.3	273.1	90	255.1	10	133.0	30
R/S(±)-bisoprolol	9.5, 10.1	326.2	120	116.0	10	74.1	30
R/S(±)-acebutolol	14.0, 15.6	337.2	90	116.1	20	319.3	10
R/S(±)-metoprolol	10.0, 10.9	268.1	110	116.0	12	191.1	10
R/S(±)-fluoxetine	15.8, 20.1	309.8	90	44.0	10	147.7	2
R/S(±)-citalopram	21.0, 23.6	325.1	110	108.9	30	261.8	20
R/S(±)-venlafaxine	11.8, 13.3	278.1	90	58.1	20	121.1	30
R/S(±)-desmethylvenlafaxine	10.8, 12.6	264.1	90	246.1	10	106.9	30
Paracetamol-d_4	3.3	155.9	90	114.0	20	-	-
Carbamazepine-d_{10}	3.6	246.9	130	204.1	20	-	-
Caffeine-$^{13}C_3$	4.2	198.0	90	139.9	20	-	-
Cotinine-d_3	3.7	180.0	90	80.0	30	-	-
R/S(±)-amphetamine-d_{11}	12.4, 14.4	147.0	70	98.0	20	-	-
R/S(±)-methamphetamine-d_{11}	16.0, 18.0	161.1	90	97.0	20	-	-
R/S(±)-MDMA-d_5	18.4	199.0	90	164.9	10	-	-
R/S(±)-chlorpheniramine-d_6	20.2, 22.2	281.0	100	229.9	10	-	-
R/S(±)-*s*albutamol-d_3	8.2, 9.3	243.0	90	150.9	10	-	-
R/S(±)-propranolol-d_7	12.4, 14.4	267.0	110	115.9	20	-	-
R/S(±)-atenolol-d_7	18.2, 19.8	274.1	110	145.0	30	-	-
R/S(±)-sotalol-d_6	13.0, 15.3	279.1	90	133.9	30	-	-
R/S(±)-bisoprolol-d_5	9.6, 10.2	331.2	120	121.0	10	-	-
R/S(±)-acebutolol-d_5	14.1, 15.8	342.2	90	121.0	20	-	-
R/S(±)-metoprolol-d_7	10.1, 10.9	275.2	110	123.0	15	-	-
R/S(±)-fluoxetine-d_6	15.8, 20.2	316.0	90	44.1	10	-	-
R/S(±)-citalopram-d_6	22.3, 25.0	331.0	130	109.0	30	-	-
R/S(±)-venlafaxine-d_6	11.8, 13.3	284.1	90	58.1	20	-	-

Key: CE, collision energy, MDMA, 3,4-methylenedioxymethamphetamine

Table S3. Sample locations of the Forth and Clyde estuaries

Estuary	**Sampling date**	**Location (Latitude/Longitude)**	**Sampling location name**	**Tide conditions**
Forth	13/6/19	56.10590/-3.83512	Alloa	Rising
	13/6/19	56.09094/-3.77781	Dunmore	Rising
	13/6/19	56.04627/-3.69451	Longannet point	Rising
	13/6/19	56.03000/-3.52913	Crombie	Rising
	11/6/19	56.02832/-3.17705	Gunnet ledge	Rising
Clyde	19/6/19	55.86416/-4.30400	Kelvin confluence	Rising
	19/6/19	55.90544/-4.43557	Dalmuir	Rising
	19/6/19	55.92849/-4.52116	Milton	Rising
	19/6/19	55.93899/-4.65588	Woodhall	Rising
	18/6/19	55.94758/ -4.89306	Dunoon	Rising

Table S4. Intraday and interday precision, and instrumental detection and quantitation limits

Analyte	Intraday precision (%)			Interday precision (%)			IDL	IQL
	5 ng mL^{-1}	50 ng mL^{-1}	250 ng mL^{-1}	5 ng mL^{-1}	50 ng mL^{-1}	250 ng mL^{-1}	(ng mL^{-1})	(ng mL^{-1})
Paracetamol[a]	3.7	1.5	1.9	0.8	2.1	1.0	0.7	2.1
Carbamazepine[a]	0.9	1.7	0.4	2.0	1.6	0.4	0.4	1.4
Carbamazepine epoxide[a]	5.9	5.5	8.8	3.3	2.2	10.4	0.3	1.1
Caffeine[a]	2.9	1.1	1.9	2.0	1.9	1.3	1.0	3.3
Cotinine[a]	2.8	0.2	0.3	1.5	1.5	2.5	0.0	0.1
S(+)-amphetamine	2.8	2.4	1.8	1.0	1.3	1.7	0.1	0.4
R(-)-amphetamine	3.4	2.7	1.4	0.9	0.6	0.2	0.1	0.4
S(+)-methamphetamine	1.2	0.4	1.7	1.8	1.1	1.4	0.1	0.2
R(-)-methamphetamine	1.9	0.9	0.4	1.7	0.3	0.2	0.1	0.2
R/S(±)-MDMA[a]	2.4	0.9	1.1	3.3	1.4	0.3	0.3	1.0
S(+)-chlorpheniramine	2.1	2.4	0.2	3.1	2.1	2.5	0.3	1.0
R(-)-chlorpheniramine	3.8	3.6	0.8	2.7	3.1	4.9	0.3	1.0
Salbutamol-E1	3.8	2.0	4.0	6.4	1.5	1.8	0.1	0.3
Salbutamol-E2	1.1	3.3	1.6	1.3	1.3	0.7	0.1	0.3
S(-)-propranolol	0.9	2.2	2.0	5.3	2.6	1.1	0.3	1.0
R(+)-propranolol	4.4	2.2	1.7	1.9	6.7	1.1	0.3	1.0
S(-)-atenolol	4.0	1.7	1.5	9.0	0.8	0.8	1.5	5.0
R(+)-atenolol	3.9	2.2	2.0	1.6	2.9	0.5	1.5	5.0
Sotalol-E1	10.5	0.5	2.2	4.1	0.7	2.1	1.3	4.2
Sotalol-E2	4.0	0.6	1.1	3.6	0.8	0.6	1.3	4.2
Bisoprolol-E1	2.8	0.5	0.8	1.7	0.8	0.5	0.1	0.4
Bisoprolol-E2	2.5	3.2	2.2	1.3	2.1	2.4	0.1	0.4
Acebutolol-E1	2.6	0.6	0.7	0.2	1.4	1.0	0.1	0.4
Acebutolol-E2	5.8	2.8	2.4	2.1	0.2	4.5	0.1	0.4
Metoprolol-E1	6.3	0.6	2.1	2.0	0.6	1.8	0.8	2.5
Metoprolol-E2	4.0	0.7	1.0	3.5	1.4	0.7	0.8	2.5
S(+)-fluoxetine	3.7	1.4	2.0	1.7	0.6	0.5	0.5	1.6
R(-)-fluoxetine	4.9	1.5	2.0	3.0	1.1	0.7	0.5	1.6
R(-)-citalopram	5.3	4.0	1.5	1.9	2.4	2.1	0.5	1.7
S(+)-citalopram	4.2	1.9	3.9	0.5	1.9	2.9	0.5	1.7
Venlafaxine-E1	8.2	2.3	2.2	11.4	10.4	2.6	0.1	0.4
Venlafaxine-E2	2.0	1.4	0.3	1.1	1.5	1.4	0.1	0.4

Desmethylvenlafaxine-E1	1.5	5.1	0.5	10.1	4.6	1.8	0.4	1.4
Desmethylvenlafaxine-E2	1.4	2.2	1.5	3.2	2.9	0.5	0.4	1.4

Key: IDL, instrument detection limit; IQL, instrument quantitation limit; MDMA, 3,4-methylenedioxymethamphetamine; [a]10, 100 and 500 ng mL^{-1}

Table S5. Metals present in a 10 µL LC-MS/MS injection (n=3)

Sample	SPE conditions		Metal in 10 µL injection (µg)					Sodium chloride equivalent (µg)[a]
	Water wash volume	Elution solvent	Sodium	Magnesium	Calcium	Potassium	Sum	
River water	10	Methanol	1.3	0.40	0.36	0.092	2.2	2.0
Seawater	10	Methanol	41	2.5	2.4	0.60	47	63
	50	Methanol	11	0.80	0.56	0.14	13	17
	10	Acetonitrile	2.3	0.52	0.17	0.13	3.1	3.5
	50	Acetonitrile	0.60	0.15	0.040	0.12	0.91	0.90

[a]Assumes all sodium is present within extract as sodium chloride

Note: all concentrations are adjusted using recovery determined from the analysis of artificial river waters and seawaters

Table S6. SPE-enantioselective LC-MS/MS methods for simultaneous determination of several therapeutic groups of chiral drugs in aqueous environmental matrices

Drugs	SPE protocol	Chromatographic column	Mobile phase conditions	Run time (min)	MS detector	Enantiomer R_S	Method recovery (%)	MDL (ng L^{-1})	Reference
Fluoxetine*, alprenolol*, metoprolol*, tramadol, propranolol*, salbutamol*, benzoylecgonine, mirtazapine, bisoprolol*, nebivolol, O-desmethylvenlafaxine, venlafaxine, O-desmethyltramadol*, N-desmethyltramadol, amphetamine, methamphetamine, norcocaine & cocaine.	• River or estuary water (500 mL) • Adjusted to pH 2 • Filtered (0.45 µm) • 150 mg 3 mL Oasis MCX SPE • Wash with 4 mL acidified water • Elution in 4 mL 5% ammonium hydroxide in methanol • Reconstituted in 0.25 mL ethanol	Chirobiotic V® 150 x 2.1 mm, I.D. 5 µm particle size @ 25 °C	92.5:7.5 ethanol: 10 mM ammonium acetate pH 6.8 @ 0.32 mL min^{-1}	30	QqQ	0.6-1.7	76-122	0.1-1.9	Coelho et al., 2019
Aspartame, caffeine, carbamazepine, carbamazepine 10,11 epoxide, cotinine, methylparaben, paracetamol, triclocarban, amphetamine*, atenolol*, chlorpheniramine*, citalopram*, fluoxetine*, MDMA, propranolol* & salbutamol*	• River water (250 mL) or septic tank effluent (25 mL) • Filtered (0.7 µm) • 60 mg 3 mL Oasis HLB SPE • Wash with 10 mL water • Elution in 4 mL methanol • Reconstituted in 0.25 mL mobile phase	Chirobiotic V2® 250 x 2.1 mm, I.D. 5 µm particle size @ 15 °C	1 mM ammonium acetate + 0.01 % acetic acid in methanol @ 0.17 mL min^{-1}	60	QqQ	1-2.3	20-118	0.1-870	Ramage et al., 2019
Aminorex, carboxyibuprofen, cephalexin, chloramphenicol, dechloroethylifosfamide, O-desmethylnaproxen, 10,11-dihydro-10-hydroxy carbamazepine, dihydroketoprofen, florfenicol, griseofuvlin, 2-hydroxyibuprofen, ibuprofen, ifosfamide, indoprofen, ketoprofen, naproxen, phenylpropionic acid, praziquantel & tetramisole	• River water (200 mL) or wastewater effluent (100 mL) • Filtered (0.7 µm) • 60mg 3mL Oasis HLB-MAX SPE. • 2mL aqueous wash • Elution in 4 mL methanol and 2 mL 2% formic acid in methanol • Reconstituted in 0.5 mL mobile phase	Chirobiotic T® 250 x 4.6 mm, I.D. 5 µm particle size @ 25 °C	10 mM ammonium acetate in water (pH 4.2): methanol (70:30, *v/v*) @ 0.08 mL min^{-1}	150	QqQ	0.4-0.9	8-127	0.1-1,300	Camacho-Muñoz and Kasprzyk-Hordern, 2017
Aminorex*, carboxyibuprofen, cephalexin, chloramphenicol*, dechloroethylifosfamide, 10,11-dihydro-10-hydroxy carbamazepine, dihydroketoprofen*, fexofenadine*, 2-hydroxyibuprofen, ibuprofen*, ifosfamide*, indoprofen, ketoprofen, mandelic acid, naproxen*, phenylpropionic acid, praziquantel & tetramisole*	• River water (500 mL) or wastewater effluent (250 mL) • Filtered (0.7 µm) • 60mg 3mL Oasis HLB-MAX SPE • 2mL aqueous wash • Elution in 4 mL methanol and 2 mL 2% formic acid in methanol • Reconstituted in 0.5 mL mobile phase	Chiral AGP 100 x 2 mm, I.D. 5 µm particle size @ 25 °C	10 mM ammonium acetate in water with 1 % acetonitrile (pH 6.7)	100	QqQ	≥0.7	2-158	0. 1-340	Camacho-Muñoz and Kasprzyk-Hordern, 2015
Flumequine, albuterol*, ketoprofen, pindolol*, propranolol*, atenolol*, metoprolol*, clenbuterol*, sotalol*, timolol*, naproxen & fluoxetine*	• River water (500 mL) or wastewater effluent (100 mL) • Filtered (0.7 µm)	Chirobiotic V® 250 x 4.6 mm, I.D. 5 µm particle size @ 25	4 mM ammonium acetate + 0.005 % formic acid in methanol @ 0.1 mL min^{-1}	65	QqQ	≥0.4-1.1	56-116	0.1-11	Lopez-Serna et al., 2013

	• 60 mg 3 mL Oasis HLB SPE • Elution in 4mL methanol • Reconstituted in 0.5 mL mobile phase	°C							
Caffeine, carbamazepine, carbamazepine 10,11 epoxide, cotinine, paracetamol, amphetamine*, methamphetamine*, atenolol, metoprolol, bisoprolol, chlorpheniramine*, citalopram*, fluoxetine*, venlafaxine*, desmethylvenlafaxine*, MDMA, propranolol* sotalol*, acebutolol*, & salbutamol*	• Sea water (500 mL) • Filtered (0.7 µm) • 200 mg 6 mL Oasis HLB SPE • Wash with 50 mL water • Elution in 6 mL acetonitrile • Reconstituted in 0.25 mL methanol	Poroshell 120 Chiral-V 150 x 2.1 mm, I.D. 2.7 µm particle size @ 15 °C	2 mM ammonium acetate + 0.01 % acetic acid in methanol @ 0.15 mL min^{-1}	30	QqQ	0.6-2.3	82-137	0.1-21	This study

Key: MDL, method detection limit; QqQ, triple quadrupole; SPE, solid phase extraction; MDMA, 3,4-methylenedioxy-methamphetamine; I.D., internal diameter; *, highlights those separated at the enantiomeric level with $R_S \geq 1$

References

Camacho-Muñoz, D., Kasprzyk-Hordern, B. Multi-residue enantiomeric analysis of human and veterinary pharmaceuticals and their metabolites in environmental samples by chiral liquid chromatography coupled with tandem mass spectrometry detection (2015) Analytical and Bioanalytical Chemistry, 407 (30), pp. 9085-9104. DOI: 10.1007/s00216-015-9075-6

Camacho-Muñoz, D., Kasprzyk-Hordern, B. Simultaneous enantiomeric analysis of pharmacologically active compounds in environmental samples by chiral LC–MS/MS with a macrocyclic antibiotic stationary phase (2017) Journal of Mass Spectrometry, 52 (2), pp. 94-108. DOI: 10.1002/jms.3904

Coelho, M.M., Lado Ribeiro, A.R., Sousa, J.C.G., Ribeiro, C., Fernandes, C., Silva, A.M.T., Tiritan, M.E. Dual enantioselective LC–MS/MS method to analyse chiral drugs in surface water: Monitoring in Douro River estuary (2019) Journal of Pharmaceutical and Biomedical Analysis, 170, pp. 89-101. DOI: 10.1016/j.jpba.2019.03.032

López-Serna, R., Kasprzyk-Hordern, B., Petrović, M., Barceló, D. Multi-residue enantiomeric analysis of pharmaceuticals and their active metabolites in the Guadalquivir River basin (South Spain) by chiral liquid chromatography coupled with tandem mass spectrometry (2013) Analytical and Bioanalytical Chemistry, 405 (18), pp. 5859-5873. DOI: 10.1007/s00216-013-6900-7

Ramage, S., Camacho-Muñoz, D., Petrie, B. Enantioselective LC-MS/MS for anthropogenic markers of septic tank discharge (2019) Chemosphere, 219, pp. 191-201. DOI: 10.1016/j.chemosphere.2018.12.007