

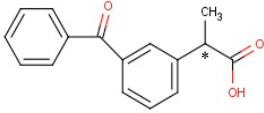
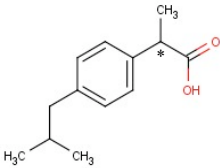
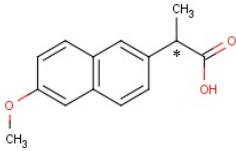
Analytical and Bioanalytical Chemistry

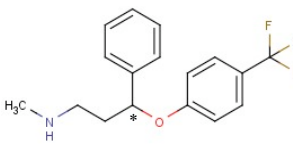
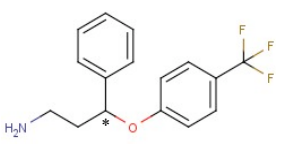
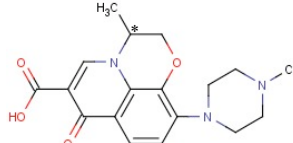
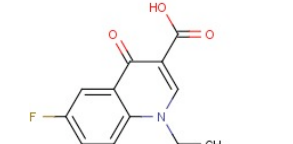
Electronic Supplementary Material

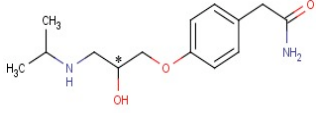
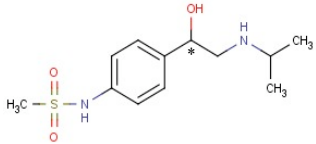
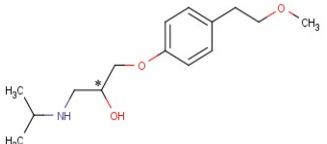
Multi-residue enantiomeric analysis of pharmaceuticals and their active metabolites in the Guadalquivir River basin (South Spain) by chiral liquid chromatography coupled with tandem mass spectrometry

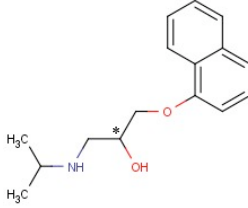
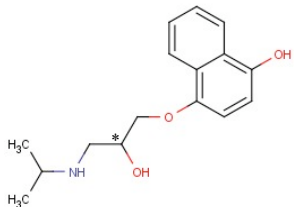
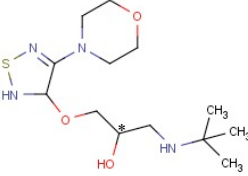
Rebeca López-Serna, Barbara Kasprzyk-Hordern, Mira Petrović and Damià Barceló

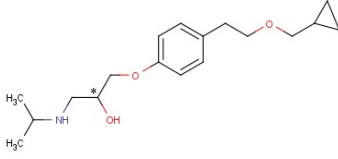
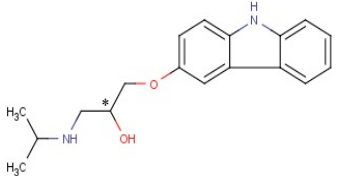
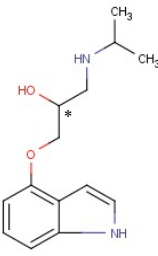
Table S1. Target compounds by therapeutic groups, used surrogates and optimized chromatographic and ESI-MS/MS parameters

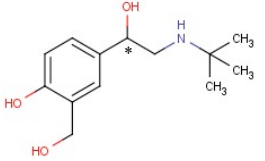
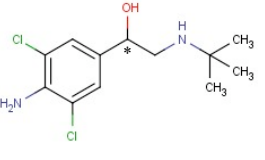
Therapeutic group	N°	Compounds	CAS N°	MW	Structure	pKa at 25°C	log P at 25°C	Pharmacological activity	Enantiomer ²	Compounds analysed by PI mode									
										Precursor ion (m/z)	SRM 1	CV-CE	SRM 2	CV-CE	Rt (min)	SRM1 / SRM2	Surrogate	EF	R _s
Analgesics/anti-inflammatories (3)	1	rac-Ketoprofen C16 H14 O3	22071-15-4	254.28		4.23 ± 0.10	2.911 ± 0.331	Yes	S(+); R(-)	255.17 [M+H] ⁺	104.97	38-24	209.11	38-10	8.35	1.42	<i>rac</i> -Ketoprofen- <i>13C-d3</i>	-	-
		<i>rac</i> -Ketoprofen- <i>13C-d3</i>	-	-					S(+); R(-)	259.01 [M+H] ⁺	213.21	40-14	-	-	8.27	-	-	-	-
	2	rac-Ibuprofen C13 H18 O2	15687-27-1	206.28		4.41 ± 0.10	3.502 ± 0.227	Yes	E1	206.87 [M+H] ⁺	170.20	56-20	132.54	56-14	21.45	20.39	<i>Clenbuterol-d9 E1</i>	0.50	1.27
								E2						24.08	19.70	<i>Clenbuterol-d9 E2</i>			
	3	rac-Naproxen C14 H14 O3	23981-80-8	230.26		4.84 ± 0.30	2.876 ± 0.239	Yes	(S+); (R-)	231.04 [M+H] ⁺	185.11	34-14	170.33	28-24	7.94	10.11	<i>rac</i> -Naproxen- <i>d3</i>	-	-
		<i>rac</i> -Naproxen- <i>d3</i>	-	-				(S+); (R-)	234.23 [M+H] ⁺	188.16	28-14	-	-	8.02	-	-	-	-	

Psychiatric drugs and transformation products (2)																				
4	rac-Fluoxetine C17 H18 F3 N O	54910-89-3	309.33		10.05 ± 0.10	3.930 ± 0.434	Yes	(S+)	(R-)	(S+)	310.17 [M+H] ⁺	43.98	34-10	148.11	34-10	38.23	14.97	<i>Fluoxetine-d5</i> (S+)	0.49	1.08
	<i>rac-Fluoxetine-d5</i>	-	-					(S+)	(R-)	(R-)	315.3 [M+H] ⁺	153.16	26-8	-	-	38.23	-	-	-	-
5	rac-Norfluoxetine C16 H16 F3 N O	83891-03-6	295.3		9.05 ± 0.13	3.763 ± 0.415	Yes	E1			296.14 [M+H] ⁺	134.09	18-6	-	-	30.72	-	<i>Fluoxetine-d5</i> (S+)	0.49	0.38
								E2						-	-	31.84	-	<i>Fluoxetine-d5</i> (R-)		
6	rac-Ofloxacin C18 H20 F N3 O4	82419-36-1	361.37		5.19 ± 0.40; 7.37 ± 0.42	1.855 ± 0.875	Yes	-			362.15 [M+H] ⁺	318.07	48-20	261.09	42-30	-	-	<i>rac-Ofloxacin-d8</i>	-	-
	<i>rac-Ofloxacin-d8</i>	-	-					-			370.27 [M+H] ⁺	265.14	54-32	-	-	-	-	-	-	-
7	rac-Flumequine C14 H12 F N O3	42835-25-6	261.25		5.70 ± 0.40; -1.98 ± 0.60	0.882 ± 0.669	Yes				262.03 [M+H] ⁺	202.06	32-32	126.04	32-48	37.67	2.35	<i>rac-Flumequine-13C3</i>	-	-
	<i>rac-Flumequine-13C3</i>	-	-								265.22 [M+H] ⁺	205.06	34-34	-	-	37.03	-	-	-	-

Cardiovascular drugs and transformation products (9)																			
8	rac-Atenolol C14 H22 N2 O3	29122-68-7	266.34		13.88 ± 0.20; 9.43 ± 0.10	0.335 ± 0.279	Yes	(R+)	(S-)	267.31 [M+H] ⁺	145.1	38-30	190.1	38-16	39.39	1.44	Atenolol-d7 (S-)	0.50	0.97
	rac-Atenolol-d7	-	-					(R+)	(S-)	274.31 [M+H] ⁺	145.09	44-30	-	-	39.23	-	-	-	-
9	rac-Sotalol C12 H20 N2 O3 S	3930-20-9	272.36		8.28 ± 0.10; 9.31 ± 0.10	0.240 ± 0.369	Yes	E1	E2	273.14 [M+H] ⁺	133.21	30-28	213.10	30-16	32.68	1.43	Sotalol-d7 E1	0.49	1.08
	rac-Sotalol-d6	-	-					E1	E2	279.03 [M+H] ⁺	134.20	32-36	-	-	32.6	-	-	-	-
10	rac-Metoprolol C15 H25 N O3	51384-51-1	267.36		13.89 ± 0.20; 9.43 ± 0.10	1.632 ± 0.263	Yes	E1	E2	268.33 [M+H] ⁺	116.09	42-20	121.1	42-22	26.2	2.25	Metoprolol-d7 E1	0.51	0.91
	rac-Metoprolol-d7	-	-					E1	E2	275.39 [M+H] ⁺	123.12	44-20	-	-	26.04	-	-	-	-
								E2		28.36				28.2					

1	rac-Propranolol C16 H21 N O2	525-66-6 259.34		13.84 ± 0.20; 9.50 ± 0.30 2.900 ± 0.247	Yes	(S-) (R+)	260.18 [M+H] ⁺	116.09	42-16	183.09	42-18	28.92	1.90	<i>Propranolol-d7 (S-)</i>	0.51	1.00
	<i>rac-Propranolol-d7</i>	-	-			(S-) (R+)	267.31 [M+H] ⁺	123.18	42-18	-	-	28.92	-	-	-	-
1	rac-4OH propranolol C16 H21 N O3	10476-53-6 275.34		10.17 ± 0.40; 9.60 ± 0.30 2.450 ± 0.254	Yes	E1 E2	276.05 [M+H] ⁺	116.39	40-20	173.34	40-20	27.04	1.10	<i>Propranolol-d7 (S-)</i>	0.50	1.00
2												29.44	1.09	<i>Propranolol-d7 (R+)</i>		
1	rac-Timolol C13 H24 N4 O3 S	- 316.42		13.38 ± 0.20; 9.35 ± 0.10 1.280 ± 0.408	Yes	(S-) (R+)	317.25 [M+H] ⁺	261.13	38-16	244.09	38-22	30.44	2.49	<i>Timolol-d5 (S-)</i>	0.51	1.13
3						(S-) (R+)						-	-	<i>Timolol-d5 (R+)</i>		
	<i>rac-Timolol-d5</i>	-	-			(S-) (R+)	322.31 [M+H] ⁺	266.19	40-18	-	-	30.52	-	-	-	-
						(R+)						34.12	-	-	-	-

1 4	rac-Betaxolol C ₁₈ H ₂₉ N O ₃	63659-18-7 307.43		13.89 ± 0.20; 9.17 ± 0.38 2.687 ± 0.401	Yes	E1	308.34 [M+H] ⁺	116.09	44-24	121.04	44-30	24.48	3.33	<i>Pindolol-d7</i> <i>E1</i>	0.51	0.77
1 5	rac-Carazolol C ₁₈ H ₂₂ N ₂ O ₂	57775-29-8 298.38		13.94 ± 0.20; 9.54 ± 0.30 3.626 ± 0.412	Yes	E1	299.24 [M+H] ⁺	116.09	44-24	222.11	44-18	27.16	5.44	<i>Metoprolol-d7</i> <i>E1</i>	1.00	0.92
1 6	rac-Pindolol C ₁₄ H ₂₀ N ₂ O ₂	13523-86-9 248.32		13.94 ± 0.20; 9.54 ± 0.30 1.680 ± 0.250	Yes	E1	249.16 [M+H] ⁺	116.11	38-16	172.12	38-18	26.12	5.01	<i>Pindolol-d7</i> <i>E1</i>	0.50	0.91
	<i>rac-Pindolol-d7</i>	-				E2	256.02 [M+H] ⁺	123.20	44-18	-	-	28.2	-	<i>Pindolol-d7</i> <i>E2</i>	-	-
						E1						26.04	-		-	-
						E2									-	-

β-agonists (2)																					
1 7	rac-Albuterol C13 H21 N O3	18559-94-9	239.31		9.99 ± 0.31; 9.62 ± 0.10	0.692 ± 0.379	Yes	E1 E2 E1 E2	240.15 [M+H] ⁺	148.11	30-18	166.12	30-14	21.01	3.12	<i>Albuterol-d3</i> <i>E1</i>	0.49	1.05			
														23.57	3.07	<i>Albuterol-d3</i> <i>E2</i>					
	21.17	-	-											-	-	-	-	-	-		
	23.73	-	-											-	-	-	-	-			
1 8	rac-Clenbuterol C12 H18 Cl2 N2 O	37148-27-9	277.19		13.29 ± 0.20; 9.51 ± 0.10	2.634 ± 0.384	Yes	E1 E2 E1 E2	276.98 [M+H] ⁺	203.09	30-16	132.00	30-30	21.41	2.99	<i>Clenbuterol-d9</i> <i>E1</i>	0.50	1.11			
														24.12	2.99	<i>Clenbuterol-d9</i> <i>E2</i>					
	21.33	-	-											-	-	-	-	-			
	24.04	-	-											-	-	-	-	-			
	<i>rac-Clenbuterol-d9</i>	-	-																		

*: Chiral carbon

Table S2. Sampling sites

Sampling site*	Locality (Province)	River	Date	Average flow (m ³ /s)	% max flow	Source of contamination	
1 2 3 4 5 6 7 8 9 Guadalquivir River	GUA1	Villacarrillo (Jaén)	Guadalquivir	03/11/2011	-	-	Agricultural activity: Olive trees
	GUA2	Baeza (Jaén)	Guadalquivir	03/11/2011	4.55	37%	Near the source of the river
	GUA3	Marmolejo (Jaén)	Guadalquivir	09/11/2011	8.54	19%	Near the source of the river
	WWTP1	Córdoba (Córdoba)	Treatment technology: Primary + Secondary (Activated sludge)				
	GUA4	Córdoba (Córdoba)	Guadalquivir	09/11/2011	-	-	Downstream WWTP1
	GUA5	Peñaflor (Sevilla)	Guadalquivir	14/11/2011	10.59	44%	Intermediate sampling site
	WWTP2	Sevilla South (Sevilla)	Treatment technology: Primary + Secondary (Activated sludge)				
	GUA6	Coria del Río (Sevilla)	Guadalquivir	25/10/2011	-	-	Downstream WWTP2 and estuary
	GUA7	Brazo del Este (Sevilla)	Guadalquivir	28/10/2011	-	-	Estuary
GUA8	Lebrija (Sevilla)	Guadalquivir	28/10/2011	-	-	Estuary	
GUA9	Sanlúcar de Barrameda (Cádiz)	Guadalquivir	28/10/2011	-	-	Estuary	
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 Tributaries	BOR	La Iruela (Jaén)	Borosa	03/11/2011	-	-	Near the source of the river
	GUAM	Úbeda (Jaén)	Guadiana Menor	03/11/2011	-	-	Before joining the Guadalquivir River
	MAG	Santa Elena (Jaén)	Magaña	04/11/2011	-	-	Near the source of the river
	GUAN	Mengíbar (Jaén)	Guadalbullón	03/11/2011	5.05	89%	Before joining the Guadalquivir River
	YEG	Cardeña (Córdoba)	Yeguas	09/11/2011	-	-	Zona contaminada por purines
	GUAL	Baena (Córdoba)	Guadalmoral	02/11/2011	-	-	Agricultural activity: Olive trees
	PIC	Fuente Palmera (Córdoba)	Picachos	14/11/2011	-	-	Agricultural activity: Orange trees
	BEM	Hornachuelos (Córdoba)	Bembézar	02/11/2011	-	-	Near the source of the river
	CAC	Arenas del Rey (Granada)	Cacín	18/11/2011	-	-	Near the source of the river
	WWTP3	Loja (Granada)	Treatment technology: Primary				
	GEN1	Loja (Granada)	Genil	18/11/2011	0	-	Downstream WWTP3
	GEN2	Écija (Sevilla)	Genil	14/11/2011	3.46	19%	Before joining the Guadalquivir River
	COR	Carmona (Sevilla)	Corbones	15/11/2011	2.95	86%	Before joining the Guadalquivir River
	WWTP4	Sevilla East (Sevilla)	Treatment technology: Primary + Secondary (Activated sludge) + Tertiary				
	HER	Alcalá del Río (Sevilla)	Herreros	15/11/2011	-	-	Agricultural activity: Cereal
WWTP5	Morón de la Frontera (Sevilla)	Treatment technology: Primary + Secondary (Activated sludge)					
GUA A	Morón de la Frontera (Sevilla)	Guadaíra	15/11/2011	-	-	Downstream WWTP5 and military camp	
GUAR	Alnalcázar (Sevilla)	Guadamar	25/10/2011	0.06	5%	Before joining the Guadalquivir River	

*: Abbreviations of the corresponding catchment river were chosen to name the sampling sites of SW

Table S3. Concentrations and enantiomeric fractions of chiral drugs in the Guadalquivir River basin

A) Analgesics and psychiatric drugs

Sampling sites			Concentration, ng L ⁻¹ (%RSD)										
			Analgesics/anti-inflammatories (3)					Psychiatric drugs and transformation products (2)					
			rac-Ketoprofen	Ibuprofen		EF / EF _{rel}	rac-Naproxen	Fluoxetine		EF / EF _{rel}	Norfluoxetine		EF / EF _{rel}
	E1	E2			S(+)	R(-)		E1	E2				
Guadalquivir River	1	GUA1	0.725 (67.9)	96.9 (33.3)	116 (35.9)	0.48/0.48	38.8 (54.7)	bloq.	n.d.	-	n.d.	n.d.	-
	2	GUA2	5.48 (74.1)	346 (13.7)	422 (6.86)	0.48/0.48	169 (7.37)	0.212 (11.8)	0.0750 (66.7)	0.66/0.66	n.d.	n.d.	-
	3	GUA3	3.60 (126)	185 (17.9)	225 (14.9)	0.48/0.48	186 (17.2)	n.d.	n.d.	-	n.d.	n.d.	-
	WWTP1	Influent	481 (1.90)	1320 (54.1)	4827 (6.69)	0.25/0.25	4283 (9.14)	6.25 (0.00)	3.50 (10.1)	0.64/0.63	12.1 (141)	5.50 (141)	0.67/0.67
		Effluent	353 (0.44)	669 (27.8)	921 (11.1)	0.46/0.46	572 (15.8)	10.9 (11.4)	6.25 (5.66)	0.60/0.62	0.875 (141)	0.375 (141)	0.69/0.69
	4	GUA4	34.5 (9.19)	208 (8.65)	254 (3.54)	0.48/0.48	145 (14.1)	0.100 (0.00)	0.0333 (86.6)	0.63/0.64	n.d.	n.d.	-
	5	GUA5	3.07 (86.7)	258 (6.23)	295 (6.42)	0.50/0.50	118 (9.90)	n.d.	n.d.	-	n.d.	n.d.	-
	WWTP2	Influent	571 (0.140)	3055 (1.48)	3563 (10.2)	0.49/0.49	5143 (6.21)	11.4 (1.55)	6.12 (14.4)	0.67/0.64	6.25 (141)	9.50 (141)	0.38/0.38
		Effluent	514 (7.12)	1392 (17.6)	16340 (8.32)	0.49/0.49	2008 (2.18)	6.75 (15.7)	3.62 (4.88)	0.63/0.64	0.875 (141)	1.13 (141)	0.42/0.42
6	GUA6	7.60 (31.6)	286 (3.67)	373 (4.92)	0.47/0.47	111 (6.17)	0.0250 (141)	bloq.	-	n.d.	n.d.	-	
7	GUA7	n.d.	253 (12.1)	322 (23.0)	0.48/0.48	275 (54.5)	bloq.	n.d.	-	n.d.	n.d.	-	
8	GUA8	n.d.	141 (8.12)	181 (10.8)	0.47/0.47	91.7 (30.8)	n.d.	n.d.	-	n.d.	n.d.	-	
9	GUA9	n.d.	104 (76.4)	134 (69.1)	0.47/0.47	37.5 (9.64)	n.d.	n.d.	-	n.d.	n.d.	-	
Tributaries	1	BOR	0.167 (173)	494 (7.07)	594 (4.06)	0.48/0.48	35.5 (5.32)	n.d.	n.d.	-	n.d.	n.d.	-
	2	GUAM	0.200 (200)	155 (42.1)	179 (37.7)	0.49/0.49	22.8 (6.94)	n.d.	n.d.	-	n.d.	n.d.	-
	3	MAG	n.d.	174 (7.60)	222 (8.49)	0.47/0.47	67.5 (124)	n.d.	n.d.	-	n.d.	n.d.	-
	4	GUAN	29.4 (86.6)	591 (19.5)	747 (8.88)	0.47/0.47	201 (15.1)	0.0333 (86.6)	bloq.	-	n.d.	n.d.	-
	5	YEG	6.63 (173)	141 (14.7)	183 (12.6)	0.47/0.47	141 (16.3)	0.0333 (86.6)	bloq.	-	n.d.	n.d.	-
	6	GUAL	0.450 (128)	143 (28.6)	168 (37.8)	0.49/0.49	125 (89.4)	n.d.	n.d.	-	n.d.	n.d.	-
	7	PIC	0.667 (87.9)	160 (19.3)	194 (28.4)	0.49/0.49	69.7 (8.24)	n.d.	n.d.	-	n.d.	n.d.	-
	8	BEM	0.433 (173)	180 (12.0)	237 (3.57)	0.46/0.46	63.5 (32.5)	n.d.	n.d.	-	n.d.	n.d.	-
	9	CAC	0.100 (173)	31.2 (35.6)	37.7 (36.3)	0.49/0.49	1.87 (134)	n.d.	n.d.	-	n.d.	n.d.	-
	WWTP3	Influent	16.3 (101)	411 (30.6)	501 (24.3)	0.48/0.48	122 (1.45)	0.750 (0.00)	0.500 (0.00)	0.61/0.60	0.125 (141)	n.d.	-
		Effluent	1.75 (15.2)	226 (17.0)	262 (6.21)	0.49/0.49	33.5 (63.3)	0.375 (47.1)	0.250 (0.00)	0.62/0.60	n.d.	n.d.	-
	10	GEN1	12.6 (2.82)	354 (6.60)	412 (4.96)	0.49/0.49	339 (6.55)	0.275 (12.9)	0.100 (0.00)	0.67/0.68	0.400 (141)	0.100 (141)	0.76/0.76
11	GEN2	n.d.	289 (104)	424 (20.2)	0.30/0.30	266 (11.2)	n.d.	bloq.	-	n.d.	n.d.	-	
12	COR	0.550 (200)	165 (15.7)	210 (15.6)	0.47/0.47	75.4 (18.1)	n.d.	n.d.	-	n.d.	n.d.	-	

WWTP4	Influent	366 (5.50)	4390 (39.2)	6201 (10.9)	0.44/0.44	5511 (1.01)	4.87 (3.63)	2.87 (18.4)	0.71/0.61	5.38 (141)	12.0 (141)	0.29/0.29
	Effluent	296 (3.38)	1111 (13.3)	1174 (7.14)	0.51/0.51	300 (2.12)	5.75 (0.00)	2.75 (0.00)	0.66/0.66	0.750 (141)	0.125 (141)	0.81/0.81
13	HER	n.d.	821 (50.2)	1043 (51.8)	0.46/0.46	221 (29.6)	bloq.	n.d.	-	n.d.	n.d.	-
WWTP5	Influent	616 (6.29)	3823 (3.99)	4703 (11.6)	0.48/0.48	5307 (10.3)	7.75 (4.56)	3.87 (4.56)	0.65/0.65	8.63 (141)	7.50 (141)	0.51/0.51
	Effluent	242 (3.62)	1094 (6.82)	1222 (2.33)	0.50/0.50	219 (7.92)	11.2 (9.43)	5.87 (3.00)	0.64/0.64	n.d.	n.d.	-
14	GUAA	7.45 (23.7)	253 (11.3)	312 (0.623)	0.48/0.48	243 (10.3)	0.0500 (0.00)	bloq.	-	n.d.	n.d.	-
15	GUAR	0.900 (173)	777 (21.6)	1024 (7.42)	0.46/0.46	61.1 (140)	bloq.	n.d.	-	n.d.	n.d.	-

B) Cardiovascular drugs I

Sampling sites			Concentration, ng L ⁻¹ (%RSD)								
			Cardiovascular drugs and transformation products (9)								
			Atenolol		EF / EF _{rel}	Sotalol			Metoprolol		
S(-)	R(+)	E1	E2	EF / EF _{rel}		E1	E2	EF / EF _{rel}			
Guadalquivir River	1	GUA1	2.30 (5.89)	2.21 (2.84)	0.50/0.50	n.d.	n.d.	-	0.0125 (200)	n.d.	
	2	GUA2	11.8 (4.25)	11.4 (2.77)	0.50/0.50	0.675 (66.9)	0.612 (67.1)	0.44/0.49	0.288 (8.70)	0.300 (68.0)	0.59/0.47
	3	GUA3	18.3 (3.42)	13.0 (3.05)	0.42/0.42	0.467 (87.3)	0.467 (87.3)	0.47/0.50	0.733 (10.4)	0.700 (12.4)	0.56/0.50
	WWTP1	Influent	445 (0.0398)	437 (1.17)	0.49/0.50	15.13 (1.17)	15.1 (3.51)	0.52/0.51	18.5 (1.91)	20.2 (1.75)	0.54/0.48
		Effluent	232 (1.14)	176 (2.21)	0.44/0.43	14.63 (3.63)	14.9 (1.19)	0.46/0.50	15.5 (0.00)	20.0 (3.54)	0.48/0.44
	4	GUA4	48.2 (2.03)	47.2 (0.922)	0.51/0.50	2.12 (3.61)	2.32 (2.49)	0.45/0.48	2.07 (5.59)	1.97 (10.3)	0.61/0.51
	5	GUA5	15.2 (5.89)	13.4 (4.83)	0.49/0.48	1.00 (0.00)	0.967 (7.90)	0.47/0.50	0.700 (7.14)	0.700 (14.3)	0.59/0.50
	WWTP2	Influent	1317 (5.03)	1315 (0.309)	0.49/0.50	45.7 (0.00)	47.9 (3.32)	0.51/0.50	36.6 (4.34)	39.6 (6.69)	0.63/0.49
		Effluent	745 (1.33)	730 (0.315)	0.51/0.50	37.13 (2.38)	32.2 (4.39)	0.48/0.54	8.88 (1.99)	11.9 (4.47)	0.55/0.43
6	GUA6	36.9 (3.16)	35.1 (4.42)	0.49/0.49	1.38 (2.57)	1.32 (2.67)	0.47/0.51	0.925 (3.82)	1.00 (7.07)	0.52/0.48	
7	GUA7	15.0 (3.98)	13.9 (8.14)	0.49/0.49	1.22 (2.37)	1.50 (5.77)	0.42/0.45	1.67 (9.17)	1.78 (9.01)	0.57/0.49	
8	GUA8	5.92 (4.17)	3.58 (4.48)	0.39/0.38	0.383 (86.8)	0.217 (87.4)	0.52/0.60	0.0667 (86.6)	0.0167 (173)	0.66/0.51	
9	GUA9	2.15 (89.4)	1.65 (87.2)	0.44/0.43	0.183 (173)	0.150 (173)	0.58/0.65	0.683 (16.9)	bloq.	-	
Tributaries	1	BOR	1.78 (8.09)	1.03 (86.7)	0.48/0.48	0.533 (5.41)	0.567 (5.09)	0.47/0.48	bloq.	bloq.	-
	2	GUAM	2.65 (5.34)	2.44 (2.58)	0.49/0.49	0.787 (3.17)	0.850 (6.79)	0.40/0.48	0.212 (11.8)	0.212 (67.6)	0.60/0.45
	3	MAG	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	4	GUAN	56.0 (3.49)	50.3 (2.14)	0.47/0.48	0.667 (8.66)	0.633 (4.56)	0.45/0.51	1.40 (3.57)	1.47 (5.21)	0.57/0.49
	5	YEG	5.60 (3.22)	4.63 (3.79)	0.47/0.46	n.d.	n.d.	-	0.200 (25.0)	0.217 (13.3)	0.48/0.48
	6	GUAL	1.04 (68.1)	0.94 (66.8)	0.48/0.47	1.58 (6.61)	1.85 (2.21)	0.39/0.46	0.262 (18.2)	0.388 (28.6)	0.58/0.42

	7	PIC	4.50 (6.19)	3.70 (5.89)	0.47/0.46	n.d.	n.d.	-	n.d.	n.d.	-
	8	BEM	0.167 (173)	0.150 (173)	0.48/0.48	0.333 (86.6)	0.700 (0.00)	0.38/0.41	n.d.	0.0333 (86.6)	-
	9	CAC	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
WWTP3	<i>Influent</i>		53.0 (0.667)	53.5 (4.63)	0.50/0.50	n.d.	n.d.	-	bloq.	0.375 (47.1)	-
	<i>Effluent</i>		8.50 (4.16)	7.88 (2.24)	0.48/0.48	n.d.	n.d.	-	n.d.	n.d.	-
	10	GEN1	90.6 (0.273)	88.4 (4.24)	0.50/0.50	3.15 (0.00)	3.40 (0.00)	0.44/0.49	3.05 (4.64)	3.45 (2.05)	0.49/0.47
	11	GEN2	19.7 (8.88)	18.5 (7.01)	0.55/0.49	0.637 (67.9)	0.762 (67.6)	0.41/0.45	0.450 (15.7)	bloq.	-
	12	COR	4.84 (5.62)	4.06 (5.98)	0.47/0.46	0.725 (67.9)	1.08 (8.06)	0.39/0.46	0.162 (68.2)	bloq.	-
WWTP4	<i>Influent</i>		556 (3.69)	557 (4.73)	0.49/0.50	23.0 (0.00)	23.8 (1.49)	0.46/0.50	38.4 (5.07)	41.2 (3.43)	0.69/0.49
	<i>Effluent</i>		218 (1.05)	171 (2.47)	0.45/0.44	20.9 (2.54)	27.5 (5.14)	0.37/0.44	29.4 (1.81)	34.5 (3.07)	0.63/0.47
	13	HER	9.67 (4.75)	8.20 (0.862)	0.48/0.47	n.d.	n.d.	-	n.d.	0.0250 (141)	-
WWTP5	<i>Influent</i>		859 (2.53)	850 (1.58)	0.57/0.50	60.6 (1.46)	62.7 (1.13)	0.48/0.50	66.0 (2.68)	71.8 (0.493)	0.58/0.49
	<i>Effluent</i>		342 (2.12)	300 (1.47)	0.47/0.47	57.0 (7.44)	71.4 (2.23)	0.41/0.45	72.13 (2.21)	85.4 (1.45)	0.51/0.46
	14	GUAA	33.8 (2.09)	29.6 (2.03)	0.47/0.47	5.38 (0.658)	7.58 (1.40)	0.40/0.42	9.58 (1.85)	10.2 (1.74)	0.51/0.49
	15	GUAR	0.0833 (173)	bloq.	-	n.d.	n.d.	-	n.d.	n.d.	-

C) Cardiovascular drugs II

Sampling sites			Concentration, ng L ⁻¹ (%RSD)									
			Cardiovascular drugs and transformation products (9)									
			Propranolol			4OH propranolol			Timolol			
S(-)	R(+)	EF / EF _{rel}	E1	E2	EF / EF _{rel}	S(-)	R(+)	EF / EF _{rel}				
Guadalquivir River	1	GUA1	bloq.	bloq.		n.d.	n.d.	-	bloq.	n.d.		
	2	GUA2	1.75 (7.00)	1.3-3 (8.98)	0.55/0.43	n.d.	n.d.	-	0.0333 (150)	n.d.	0/0	
	3	GUA3	0.700 (7.14)	0.433 (6.66)	0.46/0.38	n.d.	n.d.	-	0.100 (100)	n.d.	0/0	
	WWTP1	<i>Influent</i>		30.2 (5.84)	25.9 (0.683)	0.61/0.46	n.d.	n.d.	-	3.50 (40.4)	n.d.	0/0
		<i>Effluent</i>		46.1 (0.383)	38.0 (1.86)	0.55/0.45	n.d.	n.d.	-	3.13 (39.6)	n.d.	0/0
	4	GUA4	4.42 (2.85)	3.17 (3.97)	0.56/0.41	n.d.	n.d.	-	0.300 (100)	n.d.	0/0	
	5	GUA5	1.32 (5.80)	0.900 (9.62)	0.54/0.40	n.d.	n.d.	-	0.100 (100)	n.d.	0/0	
	WWTP2	<i>Influent</i>		32.4 (6.01)	23.3 (1.52)	0.65/0.41	n.d.	n.d.	-	6.25 (50.9)	n.d.	0/0
		<i>Effluent</i>		28.8 (9.84)	19.1 (0.924)	0.58/0.40	n.d.	n.d.	-	5.13 (37.9)	n.d.	0/0
	6	GUA6	1.22 (14.4)	0.750 (0.00)	0.49/0.38	n.d.	n.d.	-	0.150 (47.1)	n.d.	0/0	
7	GUA7	0.15 (173)	0.300 (88.2)	0.58/0.46	n.d.	n.d.	-	n.d.	n.d.	-		

	8	GUA8	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-	
	9	GUA9	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-	
Tributaries	1	BOR	0.0667 (86.6)	0.0500 (100)	0.42/0.41	n.d.	n.d.	-	bloq.	n.d.	-	
	2	GUAM	0.0500 (200)	0.0250 (200)	0.50/0.46	n.d.	n.d.	-	bloq.	n.d.	-	
	3	MAG	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-	
	4	GUAN	1.67 (8.66)	1.10 (0.00)	0.52/0.39	n.d.	n.d.	-	0.500 (52.0)	n.d.	0/0	
	5	YEG	0.617 (4.68)	0.483 (5.97)	0.45/0.43	n.d.	n.d.	-	bloq.	n.d.	-	
	6	GUAL	bloq.	0.0875 (118)	-	n.d.	n.d.	-	bloq.	n.d.	-	
	7	PIC	0.0500 (0.00)	bloq.	-	n.d.	n.d.	-	bloq.	n.d.	-	
	8	BEM	0.0333 (173)	n.d.	-	n.d.	n.d.	-	bloq.	n.d.	-	
	9	CAC	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-	
	WWTP3	<i>Influent</i>		0.250 (0.00)	0.250 (0.00)	0.37/0.37	n.d.	n.d.	-	bloq.	n.d.	-
		<i>Effluent</i>		n.d.	bloq.	-	n.d.	n.d.	-	bloq.	n.d.	-
	10	GEN1	2.30 (6.15)	1.73 (2.05)	0.51/0.42	n.d.	n.d.	-	0.525 (47.1)	n.d.	0/0	
	11	GEN2	0.225 (117)	0.200 (115)	0.58/0.62	n.d.	n.d.	-	0.0250 (200)	n.d.	0/0	
	12	COR	bloq.	bloq.	-	n.d.	n.d.	-	bloq.	n.d.	-	
	WWTP4	<i>Influent</i>		17.5 (10.1)	10.3 (3.45)	0.61/0.37	n.d.	n.d.	-	3.38 (47.1)	n.d.	0/0
<i>Effluent</i>			14.9 (1.19)	11.13 (1.59)	0.60/0.42	n.d.	n.d.	-	2.25 (47.1)	n.d.	0/0	
13	HER	0.0250 (141)	0.125 (28.3)	0.72/0.66	n.d.	n.d.	-	n.d.	n.d.	-		
WWTP5	<i>Influent</i>		21.6 (7.36)	15.0 (0.00)	0.62/0.40	n.d.	n.d.	-	5.00 (42.4)	n.d.	0/0	
	<i>Effluent</i>		14.5 (2.44)	9.62 (1.84)	0.54/0.39	n.d.	n.d.	-	3.88 (41.0)	n.d.	0/0	
14	GUAA	1.18 (9.03)	0.825 (4.29)	0.48/0.40	n.d.	n.d.	-	0.450 (47.1)	n.d.	0/0		
15	GUAR	0.0167 (173)	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-		

D) Cardiovascular drugs III

Sampling sites			Concentration, ng L ⁻¹ (%RSD)								
			Cardiovascular drugs and transformation products (9)								
			Betaxolol			Carazolol			Pindolol		
			E1	E2	EF / EF _{rel}	E1	E2	EF / EF _{rel}	E1	E2	EF / EF _{rel}
Guadalquivir River	1	GUA1	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	2	GUA2	n.d.	n.d.	-	n.d.	n.d.	-	bloq.	n.d.	-
	3	GUA3	n.d.	n.d.	-	n.d.	n.d.	-	bloq.	n.d.	-
	WWTP1	Influent	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
		Effluent	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	4	GUA4	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	5	GUA5	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	WWTP2	Influent	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
		Effluent	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	bloq.	-
6	GUA6	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-	
7	GUA7	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-	
8	GUA8	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-	
9	GUA9	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-	
Tributaries	1	BOR	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	2	GUAM	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	3	MAG	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	4	GUAN	n.d.	n.d.	-	n.d.	n.d.	-	bloq.	n.d.	-
	5	YEG	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	6	GUAL	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	7	PIC	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	8	BEM	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	9	CAC	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	WWTP3	Influent	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
		Effluent	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	10	GEN1	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
11	GEN2	n.d.	n.d.	-	n.d.	n.d.	-	0.0125 (200)	n.d.	-	
12	COR	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-	

<i>WWTP4</i>	<i>Influent</i>	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	<i>Effluent</i>	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
13	HER	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	bloq.	-
<i>WWTP5</i>	<i>Influent</i>	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
	<i>Effluent</i>	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
14	GUAA	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-
15	GUAR	n.d.	n.d.	-	n.d.	n.d.	-	n.d.	n.d.	-

E) β -agonists and antibiotics

			Concentration, ng L ⁻¹ (%RSD)						Concentration, ng L ⁻¹ (%RSD)
			β -agonists (2)						Antibiotics (1)
			Albuterol			Clenbuterol			rac-Flumequine
			E1	E2	EF / EF _{rel}	E1	E2	EF / EF _{rel}	
Guadalquivir River	1	GUA1	n.d.	n.d.		n.d.	n.d.		n.d.
	2	GUA2	n.d.	bloq.		n.d.	n.d.		n.d.
	3	GUA3	0.0667 (173)	0.0833 (173)	0.24/0.25	n.d.	n.d.		n.d.
	<i>WWTP1</i>	<i>Influent</i>	3.50 (20.2)	4.75 (7.44)	0.23/0.43	n.d.	n.d.		bloq.
		<i>Effluent</i>	2.50 (0.00)	4.00 (8.84)	0.35/0.38	n.d.	n.d.		n.d.
	4	GUA4	0.433 (6.66)	0.683 (11.2)	0.38/0.39	n.d.	n.d.		n.d.
	5	GUA5	bloq.	0.100 (173)		n.d.	n.d.		n.d.
	<i>WWTP2</i>	<i>Influent</i>	4.75 (7.44)	8.50 (0.00)	0.35/0.36	n.d.	n.d.		n.d.
		<i>Effluent</i>	3.88 (4.56)	6.63 (2.67)	0.36/0.36	n.d.	n.d.		n.d.
6	GUA6	0.325 (10.9)	0.475 (7.44)	0.38/0.40	n.d.	n.d.		n.d.	
7	GUA7	bloq.	0.200 (90.1)		n.d.	n.d.		n.d.	
8	GUA8	n.d.	0.0500 (173)		n.d.	n.d.		bloq.	
9	GUA9	n.d.	n.d.		n.d.	n.d.		6.77 (86.8)	
Tributaries	1	BOR	n.d.	n.d.		n.d.	n.d.		bloq.
	2	GUAM	n.d.	n.d.		n.d.	n.d.		n.d.
	3	MAG	n.d.	n.d.		n.d.	n.d.		n.d.
	4	GUAN	0.367 (7.87)	0.550 (0.00)	0.39/0.40	n.d.	n.d.		n.d.
	5	YEG	n.d.	0.0333 (173)		n.d.	n.d.		n.d.
	6	GUAL	bloq.	0.150 (66.7)		n.d.	n.d.		n.d.

	7	PIC	n.d.	n.d.		n.d.	n.d.	n.d.
	8	BEM	n.d.	n.d.		n.d.	n.d.	n.d.
	9	CAC	n.d.	n.d.		n.d.	n.d.	n.d.
<i>WWTP3</i>		<i>Influent</i>	0.125 (141)	0.375 (47.1)	0.36/0.36	n.d.	n.d.	n.d.
		<i>Effluent</i>	n.d.	0.125 (141)		n.d.	n.d.	n.d.
	10	GEN1	0.400 (0.00)	0.725 (4.88)	0.35/0.37	n.d.	n.d.	3.05 (2.32)
	11	GEN2	0.0625 (200)	0.325 (72.7)	0.60/0.37	n.d.	n.d.	n.d.
	12	COR	n.d.	bloq.		n.d.	n.d.	n.d.
<i>WWTP4</i>		<i>Influent</i>	3.63 (4.88)	6.25 (0.00)	0.33/0.37	n.d.	n.d.	n.d.
		<i>Effluent</i>	3.25 (0.00)	6.00 (0.00)	0.34/0.34	n.d.	n.d.	n.d.
	13	HER	bloq.	0.0500 (141)		n.d.	n.d.	n.d.
<i>WWTP5</i>		<i>Influent</i>	4.38 (4.04)	7.75 (4.56)	0.33/0.36	n.d.	n.d.	n.d.
		<i>Effluent</i>	4.50 (0.00)	8.62 (2.05)	0.35/0.34	n.d.	n.d.	n.d.
	14	GUAA	0.650 (0.00)	1.20 (0.00)	0.33/0.35	n.d.	n.d.	n.d.
	15	GUAR	bloq.	0.0333 (173)		n.d.	n.d.	n.d.