

## Supplementary information

### In-sewer stability of selected analgesics and their metabolites

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### **Section 1: Typical parameters of the feeding raw sewage**

The real sewage is weekly collected from a pump station in St Lucia, Brisbane (Australia). Wastewater in this residential area is the typical domestic sewage with pH 7.5, low sulfide (<3 mgS/L), 10 – 30 mgS/L sulfate, low methane (<5 mgCOD/L), 180 – 200 mg/L SCOD with 50 mgCOD/L acetate and 10 – 20 mgCOD/L propionate as the major VFAs contents, 200 – 400 mg/L TSS, and 180 – 380 mg/L VSS. The collected fresh sewage is stored in a cold room under 4°C to minimize biological reactions. The feeding sewage is heated by a thermoregulator in a water bath to room temperature before entering the reactor.

Table S1: Physical and chemical details of the investigated biomarkers

Biomarkers	Parent or Metabolite	Excretion rate <sup>#</sup>	Available LogKow value in PubChem*
Desmetramadol	Metabolite of tramadol	0.20	
Ibuprofen carboxylic acid	Metabolite of ibuprofen	0.16	
Valdecoxib	Parent	0.7	2.67
Parecoxib	Parent		
Celecoxib	Parent	0.026	3.47
Etoricoxib	Parent	0.01	
Indomethacin	Parent	0.27	4.27
Sulindac	Parent		
Naltrexone	Parent	0.6	1.92
Naloxone	Parent	0.6	2.09
Piroxicam	Parent	0.001	
Ketoprofen	Parent	0.9	
Lidocaine	Parent	0.03	2.26
Tapentadol	Parent	0.03	3.57
Oxymorphone	Parent	0.5	0.83
Hydrocodone	Parent	0.12	2.16
Meperidine	Parent	0.05	2.72
Hydromorphone	Parent	0.36	0.11

# (Baselt and Cravey 1982)

\*(Kim et al. 2019)

**Table S2:** Mass Spectrometry information

Compounds name	Precursor Ion	Product Ion	Declustering potential (V)	Collision Energy (V)	Collision Cell Exit Potential (V)
Hydrocodone	300.1	199	180	40	22
		241	180	36	40
Hydrocodone D3	303.1	199.1	160	38	10
Hydromorphone	286.1	185.1	140	38	21
		157.1	140	55	24
Hydromorphone D3	289.1		140	38	26
Oxymorphone	301.7	284.1	125	26	15
		227.1	125	36	26
Oxymorphone D3	305.7	287.2	130	26	15
Desmetramadol	250.2	58	45	55	10
		42.1	45	70	15
Desmetramadol D6	256	64	70	15	17
Tapentadol	222	107.1	85	30	12
		121.1	85	28	19
Tapentadol D3	225	107.1	45	22	16
Naloxone	328.2	310.2	77	27	15
		212.1	77	49	5
Naloxone D5	333.2	315.1	80	25	19
Naltrexone	342.2	270.1	130	37	30
		267.2	130	36	13
Naltrexone D3	345.1	270.2	100	39	13

Meperidine	248	220.3	122	29	11
(Pethidine)		174.2	122	25	20
Meperidine D4	252.1	224.1	80	29	13
Ibuprofen Carboxylic acid	235.1	191.1	-90	-12	-20
/Carboxybuprofen		73.1	-90	-19	-20
Ibuprofen Carboxylic acid	238.1	194.1	-60	-11	-10
/Carboxybuprofen D3					
Diclofenac	296	214	60	42	25
		250	60	18	15
Diclofenac D4	300	219	80	28	12
Parecoxib	369	119.1	-120	-39	-19
		172	-120	-70	-53
Parecoxib D5	374	119.2	-110	-42	-15
Valdecoxib	313	118	-120	-35	-17
		190.1	-120	-58	-22
Valdecoxib D3	316.1	119.1	-116	-41	-12
Celecoxib	382.1	362	120	35	18
		303.1	120	33	16
Celecoxib D4	386.1	366	140	38	19
Etoricoxib	359	280.1	150	40	15
		279.1	150	52	35
Etoricoxib D3	362.1	280.1	180	43	14
Indomethacin	358	139	60	23	25
		111	60	70	20
Indomethacin D4	362.1	143.1	100	22	22
		115.1		69	25
Ketoprofen	255	209	75	15	33
		105	75	38	16
Ketoprofen D3	258.1	212.2	110	18	12

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Sulindac	357	233.2	96	58	25
		248.1	96	49	25
Sulindac d6	363.2	236.1	130	57	30
Lidocaine	235.2	86.2	50	28	11
		58.1	50	48	30
Lidocaine D10	245	96.3	70	23	11

**Table S3:** Method performance data for the direct injection analytes

Compounds	Linearity	LOD	LOQ	Intraday (RSD in %)			Interday (RSD in %)			Relative Matrix Effect (%)	Accuracy (%)		
		ng/L	ng/L	50 ng/L	100 ng/L	1000 ng/L	50 ng/L	100 ng/L	1000 ng/L		100 ng/L	1000 ng/L	5000 ng/L
Tapentadol	0.9995	6	17	2.8	3.2	4.9	3.0	2.9	4.4	103.3	103.6	94.4	110.8
Lidocaine	0.9996	10	40	3.0	3.0	3.4	1.2	4.2	4.2	105.3	107.5	93.9	110.8
Desmetramadol	0.9986	5	15	2.4	3.1	4.1	2.5	2.3	5.9	99.4	107.8	102.0	113.4
Diclofenac	0.9984	13	41	6.7	2.7	4.7	5.5	4.9	6.4	99.4	111.8	100.2	112.2
Ibuprofen carboxylic acid*	0.9977	45	135		6.3	4.9		4.1	4.4	110.5		109.8	107.0

*\*For Ibuprofen carboxylic acid, only 1000 ng/L and 5000 ng/L were used to calculate the method validation results. Intraday and interday, n= 7, Accuracy n= 7*

**Table S4:** Method performance data of SPE-based analytes

Compounds	Linearity	LOD	LOQ	Intraday (RSD in %)			Interday (RSD in %)			Relative Matrix Effect (%)	Relative recovery (%)	Accuracy (%)		
		ng/L	ng/L	50 ng/L	100 ng/L	1000 ng/L	50 ng/L	100 ng/L	1000 ng/L			5 ng/L	100 ng/L	1000 ng/L
Meperidine	0.9992	5	13	2.7	2.0	0.7	3.8	1.0	1.3	99.5	83.6	97.9	98.9	100.8
Natrexone	0.9956	36	110	7.9	5.1	3.3	7.9	4.3	4.2	97.6	91.2	104.2	94.6	94.5
Hydromorphone	0.9994	20	60	4.9	2.9	2.9	7.0	3.3	2.5	99.0	96.2	95.9	97.5	96.7
Hydrocodone	0.9993	15	46	5.4	3.1	1.9	4.3	3.2	1.4	97.6	97.4	93.2	105.3	102.4
Oxymorphone	0.9995	23	71	5.8	2.3	1.4	8.5	1.3	2.3	92.8	105.4	91.4	88.1	94.2
Naloxone	0.9995	11	35	6.6	2.0	1.8	6.3	1.1	2.2	95.8	90.2	104.5	92.6	93.2
Ketoprofen	0.9994	24	74	6.2	2.9	2.1	3.2	1.7	1.8	100.4	103.5	102.3	97.5	96.1
Piroxicam	0.9994	31	93	8.8	4.2	5.5	5.4	6.6	5.5	103.7	83.7	91.6	105.7	103.3
Indomethacin	0.9994	5	13	5.9	2.0	2.7	4.9	1.0	0.9	103.4	116.4	104.2	96.8	95.2
Etoricoxib	0.9993	5	14	8.0	2.7	1.2	4.6	2.3	2.8	99.5	85.3	107.1	101.1	100.2
Celecoxib	0.9994	6	13	3.8	2.0	4.1	3.2	2.2	1.7	104.2	109.6	107.2	98.7	94.3
Valdecoxib	0.9997	29	88	7.8	4.0	3.3	7.6	4.4	3.8	102.1	79.9	120.5	104.2	100.7
Parecoxib	0.9997	7	21	8.5	3.1	2.4	3.7	2.9	3.7	99.7	83.1	108.6	103.5	97.9

*\*Interday and intraday n= 7, Accuracy n= 7*



**Table S5. Results of Quality Assurance/Quality Control**

Analytes	QA/QC parameters				
	A calibration point ( $\mu\text{g/L}$ , mean $\pm$ SD)	Duplicate samples differences (in average, %)	Pooled wastewater sample ( $\mu\text{g/L}$ , mean $\pm$ SD)	Pooled wastewater spiked sample (spiked native $10 \mu\text{g/L}$ ; $\mu\text{g/L}$ , mean $\pm$ SD)	Method blank
Diclofenac	9.9 $\pm$ 0.03	3%	0.5 $\pm$ 0.03	10.1 $\pm$ 0.2	Not detected.
Desmetramadol	10.12 $\pm$ 0.04	2%	0.4 $\pm$ 0.05	9.9 $\pm$ 0.2	Not detected.
Ibuprofen carboxylic acid	10.3 $\pm$ 0.05	5%	5.3 $\pm$ 0.01	16.1 $\pm$ 0.3	Not detected.
Valdecoxib	9.8 $\pm$ 0.03	2%	Not detected	10.1 $\pm$ 0.3	Not detected.
Parecoxib	10.3 $\pm$ 0.03	4%	Not detected	9.8 $\pm$ 0.3	Not detected.
Celecoxib	9.95 $\pm$ 0.06	4%	0.6 $\pm$ 0.04	12.1 $\pm$ 0.05	Not detected.
Etoricoxib	10.4 $\pm$ 0.08	5%	Not detected	10.5 $\pm$ 0.04	Not detected.
Indomethacin	9.9 $\pm$ 0.01	5%	Not detected	10.6 $\pm$ 0.23	Not detected.
Sulindac	10.03 $\pm$ 0.3	4%	Not detected	9.8 $\pm$ 0.25	Not detected.
Naltrexone	9.87 $\pm$ 0.2	4%	Not detected	9.7 $\pm$ 0.34	Not detected.
Naloxone	10.3 $\pm$ 0.4	5%	Not detected	10.2 $\pm$ 0.85	Not detected.
Piroxicam	9.9 $\pm$ 0.5	5%	Not detected	10.6 $\pm$ 0.67	Not detected.
Ketoprofen	10.4 $\pm$ 0.2	2%	Not detected	10.8 $\pm$ 0.73	Not detected.
Lidocaine	9.9 $\pm$ 0.1	2%	Not detected	9.9 $\pm$ 0.34	Not detected.
Tapentadol	10.4 $\pm$ 0.5	2%	Not detected	11.1 $\pm$ 0.45	Not detected.
Oxymorphone	10.2 $\pm$ 0.6	6%	Not detected	10.4 $\pm$ 0.34	Not detected.
Hydrocodone	10.1 $\pm$ 0.04	4%	Not detected	10.3 $\pm$ 0.56	Not detected.
Meperidine	9.9 $\pm$ 0.2	2%	Not detected	10.9 $\pm$ 0.23	Not detected.
Hydromorphone	10.2 $\pm$ 0.6	5%	Not detected	9.8 $\pm$ 0.67	Not detected.

**Table S6:** Background wastewater concentration before spiking the native mix

Analytes	Background concentration ( $\mu\text{g/L}$ ) in wastewater
Diclofenac	0.73
Desmetramadol	0.15
Ibuprofen carboxylic acid	20.2
Valdecoxib	n.d
Parecoxib	n.d
Celecoxib	n.d
Etoricoxib	n.d
Indomethacin	n.d
Sulindac	n.d
Naltrexone	n.d
Naloxone	n.d
Piroxicam	n.d
Ketoprofen	n.d
Lidocaine	n.d
Tapentadol	n.d
Oxymorphone	n.d
Hydrocodone	0.08
Meperidine	n.d
Hydromorphone	n.d

n. d = not detected.

## References:

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