Pharmaceuticals and Transformation Products in Hospital Wastewater and a Rural Conventional Wastewater Treatment Plant

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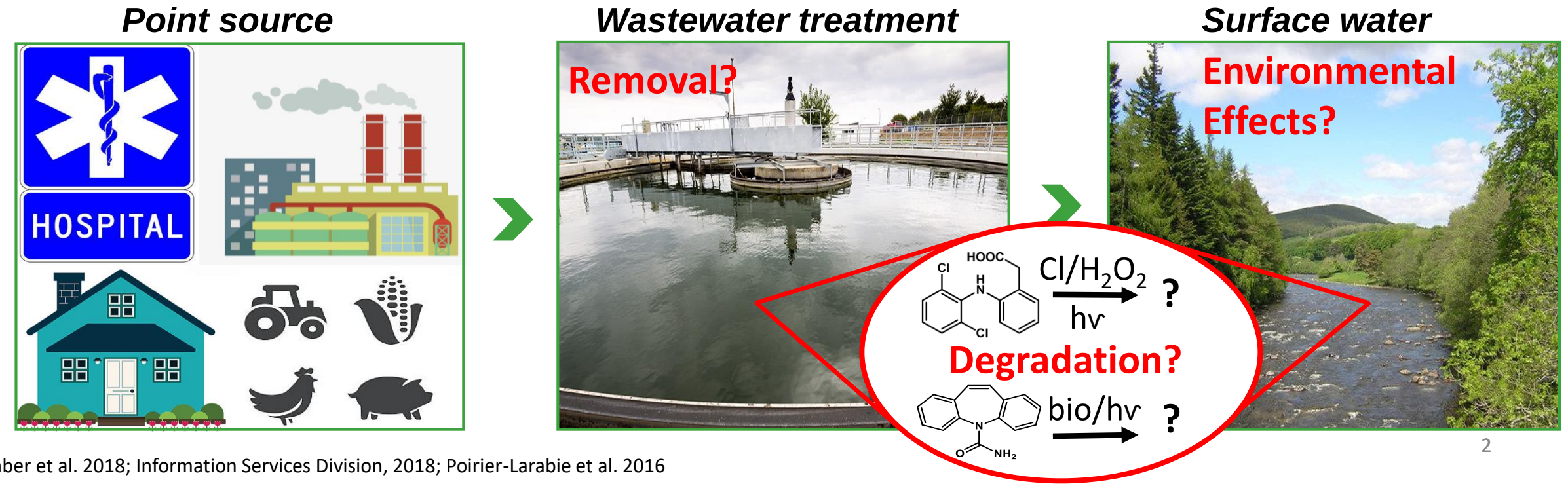
Hydro Nation Scholars Programme

Pharma: 'Emerging' Environmental Contaminants

- Pharma extensively used: >102 mil prescriptions in Scotland (2016/17)
- Enter environment mainly with WWTP effluent



Comber et al. 2018; Information Services Division, 2018; Poirier-Larabie et al. 2016

Research Objectives

1. Monitor hospital impact on pharma in municipal wastewater
2. Determine pharma change within conventional WWTP
3. Characterise transformation product presence

Study location:

Wick, Caithness County, Scottish Highlands

Study Sites & Sampling

Sampling frequency:

1x per week,

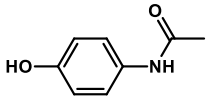
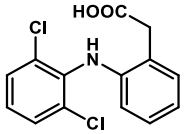
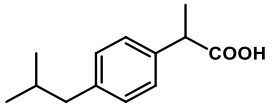
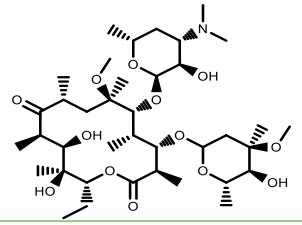
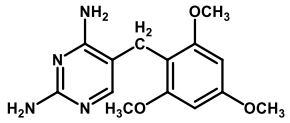
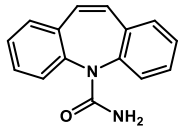
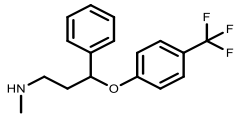
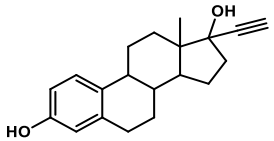
7 weeks May – July 2018

- Only 24h A&E 'major' injuries unit in region (>6800 km^2)
- 50 medical/surgical beds

- 13500 PE
- 171 L/sec max. flow
- Conventional AS
- North Sea discharge

Caithness General Hospital 1 → WWTP Combined Influent 2 → WWTP Primary Sample 3 → WWTP Secondary Sample 4 → WWTP Final Effluent 5

Target pharmaceuticals

	Class	Molecular Structure	Molecular Weight (g/mol)	pK_a	LogP	Water Solubility (mg/L)	Prescription Items, Scotland	Prioritised Compound
Paracetamol	Analgesic		151.1	9.4	0.4	14000	2680000	No
Diclofenac	NSAID		296	4.1	4.5	50000	283150	Yes, UK and EU
Ibuprofen	NSAID		206	4.4	3.9	21	325281	Yes, UK
Clarithromycin	Macrolide Antibiotic		748	8.9	3.1	0.33	254270	Yes, UK and EU
Trimethoprim	Antibiotic		290	7.1	0.9	400	481168	Yes, UK
Carbamazepine	Anticonvulsant		236	13.9	2.4	17	216405	Yes, UK
Fluoxetine	Antidepressant		309.3	10.1	4.1	14000	844744	Yes, UK
17a-ethynyl estradiol	Synthetic Hormone		296	10.3	3.6	11	444944	Yes, UK and EU

Sample Processing & Analysis

1. 1L 0.7µm filtration, surrogate spike
2. 1L SPE Oasis Prime HLB, elution 12mL 1:1(v:v) Ace:EtOAc
3. 0.5mL reconstitute 1:1(v:v) MilliQ:MeOH
4. Instrumental analysis

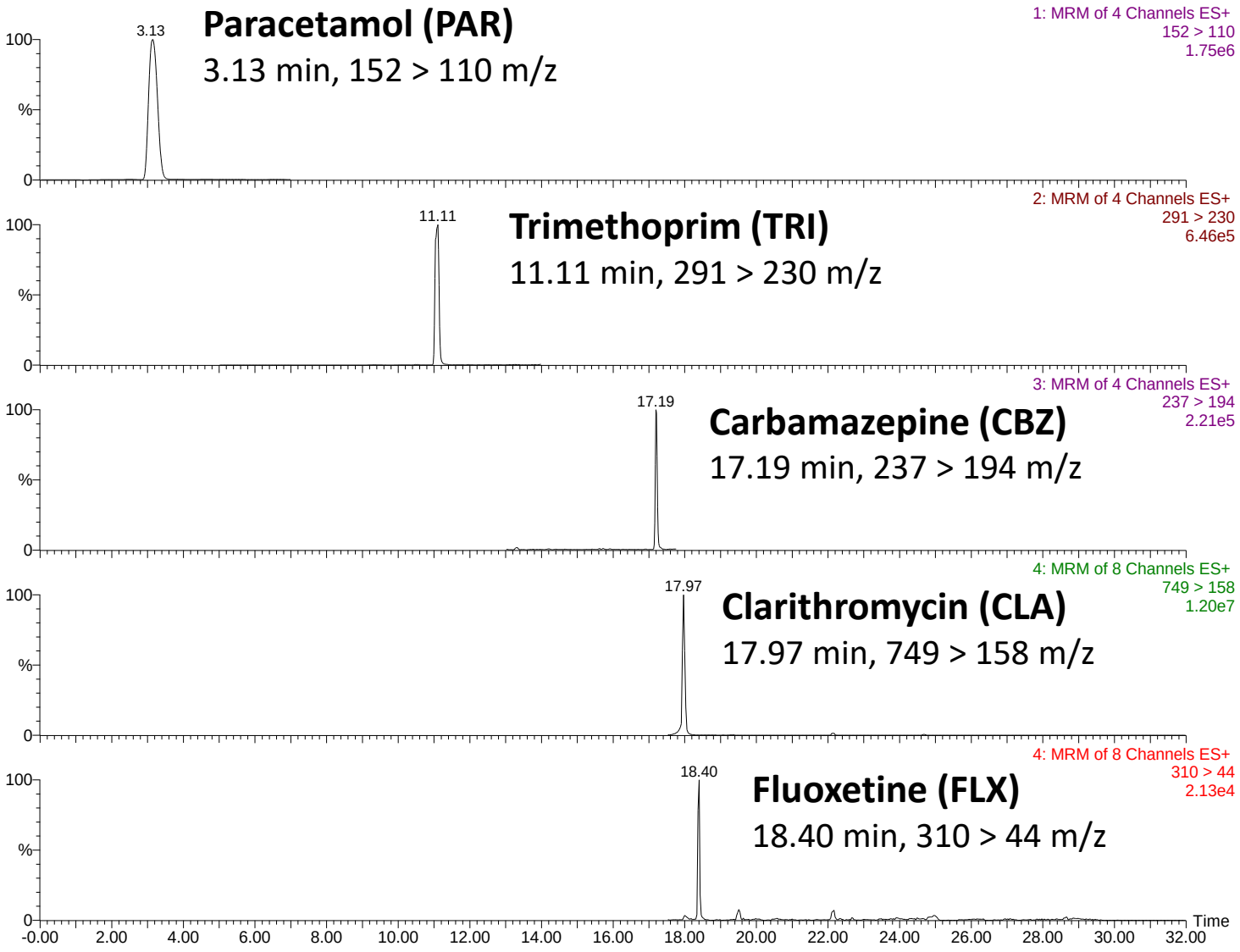
Bruker Triple Quadrupole QQQ HPLC-ESI-MS/MS

- ***$ESI^{+/-}$***

Thermo Exactive Orbitrap Q1 UPLC-HESI-MS

- ***$HESI^{+/-}$***

HPLC-MS/MS Detection

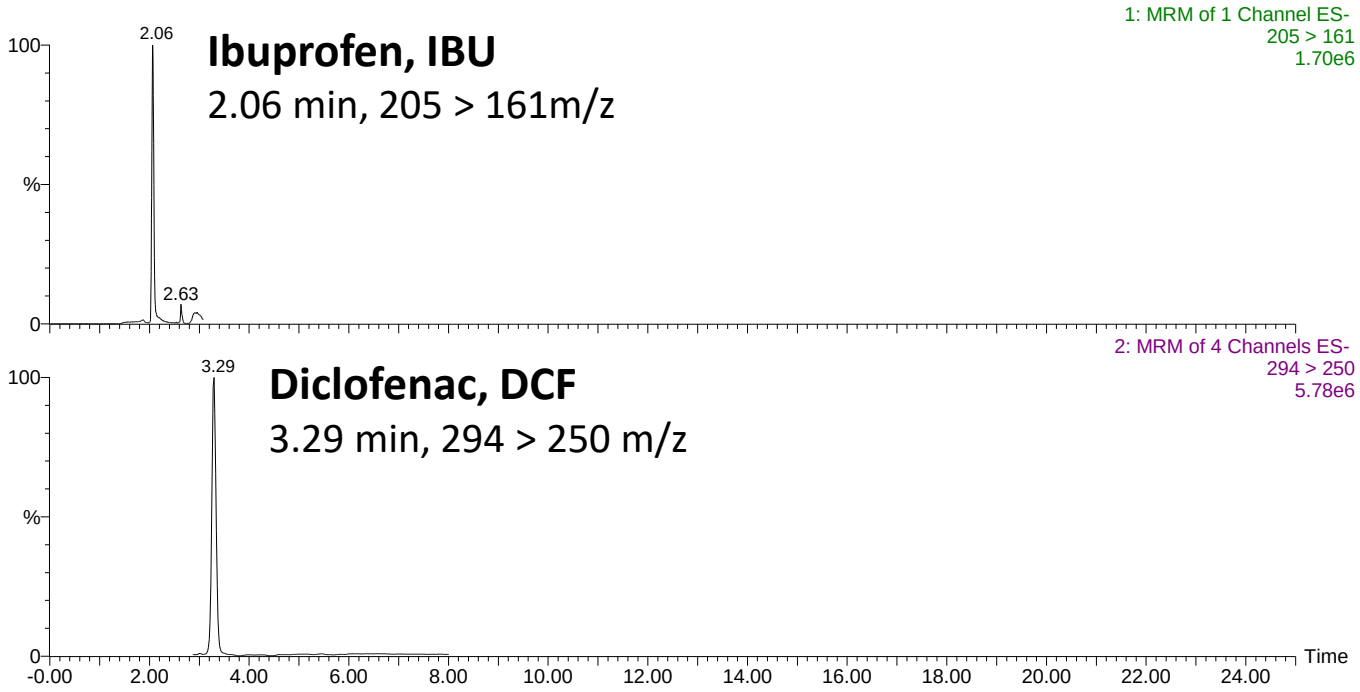


HPLC separation ESI⁺ mode pharma in a hospital discharge sample.

Detection frequency (%) of ESI⁺ mode pharma in wastewater samples. Limit of quantification (LOQ, ng/L).

	PAR	TRI	CBZ	CLAR	FLX
Hospital discharge (n=7,%)	85	85	100	57	14
WWTP Influent (n=7,%)	100	100	100	71	14
WWTP Primary (n=6,%)	100	100	100	66	n.d.
WWTP Secondary (n=6,%)	50	100	100	100	100
WWTP Effluent (n=7,%)	85	100	100	100	100
LOQ (ng/L)	0.78	0.78	0.81	0.81	3.60

HPLC-MS/MS Detection

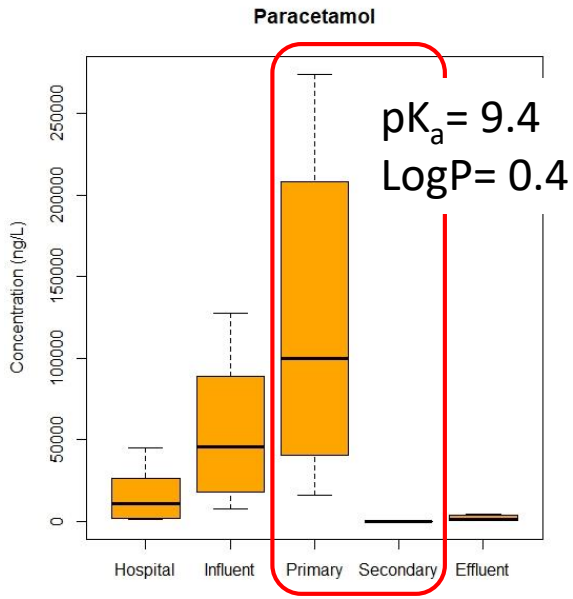


HPLC separation ESI$^-$ mode pharma in a hospital discharge sample.

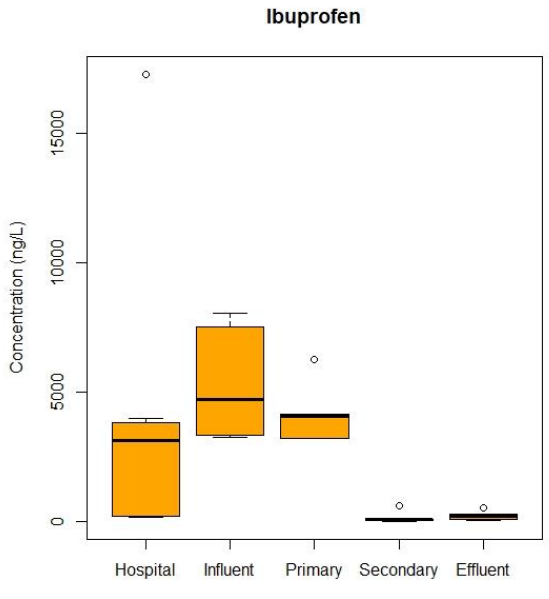
Detection frequency (%) of ESI$^-$ mode pharma in wastewater samples. Limit of quantification (LOQ, ng/L). 17a-ethynyl estradiol (EE2) not detected (n.d.).

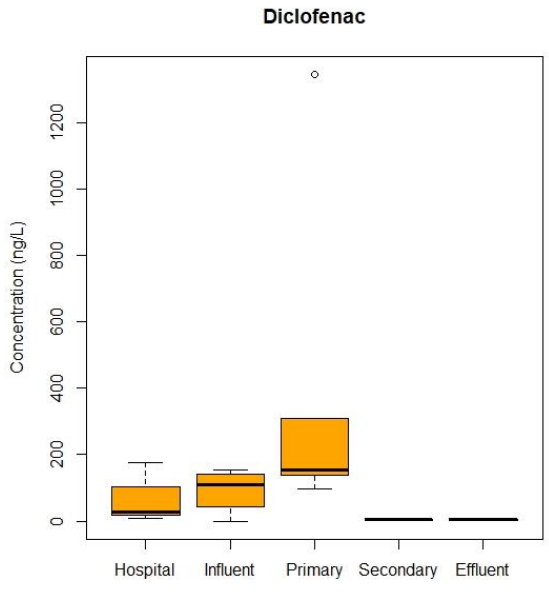
	IBU	DCF	EE2
Hospital discharge (n=7,%)	100	57	n.d.
WWTP Influent (n=7,%)	85	57	n.d.
WWTP Primary (n=6,%)	83	83	n.d.
WWTP secondary (n=6,%)	100	66	n.d.
WWTP effluent (n=7,%)	100	57	n.d.
LOQ (ng/L)	0.78	0.77	4.01

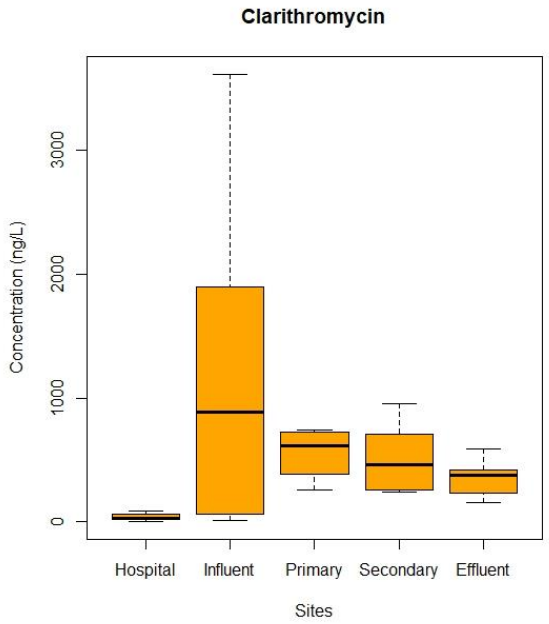
Pharma Concentrations

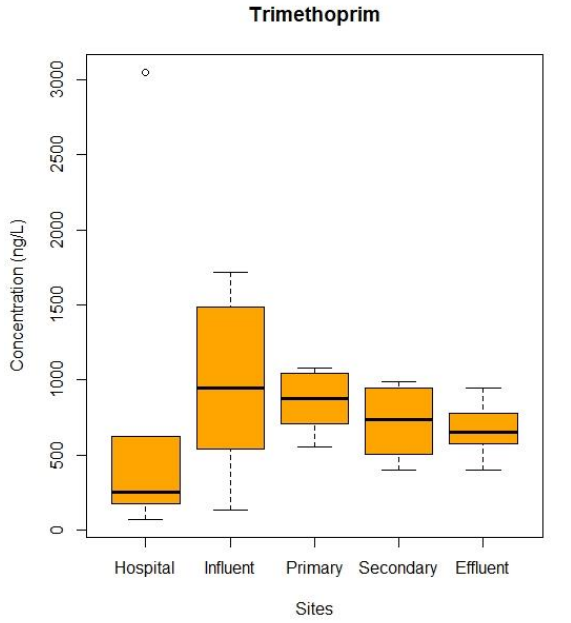


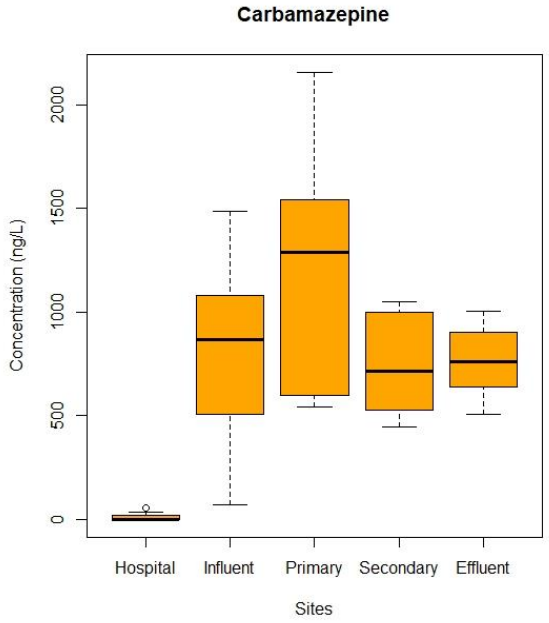
pK_a= 9.4
LogP= 0.4

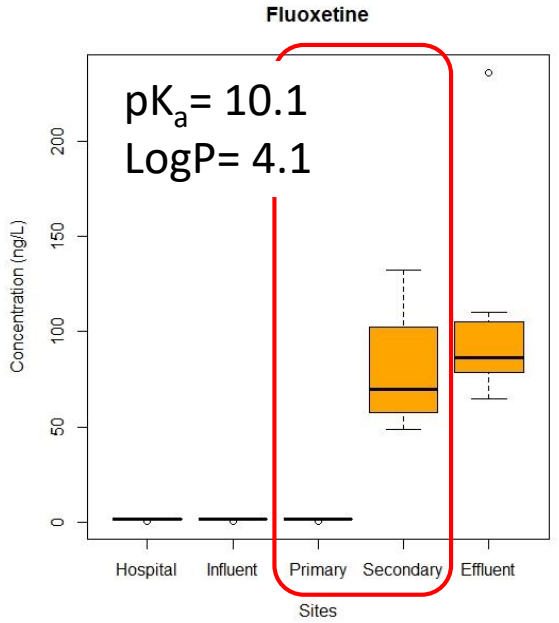








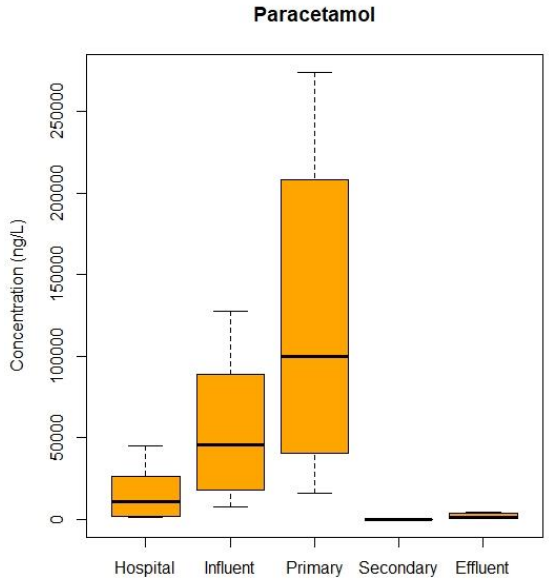


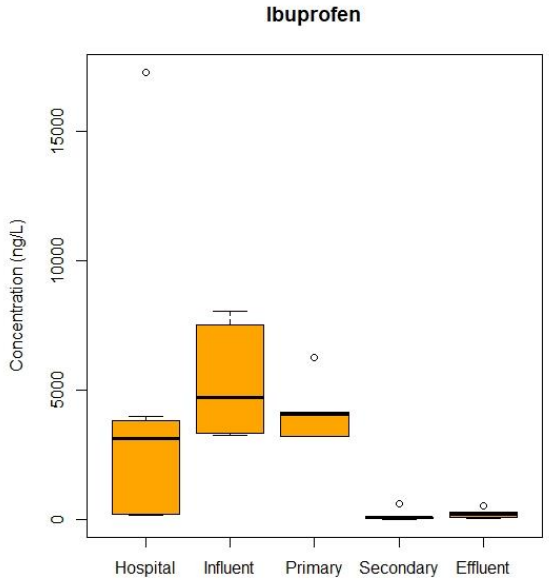


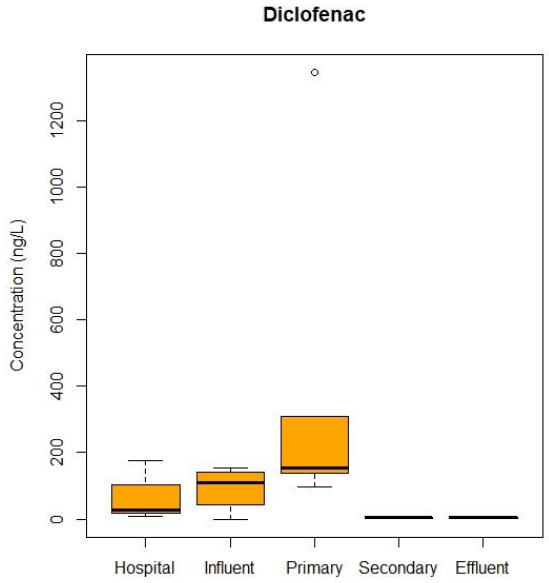
pK_a= 10.1
LogP= 4.1

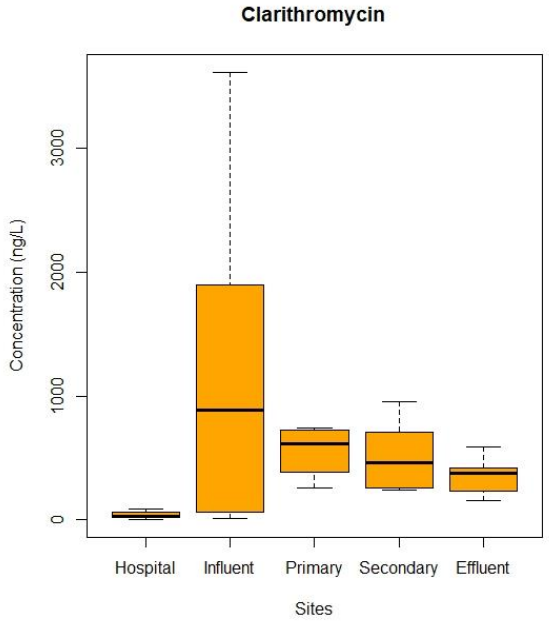
Hospital Discharge (n=7)
WWTP Influent (n=7)
WWTP Primary sample (n=6)
WWTP Secondary sample (n=6)
WWTP Effluent (n=7)

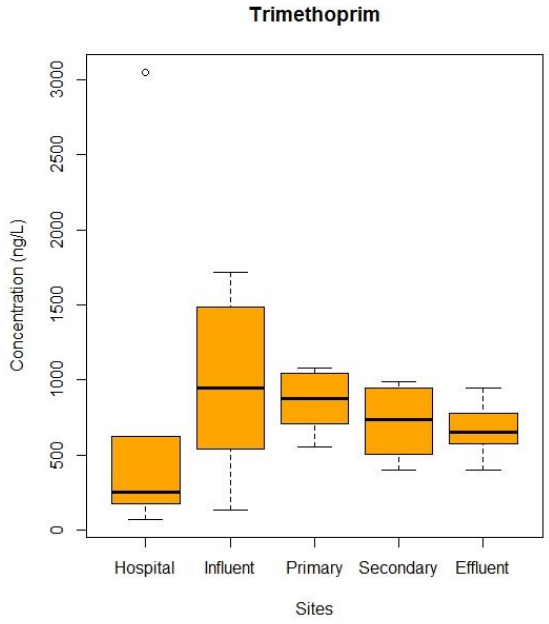
Pharma Concentrations & Hospital Impact

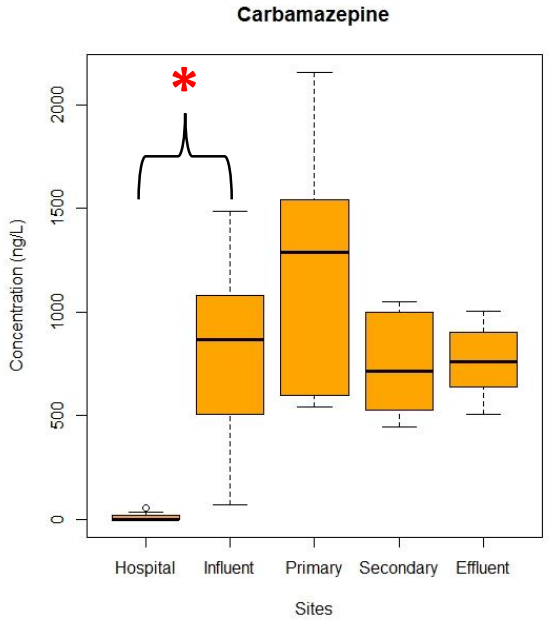


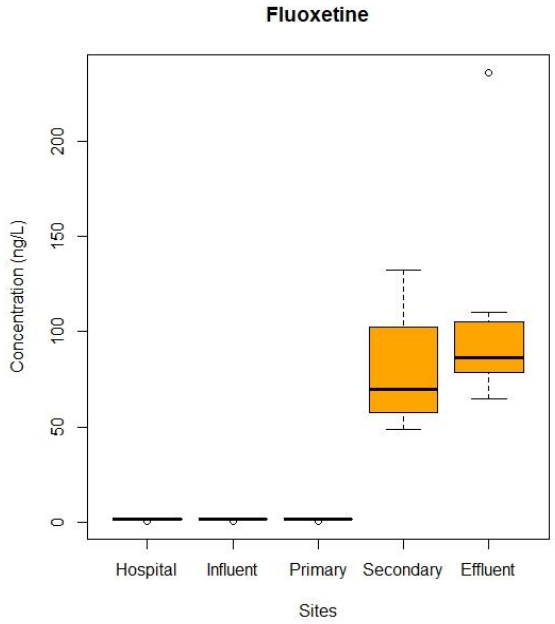








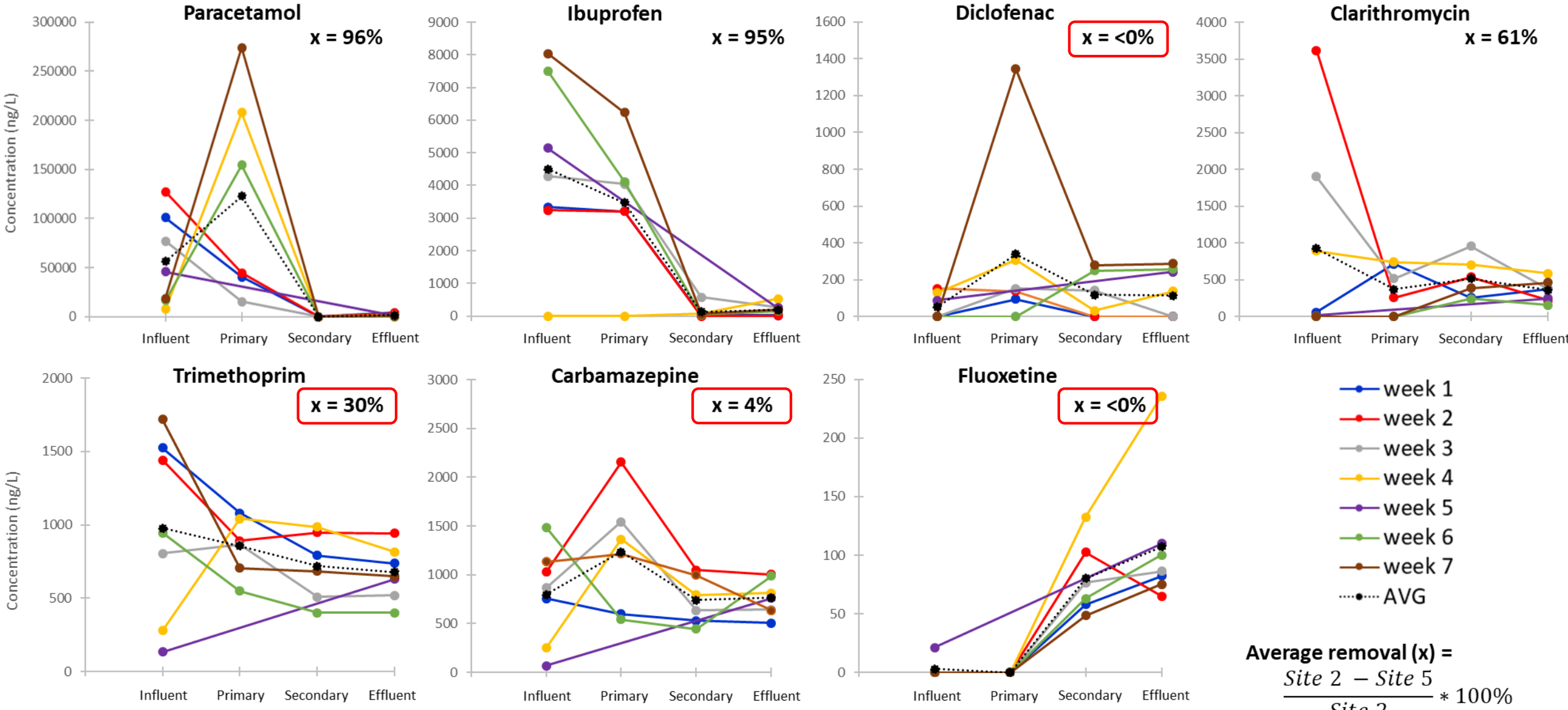




Hospital Discharge (n=7)
WWTP Influent (n=7)
WWTP Primary sample (n=6)
WWTP Secondary sample (n=6)
WWTP Effluent (n=7)

* indicates significant difference ($p<0.05$) between hospital discharge and WWTP influent, Welch two sample t-test

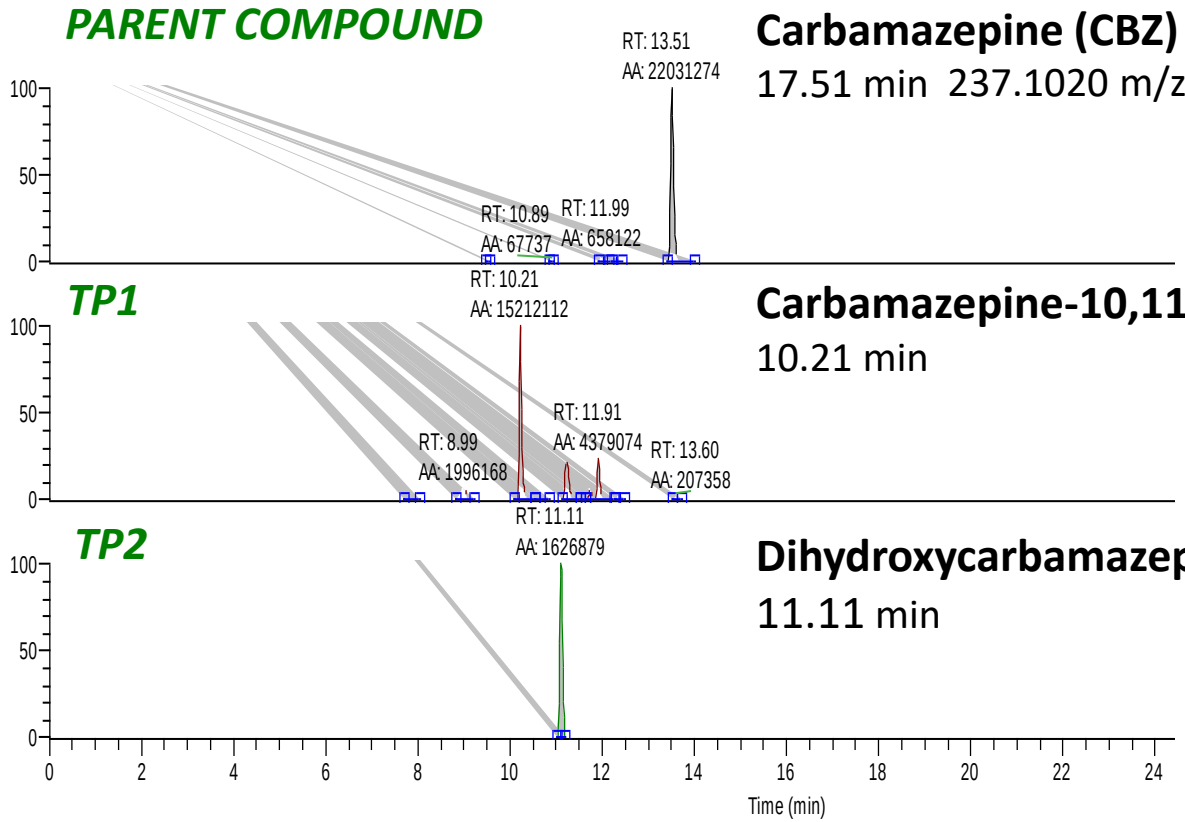
Pharma Removal in WWTP



Average removal (x) =

$$\frac{Site\ 2\ -\ Site\ 5}{Site\ 2} * 100\%$$

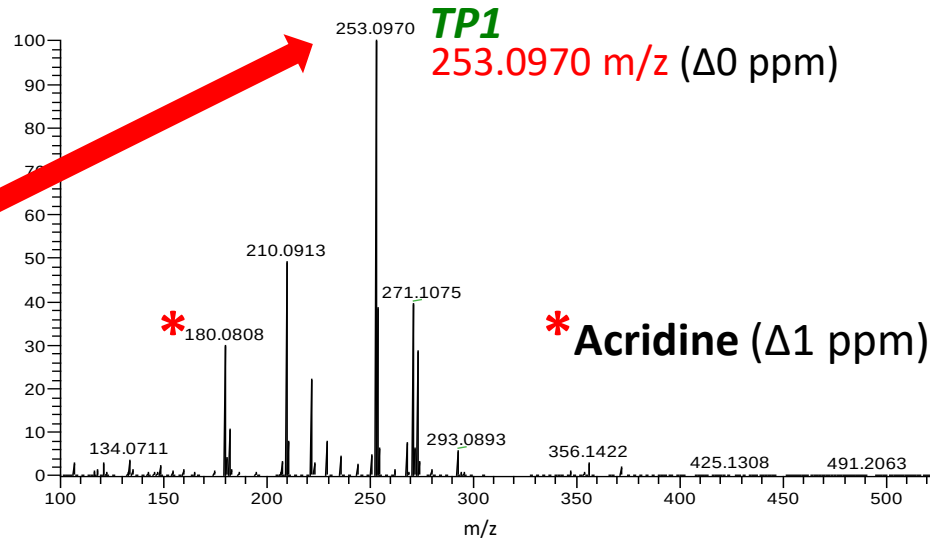
Transformation Products (TP)



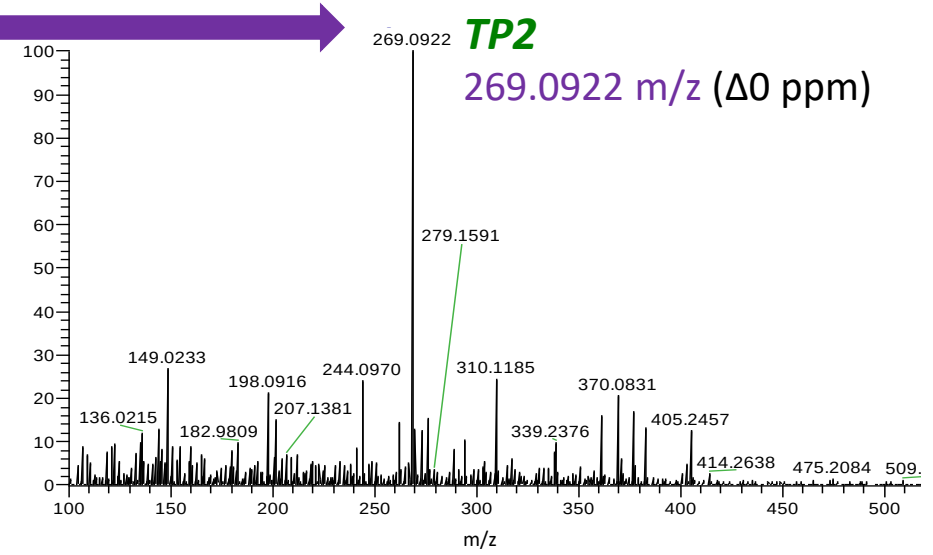
Carbamazepine (CBZ)
17.51 min 237.1020 m/z (Δ1 ppm)

Carbamazepine-10,11-epoxide
10.21 min

Dihydroxycarbamazepine
11.11 min



***Acridine** (Δ1 ppm)



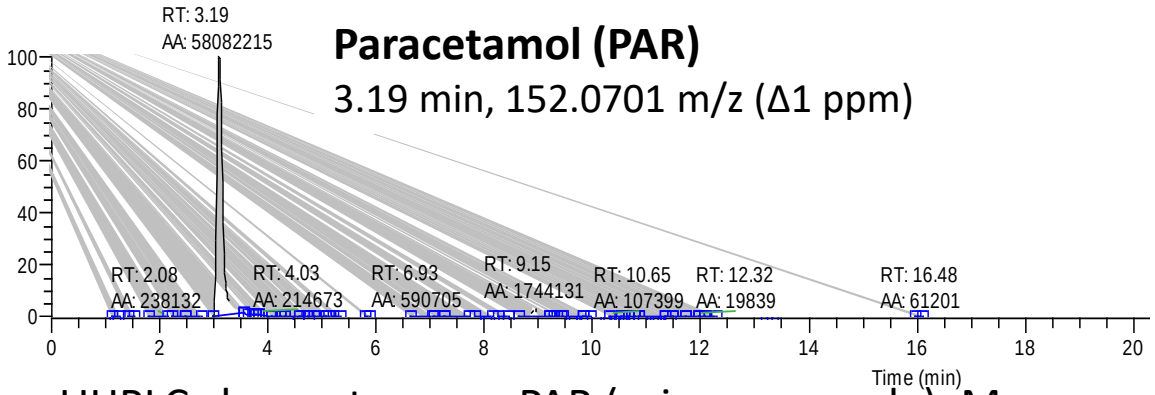
Carbamazepine and 2 transformation products in secondary sample, week 2.

- ID after direct/indirect photolysis and biological degradation
- 1 potential carcinogenic compound - acridine *

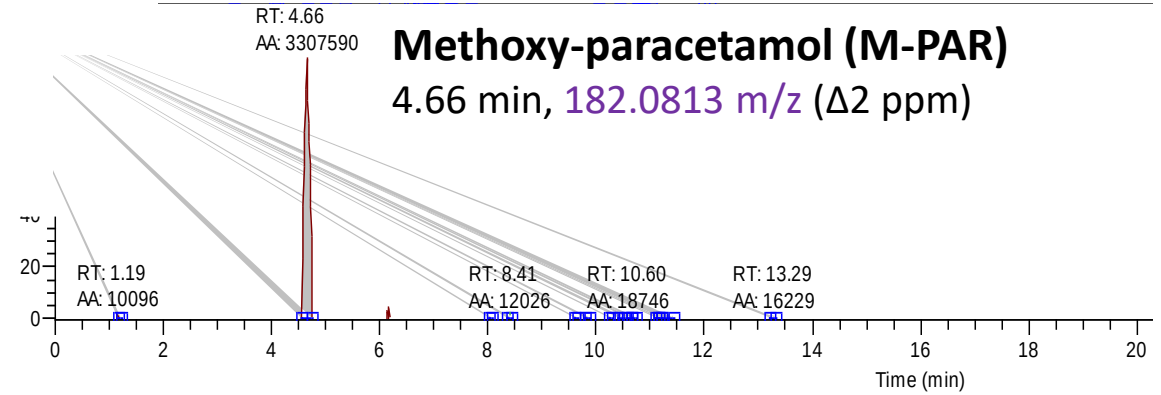
Mathon et al. 2016; Lekkerkerker-Teunissan et al. 2012; Donner et al. 2013

Transformation Products (TP)

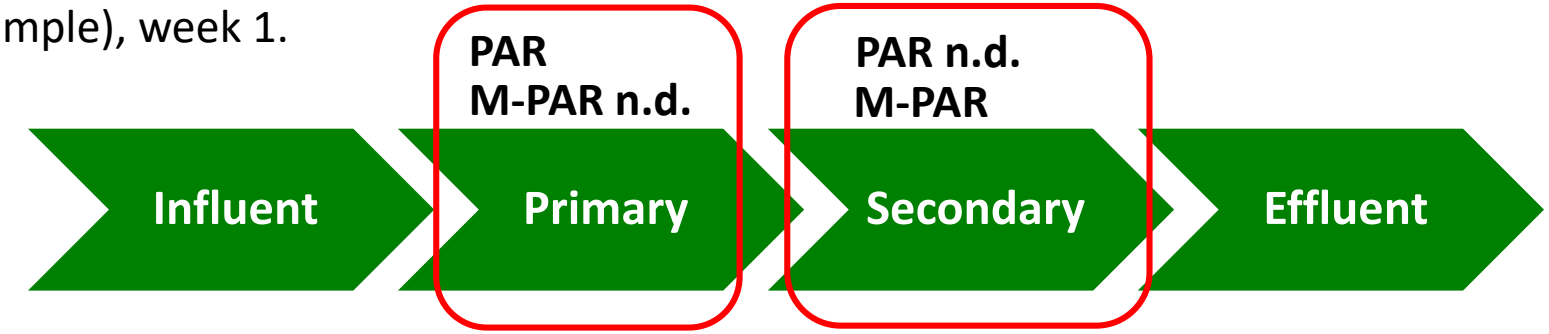
PARENT COMPOUND



TP



UHPLC chromatograms PAR (primary sample), M-PAR (secondary sample), week 1.



- PAR effective biological degradation (avg 96% removal)
- Methoxy-PAR formed during biological treatment

	WWTP Influent	WWTP Primary	WWTP Secondary	WWTP Effluent
PAR (ng/L)	56307 7616-127437 (100%)	122806 15596-273859 (100%)	33 n.d.-61 (50%)	1890 360-4248 (100%)

Ibáñez et al. 2017

Conclusions & Significance

- 1st study of pharma behaviour in rural Scottish Highlands WWTP
- Pharma observable in hospital discharge, but other significant sources impacting municipal wastewater
- Wick WWTP ineffective for complete pharma removal
  - <50% avg removal TRI, CBZ; <0% avg removal DCF, FLX
  - Transformation product formation and persistence observed
- Wick harbour and rural environment potential impact from pharma pollution
  - Tidal zones and estuaries are sink for pharma/organic pollutants (Letsinger et al. 2019; Alygizakis et al. 2016)

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Thank you!

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References

- Poirier-Larabie, S., Segura, P. A., & Gagnon, C. (2016). Degradation of the pharmaceuticals diclofenac and sulfamethoxazole and their transformation products under controlled environmental conditions. *Science of the Total Environment*, *557*, 257–267.
- aus der Beek, T., Weber, F. A., Bergmann, A., et al. (2016). Pharmaceuticals in the environment-Global occurrences and perspectives. *Environmental Toxicology and Chemistry*, 35(4), 823–835.
- Comber, S., Gardner, M., Sörme, P., et al. (2018). Active pharmaceutical ingredients entering the aquatic environment from wastewater treatment works: A cause for concern? *Science of the Total Environment*, *613–614*, 538–547.
- Information Services Division, 2018, Prescribing & Medicines: Prescription Cost Analysis. NHS Publication Report, website (accessed Apr 2019), https://www.isdscotland.org/.
- Verlicchi, P., Al Aukidy, M., Zambello, E. (2012) Occurrence of pharmaceutical compounds in urban wastewater: Removal, mass load and environmental risk after secondary treatment – A Review. *Science of the Total Environment*, *429*, 123 – 155.
- Letsinger, S., Kay, P., Rodrigues-Mozaz, S. et al. (2019). Spatial and temporal occurrence of pharmaceuticals in UK estuaries. *Science of the Total Environment*, *678*, 74-84.
- Alygizakis, N., Gago-Ferrero, P., Borova, V., et al. (2016). Occurrence and spatial distribution of 158 pharmaceuticals, drugs of abuse and related metabolites in offshore seawater. *Science of the Total Environment*, *541*, 1097-1105.
- Samson, S. (2003). Wick Wastewater Treatment Plant, *UK Water Projects Online*, website (accessed Apr 2019), http://www.waterprojectsonline.com/case_studies/2004/Scottish_Wick_2004.pdf.
- Caithness General Hospital Services, NHS Highland, website (accessed Apr 2019), https://www.nhshighland.scot.nhs.uk/services/pages/.
- Ibáñez et al. 2017
- Mathon, B., Choubert, J.-M., Miege, C., & Coquery, M. (2016). A review of the photodegradability and transformation products of 13 pharmaceuticals and pesticides relevant to sewage polishing treatment. Science of The Total Environment, 551, 712–724. Lekkerkerker-Teunissan et al. 2012
- Donner, E., Kosjek, T., Qualmann, S., Kusk, K. O., Heath, E., Revitt, D. M., Andersen, H. R. (2013). Ecotoxicity of carbamazepine and its UV photolysis transformation products. Science of the Total Environment, The, 443, 870–876.
- Lekkerkerker-Teunissen, K., Benotti, M. J., Snyder, S. A., & van Dijk, H. C. (2012a). Transformation of atrazine, carbamazepine, diclofenac and sulfamethoxazole by low and medium pressure UV and UV/H2O2 treatment. Separation and Purification Technology, 96, 33–43.