Topic/Special Session
3. Drainage Impacts

Subtopic
3.2 Receiving environment impacts

The fate of bezafibrate, carbamazepine, ciprofloxacin and clarithromycin in the wastewater treatment process

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Summary
The progress of four pharmaceuticals (bezafibrate, carbamazepine, clarithromycin and ciprofloxacin) is followed through the treatment stages (screened sewage, settled sewage and final effluent) of a large urban wastewater treatment plant (WWTP) employing activated sludge treatment. Concentrations at the inlet to the WWTP are generally higher than those predicted from consideration of local pharmaceutical consumption and typical excretion data. Percentage removal efficiencies are variable (22.5 – 94.3%) with carbamazepine being the most resistant to elimination.

Introduction
Future global predictions suggest that the number of drugs being dispensed by 2020 will be 4.5 trillion doses. The prescribed pharmaceuticals find their way to wastewater treatment plants (WWTPs) through excretion or disposal of unused or expired drugs and may be present in the discharged effluent as conventional treatment processes, consisting of sedimentation and biological transformation, are not designed to efficiently remove them. Therefore, an investigation into the fate of pharmaceuticals in the wider aquatic environment is warranted. In this paper, a carefully developed analytical method is applied to the detection of bezafibrate, carbamazepine, clarithromycin and ciprofloxacin as they pass through a WWTP serving a population of 870,000 and receiving 244,000 m^3 of wastewater per day.

Methods and Materials
Wastewater samples (7.5 L) were collected at three stages in the treatment process representing screened sewage (following gross solids and grit removal), settled sewage (following passage through primary settlement tanks) and final treated effluent (following activated sludge treatment and final sedimentation). Surface water samples (20 L) were collected from the River Lee (Lee navigation channel) at positions representing both up- and down-stream locations relative to the WWTP treated effluent discharge point. Pharmaceuticals were removed from the collected water samples using solid phase extraction procedures and subsequently analysed by reverse phase high performance liquid chromatography - mass spectrometry (LC-MS). Quantification was achieved against clean external standard solutions of known concentration prepared by dissolving the pharmaceutical compounds in 5 % v/v methanol/water.

Results and Discussion
The concentration ranges and mean values of bezafibrate, carbamazepine, ciprofloxacin and clarithromycin monitored at the three different defined treatment stages in the WWTP (together with the frequencies of detection) are compared with previously published data in Table 1. There is considerable variability in the data, particularly in the most contaminated samples (screened and settled sewage) for bezafibrate, carbamazepine and ciprofloxacin but the concentrations are

compatible with the ranges found in the literature. Bezafibrate and carbamazepine were detected on most occasions at all wastewater sampling sites.

Table 1. Pharmaceuticals detected in wastewater sampled at different points throughout the wastewater treatment process compared with published data.

		Measured values			Published values	
Compound		Screened sewage	Settled sewage	Treated effluent	WWTP influent	WWTP effluent
Bezafibrate	Range (ng/L)	628-2147	121-1342	39-411	121-7600	20-4800
	Mean (±SD) (ng/L)	1356.8 ± 689.6	783.5 ± 520.9	202.6 ± 156.5		
	Frequency	100%	83%	100%		
Carbamazepine	Range (ng/L)	369-1460	206-1502	47-1010	28-4596	8-3110
	Mean (±SD) (ng/L)	871.7 ± 547.4	680.7 ± 494.4	559.9 ± 272.7		
	Frequency	100%	100%	100%		
Ciprofloxacin	Range (ng/L)	731-2696	297-3478	44-229	143-1800	46-720
	Mean (±SD) (ng/L)	1713.4 ± 1389.4	1248.2 ± 1505.1	133.3 ± 81.4		
	Frequency	67%	67%	83%		
Clarithromycin	[a]Range (ng/L)	ND		57-598	138-724	103-996
	Mean (±SD) (ng/L)	ND	783.5	395.0 ± 46.6		
	Frequency	0%	17%	83%		

Frequency (%) = frequency of detection; ND = not detected on any sampling occasion
[a]Only detected on one occasion and therefore no range given.

Scaling down the national data for quantities of pharmaceuticals dispensed nationally in the community to the population size located within the WWTP catchment provides estimates of influent concentrations of the order of 660, 670, 860 and 560 ng/L for bezafibrate, carbamazepine, ciprofloxacin and clarithromycin after taking into account the percentages expected to be excreted unchanged. These predicted influent concentrations are towards the lower end of the measured ranges (Table 1) which exhibit the expected decreasing trend within the wastewater treatment process. The mean percentage reductions based on the measured concentration changes (with standard deviations) achieved during primary sedimentation and activated sludge treatment and for the overall wastewater treatment process are shown in Figure 1. Only small percentage reductions (15-22%) occurred during the primary sedimentation process however this noticeably increased in the activated sludge phase for bezafibrate and ciprofloxacin leading to high overall removal percentages of 89.7 ± 5.7% and 94.3 ± 0.5%, respectively. Conversely, carbamazepine demonstrated only a modest overall removal efficiency (22.5 ± 11.9%) as a consequence of a highly variable but negative average removal efficiency (-4.7 ± 52.9%) for the activated sludge treatment stage. None of the target pharmaceuticals were completely removed during the wastewater treatment process.

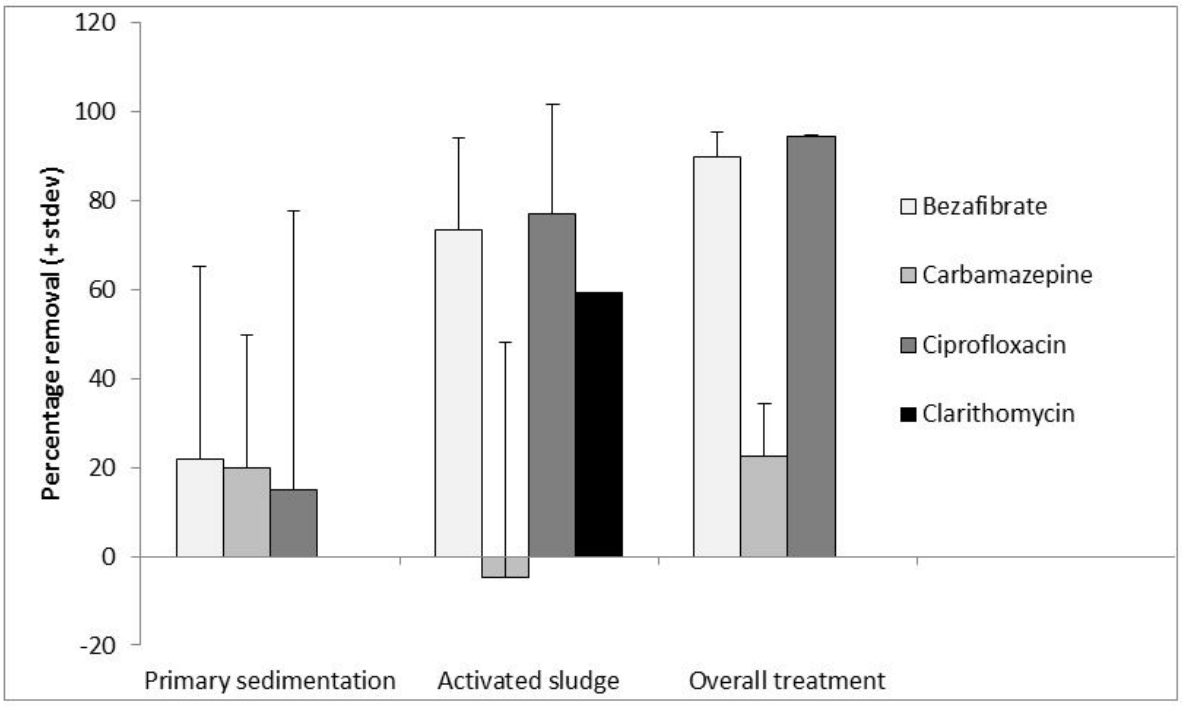

Figure 1. The percentage reductions of bezafibrate, carbamazepine, ciprofloxacin and clarithromycin following primary sedimentation, activated sludge treatment and overall treatment.

The monitored removal efficiencies of the different pharmaceuticals can be explained by their tendencies to sorb to sludge/suspended solids and/or by the extent of their biodegradation by micro-organisms. These characteristics are, in turn, dependent on the varying properties of pharmaceutical molecules due to their typically large, chemically complex structures, containing multiple ionisation sites spread throughout the molecules resulting in wide varieties of physico-chemical characteristics.

The incomplete removal of pharmaceuticals during wastewater treatment processes poses problems for receiving waters as evidenced by the down-stream concentrations reported in Table 2. As contaminants of emerging concern, the impact of pharmaceuticals on receiving waters needs to be assessed. The ratio of the predicted or measured surface water pharmaceutical concentration to the predicted no-effect concentration defines the hazard quotient and identifies an unacceptable environmental risk when values exceed unity. The calculated hazard quotients for fish, daphnids and algae (Table 3) indicate that the levels of pharmaceuticals found in both the final effluent and in the receiving surface water do not pose a potential ecological impact except in the case of clarithromycin in the final effluent when a high risk of causing ecological damage to algae is predicted. However, in the presence of multiple pharmaceuticals, which can be expected in most aquatic environments, the overall ecological threat can be expected to be enhanced. However, comprehensive environmental risk assessments are only required for new medicines and so the monitored pharmaceuticals are exempt.

Table 2. Pharmaceuticals detected in receiving waters above and below WWTP discharge point compared with published data.

		Measured values		Published values	
Compound		Up-stream	Down-stream	Surface waters upstream of WWTP	Surface waters downstream of WWTP
Bezafibrate	Range (ng/L)	22-40	44-88	4-66	4.5-200
	Mean (±SD) (ng/L)	31.0 ± 6.5	67.5 ± 12.7		
	Frequency	60 %	100 %		
Carbamazepine	Range (ng/L)	39-25	156-585	5.6-647	4-684
	Mean (±SD) (ng/L)	116.7 ± 97.7	305.5 ± 169.8		
	Frequency	80 %	100 %		
Ciprofloxacin	Range (ng/L)	ND	65–150	-	4.5-1300
	Mean (±SD) (ng/L)	ND	107.4 ± 35.5		
	Frequency	0 %	40 %		
Clarithromycin	Range (ng/L)	ND	19-34	1.4-60	0.89-1727
	Mean (±SD) (ng/L)	ND	27.0 ± 5.7		
	Frequency	0 %	60 %		

Frequency (%) = frequency of detection; ND = not detected on any sampling occasion

Table 3. The application of PNEC values (a) to calculate hazard quotients for bezafibrate, carbamazepine, ciprofloxacin and clarithromycin in the final sewage effluent (b) and in the receiving water (c).

(a)

	PNEC values (µg/L)		
	Fish	Daphnid	Algae
Bezafibrate	5.3	25	18
Carbamazepine	35.4	76.3	70
Ciprofloxacin*	2.45×10^5	991	938
Clarithromycin	280	25.7	0.09

(b)

		Hazard quotient		
	Maximum measured environmental concentration (MEC) (µg/L)	Fish	Daphnid	Algae
Bezafibrate	0.411	0.0775	0.0164	0.0228
Carbamazepine	1.010	0.0285	0.0132	0.0144
Ciprofloxacin	0.229	9.34×10^{-7}	2.31×10^{-4}	2.44×10^{-4}
Clarithromycin	0.598	0.0021	0.0233	6.64

(c)

		Hazard quotient		
	Maximum measured environmental concentration (MEC) (µg/L)	Fish	Daphnid	Algae
Bezafibrate	0.088	0.0166	0.0035	0.0049
Carbamazepine	0.585	0.0165	0.0077	0.0084
Ciprofloxacin	0.150	6.12×10^{-7}	1.51×10^{-4}	1.60×10^{-4}
Clarithromycin	0.034	1.21×10^{-4}	0.0013	0.378

*EC50 estimated using ECOSAR