Degradation Behaviour of Diclofenac, Trimethoprim and Carbamazepine Under Controlled Environmental Conditions

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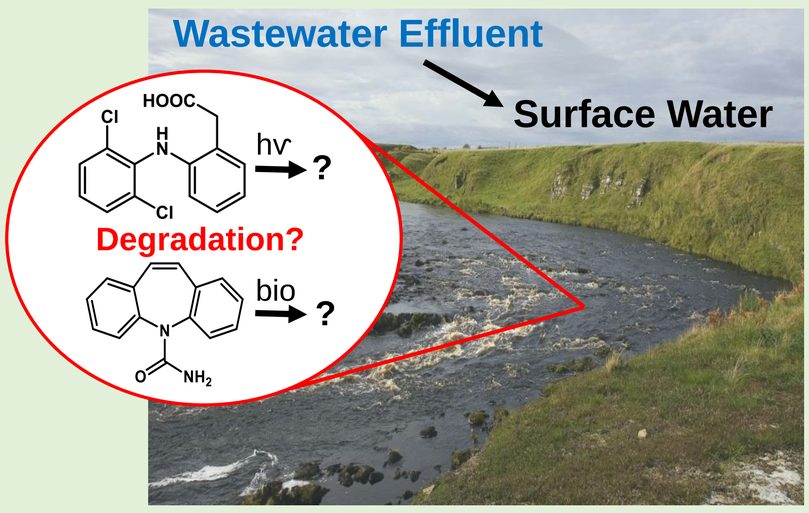
INTRODUCTION

Pharmaceuticals are extensively used and introduced into our wastewater where inadequate removal leads to release into surface waters. The effects of wastewater treatment on pharmaceutical behaviour is not fully understood – especially the formation and fate of secondary degradation products.[1,2] Advanced tertiary treatment (chemical oxidation, disinfection) and natural degradation (photolysis, biodegradation) may form toxic and/or bioactive products.[1-4] Therefore, to protect water quality and aquatic ecosystems, **research is needed to investigate pharmaceutical degradation, product distribution, persistence and eco-toxicity.**



Here, the degradation of target pharmaceuticals in water is explored under controlled conditions. We consider light exposure, temperature, humidity and oxygenation. Diclofenac (DCF, non-steroidal anti-inflammatory drug), trimethoprim (TRI, antibiotic) and carbamazepine (CBZ, anti-epileptic) were selected, as these are considered priority compounds in the UK[3] and have contrasting physicochemical properties (**Table 1**). Spiked tap water and river water were exposed to artificial sunlight and aerobic bacteria in single and mixed process conditions over 10 days to investigate photolytic and microbial degradation.

METHODOLOGY

Tap water samples were spiked with target pharmaceuticals (at 10 mg/L), and some were spiked with 0.1% river water to introduce bacteria and organic carbon (**Figure 1**). Samples were placed in plant growth cabinets (Weiss Gallenkamp, Fitotron SGC 170), programmed as below. Sampling took place at 0, 6, 24, 96 and 240 hr.

- *Light = 6 x 36W Fluorescent + Tungsten lamps (λ 185 – 1100 nm)*
- *Irradiance = max. 1000 µmol PAR photons m^{-2} s^{-1}*
- *T = 12 ± 1.5 °C, Humidity = 50 %*
- *Air bubbling with Blagdon Koi Air, KA65 pump*

1	BLK 1	2	BLK 2	3	BLK 3	4
Pharma + TW (hv)	TW (hv)	Pharma + TW+ RW (hv + bio)	TW+RW (hv + bio)	Pharma + TW + RW (bio)	BLK TW + RW (bio)	Pharma + TW (dark)

Figure 1. Seven samples; tap water (TW), river water (RW) and light conditions (hυ) and biological (bio) conditions. BLK = blank.

Table 1. Pharmaceutical physicochemical properties, and LC-MS/MS parameters indicated.

Analyte	Mol. weight	pK_a	Log K_{ow}	Water Sol. (mg/L)	R.T. (min)	ESI+/-	Parent Ion (m/z)	Cone (V)	Product Ions	Collision energy (eV)
DCF	296	4.15-4.51	4.02 - 4.51	50000	4.3	-	294	35	250, 214	8, 18
TRI	290	3.2, 7.1	0.91	400	6.6	+	291	60	230, 261	20, 20
CBZ	236	13.9	2.25-2.47	17.7	12.4	+	237	60	194, 192	14, 16

Figure 2. (A) Samples in growth cabinet, (B) LC-MS/MS and (C) LC-TOF systems.

RESULTS

The three pharmaceuticals exhibited varying behaviour under photolytic and biological degradation in the presence of organic carbon (**Figure 3**). Net removal indicated that photolytic and mixed process conditions were optimal for DCF (100%), while TRI and CBZ had limited removal (<30%) in both single and mixed processes (**Table 2**).

- **DCF:** Half-lives were calculated for samples 1 and 2 ($t_{1/2}$= 4.7, 3.6 hr, respectively). Hydroxylated diclofenac (addition –OH) was identified in samples (1, 2) after 6 hr with varying persistence (**Fig 4**).
- **TRI:** Recalcitrant to both degradation processes (<9% net removal) with increased concentration over time observed, as previously reported.[1]
- **CBZ:** Increased net removal (27-29%) observed in samples 2, 3 with presence of bacteria and organic carbon, compared to pure tap water (-2-9%). Persistence under simulated light in pure media previously reported.[1,6]

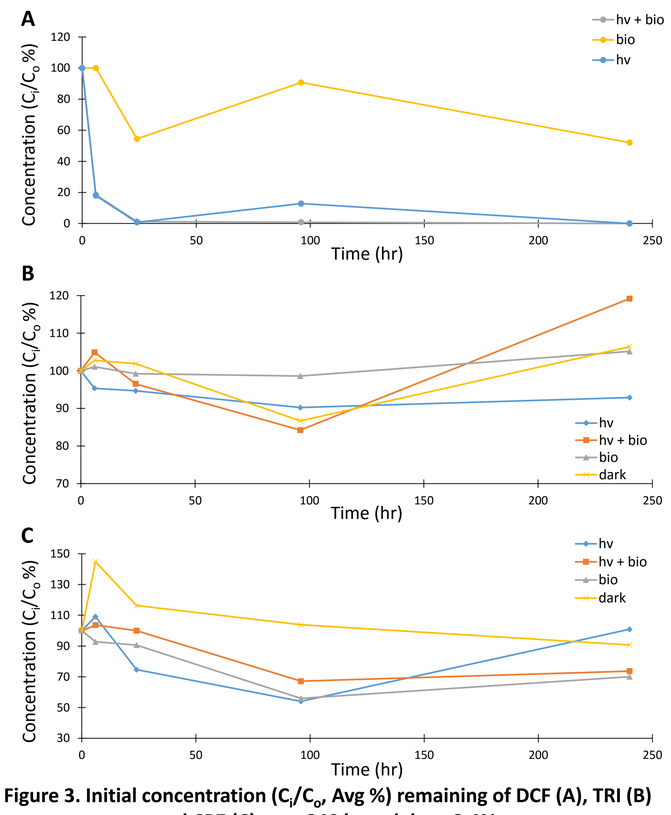


Figure 3. Initial concentration (C_i/C_o, Avg %) remaining of DCF (A), TRI (B) and CBZ (C) over 240 hr, std dev <8.4%.

Table 2. Net % removal during 240 hr (avg ± stdev), samples with degradation process indicated.

Samples	Net Removal (%)		
	DCF	TRI	CBZ
hυ	100 ± 0.02	7.12 ± 1.11	-2.24 ± 1.21
hυ + bio	100 ± 0.02	-18.9 ± 3.04	27.2 ± 9.67
bio	47.9 ± 5.48	-5.15 ± 2.86	29.9 ± 7.02
dark	NA	-7.34 ± 4.88	9.31 ± 3.94

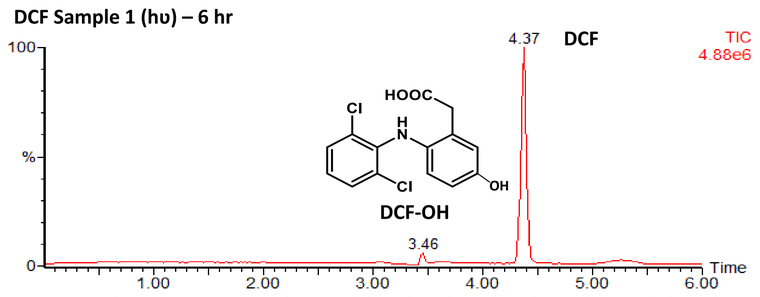


Figure 4. Chromatogram DCF (4.37 min) and Hydroxylated-DCF (3.46 min) peaks.

CONCLUSIONS AND FUTURE WORK

- Results suggested that the degradation behaviour was dependent on the pharmaceutical, process (photolysis vs biological) and environmental conditions (i.e., presence of organic carbon).
- Photolysis was dominant in terms of DCF removal, with half-lives of <5 hr calculated. Effective DCF degradation can be expected under real-water conditions, but formation of persistent degradation products is likely. CBZ and TRI were recalcitrant to significant removal, however increased CBZ degradation may occur in media with diverse bacteria communities and high organic carbon content. This suggests the importance of indirect photolysis and biodegradation in CBZ removal pathways.
- Future work will investigate pharmaceutical behaviour in simulated surface waters with natural light exposure. Also, confirmation of degradation products and pathways will be undertaken using HRMS.

REFERENCES

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