Removal of pharmaceuticals and related compounds by a bench-scale drinking water treatment system

Michael M. Bundy, William J. Doucette, Laurie McNeill and Jon F. Ericson

ABSTRACT

Reports of low-level subtherapeutic concentrations of pharmaceuticals in surface and ground waters have raised questions as to whether such compounds would survive typical drinking water treatment (i.e., coagulation, settling, filtration, and disinfection) and ultimately result in inadvertent human exposure. To examine the impact of these processes, a bench-scale drinking water treatment plant (DWTP) was constructed and used to examine the potential removal of caffeine, trovafloxacin mesylate, estradiol and salicylic acid relative to a conservative bromide (Br^-) tracer at pH 8. Radiolabeled compounds were used to provide good sensitivity within the small sample volume constraints of the system and to enable a more rigorous mass balance analysis. The bench-scale system was comprised of several unit operations including: coagulation, flocculation, sedimentation, dual-media gravity filtration, granular activated carbon treatment (GAC), and chlorination. Without GAC treatment, steady state analyses indicate removals of 3.4 to 13%, 21 to 31%, 6.9 to 12%, and 31 to 39% (95% confidence interval) for caffeine, trovafloxacin mesylate, estradiol, and salicylic acid, respectively, with most removal associated with flocculation/sedimentation and filtration. Biological degradation was likely the main process contributing to the removal of salicylic acid. The addition of GAC treatment was found to significantly enhance the overall removal of caffeine (>94%), trovafloxacin mesylate (>95%), and estradiol (93–95%), but had limited effectiveness for salicylic acid (39–56%).

Key words | anthracite, antibiotic, hormone, physical-chemical properties, sorption, zwitterions

Michael M. Bundy
MWH,
671 E Riverpark Ln, Ste 200,
Boise, ID 83706,
USA

William J. Doucette (corresponding author)
Laurie McNeill
Utah Water Research Laboratory,
Utah State University,
8200 Old Main Hill, Logan UT 84322-8200,
USA
E-mail: *doucette@cc.usu.edu*;
Lmcneill@cc.usu.edu

Jon F. Ericson
Pfizer Global Research & Development,
Eastern Point Road, Groton CT 06340,
USA
E-mail: *jon.f.ericson@pfizer.com*

INTRODUCTION

The detection of low-level, subtherapeutic concentrations of pharmaceuticals in surface and ground waters (e.g. Heberer *et al.* 1998; Seiler *et al.* 1999; Zuccato *et al.* 2000; Heberer 2002; Kolpin *et al.* 2002) has raised questions regarding the effectiveness of conventional drinking water treatment in the removal of these compounds (Breton & Boxall 2003).

While only a few isolated cases of pharmaceuticals being identified in drinking water have been reported (e.g. Heberer & Stan 1997), preliminary exposure assessments have often assumed that levels detected in surface waters and WWTP effluents are the levels that one would find in drinking water. This is a worst-case scenario since it is expected that additional removal of pharmaceuticals would occur during drinking water treatment. However, until quantitative information regarding the extent of pharmaceutical removal during drinking water treatment is generated, it is likely that this conservative scenario will continue to be used.

Treatment prior to human consumption depends on the source water quality. Conventional surface water treatment typically consists of coagulation using alum, ferric chloride, and/or synthetic polymers, settling, filtration, and disinfection. Additional treatments, such as softening, chemical oxidation of organics, iron and manganese removal, and filtration with activated carbon may also be used (Droste 1997). Ground water sources are generally less treated than

doi: 10.2166/aqua.2007.091

surface water sources and may only be subjected to aeration and disinfection prior to consumption.

During coagulation/flocculation, sedimentation, and filtration, sorption has the potential to remove compounds from the aqueous phase. However, the extent of sorption is a function of compound charge and hydrophobicity and properties of the solid phase (e.g. Adams *et al.* 2002; Ternes *et al.* 2002; Lorphensri *et al.* 2006; Vieno *et al.* 2006). Granular activated carbon (GAC) treatment has been shown to remove pharmaceuticals (Ternes *et al.* 2002) but the presence of more polar or larger molecular weight natural organic compounds may impact removal (Snyder *et al.* 2003). Disinfection also has the potential to remove pharmaceuticals through oxidation (e.g. Adams *et al.* 2002; Chamberlain & Adams 2006; Hua *et al.* 2006).

The focus of the project was to design and construct a bench-scale drinking water treatment plant (DWTP) that could be used to provide a practical approach to quantitatively determine the impact of conventional drinking water treatment processes on removal of pharmaceutical and pharmaceutical-like compounds. The bench-scale DWTP was used to evaluate the potential removal of four compounds (caffeine, trovafloxacin mesylate, 17-β estradiol, and salicylic acid (Table 1), under treatments of flocculation, sedimentation, dual-media filtration (anthracite and sand), GAC, and chlorine disinfection. The compounds were selected to represent a variety of chemicals in terms of charge (positive, negative, zwitterion, and neutral) and sorption within DWTPs. Caffeine and estradiol have also been observed in surface waters (Kolpin *et al.* 2002). Radiolabeled compounds were used to provide good sensitivity within the small sample volume constraints of the system and to enable a more rigorous mass balance analysis by enabling the direct analysis of the solid phases.

MATERIALS

Bench-scale plant design

The principal considerations for the design of the bench-scale drinking water system were that it occupy minimum bench space (<1.5 linear meters); have a low volume (6–7 L) to minimize hazardous waste generation when using

Table 1 | Test chemical properties

Compound (CAS #)	Formula	Test Conc. (μg/L)	Aqueous Solubility (mg/L)	pK_a	Log K_{ow}	Charge at pH = 8	Uses
Caffeine (58-08-2)	$C_8H_{10}N_4O_2$	1.0	2100[a]	0.61[a], 3.6[b]	−0.07[d]	Neutral	Used in combination with aspirin, acetaminophen, and various antihistamines; key ingredient in beverages
Trovafloxacin Mesylate (147059-75-4)	$C_{20}H_{15}F_3N_4OCH_3SO_3$	38	50[c]	4.4, 9.6[c]	1.9[c]	+/−	Antibiotic
17b-Estradiol (50-28-2)	$C_{18}H_{24}O_2$	1.0	3.6[c]	10.7[c]	4.01[c]	Neutral	Hormone replacement therapy; prevention of bone fractures associated with osteoporosis.
Salicylic Acid (69-72-7)	HOC_6H_4COOH	3.0	1800[c]	2.97, 13.9[c]	2.26[e] (neutral form)	–	Production of aspirin; acne and wart treatment

[a]Handbook of Chemistry and Physics.
[b]Estimated using SPARC (http://ibmlc2.chem.uga.edu/sparc/index.cfm).
[c]Howard & Meylan 1997.
[d]Lewis & Archer 1979.
[e]log K_{ow} for neutral form (Hansch & Anderson 1967)

radiolabeled chemicals; use gravity flow to move water through each treatment unit; have the ability to easily add or subtract treatment units; and operate, where possible, within recommended parameters of a full-scale system. Based on these constraints, a design flow rate of 30 ml/min was used to construct a bench-scale DWTP consisting of the following treatment units: rapid mix, coagulation/flocculation, sedimentation, dual-media filtration, GAC filtration, and disinfection (Figure 1). Plexiglas® (or Lexan®) was used in construction because it is transparent, durable, and lightweight. A summary of the bench-scale DWTP specifications is presented in Table 2. A complete description of the plant construction is provided by Bundy (2003). The bench-scale plant was designed to match the operating parameters of a typical full-scale conventional drinking water treatment plant, however, because of the low flow rate this was not possible for all factors (Table 3).

Test compounds

The four compounds evaluated in this study were caffeine, trovafloxacin mesylate, 17β-estradiol, and salicylic acid (Table 1). These compounds were selected to represent a range of pharmaceutical-type compounds in terms of charge (positive, negative, zwitterions, and neutral) and hydrophobicity that could impact removal via sorption during drinking water treatment. Unlabeled and ^{14}C-labeled caffeine (purity 98%, specific activity 53 mCi/mmol) and salicylic acid (purity 98%, specific activity 5.9 mCi/mmol), and unlabeled and ^{3}H-labeled estradiol (purity NA, specific activity 2900 mCi/mmol) were obtained from Sigma Chemical (St. Louis, MO, USA). Unlabeled and ^{14}C-labeled trovafloxacin mesylate (purity 98%, specific activity 0.24 mCi/mg) were kindly donated by Pfizer Global Research & Development. The chemical structures of the four compounds and location of each radiolabeled atom are illustrated in Figure 2. A summary of relevant physical/chemical properties for these compounds and the concentrations at which they were tested is provided in Table 1. The concentrations were based on environmental relevance and analytical constraints. The main analytical consideration was to use a low enough concentration to be environmentally relevant while still being able to detect the compound in the effluent if 99% were removed during treatment. Differences in test concentrations among the four compounds were due to the difference in the specific activities of the radiolabeled compounds. For estradiol, a combination of labeled and

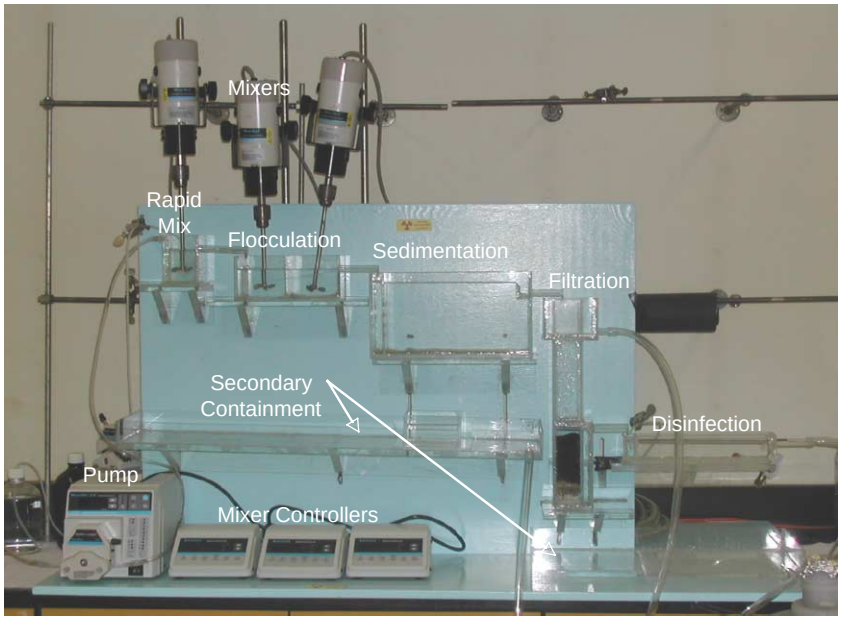

Figure 1 | Photograph of bench-scale drinking water treatment plant.

Table 2 | Bench-scale drinking water treatment plant design parameters

Process	Key parameters
Inlet reservoir	20 L carboy, impeller speed = 500 rpm
Rapid mix basin	6.4 × 6.4 × 6.6 cm, G = 96 sec^{-1}, impeller speed = 3 rps
Flocculation basins (2)	10.2 × 10.2 × 5.3 cm (each), impeller speed = 40 rpm, 20 rpm
Sedimentation basin	31.8 × 7.6 × 15.2 cm
Filter column	5.1 × 5.1 × 43.2 cm, 10.2 cm of anthracite, 2.5 cm sand
GAC filter	17.7 × 5.7 × 14.6 cm, Calgon Filtrasorb 100
Disinfection basin	30.5 × 3.8 × 3.2 cm, Cl_2 dose = 4.2 mg/L, t_{10} = 8 minutes

unlabeled compound was used. Estradiol and trovafloxacin mesylate were dissolved in ethanol for stock solutions. After chemical dosing, the amount of ethanol in the reservoir was less than 0.001%.

Source water (Logan River)

Logan River water (pH = 8.0, turbidity = 1 NTU, hardness = 200 mg/L $CaCO_3$, alkalinity = 150–200 mg/L $CaCO_3$) was used as the source water for all trials. Logan River sediment was added to increase the source water turbidity to approximately 10–15 NTU so that sufficient floc would be generated for sampling.

ANALYTICAL METHODS

Bromide

The concentration of bromide, used as a hydraulic tracer, was determined potentiometrically using an Orion® bromide ion selective electrode (ISE) in conjunction with an Orion® double-junction reference electrode and an Accumet® Model 50 pH meter with an expanded millivolt scale. Samples and standards (5 ml) were mixed with 10 ml Logan River water and 0.3 ml of ionic strength adjustor (5 M $NaNO_3$) prior to measurement. A continuing calibration check was performed a minimum of every 10 samples. The detection limit for bromide was approximately 0.8 mg/L.

Table 3 | Comparison between operating parameters for full-scale and bench-scale drinking water treatment plants

Process	Parameter	Typical full-scale Value	Bench-scale value
Rapid mix	Retention time	20–60 sec	9.3 min
Flocculation	Retention time	15–45 min	39.2 min
Flocculation	Alum dose (as $Al_2(SO_4)_3.18H_2O$)	1–50 mg/L	25 mg/L
Sedimentation	Surface loading rate	32–49 $m^3/m^2/d$	1.8 $m^3/m^2/d$
Sedimentation	Retention time	2–4 hr	2 hr
Sedimentation	Length:width ratio	3:1 to 5:1	4:1
Dual-media filtration	Filtration rate	7–20 m/hr	0.71 m/hr
Dual-media filtration	Anthracite:sand depth ratio	4:1	4:1
GAC filtration	Empty bed contact time	5–25 min	22 min
Disinfection	CT-value* (giardia)	15 mg-min/L	15 mg-min/L
Disinfection	CT-value* (viruses)	1 mg-min/L	15 mg-min/L

*CT value = disinfectant concentration (mg/L) times detention time (min).

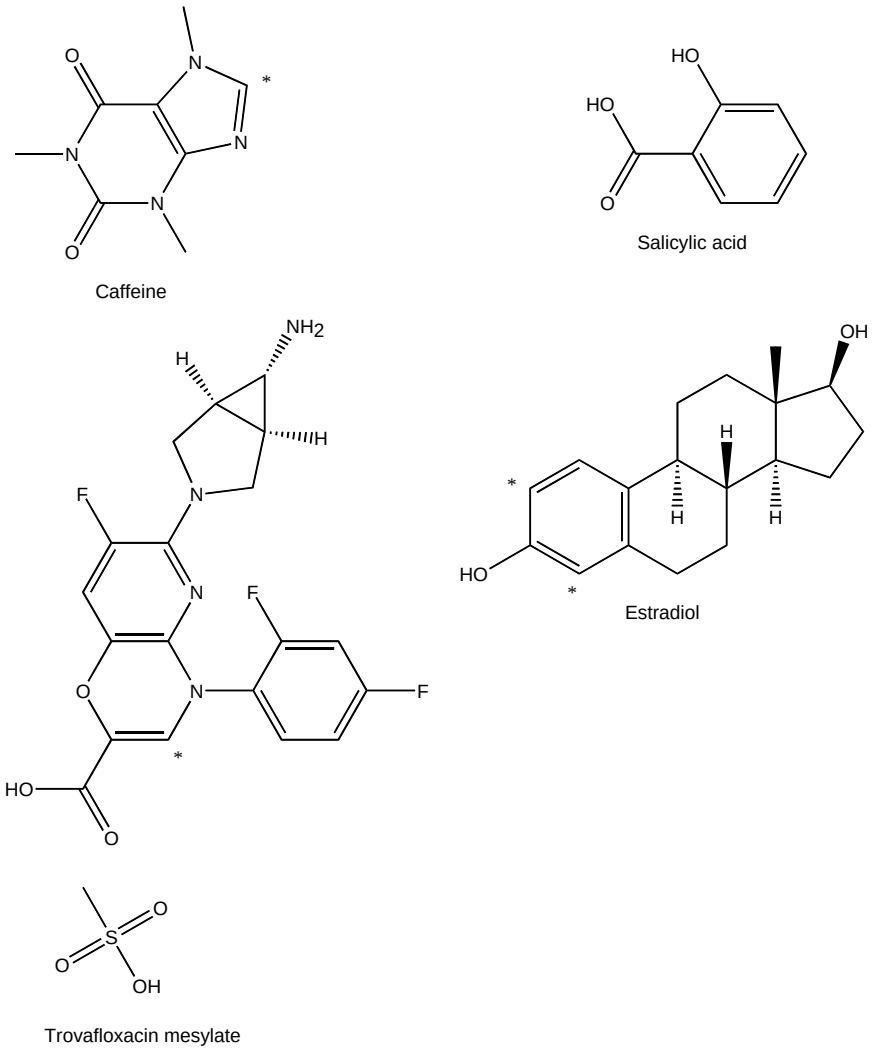

Figure 2 | Structures of test chemicals. Asterisk denotes location of labeled atom(s). Salicylic acid was uniformly ring labeled.

Turbidity

Influent and effluent samples were collected and analyzed periodically for turbidity to evaluate the performance of the DWTP. Turbidity was measured using a Monitek® TA1 Nephelometer standardized with a 7.0 or 82.5 NTU Gelex® Secondary Turbidity Standard.

Radiochemical analysis - aqueous samples

Aqueous samples of the influent and effluent of the total plant and each of the treatment units were collected in triplicate and analyzed for ^{14}C (caffeine, salicylic acid, trovafloxacin mesylate) or ^{3}H (estradiol) using a Beckman LS 6000SE Liquid Scintillation Counter (LSC). Five ml samples were collected directly into 20 ml scintillation vials containing 15 ml of Ready Gel® scintillation cocktail and analyzed by LSC. Detection limits, calculated as the concentration of labeled compound producing a response 3 times above the variation of the background signal (10 dpm), were 0.0033, 0.021, 0.0000085, and 1.9 μg/L for caffeine, salicylic acid, estradiol and trovafloxin mesylate, respectively. The very low detection limit for estradiol was due to the high specific activity of the labeled compound. Parent compound analysis was not conducted due to the sample volume limitations associated with the bench top system.

Radiochemical analysis – solid samples

A thermal oxidation procedure was used to determine the quantity of ^{14}C-labeled chemicals (caffeine, salicylic acid, trovafloxacin mesylate) associated with the solid media (floc, filter media). Samples of wet floc or media (0.4 – 1.0 g) were combusted at 925°C for four minutes using an R. J. Harvey Model OX-600 biological oxidizer. The evolved $^{14}CO_2$ was collected in 20 ml of a trapping solution consisting of 50% Ready Gel®:40% methanol:10% monoethanolamine (v:v:v). The trapping solution was analyzed by LSC. Spike recoveries for the thermal oxidation procedure were 95% or greater for all three ^{14}C-labeled compounds. Detection limits for the ^{14}C-labeled caffeine, salicylic acid, and trovafloxin mesylate were 0.033, 0.21, and 19 μg/kg, respectively.

For the ^{3}H-labeled 17-βestradiol, floc or media samples (1 g) were extracted three times with ethanol (1.5 ml) in a 10 ml centrifuge tube. After adding the sample and ethanol, each tube was agitated for 20 seconds using a Fisher Scientific mini vortex mixer. After mixing, the ethanol was separated from the solid by centrifugation at 5000 rpm for 7.5 minutes then decanted directly into a pre-weighed, 20 ml scintillation vial. After the third extraction, the scintillation vials were weighed to determine the total volume of ethanol recovered and analyzed by LSC after addition of 15.5 ml Ready Gel® scintillation cocktail. The detection limit for the ^{3}H-labeled estradiol was 0.00085 μg/kg.

Experimental design

For each compound, three trials were conducted: 1) blank DWTP, 2) DWTP without GAC filtration, and 3) DWTP with GAC filtration. In between each test, the system was rinsed once with water and three times with methanol, and the rinses monitored with LSC to ensure that activity was below background.

Blank DWTP trials

The blank DWTP trials were conducted to evaluate any losses to the system (i.e., sorption to system walls, volatilization) independent of treatment. In these trials, the dual-media filter and GAC basins were not initially filled. No coagulants or disinfectant were added; however, all the mixers were operated to simulate actual flow-through conditions. To pre-saturate the system walls and minimize any surface sorption, an unlabeled test chemical was run through the DWTP for approximately two days prior to the start of the test at the same concentration to be used in the fully operational system. After the pre-saturation period, the radiolabeled chemical and bromide tracer (40 mg/L) were added to the supply reservoir. Samples were frequently collected at the effluent of each basin and analyzed for radiolabel and bromide until breakthrough was achieved, approximately 11 hours.

DWTP without GAC filtration

The same approach used in the blank DWTP trials was followed except that the treatment units were operational, excluding GAC filtration. Aluminum sulfate (25 mg/L) was used as the coagulant and household bleach was used as the disinfectant (2 mg/L residual). The filter housing was packed with anthracite and sand. The system was pre-saturated with unlabeled compound prior to the introduction of the radiolabeled chemical and bromide tracer as previously explained. Samples were collected periodically from the effluent of each treatment unit and analyzed for bromide and radiolabel. Turbidity samples were also periodically taken from the reservoir, sedimentation basin, and plant effluent to evaluate system performance.

After the breakthrough (about 11 hours), bromide addition to the supply water was stopped. Influent and effluent samples continued to be collected for radiolabel analysis for another 24 – 28 hours (seven to eight system volumes). Samples of the filter media and floc were also collected and analyzed for radiolabel.

DWTP with GAC filtration

The GAC trial was conducted like the non-GAC trial with the addition of the GAC treatment basin in between the dual media filter and chlorine disinfection units. Also, no bromide tracer was added to the source water since preliminary batch tests showed significant sorption to the GAC. Floc and filter media samples were also collected as previously described.

Data analysis

Plots of relative concentrations (C/C_o) versus time (x-axis) were generated for bromide and each test compound. For bromide, caffeine, trovafloxacin mesylate, and estradiol, C_o was calculated by taking an average of all the measured reservoir concentrations throughout testing. However, because the concentration of salicylic acid in the source reservoir decreased over time, only the initial measurements were used in salicylic acid tests.

Data from trials with and without GAC were evaluated in order to determine the amount of compound removal associated with each treatment process. After steady state was approached (approximately 11 hours), seven sets of paired effluent and influent samples that were collected within minutes of one another were taken over a period of several hours. Each pair of samples was compared using a paired t-test with 95% confidence intervals. For each treatment process that showed statistically significant removals, the 95% confidence intervals were used to calculate an overall percent removal range.

Operational distribution coefficients associated with the solid phases (floc and filter media) were determined for each of the chemicals by collecting samples of solid and water at the same time during the appropriate trial. Distribution coefficients (L/kg) were calculated by dividing the chemical concentration in the solid phase (mg/kg, dry weight basis) by the aqueous phase concentration (mg/L).

Radiolabel mass recoveries were performed for each test by summing the mass of radiolabel in solution (in sample aliquots removed for analysis, liquid left in the system at test end, source water unused in the reservoir, and liquid leaving the system in the effluent) and radiolabel sorbed to the floc and filter media. The total mass of radiolabel associated with solid materials was calculated by extrapolating the analyzed media concentrations to the total media used in the system. The mass in the effluent was calculated by integrating the area under the plant effluent curve. It should be noted that analysis by LSC does not provide any information on compound transformation within the system.

RESULTS AND DISCUSSION

Blank system trials

Blank system trials were performed to determine if there was any significant loss of the test compounds by non-treatment processes (i.e., sorption to the system walls, volatilization). Breakthrough curves for the bromide tracer and the four test compounds (Figure 3 shows example for caffeine) showed

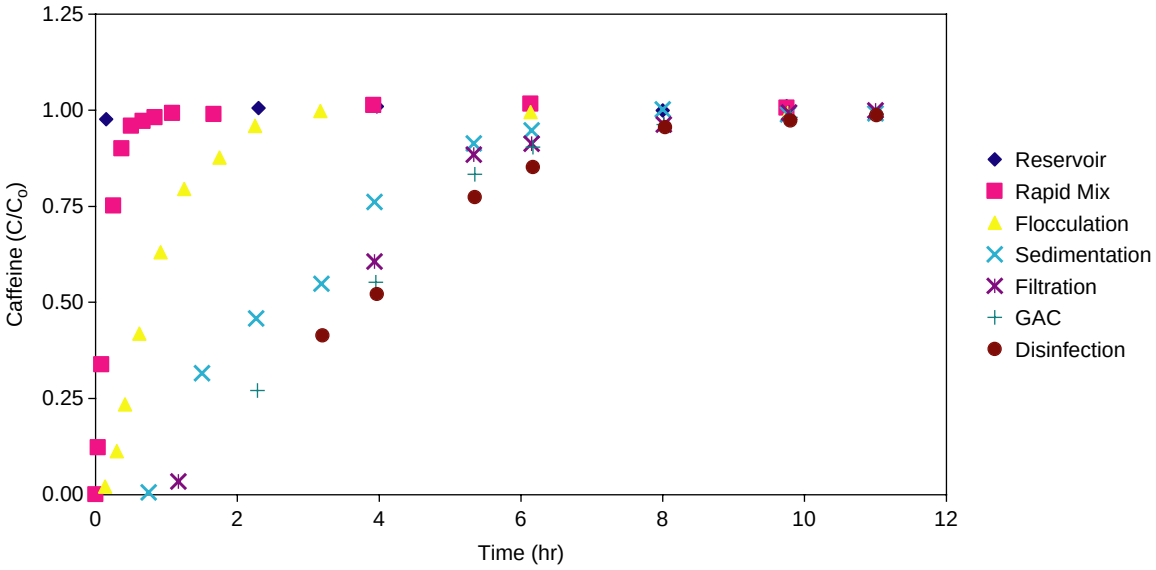

Figure 3 | Breakthrough curves for caffeine in blank system.

similar behavior, except for salicylic acid that seemed to be removed from the system. A second blank system trial conducted for salicylic acid verified the behavior observed in the first trial. Mass recoveries (Table 4) were essentially complete (99–104%), apart from salicylic acid (59%). Subsequent microcosm experiments compared reactors containing Logan River water and ^{14}C-salicylic acid with and without the bacteriostatic agent sodium azide. The reactor without azide showed a 30% loss of salicylic acid over a seven-day period, while the reactor with azide showed no loss. A further mass balance analysis was performed by subtracting the mass leaving and remaining in each treatment unit from the total mass of salicylic acid entering each unit. Most of the loss took place in the reservoir followed by the flocculation/sedimentation process, where contact times between the river water and salicylic acid were longest. These results are consistent with the hypothesis that biodegradation is the primary loss mechanism for salicylic acid in the blank system. Because of the decrease of source concentration over time for salicylic acid, mass balances on each treatment process were calculated by integrating the areas under the effluent curves of the reservoir, sedimentation basin, dual-media filter, GAC filter, and disinfection basin. The results were compared to determine how much compound was removed in each treatment process.

DWTP without GAC filtration

DWTP influent turbidities ranged from 2 to 16 NTU with an average for all test runs of approximately 9 NTU. The turbidity of the sedimentation basin effluent ranged from 0.6 to 1.0 NTU, the filter effluent did not exceed 0.3 NTU, and the average plant effluent was less than 0.1 NTU.

For caffeine, paired t-test comparisons (95% confidence interval) between paired plant inlet and outlet concentrations show a total removal of between 3.4 and 12.7% and that statistically significant removals only occurred during the filtration process (0.62 to 5.3%) (Table 5). The mass recovery data (Table 4) show that 90.8% of the ^{14}C introduced into the plant left the system in the effluent, 0.4% of the mass was found in the floc, 1.3% in the filter media, and about 6% was associated with the water remaining in the various basins at the end of testing. Again, it should be noted that the radiolabel analysis does not indicate whether the caffeine (or other chemicals) was transformed during the treatment process.

Caffeine distribution coefficients (Table 6) for anthracite and sand were determined to be 3.3 ± 0.2 L/kg and 1.6 ± 0.2 L/kg, respectively, while the value for the floc was 112 ± 10 L/kg (mean of triplicate determinations $\pm$ standard deviation). Despite the higher distribution coefficient for the floc, the sand/anthracite filter was responsible

Table 4 | Mass recoveries (%) for blank, non-GAC, and GAC trials from radiolabel analysis

	Caffeine			Trovafloxacin mesylate			Estradiol			Salicylic acid		
	Blank	No GAC	GAC	Blank	No GAC	GAC	Blank	No GAC	GAC	Blank	No GAC	GAC
Basins	30.9	6.6	7.6	34.2	9.0	8.2	33.5	10.0	9.4	18.5	6.7	7.0
Reservoir	0.0	0.0	3.7	0.0	0.0	3.0	0.0	1.9	1.1	0.0	0.0	1.9
Floc	NA	0.4	0.2	NA	11.2	7.9	NA	0.7	0.5	NA	12.7	14.6
Filter media	NA	1.3	1.7	NA	6.9	6.5	NA	1.9	1.2	NA	2.2	13.7
GAC	NA	NA	88.1	NA	NA	101.0	NA	NA	15.1 *	NA	NA	6.6
Samples	1.1	0.8	0.5	1.4	0.5	0.5	1.2	0.6	0.5	0.8	0.1	0.4
Effluent	67.3	90.8	0.3	68.4	70.9	1.0	67.5	87.4	3.5	39.5	53.5	32.0
Total	99.3	99.9	102.1	104.0	98.5	128.1	102.1	102.4	31.3	58.7	75.2	76.2

NA = Not Applicable.
*Estradiol recoveries from GAC were low (see text).

Table 5 | Percent removal (95% confidence intervals) for DWTP trials without and with GAC based on paired influent and effluent samples

	Caffeine		Trovafloxacin mesylate		Estradiol		Salicylic Acid[+]	
	No GAC	GAC	No GAC	GAC	No GAC	GAC	No GAC	GAC
Flocculation/ Sedimentation	0 *	2.8–6.1	0	7.5–17.8	0	0.5–6.0	2.7–13.7	20.0–33.8
Dual media filtration	0.6–5.3	0	3.3–27.1	4.2–10.2	2.7–7.7	0	20.8–30.2	9.9–18.2
GAC filtration	NA	92.0–97.4	NA	76.6–81.4	NA	89.1–95.1	NA	5.8–8.5
Disinfection	0	0–0.3	0.5–8.6	0	0	0	0	0–1.6
Total	3.4–12.7	>94	20.5–30.8	>95	6.9–11.5	92.9– > 97	31.1–38.6	38.8–59.1

*"0" means the removal was not statistically significant at 95% confidence.
[+]Approximately 25–40% of salicylic acid was lost to mineralization.

for more caffeine removal because of its greater mass. Assuming that most of the 6% of caffeine remaining in the basins would pass through the system untreated, the total removal of caffeine based on the mass recovery analysis is about 5%, which is within the statistical range of values determined directly from the influent and effluent samples.

For the zwitterion trovafloxacin mesylate, a total removal of 20.5 to 30.8% was calculated from the paired influent and effluent samples (Table 5) with statistically significant removals in the filtration (3.3 to 27.1%) and disinfection processes (0.53 to 8.6%). The mass recovery data (Table 5) yielded similar results (20 to 30% total removal) with 11.2 and 6.9% of the total ^{14}C used associated with the floc and filter media, respectively. Even though significant removals of trovafloxacin mesylate in the flocculation/sedimentation process were not observed, the distribution coefficient for the floc (6500 ± 310 L/kg) was considerably larger than that observed for caffeine (Table 6) due to the interaction of the negatively charged portion of the zwitterion with the positively charged floc. The lack of significant removal in the flocculation/sedimentation process despite the relatively large distribution coefficient may be due to the relatively small amount of floc formed in the system or may indicate that the sorption of trovafloxacin mesylate to the floc is reversible. Distribution coefficients of 21.0 ± 8.7 L/kg (anthracite) and 12.6 ± 1.7 L/kg (sand) were also larger than those observed for caffeine (Table 6).

Estradiol breakthrough curves within the bench-scale DWTP were similar to caffeine, with total removals calculated from paired influent and effluent samples of 6.9 to 11.5% (Table 5). Most of this removal took place in the dual-media filter (2.7 to 7.7%). The overall mass recovery for estradiol was 102% and the mass balance analysis (Table 4) shows that only small amounts of the total label used were associated with the floc (0.7%) and filter media (1.9%).

Table 6 | Distribution coefficients (mean ± standard deviation) for triplicate samples of floc, sand, and anthracite

Compound	Floc/water distribution coefficient (L/kg)	Sand/water distribution coefficient (L/kg)	Anthracite/water distribution coefficient (L/kg)
Caffeine	112 ± 9.7	1.6 ± 0.2	3.3 ± 0.2
Trovafloxacin Mesylate	6500 ± 310	12.6 ± 1.7	21.0 ± 8.7
Estradiol	295 ± 25.7	1.0 ± 0.2	5.5 ± 1.1
Salicylic Acid	6170 ± 1260	4.3 ± 0.7	7.5 ± 1.5

The distribution coefficients for estradiol were 295 ± 26 L/kg for the floc, 5.5 ± 1.1 for the anthracite, and 1.0 ± 0.2 for the sand (Table 6).

Based on the results of blank system trials, it was anticipated that a significant percentage of salicylic acid would be removed by mineralization during the non-GAC test. Paired t-tests showed 31.1 to 38.6% removal for the entire plant (Table 5) with statistically significant removals for flocculation/sedimentation (2.7 to 13.7%) and filtration (20.8 to 30.2%). Since the removal of salicylic acid in this test is influenced by biodegradation, all of the removal cannot be attributed to sorption as it was in the caffeine tests. The radiolabeled mass balance (Table 4) for this test indicates that approximately 25 - 40% of the label used went unaccounted for. The mass balance shows that 12.7% of the salicylic acid was associated with the floc while 2.2% was associated with the filter media. This corresponds to distribution coefficients of 6170 ± 1260 L/kg for the positively charged floc, 7.5 ± 1.5 L/kg for the anthracite, and 4.3 ± 0.7 L/kg for the sand (Table 6).

DWTP with GAC filtration

The addition of GAC filtration significantly enhanced the overall removals for caffeine, trovafloxacin mesylate, and estradiol, but only slightly increased the removal of salicylic acid. Based on a paired *t*-test analysis of the influent and effluent samples (Table 5), the overall removals increased from a range of 3.4–12.7% to >94% for caffeine, from 20.5–30.8% to >95% for trovafloxacin mesylate, and from 6.9–11.5% to 92.9– > 97% for estradiol. For the negatively charged salicylic acid, the addition of GAC only increased overall removals from 31.1–38.6% to 38.8–59.1%.

As shown in Table 4, mass recoveries were similar to those obtained in the trials without GAC except for estradiol. However, the low estradiol recovery in the GAC trials was likely not due to losses within the system but poor extraction efficiencies associated with the analysis of the GAC. A solvent (ethanol) extraction/LSC procedure was used for the ^{3}H-labeled estradiol instead of the combustion/LSC procedure used for the other ^{14}C-labeled compounds. Recoveries of estradiol spiked on GAC were reproducible but typically less than 50% while the combustion procedure yielded recoveries of greater than 95% for the other three ^{14}C-labeled compounds.

The distribution coefficients for the floc, sand, and anthracite were similar to those obtained in the non-GAC trials (data not shown).

SUMMARY AND CONCLUSIONS

A modular, bench-scale drinking water treatment plant (DWTP) was designed, constructed, and used to assess the potential removal of four pharmaceutical compounds (caffeine, trovafloxacin mesylate, 17-β estradiol and salicylic acid at 1 to 38 μg/L) under conventional drinking water treatments including flocculation, sedimentation, dual-media filtration (anthracite and sand), GAC, and chlorine disinfection. The plant was effective in lowering influent turbidity from 2 to 16 NTU to less than 1.0 NTU.

Blank system trials, performed to determine if there was any significant loss of the test compounds by non-treatment processes, found no loss of the compounds except for salicylic acid. Additional experiments conducted, subsequent to the blank system trials, showed that salicylic acid was rapidly biodegraded within the Logan River water used as the source water for all bench-scale studies.

Using conventional treatment without GAC, removals of approximately 3.4 to 13%, 21 to 31%, 31 to 39%, and 6.9 to 12% relative to a conservative tracer (Br^{-}) were observed for caffeine, trovafloxacin mesylate, salicylic acid, and estradiol, respectively. The addition of GAC treatment was found to significantly enhance the overall removal of caffeine, trovafloxacin mesylate, and estradiol with total removals greater than 94% but had limited impact on salicylic acid.

ACKNOWLEDGEMENTS

Funding for this project was provided by Chemical R&D, Pfizer Global Research & Development, Groton, CT.

REFERENCES

Adams, C., Wang, Y., Loftin, K. & Meyer, M. 2002 Removal of antibiotics from surface and distilled water in conventional water treatment processes. *Journal of Environmental Engineering-ASCE* **128**(3), 253–260.

Breton, R. & Boxall, A. 2003 Pharmaceuticals and personal care products in the environment: Regulatory drivers and research needs. *QSAR Comb. Sci.* **22**, 399–409.

Bundy, M. M. 2003 *Removal of Pharmaceutical-like Compounds by Drinking Water Treatment Processes Using a Laboratory System*. M.S. Thesis, Utah State University.

Chamberlain, E. & Adams, C. 2006 Oxidation of sulfonamides, macrolides, and carbadox with free chlorine and monochloramine. *Water Research* **40**(13), 2517–2526.

Droste, R. L. 1997 *Theory and Practice of Water and Wastewater Treatment*. John Wiley & Sons, Inc., New York.

Hansch, C. & Anderson, S. M. 1967 The Effect of intramolecular hydrophobic bonding on partition coefficients. *Journal of Organic Chemistry* **32**, 2583–2586.

Heberer, T. & Stan, H. J. 1997 Determination of clofibric acid and N-(phenylsulfonyl)-sarcosine in sewage, river and drinking water. *Intern. J. Environ. Anal. Chem.* **67**, 113–124.

Heberer, T., Schmidt-Baumler, K. & Stan, H.-J. 1998 Occurrence and distribution of organic contaminants in the aquatic system in Berlin. Part 1: Drug residues and other polar contaminants in Berlin surface and groundwater. *Acta Hydrochimica Et Hydrobiologica* **26**(5), 272–278.

Heberer, T. 2002 Occurrence, fate, and removal of pharmaceutical residues in the aquatic environment: A review of recent research data. *Toxicology Letters* **131**(1–2), 5–17.

Howard, P. H. & Meylan, W. M. (eds) 1997 *Handbook of Physical Properties of Organic Chemicals*. Lewis Publishers, New York, USA.

Hua, W. Y., Bennett, E. R. & Letcher, R. J. 2006 Ozone treatment and the depletion of detectable pharmaceuticals and atrazine herbicide in drinking water sourced from the upper Detroit River, Ontario, Canada. *Water Research* **40**(12), 2259–2266.

Kolpin, D. W., Furlong, E. T., Meyer, M. T., Thurman, E. M., Zaugg, S. D., Barber, L. B. & Buxton, H. T. 2002 Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999–2000: A national reconnaissance. *Environ. Sci. Technol.* **36**(6), 1202–1211.

Lewis, K. M. & Archer, R. D. 1979 pKa values of estrone, 17B-estradiol and 2-methoxyestrone. *Steroids* **34**(5), 485–499.

Lorphensri, O., Intravijit, J., Sabatini, D. A., Kibbey, T. C. G., Osathaphan, K. & Saiwan, C. 2006 Sorption of acetaminophen, 17 alpha-ethynyl estradiol, nalidixic acid, and norfloxacin to silica, alumina, and a hydrophobic medium. *Water Research* **40**(7), 1481–1491.

Seiler, R. L., Zaugg, S. D., Thomas, J. M. & Howcroft, D. L. 1999 Caffeine and pharmaceuticals as indicators of waste water contamination in wells. *Ground Water* **37**(3), 405–410.

Snyder, S. A., Westerhoff, P., Yoon, Y. & Sedlak, D. L. 2003 Pharmaceuticals, personal care products, and endocrine disruptors in water: Implications for the water industry. *Environmental Engineering Science* **20**(5), 449–469.

Ternes, T. A., Meisenheimer, M., McDowell, D., Sacher, F., Brauch, H., Haist-Gulde, B., Preuss, G., Wilme, U. & Zulei-Seibert, N. 2002 Removal of pharmaceuticals during drinking water treatment. *Environmental Science & Technology* **36**(17), 3855–3863.

Vieno, N., Tuhkanen, T. & Kronberg, L. 2006 Removal of pharmaceuticals in drinking water treatment: Effect of chemical coagulation. *Environmental Technology* **27**(2), 183–192.

Zuccato, E., Calamari, D., Natangelo, M. & Fanelli, R. 2000 Presence of therapeutic drugs in the environment. *The Lancet* **355**(9217), 1789–1790.

First received 22 October 2006; accepted in revised form 5 December 2006