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# Occurrence of Pharmaceuticals in River Water and Their Elimination in a Pilot-Scale Drinking Water Treatment Plant

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The occurrence of four beta blockers, one antiepileptic drug, one lipid regulator, four anti-inflammatories, and three fluoroquinolones was studied in a river receiving sewage effluents. All compounds but two of the fluoroquinolones were observed in the water above their limit of quantification concentrations. The highest concentrations (up to 107 ng L<sup>-1</sup>) of the compounds were measured during the winter months. The river water was passed to a pilot-scale drinking water treatment plant, and the elimination of the pharmaceuticals was followed during the treatment. The processes applied by the plant consisted of ferric salt coagulation, rapid sand filtration, ozonation, two-stage granular activated carbon filtration (GAC), and UV disinfection. Following the coagulation, sedimentation, and rapid sand filtration, the studied pharmaceuticals were found to be eliminated only by an average of 13%. An efficient elimination was found to take place during ozonation at an ozone dose of about 1 mg L<sup>-1</sup> (i.e., 0.2–0.4 mg of O<sub>3</sub>/mg of TOC). Following this treatment, the concentrations of the pharmaceuticals dropped to below the quantification limits with the exception of ciprofloxacin. Atenolol, sotalol, and ciprofloxacin, the most hydrophilic of the studied pharmaceuticals, were not fully eliminated during the GAC filtrations. All in all, the treatment train was found to very effectively eliminate the pharmaceuticals from the raw water. The only compound that was found to pass almost unaffected through all the treatment steps was ciprofloxacin.

## Introduction

Human pharmaceuticals and their metabolites are discharged by sewage treatment plants to river, lake, and sea water. Numerous studies have shown that the pharmaceutical residues are widespread in the aquatic environment (reviewed in ref 1). Surface waters are important raw water sources for drinking water treatment plants, and a few studies have shown that pharmaceuticals and/or their metabolites may pass the treatment process and end up in drinking water (2–5).

To protect human health, the drinking water treatment processes that are applied should as efficiently as possible hinder the anthropogenic compounds from entering drinking water. The main purpose of drinking water treatment plants using surface water as raw water is to remove natural organic matter (NOM), turbidity, and microorganisms from the water. Techniques, such as coagulation and sand filtration, that effectively reduce the amount of NOM and turbidity have been found to be inefficient in the elimination of pharmaceuticals (2, 3, 6–11). According to present knowledge, adsorption to activated carbon (either powered or granular), oxidation by ozone, and separation by membranes are the most promising methods for the elimination of pharmaceuticals (6–14).

The aim of this work was to study the elimination of 13 pharmaceuticals (Table 1) found in the River Vantaa (in southern Finland) by a treatment train applied in a pilot-scale drinking water treatment plant. The treatment train mimicked the full-scale treatment plant that supplies Helsinki City with drinking water. In the case that the primary raw water source of the Helsinki water treatment plant cannot be used, the River Vantaa water will serve as the drinking water source for the city. Very few studies have reported on the elimination of pharmaceuticals from contaminated natural water sources in pilot- or full-scale treatment plants (3, 6, 7, 9, 11). Further, the elimination of many of the compounds studied here has not been evaluated previously.

## Materials and Methods

**Raw Water.** The water of the River Vantaa was the raw water source of the pilot plant. Some of the water quality parameters at the time of sampling are listed in Table 2. The River Vantaa catchment area (1686 km<sup>2</sup>) is situated in densely populated southern Finland. The length of the river with its tributaries is over 300 km, the yearly average flow is 17 m<sup>3</sup> s<sup>-1</sup>, and the river drains into the Gulf of Finland. Almost 40% of the soil in the catchment area consists of clay. The main loadings of nutrients, particles, and organic matter to the river originate from agriculture, natural leaching, and 12 wastewater treatment plants, which release the treated wastewater to the river.

**Pilot-Scale Treatment Process.** The processes applied at the pilot-scale water treatment plant consisted of coagulation with ferric sulfate, flocculation, vertical sedimentation, rapid sand filtration (quartz sand or anthracite + quartz sand), ozonation, two-step granular activated carbon filtration, and UV disinfection (Figure 1).

The raw water was collected in containers where the water was passed through the pilot plant at flow rate of 0.1 m<sup>3</sup> h<sup>-1</sup>. Prior to the coagulation with ferric sulfate, the pH of the raw water was adjusted to 4.9–5.0 with either lime or sulfuric acid. The amount of ferric sulfate was calculated according to the amount of NOM (the amount determined as the KMnO<sub>4</sub> number) present in the raw water (Table 2) except in July 2005, when ferric sulfate was fed to the process according to the pH.

Following flocculation, vertical sedimentation, and rapid sand filtration (operated at a surface load of 12 m h<sup>-1</sup>), the pH was raised to 7.3. Ozone was produced continuously from compressed, dried air with an Argentox GLX 4 O<sub>3</sub> generator (maximum output 2 g of O<sub>3</sub> h<sup>-1</sup>). The ozonation unit consisted of three columns operating in series. The height of the columns was 4 m, and the diameter was 80 mm, giving a contact time of 10 min per column with a flow rate of 0.1 m<sup>3</sup> h<sup>-1</sup>. In the experiment carried out in July 2005, O<sub>3</sub> was applied only to the first column. In November 2005, January 2006,

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**TABLE 1. Studied Pharmaceuticals, Their Properties, and Limit of Quantification of the Analytical Method in Drinking (LOQ<sub>DW</sub>) and Surface (LOQ<sub>SW</sub>) Water**

Therapeutic class	Compound	Molecular structure	log K <sub>ow</sub> <sup>(15)</sup>	pK <sub>a</sub>	LOQ <sub>DW</sub> (ng L <sup>-1</sup> ) <sup>(21, 22)</sup>	LOQ <sub>SW</sub> (ng L <sup>-1</sup> ) <sup>(21, 22)</sup>
Beta blocker	Acebutolol		1.71	9.2 <sup>(17)</sup>	0.4	0.8
	Atenolol		0.16	9.6 <sup>(15)</sup>	6.5	11.8
	Metoprolol		1.69	9.7 <sup>(17)</sup>	2.2	3.8
	Sotalol		0.24	9.55 <sup>(18)</sup>	1.6	3.9
Antiepileptic	Carbamazepine		2.45	13.9 <sup>(19)</sup>	0.2	0.5
Lipid regulator	Bezafibrate		4.25	3.61 <sup>(16)</sup>	1.0	1.0
Antiphlogistic	Diclofenac		4.51	4.15 <sup>(15)</sup>	1.0	1.0
	Ibuprofen		3.97	4.91 <sup>(15)</sup>	1.0	1.0
	Ketoprofen		3.12	4.45 <sup>(15)</sup>	5.0	5.0
	Naproxen		3.18	4.15 <sup>(15)</sup>	5.0	5.0
Fluoroquinolone antibiotic	Ciprofloxacin		0.28	6.27 <sup>-COOH, (20)</sup> 8.87 <sup>=NH2+, (20)</sup>	8.4	24
	Norfloxacin		-1.03	6.26 <sup>-COOH, (20)</sup> 8.85 <sup>=NH2+, (20)</sup>	7.0	24
	Ofloxacin		-0.39	5.97 <sup>-COOH, (20)</sup> 7.65 <sup>=NH+, (20)</sup>	1.6	2.6

and April 2006, O<sub>3</sub> was applied to the first and second columns. The applied O<sub>3</sub> dose was adjusted according to the measured residual ozone amount in the outflow of the third column (in July 2005, the second column was used). The target residual was 0.3 mg of O<sub>3</sub> L<sup>-1</sup>. The O<sub>3</sub> residual was measured with a Digox-O online monitor and checked daily

by iodimetric titrations. The applied ozone doses ranged from 1.0 to 1.3 mg of O<sub>3</sub> L<sup>-1</sup> corresponding to about 0.2–0.4 mg of O<sub>3</sub>/mg of TOC (Table 2).

Ozonated water was pumped upstream to the first GAC column from which it flowed downstream to the second column. Each filter contained 0.03 m<sup>3</sup> (i.e., 12.5 kg) activated

**TABLE 2. Water Quality of Raw Water and Treatment Parameters in Pilot Plant Experiments**

	July 2005	November 2005	January 2006	April 2006
<b>Raw water</b>				
pH	7.3	7.6	7.3	7.5
temp (°C)	21	7.5	0.5	1.0
TOC (mg L <sup>-1</sup> )	8.6	15.3	12.4	8.9
KMnO <sub>4</sub> (mg L <sup>-1</sup> )	33	63	50	38
UV absorbance at 254 nm	0.308	1.183	0.590	0.503
turbidity (FTU)	7.2	78	11.7	31.2
alkalinity (mmol L <sup>-1</sup> )	1.12	0.92	0.91	0.75
flow (m <sup>3</sup> s <sup>-1</sup> )	0.8	6.5	4.9	11.0
<b>Treatment parameters</b>				
ferric sulfate dose (g m <sup>-3</sup> )	200	155	125	94
pH in coagulation	4.9–5.2	4.9–5.0	4.9	4.9
TOC after sand filtration (mg L <sup>-1</sup> )	4.5	3.2	3.1	3.4
ozone dose (mg of O <sub>3</sub> )	1.0	1.1	1.1	1.3
ozone dose (mg of O <sub>3</sub> / mg of TOC)	0.2	0.3	0.4	0.4
residual ozone (mg L <sup>-1</sup> )	0.2	0.19–0.26	0.37	0.34
pH in ozonation	7.3	7.4	7.3	7.4
GAC I: bed volumes treated <sup>a</sup>	60280	60410	60480	60600
GAC II: bed volumes treated <sup>a</sup>	234	367	435	570

<sup>a</sup> After the experiment.

carbon, and the empty bed contact time in each filter was 18 min. The carbons in both filters were of the type Chemviron Filtrasorb F400. The carbon in the first filter (referred to as GAC I) was taken from the full-scale treatment plant, where the carbon had been in operation for about 760 days, and about 60 000 bed volumes of water (corresponding to 115 m<sup>3</sup> water per kilogram of activated carbon) containing about 2.0 mg L<sup>-1</sup> TOC had passed the filter. Fresh carbon was used in the second filter (referred to as GAC II), and 167 bed volumes (i.e., 0.4 m<sup>3</sup> kg<sup>-1</sup>) of water had passed the filter prior to the experiments. GAC I was considered to be a biologically active filter, while GAC II worked as an adsorption filter. Following GAC filtration, the water was led to a Katadyn UV disinfection unit (type AR-14–72-D, power of 24 W) giving a UV dose of about 250 J m<sup>-2</sup>.

For the determination of pharmaceuticals, 1 L grab samples from sampling taps were taken from the raw water and from the pilot-scale water treatment plant following coagulation and sedimentation, rapid sand filtration, ozonation, both GAC filtrations, and UV disinfection. The residence time of the water through the pilot plant (see Figure 1) was considered in the sampling. The aim was to follow the same plume of water throughout the pilot plant.

**Analytical Methods.** Two previously developed procedures were used for the analysis of pharmaceuticals (21, 22). The procedures are depicted in Figure S1. Pharmaceuticals were separated from the aqueous media using solid-phase extraction (SPE). The SPE extracts were chromatographed on a C<sub>18</sub> column using an Agilent 1100 HPLC system (Agilent Technologies, Espoo, Finland), and the occurrence of pharmaceuticals was monitored by using a Quattro Micro triple-quadrupole mass spectrometer (Micromass, Manchester, U.K.) The mass spectrometer was equipped with an electrospray ionization source, and positive or negative ions were acquired in the multiple reaction monitoring mode.

Detailed information about the quality parameters of the method, such as recoveries, and a detailed description of the calibration is presented elsewhere (21, 22). Limits of quantification (LOQ) of the target pharmaceuticals in ground and

surface waters (LOQ<sub>GW</sub> and LOQ<sub>SW</sub>, respectively) are presented in Table 1. The LOQ<sub>SW</sub> was applied for the raw waters (TOC = 8.6–15.3 mg L<sup>-1</sup>) and LOQ<sub>GW</sub> for the samples after the purification processes (TOC < 4 mg L<sup>-1</sup>).

## Results and Discussion

**Raw Water Characteristics and Occurrence of Pharmaceuticals.** Raw water for the pilot plant was collected from the River Vantaa. The raw water was sampled in July 2005, November 2005, January 2006, and April 2006, and parameters describing the water characteristics at the time of sampling are listed in Table 2. The concentrations of pharmaceuticals were determined in these samples and in two additional samples collected in March 2006. In every sample, all the studied pharmaceuticals, but the fluoroquinolones, were detected above their LOQ (Table 3). Most of the compounds were found in concentrations above 10 ng L<sup>-1</sup>. The dominating pharmaceuticals were metoprolol, sotalol, carbamazepine, ibuprofen, and atenolol, whose concentration maxima varied from about 60 to 100 ng L<sup>-1</sup>. These are common concentration ranges that were reported for surface waters receiving sewage (reviewed in ref 1).

The highest concentration of pharmaceuticals was observed in the samples collected in March. This is most probably due to the high proportion of treated sewage effluents in the river (river flow rates 1.5–1.8 m<sup>3</sup> s<sup>-1</sup>) and to the slow rate by which the pharmaceuticals undergo transformation reactions at the conditions prevailing in winter-time. In November, January, and April, the higher water flow rate lowered the portion of sewage effluent in the river, and consequently, a decrease in the concentration of pharmaceuticals could be observed (Figure S3). In July, the flow rate and the portion of sewage effluent were approximately the same as in March, but the concentration of the pharmaceuticals was markedly lower in the July sample. This may be attributed to the higher rates of transformation of the pharmaceuticals in the river during summertime. Many of the studied compounds have been suggested to undergo phototransformation or biotransformation/-degradation in surface waters (23–28). Diclofenac, for example, has been proven to be readily photodegradable (28), and in our study, its concentration was 46–55 ng L<sup>-1</sup> in the March samples but only 10 ng L<sup>-1</sup> in the July sample. On the other hand, ibuprofen and carbamazepine, which do not undergo rapid phototransformation (23), were found at similar concentrations in both the July and the March samples. All in all, the results indicate that the highest risk for contamination of drinking water by pharmaceuticals present in the raw water source occurs during the winter months when the river flow rate is low.

**Elimination of Pharmaceuticals in the Pilot Plant. Coagulation and Sedimentation.** In the coagulation with ferric sulfate and the subsequent sedimentation, the elimination of the studied pharmaceuticals was marginal (Figure 2 and Tables S1–S11). Previously, coagulation had not been found to affect the concentration of pharmaceuticals in water (2, 3, 6–11). Coagulation primarily removes high molecular weight NOM (Figure S2) and micropollutants with a log *K*<sub>ow</sub> value > 5 (13). Many of the studied pharmaceuticals are ionic, and theoretically, they may adsorb to particles and to the flocs formed in the coagulation by electrostatic interactions. However, this seems not to take place since the elimination of the pharmaceuticals was on average only 3%. Only ciprofloxacin was eliminated to a higher degree (i.e., to 30%) during coagulation. However, this figure is based on only one measurement (April 2006) since in the other samples, the concentration of ciprofloxacin was near or below the LOQ.

**Rapid Sand Filtration.** Rapid sand filtration following coagulation and sedimentation eliminated only an additional

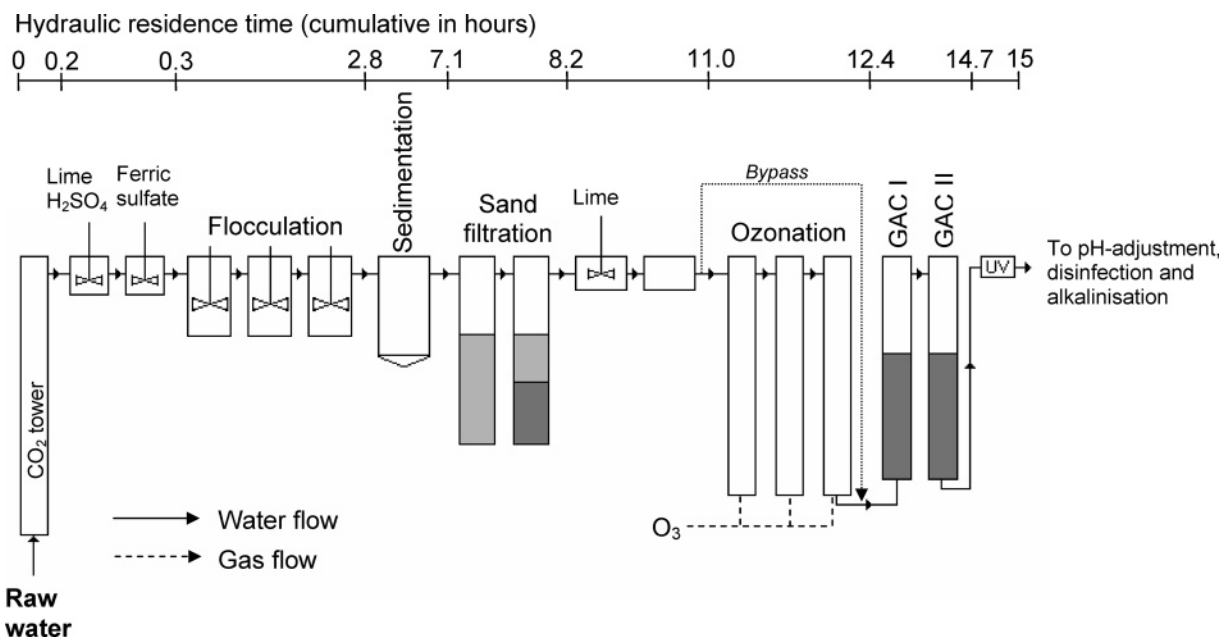


FIGURE 1. Process flow sheet of the pilot-scale water treatment plant.

TABLE 3. Concentrations of Studied Pharmaceuticals (ng L<sup>-1</sup>) at Sampling Days in the River Vantaa

	July 27, 2005 <sup>a</sup>	November 10, 2005 <sup>a</sup>	January 24, 2006 <sup>a</sup>	March 16, 2006	March 22, 2006	April 6, 2006 <sup>a</sup>
acebutolol	3	5	9	12	14	8
atenolol	17	19	26	55	47	33
metoprolol	39	42	59	101	107	64
sotalol	37	30	68	86	81	49
carbamazepine	66	32	21	80	75	32
bezafibrate	3	5	6	19	20	11
diclofenac	10	26	18	46	55	28
ibuprofen	56	14	12	21	37	69
ketoprofen	8	13	17	24	28	17
naproxen	na <sup>b</sup>	16	13	23	32	30
ciprofloxacin	<LOQ <sup>c</sup>	<LOQ	<LOQ	36	35	31
norfloxacin	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
ofloxacin	<LOQ	5	<LOQ	<LOQ	<LOQ	<LOQ

<sup>a</sup> Used as raw water in the pilot plant experiments. <sup>b</sup> na = not analyzed. <sup>c</sup> LOQ = limit of quantification.

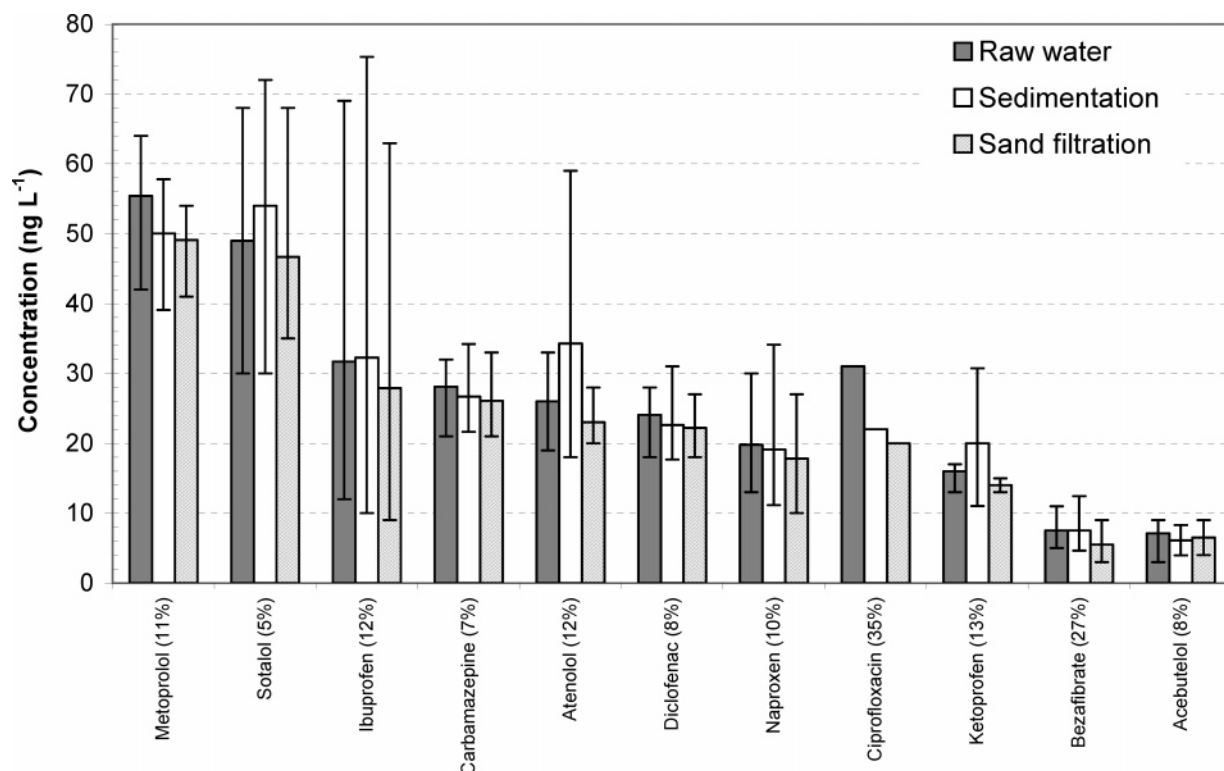
10% of the studied pharmaceuticals (Figure 2 and Tables S1–S11). Only bezafibrate exhibited a slightly higher elimination (average of 29%) during rapid sand filtration than the other compounds. Our results are consistent with the previously published ones, where rapid sand filtration was not found to result in a significant elimination of pharmaceuticals (3, 6, 11). The primary function of the rapid sand filter is to remove the excess floc after the sedimentation. Thus, the dissolved NOM measured as TOC was not reduced during the filtration step (Figure S2). It can be concluded that the elimination of the studied pharmaceuticals is negligible in treatment processes that consist only of metal salt coagulation, sedimentation, and rapid sand filtration.

**Ozonation.** Ozonation previously has been shown to be one of the most efficient techniques for the elimination of pharmaceuticals during wastewater and drinking water treatment (6, 8–11, 29, 30). In this study, the applied ozone doses (1.0–1.3 mg of O<sub>3</sub> L<sup>-1</sup>) were sufficiently high to result in an elimination of most of the studied compounds to below their LOQ values (Figure 3, Tables S1–S10). Ciprofloxacin was the most recalcitrant compound to ozonation as its concentration was reduced by an average of 16% only. Ibuprofen, naproxen, bezafibrate, and sotalol were occasionally detected in the ozonated water. In the case of ibuprofen and naproxen, the compounds occurred in the ozonated water only when they were found at elevated

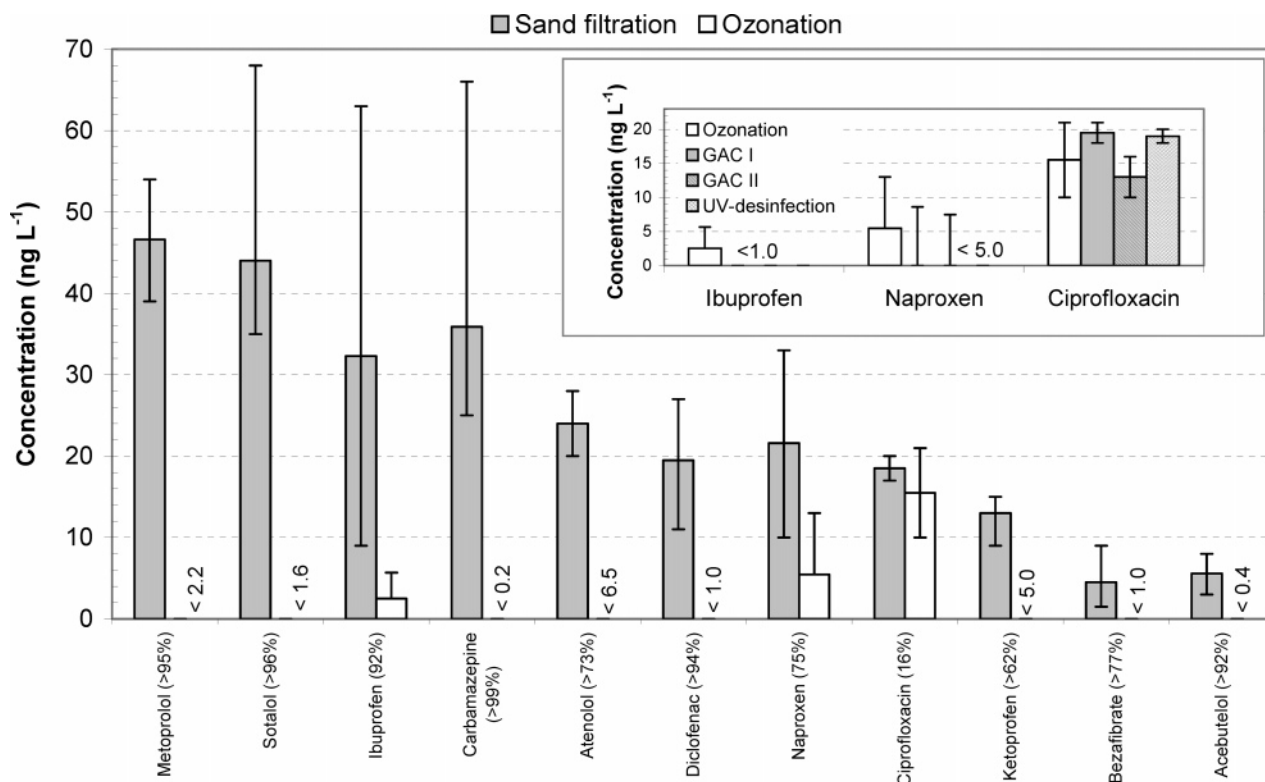
concentrations in the sand filtered water (Tables S8 and S10). On average, the elimination of ibuprofen and naproxen during ozonation was 92 and 75%, respectively. In the April 2006 experiment, sotalol was detected in the ozonated water, but it could not be accurately quantified (i.e., the concentration was <LOQ). Similarly, bezafibrate was detected after ozonation in the November 2005 experiment, but the concentration was <LOQ. On average, the elimination of sotalol and bezafibrate in ozonation was >96 and >77%, respectively.

During ozonation, the compounds may react with molecular ozone and with hydroxyl radicals (•OH) that are formed as the ozone decomposes. The rate of •OH formation depends greatly on the water matrix, especially the alkalinity of the water and the amount of TOC. Typically, ozone decomposes more rapidly in waters with a high TOC and low alkalinity (31). Reaction rate constants of ozone and of hydroxyl radicals with pharmaceuticals can be found in the literature, and the values can be used to predict the effectiveness of the oxidation (Table 4). Ozone is a very selective oxidant and reacts preferentially with unsaturated bonds and aromatic rings substituted by electron donor groups (e.g., OH, NH<sub>2</sub>, and OCH<sub>3</sub>) (31). Therefore, the reported rate constants with ozone vary drastically between the studied pharmaceuticals. According to von Gunten et al. (32), compounds with  $k_{O_3} > \sim 10^4 \text{ M}^{-1} \text{ s}^{-1}$  can be considered to





**FIGURE 2.** Concentrations of the studied pharmaceuticals in the raw water, after ferric coagulation and sedimentation and after the rapid sand filtration (on average with a variation of minimum and maximum values,  $n = 3$  except for ciprofloxacin  $n = 1$ ). The elimination of the compounds after the sand filtration is presented in parentheses (calculated from the average values).



**FIGURE 3.** Concentrations of the studied pharmaceuticals after the rapid sand filtration and after ozonation (on average with a variation of minimum and maximum values,  $n = 4$  except for ciprofloxacin  $n = 2$ ). In the inset, the concentrations in GAC filtrations and UV disinfection are presented for those compounds still present after ozonation. The values with a less than sign (<) correspond to below the limit of quantification. The elimination of the compounds in the ozonation is presented in parentheses (calculated from the average values).

react quickly with ozone and are rapidly oxidized with ozone doses typically applied in drinking water treatment (i.e., about

1 mg of  $O_3 L^{-1}$ ). Hydroxyl radicals, on the other hand, are unselective oxidants, and the rate constants of pharmaceu-

**TABLE 4. Apparent Rate Constants in Distilled Water Reported in the Literature for Reactions of Pharmaceuticals with Ozone ( $k_{O_3}$ ) and Hydroxyl Radicals ( $k_{OH}$ )<sup>a</sup>**

	apparent $k_{O_3}$ ( $10^5 \text{ M}^{-1} \text{ s}^{-1}$ )	apparent $k_{OH}$ ( $10^9 \text{ M}^{-1} \text{ s}^{-1}$ )
acebutolol	dnf <sup>b</sup>	dnf
atenolol	dnf	dnf
metoprolol	dnf	dnf
sotalol	dnf	dnf
carbamazepine	~3	$8.8 \pm 1.2$
bezafibrate	0.0059	$7.4 \pm 1.2$
diclofenac	~10	$7.5 \pm 1.5$
ibuprofen	0.000096	$7.4 \pm 1.2$
ketoprofen	dnf	dnf
naproxen	~2	$9.6 \pm 0.5$
ciprofloxacin	0.004 <sup>c</sup>	$4.1 \pm 0.3$
	0.075 <sup>d</sup>	
	0.19 <sup>e</sup>	
norfloxacin	dnf	dnf
ofloxacin	dnf	dnf

<sup>a</sup> From ref 12, except for naproxen (29) and ciprofloxacin (33). <sup>b</sup> dnf = data not found. <sup>c</sup> For diprotonated species. <sup>d</sup> For monoprotonated species at neutral pH. <sup>e</sup> For deprotonated species.

tics with the radicals are normally around  $10^9 \text{ M}^{-1} \text{ s}^{-1}$  (12, 29, 33). Some pharmaceuticals (e.g., ibuprofen) that react slowly with ozone are preferentially oxidized by hydroxyl radicals (12). Their elimination in the ozonation of drinking water is difficult to predict since the elimination depends strongly on the formation of hydroxyl radicals and thus on the water matrix (12).

Amine functionalities are structural components of beta blockers, fluoroquinolones, carbamazepine, and diclofenac, rendering the compounds highly reactive with respect to ozone (31). Carbamazepine and diclofenac have been extensively eliminated (>95%) already at ozone doses of 0.5 mg of  $\text{O}_3 \text{ L}^{-1}$  (11, 12). The concentrations of sotalol, atenolol, and metoprolol in an STP effluent have been reduced by >60% with an ozone dose of 5 mg  $\text{L}^{-1}$  (i.e., 0.2 mg of  $\text{O}_3/\text{mg}$  of TOC) (30). About 65% of ciprofloxacin has been eliminated from STP effluent by ozonation with a dose of 1.5 mg  $\text{L}^{-1}$  (i.e., 0.3 mg of  $\text{O}_3/\text{mg}$  of TOC) (33). Our results concerning carbamazepine, diclofenac, and beta blockers are consistent with the literature data, as these compounds were mainly reduced to <LOQ concentrations in the pilot plant with ozone doses of 1–1.3 mg  $\text{L}^{-1}$  (i.e., 0.2–0.4 mg of  $\text{O}_3/\text{mg}$  of TOC). However, ciprofloxacin was not in any significant degree eliminated by ozone in the pilot plant, and the reason for this is not fully understood. It has been suggested that ciprofloxacin reacts with ozone primarily via the amine group in the piperazine ring moiety and that the kinetic constant for the reaction is highly pH dependent (33). At low or neutral pH, the ozone rate constants of ciprofloxacin are lower than at higher pH (Table 4). The pH of the ozone treated water was 7.5, and at these conditions, ciprofloxacin is protonated, and consequently, the oxidation reaction is hampered.

Naproxen has a high apparent rate constant for reaction with ozone, and it has previously been shown that the compound is almost fully eliminated by ozonation with doses similar to those used in our study (14). In our study, naproxen was not fully eliminated in the July 2005 and November 2005 experiments, and this was probably due to the application of a too low dose of ozone (0.2–0.3 mg of  $\text{O}_3/\text{mg}$  of TOC). When the ozone dose was raised to 0.4 mg of  $\text{O}_3/\text{mg}$  of TOC, as in the January 2006 and April 2006 experiments, the compound could not be observed in the ozonated samples.

The incomplete elimination of ibuprofen was likely due to its low reactivity toward ozone (Table 3). The degree of elimination was slightly higher than reported in other studies

**TABLE 5. Concentrations of Pharmaceuticals After Unit Operations in the April 6, 2006 Experiment Where Sand Filtered Water Was Either Lead to Ozonation or Directly to Granular Activated Carbon (GAC) Filtration<sup>a</sup>**

	atenolol	sotalol	ciprofloxacin
raw water	33	49	31
sedimentation	59	60	22
sand filtration	20	35	20

	to ozonation	to GAC	to ozonation	to GAC	to ozonation	to GAC
ozonation	<6.5		<1.6 <sup>b</sup>		21	
GAC I	<6.5 <sup>b</sup>	<6.5	3.4	3.0	21	16
GAC II	<6.5	22	<1.6 <sup>b</sup>	1.6	16	24
UV des-infection	<6.5 <sup>b</sup>	<6.5	<1.6	<1.6	20	19

<sup>a</sup> Only those pharmaceuticals whose concentrations were >LOQ in GAC filtered water (without the ozonation) are presented. Values with a less than sign refer to <LOQ. Blank cells indicate that water was not ozonated. <sup>b</sup> Peak was detected in the chromatogram but could not be quantified.

where equal ozone doses have been applied in the ozonation of natural waters (77% in ref 12 and 51% in ref 14). One possible reason for this is that the residual ozone was not quenched after the sampling, whereas in the other studies, the residual ozone has been quenched after reaction times of 10–24 min (12, 14).

Also, bezafibrate has a relatively low apparent  $k_{O_3}$  value, but the determination of the extent of its oxidation during ozonation was not possible due to its low concentration (<10 ng  $\text{L}^{-1}$ ) in the sand filtered water. Previously, it has been found that ozone doses of 1–3 mg  $\text{L}^{-1}$  (i.e., 0.3–2.3 mg of  $\text{O}_3/\text{mg}$  of TOC) have been required for 70–80% elimination of bezafibrate (11, 12).

The objective of the ozonation of pharmaceuticals in water treatment is to transform the compound in such a way that it loses its biological activity. However, recent studies have shown that this objective may not always be achieved. For example, in the case of ciprofloxacin, ozone does not primarily react with the quinolone moiety, which is the part of the compound that is the major contributor to its pharmacological effect (33). Also, the risks connected to the recently identified oxidation products of carbamazepine and diclofenac are unknown (36, 37).

**GAC Filtration.** Following ozonation, the water was passed through a two-stage GAC filtration step. This treatment eliminated the residues of ibuprofen present in the ozonated water, but the residue of naproxen was still occasionally detected in the filtered water, however, at reduced concentrations (Figure 3 and Tables 5 and S6). The concentrations of sotalol, atenolol, and bezafibrate were <LOQ in the ozonated water, but the compounds could occasionally be detected in the GAC filtered water. Only marginal elimination of ciprofloxacin took place during the GAC filtrations (Figure 3).

In one experiment (April –2006), the ozonation was bypassed, and the water was allowed to pass directly from the rapid sand filter to the GAC filters (see Figure 1). In the GAC I and GAC II filtered water, ciprofloxacin and sotalol could be detected, while atenolol was found after the GAC II only (Table 5). The other compounds could not be detected after the GAC filtrations. The occasional reappearances of compounds in GAC filtered waters probably were caused by source variation or fluctuations in the performance of the pilot plant.

During GAC filtration, adsorption occurs mainly by hydrophobic interactions, but also ion exchange processes

may take place (13). Adsorption through hydrophobic interactions tends to increase with an increasing  $K_{ow}$  value of a substance (13). For example, the neutral pharmaceutical carbamazepine has been found to have a higher affinity to GAC as compared to ionic pharmaceuticals such as naproxen (38). Also, the amount of water treated with the carbon affects the breakthrough of the compounds (38). The more hydrophobic pharmaceuticals, such as carbamazepine, have been reported to be efficiently eliminated by GAC filtration even after treatment of >70 000 bed volumes of water (38). The more hydrophilic compounds, however, have been found to pass the GAC already after treatment of 2000–3000 bed volumes of water (38). The incomplete elimination observed for atenolol, sotalol, and ciprofloxacin during the GAC filtrations probably was caused by their high hydrophilicity (their log  $K_{ow}$  values were 0.16, 0.24, and 0.28, respectively).

Our results are consistent with the previous studies where GAC filtration has been found to be a viable tool for the elimination of pharmaceuticals from water (7, 8, 10, 11, 38). However, to achieve efficient elimination of pharmaceuticals in full-scale GAC filtration, one of the key factors is the regular regeneration of the carbon (38).

**UV Disinfection.** Most of the pharmaceuticals could not be detected in the GAC filtered water, and thus, any further elimination could not be established by UV treatment. But, low concentrations of ciprofloxacin, naproxen (Figure 3), and sotalol (Table S4) were found following the GAC filtration, and their elimination by UV treatment was studied. It was found that ciprofloxacin was not affected by UV irradiation, whereas the concentration of naproxen and sotalol was lowered, and the compounds were not detectable in the treated water. In one experiment, bezafibrate was found in the UV treated water, although it could not be detected in the GAC filtered water. This occurred during the November 2005 experiment, where bezafibrate was detected after ozonation and GAC I filtration, even though the compound could not be quantified (i.e., concentration was <LOQ). Thus, the occurrence of bezafibrate in the UV disinfected water at concentrations near its LOQ probably was due to source variation or fluctuation in the performance of the pilot plant. Even though many pharmaceuticals adsorb UV light, the UV intensity used for disinfection purposes was often too low to induce transformations in compounds (10, 13, 32), and therefore, it is likely that pharmaceuticals would pass the UV treatment more or less unaffected.

Overall, the treatment train in the studied pilot plant was very efficient in the elimination of compounds detected in the river water since after the water had passed the whole treatment train, the majority of the studied pharmaceuticals was eliminated to <LOQ concentrations. Only ciprofloxacin was found to pass almost unaffected through the pilot plant, and more work is needed where the fate of ciprofloxacin in treatment plants is studied more in depth. In general, pharmaceuticals have been detected in drinking water at extremely low concentrations (in the range of low nanograms per liter) as compared to their therapeutic doses (in the range of milligrams) (39). In our study, lifetime ingestion (70 years, 2 L day<sup>-1</sup> water) of ciprofloxacin via drinking water (concentration of 20 ng L<sup>-1</sup>) would be about 1 mg. This is 1000 times lower than the oral daily therapeutic dose of ciprofloxacin (1000 mg). However, the effects caused by chronic exposure to low concentrations of pharmaceuticals over a long period of time are unknown. Still, the risk for the consumers posed by a low concentration of pharmaceuticals in drinking water is most probably negligible.

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## Supporting Information Available

Analytical methods applied in the study as well as results (Figures S1–S3 and Tables S1–S11). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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