Occurrence and Fate of Carbamazepine, Clofibric Acid, Diclofenac, Ibuprofen, Ketoprofen, and Naproxen in Surface Waters

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Although various single-concentration measurements of pharmaceuticals are available in the literature, detailed information on the variation over time of the concentration and the load in wastewater effluents and rivers and on the fate of these compounds in the aquatic environment are lacking. We measured the concentrations of six pharmaceuticals, carbamazepine, clofibric acid, diclofenac, ibuprofen, ketoprofen, and naproxen, in the effluents of three wastewater treatment plants (WWTPs), in two rivers and in the water column of Lake Greifensee (Switzerland) over a time period of three months. In WWTP effluents, the concentrations reached 0.95 μg/L for carbamazepine, 0.06 μg/L for clofibric acid, 0.99 μg/L for diclofenac, 1.3 μg/L for ibuprofen, 0.18 μg/L for ketoprofen, and 2.6 μg/L for naproxen. The relative importance in terms of loads was carbamazepine, followed by diclofenac, naproxen, ibuprofen, clofibric acid, and ketoprofen. An overall removal rate of all these pharmaceuticals was estimated in surface waters, under real-world conditions (in a lake), using field measurements and modeling. Carbamazepine and clofibric acid were fairly persistent. Phototransformation was identified as the main elimination process of diclofenac in the lake water during the study period. With a relatively high sorption coefficient to particles, ibuprofen might be eliminated by sedimentation. For ketoprofen and naproxen, biodegradation and phototransformation might be elimination processes. For the first time, quantitative data regarding removal rates were determined in surface waters under real-world conditions. All these findings are important data for a risk assessment of these compounds in surface waters.

Introduction

Although pharmaceuticals are used in large quantities in modern society, their potential to reach surface waters and their impact on the environment have received little attention during the last three decades. However, since the 1980s, some investigations have been carried out on the occurrence and fate of pharmaceuticals in the environment (*1*). The majority of these field investigations focused on the determination of concentration levels of specific compounds in various compartments of the aquatic environment. Detectable concentrations of drugs or of their metabolites have then been reported in wastewater treatment plant (WWTP) effluents and natural waters (*1*−*3*). However, the data collected in such studies rarely provide quantitative information on the various processes that determine the fate of the compound in the system considered.

We investigated carbamazepine, an antiepileptic agent, clofibric acid, the metabolite of three lipid regulators, and diclofenac, ibuprofen, ketoprofen, and naproxen, which are analgesic/antiinflammatory drugs (Figure 1). All these compounds enter the surface waters, because they are only partially eliminated in wastewater treatment plants (ibuprofen showed the highest elimination rate (75−90%), carbamazepine the lowest (7%)) (*4*, *5*). The following behavior in surface waters is known; however, their behavior simultaneously evaluated in a real-world system is missing. In surface waters, clofibric acid, which was detected in several Swiss lakes and in the North Sea, has been described as a "persistent" compound (*6*, *7*). Carbamazepine also seems to be persistent: Sacher et al. (*8*) reported a permanent contamination in various German rivers, with relatively high concentrations compared to other drugs. Despite carbamazepine's absorbance of sunlight, Andreozzi et al. (*9*) observed only a slight elimination through phototransformation. Laboratory experiments with natural waters showed that phototransformation was also negligible for ibuprofen, whereas biodegradation appeared to be an important elimination process (*10*). For diclofenac, laboratory assays performed with lake water highlighted a high elimination by phototransformation and measurements in the lake revealed an efficient elimination process in the epilimnion (*11*, *12*). To our knowledge, no information on the fate of ketoprofen and naproxen is available in the literature.

We evaluated the occurrence and the behavior of these six pharmaceuticals in wastewater effluents, in rivers, and in a lake. Over a time period of three months, continuous concentration measurements were carried out in the effluents of three WWTPs, in two rivers, and in lake Greifensee in Switzerland (Figure 2). The goals were manifold: (i) to obtain representative results on the variation in the concentrations and loads of pharmaceuticals in WWTPs and in rivers, (ii) to get an overall view of the mass fluxes of the pharmaceuticals in a 130-km^2 large hydrological catchment area with ∼89 000 inhabitants, and (iii) to quantify overall removal rates of the compounds under "real-world" conditions in a lake using a combination of field data and computer modeling. Comparisons of the rates determined in our study with literature data provide detailed information on the processes that govern the fate of these compounds, which is essential for risk assessment.

Experimental Section

Chemical Standards. Carbamazepine, clofibric acid, diclofenac, ibuprofen, and ketoprofen were purchased from Sigma-Aldrich Chemie (Steinheim, Germany). Naproxen was obtained from Fluka AG (Buchs, Switzerland).

Field Study. From August 16, 1999, to October 22, 1999, an intensive sampling program was conducted (*13*) in the catchment area of Lake Greifensee (Figure 2). The study area is of ∼130 km^2 with ∼89 000 inhabitants. No pharmaceutical factories are in this area.

Wastewater Treatment Plants. The treatment in the three WWTPs investigated (WWTP of Moenchaltorf, Uster, and

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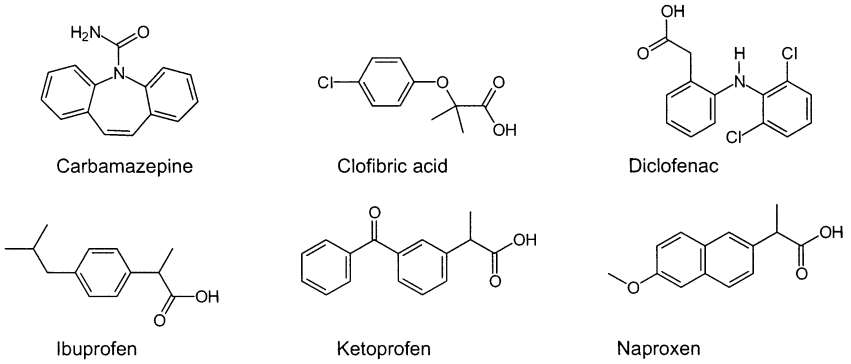

FIGURE 1. Chemical structures of the pharmaceuticals investigated.

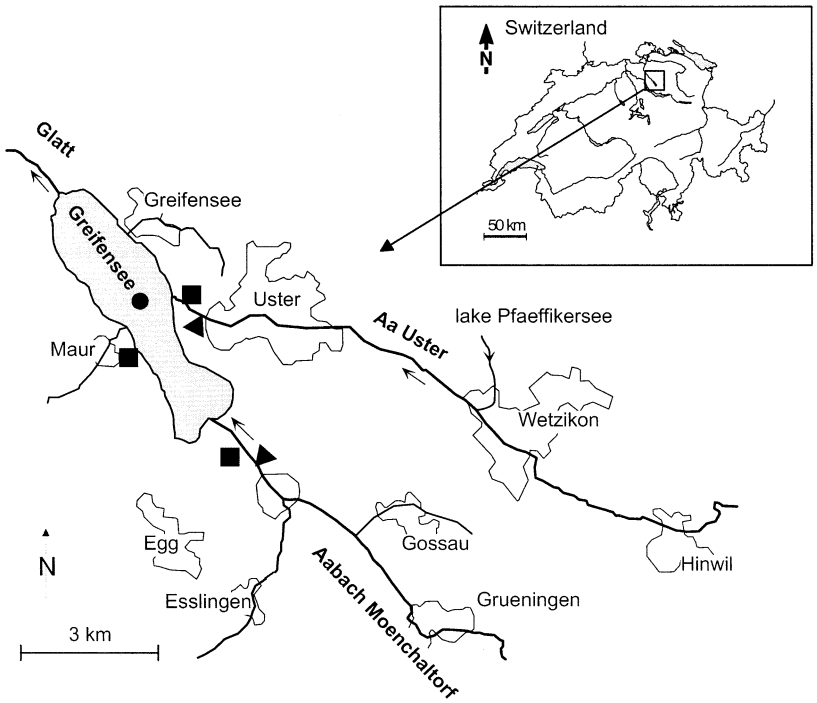

FIGURE 2. Sampling sites in the catchment area of Lake Greifensee: ■, effluents of wastewater treatment plants; ▲, sampling stations of the main tributaries; ●, water from the deepest point of the lake; polygons, village.

Maur; see squares in Figure 2) consists of three steps: mechanical clarification, biological treatment, and flocculation filtration. Under regular operation, all WWTPs remove 85% of influent *$KMnO_4$ demand* and 95% of the influent *biological oxygen demand* (BOD) and phosphorus load in minimum. As almost everywhere in Switzerland, the sewer system is equipped additionally with combined sewer overflows (CSOs), which can lead to a discharge of untreated wastewater directly into the watercourses during storm events.

From August 16 to October 22, 1999, 72-h flow proportional composite samples were collected from the effluent of all three WWTPs. The samples were kept inside the fixed installed sampler at 4 °C. Every third day, the samples were transported to the laboratory and mixed to weekly flow proportional samples.

Rivers. From August 16 to October 22, 1999, the two main tributaries Aa Uster and Aabach Moenchaltorf were sampled. Portable samplers (Manning Products) were installed (triangles in Figure 2) and the flow proportional sampling was controlled by an on-line flow measurement (water gauge—flow-calibrated installation). The samples were picked up every third day and combined to weekly volume proportional samples in the laboratory.

Lake Greifensee. Lake Greifensee is a small eutrophic lake (surface area 8.46 km^2; maximum depth 32 m) located 10 km east of Zürich, Switzerland (47°21′N−8°41′E). It is a holomictic lake with regular deep mixing in winter (December/March) and a mean water residence time of 408 days. The hydraulics and morphology of this lake have been described in detail elsewhere (*14*). The effluents of three municipal wastewater treatment plants (WWTP of Moenchaltorf, Uster, and Maur) are directly discharged into the epilimnion, and the two main tributaries, Aa Uster and Aabach Moenchaltorf, receive the discharge of four other WWTPs. The Glatt River is the only outflow of the lake.

From August 16 to October 22, 1999, samples were collected above the deepest point of the lake (black dot in Figure 2), at seven depths, with a stainless steel sampling bottle (Friedinger, Lucerne, Switzerland) from which the water was transferred to 1-L glass bottle. Vertical concentration profiles at this location were assumed to be representative for the whole lake due to the fast horizontal mixing compared to the slow vertical one (*14*).

Analytical Procedure. The analytical procedure used and its validation are described in detail elsewhere (*15*). Briefly, the samples were filtered in the laboratory (1 L, pH previously adjusted to pH 3), spiked with internal standards (mecoprop-

TABLE 1. Average Daily Load into the Lake of the Six Pharmaceuticals from the Three WWTP Effluents and the Two Rivers

	inhabitants serviced (persons)	daily load (g/day)					
		carbamazepine	clofibric acid	diclofenac	ibuprofen	ketoprofen	naproxen
WWTP							
Moenchaltorf	3100	0.24		0.56	0.20	0.01	1.34
Uster	34000	11.65	0.78	7.50	0.38	0.15	3.11
Maur	4500	1.16	0.01	1.18	0.74	0.10	1.61
load of the 3 WWTPs (g/day)		13.05	0.79	9.24	1.32	0.26	6.06
rivers							
Aabach Moenchaltorf		8.99		2.93	0.69		3.71
Aa Uster		7.18	2.06	6.71	4.06	0.15	1.93
load of the 2 rivers (g/day)		16.17	2.06	9.64	4.75	0.15	5.64
total load (g/day)		29.2	2.85	18.9	6.07	0.41	11.7

d_3, dihydrocarbamazepine), and enriched by solid-phase extraction on Waters Oasis HLB sorbent (Waters, Bergen op Zoom, The Netherlands). Carbamazepine was analyzed by GC/MS directly after reduction of the elution solvent, whereas the acidic pharmaceuticals were first derivatized with diazomethane and then analyzed by GC/MS. The GC/MS system consisted of a HRGC 8060, a MD 800 mass spectrometer, and an autosampler A200S, all Fisons Instruments (Beverly, MD).

Lake Model. Vertical concentration profiles were simulated using the computer software AQUASIM (*16*), which allows to construct mathematical models describing the dynamic behavior of chemicals in lakes. Lake Greifensee was represented with 64 horizontal boxes of 50-cm thickness. Complete horizontal homogeneity was assumed for each layer. In contrast, vertical mixing was explicitly described by turbulent diffusion with time- and depth-dependent diffusivities, which were calibrated by means of vertical temperature profiles.

Vertical profiles of all the pharmaceuticals were simulated with measured input mass fluxes calculated from the measured pharmaceuticals concentrations and water inflow of WWTP and rivers. They were determined by independently measured data: they were not fitted and thus served as good criteria for the validity of model assumptions. Flushing was considered as the sole elimination process or another elimination process was included. For diclofenac, a phototransformation process was implemented in order to evaluate the importance of this process compared to flushing.

Theoretical Background of the Phototransformation Process of Diclofenac. The pseudo-first-order rate constant for direct phototransformation of a compound of interest in a given volume element, $k_{p,direct}$ can be described by eq 1 (*17*), where λ is the wavelength of light, $\epsilon(\lambda)$ is the decadic

$$k_{p,direct} = 2.303 \int_{\lambda} \epsilon(\lambda)\Phi(\lambda)\,(dI(\lambda)/d\lambda)\,d\lambda \qquad (1)$$

molar extinction coefficient of the compound of interest (m^2 mol^{-1}), $\Phi(\lambda)$ is the reaction quantum yield (mol $einstein^{-1}$), and $dI(\lambda)/d\lambda$ is the irradiation spectrum (einstein m^{-2} s^{-1} nm^{-1}).

For the anionic form of diclofenac, a quantum yield of 0.22 was used (*18*). Calculations of rate constants for photochemical transformations under terrestrial sunlight were performed with the computer program GCSOLAR (*19*), which implements the use of eq 1 as a function of season, latitude, time of day, depth in water body, and ozone layer thickness, assuming a perfectly clear sky. Considering the pH (pH 8.6) of lake Greifensee during the field study, diclofenac is mainly present in its anionic form.

Daily ephemeris values for Dübendorf, Switzerland (47°24′N/8°37′E) were calculated (*20*) and ozone layer thickness values obtained from satellite data (*21*). Rate constants were calculated for a well-mixed water layer of 50-cm thickness for implementation into the lake model. To calculate effective diclofenac phototransformation rate constants, a further correction accounting for reduced sunlight transmission through the atmosphere was considered.

$$k_{p,direct}(calc) = k_{p,direct}(GCSOLAR)(W_{measured}/W_{theory}) \quad (2)$$

$W_{measured}$ is the measured global radiation at Dübendorf and W_{theory} is the daily averaged theoretical global radiation, calculated as described by Gerecke et al. (*22*).

Results and Discussion

Occurrence and Dynamic Input of the Drugs from WWTP Effluents into Surface Waters. Figure 3 shows the concentration time courses of the drugs in the effluents of the WWTPs, ranging from the limit of detection (1.5−10 ng/L, depending on the compound) to more than 3 μg/L. Pronounced fluctuations in the concentrations of all compounds were observed. The highest concentrations were found for naproxen and ibuprofen in the effluent of the WWTP of Maur (around October 15). Clofibric acid and ketoprofen always presented the lowest concentrations, not exceeding 60 or 180 ng/L, respectively (note the lower scale in the corresponding figures). During rain events, the increase in water flow was accompanied either by a parallel increase of the concentration (see Figure 3, naproxen in the WWTP of Moenchaltorf between the September 17 and October 4) or by a decrease of the concentration (see Figure 3, carbamazepine in WWTP of Maur, same time period). The first scenario may result from a lower efficiency of the WWTP during rain events or from a higher input to the WWTP coming from an efficient flushing of the sewer system. On the other hand, the measured carbamazepine concentration may decrease due to dilution. The very high increase in the concentration of naproxen, ibuprofen, and ketoprofen at the end of October during a low and constant water level can be explained by an increase in the consumption of these pharmaceuticals.

The average daily loads from the WWTPs are given in Table 1. Carbamazepine presented the highest total daily loads, ∼13 g/day, followed by diclofenac (9.24 g/day) and naproxen (6.06 g/day). For ibuprofen, clofibric acid, and ketoprofen, lower loads (between 0.26 and 1.32 g/day) were observed. The daily loads normalized per person varied in the different WWTPs by a factor of 4−70. This large factor illustrates the difficulty of assessing general information of the input of pharmaceuticals into surface waters from the numbers of inhabitants.

Occurrence, Concentration Variations, and Loads in Rivers. The pronounced variation in pharmaceutical concentrations observed in the rivers (Figure 4) can be explained by the variation of the pharmaceutical discharge from WWTPs

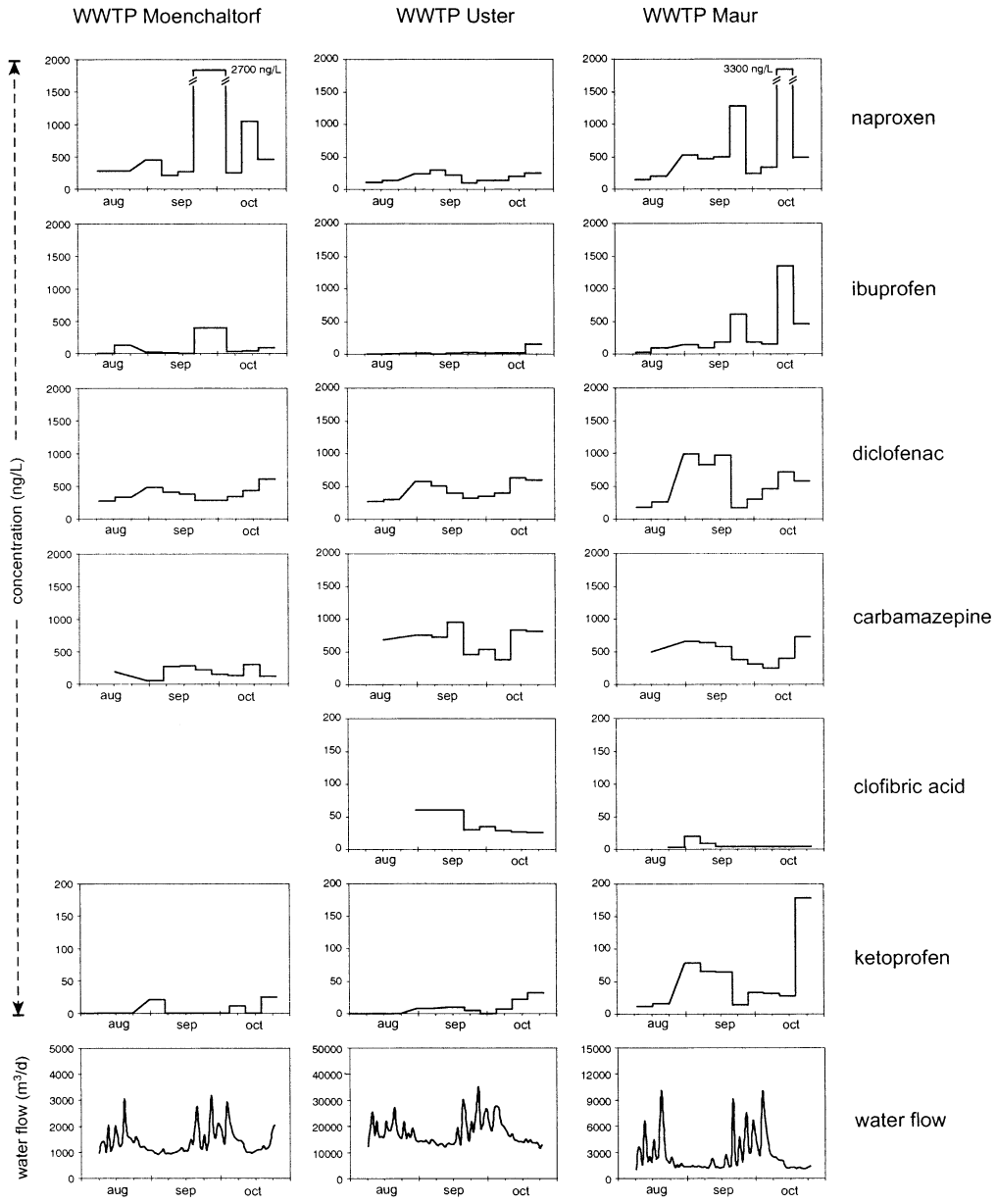

FIGURE 3. Continuous concentration measurements from August to October 1999 of the six pharmaceuticals and water flows in the effluents of three wastewater treatment plants directly discharging into the lake.

located upstream and by the variation of the streamflow. The concentrations in the rivers ranged from the limit of detection (ranging from 1.5 to 10 ng/L depending on the compound) to 400 ng/L. The highest concentrations were observed for naproxen and carbamazepine in the River Aabach Moenchaltorf (around October 15). Clofibric acid and ketoprofen could only be detected in the Aa Uster River and at very low concentrations, not exceeding 30 or 10 ng/L, respectively.

If we now evaluate the average daily loads into the lake from the rivers (Table 1), we see that, as observed in WWTP effluents, carbamazepine presented the highest load at ∼16 g/day, followed by diclofenac, (9.6 g/day), naproxen (5.6 g/day), and ibuprofen (4.75 g/day). For clofibric acid and ketoprofen, the loads were lower: 2 and 0.2 g/day, respectively. The measurement in WWTP effluents and in rivers illustrate clearly that drug concentrations vary drastically and that interpretations of studies with only a few grab samples must be considered very carefully.

Occurrence in the Water Column of Lake Greifensee. Four vertical concentration profiles were determined above the deepest point in the lake (Figure 5). In the hypolimnion, the concentrations of the pharmaceuticals remained rather constant over the whole sampling period. Carbamazepine presented the highest concentrations, ∼40 ng/L, whereas for the other compounds, a concentration of about 8−10 ng/L was measured. In the epilimnion, naproxen and diclofenac concentrations showed strong fluctuations. For example, despite the high input, the concentration of both compounds decreased from August to September. Such fluctuations indicate a removal process in the epilimnion. However, for a definitive statement on the behavior of each pharmaceutical in the lake, the variation of the input and the mixing conditions in the lake must be considered (see discussion below). Note that ketoprofen could not be detected in the lake water column (concentration lower than 1.5 ng/L). The lake content of the pharmaceuticals was quantified using the measured concentrations and the corresponding lake−layer volume. Similar amounts in the lake of ∼1 kg were determined for clofibric acid, diclofenac, ibuprofen, and naproxen whereas the amount of carbamazepine was ∼7 times higher (∼7 kg).

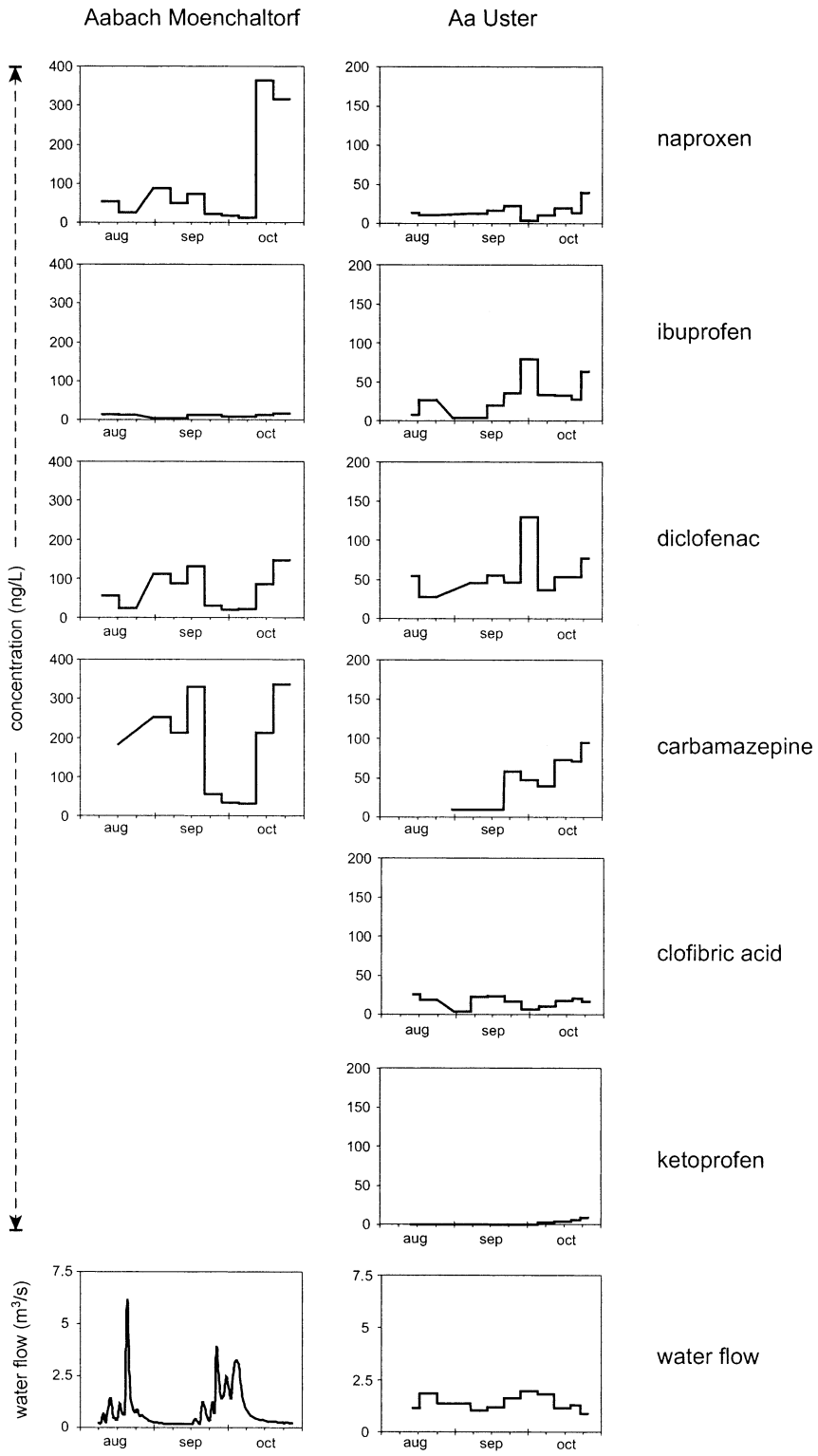

FIGURE 4. Continuous concentration measurements from August to October 1999 of the six pharmaceuticals and water flows in two rivers that receive wastewater from other four WWTPs.

Fate of the Pharmaceuticals in the Lake Greifensee. A simple mass balance (inflow − outflow of the lake) was established over the three-month study period (*14*). The total input of the compounds into the lake was defined as the sum of the input by the three WWTPs directly discharging into the lake and the two rivers (Aa Uster and Aabach Moenchaltorf). A continuous one-dimensional model, considering measured input, mixing, and elimination by flushing (see Experimental Section for details), was then used to simulate the vertical concentration profiles from August to October 1999 (except ketoprofen because the concentrations were below the detection limit). Based on the hydraulics data of the lake, a flushing rate of 0.006 day^{-1} was determined, which holds for all compounds. In a first step, we considered a scenario corresponding to a conservative behavior of the compounds, i.e., assuming flushing as the sole elimination process. The concentration profiles measured on August 16 were used as initial values for the calculations. The simulated

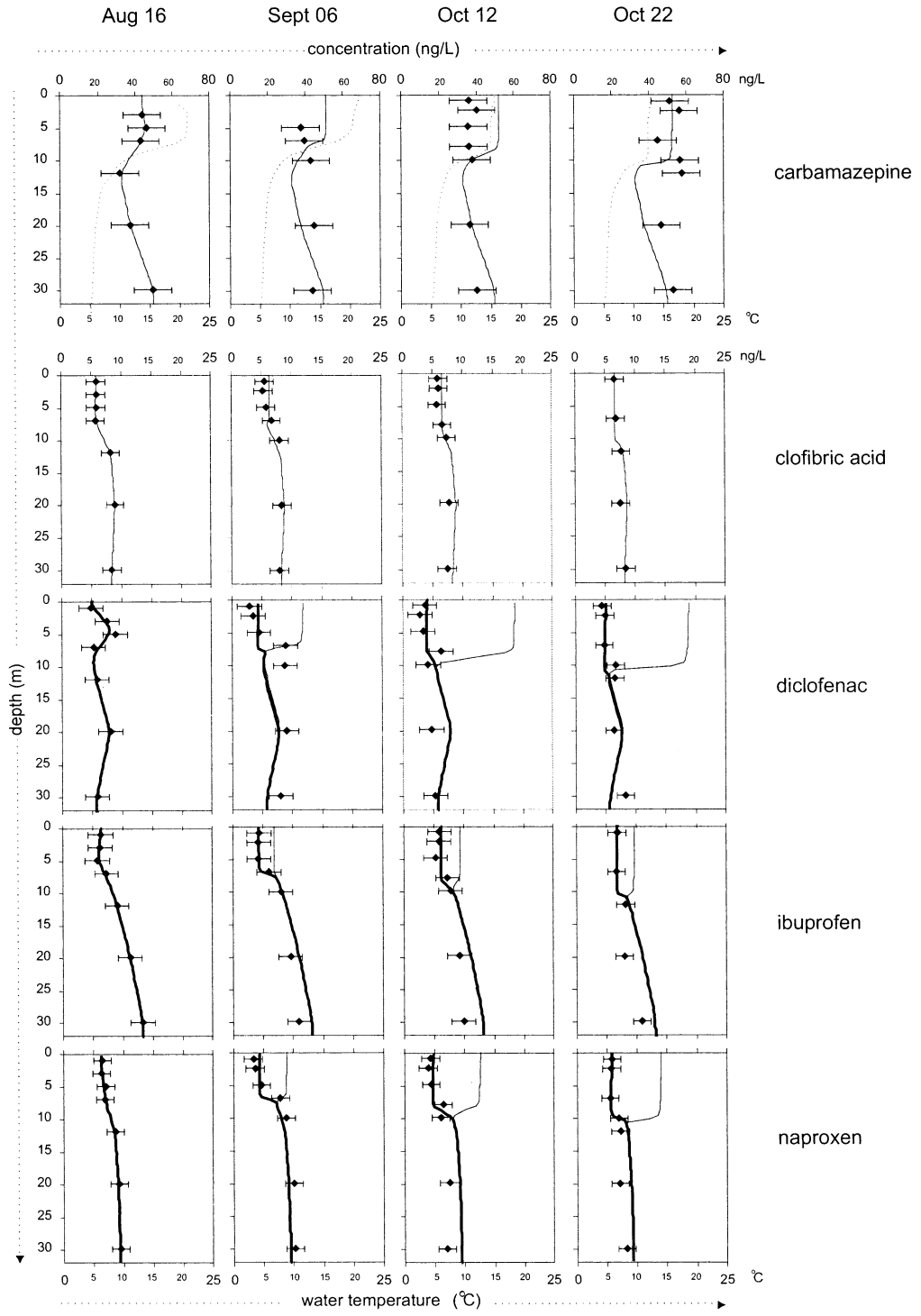

FIGURE 5. Monthly vertical concentration profiles of the six pharmaceuticals in Lake Greifensee: ◆, measured concentrations; ⋯, temperature profile; simulation results considering flushing as the sole elimination process (—) or considering flushing and another elimination process (—). (i) In the case of diclofenac, the second elimination process corresponds to the phototransformation; (ii) missing concentrations are due to analytical problems.

concentrations of carbamazepine and clofibric acid matched the measured data very well. Only a very low degradation rate (lower than 0.01 day^{-1}) was determined, and therefore, these compounds must be considered as persistent in surface waters. In contrast, the simulated concentrations in the epilimnion of diclofenac, ibuprofen, and naproxen (see Figure 5) were compared to the measured concentrations, overestimated. For example, the simulated results for naproxen revealed a continuous increase of the concentration over time to reach 13 ng/L at the end of October instead of the measured value of 6 ng/L. Thus, in the epilimnion, removal processes other than flushing must be considered to explain the observed concentration profiles of diclofenac, ibuprofen, and naproxen. To quantitatively assess the importance of these elimination processes, an average elimination rate (and its corresponding half-life time) in the epilimnion was determined for the pharmaceuticals by parameter estimation (Table 2). Overall removal rates of 0.09, 0.05, and 0.02 day^{-1} were determined for diclofenac, naproxen, and ibuprofen, respectively.

Identification of the Elimination Processes of Diclofenac, Ibuprofen, Ketoprofen, and Naproxen. The quantified

TABLE 2. Physicochemical Constants, Back-of-the-Envelope Calculations and Overall Elimination Rates in the Epilimnion for the Six Pharmaceuticals

	carbamazepine	clofibric acid	diclofenac	ibuprofen	ketoprofen	naproxen
Henry's law constant (atm m^3 mol^{-1})[a]	1.08×10^{-10}	2.19×10^{-8}	4.73×10^{-12}	1.5×10^{-7}	2.12×10^{-11}	3.39×10^{-10}
octanol/water partition coefficient (log)	2.45[b]	2.57[c]	4.51[d]	4.13−4.91[b,d]	3.12−3.16[b,d]	3.18−3.24[c,d]
pK_a[d]			4.15	4.91	4.45	4.15
qualified overall elimination rate constant (day^{-1})[e]	**0.011± 0.002**	**<0.01**	**0.088 ± 0.012**	**0.022 ± 0.003**	**n.d.**	**0.051 ± 0.002**
corresponding half-life time (day)	**63**	**>63**	**8**	**32**	**n.d.**	**14**
rate constant (day^{-1}) for						
outflow	0.006	0.006	0.006	0.006	0.006	0.006
chemical degradation	nr[f]	nr	nr	nr	nr	nr
gas exchange	nr	nr	nr	nr	nr	nr
sedimentation	<0.001	<0.001	0.005	0.005−0.01	<0.001	<0.001
direct phototransformation	(−)?[g]	nr	0.082 ± 0.012	nr	possible	possible
indirect ($OH^•$) phototransformation	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
biodegradation	(−)?	(−)?	(−)?	(+)?	??	??

[a] Reference 24. [b] Reference 25. [c] Reference 26. [d] Reference 27. [e] Obtained by model simulation based on field measurements. [f] nr, not relevant. [g] Reference 9.

TABLE 3. Characteristic Data of Lake Greifensee

Lake Morphology	
volume (m^3)	1.51×10^8
area	
surface (m^2)	8.49×10^6
10 m (m^2)	6.55×10^6
20 m (m^2)	3.51×10^6
30 m (m^2)	1.02×10^6
max depth (m)	32
Lake Hydraulics	
mean residence time of water (year)	1.1
mean throughflow of water (m^3/day)	3.7×10^5
mean epilimnion depth (summer) (m)	5
mean epilimnion volume (summer) (m^3)	4.2×10^7
Sedimentation Parameters	
particle concn in water column (max value) (kg L^{-1})	5×10^{-6}
fraction of organic carbon in particles (kg_{oc} kg^{-1})	0.4
range of average settling velocity of particles (m day^{-1})	0.5−2.5

overall elimination rates in the lake (see above) corresponds to the sum of different transport and transformation processes summarized in Table 2. The relative importance of each process can be estimated with simple back-of-the-envelope calculations (for details, see refs *14* and *17*) based on the physicochemical properties of the pharmaceuticals (Table 2) and lake properties (Table 3). Table 2 presents the rate constants obtained for each process. Due to the very low Henry's law constant and the resistance against strong bases and acids, we can expect that gas exchange and hydrolysis can be neglected for all compounds. The sedimentation rate constants were calculated using the parameters listed in Tables 2 and 3, assuming sorption equilibrium and a linear sorption isotherm. Direct phototransformation comes from the direct absorption of sunlight by the compound: there must be a good overlap between the absorption spectrum of the studied compound and sunlight intensity spectrum. Using the UV spectra of these pharmaceuticals (data not shown), we were able to discern whether direct phototransformation was possible. However, to evaluate the importance of such a process, further parameters such as the quantum yield have to be known: this could only be done for diclofenac (see below). For the indirect photodegradation, which corresponds mainly to the reaction with hydroxyl radicals ($^•OH$), a maximum first-order rate constant of 0.002 day^{-1} in summertime (*17*) was estimated for all compounds. However, according to actual meteorological data, we calculated that this rate constant is reduced by a factor of 2 over the time period considered yielding to a rate of ∼0.001 day^{-1} (*23*).

For diclofenac, the direct phototransformation has already been described as an elimination process in surface waters (*11*, *12*). To evaluate the relative importance of this process in relation to the others, we implemented a phototransformation process (see Experimental Section) in our model and compared the simulated profiles with the measured ones: the two series of profiles fitted very well (see Figure 5). Over this three-month period, an average elimination rate of 0.082 day^{-1} could be estimated for the phototransformation process, which appeared as the main elimination process for diclofenac. Note that phototransformation processes are strongly time and site specific and may vary by orders of magnitude (for details, see ref *23*).

For ibuprofen, the direct phototransformation can be neglected because this compound does not absorb sunlight. However, a relatively high sorption coefficient to particles combined with a particulate organic carbon of 2 mg L^{-1} and a settling velocity of 1 m day^{-1} in the lake water column (*17*) leads to a relevant elimination by sedimentation; biodegradation might also be relevant (*10*).

For ketoprofen and naproxen, direct phototransformation and biodegradation must be considered as possible elimination processes. To date, however, no further information on the processes is available for these compounds.

Basis for an Improved Risk Assessment in the Aquatic Environment. The measurements, simulation results, and calculations of this intensive three-month field study provide important information on the concentration range (dynamics) of these pharmaceuticals in WWTP effluents, in rivers, and in a lake. For the first time, quantitative data regarding the removal rates were determined in surface waters under real-world conditions. For a proper risk assessment, it is crucial to know that carbamazepine and clofibric acid were found to be quite persistent whereas diclofenac, ibuprofen, and naproxen are eliminated.

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Literature Cited

(1) Kümmerer, K. *Pharmaceuticals in the Environment, Sources, Fate, Effects and Risks*; Springer-Verlag: Berlin, 2001.
(2) Daughton, C. G.; Ternes, T. A. *Environ. Health Perspect.* **1999**, *107* (6), 907−938.
(3) Kolpin, D. W.; Furlong, E. T.; Meyer, M. T.; Thurman, E. M.; Zaugg, S. D.; Barber, L. B.; Buxton, H. T. *Environ. Sci. Technol.* **2002**, *36*, 1202−1211.
(4) Ternes, Th. A. *Water Res.* **1998**, *32*, 1−16.
(5) Stumpf, M.; Ternes, Th. A.; Wilken, R.-D.; Rodrigues, S. V.; Baumann, W. *Sci. Total Environ.* **1999**, *225*, 135−141.
(6) Buser, H. R.; Müller, M. D.; Theobald, N. *Environ. Sci. Technol.* **1998**, *32*, 188−192.
(7) Stan, H.-J.; Heberer, Th.; Linkerhägner, M. *Vom Wasser* **1994**, *83*, 57−68.
(8) Sacher, F.; Lochow, E.; Bethmann, D.; Brauch, H.-J. *Vom Wasser* **1998**, *90*, 233−243.
(9) Andreozzi, R.; Marotta, R.; Pinto, G.; Pollio, A. *Water Res.* **2002**, *36*, 2869−2877.
(10) Buser, H. R.; Poiger, T.; Müller, M. D. *Environ. Sci. Technol.* **1999**, *33*, 2529−2535.
(11) Buser, H. R.; Poiger, T.; Müller, M. D. *Environ. Sci. Technol.* **1998**, *32*, 3449−3456.
(12) Poiger, T.; Buser, H. R.; Müller, M. D. *Environ. Toxicol. Chem.* **2001**, *20*, 256−263.
(13) Singer, H. P.; Müller, S. R.; Tixier, C.; Pillonel, L. *Environ. Sci. Technol.* **2002**, *36*, 4998−5004.
(14) Ulrich, M. M.; Müller, S. R.; Singer, H. P.; Imboden, D. M.; Schwarzenbach, R. P. *Environ. Sci. Technol.* **1994**, *28* (9), 1674−1685.
(15) Oellers, S.; Singer, H. P.; Fässler, P.; Müller, S. R. *J. Chromatogr., A* **2001**, *911*, 225−234.
(16) Reichert, P. *Water Sci. Technol.* **1994**, *30*, 21−30.
(17) Schwarzenbach, R. P.; Gschwend, P. M.; Imboden, D. M. *Environmental Organic Chemistry*; Wiley: New York, 1993.
(18) Moore, D. E.; Roberts-Thomson, S.; Zhen, D.; Duke, C. C. *Photochem. Photobiol.* **1990**, 685−690.
(19) Zepp, R. G.; Cline, D. M. *Environ. Sci. Technol.* **1977**, *11*, 359−366.
(20) Meeus, J. *Astronomical formulae for calculators*, 4th ed.; Willmann-Bell, Inc.: Richmond, VA, 1988.
(21) http://jwocky.gsfc.nasa.gov/.
(22) Gerecke, A. C.; Canonica, S.; Müller, S. R.; Schärer, M.; Schwarzenbach, R. P. *Environ. Sci. Technol.* **2001**, *35* (19), 3915−3923
(23) Tixier, C.; Singer, H. P.; Canonica, S.; Müller, S. R. *Environ. Sci. Technol.* **2002**, *36* (16), 3482−3489.
(24) Meylan, W. M.; Howard, P. H. *Environ. Toxicol. Chem.* **1991**, *10*, 1283−1293.
(25) Hanna, M.; Bebiasi, V.; Bond, B.; Salter, C.; Hutt, A. J.; Camilleri, P. *Anal. Chem.* **1998**, *70*, 2092−2099.
(26) Alcock, R. E.; Gemmill, R.; Jones, K. C. *Chemosphere* **1999**, *38*, 759−770.
(27) Avdeef, A.; Berger, C. M.; Brownell, C. *Pharm. Res.* **2000**, *17*, 85−89.

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