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Citation for the published paper:

Radke, M., Ulrich, H., Wurm, C., Kunkel, U. (2010)

"Dynamics and Attenuation of Acidic Pharmaceuticals along a River Stretch"

Environmental Science and Technology, 44(8): 2968-2974

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Dynamics and attenuation of acidic pharmaceuticals along a river stretch

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5524 Words (including abstract: 190 words)

3 Figures (900 words)

2 Tables (600 words)

21 ABSTRACT.

22 While substantial knowledge on the occurrence of pharmaceuticals in the environment is
23 available, their behavior and fate in surface waters is still poorly understood. Therefore, the
24 aims of this study were to analyze the short-term dynamics of selected pharmaceuticals
25 along a 13.6 km long river stretch downstream of a wastewater treatment plant (WWTP),
26 and to quantify their attenuation by a mass balance approach. Four acidic pharmaceuticals
27 (bezafibrate, clofibric acid, diclofenac, naproxen) with different degradation properties were
28 measured over a period of three weeks at high temporal resolution, and in-situ photolysis
29 experiments were carried out. The average concentrations of pharmaceuticals were between
30 $9 \pm 4 \text{ ng L}^{-1}$ and $339 \pm 133 \text{ ng L}^{-1}$, corresponding to loads between 1.9 ± 1.2 and $63 \pm 37 \text{ g d}^{-1}$
31 ($n=134$). The temporal dynamics of pharmaceuticals was closely related to discharge of the
32 WWTP and precipitation, and highest concentrations were observed at the beginning of a
33 discharge event. During a dry period, naproxen was eliminated along the river stretch with a
34 dissipation time (DT_{50}) of 3.6 ± 2.1 days while the other compounds did not exhibit
35 significant attenuation. As photolysis and other abiotic processes were of limited quantitative
36 relevance, the attenuation of naproxen can most likely be attributed to biotransformation.

37
38 KEYWORDS. Acidic Pharmaceuticals. River. Attenuation. Photolysis. Diclofenac.
39 Naproxen.

42 BRIEF. The behavior and fate of several acidic pharmaceuticals in a small river is studied
43 with the aim of identifying key processes contributing to their attenuation.

44

Introduction

Human pharmaceuticals are organic micropollutants which are frequently detected in aquatic systems (1). The main sources of these compounds in rivers and streams are the discharge of treated sewage from wastewater treatment plants (WWTPs) and the direct discharge of raw sewage through sewer overflows (2). Typical concentrations of individual compounds in rivers are in the nano- to microgram per liter range (3-5), and due to their continuous input many pharmaceuticals have been classified as so-called “pseudo-persistent” compounds (6), even though they might be susceptible to transformation processes in the environment.

To date, the in-stream fate of pharmaceuticals in rivers is still only partly understood. In laboratory experiments, it has been shown that several pharmaceuticals are quickly transformed by photolysis (7), and this was also verified in field experiments (8). In a shallow Californian river, removal rates between 67 % and 100 % have been determined for – among other compounds – the pharmaceuticals gemfibrozil, ibuprofen, naproxen, and ketoprofen within 11 km (9). In a subsequent study the dominant attenuation processes were then identified to be either photolysis (naproxen) or biotransformation (ibuprofen, gemfibrozil) (10). Measurements in a larger river suggest that biotransformation is the more important attenuation mechanism than photolysis for a number of pharmaceuticals, especially in turbid or deep rivers (11).

The aim of this study was to analyze the short-term dynamics of pharmaceutical compounds and to determine a mass balance for a river stretch. From these data, the importance of different attenuation mechanisms in the river was evaluated. To this end, four acidic pharmaceuticals (diclofenac, bezafibrate, naproxen, clofibric acid) with similar physico-chemical properties but different attenuation properties in surface water were

studied. In the context of this study, processes reducing the load of the pharmaceuticals along the river stretch are subsumed under the term attenuation; it thus does not cover mere dilution.

Experimental Methods

Chemicals. All pharmaceuticals (purity > 97 %) and fenoprop were purchased from Sigma-Aldrich (Seelze, Germany). The surrogate standards D₄-bezafibrate, D₄-clofibric acid, D₄-diclofenac, and D₃-naproxen were purchased from Toronto Research Chemicals (North York, ON, Canada). LC-MS-grade acetonitrile and acetic acid were purchased from Sigma-Aldrich, LC-MS-grade water from J.T. Baker (Deventer, The Netherlands).

Analytical Methods. The pharmaceuticals were enriched by solid phase extraction (SPE) as previously described by Löffler and Ternes (12). Briefly, water samples were vacuum filtered and extracted by OASIS MCX cartridges (60 mg/3 mL; Waters, Eschborn, Germany) after addition of deuterated surrogate standards. After elution, pharmaceuticals were analyzed by HPLC-MS/MS and quantified by isotope dilution. The recovery of the target compounds was verified by analyzing spiked river water, yielding acceptable recovery rates between 80±5 % and 106±15 %. Blank samples (drinking water) were regularly extracted to verify that no contamination occurred. A detailed description of the analytical methodology is available as Supporting Information.

Sampling site and sampling methods. Samples were taken at two points along a 13.6 km long stretch of the river Roter Main near Bayreuth, Germany (49°58' N, 11°33' E), between 08/22/2007 and 09/13/2007. The WWTP of Bayreuth is the major source of organic contaminants into the river; it has a capacity of 300,000 population equivalents and serves a population of 90,000 (13). Its maximum discharge capacity is 1.3 m³ s⁻¹. If this limit is

reached during precipitation events, wastewater is diverted to retention tanks throughout the sewer system (26,000 m³). Once the storage capacity of these tanks is exceeded, combined sewer overflows upstream of the WWTP discharge untreated wastewater into the river. Information on the periods when these overflows were discharging into the river are available on an hourly basis. The sampling period comprised several rainfall events of different magnitudes, ranging from a precipitation of 6.6 mm in 16 hours to 23.9 mm in 46 hours, as well as a 6-day period of dry weather with nearly baseflow conditions in the river. The average short wave radiation (<400 nm) during this dry period varied from 307 to 432 W m⁻² (daylight hours only), measured at a station operated by the Department of Micrometeorology at the University of Bayreuth (see <http://www.bayceer.uni-bayreuth.de/mm/>) approx. 5.3 km southeast of the upstream sampling site. The radiation intensity during the other periods was lower.

Samples were taken at two locations: the “upstream” site was located 900 m downstream of the WWTP, and the “downstream” site was 13.6 km further downstream. Between the two sampling sites, no continuous input of wastewater occurred. Several sewer overflows are located along the river stretch; no information on discharge of wastewater through these overflows into the river is available. A theoretical and an empirical approach were used to verify that the WWTP effluent was completely mixed with the river water before it reached the upstream site (see Supporting Information for details). The proportion of treated wastewater in the river during the sampling period was on average 18±6 % of total flow at the upstream site. Substantial diel variations of this proportion were observed, and generally it was highest during rainfall events with a maximum of 38 %.

The river morphology is modified by anthropogenic impacts, e.g. by several weirs, but usually no dredging of sediment or other anthropogenic modifications occur today. The

average depth of the river section is approx. 100 cm, and its width varies from 5 to 20 m. Twenty to forty percent of the riverbanks are occupied by bushes and trees which are at least partly shading the water surface. The texture of the river sediment varies from sand to clay. The color of the water is reddish-brown due to the geology of the upstream catchment; an absorption spectrum of the river water is provided as Figure S1 (Supporting Information).

Discharge at the upstream site was calculated as the sum of discharge measured at a gauging station 2.6 km upstream of the first sampling site (<http://www.hnd.bayern.de/>, station “Bayreuth/Roter Main”) and the discharge measurements at the WWTP outfall. The time lag between the gauge and the upstream site was accounted for (see Supporting Information, Figure S2). Along the river stretch, a few minor creeks are discharged into the river. At the downstream site, discharge was measured with an ultrasonic doppler instrument (PCM-4, Nivus, Eppingen, Germany). Due to the immanent uncertainties in the absolute discharge measurements at such temporary gauging stations (e.g., due to no long-term calibration and non-uniform cross section), the data from this site were only used for visualizing the temporal dynamics of pharmaceutical loads (in Figure 2 and Figure 3) but not for estimating attenuation rates. Using clofibric acid as a conservative tracer, the discharge at the downstream site was approx. 1.3 ± 0.1 times the discharge at the upstream site during dry weather (see Supporting Information, Table S3). Over the whole sampling period, the average discharge at the upstream site was $2.2 \pm 1.0 \text{ m}^3 \text{ s}^{-1}$; during the dry period it was $1.5 \pm 0.1 \text{ m}^3 \text{ s}^{-1}$. The hydrograph for the upstream site is available as Supporting Information (Figure S3), as well as further information on general physical/chemical characteristics of the river water. Under baseflow conditions, the travel time of water and (non-sorbing) solutes from the upstream to the downstream site was approx. 30 h as determined by dye-

tracing; during the discharge peaks, the travel time of the pressure wave between the sites was as low as 6 h.

Water samples were collected at both sites as time-averaged composite samples using automatic water samplers (3700 compact, Teledyne-ISCO, Lincoln, USA). Every 30 min (until 08/27/2007) or 40 min (from 08/27/2007), 50 mL of water was sampled; 6 of these samples were combined in one glass bottle, yielding 3 and 4 hour composite samples, respectively. Ice was added to the base of the sampler, and the samples were stabilized by adding NaN_3 to the bottles prior to sampling (final concentration 0.1 %). Samples were collected every second day and stored at 4°C (max. 2 days) until extraction. The addition of NaN_3 did not negatively affect the concentration of pharmaceuticals (see Supporting Information, Table S1).

In-situ photolysis experiments. The aim of the in-situ photolysis experiments was to estimate the contribution of photolysis to the overall attenuation of the pharmaceuticals. A complete assessment of the pharmaceuticals' photolytic fate was beyond the scope of this study. Experiments were carried out with ultrapure water (Milli-Q water) and river water (unfiltered). The water was spiked with the target pharmaceuticals to a concentration of approx. $100 \mu\text{g L}^{-1}$ (no addition of NaN_3) and transferred to quartz glass tubes (length: 36 cm; diameter: 2 cm). At 8:00 UTC on a summer day (07/27/2009), two replicate tubes were placed horizontally directly below the water surface in the river and exposed to sunlight irradiation. The experiment was carried out close to the upstream sampling site at a location with optimum radiation conditions. At $t=0, 1, 2, 4$, and 6 hours, the tubes were removed, an aliquot of 1 mL was sampled from each tube, and the tubes were exposed again. The deuterated surrogate standards were added and the samples were stored frozen until analysis. Results of preliminary experiments confirmed that freezing did not negatively affect the

results (see Supporting Information, Table S1). Before analysis, samples were allowed to thaw, fenoprop – which was used to monitor instrument performance – was added, and samples were analyzed by HPLC-MS/MS without any additional pretreatment. Dark and sterile controls were carried out to determine losses due to processes other than photolysis (e.g., sorption to the PTFE-lined lid, biotic or other abiotic transformations). The pH of the river water was 7.7 and remained constant during the experiment, the pH of the ultrapure water increased from 5.9 to 6.6. The average short wave radiation (<400 nm) over the incubation period was 807 W m⁻².

Calculations. The concentration of each composite sample was multiplied with the corresponding discharge to calculate the load of pharmaceuticals at the upstream site. Concentrations at both sampling sites were analyzed for statistical differences by checking the confidence intervals for overlap. For correlation analysis, the Spearman's rank correlation coefficient (r_s) was calculated. The Mann-Whitney U test was used to test the calculated attenuation rates for significance.

For each hydrologic event (see Figure 2) the dilution factor along the river stretch was calculated by comparing the integrals of the clofibric acid concentrations for the two sites. The uncertainty of this approach was addressed by Monte Carlo simulations (see Supporting Information for details). The calculation of loads at the downstream site was impaired by uncertain discharge data at that site. Therefore, attenuation rates were estimated from the concentration ratio of the individual compounds to clofibric acid. Briefly, the concentration of each pharmaceutical was normalized to the concentration of clofibric acid, and the relative attenuation along the river stretch was calculated from the averaged ratios. This approach retains the combined uncertainties of the analytical methodology and the environmental conditions, and due to the high number of samples it provides a robust

estimate of the attenuation rate. A detailed description of this procedure is available as Supporting Information. For the dry period (event E2), the time interval used to calculate attenuation along the river stretch was delineated using the hydrograph, taking into account the approximate travel time of solutes between the sampling sites. For peak discharge events (events E1, E3, E4, E5), we used the load chemograph to delineate the beginning and end of the integration range.

Data from photolysis experiments were normalized to the measured initial concentration ($t=0$ h) in each tube. The photolysis rate constant at the surface was then determined by a linear regression of the logarithmic concentration versus time. Based on this rate, the photolysis rate over the whole water column was derived following procedures described by Schwarzenbach et al. (14) and Fono et al. (11), and this rate was then used to estimate the attenuation by photolysis along the river stretch. To this end, two scenarios were used representing “optimistic” and “realistic” conditions for photolysis. A detailed description of this procedure and the input parameters is available as Supporting Information.

Results and Discussion

Concentrations and Loads. The statistical distribution of concentrations and loads (upstream site only) are shown in Figure 1a and in Table S4 (Supporting Information). All four compounds were detected continuously at both sites. The average concentration of each compound was significantly higher at the upstream site than at the downstream site. The concentration distributions are positively skewed with more observations in the lower concentration range (Figure 1a); extreme values outside the 1.5 interquartile range (1.5IQR) were only observed at the highest concentrations. The concentrations of all four pharmaceuticals were significantly correlated with each other (r_s from 0.50 to 0.77, $p<0.001$;

see Supporting Information, Table S5), indicating that they shared one common source. The statistical distribution of the loads at the upstream site are also positively skewed, but compared to the distribution of concentrations extreme values at high loads were much more pronounced (Figure 1a). For the dry period, the differences between the average concentrations at the two sites were bigger, and only a few outliers were observed (Figure 1b).

Figure 1: Statistical distribution of concentrations (left column) and loads (right column) for a) the whole dataset, and b) the dry weather period (E2; see Figure 2). The box designates median and 25th and 75th percentiles, respectively; the whiskers denote the 1.5 interquartile range (1.5IQR); outliers (outside the 1.5IQR) are plotted individually. US: upstream site (whole dataset: n=134; dry period: n=40); DS: downstream site (n=136 and 41, respectively). Due to uncertain discharge data, no loads are reported for the downstream site. Downstream concentrations were significantly smaller than upstream concentrations at p<0.05 (*) and p<0.01 (**), respectively.

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Temporal Dynamics. The temporal dynamics of concentrations and loads at both sampling sites are illustrated for clofibric acid in Figure 2. The dynamics were closely connected to the hydrological conditions: at the beginning of a discharge peak, we observed a peak in concentration and load. While the peaks of discharge and concentration/load were synchronous at the upstream site, the clofibric acid peaks arrived slightly later than the discharge peaks at the downstream site. This is a common observation in rivers which can be attributed to the discharge (pressure) responding like a kinematic wave which travels faster downstream than the physical water body (15, 16).

Figure 2: Concentration and load of clofibric acid at the upstream and downstream sampling site together with the corresponding hydrograph for each site. Times when untreated wastewater was discharged through combined sewer overflows (upstream of the first sampling site) are indicated by columns in the top-left plot. The periods used for integration of loads are indicated by the gray areas in the right plots, the individual events are labeled with E1 to E5. The discharge and thus the load at the downstream site were corrected by the average dilution factor derived from clofibric acid (see Supporting Information for details).

237

238 The temporal dynamics of the other three compounds were similar to clofibric acid (Figure
239 3). For all compounds, the peaks of concentration and load were associated with rainfall
240 events. The concentration differences between the period with low discharge and the high
241 discharge periods was least pronounced for diclofenac. The outliers observed in the
242 statistical distribution (Figure 1a) can all be attributed to precipitation events which caused
243 both higher concentrations and loads compared to baseflow conditions. This is similar to
244 observations from the river Glatt where higher loads of pharmaceuticals (β -blockers) were
245 associated with rainfall events (17). Higher concentrations of organic wastewater
246 contaminants during wet periods compared to baseflow have also been reported by Frick and
247 Zaugg for a long-term dataset (18).

248 The concentration peaks (Figure 2) can be attributed to the accelerated displacement of
249 wastewater from the sewer system and the WWTP into the river at the beginning of a rainfall
250 event. Thereby, the mass flow of pharmaceuticals into the river increases substantially. After
251 this initial “purging” of the sewer system, the mass flow of pharmaceuticals through the
252 WWTP into the river decreases again since the delivery rate by human excretion is relatively
253 constant and independent from precipitation. This explanation is plausible based on the
254 back-of-the-envelope calculation provided as Supporting Information. Moreover, it is in
255 agreement with the significant ($p < 0.001$) correlation between the concentrations of the
256 pharmaceuticals and the proportion of wastewater in the river (r_s between 0.54 and 0.75;
257 Supporting Information, Table S5). Additionally, the residence time of wastewater in the
258 treatment plant is reduced during periods with increased wastewater flow which might
259 decrease the removal efficiency of the treatment plant. This would affect the magnitude of
260 the concentration peaks. Discharge of untreated wastewater through combined sewer

overflows upstream of the WWTP did not substantially contribute to the observed concentration peaks during rainfall events. With the exception of the event E1, the overflows were discharging only after the pharmaceutical peak already passed the upstream site (E3, E4; see Figure 2) or they were not activated at all (E5).

Most of the rainfall events during the sampling period were of short duration and caused only short periods of high discharge (Supporting Information, Figure S3). Therefore, no substantial dilution of the river water was observed with respect to pharmaceuticals. Only event E5 was characterized by a comparatively long period of high discharge causing dilution both at the upstream and the downstream site after the initial peak. This is different from settings with extended discharge periods triggered for example by snow melt where lower concentrations due to dilution can be expected over a longer period (19).

Due to dispersion, rainfall associated peaks of pharmaceutical load and concentration at the downstream site were usually broader and smaller than at the upstream site, but the peak shape was well preserved. During the dry period (E2) a diel variation of the concentration of pharmaceuticals was observed which was most pronounced for clofibric acid. This pattern with highest concentrations during the afternoon was closely related to the daily discharge variations of the WWTP and thus the proportion of wastewater in the river (see Supporting Information, Figure S4).

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282 Figure 3: Time trends of concentration (left column) and load (right column) of bezafibrate,
 283 diclofenac, and naproxen for the complete sampling period at the two sampling sites. For
 284 visualization, the measured discharge and thus the load at the downstream site were
 285 corrected by the average dilution factor derived from clofibric acid (see text and Supporting
 286 Information for details).

287

288 **Photolysis.** The results of the in-situ photolysis experiments are summarized in Table 1,
 289 and kinetic plots are available as Supporting Information (Figure S5). The highest photolysis
 290 rate was measured for diclofenac. Its transformation rates determined in ultrapure and river
 291 water were identical; this has also been reported previously (20). The measured rate
 292 constants are in good agreement with rates reported by others (8, 20), given the different
 293 experimental set-ups and radiation conditions in these studies. For naproxen, the photolysis

rate in river water was higher than in ultrapure water, indicating a substantial contribution of indirect photolysis. This is in agreement with observations by Fono et al. (11) and Lin and Reinhard (21), whereas Packer et al. (20) determined a lower photolysis rate in river water (see Supporting Information, Table S7 the for a compilation of these data). Such contrasting results can be attributed to differences in the concentration or type of light absorbing compounds and photosensitizers (i.e., radical sources) like dissolved organic matter in the different waters. The absolute photolysis rates (k_{surf}) of naproxen in river and ultrapure water determined in this study were between 9 % and 33 % of the rates reported by Packer et al. (20) and Lin and Reinhard (21). As for diclofenac, these differences could be due to details of the experimental set-ups and radiation conditions. Moreover, since we exposed the solutions directly below the water surface, some additional shielding effects by river water above the test tubes could slightly reduce the photolysis rate compared to the direct exposure of the test tubes by others. Compared to naproxen, the photolysis of diclofenac was much faster in river as well as in ultrapure water (Table 1), which is in agreement with results from experiments we carried out in a sunlight simulator (data not shown). In contrast, Packer et al. (20) reported almost identical photolysis rates for both compounds; the reason for these different findings remain unresolved. Clofibric acid was photodegraded in river water at a very low rate and not at all in ultrapure water. The absolute rate is in agreement with results from Packer et al. (20), and the contribution of indirect photolysis to the phototransformation of clofibric acid has also previously been described (20, 22). In agreement with previous reports (23), bezafibrate was not susceptible to photolysis on the time-scale of this study. Results from the dark and sterile controls confirmed that processes other than photolysis did not contribute to the transformation of pharmaceuticals (see Supporting Information, Table S6).

For the whole water column, photolysis rates between 0.01 d^{-1} and 0.37 d^{-1} were estimated (Table 1). Based on these rates and the two scenarios for photolysis, we calculated relative attenuation rates by photolysis between 3.4 and 15 % along the river stretch for diclofenac and naproxen (see Supporting Information for further details). The concentration of clofibric acid and bezafibrate should not be affected by photolysis (Table 1).

Table 1: Summary of in-situ photolysis experiments with ultrapure and river water. k_{surf} : measured photolysis rate constant at the water surface; k_{total} : calculated photolysis rate over the whole water column; RA_{photo} : estimated relative attenuation along the river stretch for the two scenarios (min: realistic; max: best case). Kinetic plots for these experiments and detailed information on the calculations are available as Supporting Information.

	Ultrapure Water		River Water		
	k_{surf} (d^{-1})	k_{total} (d^{-1})	k_{surf} (d^{-1})	k_{total} (d^{-1})	RA_{photo} (min-max) (%)
Bezafibrate	n.s.		n.s.		
Clofibric Acid	n.s.		0.29 ± 0.10 *	0.009 ± 0.005	0.1-0.5
Diclofenac	11.3 ± 0.5 **	0.36 ± 0.09	11.6 ± 0.6 **	0.37 ± 0.09	5.2-15.0
Naproxen	2.6 ± 0.2 **	0.11 ± 0.03	3.9 ± 0.2 **	0.16 ± 0.04	3.4-11.5

Significance level for the rate constants: * $p < 0.05$; ** $p < 0.0001$; n.s.: slope of regression line not significantly different from zero

Mass Balancing. On the time-scale of our experiments, clofibric acid can be used as a conservative tracer since it is resistant against biodegradation (24, 25) and photolysis (Table 1 and (26)), and sorption to sediments from the river Roter Main is also negligible (24). Therefore, the attenuation of bezafibrate, diclofenac, and naproxen was determined relative to clofibric acid for events E2, E4, and E5. For the other two events, the normalization to

clofibric acid was not possible due to the suspected additional input of clofibric acid through sewer overflows along the river stretch (see Supporting Information, Table S3). During the two peak events (E4 and E5), no significant attenuation of bezafibrate, diclofenac, and naproxen occurred (Table 2). This was expected since the travel time between the sampling sites was comparatively low and the sky was clouded during rainfall events, making conditions unfavorable for biotransformation and photolysis. During the dry period (E2), the attenuation rate of naproxen was significantly different from zero ($23 \pm 6\%$), whereas for diclofenac and bezafibrate attenuation was not significant (Table 2). Thus, we can deduce that even for a compound which is highly susceptible to photolysis like diclofenac (see references (8, 20) and Table 1), attenuation by photolysis was of minor importance. This is in agreement with the estimated low attenuation rate by photolysis in the “realistic” photolysis scenario (Table 1). Photolysis of naproxen can be ruled out as quantitatively relevant attenuation mechanism during the dry period since it was less susceptible to photolysis than diclofenac and the attenuation rate by photolysis estimated for the “realistic” scenario was $<3\%$. Moreover, based on the photolysis control experiments and our previous studies we can also exclude other abiotic transformation processes, biodegradation in the flowing water, and adsorption to suspended matter or sediment on the time-scale relevant for this study (24). The most likely mechanism responsible for the attenuation of naproxen is thus biotransformation in biofilms in the hyporheic zone or on submerged macrophytes.

Based on results from a previous laboratory study with sediment and water from the same river, we would also expect biodegradation of bezafibrate and diclofenac (24). However, these experiments were carried out with sandy sediment and at least the top sediment layer was continuously aerobic. In contrast, we learned from field observations that sediments in many parts of the river stretch were anaerobic. Although there is no direct evidence, we thus

hypothesize that the attenuation of naproxen was due to primary degradation in anaerobic sediments and that this process is less efficient for bezafibrate and diclofenac. However, knowledge on the behavior and fate of polar organic micropollutants under anaerobic conditions is still limited, and therefore this has to remain a hypothesis.

Table 2: Relative attenuation (RA_{tot} ; %) of bezafibrate, diclofenac, and naproxen between the upstream and downstream sampling site for the hydraulic events E2, E4, and E5. n_{up} , n_{down} : number of samples at the upstream and downstream site averaged for the specified event.

	Bezafibrate	Diclofenac	Naproxen	n_{up}/n_{down}
E2 (dry period)	9±7	4±6	23±6 *	40 / 41
E4 (peak)	-2±9	-5±7	4±9	22 / 23
E5 (peak)	10±20	5±15	8±11	13 / 10

* relative attenuation different from zero, $p < 0.05$

Implications. The connection between highest loads of pharmaceuticals to precipitation and discharge events (Figure 3) has implications for their environmental fate. Under such conditions, photolysis is unlikely to occur since UV radiation is typically low during precipitation events and is further reduced by increased loads of suspended solids at higher discharge. Moreover, due to the fast downstream transport of water and solutes during discharge peaks (6 h vs. 30 h during baseflow), the residence time is too short for biodegradation processes to substantially reduce micropollutant loads. Thus, when the highest input of pharmaceuticals occurs, their attenuation is least effective.

Against our initial assumption the concentrations were highest at the beginning of peak discharges due to rapid displacement of wastewater from the sewer system and the WWTP. This is relevant in cases where river water is used for production of drinking water. As a consequence of our observations, river water should not be abstracted for production of drinking water during the initial phase of discharge peaks to avoid an unnecessary high concentration of pharmaceuticals in the raw water.

Only naproxen can be used to compare results from this study to previous research on in-stream fate of pharmaceuticals since it is the only common compound between these studies. Based on first-order kinetics, the measured relative attenuation and a travel time of 30 hours, we calculated a dissipation time (DT_{50}) of naproxen in the river of 3.6 ± 2.1 days. This is in the same range as the half-life of 4.2 days reported by Fono et al. (11) for the Trinity river, a large river in Texas, USA; there, biotransformation and photolysis were considered equally important for the attenuation of naproxen. The higher importance of photolysis can be attributed to a higher radiation intensity (latitude 33°N compared to 50°N), but also to a lower absorption of light in the river water (beam absorption coefficient at 330 nm: 0.06 cm^{-1} vs. 0.11 cm^{-1} in this study). In contrast, a naproxen removal between 75 and 100 % within only 0.31 days (7.5 hours) was measured by Lin et al. (10) in the Santa Ana river (California, USA). Forty percent of this removal was attributed to photolysis, the remainder mainly to sorption processes. The comparatively high contribution of photolysis to the attenuation of naproxen in the Santa Ana river is consistent with the high photolysis rate determined in laboratory experiments with water from the same river (21). However, the large difference to the river Roter Main (and the Trinity river) can not be explained by higher solar radiation alone since the overall irradiation was in the same order of magnitude than in this study (4.1 to 4.9 hours of 760 W m^{-2} ; this study: approx. 15 hours between 307 and 432 W m^{-2}). Other

factors like the optical properties of the river water (e.g., an increased absorption of radiation by dissolved organic matter or other dissolved or suspended species in the river Roter Main) or higher vegetation along the river banks must have substantially contributed to this difference. At present, no final explanation for the observed differences can be given since information is not available for most relevant parameters. The comparison of these two studies highlights the need for a better characterization and quantification of the constraints of photolysis on the field scale, especially under circumstances where the influence of vegetation can be comparatively high.

The different findings regarding the importance of individual attenuation mechanisms between the few studies on the fate of pharmaceuticals in rivers are most likely due to parameters constraining biotransformation and photolysis. Knowledge on the influence of these parameters – e.g., the type and concentration of suspended matter, composition and activity of microbial communities, quality and quantity of dissolved organic matter, redox conditions in the sediment, and the exchange of surface water with the river sediment (hyporheic zone) – on the attenuation of pharmaceuticals is currently sparse. At present, we are not able to quantify common constraints or to generalize our observations because we are lacking either a mechanistic understanding of the relation between these parameters and micropollutant attenuation or methods for determining the relevant properties of rivers on a spatial scale from 10 to 100 km.

Acknowledgements

We thank the local water board (Wasserwirtschaftsamt Hof) and the staff of the wastewater treatment plant Bayreuth for providing discharge data and Jutta Eckert for

assistance in the laboratory. Financial support by the Deutsche Forschungsgemeinschaft (DFG; project RA 896/8-1) is acknowledged. We thank three reviewers and James M. Armitage for their constructive comments on an earlier version of the manuscript.

Supporting Information Available

A summary of physical-chemical characteristics of the river water, estimation of mixing of WWTP effluent with river water, temporal correction of discharge data, hydrograph for the upstream sites, details on the analytical method and sample stability, procedures to calculate dilution, attenuation, and photolysis rates, average concentrations and loads, the correlation matrix for pharmaceuticals and proportion of wastewater in the river, diel variation of concentrations during the dry period, a back-of-the-envelope calculation, results of photolysis experiments, and comparison of photolysis data to literature. This material is available free of charge via the Internet at <http://pubs.acs.org>.

References

1. Ternes, T. A., Occurrence of drugs in German sewage treatment plants and rivers. *Water Research* **1998**, 32 (11), 3245-3260.
2. Alder, A. C.; McArdell, C. S.; Golet, E. M.; Kohler, H.-P. E.; Molnar, E.; Anh Pham Thi, N.; Siegrist, H.; Suter, M. J.-F.; Giger, W., Environmental Exposure of Antibiotics in Wastewaters, Sewage Sludges and Surface Waters in Switzerland. In *Pharmaceuticals in the Environment*, 2nd ed.; Kümmerer, K. (Ed.), Springer, Berlin, **2004**.
3. Kolpin, D. W.; Furlong, E. T.; Meyer, M. T.; Thurman, E. M.; Zaugg, S. D.; Barber, L. B.; Buxton, H. T., Pharmaceuticals, hormones, and other organic wastewater contaminants in US streams, 1999-2000: A national reconnaissance. *Environmental Science & Technology* **2002**, 36 (6), 1202-1211.
4. Ashton, D.; Hilton, M.; Thomas, K. V., Investigating the environmental transport of human pharmaceuticals to streams in the United Kingdom. *Science of the Total Environment* **2004**, 333 (1-3), 167-184.
5. Loos, R.; Gawlik, B. M.; Locoro, G.; Rimaviciute, E.; Contini, S.; Bidoglio, G., EU-wide survey of polar organic persistent pollutants in European river waters. *Environmental Pollution* **2009**, 157 (2), 561-568.
6. Daughton, C. G., Cradle-to-cradle stewardship of drugs for minimizing their environmental disposition while promoting human health. I. Rationale for and avenues toward a green pharmacy. *Environmental Health Perspectives* **2003**, 111 (5), 757-774.
7. Tixier, C.; Singer, H. P.; Oellers, S.; Müller, S. R., Occurrence and fate of carbamazepine, clofibric acid, diclofenac, ibuprofen, ketoprofen, and naproxen in surface waters. *Environmental Science & Technology* **2003**, 37 (6), 1061-1068.
8. Bartels, P.; von Tümpling, W., Solar radiation influence on the decomposition process of diclofenac in surface waters. *Science of the Total Environment* **2007**, 374 (1), 143-155.
9. Gross, B.; Montgomery-Brown, J.; Naumann, A.; Reinhard, M., Occurrence and fate of pharmaceuticals and alkylphenol ethoxylate metabolites in an effluent-dominated river and wetland. *Environmental Toxicology and Chemistry* **2004**, 23 (9), 2074-2083.
10. Lin, A. Y. C.; Plumlee, M. H.; Reinhard, M., Natural attenuation of pharmaceuticals and alkylphenol polyethoxylate metabolites during river transport: Photochemical and biological transformation. *Environmental Toxicology and Chemistry* **2006**, 25 (6), 1458-1464.
11. Fono, L. J.; Kolodziej, E. P.; Sedlak, D. L., Attenuation of wastewater-derived contaminants in an effluent-dominated river. *Environmental Science & Technology* **2006**, 40 (23), 7257-7262.
12. Löffler, D.; Ternes, T. A., Determination of acidic pharmaceuticals, antibiotics and ivermectin in river sediment using liquid chromatography-tandem mass spectrometry. *Journal of Chromatography A* **2003**, 1021 (1-2), 133-144.

13. City of Bayreuth, Land use planning - Chapter 3: Inventory (Flächennutzungsplan, Kapitel 3: Bestand), in German.
http://www.bayreuth.de/files/pdf/Planungsamt/FNP/Kap_3.pdf (2009/09/05),
14. Schwarzenbach, R. P.; Gschwend, P. M.; Imboden, D. M., *Environmental Organic Chemistry*. 2 ed.; Wiley & Sons: **2002**.
15. Kurtenbach, A.; Möller, S.; Krein, A.; Symader, W., On the relationship between hydrographs and chemographs. *Hydrological Processes* **2006**, 20 (14), 2921-2934.
16. Krein, A.; de Sutter, R., Use of artificial flood events to demonstrate the invalidity of simple mixing models. *Hydrological Sciences* **2001**, 46 (4), 611-622.
17. Alder, A. C.; Schaffner, C.; Majewsky, M.; Klasmeier, J.; Fenner, K., Fate of β -blocker human pharmaceuticals in surface water: Comparison of measured and simulated concentrations in the Glatt Valley Watershed, Switzerland. *Water Research* In Press (doi: 10.1016/j.watres.2009.10.002).
18. Frick, E. A.; Zaugg, S. D., Organic wastewater contaminants in the Upper Chattahoochee River Basin, Georgia, 1999-2002. In *Proceedings of the 2003 Georgia Water Resources Conference*, Hatcher, K. J. (Ed.), Institute of Ecology, The University of Georgia, Athens, Georgia, **2003**.
19. Barber, L. B.; Murphy, S. F.; Verplanck, P. L.; Sandstrom, M. W.; Taylor, H. E.; Furlong, E. T., Chemical loading into surface water along a hydrological, biogeochemical, and land use gradient: a holistic watershed approach. *Environmental Science & Technology* **2006**, 40 (2), 475-486.
20. Packer, J. L.; Werner, J. J.; Latch, D. E.; McNeill, K.; Arnold, W. A., Photochemical fate of pharmaceuticals in the environment: Naproxen, diclofenac, clofibric acid, and ibuprofen. *Aquatic Sciences* **2003**, 65 (4), 342-351.
21. Lin, A. Y.-C.; Reinhard, M., Photodegradation of common environmental pharmaceuticals and estrogens in river water. *Environmental Toxicology and Chemistry* **2005**, 24 (6), 1303-1309.
22. Lam, M. W.; Tantuco, K.; Mabury, S. A., PhotoFate: A new approach in accounting for the contribution of indirect photolysis of pesticides and pharmaceuticals in surface waters. *Environ. sci. tech.* **2003**, 37 (5), 899-907.
23. Cermola, M.; DellaGreca, M.; Iesce, M. R.; Previtera, L.; Rubino, M.; Temussi, F.; Brigante, M., Phototransformation of fibrates drugs in aqueous media. *Environ. Chem. Lett.* **2005**, 3, 43-47.
24. Kunkel, U.; Radke, M., Biodegradation of acidic pharmaceuticals in bed sediments: insight from a laboratory experiment. *Environ. Sci. Technol.* **2008**, 42 (19), 7273-7279.
25. Löffler, D.; Römbke, J.; Meller, M.; Ternes, T. A., Environmental fate of pharmaceuticals in water/sediment systems. *Environmental Science & Technology* **2005**, 39 (14), 5209-5218.
26. Andreozzi, R.; Raffaele, M.; Paxeus, N., Pharmaceuticals in STP effluents and their solar photodegradation in aquatic environment. *Chemosphere* **2003**, 50, 1319-1330.