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# Contribution of effluents from hospitals and private households to the total loads of diclofenac and carbamazepine in municipal sewage effluents—modeling versus measurements

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**Abstract**

The anti-epileptic drug carbamazepine and the non-steroidal anti-inflammatory drug diclofenac are frequently found as residues in the aquatic environment and also in samples of ground and drinking water. For both compounds, their loads occurring in the effluents from a military hospital and in the combined (household and hospital) sewage of a sewage pumping station (SPS) and a large municipal sewage treatment plant (STP) were predicted and measured within a field trial by collecting and analyzing defined composite samples over a time period of 1 week. The use of pharmacokinetic data and precise information on the administration of the individual medicinal formulation was found to be essential for the validity of the predicted data. The measured data confirmed the validity of the predicted loads with recoveries between 63 and 102% for carbamazepine and around 35% for diclofenac in the hospital wastewater. A comparison of the weekly loads predicted and measured in the influents and effluents of a STP in Berlin (Germany) yielded a very low removal rate for diclofenac (less than 15%) and a removal rate of up to 40% for carbamazepine. In total, 2.0 kg of carbamazepine per week (105 kg/a) and 4.4 kg of diclofenac per week (226 kg/a) were discharged into Berlin's surface water by the municipal STP, which treats both household sewage from approximately one million inhabitants and large amounts of hospital effluents (approximately 12,060 hospital beds).
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## 1. Introduction

In recent years, a large number of pharmaceutical residues have been reported to occur in the aquatic environment [1,2]. However, only a few of these compounds have also been detected in ground or drinking water samples, and were therefore recognized as being important for public drinking water supply [2]. Two of these compounds are the analgesic diclofenac and the anti-epileptic drug carbamazepine which are commonly found in sewage and surface waters at low μg/L concentrations. Besides dilution, the concentrations of diclofenac in surface waters can also significantly be decreased by photochemical degradation [3–5]. Nevertheless, residues of diclofenac have also been detected in ground and drinking water samples [2,6–9]. Carbamazepine was recognized as a compound that is not affected by conventional sewage treatment and that is also highly persistent in the aquatic environment [2,4,5,10]. Under influent (recharge) conditions, it can be leaching into ground water both because of its persistence and its documented mobility in the subsoil [7–10]. Depending on the geochemical and hydrochemical conditions during ground water recharge, only small to medium quantities of carbamazepine are attenuated [7–10], which also explains the occurrence of this compound in samples from public drinking water supply at ng/L concentrations [2,6]. Aside from special sources such as landfill leachates or production spills, the main source of pharmaceutical residues is municipal sewage effluents. However, the contributions of

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hospital and household effluents to the loads of pharmaceuticals occurring in the aquatic environment are still discussed. In a recent research project, this issue was investigated by creating a theoretical model for the prediction of the loads of pharmaceuticals originating from different sources (various hospitals and private households) in the sewer system and the receiving sewage treatment plants (STPs). Thus, consumption data were combined with information on the mode of administration and pharmacokinetic data. The results from these calculations were then compared and verified with analytical data obtained from actual measurements of composite samples collected from the sewers and the receiving STP in terms of a field trial. This paper describes and discusses the results obtained for the two above-mentioned pharmaceuticals.

## 2. Materials and methods

### 2.1. General model for the calculation of the predicted pharmaceutical loads

Important prerequisites for the occurrence of pharmaceutical residues from human medical care in the aquatic environment are: (1) the total amounts of the individual drug administered to patients in hospitals and private households (including both prescribed and over-the-counter drugs); (2) the mode of application (e.g. oral, dermal, intestinal or rectal) resulting in different rates of absorption; (3) the fate in the human organism (metabolism, formation of conjugates); and (4) the behavior of the drug residues inside the sewers, during the sewage treatment process and in the environment (persistence, sorption, bioaccumulation, metabolism). The first three factors have been taken into account for the calculation of the predicted loads of the individual pharmaceutical compound discharged by hospitals and/or private households. The last factor was estimated and addressed by comparing the measured loads in the influents and the effluents of the investigated STP and by comparing the predicted with the measured loads.

The predicted weekly load $M_{\text{totweek}}$ in kg/week of the individual pharmaceutical parent compound was calculated using the following equation:

$$M_{\text{totweek}} = \sum_{i=1}^{n} a_i \times b_i \times m_i \times s_i((1 - R_{\text{p}}) + R_{\text{p}}(x_{\text{p}} + x_{\text{c}}))_i \times 10^{-6} \quad (1)$$

were $a_i$ is the number of administered packages per week for each formulation or brand per week $i$, $b_i$ is the number of units per package for each formulation or brand $i$, $m_i$ is the content of active compound per unit in mg for each formulation or brand $i$, $s_i$ is the release rate of the pharmaceutical compound from the individual formulation $i$, $R_{\text{p}}$ is the absorption rate which depends on the mode of application of each formulation $i$, $x_{\text{p}}$ is the portion of the pharmaceutical which is excreted unchanged (as parent compound) after its absorption and $x_{\text{c}}$ is the percentage excreted as conjugate. Eq. (1) contains all important parameters for the calculation of the individual pharmaceutical loads. Nevertheless, this equation is not sufficient because pharmacokinetic data are mostly given as minimum–maximum information, e.g. the reported absorption rate for carbamazepine is 85–90% and the excretion rate of the reabsorbed but non-metabolized (parent) compound is 1–3%. Thus, a range of predicted loads is derived from minimum and maximum values calculated using the refined Eqs. (2) and (3):

$$M_{\text{totweek[min]}} = \sum_{i=1}^{n} a_i \times b_i \times m_i \times s_i((1 - R_{\text{p[max]}}) + R_{\text{p[max]}}(x_{\text{p[min]}} + x_{\text{c[min]}}))_i \times 10^{-6} \quad (2)$$

$$M_{\text{totweek[max]}} = \sum_{i=1}^{n} a_i \times b_i \times m_i \times s_i((1 - R_{\text{p[min]}}) + R_{\text{p[min]}}(x_{\text{p[max]}} + x_{\text{c[max]}}))_i \times 10^{-6} \quad (3)$$

### 2.2. Description of the location and the design of the study

The sewage effluents of a military hospital located in the central districts of Berlin, Germany, were investigated in terms of a field trial carried out between 8 and 16 April 2002. During the field trial, the total amounts of pharmaceuticals administered to the patients were recorded for each individual drug. This was achieved by recording the number and type of medication donated to the individual wards by the hospitals pharmacy before and during the field trial taking into account the pharmacokinetic data (lag times for excretion). Additionally, a form was created and distributed to all wards for the cumulative and anonymous recording of the number and type of medication administered to the patients. Both figures were acquired and compared to check for plausibility, which was confirmed. From these data, the predicted weekly loads originating from the military hospital were calculated for the individual drug as described earlier.

The investigated facility has a capacity of 300 hospital beds and is located “end of the pipe” (Fig. 1) with only a few private households discharging neglectable quantities of effluents into the sewer upstream from this hospital. Twenty-four hour composite samples were collected over a time period of 7 days from the sewer pipe in the Boyenstreet (Fig. 1) downstream from the hospital using a MIC B EX sampler from Ori-Abwassertechnik GmbH & Co. KG (Hille, Germany). The flow rate inside the sewer pipe was measured continuously using a Flo-Tote 3 flow meter device from Marsh-Mc Birney (Frederick, MD, USA) calibrated with the magnetic inductive flow meter Flo-Mate from Marsh-McBirney (Frederick, MD, USA).

In a neighboring sewage pumping station (SPS) (Fig. 1), the effluents from the military hospital merge with effluents

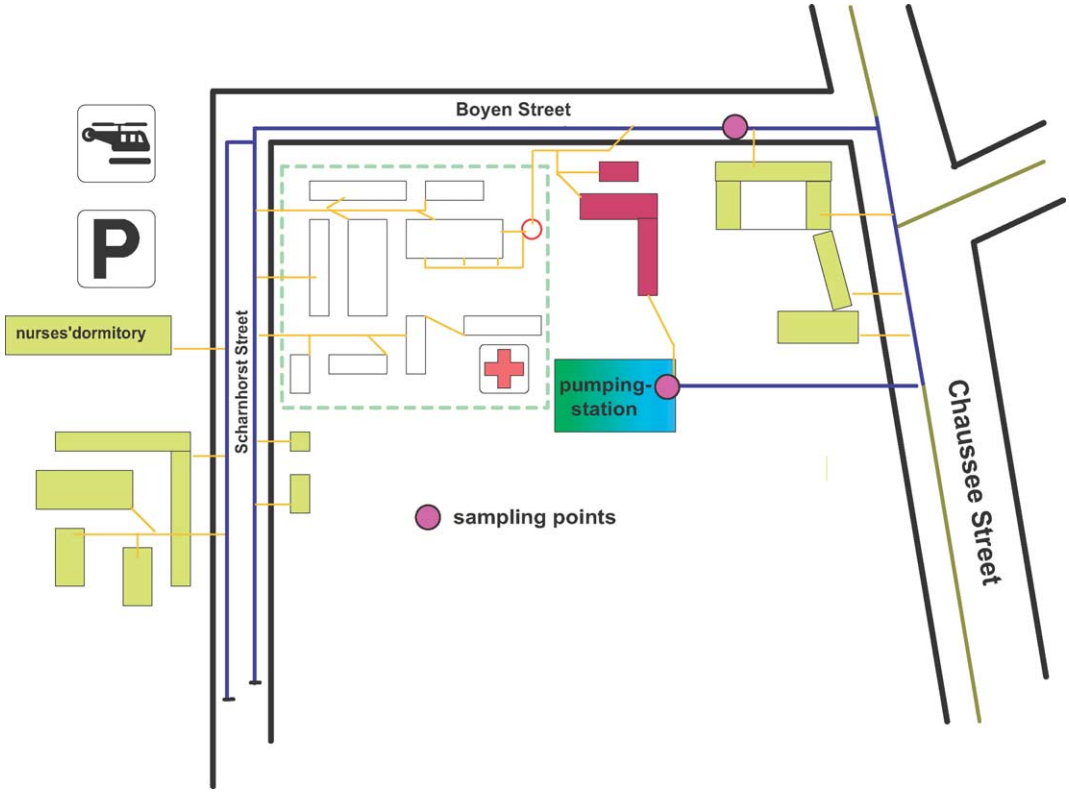


Fig. 1. Map showing the investigated military hospital and the receiving sewage pumping station.

from other civil hospitals and from private households discharged by about 96,000 inhabitants living in this drainage area. The SPS receives the effluents from four additional hospitals including Berlins largest hospital the Charité (1079 hospital beds), the DRK hospital (260 beds), the Jewish hospital (363 beds), and the St. Hedwig hospital (337 beds). These four hospitals provided monthly consumption data that were used for the estimation of the amounts administered for the individual drugs during the week of sampling. As shown earlier, the predicted loads of pharmaceuticals originating from private households were calculated from the data of prescription and over-the-counter drugs sold by Berlins pharmacies in 2001. Twenty-four hour composite samples were taken in the SPS using a PB-MOS sampler from Bühler (Dr. Bruno Lange GmbH, Düsseldorf, Germany). Information on the daily flow rates was provided by the Berlin Water Company.

The total sewage from the SPS was directed to the municipal STP in Ruhleben, Berlin's largest STP located in the central western districts of Berlin, Germany. The investigated STP purifies household sewage effluents from about one million inhabitants and hospital sewage effluents from approximately 12,060 hospital beds. The predicted STP influent loads were calculated from the data of prescription and over-the-counter drugs sold by Berlin's pharmacies in 2001 and from the hospital consumption data provided by the five hospitals located in the drainage area of the SPS, which was extrapolated to the total number of beds of all hospitals discharging their effluents into the STP in Ruhleben. There the sewage is purified by mechanical and an extended biological (activated sludge) sewage treatment for biological phosphorus and nitrogen removal. Thus, the treatment train of the STP also includes a nitrification and a denitrification step with sludge recirculation. The sewage sludge is dewatered in centrifuges and incinerated in fluidized bed furnaces, followed by waste heat utilization and flue gas cleaning. More than 200,000 $m^3$ of sewage per day is processed in this STP during dry weather conditions with an approximate residence time of up to 24 h. Daily composite samples of raw (influent) and treated (effluent) sewage water samples were taken between 8 and 16 April 2002. The influent and the effluent samples were collected with a time shift taking into account the residence time of the sewage in the sewer system between the SPS and the STP (6 h) and inside the STP (24 h). Information on the daily influent and effluent flow rates of the STP during the field trial were provided by the Berlin Water Company. These figures were used for the calculation of the measured STP's loads.

### 2.3. Analytical methods

Diclofenac and carbamazepine were analyzed by using two different methods described by Reddersen and Heberer [11]. All water samples were collected in glass bottles and, as far as possible, analyzed within 24 h or stored at 4 °C for less than 2 days. Depending on the matrix content, the samples were concentrated from a volume

of 100/500 mL (raw/purified sewage) down to a final sample volume of 0.1 μL (concentration factor: up to 5000). The methods apply solid-phase extraction (SPE) with non-endcapped reversed-phase octadecyl adsorbents for the extraction of the analytes from the water samples. The extracted residues were then derivatized using pentafluorobenzyl bromide (for diclofenac) or *N*-(*tert*-butyldimethylsilyl)-*N*-methyl-trifluoroacetamide (for both analytes) as derivatization reagents, respectively. The remaining residues were dissolved and analyzed using gas chromatography–mass spectrometry (GC–MS) in selected ion monitoring (SIM) mode. Using these methods, recoveries of around 90 and 110% are obtained for dicofenac and carbamazepine, respectively [11]. For both compounds, limits of detection (LODs) and limits of quantitation (LOQs) in samples of raw sewage were 10 and 20 ng/L, respectively. For purified sewage, LODs and LOQs were 2 and 4 ng/L, respectively [11]. For quality control, two suitable surrogate standards 2-(4-chorophenoxy)butyric acid (for the analysis of diclofenac) and dihydrocarbamazepine (for carbamazepine) were added to the samples before sample preparation. Sample analysis was repeated when the recoveries of the surrogates were below 70%. Additionally, the results obtained for both different methods were compared and verified for diclofenac. Carbamazepine was only accessible with one of the methods applying derivatization with *N*-(*tert*-butyldimethylsilyl)-*N*-methyl-trifluoroacetamide. But, the recoveries obtained for the surrogate standard dihydrocarbamazepine could be used to compensate for matrix interferences [11].

### 2.4. Calculation of measured loads and recoveries

The measured weekly loads $M_{\text{measweek}}$ (in kg/week) for diclofenac and carbamazepine were calculated for the sewer at Boyenstreet, the pumping station, and the sewage influents using Eq. (4):

$$M_{\text{measweek}} = \sum_{i=1}^{n=7} (c_{\text{d}} \times V_{\text{d}} \times 10^{-9})_i \quad (4)$$

were $c_{\text{d}}$ is the measured concentration in μg/L on each sampling days ($i = 1$–7) and $V_{\text{d}}$ is the daily sewage flow rate ($i = 1$–7) in L/d.

Eqs. (5) and (6) were used for the calculation of minimum and maximum recovery rates to compare the measured loads (Eq. (4)) with those predicted using Eqs. (2) and (3):

$$\text{REC}\,(\%)_{[\text{min}]} = \frac{M_{\text{measweek}}}{M_{\text{totweek}\,[\text{max}]}} \times 100 \quad (5)$$

$$\text{REC}\,(\%)_{[\text{max}]} = \frac{M_{\text{measweek}}}{M_{\text{totweek}\,[\text{min}]}} \times 100 \quad (6)$$

## 3. Results and discussion

### 3.1. Calculation of the predicted loads originating from the military hospital

Table 1 shows the ranges of the predicted weekly loads ($M_{\text{totweek}}$) of carbamazepine and diclofenac in the effluents from the military hospital. These loads were calculated from the amounts administered in the different wards of the hospital applying Eqs. (2) and (3). For the calculation of the loads, the administered amounts of both pharmaceuticals were acquired taking into account the modes of applications of the individual formulations. Additionally, it was assumed that the excreted conjugates were cleaved immediately after reaching the sewer. This assumption was confirmed in previous investigations of untreated sewage samples (hospital effluents), which were analyzed with and without enzymatic pretreatment. The analytical results obtained from these studies did not show any significant differences for both types of samples.

Although the amounts of diclofenac and carbamazepine administered in the military hospital were comparable, the predicted loads differ by a factor of four. This dissimilarity is mainly caused by compound-dependent differences in the modes of application. As can be seen in Table 1, dermal application was identified as the main source (> 68%) for the occurrence of residues of diclofenac in the effluents of the military hospital. This is caused by the low absorption rate reported for this type of application. Incomplete absorption was also identified as the most important cause for the occurrence of carbamazepine residues in the aquatic environment. Thus, the non-reabsorbed amounts of carbamazepine add the highest contributions to the overall loads of the parent compound detected in sewage.

Table 1
Calculation of the predicted weekly loads of carbamazepine and diclofenac in the effluents from the military hospital

| Compound | Mode of application | Amount administered (g/week)[a] | Absorption rate ($R_{\text{p}}$) (%) | Parent compound[b] excreted ($x_{\text{p}}$) (%) | Conjugates excreted[b] ($x_{\text{c}}$) (%) | Predicted sewage loads (g/week) ($M_{\text{totweek}}$) |
|---|---|---|---|---|---|---|
| Carbamazepine | Oral | 32.50 | 85–90 | 1–3 | 0 | 3.54–5.70 |
| Diclofenac | Oral | 35.73 | 100 | 1 | 10–15 | 3.93–5.72 |
| | Rectal | 2.47 | 100 | 1 | 10–15 | 0.27–0.40 |
| | Parenteral | 0.14 | 100 | 1 | 10–15 | 0.02 |
| | Dermal | 13.96 | 5–10 | 1 | 10–15 | 12.72–13.37 |
| | Total | 52.30 | – | – | – | 16.94–19.51 |

[a] Amount of parent compound administered in the military hospital during the field trial.
[b] Parent compounds and conjugates excreted after absorption.

Table 2
Calculation of the predicted weekly loads of carbamazepine and diclofenac in the drainage area of the pumping station

| Compound | Mode of application | Amount administered (g/week)[a] | | | Predicted sewage loads in the drainage area of the pumping station in g/week ($M_{totweek}$) |
|---|---|---|---|---|---|
| | | Military hospital | Other hospitals | Private households | |
| Carbamazepine | Oral | 32.5 | 514.5 | 1564.2 | 230.1–370.5 |
| Diclofenac | Oral | 35.7 | 92.8 | 843.4 | 106.0–154.1 |
| | Rectal | 2.5 | 30.1 | 71.7 | 10.7–15.6 |
| | Parenteral | 0.1 | 1.1 | 26.1 | 3.0–4.4 |
| | Dermal | 14.0 | 75.4 | 291.1 | 346.6–364.5 |
| | Total | 52.3 | 199.4 | 1232.3 | 466.3–538.6 |

[a] Amounts of parent compound administered during the field trial.

### 3.2. Calculation of the predicted loads for the pumping station

The effluents from the military hospital (300 beds) are directed into the neighboring SPS that also receives the effluents from four civil hospitals (with a total of 2039 beds) and from numerous private households representing about 96,000 inhabitants. Table 2 compiles the amounts of carbamazepine and diclofenac administered in all hospitals and private households of the drainage area of the SPS. The table also compiles the results from the calculation of the total loads predicted to occur in the SPS. The results were calculated using Eqs. (2) and (3) again taking into account the modes of application for the individual formulation.

One of the objectives of the field trial was to estimate the contribution of the military hospital but also of the civil hospitals to the total loads of pharmaceuticals in the sewers and the aquatic system. This was possible by using the data presented in Table 2. For the military hospital, a contribution of only 1.54% to the total loads of carbamazepine in the SPS was calculated. For the sum of all five military or civil hospitals located in the drainage area, a 26% contribution to the total loads of carbamazepine was determined. A similar picture was observed for diclofenac, where only 3.5 or 17% of the total amounts were administered in the military hospital or in all five hospitals, respectively. These figures are indicating that for such types of pharmaceuticals, the contributions of hospital effluents to the total loads of drug residues occurring in municipal sewers are much lower than those from private households. This result is also interesting because of the large number of hospital beds in this drainage area. Thus, the relative number of 24.7 hospital beds per 1000 inhabitants in the drainage area of the SPS is about twice as high as that in the total drainage area of the receiving STP in Berlin-Ruhleben (12.1 hospital beds per 1000 inhabitants). In conclusion, for hospital effluents, contributions of less than 15 and 10% can be expected for carbamazepine and diclofenac, respectively. Of course, this assumption will not apply to pharmaceuticals and diagnostics predominantly or even exclusively administered in hospitals such as X-ray contrast media.

### 3.3. Calculation of the predicted loads for the receiving STP

The sewage from the military hospital and the combined sewage from the SPS was directed to and treated in the municipal STP in Berlin-Ruhleben that purifies household sewage from about one million inhabitants and hospital sewage effluents from hospitals with approximately 12,060 hospital beds. The predicted STP influent loads for carbamazepine and diclofenac shown in Table 3 were calculated from the data of prescription and over-the-counter drugs sold by Berlins

Table 3
Calculation of the predicted weekly loads of carbamazepine and diclofenac in the influents from the sewage treatment plant (STP) Berlin-Ruhleben and contributions from the military hospital to the total loads

| Compound | Mode of application | Military hospital | | STP Ruhleben (influents) | | Contribution of the military hospital to the total loads[c] (%) |
|---|---|---|---|---|---|---|
| | | Amount administered (g/week)[a] | Predicted sewage loads ($M_{totweek}$) (g/week) | Amounts administered (g/week)[b] | Predicted sewage loads ($M_{totweek}$) (g/week) | |
| Carbamazepine | Oral | 32.5 | 3.5–5.7 | 19145 | 2087–3360 | 0.17 |
| Diclofenac | Oral | 35.7 | 3.9–5.7 | 9428 | 1037–1508 | (0.38) |
| | Rectal | 2.5 | 0.27–0.40 | 881 | 97–141 | (0.28) |
| | Parenteral | 0.1 | 0.02 | 279 | 31–45 | (0.05) |
| | Dermal | 14.0 | 12.7–13.4 | 3499 | 3188–3352 | (0.40) |
| | Total | 52.3 | 16.9–19.5 | 14087 | 4353–5047 | 0.39 |

[a] Parent compounds and conjugates excreted after absorption.
[b] Amount of parent compound administered in hospitals and private households during the field trial.
[c] Comparison of the predicted average loads of the military hospital and the influents of the sewage treatment plant in Berlin-Ruhleben.

Table 4
Comparison of predicted and measured weekly loads of carbamazepine and diclofenac at Boyenstreet (effluents from the military hospital) and in the sewage pumping station

| Compound | Sewer at Boyenstreet | | | Sewage pumping station | | |
|---|---|---|---|---|---|---|
| | Predicted loads (g/week) | Measured loads (g/week) | Recovery (%) | Predicted loads (g/week) | Measured loads (g/week) | Recovery (%) |
| Carbamazepine | 3.54–5.70 | 3.60 | 63–102 | 230.1–370.5 | 462.6 | 125–201 |
| Diclofenac | 19.24–19.83 | 6.21 | 32–37 | 466.3–538.6 | 354.3 | 66–76 |

pharmacies in 2001 and from the hospital consumption data provided by the five hospitals located in the drainage area of the SPS extrapolated to the total number of beds of all hospitals discharging their effluents into the STP in Ruhleben. For the effluents from the military hospital, contributions of only 0.17 and 0.39% to the predicted total loads in the STP were calculated for carbamazepine and diclofenac, respectively.

### *3.4. Results from the field measurements and comparison of predicted and measured loads*

A comparison of the predicted and the measured loads of carbamazepine and diclofenac is shown in Table 4. The sewer at Boyenstreet almost exclusively contains the effluents discharged by the military hospital whereas the sewage in the SPS is a merger of effluents originating from private households and all five hospitals located in the drainage area of the SPS (see also Sections 2.2 and 3.2). In general, the comparison with the empirically (analytically) determined loads showed a very good agreement for the predicted values. The recovery rates for the predicted loads were calculated using Eqs. (5) and (6) taking into account the spans of the reported pharmacokinetic data as described in Section 2.4.

For carbamazepine, maximum recovery rates of around 100% were obtained for the military hospital effluents and also for the combined sewage effluents in the SPS. For diclofenac, a recovery rate of around 70% was determined for the SPS, but only about 35% of the predicted loads were found in the military hospital effluents. The possible reasons for this observation will be discussed in Section 3.5.

In Table 5, the predicted loads for carbamazepine and diclofenac in the influents of the STP Berlin-Ruhleben are compared with their measured loads. Again, a very good agreement was found for carbamazepine with a calculated recovery rate of between 65 and 105%. The recovery rate for diclofenac was lower, but still around 70%. A comparison of the weekly loads measured in the influents and effluents of the STP yielded a removal rate of 37% for carbamazepine. For diclofenac, the loads detected in the effluents exceeded those found in the influents of the STP (case I) even though the influents and effluents were collected as daily composite samples with a time shift of 24 h taking into account the residence time of the sewage inside the STP. More reasonable results were obtained when using the predicted instead of the measured influent loads for the calculation of the removal rate (case II). The calculated removal rate of less than 15% for diclofenac is also in line with earlier investigations that were also carried out in Berlin [5,7]. In these studies, an average removal rate of 17% was calculated for diclofenac based on concentration data measured for the influents and effluents of different STPs. For carbamazepine, the removal rate calculated from the predicted influent and the measured effluent loads was between 3 and 40%. This result is in line with the value of 37%, which was calculated from measured influent and effluent loads. An average removal rate of 8% was determined for carbamazepine in previous investigations of influents and effluents from different STPs in Berlin [5,7].

### *3.5. Possible reasons for the low recovery of diclofenac*

During dermal application of diclofenac, significant parts of the used ointment or gel are absorbed by clothes or bandages. Although diclofenac will appear in the waste water after the washing of these items, the loads resulting from this source will not appear in the military hospital effluents because the laundry of the military hospital is not located inside the drainage area. This also explains the very low recovery of only around 35% of the predicted loads in the effluents of the military hospital. Additionally, paper towels, e.g. those used in hospitals to remove excess ointment during

Table 5
Comparison of predicted and measured weekly loads of carbamazepine and diclofenac in the influents and effluents of the sewage treatment plant (STP) in Berlin-Ruhleben

| Compound | STP influents | | | STP effluents | | |
|---|---|---|---|---|---|---|
| | Predicted loads (g/week) | Measured loads (g/week) | Recovery (%) | Measured loads (g/week) | Removal (%) | |
| | | | | | Case I[a] | Case II[b] |
| Carbamazepine | 2087–3360 | 3218 | 65–105 | 2022 | 37 | 3–40 |
| Diclofenac | 4353–5047 | 3219 | 64–74 | 4354 | (−35) | 0–14 |

[a] Recovery calculated on the basis of measured influent and effluent loads.
[b] Recovery calculated on the basis of measured effluent vs. predicted influent loads.

Voltaren® iontophoresis therapy, and gauze bandages will for the most part be disposed of after use. Residues of diclofenac from such sources will more likely appear in the solid waste and not in the waste water. Other possible reasons for the low recoveries of diclofenac and for measuring lower loads in the influents compared to the effluents of the STP might be the sorption and/or conjugation of diclofenac in raw sewage or potential analytical problems caused by matrix effects [12]. As described in Section 3.1, the presence of conjugated residues in raw sewage was excluded in a preceding study. Hydrophobic adsorption of diclofenac residues to suspended solids is also possible, but less likely because diclofenac is mostly dissociated at the pH of the raw sewage.

## 4. Conclusions

The results from the prediction of the loads and the field measurements have proven the validity of the model calculations for carbamazepine and diclofenac. The implementation of pharmacokinetic data into these calculations was found as being essential to obtain valid data also being superior to the commonly applied practice of using estimated prescription data for the calculation of concentrations or loads of pharmaceuticals in the environment. Especially, the type of application of the individual formulation was identified as being most important for the quantities of residues expected to occur in the municipal sewers. For both compounds, the non-absorbed part of the pharmaceutical substance contributed most to the total loads of these compounds in the sewers and the aquatic environment. Absorption depends on the type of application, which depends on the individual formulation of the administered medicine. Therefore, it is not sufficient to acquire only the total amounts of the administered pharmaceuticals but the individual amounts for each formulation. For carbamazepine, very good experimental recoveries of around 100% of its predicted loads were found in the sewage effluents from the military hospital and the combined sewage processed by the SPS and the receiving STP in Berlin-Ruhleben. Diclofenac was only found with lower recoveries (32–76%) in the combined municipal sewage and especially in the effluents from the military hospital. The lower recoveries could be explained by different types of application resulting in a different fate of these residues. For diclofenac, dermal application was identified as the main source for the occurrence of its residues in municipal sewage. Thus, “losses” of predicted diclofenac loads to solid waste (paper towels, gauze bandages, etc.) and to effluents from laundries (diclofenac absorbed by clothes or bandages) located outside the drainage area are possible. The example of diclofenac also shows that the loads of an individual drug in municipal sewage effluents might be overestimated whenever dermal application adds a relevant proportion to its total loads.

For diclofenac, the value of the measured weekly effluent load exceeded that of the measured weekly influent load, which might have been caused by problems in analyzing diclofenac in samples of raw sewage. Using the predicted weekly STP influent loads for diclofenac resulted in a low but reasonable removal rate of less than 15% which is consistent with results from earlier investigations. For carbamazepine, such problems were not observed and removal rates between 3 and 40% were calculated and measured for this compound. In total, 2.0 kg/week (105 kg/a) of carbamazepine and 4.4 kg/week (226 kg/a) of diclofenac are discharged into Berlin’s surface water by the municipal STP in Berlin-Ruhleben which treats household sewage discharged by approximately one million inhabitants (total population of Berlin including its surroundings: approximately four million) and by various hospitals with a capacity of approximately 12,060 hospital beds.

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