CrossMark

RESEARCH ARTICLE

# The different fate of antibiotics in the Thames River, UK, and the Katsura River, Japan

Seiya Hanamoto[1,2] · Norihide Nakada[1] · Monika D. Jürgens[3] · Andrew C. Johnson[3] ·
Naoyuki Yamashita[1] · Hiroaki Tanaka[1]

**Abstract** Little is known about the mechanisms influencing the differences in attenuation of antibiotics between rivers. In this study, the natural attenuation of four antibiotics (azithromycin, clarithromycin, sulfapyridine, and sulfamethoxazole) during transport along the Thames River, UK, over a distance of 8.3 km, and the Katsura River, Japan, over a distance of 7.6 km was compared. To assist interpretation of the field data, the individual degradation and sorption characteristics of the antibiotics were estimated by laboratory experiments using surface water or sediment taken from the same rivers. Azithromycin, clarithromycin, and sulfapyridine were attenuated by 92, 48, and 11% in the Thames River stretch. The first-order decay constants of azithromycin and sulfapyridine were similar to those in the Katsura River, while that of clarithromycin was 4.4 times higher. For sulfamethoxazole, the attenuation was limited in both rivers. Loss of sulfapyridine was attributed to both direct and indirect photolysis in the Thames River, but to only direct photolysis in the Katsura River. Loss of azithromycin and clarithromycin was attributed to sorption to sediment in both rivers. The probable explanation behind the difference in loss rates of clarithromycin between the two rivers was considered to be sediment sorption capacity.

## Introduction

Antibiotics have been detected worldwide in various environmental media including fresh water (Kolpin et al. 2002; Kasprzyk-Hordern et al. 2008; Shimizu et al. 2013), coastal water (Managaki et al. 2007; Jia et al. 2011; Shimizu et al. 2013), and sediments (Feitosa-Felizzola and Chiron 2009; Blair et al. 2013; Xu et al. 2014). Due to the potential risk to aquatic organisms (Cooper et al. 2008; Boxall et al. 2012; Cizmas et al. 2015) and possible links to antibiotic resistance (Ågerstrand et al. 2015), antibiotics are considered some of the most important emerging contaminants in aquatic environments. Studies on antibiotic-resistant bacteria have shown their wide prevalence in natural environments, including drinking water resources (Sharma et al. 2016), which is one of the most important challenges to the health care sector in the twenty-first century (Carvalho and Santos 2016). Therefore, in order to assess their risk and to aid in their management, the environmental fate and behavior of antibiotics should be modeled.

In the aquatic environment, antibiotics may be attenuated by physical, chemical, and/or biological processes. Studies on the natural attenuation of antibiotics during river transport suggest rapid removal is possible for some macrolide, quinolone, and tetracycline antibiotics (Hanamoto et al. 2013; Barber et al. 2013; Luo et al. 2011). However, the reported

✉ Seiya Hanamoto
hanamoto64@gmail.com

1 Research Center for Environmental Quality Management, Graduate School of Engineering, Kyoto University, 1-2 Yumihama, Otsu, Shiga 520-0811, Japan

2 Public Works Research Institute (PWRI), 1-6 Minamihara, Tsukuba, Ibaraki 305-8516, Japan

3 Centre for Ecology and Hydrology, Maclean Building, Crowmarsh Gifford, Wallingford, Oxfordshire OX10 8BB, UK

✑ Springer

attenuation of pharmaceuticals, including antibiotics, often differs between rivers (Li et al. 2016; Radke et al. 2010; Kunkel and Radke 2011; Dickenson et al. 2011; Acuña et al. 2015; Aymerich et al. 2016).

To understand natural attenuation, we must identify the key factors or processes that can explain the different loss rates between rivers. The mechanisms influencing the different attenuation of antibiotics between rivers have been estimated based on general characteristics of rivers such as hydrological, meteorological, and water quality parameters (Li et al. 2016; Dickenson et al. 2011; Acuña et al. 2015). Li et al. (2016) observed the attenuation of pharmaceuticals in four European rivers, and suggested that shallow depth and low turbidity made the photochemical attenuation more efficient in a small river, compared with larger rivers. However, in most cases, no obvious explanation was found for the difference between rivers. It is presumed that river characteristics, such as the composition of sediments, dissolved matter, and microbial communities (which are related to sorption, photolysis, and biodegradation processes, respectively), are determining the different fates of antibiotics among rivers. But to date, little research has been carried out to resolve the importance of these processes on the different fates.

Thus, the aim of this study was to identify the mechanisms influencing the different fate and behavior of selected antibiotics between rivers. The natural attenuation of the antibiotics in the Thames River (UK) was compared with the observations for the Katsura River (Japan) examined previously (Hanamoto et al. 2013). To help distinguish the roles of the local degradation potential and sorption characteristics for the antibiotics in both rivers, laboratory experiments and model estimations were used. The antibiotics studied were two macrolides (azithromycin and clarithromycin) and two sulfonamides (sulfapyridine and sulfamethoxazole). Their physical properties are summarized in the Supporting Information (SI) Table S1. It is desirable to be in a better position to predict the fate of pharmaceuticals and particularly antibiotics in rivers. In this case, the significance of the fate and behavior of the same compounds in very different rivers/climates/topologies was examined essentially to ask how predictable their loss is.

## Materials and methods

### Site descriptions

Samplings were conducted along an 8.3-km stretch of the Thames River (Fig. 1a), between site 1 (51° 42′ 55″ N, 1° 14′ 11″ W) and site 3 (51° 40′ 14″ N, 1° 16′ 8″ W), in Oxfordshire. The stretch receives water from Littlemore Brook (site 2), where treated wastewater is discharged 1.6 km upstream of site 2. The Katsura River stretch (7.6 km) receives water from two wastewater treatment plants

(sites a–c) and two tributaries (sites d and e) (Fig. 1b). There is little vegetation and no significant additional inflows along the two river stretches. The Thames River stretch catchment is mostly composed of limestone, clay/mudstone, and sandstone (Smith 2013), while the Katsura River stretch catchment is mostly granite, chalk, clay/mudstone, and sandstone (Ministry of Land, Infrastructure and Transport 2014). Most residents in both catchments are connected to the respective sewer system. These stretches were selected because they are highly impacted by treated wastewater, and antibiotic concentrations were expected to be higher there than elsewhere in each river. The general characteristics of the Thames River stretch and the Katsura River stretch are summarized in Table 1.

### Field study

The details of the sampling method in the Thames River stretch are described elsewhere (Nakada et al. 2017). Surface water samples were collected at three sites, once or twice a summer between 2012 and 2015, yielding a total of seven samplings. All the samples were collected hourly for 24 h by using automatic water samplers (ISCO Avalanche, ISCO 6712, Hach Sigma SD 900 or Bühler Montec Xian 1000). For the samples collected in 2012 and 2013, the 24-hourly samples were combined to 12 2-hourly samples and subjected to the antibiotic analysis separately. Since the diurnal variations of mass loading of the selected antibiotics were not significant (see "Natural attenuation of antibiotics in the rivers Thames and Katsura" section below), the samples collected in 2014 and 2015 were collected as 24-h composite samples by combining the 24-hourly samples. The samples were stored in plastic bottles with ascorbic acid at 1.0 g/L in darkness (to reduce sample deterioration) and taken to the laboratory. The samples were stored in a dark room at 4 °C until treatment. Details of the sample analysis are described in SI "Analysis of Antibiotics." Briefly, samples were filtered and concentrated by solid-phase extraction within 2 days of collection and the four selected antibiotics and the antiepileptic agent carbamazepine were measured by ultra-high-performance liquid chromatography coupled to a tandem mass spectrometer and quantified by a surrogate method (Narumiya et al. 2013). Carbamazepine can be considered as a relatively conservative tracer and so was used to estimate the flow rate (see below).

The mass balance approach was used to estimate the attenuation of the antibiotics. The amount of an antibiotic attenuated during the transport along the stretch relative to total mass loadings from sites 1 and 2 is defined as the attenuation rate (Eq. 1). In addition, since most attenuation processes in a river can be regarded as first-order reactions (see the "Laboratory experiment and model estimation" section described below), a first-order decay constant was determined by Eq. 2, using the Goal Seek function of Microsoft Excel. The flow rate at site 3
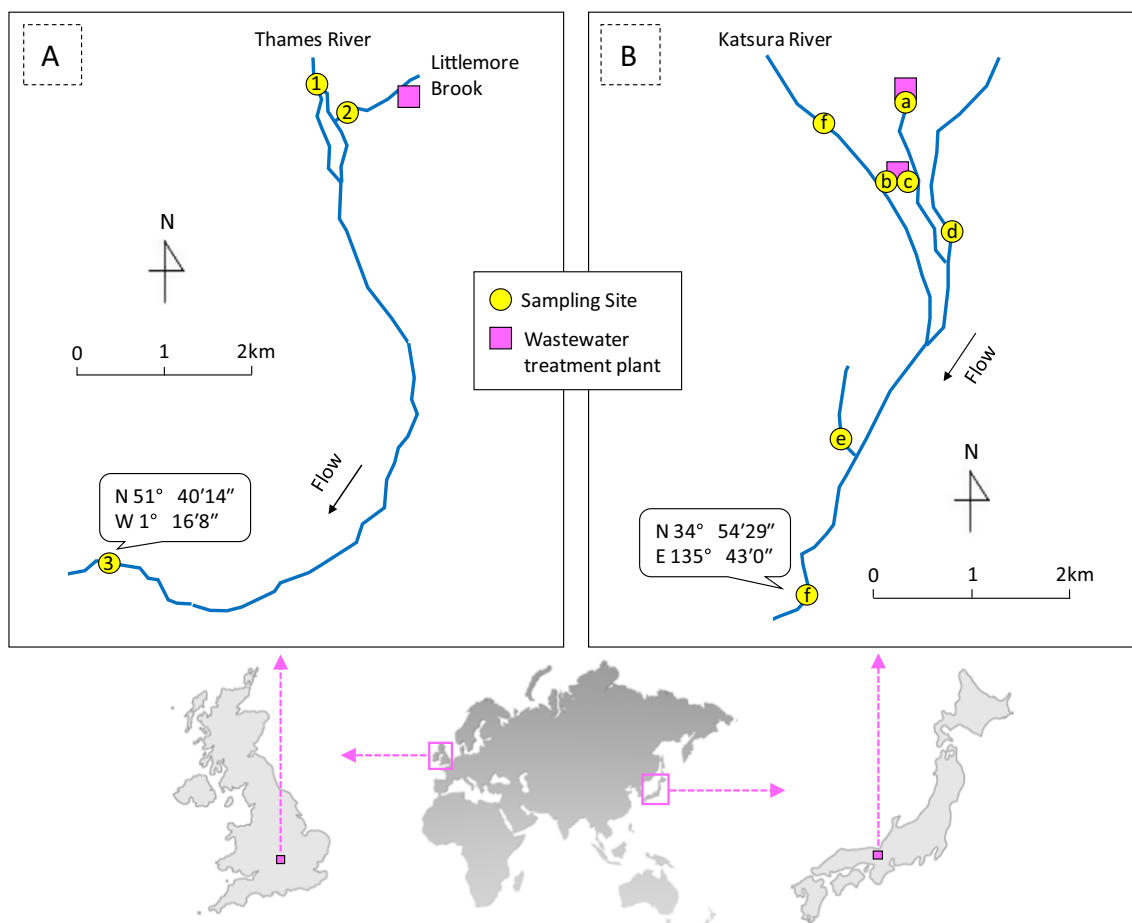
**Fig. 1** Locations of sampling sites on the **a** Thames River stretch and **b** Katsura River stretch

was estimated by subtracting the reported flow rate at the Ock River from that at Sutton Courtenay on the Thames River (Centre for Ecology and Hydrology, 2016). The flow rates at sites 1 and 2 were estimated by using the mass balance of

carbamazepine, which is persistent in aquatic environments (Nakada et al. 2008; Yamamoto et al. 2009) (Eqs. 3 and 4). The laboratory experiments indicated that carbamazepine was also persistent in the Thames River stretch (see the "Biotic and

**Table 1** General characteristics of the Thames and Katsura River stretches

| | | Thames River stretch | Katsura River stretch |
|---|---|---|---|
| Water quality parameters[a] | Temperature (°C)[b] | 18.0 (16.0–19.9) | 21.6 (9.4–27.3) |
| | pH[b] | 8.0 (7.8–8.1) | 7.4 (7.4–7.5) |
| | Suspended solids (mg/L)[b] | 8.9 (6.9–23.6) | 5.8 (3.5–19.8) |
| | Flow rate (m$^3$/s)[c] | 7.6 (4.0–49.5) | 22.4 (18.0–36.6) |
| | Flow velocity (m/s)[c] | 0.35 (0.26–0.90) | 0.54 (0.50–0.67) |
| | Depth (m)[c] | 0.53 (0.39–1.38) | 0.48 (0.44–0.56) |
| Hydrological conditions[a] | Hydraulic radius (m)[c] | 0.52 (0.38–1.30) | 0.47 (0.44–0.55) |
| | Friction velocity at sediment-water interface (m/s)[c] | 0.031 (0.024–0.067) | 0.048 (0.045–0.058) |
| | Travel time (h) | 6.5 (2.6–8.9) | 8.6 (7.0–9.4) |

[a] Median (minimum–maximum) in the field studies (n = 7, the Thames River; n = 6, the Katsura River), obtained as described in SI "General Characteristics of the Rivers"

[b] Data at the most downstream site in each stretch

[c] Average of several sites in each stretch

abiotic degradation and sorption characteristics of antibiotics in the Thames and 305 Katsura Rivers" section described below). The travel time was calculated from length and flow velocity, which was estimated from the flow rate using an empirical general relationship for rivers in the UK (Round et al. 1998).

$$R_a = \frac{C_1 Q_1 + C_2 Q_2 - C_3 Q_3}{C_1 Q_1 + C_2 Q_2} \times 100 \tag{1}$$

$$C_3 Q_3 = C_1 Q_1 e^{-k_a t_1} + C_2 Q_2 e^{-k_a t_2} \tag{2}$$

$$Q_1 = \frac{Q_3 (C_{CBZ3} - C_{CBZ2})}{C_{CBZ1} - C_{CBZ2}} \tag{3}$$

$$Q_2 = Q_3 - Q_1 \tag{4}$$

where $R_a$ is the attenuation rate (%); $k_a$ is the first-order decay constant (h$^{-1}$); $C$ is the concentration of an antibiotic in surface water (ng/L); $C_{CBZ}$ is the concentration of carbamazepine in the surface water (ng/L); $Q$ is the flow rate (m$^3$/s); $t$ is the travel time to site 3 (h); and the subscripts are site IDs in Fig. 1.

The sampling and calculation methods for the Katsura River stretch were similar to those for the Thames River stretch. The samples were collected from seven sites (Fig. 1b) three times in summer and three times in winter between 2011 and 2012. The details were described in our previous study (Hanamoto et al. 2013).

**Laboratory experiment and model estimation**

Indirect photolysis, biodegradation, and sorption tests, and model estimations of direct photolysis for the selected antibiotics and carbamazepine (test compounds) were carried out. Carbamazepine, a compound used to estimate the flow rate in the field study, was included here to test its persistence in the river stretches studied.

*Direct photolysis estimation*

Direct photolysis represents degradation of a compound derived from direct absorption of light by the compound, which follows a first-order reaction (Direct photolysis rate in water by sunlight 1998). Direct photolysis rate constants of the test compounds in the Thames River stretch under average summer conditions were estimated by an equation proposed in our previous study (Hanamoto et al. 2013). The equation considers the attenuation of sunlight in the atmosphere and water, and was derived from equations proposed by Zepp and Cline (1977) and Tixier et al. (2002) (see SI Eq. S2). The parameters used in the estimation were set as follows. Reported values (Hanamoto et al. 2013) were used for the photochemical properties (i.e., quantum yields and molar absorption coefficients). The depth of water was estimated from the reported flow rate (Centre for Ecology and Hydrology,

2016), estimated flow velocity (Round et al. 1998), and river width measured in Google Maps©, assuming the river cross section to be a rectangle. To determine light penetration in water, we collected surface water at site 3 under low flow conditions in 2013 summer and measured the absorptivity between 290 and 490 nm with a UV-Vis spectrophotometer (UV-2500PC, Shimadzu, Kyoto, Japan). The measured value was used for the light absorption coefficient of the water body. Reported values at latitude 50° N in summer under clear sky (Direct photolysis rate in water by sunlight 1998) were used for the spectrum of sunlight at the water surface. Since we could not obtain any monitoring data for UVB or UVA in the UK, those measured in Kyoto city, Japan (Project for monitoring sunlight intensity, 2013), were substituted to estimate the average fraction of sunlight blocked by the clouds. Theoretical values for sky radiation were used for the fraction of sunlight reflected at the water surface and the path length of sunlight in the water (Zepp and Cline 1977). Since there was little overhanging vegetation along the river stretch, the fraction of sunlight shaded by plants was set to 0. Direct photolysis rate constants in the Katsura River stretch were estimated using the same equation under average summer and winter conditions, because the field studies in the stretch were conducted in both summer and winter (see Table 1). The parameters used in the estimation were obtained in our previous study (Hanamoto et al. 2013) for the Katsura River stretch. The parameters for the Thames and Katsura river stretches are summarized in SI Table S3.

*Indirect photolysis test*

Indirect photolysis represents degradation of a compound driven by reactive species (e.g., singlet oxygen and hydroxyl radical) produced under light irradiance to dissolved matter (e.g., humic substance and nitrate) in surface water. Indirect photolysis rate constants of test compounds in the river stretches were assessed by applying US Environmental Protection Agency's (USEPA) harmonized test guideline 835.5270 (Indirect photolysis screening test 1998) to the surface water with an assumption of extrapolation as described below. Grab samples collected at site 3 in the Thames River stretch were brought to the laboratory, and filtered through a 1-μm-pore size glass fiber filter (GF/B, Whatman, UK) to prevent sorption of test compounds to suspended solids. A phosphate buffer solution (10 mM) at pH 7.8 (same as the surface water) was prepared with ultrapure water. The test compounds were added to the filtered surface water and phosphate buffer to give an initial concentration of 5 μg/L each. The 10-mL solutions in 20-mL quartz tubes were exposed to natural sunlight under a clear sky in the daytime for 4 h. The test compounds before and after the exposure were analyzed as described above. The change

in concentrations in darkness was negligible (data not shown). The surface water sample was collected in 2015 summer under low flow condition (7th percentile in 2010–2014, obtained in Centre for Ecology and Hydrology, 2016), and the experiment was conducted in duplicate in an open space at the Centre for Ecology and Hydrology, UK (51° 36′ 9″ N, 1° 6′ 45″ W), within 2 days of the sample collection. The same laboratory conditions and procedures were applied to the surface water sample collected at the Miyamae Bridge, the most downstream site in the Katsura River stretch (site g in Fig. 1b), under low flow condition (9th percentile in 2010–2014, obtained in Ministry of Land, Infrastructure and Transport, 2016). The sunlight exposure to the Katsura River water was conducted in open space at the Research Center for Environmental Quality Management, Japan (35° 0′ 9″ N, 135° 53′ 24″ E).

Since the indirect photolysis is generally a pseudo-first-order reaction (Indirect photolysis screening test 1998), the indirect photolysis rate constant in the test tube was estimated by subtracting the first-order rate constant in the phosphate buffer from that in the surface water (Eqs. 5 and 6). To extrapolate from the rate in the quartz test tube to that in the Thames River stretch, the ratio of sunlight absorbed by influential dissolved matter (i.e., dissolved matter producing reactive species influential on the antibiotics degradation) in the stretch to that in the tube is needed. Calculated sunlight intensities in the tubes with surface water and phosphate buffer were similar (data not shown) due to the short light path length in the tube. Most dissolved matter and also antibiotics absorb sunlight mainly in the 300–400-nm range (Hanamoto et al. 2013). Therefore, the ratio was estimated by dividing the direct photolysis rate constants of antibiotics estimated in the stretch ($k_{denv}$) by those observed in the test tube ($k_{pwtub}$), assuming that the shape of the solar action spectrum of the influential dissolved matter is similar to that of the antibiotics. The indirect photolysis rate constant in the Thames River stretch was then estimated using this ratio (Eq. 7).

$$k_{sw/pw_{tub}} = -\frac{1}{t_i} ln \frac{C_{sw/pw_{aft}}}{C_{sw/pw_{bef}}} \tag{5}$$

$$k_{i_{tub}} = k_{sw_{tub}} - k_{pw_{tub}} \tag{6}$$

$$k_{i_{env}} = \frac{k_{i_{tub}} k_{d_{env}}}{k_{pw_{tub}}} \tag{7}$$

where $k$ is the first-order rate constant ($h^{-1}$); $C$ is the concentration in the water (ng/L); $t_i$ is the exposure time (h); $k_i$ is the indirect photolysis rate constant ($h^{-1}$); $k_d$ is the direct photolysis rate constant ($h^{-1}$); and subscripts $tub$, $env$, $sw$, $pw$, $bef$, and $aft$ are values in the test tube, aquatic environment, surface water, ultrapure water, before the exposure, and after the exposure.

## Biodegradation test

To assess the degradation of test compounds resulting from the activity of microorganisms which live in surface water in the river stretches, a simple simulation test was conducted with reference to USEPA's harmonized test guideline 835.3170 (Shake Flask Die-Away Test 1998). Surface water grab samples collected at site 3 in the Thames River stretch were brought to the laboratory. The test compounds were first dissolved in ultrapure water and then added to the river water samples to give an initial concentration of 0.5 μg/L of each. The solutions were incubated at 20 ± 1 °C in the dark on a rotating shaker at 100 rpm for 24 h. The test compounds in the dissolved phase before and after the incubation were analyzed as described above, and those in the particulate phase were analyzed as described in SI "Analysis of Antibiotics." The amount of a compound in the solution (i.e., total of dissolved and particulate phase) that was lost in the incubation relative to the amount before the incubation was defined as a biodegradation loss (Eq. 8). Sorption of test compounds to glassware was negligible (Hanamoto et al. 2013). The change in suspended solid concentration during the incubation was negligible (data not shown). The surface water samples were collected twice in 2015 summer under low flow conditions (7th and 12th percentiles of the 5-year daily flow data 2010–2014, obtained in Centre for Ecology and Hydrology, 2016), and the experiments were conducted in duplicate within a day after the sample collection. The same laboratory conditions and procedures were applied to the surface water samples collected at the Miyamae Bridge in the Katsura River stretch (site g in Fig. 1b), although the experiment was conducted only once using sample collected under high flow condition (83rd percentile of the 5-year daily flow data 2010–2014, obtained in Ministry of Land, Infrastructure and Transport, 2016). Since the biodegradation of a compound of low concentration is a first-order reaction (Shake Flask Die-Away Test 1998), a biodegradation rate constant was determined by Eq. 9.

$$L_b = \frac{M_{bef} - M_{aft}}{M_{bef}} \times 100 \tag{8}$$

$$k_b = -\frac{1}{t_b} ln \left(1 - \frac{L_b}{100}\right) \tag{9}$$

where $L_b$ is the biodegradation loss (%); $k_b$ is the biodegradation rate constant ($h^{-1}$); $M$ is the mass of a compound in the solution (i.e., total of dissolved and particulate phase) (ng); $t_b$ is the incubation time (h); and subscripts $bef$ and $aft$ are values before and after the incubation.

## Sorption test

Since the sorption rate of a compound to river sediment is difficult to determine at laboratory scale due to

complications by hydrological factors such as hyporheic exchange, the sediment-water partition coefficient was measured to evaluate sediment sorption capacity. The sediment-water partition coefficients of test compounds were estimated in accordance with OECD test guideline No. 106 (Adsorption–desorption using a batch equilibrium method 1995). Sediment grab samples were collected from the top 5 cm in the Thames River stretch—two mixture sites—and in the Katsura River stretch—three mixture sites in 2014 summer under low flow conditions and brought to the laboratory, air-dried, and passed through a 2-mm sieve. The solvent used for the sorption experiments with the sediments was surface water from the Katsura River at the Miyamae Bridge (site g in Fig. 1b) which was filtered through a 1-μm pore size glass fiber filter, and to which 0.02% sodium azide was added to minimize microbial activity. Sediments (0.15–0.20 g) and river water (50 mL) were put into glass centrifuge tubes, and the test compounds were added to give an initial concentration of 200 ng/L each. The tubes were then rotated at 20 ± 1 °C in the dark. After 2 days, the test compounds in the water and sediment were analyzed as described above and in SI "Analysis of Antibiotics," respectively. We had previously observed that the sediment-water equilibrium for the test compounds was nearly reached within 2 days and that changes in concentration without sediment were negligible (Hanamoto et al. 2013). The sediment-water partition coefficients were determined by dividing the concentration in the sediment by that in the water (Eq. 10). A higher coefficient indicates a greater

sorption capacity of the sediment. The experiment was conducted in duplicate.

$$K_p = \frac{C_{seq}}{C_{weq}} \qquad (10)$$

where $K_p$ is the sediment-water partitioning coefficient (L/kg); $C_{weq}$ is the concentration in the water at equilibrium (ng/L); and $C_{seq}$ is the concentration in the sediment at equilibrium (ng/kg).

## Results and discussion

### Natural attenuation of antibiotics in the rivers Thames and Katsura

Concentrations of the selected antibiotics and carbamazepine in the Littlemore Brook (site 2), a wastewater-impacted tributary, were much higher than those in the Thames River (sites 1 and 3, Fig. 2a). The mass loadings from site 2 were higher than those from site 1 for azithromycin and clarithromycin, and vice versa for the others (Fig. 2b). This difference between compounds would be mainly attributable to the attenuation of the two macrolides during the transport in the stretch upstream of site 1. Coefficients of variations (CVs) of concentrations within a day at the major sources (i.e., site 2 for the two macrolides and site 1 for the others) were low (below 20%, see SI Fig. S1), indicating diurnal variation of concentration would not produce substantial errors in estimating attenuations and flow rates by Eqs. 1–4. Higher CVs of the two
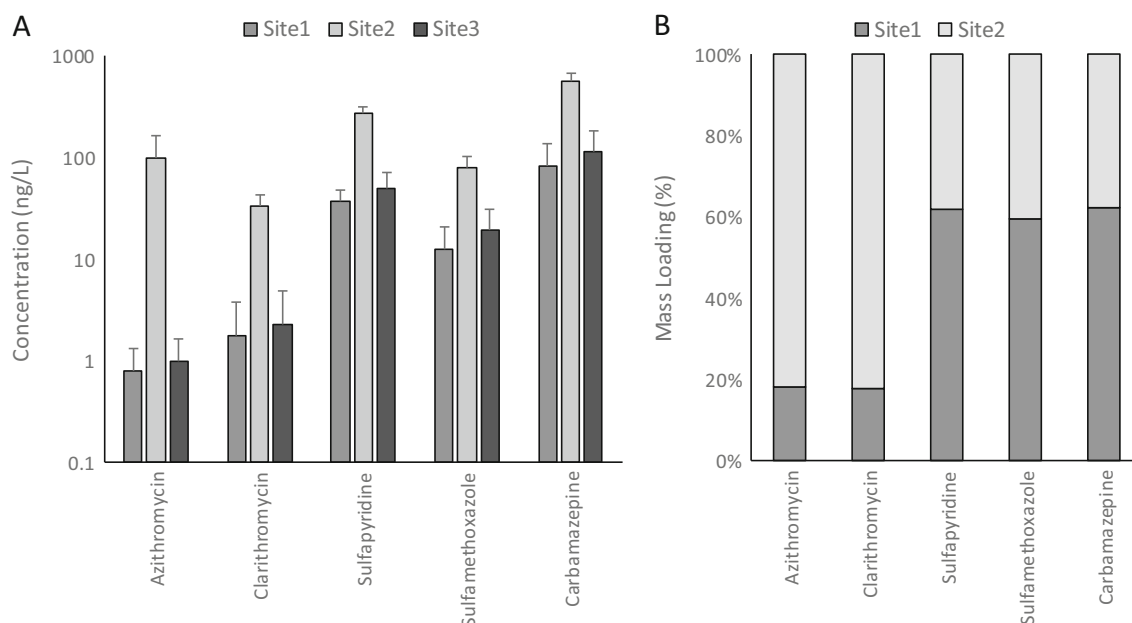


**Fig. 2 a** Measured concentrations. **b** Source distribution of antibiotics and carbamazepine in the Thames River stretch. For **a**, the vertical bars denote means, and the error bars denote standard deviations ($n = 7$). For **b**, the vertical bars denote medians ($n = 7$)

macrolides in sites 1 and 3 might be attributed to temporal variability of attenuation in the Thames River.

The attenuation rates for the Thames River stretch were low for the two sulfonamides, sulfamethoxazole (−2% on average) and sulfapyridine (11%), and higher for the two macrolides, clarithromycin (48%) and azithromycin (92%), indicating substantial losses for the macrolides. The estimated average half-lives in the Thames River stretch were 29.2, 4.5, and 1.9 h for sulfapyridine, clarithromycin, and azithromycin, respectively. The decay constants in the Thames River were 4.4, 1.2, and 1.2 times higher than those in the Katsura River for clarithromycin, azithromycin, and sulfapyridine, respectively (Fig. 3). Thus, the fate of clarithromycin, in particular, was very different between the rivers. Though there was no statistically significant difference in the decay constants of antibiotics between the rivers even for clarithromycin ($p = 0.087$), this was attributable to their high fluctuation between sampling days and the limited number of samples. The fluctuation of the decay constants would be mainly driven by the daily variation in environmental factors such as sunlight intensity and flow velocity (see "Mechanistic considerations for the difference in attenuation between the rivers" section described below). Since surface water samples were collected as composite samples, the sampling error is minimal.

The limited attenuation of the sulfonamides in both rivers is similar to several observations in Swedish rivers (Bendz et al. 2005; Li et al. 2016), American rivers (Barber et al. 2013), and
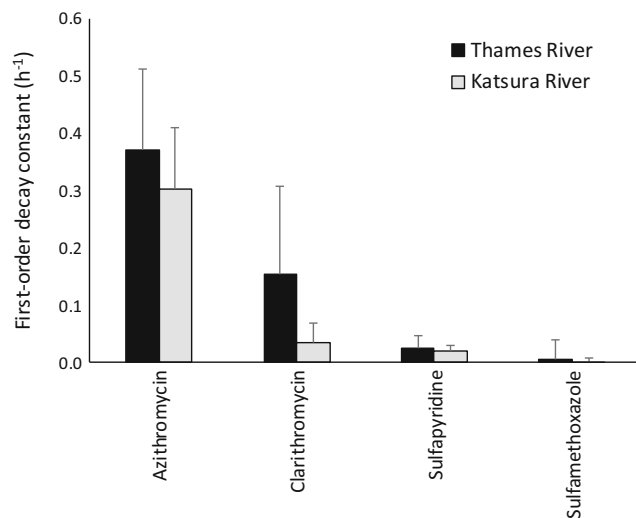


**Fig. 3** Comparison of the first-order decay constants of the antibiotics between the Thames River stretch and the Katsura River stretch (means and standard deviations). The decay constant in the Katsura River was measured in a previous study (Hanamoto et al. 2013). For sulfapyridine, there was a significant difference between the summer and winter sampling campaigns in the Katsura River stretch (see SI Fig. S2), so only the three decay constants obtained in summer were included, while all six decay constants were included for the other antibiotics. The number of samples was $n = 7$ for all antibiotics in the Thames River; $n = 3$ for sulfapyridine in the Katsura River; and $n = 6$ for the other antibiotics in the Katsura River

a Spanish river (Aymerich et al. 2016). No report on the decay constant was found for the investigated macrolides, but that of erythromycin, a similar macrolide antibiotic, was reported in Iberian rivers (0.17 h$^{-1}$) (Acuña et al. 2015). This is comparable to that of clarithromycin observed in the Thames River stretch.

## Biotic and abiotic degradation and sorption characteristics of antibiotics in the Thames and Katsura rivers

The direct photolysis rate constant of sulfapyridine was 0.011 h$^{-1}$ in the Thames River stretch and 0.022 h$^{-1}$ in the Katsura River stretch under average summer conditions and below 0.010 h$^{-1}$ in the Katsura River stretch in winter. The lower rate constant in the Thames River compared to the Katsura in summer was mainly due to a higher light absorption coefficient of the water body (see SI Fig. S3). The direct photolysis of sulfapyridine was attributed to desulfonation and/or denitrification, as well as hydroxylation of photooxidized heterocyclic rings (Baena-Nogueras et al. 2017). The rate constants of the other antibiotics were below 0.010 h$^{-1}$ in both rivers.

The first-order rate constant of sulfapyridine observed in the indirect photolysis experiment in the Thames River water was 2.4 times higher than that in the ultrapure water, while the constant of sulfapyridine in the Katsura River water was similar to that in the ultrapure water (see SI Fig. S4). The estimated indirect photolysis rate constant of sulfapyridine in the Thames River stretch was 0.015 h$^{-1}$, while that in the Katsura River stretch was below 0.010 h$^{-1}$. Previously, significant indirect photolysis of sulfapyridine was reported in water from a constructed wetland, and this was attributed not to nitrate but to a portion of dissolved organic matter (Challis et al. 2013). Since there is no other study on indirect photolysis of sulfapyridine under sunlight, further mechanistic studies should be conducted to elucidate constituents of dissolved organic matter determining the indirect photolysis of sulfapyridine. The decrease in concentrations of the other antibiotics during the sunlit experiment was below 20%, yielding indirect photolysis rate constants of below 0.010 h$^{-1}$ in both rivers.

The biodegradation losses derived from the laboratory experiments over 24 h were below 20%, and the biodegradation rate constants were below 0.010 h$^{-1}$ for all antibiotics in both rivers. The reported biodegradation rate constants of the antibiotics, which were observed in Katsura River water under the 5-day incubation test, were also below 0.010 h$^{-1}$ (Hanamoto et al. 2013).

The relative sediment-water partitioning coefficients were azithromycin > clarithromycin ≫ sulfapyridine > sulfamethoxazole in both rivers. The partitioning coefficients for the Thames River sediments were 1.4 and 5.5 times (on average)

higher than those for the Katsura River sediment for azithromycin and clarithromycin, respectively. Since the two macrolides mostly exist in cationic forms in surface water (Sibley and Pedersen 2008), their sorption is likely to be due to coulombic attraction to negatively charged surface sites on sediments (e.g., permanent negative charge on aluminosilicate clays, deprotonated surface hydroxyl groups on sediment metal oxides, and deprotonated surface hydroxyl or carboxylic acid groups on sediment organic matter, Vasudevan et al. 2009). Because of the multiple sorption sites, sorption capacities of macrolides did not correlate with general properties of soils (e.g., organic carbon content, cation exchange capacity) (Kodešová et al. 2015; Srinivasan et al. 2014), and there is no related mechanistic study with sediments. Given the geologic differences between the two catchments (see the "Site descriptions" section above), mineralogical compositions of sediments seem to be different between the rivers, and this might have caused the much higher partitioning coefficient of clarithromycin in the Thames River than in the Katsura River. Therefore, further mechanistic studies should be conducted to elucidate sediment constituents determining the sorption capacity of clarithromycin. As for the difference in partitioning coefficients between the compounds, previous studies on sediments indicated that the octanol-water partitioning coefficient ($K_{ow}$), the indicator of hydrophobicity of a compound, could not explain the different sorptivity between pharmaceuticals (Yamamoto et al. 2009; Schaffer et al. 2012). Given the hydrophilic and ionizable properties of pharmaceuticals and negatively charged surface sites on sediments, the fraction of pharmaceuticals existing in cationic form would be the most influential factor differentiating antibiotics sorptivities. Therefore, the observed low sorptivities of the two sulfonamides could be because they mostly exist in anionic or neutral forms within the common environmental pH range (Gao and Pedersen 2005).

For carbamazepine, all the degradation rate constants were below 0.010 $h^{-1}$, the partitioning coefficient was not measurable due to its low sorptivity, and its predicted volatilization is expected to be negligible (Hanamoto et al. 2013) in both rivers, indicating the validity of using it as a conservative tracer to estimate the flow rate in the river stretches.

## Mechanistic considerations for the difference in attenuation between the rivers

The degradation and volatilization (Hanamoto et al. 2013) rates were negligible, and sediment sorption capacity was low in both rivers for sulfamethoxazole, which is consistent with its limited natural attenuation (see Fig. 3). Since biodegradation and volatilization (Hanamoto et al. 2013) were negligible and sediment sorption capacity was low in both rivers for sulfapyridine, its major loss mechanism during transport

along the river stretches was direct and/or indirect photolysis. The decay constants of sulfapyridine observed in the river stretches were comparable to the sum of its direct and indirect photolysis rate constants under average summer conditions (Fig. 4), indicating the assumption made in extrapolating the indirect photolysis rate constants observed in the test tubes into those in the river stretches (see the "Indirect photolysis test" section described above) did not produce a substantial error in the estimate. Therefore, the attenuation of sulfapyridine can be considered to be mainly due to both direct and indirect photolysis in the Thames River, but to only direct photolysis in the Katsura River. The difference in indirect photolysis between the rivers is attributable to constituents of dissolved organic matter (see the "Biotic and abiotic degradation and sorption characteristics of antibiotics in the Thames and 305 Katsura Rivers" section above).

The degradation and volatilization (Hanamoto et al. 2013) rates were also negligible, but the sediment sorption capacity was high in both rivers for azithromycin and clarithromycin. Therefore, the major loss mechanism during transport along the river stretches for the two macrolides would be sorption to sediment, which is consistent with their reported high concentrations in sediments (Blair et al. 2013; Feitosa-Felizzola and Chiron 2009; Xu et al. 2014; Luo et al. 2011). The much higher decay constant of clarithromycin in the Thames River than in the Katsura River was attributable to the higher sediment sorption capacity in the former, given their positive relationship shown in Fig. 5. The sorption rate constant of a compound (i.e., mass transferred from overlaying water into sediment per unit time) is determined by a driving force, which is defined as the difference in sediment pore water
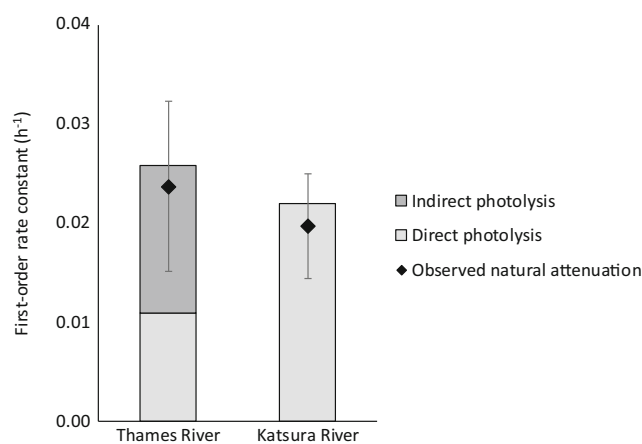


**Fig. 4** Comparison of the observed first-order decay constant and the estimated photolysis rate constants for sulfapyridine under average summer conditions. Since there was a significant difference in the decay constants between the summer and winter sampling campaigns in the Katsura River stretch, the comparison was conducted under summer conditions. Means and standard errors of measurements in summer sampling campaigns were substituted for the decay constants ($n = 7$ for the Thames River; $n = 3$ for the Katsura River). The decay constant in the Katsura River was measured in a previous study (Hanamoto et al. 2013)
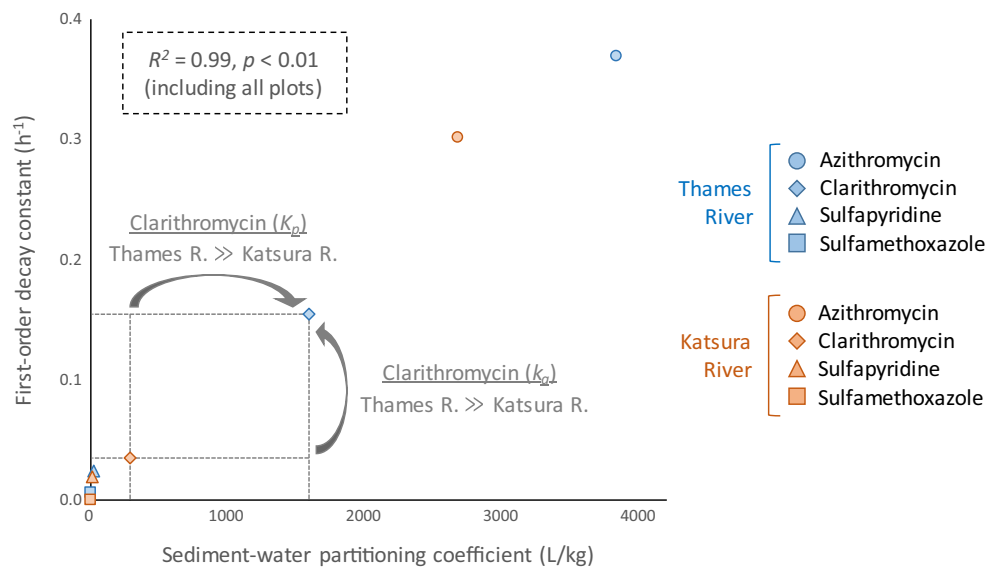
**Fig. 5** Comparison of the first-order decay constants ($k_a$) and the sediment-water partitioning coefficients ($K_p$) for antibiotics. Means were substituted for the decay constant ($n = 7$ for all antibiotics in the Thames River; $n = 3$ for sulfapyridine in the Katsura River; $n = 6$ for the other antibiotics in the Katsura River). The decay constants in the Katsura River were measured in a previous study (Hanamoto et al. 2013). A higher partitioning coefficient indicates a greater sorption capacity of the sediment. Since the partitioning coefficient of sulfamethoxazole was not available due to its low sorptivity, it was plotted as 0

and overlaying water concentrations, and a mass transfer coefficient (Thibodeaux 1996). The sediment sorption capacity is an influential factor determining the driving force of sorption to sediment.

Another possible factor differentiating the driving force of sorption between the rivers could be biodegradation of clarithromycin within the sediment. Though there is no related study on sediments, degradation rates of the macrolides were quite low within soils (Kodešová et al. 2016) and biosolid-amended soils (Walters et al. 2010) (half lives were mostly over 100 days), which indicates biodegradation within sediment is likely to be low for clarithromycin. The sorption rate constant is also affected by hydrological parameters such as flow velocity, hydraulic radius, and hyporheic exchange, which are determinants of the mass transfer coefficient, and replacement of surface sediment during high flow events, which affects the driving force. However, these parameters could not explain the fact that the fate of only clarithromycin was very different between the two rivers, since such parameters do not have substance-specific effects (Thibodeaux 1996). The sorption to suspended solids was also not considered to be playing an important role given that the concentration was low in both rivers (see Table 1). Thus, though there are some unquantified factors, the sediment sorption capacity would be a key factor explaining the different fate of clarithromycin between the rivers. Further studies to estimate the sorption rate constant should be conducted and compared with the observed attenuation to help confirm this.

## Conclusions

The field study revealed that the decay constants in the Thames River were 4.4, 1.2, and 1.2 times higher than those in the Katsura River for clarithromycin, azithromycin, and sulfapyridine, respectively, while the attenuation was limited in both rivers for sulfamethoxazole. River characterization highlighted sediment sorption capacity which played an important role in the different loss rates of clarithromycin between the two rivers. Attenuation of azithromycin was also attributed to sorption to sediment in both rivers. Both direct and indirect photolysis affected attenuation of sulfapyridine in the Thames River, while indirect photolysis was negligible in the Katsura River. These findings provide a better understanding of the key factors differentiating natural attenuation of antibiotics between rivers. Future work should focus on the sediment properties which determine the sorption capacity of the macrolides. In addition, more information is needed on the types of dissolved organic matter determining indirect photolysis of sulfapyridine, as well as on sorption rate constants of the macrolides in the rivers.

# References

Acuña V, Schiller D, García-Galán MJ, Rodríguez-Mozaz S, Corominas L, Petrovic M, Poch M, Barceló D, Sabater S (2015) Occurrence and in-stream attenuation of wastewater-derived pharmaceuticals in Iberian rivers. Sci Total Environ 503-504:133–141

Adsorption–desorption using a batch equilibrium method (1995) OECD test guidelines for chemicals No. 106. In: OECD

Ågerstrand M, Berg C, Björlenius B, Breitholtz M, Brunström B, Fick J et al (2015) Improving environmental risk assessment of human pharmaceuticals. Environ Sci Technol 49:5336–5345

Aymerich I, Acuna V, Barcel D, García MJ, Petrovic M, Poch M, Rodriguez-Mozaz S, Rodríguez-Roda I, Sabater S, von Schiller D (2016) Corominas, Ll. Attenuation of pharmaceuticals and their transformation products in a wastewater treatment plant and its receiving river ecosystem. Water Res 100:126–136

Baena-Nogueras RM, González-Mazo E, Lara-Martín PA (2017) Photolysis of antibiotics under simulated sunlight irradiation: identification of photoproducts by high-resolution mass spectrometry. Environ Sci Technol 51(6):3148–3156

Barber LB, Keefe SH, Brown GK, Furlong ET, Gray JL, Kolpin DW, Meyer MT, Sandstrom MW, Zaugg SD (2013) Persistence and potential effects of complex organic contaminant mixtures in wastewater-impacted streams. Environ Sci Technol 47:2177–2188

Bendz D, Paxéus NA, Ginn TR, Loge FJ (2005) Occurrence and fate of pharmaceutically active compounds in the environment, a case study: Höje River in Sweden. J Hazard Mater 122:195–204

Blair BD, Cargo JP, Hedman CJ, Klaper RD (2013) Pharmaceuticals and personal care products found in the Great Lakes above concentrations of environmental concern. Chemosphere 93:2116–2123

Boxall ABA, Rudd MA, Brooks BW, Caldwell DJ, Choi K, Hickmann S, Innes E, Ostapyk K, Staveley JP, Verslycke T, Ankley GT, Beazley KF, Belanger SE, Berninger JP, Carriquiriborde P, Coors A, DeLeo PC, Dyer SD, Ericson JF, Gagné F, Giesy JP, Gouin T, Hallstrom L, Karlsson MV, Larsson DGJ, Lazorchak JM, Mastrocco F, McLaughlin A, McMaster ME, Meyerhoff RD, Moore R, Parrott JL, Snape JR, Murray-Smith R, Servos MR, Sibley PK, Straub JO, Szabo ND, Topp E, Tetreault GR, Trudeau VL, Kraak GVD (2012) Pharmaceuticals and personal care products in the environment: what are the big questions? Environ Health Perspect 120:1221–1229

Carvalho IT, Santos L (2016) Antibiotics in the aquatic environments: a review of the European scenario. Environ Int 94:736–757

Centre for Ecology and Hydrology (2016) The UK, National River Flow Archive, Website; http://nrfa.ceh.ac.uk. Accessed 20 Sept 2016

Challis JK, Carlson JC, Friesen KJ, Hanson ML, Wong CS (2013) Aquatic photochemistry of the sulfonamide antibiotic sulfapyridine. J Photochem Photo boil A Chem 262:14–21

Cizmas L, Sharma VK, Gray CM, McDonald TJ (2015) Pharmaceuticals and personal care products in waters: occurrence, toxicity, and risk. Environ Chem Lett 13:381–394

Cooper ER, Siewicki TC, Phillips K (2008) Preliminary risk assessment database and risk ranking of pharmaceuticals in the environment. Sci Total Environ 398:26–33

Dickenson ERV, Snyder SA, Sedlak DL, Drewes JE (2011) Indicator compounds for assessment of wastewater effluent contributions to flow and water quality. Water Res 45:1199–1212

Direct photolysis rate in water by sunlight (1998) Fate, transport, and transformation test guidelines, OPPTS 835.2210. U.S. EPA, Washington, DC

Feitosa-Felizzola J, Chiron S (2009) Occurrence and distribution of selected antibiotics in a small Mediterranean stream (Arc River, Southern France). J Hydrol 364:50–57

Gao J, Pedersen JA (2005) Adsorption of sulfonamide antimicrobial agents to clay minerals. Environ Sci Technol 39(24):9509–9516

Hanamoto S, Nakada N, Yamashita N, Tanaka H (2013) Modeling the photochemical attenuation of down-the-drain chemicals during river transport by stochastic methods and field measurements of pharmaceuticals and personal care products. Environ Sci Technol 47(23): 13571–13577

Indirect photolysis screening test (1998) Sunlight photolysis in waters containing dissolved humic substances., fate, transport, and transformation test guidelines, OPPTS 835.5270. U.S. EPA, Washington, DC

Jia A, Hu J, Wu X, Peng H, Wu S, Dong Z (2011) Occurrence and source apportionment of sulfonamides and their metabolites in Liaodong Bay and the adjacent Liao River basin, North China. Environ Toxicol Chem 30:1252–1260

Kasprzyk-Hordern B, Dinsdale RM, Guwy AJ (2008) The occurrence of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs in surface water in South Wales, UK. Water Res 42: 3498–3518

Kodešová R, Grabic R, Kočárek M, Klement A, Golovko O, Fér M, Nikodem A, Jakšík O (2015) Pharmaceuticals' sorptions relative to properties of thirteen different soils. Sci Total Environ 511:435–443

Kodešová R, Kočárek M, Klement A, Golovko O, Koba O, Fér M, Nikodem A, Vondráčková L, Jakšík O, Grabic R (2016) An analysis of the dissipation of pharmaceuticals under thirteen different soil conditions. Sci Total Environ 544:369–381

Kolpin DW, Furlong ET, Meyer MT, Thurman EM, Zaugg SD, Barber LB, Buxton HT (2002) Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999−2000—a national reconnaissance. Environ Sci Technol 36:1202-−1211

Kunkel U, Radke M (2011) Reactive tracer test to evaluate the fate of pharmaceuticals in rivers. Environ Sci Technol 45:6296–6302

Li Z, Sobek A, Radke M (2016) Fate of pharmaceuticals and their transformation products in four small European rivers receiving treated wastewater Environ. Sci Technol 50:5614–5621

Luo Y, Xu L, Rysz M, Wang YQ, Zhang H, Alvarez PJJ (2011) Occurrence and transport of tetracycline, sulfonamide, quinolone, and macrolide antibiotics in the Haihe River Basin, China. Environ Sci Technol 45:1827–1833

Managaki S, Murata A, Takada H, Tuyen BC, Chiem NH (2007) Distribution of macrolides, sulfonamides, and trimethoprim in tropical waters: ubiquitous occurrence of veterinary antibiotics in the Mekong Delta. Environ Sci Technol 41:8004–8010

Ministry of Land, Infrastructure and Transport (2014) Japan, Report (in Japanese, https://www.mlit.go.jp/river/shinngikai_blog/tisuinoarikata/dai33kai/dai33kai_siryou2-1-2.pdf

Ministry of Land, Infrastructure and Transport (2016) Japan, Water information system (in Japanese) Website; http://www1.river.go.jp/. Accessed 20 Sept 2016

Nakada N, Hanamoto S, Jürgens MD, Johnson AC, Bowes MJ, Tanaka H (2017) Assessing the population equivalent and performance of wastewater treatment through the ratios of pharmaceuticals and personal care products present in a river basin: application to the River Thames basin, UK. Sci Total Environ 575:1100–1108

Nakada N, Kiri K, Shinohara H, Harada A, Kuroda K, Takizawa S, Takada H (2008) Evaluation of pharmaceuticals and personal care products as water-soluble molecular markers of sewage. Environ Sci Technol 42(17):6347–6353

Narumiya M, Nakada N, Yamashita N, Tanaka H (2013) Phase distribution and removal of pharmaceuticals and personal care products during anaerobic sludge digestion. J Hazard Mater 260:305–312

Project for monitoring sunlight intensity (2013) (in Japanese) Website; http://www.cs.kyoto-wu.ac.jp/%7Ekonami/climate/index.shtml. Accessed 12 July 2013

Radke M, Ulrich H, Wurm C, Kunkel U (2010) Dynamics and attenuation of acidic pharmaceuticals along a river stretch. Environ Sci Technol 44:2968–2974

Round CE, Young AR, Fox K (1998) A regionally applicable model for estimating flow velocity at ungauged river sites in the UK. J Chart Inst Water Environ Manag 6:402–405

Schaffer M, Boxberger N, Börnick H, Licha T, Worch E (2012) Sorption influenced transport of ionizable pharmaceuticals onto a natural sandy aquifer sediment at different pH. Chemosphere 87:513–520

Shake Flask Die-Away Test (1998) Fate, transport, and transformation test guidelines, OPPTS 835.3170; U.S. EPA, Washington, DC

Sharma VK, Johnson N, Cizmas L, McDonald TJ, Kim H (2016) A review of the influence of treatment strategies on antibiotic resistant bacteria and antibiotic resistance genes. Chemosphere 150:702–714

Shimizu A, Takada H, Koike T, Takeshita A, Saha M, Rinawati, Nakada N, Murata A, Suzuki T, Suzuki S, Chiem NH, Tuyen BC, Viet PH, Siringan MA, Kwan C, Zakaria MP, Reungsang A (2013) Ubiquitous occurrence of sulfonamides in tropical Asian waters. Sci Total Environ 452–453:108–115

Sibley SD, Pedersen JA (2008) Interaction of the macrolide antimicrobial clarithromycin with dissolved humic acid. Environ Sci Technol 42(2):422–428

Smith, A., (2013). User guide for the BGS DiGMapGB-50 data (V7). British Geological Survey Open Report, OR/13/008

Srinivasan P, Sarmah AK, Manley-Harris M (2014) Sorption of selected veterinary antibiotics onto dairy farming soils of contrasting nature. Sci Total Environ 472:695–703

Thibodeaux LJ (1996) Environmental chemodynamics, 2nd edn. Wiley-Interscience, New York

Tixier C, Singer HP, Canonica S, Müller SR (2002) Phototransformation of triclosan in surface waters: a relevant elimination process for this widely used biocide—laboratory studies, field measurements, and modeling. Environ Sci Technol 36(16):3482–3489

Vasudevan D, Bruland GL, Torrance BS, Upchurch VG, MacKay AA (2009) pH-dependent ciprofloxacin sorption to soils: interaction mechanisms and soil factors influencing sorption. Geoderma 151: 68–76

Walters E, McClellan K, Halden RU (2010) Occurrence and loss over three years of 72 pharmaceuticals and personal care products from biosolids-soil mixtures in outdoor mesocosms. Water Res 44:6011–6020

Xu J, Zhang Y, Zhou C, Guo C, Wang D, Du P, Luo Y, Wan J, Meng W (2014) Distribution, sources and composition of antibiotics in sediment, overlying water and pore water from Taihu Lake, China. Sci Total Environ 497–498:267–273

Yamamoto H, Nakamura Y, Moriguchi S, Honda Y, Tamura I, Hirata Y, Hayashi A, Sekizawa J (2009) Persistence and partitioning of eight selected pharmaceuticals in the aquatic environment: laboratory photolysis, biodegradation, and sorption experiments. Water Res 43(2):351–362

Zepp R, Cline D (1977) Rates of direct photolysis in aquatic environment. Environ Sci Technol 11(4):359–366