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Potential for biodegradation and sorption of acetaminophen, caffeine, propranolol and acebutolol in lab-scale aqueous environments

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ABSTRACT

Sorption and combined sorption-biodegradation experiments were conducted in laboratory batch studies with 100 g soil/sediments and 500 mL water to investigate the fates in aqueous environments of acetaminophen, caffeine, propranolol, and acebutolol, four frequently used and often-detected pharmaceuticals. All four compounds have demonstrated significant potential for degradation and sorption in natural aqueous systems. For acetaminophen, biodegradation was found to be a primary mechanism for degradation, with a half-life ($t_{1/2}$) for combined sorption-biodegradation of 2.1 days; in contrast, sorption alone was responsible only for a 30% loss of aqueous-phase acetaminophen after 15 days. For caffeine, both biodegradation and sorption were important ($t_{1/2}$ for combined sorption-biodegradation was 1.5 days). However, for propranolol and acebutolol, sorption was found to be the most significant removal mechanism and was not affected by biodegradation. Desorption experiments revealed that the sorption process was mostly irreversible. High values were found for K_d for caffeine, propranolol, and acebutolol, ranging from 250 to 1900 L kg^{-1}, which explained their greater tendency for sorption onto sediments, compared to the more hydrophilic acetaminophen. Experimentally derived values for log K_{oc} differed markedly from values calculated from correlation equations. This discrepancy was attributed to the fact that these equations are well suited for hydrophobic interactions but may fail to predict the sorption of polar and ionic compounds. These results suggest that mechanisms other than hydrophobic interactions played an important role in the sorption process.

1. Introduction

Pharmaceuticals and personal care products (PPCPs) have provoked considerable concern because of their widespread occurrence, potential toxicity for aqueous environments, and risk to human health. Even though the concentrations released are generally low (in the range of ng L^{-1} to μg L^{-1}), their potential impact on human health cannot be overlooked, particularly for those commonly used substances that may accumulate in human tissues [1]. Trace levels of PPCPs and their metabolites are ubiquitous and have been found in sources as diverse as drinking water, sewage treatment plant effluents, and even surface water [2–5]. Several studies have reported that the low removal efficiency of PPCPs in conventional treatment processes inevitably results in their release into aqueous environments [6,7]. Others have found sulfamethoxazole concentrations of 390 ng L^{-1} in influent samples and minimal elimination in effluents (310 ng L^{-1}) [8], and little PPCP degradation in pre-treatment or in sedimentation treatment processes that are specific for acidic, low K_{ow} compounds such as PPCPs [9].

Environmental analysis of Taiwan's surface waters has revealed the presence of multiple pharmaceuticals at detectable concentrations that may represent a source of risk to the local flora, fauna, and human inhabitants [11,12]. It is therefore essential that Taiwan acknowledge this issue by monitoring PPCP occurrence, designing and implementing a registry in which scrupulous records of PPCP occurrences can be maintained, and investigating the fate and risk of these pharmaceuticals. Following the establishment of universal health care coverage for Taiwanese residents, pharmaceutical usage in the population increased significantly; moreover, 3.6 tons of pharmaceuticals are thrown away annually [10]. This suggests potentially significant contamination of Taiwan's aqueous environment from pharmaceutical production processes, disposal of unused drugs and ineffective wastewater treatment; of even greater concern are the potential environmental consequences. Previous investigations have already demonstrated that discarding these contaminants directly into surface waters can result in adverse ecological and human health effects. Studies reporting specifically on the occurrence of pharmaceuticals in Taiwan [11,12] have detected numerous distinct PPCP species, results that are consistent with analyses from other sites worldwide. These findings warrant in-depth research into the occurrence, fate, and risk assessments of these potentially harmful pharmaceuticals.

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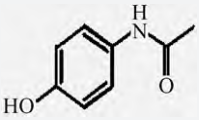
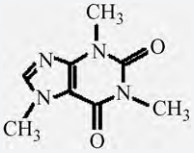
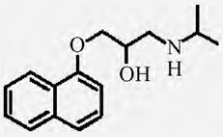
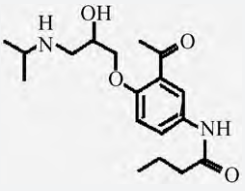
Table 1
Physicochemical properties and application of target compounds.

Compounds	Chemical structure	CAS number	M.W.	pK_a	log K_{ow}	Application
Acetaminophen		103-90-2	151.2	9.7[a]	0.46[a]	Non-steroidal anti-inflammatory drug
Caffeine		58-08-2	194.2	6.1[a]	<0[a]	Psycho stimulant
Propranolol		525-66-6	259.8	9.5	1.2–3.48	Beta-blocker
Acebutolol		37517-30-9	336.4	9.2[b]	1.71[b]	Beta-blocker

[a] Ref. [14].
[b] Ref. [16].

Natural attenuation is a combination of naturally occurring processes that take place without human involvement. These processes involve dilution, hydrolysis, photolysis, biodegradation, dispersion, irreversible sorption and sometimes radioactive decomposition. Furthermore, these processes most likely reduce the toxicity of contaminants towards the environment and human populations [13]. The degree and type of attenuative processes that take place determine the subsequent occurrence and distribution of pharmaceutical contaminants and are a key factor when considering risk assessment and management. Previous studies have shown that many PPCPs are susceptible to some of the natural attenuation processes which occur in surface waters [4,14]. These processes can be classified as mechanisms for physical transport or for chemical/biochemical transformation by alternate pathways; both mechanisms are critical for determining the fate and mobility of PPCPs in the environment. Studies of natural attenuation have been widely reported for environmental contaminants; however, very limited information is available for Taiwan, especially with regards to pollution by pharmaceuticals. Our understanding of the ultimate fate of PPCPs in aqueous environments must be preceded by a better understanding of the natural attenuation processes that PPCPs undergo en route to their eventual fates.

The physicochemical properties and applications of target compounds are presented in Table 1. Acetaminophen (also known as paracetamol) is a widely used analgesic, antipyretic drug that relieves fever, headache, and minor aches. Its alkalinity ($pK_a = 9.7$) and octanol–water partition coefficient (K_{ow}) of 2.88 suggest that biodegradation may play a crucial role in its degradation [14]. Caffeine, which has a neutral pH ($pK_a = 6.1$) and small K_{ow} [14], acts as a stimulant in humans and other animals. Despite its negative K_{ow}, the removal efficiency of caffeine by sludge treatment plants is excellent [15]. Propranolol and acebutolol are beta-blockers that are mainly used to treat hypertension. Acebutolol is alkaline ($pK_a = 9.2$) with a K_{ow} of 51.3 [16]; these properties indicate that biodegradation by microorganisms and/or sorption on high-organic-content sediment are likely to play a significant role in its natural attenuative processes.

This study of the sediments and waters of the Ji-Lung River is the first of its kind and provides a fuller description of the concentrations of certain target pharmaceuticals in its waters and sediments, the potential risks they pose, and mechanisms of natural attenuation to which they are subjected.

Our objectives were, therefore: (1) to determine the occurrence of the pharmaceuticals acetaminophen, caffeine, propranolol, and acebutolol, which are frequently found in significant concentrations (up to $\mu g\,L^{-1}$) in Taiwanese rivers [11,12]; (2) to perform batch studies to determine their potential for natural attenuation (specifically for sorption and biodegradation) in aqueous environments; (3) to describe the mechanisms of sorption and desorption and quantify the solid-water distribution coefficient (K_d); and (4) to consider our findings in the context of what is known about natural attenuation processes and their implications for the fate of the targeted compounds in the natural aqueous environment.

2. Experimental methods

2.1. Description of study site and sampling

River water and sediment samples were collected from four different locations in the Ji-Lung River. The Ji-Lung River is 86.4 km long, with a drainage area of 491 km^2 [17], and is directly downstream from one of Taipei's major wastewater treatment plants [18]. This plant receives 1.15 million m^3 water per day [19], and after treatment, its effluent is released into the Ji-Lung River, where it represents a primary source of pollution. In addition, the river runs through urban Taipei, and many hospitals are located on its banks. These hospitals indiscriminately dump their untreated waste into the river, producing the pharmaceutical and other chemical contamination observed in previous studies of Taiwanese rivers in this area [12]. Sampling points for this study were

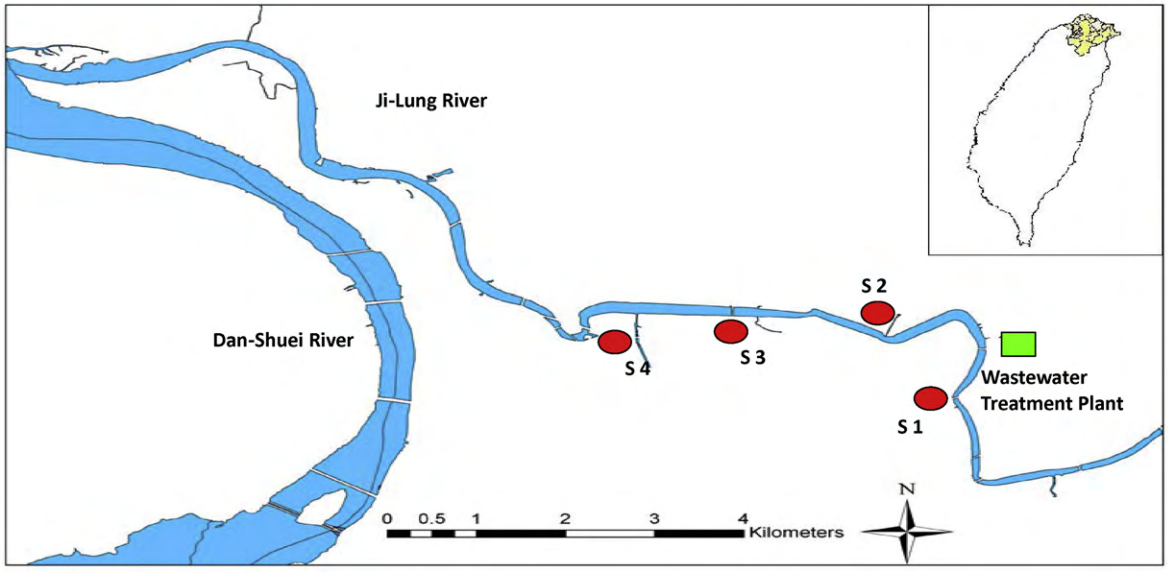


Fig. 1. Map showing the Ji-Lung River study area and sampling sites.

selected in zones directly downstream of likely sources of pollution (Fig. 1).

Samples of water and sediment were also collected from upstream regions of the Ji-Lung River that flow through sparsely populated areas. The water and sediment samples collected there provided background data (Supplementary information, Table 1), against which the results from samples taken in more densely populated areas were compared. The grab-sampling method was applied to collect river samples, and sediment samples were collected in triplicate. The sediment samples were air-dried, gently crushed, sieved (2 mm), and stored at 4 °C. River water samples (1 L) were collected in new or previously autoclaved amber glass bottles, which were washed three times with tap water and once with deionized (DI) water. After collection, the water samples were filtered through 0.45-μm glass fiber filters to remove organic debris and stored at 4 °C.

The sediment was analyzed with a TOC analyzer (TOC-5000A and SSM-5000A solid sample module, Shimadzu). The moisture content was determined via a standard protocol from the Taiwan Environmental Protection Agency, and the surface area and pore size were determined by the BET method (SA3100, Beckman Coulter). The nitrate concentration in river waters was analyzed using a spectrophotometer (DR2800, Hach, CO, USA) at 410 nm.

2.2. Analytical methods

Acetaminophen, caffeine and acebutolol of >99% purity were obtained from Sigma-Aldrich (St. Louis, MO, USA), and propranolol (>99% pure) was obtained from USP (Rockville, MD, USA). Stock solutions of each compound were prepared by dilution with methanol to 1000 mg L^{-1} and were stored in amber glass bottles at −20 °C. Formic acid (ACS-grade) was purchased from Riedel-deHaën (Seelze, Germany).

Analyses were performed using high performance liquid chromatography/tandem mass spectrometry (HPLC–MS/MS) (Applied Biosystems API 4000 with data processing software, Analyst 1.4.2). The HPLC module consisted of a pump (Agilent 1200 Series Binary Pump), degasser (Agilent 1200 Series Micro Vacuum Degasser), and autosampler (Agilent 1200 Series Autosampler). The analytes were chromatographed on a guard column (Eclipse XDB-C18, 4.6 × 12.5 mm, 5-μm pore size) with a flow rate of 1 mL min^{-1}. Formic acid (0.1%) in DI water (mobile phase A) or methanol (mobile phase B) was used as the binary gradient. The injection volume of each sample was 50 μL, and the autosampler was operated at room temperature.

The detector was a triple quadrupole mass spectrometer equipped with an electrospray ionization source. For all compounds, analyses were performed in positive multiple reaction monitoring transition mode.

Solid-phase extraction was performed before analysis by HPLC–MS/MS. Oasis HLB cartridges (500 mg, 6 mL, Waters, Milford, MA, USA) were conditioned by rinsing with 6 mL 100% methanol and 6 mL DI water. Water samples (400 mL) were loaded at a flow rate of 3–6 mL min^{-1}. After loading, the cartridges were rinsed with 6 mL DI water and dried. The analytes were then eluted with 4 mL 100% methanol and 4 mL methanol–diethylether (50/50, v/v). Finally, the extracts were dried by nitrogen at 37 °C and reconstituted to 0.4 mL with 25% methanol. The final solutions were filtered through 0.45 μm polyvinylidene difluoride membrane filters before analysis with HPLC–MS/MS. A detailed description of the analytical procedure and methods validation has been previously reported [11]. Percent recovery was 85, 115, 69 and 105% for acetaminophen, caffeine, propranolol, and acebutolol, respectively. The corresponding method detection limit was 0.1 ng L^{-1}, and detailed LC–MS/MS parameters are given in the accompanying Supplement.

2.3. Sorption and biodegradation experiments

Sorption and combined sorption-biodegradation experiments were conducted in triplicate in three separate experimental bottles. The first set of experiments (intended to investigate sorption uptake) consisted of 500 mL autoclaved DI water and 100 g autoclaved sediments spiked with 50 μg L^{-1} of the target compounds. Sterile and neutral conditions (pH = 7) during the experiment were maintained by adding 0.1 mL 0.02% sodium azide and 1 mL 0.5 M phosphate buffer to each bottle. The second set of experiments (intended to investigate the effect of combined sorption-biodegradation) included 500 mL filtered (0.45 μm) river water and 100 g sediments spiked with 50 μg L^{-1} of pharmaceuticals. One milliliter of 0.5 M phosphate buffer was added to maintain neutral conditions. The third set served as a control and contained 500 mL autoclaved DI water and spiked target compounds. Amber glass bottles were utilized to prevent photodegradation. All glass-

stoppered bottles were then shaken (120 rpm) in a shaker bath in an incubator set at a constant temperature (20 °C).

The sorption experiments were continued until target compounds equilibrated. For the combined sorption-biodegradation experiments, the same bottles were spiked and respiked two more times with 50 μg L^{-1} concentration of target compound. Because we had added phosphate buffer, pH adjustment was not performed every time the bottles were spiked, but the pH was verified and recorded as near neutral conditions (pH 7 ± 0.2). At predetermined intervals, 0.5 mL aliquots were collected from each sample, filtered (0.22 μm), and quantified using HPLC–MS/MS.

2.4. Desorption tests

To further quantify the amount of each sorbed target compound that could be desorbed and to understand the sorption mechanism, sediments were subjected to desorption studies at the end of our sorption experiments. Samples from the sorption experiments were centrifuged, and the supernatants were collected. The sediments were air-dried for one day, after which 500 mL of autoclaved river water was introduced into the bottles. Again, 1 mL of 0.5 M phosphate buffer and 0.1 mL of 0.02% sodium azide were added to maintain a pH of 7 and sterile conditions. The bottles were shaken (120 rpm) in a shaker bath in an incubator set at a constant temperature (20 °C). At predetermined intervals, 0.5 mL aliquots of sample were taken from each bottle, filtered (0.22 μm), and analyzed by HPLC–MS/MS.

2.5. K_d determination experiments

To determine K_d, we used autoclaved river water and sediments in the same three proportions used for the sorption uptake and combined sorption-biodegradation experiments. The first sample contained 25 mL autoclaved river water and 5 g autoclaved sediments spiked with pharmaceuticals at several concentrations (10–500 μg L^{-1}). The second tube contained 25 mL autoclaved river water with no sediment and was spiked with predetermined concentrations of target compounds to enable identification of other degradation mechanisms that might be present. Lastly, a control sample (no sediment, 25 mL autoclaved river water) was analyzed to define the background effect. All tubes were wrapped with aluminum foil to prevent photolysis, and 5 μL 0.02% sodium azide and 50 μL 0.5 M phosphate buffer were added to all tubes to maintain sterile and neutral conditions, respectively. All tubes were shaken continuously (120 rpm) in a mechanical shaker with a water bath in an incubator (20 °C). All tubes were centrifuged, filtered (0.22 μm), and subjected to HPLC–MS/MS analysis.

2.6. Calculation of the sorption coefficient

In order to compare the experimental vs. calculated K_d values, the organic carbon distribution coefficient (K_{oc}) was calculated with the pH-dependent octanol–water distribution (D_{ow}), which considers the pK_a at the ambient pH. The relationship between K_{oc} and D_{ow} is as follows [35]:

$$\log K_{oc} = 0.74 \times \log D_{ow} + 0.15$$

The equation for D_{ow} is as follows:

For neutral functional groups:

$$\log D_{ow} = \log K_{ow}$$

Table 2
Detected concentrations (ng L^{-1}) of target compounds at sampling sites (n = 3).

Item	Site 1	Site 2	Site 3	Site 4
Acetaminophen	14 ± 5.0	1600 ± 46	31 ± 5.0	19 ± 2.0
Caffeine	3800 ± 400	6000 ± 230	3500 ± 270	3600 ± 90
Propranolol	9.0 ± 8.0	3.0 ± 0.2	12 ± 8.0	2.0 ± 0.2
Acebutolol	11 ± 6.0	11 ± 1.0	17 ± 4.0	10 ± 0.7

For acidic functional groups:

$$\log D_{ow} = \log K_{ow} + \log \frac{1}{1 + 10^{pH - pK_a}}$$

For basic functional groups:

$$\log D_{ow} = \log K_{ow} + \log \frac{1}{1 + 10^{pK_a - pH}}$$

K_d values were calculated from the predicted K_{oc} values [20].

3. Results and discussion

3.1. Investigation of field data

All experiments were conducted in triplicate, and the results are reported as means ± standard deviations, which are represented in the figures by the error bars. Since standard error did not appear to influence our results significantly, these are not discussed in this research. Characterization of Ji-Lung River sediment found a pH = 5.8–6.2 and texture consisting of sand (99.6%), silt (0.2%) and clay (0.2%). The Ji-Lung sediments could generally be classified as sand, since sediment particles were 0.15–0.84 mm and dominated by sand-size particles (0.050–2.0 mm). The total organic content was found to be 1.7 ± 0.2%. All sediment samples had negative zeta potential values ranging between −19.9 and −20.3 mV. The cation exchange capacity was 4.2–4.6 meq $(100\,g)^{-1}$, which agrees well with the pH and clay content of the sediment. The moisture content was determined to be 21.7 ± 0.6%, with a BET surface area of 6.1 $m^2\,g^{-1}$. Taiwanese river sediments have been typically shown to have an organic content of <2% [21]. The limited organic content and the available surface area of these sediments would make any organic matter present crucial for the sorption process.

The concentrations of acetaminophen, caffeine, propranolol and acebutolol found in each of the four sampling sites are presented in Table 2. Pharmaceutical concentrations in the river water were at ng μg L^{-1} levels and were higher where wastewater treatment plant effluents were discharged (Site 2, Fig. 1) and lower in downstream segments of the river. Since water samples were collected on sunny days, with no rainfall, river branches, or large pipes entering the river in the area studied, dilution seems unlikely. Although different degrees of attenuation were found for all four target compounds during the river transport, these data indicated that the possibility of loss during the aqueous phase through natural processes such as sorption/degradation was highly likely. Therefore, we conducted batch studies of river water samples to investigate their potential for sorption and biodegradation and to characterize the fate of our target compounds in this aqueous environment.

3.2. Sorption and biodegradation studies

The term "biodegradation" used in this study refers to the loss of the parent compound in active cultures relative to a sterile control. It is not known if the compound is mineralized or

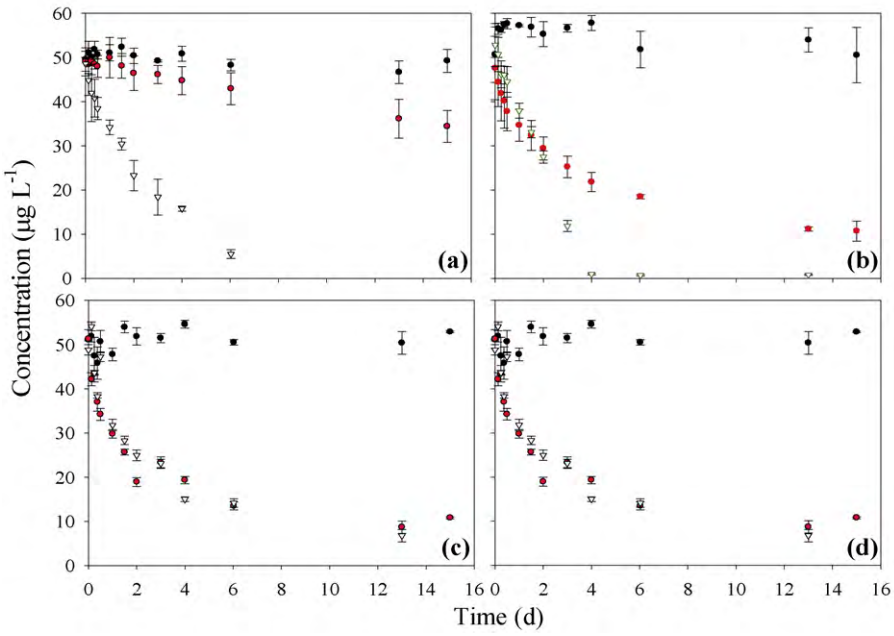


Fig. 2. Sorption and combined sorption-biodegradation study of (a) acetaminophen, (b) caffeine, (c) propranolol, (d) acebutolol. (●) Control; (●) sorption; (▽) combined sorption-biodegradation. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

transformed to a metabolite. Both biodegradation and sorption are components of the natural attenuation process, during which parent compounds are lost from the aqueous phase. It is difficult at best and often nearly impossible to separate the influence of biodegradation from that of sorption. Therefore our experiments were designed to simplify the complexities of natural systems and to focus on selected key parameters. Studies of each pharmaceutical were carried out at two different concentrations (50 and 500 $\mu g\,L^{-1}$). Experiments were designed to simulate natural systems, and similar conditions were used to study both sorption and combined sorption-biodegradation. Despite the fact that the highest concentration of pharmaceuticals that we detected in Ji-Lung River waters was only 6.2 $\mu g\,L^{-1}$, they have been reported to occur at much higher concentrations (e.g., in the Dahan River (maximum 13 $\mu g\,L^{-1}$) and in effluents from hospitals (187 $\mu g\,L^{-1}$) and drug production facilities (418 $\mu g\,L^{-1}$) just before their release into surface water bodies) [12]. Therefore, 50 and 500 $\mu g\,L^{-1}$ concentrations were used to test attenuation potentials in this study. Each set of experiments simultaneously investigated sorption and biodegradation. Another set of experiment simulated a sorption system only, allowing us to characterize the influence of sorption alone on our target compounds. A third set of bottles (control) was set up to ensure that other possible degradative mechanisms (e.g., hydrolysis, photolysis) were eliminated. Fig. 2 shows the results of decreased compound concentrations over time at the 50 $\mu g\,L^{-1}$ concentration.

Fig. 2a represents sorption alone and combined sorption-biodegradation of acetaminophen against a control. From the figure it is clear that the rate of combined sorption-biodegradation is much faster than sorption alone. The acetaminophen added to the combined sorption-biodegradation system was consumed within 13 days, whereas the sorption-only system achieved a mere 30% decrease in compound concentrations. Degradation by combined sorption-biodegradation can be assumed to follow pseudo-first-order kinetics ($R^2 = 0.97$) with half-lives ($t_{1/2}$) calculated to be 2.1 days. (The figures pertaining to the R^2 and K values are presented in the Supplement for clarity.) The concentration of acetaminophen in the control system remained stable throughout, indicating that the influence of other degradation mechanisms (e.g., hydrolysis and oxidation-reduction reactions) was negligible. At neutral pH, acetaminophen exists entirely in neutral form (pK_a of 9.5–9.7) and possesses very low hydrophobicity ($\log K_{ow}$ 0.46–0.49). These properties probably contribute to the low sorption rates observed in our study. Furthermore, our results agree well with earlier studies that examined sorption of acetaminophen using silica, alumina and low-organic-content sand [22]. These studies reported that acetaminophen engaged in few hydrophobic interactions, resulting in negligible sorption rates. Lam et al. [23] carried out biodegradation studies of eight pharmaceuticals (including acetaminophen) in a microcosm study and reported that biodegradation, with a $t_{1/2}$ of 0.9 ± 0.2 days, was more important than photolysis. Yamamoto et al. [24] also studied pharmaceutical partitioning in aquatic environments and reported 80% biodegradation for acetaminophen in a period of 72 h ($t_{1/2}$ of 2.1 days) in river water experiments. When these findings are compared with our results, it is evident that biodegradation is the primary natural attenuative mechanism responsible for acetaminophen breakdown.

Fig. 2b presents results from studies of sorption uptake and combined sorption-biodegradation of caffeine. Concentrations in the control system were stable at all times; in contrast, caffeine levels in the two experimental systems were similar only for the first two days, after which the rate of breakdown by combined sorption-biodegradation greatly exceeded the rate for sorption alone. The concentration of caffeine in the sorption-only system decreased by 76% within 13 days and subsequently remained stable, while all of the caffeine in the combined sorption-biodegradation system was consumed by the fourth day ($t_{1/2} = 1.5$ days). Caffeine biodegradation has been documented in single culture [25,26], mixed consortium [27] and in wastewater treatment plants (WWTPs) that used biological treatment systems [15,28]. Santos et al. [15] monitored several pharmaceutically active compounds over a one-year period in the influents and effluents of WWTPs and found that more than 80% of the caffeine had been removed by the stipulated hydraulic retention time. We observed similar results for caffeine removal in WWTPs in Taiwan, where removal efficiencies were 86–100% [28]. We thus conclude that sorption and biodegradation are both significant mechanisms for caffeine removal in water systems.

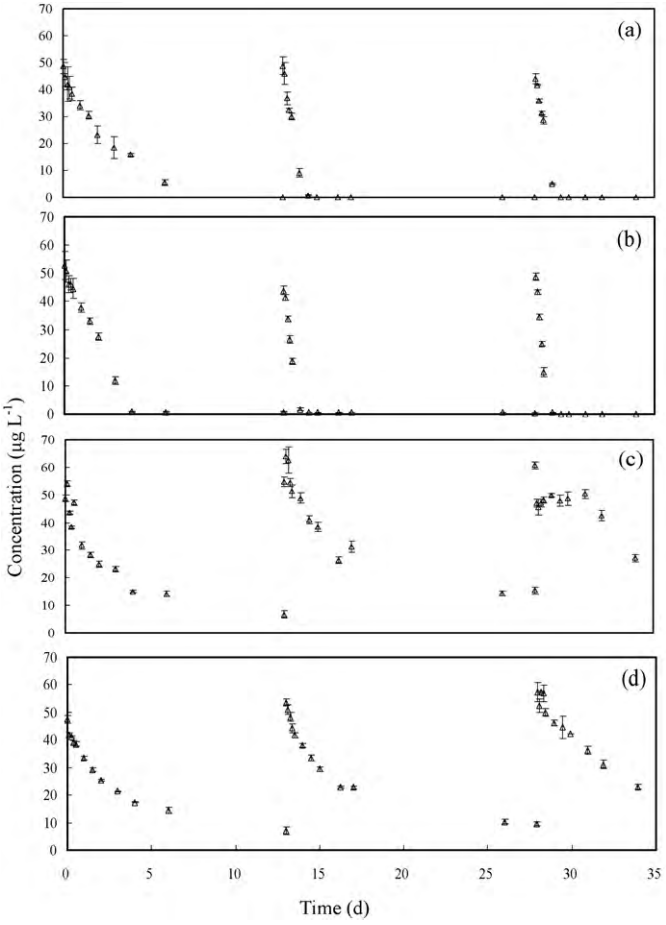


Fig. 3. Combined sorption-biodegradation respike experiments (a) acetaminophen, (b) caffeine, (c) propranolol, (d) acebutolol.

For propranolol and acebutolol (Fig. 2c and d), the effect of sorption alone was similar to that of combined sorption-biodegradation, indicating that the influence of biodegradation alone was almost negligible. The concentrations of propranolol and acebutolol were found to be decreased by 83% and 90% respectively after 14 days, and their half-lives were 2.2 days (propranolol) and 2.4 days (acebutolol). The micro-flora responsible for the biodegradation of these two compounds may have been absent in the pocket of sediment considered in this study. Drillia et al. [29] studied the mobility and sorption of six pharmaceuticals (including propranolol) with low- and high-organic-content soils. They reported high sorption in soils as well as in activated sludge samples, as reflected by high K_d and high K_F values. Daniel et al. [30] reported significant propranolol degradation (at 10 $\mu g L^{-1}$ levels) in laboratory batch experiments using acclimatized and non-acclimatized sludge. Thus our findings and those of earlier investigators suggest that sorption is the dominant mechanism behind the loss of both propranolol and acebutolol.

With the exception of acetaminophen, we found that consumption rates by sorption alone for our target compounds (caffeine, propranolol, and acebutolol) were higher than by combined sorption-biodegradation during the first few days. This may have been an artifact of the preparation process. Previous studies have shown that the rate of sorption is enhanced by pre-treatment methods such as autoclaving, drying, and exposure to chemicals (e.g., NaOH, $CaCl_2$) [31], while Hildebrand et al. [32] showed that sorption of 17β-estradiol in autoclaved soil was slightly higher than in sodium azide or mercuric chloride-treated soil. However, an earlier study [33] reported otherwise and concluded that sterilization by autoclaving results in negligible change. Our samples were autoclaved, potentially changing sediment characteristics or altering sorption rates. To clarify the impact of autoclaving on the results from this study, two other sterilizing methods were investigated: heat treatment (250 °C, 60 min) and addition of 1% (w/v) NaN_3. We found that heat treatment and autoclaving resulted in the same sorption behavior for all four target compounds. However, NaN_3-treated soil/sediments exhibited different sorption potentials. Acetaminophen was 40% more sorbed, while propranolol and acebutolol were approximately 20% less sorbed in the NaN_3-treated soil than in the autoclaved soil. The sorption of caffeine was unchanged in all cases. The exact explanation for these observations is as yet unknown and merits further studies that will clarify the effect of autoclaving on the sorption potential.

3.3. Respike experiments

Respike experiments were conducted to determine the potential of target compounds for biodegradation. The combined sorption-biodegradation systems were respiked on days 13 and 28; samples were retrieved at predetermined intervals and analyzed using HPLC–MS/MS. Results are presented in Fig. 3. For acetaminophen and caffeine (Fig. 3a and b), degradation was faster after the second respike, suggesting that significant adaptation of microbial flora and potential for biodegradation were present. These findings agree closely with our sorption/biodegradation results (Fig. 2a and b), which indicated that sorption and biodegradation were both significant for the natural attenuation of acetaminophen and caffeine over a short period of time in the aqueous environment. In contrast, the reaction rates of propranolol and acebutolol (Fig. 3c and d) remained unchanged over the course of the respike study, findings that agree closely with the sorption results (Fig. 2c and d); thus, we conclude that sorption is the dominant removal mechanism in aqueous environments.

3.4. Desorption tests

To determine whether sorption was reversible or irreversible, we conducted desorption experiments using 50 and 500 $\mu g L^{-1}$ concentrations of target compounds. Similar desorption trends were seen for both concentrations and are presented in Fig. 4 (50 $\mu g L^{-1}$ data not shown), along with the sorption and desorption processes over time for all four target compounds.

At the initial 50 $\mu g L^{-1}$ concentration, desorption was very weak ($9 \pm 3\%$ (acetaminophen) and <3% each for caffeine, propranolol, and acebutolol), indicating irreversible sorption for all four compounds. These results also suggest that chemical sorption may be the mechanism of sorption of the target compounds onto sediments. Due to the low-organic content (1.7%) of the sediments, the sorption process might have occurred due to the possible dominance of mineral surfaces rich in clay, as has been reported for sorption of chlorophenol and triazine [34]. Therefore, we assume that sorption might have occurred due to ionic bond formation in the system.

Desorption results for 500 $\mu g L^{-1}$ concentrations (Fig. 4a–d) were very similar to the 50 $\mu g L^{-1}$ results. The extent to which compounds were desorbed was the same in both cases; however, the desorption rate increased as concentration decreased, which was inconsistent with pseudo-first order reaction characteristics. A possible explanation could be that external mass transfer and intraparticle diffusion were the crucial processes for this system, such that the sediment required more contact time to reach equilibrium after the initial spiked concentration was increased.

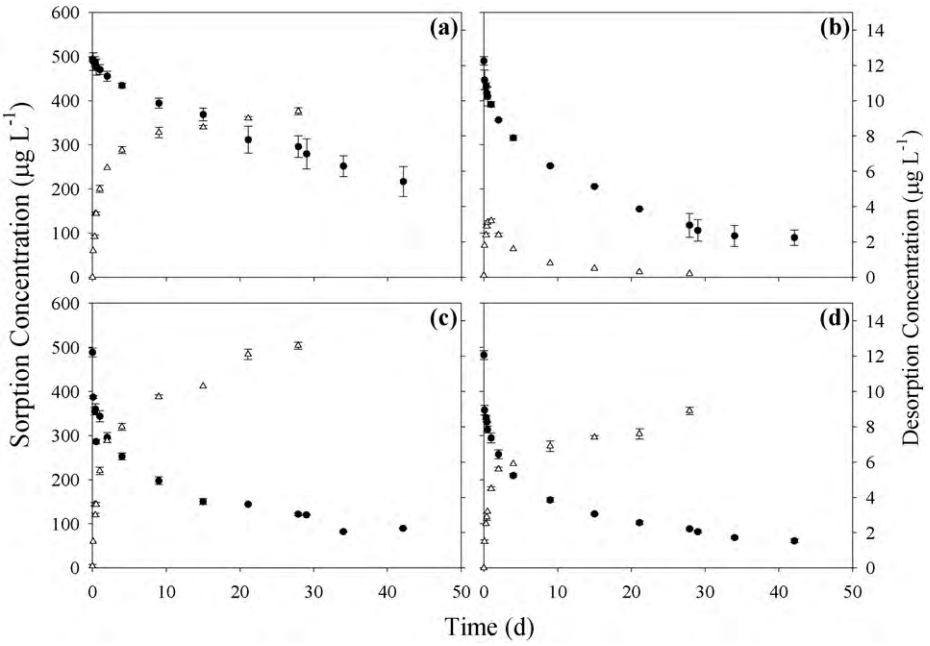


Fig. 4. Sorption and desorption of (a) acetaminophen, (b) caffeine, (c) proproanolol, (d) acebutolol at 500 μg L^{-1}. (●) Sorption, (△) desorption.

3.5. K_d determination experiments

3.5.1. Determination of K_d values

The K_d values for the four pharmaceuticals were obtained experimentally and from theoretical calculations. In the experimental part, the concentration in solid phase was measured as the difference between the initial concentration and the concentration in aqueous phase at equilibrium, thereby minimizing any error introduced by the extraction procedures [35]. Our experimental controls demonstrated that other mechanisms of degradation could be eliminated, confirming the reliability of the method.

Table 3 depicts the K_d and K_F for all target compounds and compares them with available literature values. Results for caffeine, propranolol, and acebutolol fit the Freundlich isotherm (although some values were below detection limits), and the linearity (coefficient of determination) was found to be >0.94. These findings imply nonlinear sorption in the concentration range studied, as well as a high affinity between the compounds and sediment early in the sorption process, which decreased as sorption sites were saturated. The linearity parameters ($1/n$) of caffeine, propranolol, and acebutolol were 0.72, 0.84, and 0.67, respectively. Acebutolol displayed great potential for sorption onto sediment, suggesting the significance of this mechanism in acebutolol's removal by natural attenuation. In the case of acetaminophen, the water- and solid-phase concentrations were less correlated, suggesting that the system might not have reached equilibrium even after two weeks.

The K_d values were obtained from the linear region (0.4–120 μg L^{-1} (acetaminophen), 0.1–6.6 μg L^{-1} (caffeine), 0.1–5.8 μg L^{-1} (propranolol); 0.1–0.7 μg L^{-1} (acebutolol)) of the Freundlich isotherm. With the exception of acetaminophen, all target compounds (caffeine, propranolol, and acebutolol) exhibited high K_d values ranging from 240 to 1900 L kg^{-1}, demonstrating the strong tendency for target compounds to be sorbed onto sediment even in a low-organic-content system. In comparison, the calculated sorption coefficient values were found to be similar to those from earlier studies. Drillia et al. [29] found that the K_d and K_F values for propranolol in high- and low-organic-content soils were in the range of 15–250 L kg^{-1} and 6.8–250 $\mu g^{(1-1/n)}\, L^{(1/n)}\, kg^{-1}$, respectively. Yamamoto et al. [24] also reported K_d values for acetaminophen and propranolol in the range of 2.6–10 and 2.2–160 L kg^{-1}, respectively.

3.5.2. Comparison of measured K_d values vs. modeled values based on K_{ow}

The log K_{oc} values were calculated using empirical correlation equations [20,36,37] and compared to experimentally derived values (see Supplementary information). Experimental results were much higher than theoretically derived log K_{oc} values, most likely because these methods can model hydrophobic interactions but cannot predict sorption of polar and ionic compounds [38] (with the exception of acetaminophen, which engages in few hydrophobic interactions at neutral pH values, resulting in negligible sorption

Table 3
Results from the K_d experiment: the distribution coefficient (K_d) and the Freundlich constant (K_F).

Compound	f_{oc} = 0.017						K_d literatures	K_F literatures
	Linear range for K_d (μg/L)	K_d	R^2	K_F	$1/n$	R^2		
Acetaminophen	0.4–120	5.0	0.6	59	0.53	0.63	2.6–10[b]	–
Caffeine	0.1–6.6	250	0.9	360	0.72	0.97	–	–
Propranolol	0.1–5.8	270	1.0	330	0.84	0.97	2.2–250[a,b]	210–250[b]
Acebutolol	0.1–0.7	1900	0.9	1900	0.67	0.94	–	–

f_{oc} is the organic carbon fraction (mass/mass); K_d expressed in L kg^{-1}; K_F expressed in $\mu g^{(1-1/n)}\, L^{(1/n)}\, kg^{-1}$.
[a] Ref. [24].
[b] Ref. [29].

Table 4
Half-life ($t_{1/2}$) values of natural attenuation processes of target compounds (unit: day).

Item	Photolysis	Sorption and biodegradation
Acetaminophen	1.4–2.3[a]	2.1 (1.08–2.08)[a,d]
Caffeine	–	1.5
Propranolol	0.04–0.34[a,b]	2.2 (5–25.8)[a]
Acebutolol	0.8–6[c]	2.4

Values in parenthesis are from previous reported studies.
[a] Ref. [24].
[b] Ref. [39].
[c] Ref. [40].
[d] Ref. [23].

rates [22]). Consequently the sorption process can be understood to result from ionic interaction.

Table 4 presents $t_{1/2}$ for natural attenuation of the target compounds from our experimental study and from other investigators and shows that most target compounds require a minimum of one day for attenuation. The Ji-Lung River is 86.4 km in length, with a measured velocity of 0.3–0.5 m/s [17], resulting in a projected traveling time for residual pharmaceuticals through the Ji-Lung River of 2–3 days, which should be sufficient for complete removal by natural attenuation. However, it is important to note that environmental factors that were not modeled in this simplified batch system, such as river traveling velocities and suspended solids, are also important determinants of the degree of natural attenuation that occurs.

It is well known that high-organic content, high CEC and more negative zeta potential values encourage sorption of hydrophobic compounds. Sediments, like the low-organic-content samples in our study, and low CEC should be studied further to define their sorption characteristics. The aromatic ring in each compound, with its electron-donor/electron-accepting groups, might affect the electrochemical affinity and should be further investigated to better understand the sorption process for polar compounds. In combination with the known physicochemical properties of the four selected target pharmaceuticals, our results point toward sorption mechanisms other than hydrophobic interactions. Investigations of metabolites (especially of compounds that undergo biodegradation) and of mass balance with these metabolites are also necessary and are a focus of our future work.

4. Conclusions

This is the first report on the occurrence of pharmaceuticals in Taiwan's Ji-Lung River. This work enhances our understanding of the fate of these pharmaceuticals in aqueous systems. Furthermore, we have identified the nature and relative significance of the natural attenuation processes that may affect these pharmaceuticals in a river system.

Each of the four pharmaceuticals chosen for this study can be removed from the natural aqueous system. For acetaminophen, biodegradation was found to be the major mechanism of degradation, whereas for caffeine, sorption and biodegradation were the primary processes. For propranolol and acebutolol, sorption was the dominant mechanism of removal. The physicochemical properties of caffeine, propranolol, and acebutolol fit the Freundlich isotherm with a linearity >0.94 (nonlinear sorption). The sorption affinity was high during the early hours of the sorption process and continued rapidly until all sorption sites were saturated, after which the process slowed.

For natural systems with low (ng L^{-1} to low μg L^{-1}) concentrations of target compounds, the linearity of sorption is best expressed by K_d values. Caffeine, propranolol, and acebutolol had K_d values ranging from 250 to 1900 L kg^{-1}, suggesting a strong tendency for the target compounds to be sorbed onto sediment despite the low-organic content.

Taiwanese river sediments typically contain a total organic content under 2% [21]. Most sorption characteristics of river sediments correlate with the relative amount of organic matter and the corresponding clay content, and the present study reveals similar sorption tendencies. The sediment was largely composed of sand with a low-organic content, consistent with its neutral pH and low CEC values. This low-organic content was compensated for by the sediment's surface area, which improves sorption conditions by enhancing the initial attenuation of a compound early in the sorption process, and which is especially important in Taiwan's high-velocity rivers, where sorption depends mainly on contact time between the organic materials and sediments. Sorption increases the chances of biodegradation, a crucial degradation mechanism for organic materials such as acetaminophen [14]. Thus the surface area of sediments significantly affects the extent to which organic materials can undergo natural attenuation. Based on simulations of sorption and biodegradation processes in the Ji-Lung River, we have demonstrated that removal of our four target pharmaceuticals by natural attenuation is possible. Nevertheless, it would be a stretch to assert that the half-lives and sorption parameters determined in the batch studies are appropriate for the water column or sediments in the field. The river traveling velocities, temperature variations, existence and complexity of local biota and the occurrence of suspended solids can significantly affect the behavior and fate of target contaminants in the intricate aqueous environment. Further studies of these factors will better characterize the complexities of this system and the extent to which natural attenuation of contaminants occurs in aqueous environments.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jhazmat.2010.07.017.

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