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Stability and Degradation of Opioids in River Water

Varsha Niroula and Sheree A. Pagsuyoin*

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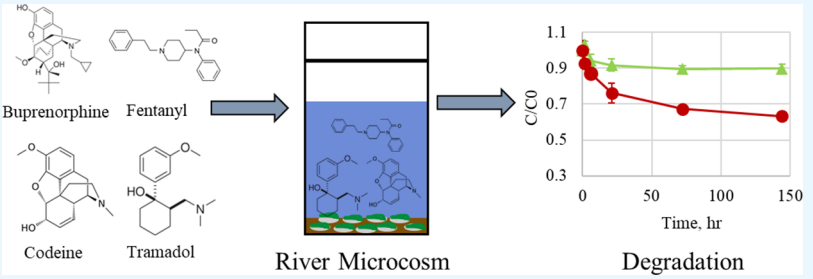

ABSTRACT: As the level of consumption of opioids continues to rise globally, there is increasing concern over the potential impacts of continuous opioid discharges into aquatic ecosystems. Opioids are psychoactive compounds that are not completely removed during wastewater treatment, and little is known about their stability and fate in the environment. In the present study, we evaluated the stability of four highly used opioids, buprenorphine, codeine, fentanyl, and tramadol, in river water via batch degradation experiments. The opioids were spiked at environmentally relevant concentrations into 150 mL of river microcosms designed to distinguish among hydrolysis, abiotic degradation, biodegradation, and sorption. All opioids exhibited relatively high stability in river water, with removal rates of only 15% (tramadol) to 26% (buprenorphine) after 6 days. Biodegradation was the most important attenuation pathway for all four opioids, with first-order biodegradation constants ranging from 0.011 d^{-1} (tramadol) to 0.018 d^{-1}(buprenorphine). Overall, degradation rates were 1−4 orders of magnitude lower compared to the reported rates for wastewater systems. These results offer insights into the stability of opioids in freshwater systems and raise questions about the potential effects of their pseudopresence in surface waters on aquatic organisms.

1. INTRODUCTION

Drugs of abuse (DAs) pertain to substances that have the potential for addiction and encompass licitly (i.e., prescribed medications) and illicitly used (i.e., abused/misused prescriptions and illicit drugs) drugs.[1] Increased global drug consumption, particularly for opioids, has given rise to public health problems, e.g., the opioid epidemic. Medical opioids are prescribed primarily for pain relief because of their analgesic properties.[2] In the United States, dispensing rates for prescription opioids peaked in 2012 (255 M prescriptions) and continued to decrease annually (143 M in 2020) although the rates remain high in southeastern regions.[3] However, illicit use of opioids continued to increase (from 1.08% in 2018 to 1.12% in 2020).[4] Opioid overdose deaths in the U.S. more than doubled between 2010 (21,000 deaths) and 2017 (48,000) and quadrupled in 2021 (80,000).[5]

Due to high drug consumption and the incomplete removal of drugs during wastewater treatment, there is growing scientific interest in the potential ecological impacts of residual drug discharges to the environment.[6] DAs are highly psychoactive, but little is known about their individual and synergistic effects on aquatic organisms. In Australia, codeine, a prescription opioid, was among the most frequently detected pharmaceuticals in stream invertebrates.[7] Lab-scale ecotoxicity studies indicate a range of effects on organisms; for instance, Fischer et al. found that codeine bioaccumulated in fish and reduced the hormone levels in female medaka.[8] Exposure to environmental concentrations of tramadol, another commonly prescribed opioid, has been found to alter the behavior and mobility of crayfish.[9] Kirla et al. found that exposure to fentanyl and its derivatives adversely impacted the survival and locomotion of zebrafish larvae.[10]

Residual DAs enter streams through various point (e.g., sewage facilities,[11] and hospitals[11]) and nonpoint (e.g., septic systems[12] and illegal dumping[13]) sources. They have been detected in effluents (1−10^5 ng/L)[14] and streams (1−10^4 ng/L)[15] around the globe. Discharges from septic systems also tend to have higher drug concentrations than treatment plant effluents.[16] Compared to other emerging organic pollutants, there are limited studies on the stability of DAs in sewage and even fewer studies on their fate in streams. These earlier

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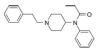
Table 1. Chemical Properties and Uses of Target Opioids[a]

Opioid (CODE)	Molecular Structure	Molecular Weight	Log K_{ow}	pKa	Medical Use
Buprenorphine (BUP)		467.6	4.98	8.31	Treatment option for managing opioid dependence and prevention strategy for HIV infection
Codeine (COD)		299.4	1.19	10.6	Treatment for mild to moderate pain
Fentanyl (FEN)		336.5	4.05	8.99	Treatment for severe pain
Tramadol (TRA)		263.37	3.01	9.41	Treatment for moderate pain

[a]MW data are for the unlabeled drug standards. Log K_{ow} and pK_a values are for 298.15K (data from refs 28 and 29).

studies have found psychoactive drugs to be highly persistent, for instance, methamphetamine has a half-life of 42 h in sewage[17] while amphetamine has a half-life of 88 h.[18] Lin et al. found that the opioids codeine and morphine are resistant to hydrolysis and biodegradation in aquatic environments. Given the high consumption of psychoactive drugs and their continuous discharge into the environment, there is a need to understand their environmental fate to assess and manage the potential risks they pose on aquatic organisms.

The goals of the present study are to (1) evaluate the stability of opioids and (2) identify the most relevant attenuation processes for opioids in riverine ecosystems. The study was carried out using batch degradation experiments in river microcosms designed to distinguish among abiotic degradation, biodegradation, and sorption. Four target opioids were selected based on their high consumption[19] and frequent detection in streams:[20] buprenorphine, codeine, fentanyl, and tramadol (Table 1). Except for codeine, all are synthetic opioids prescribed for various medical purposes. Buprenorphine is used in opioid addiction therapy (medication-assisted treatment);[21] it has been detected in surface waters at 10^1−10^2 ng/L levels.[22] Codeine is used for pain relief and is the most abundant opiate in urban wastewater (10^1−10^2 ng/L)[23] and surface water (10^1−10^3 ng/L).[20] Fentanyl is used to treat severe pain and is the leading abused opioid involved in drug overdose deaths in the U.S.[24] and worldwide.[25] Fentanyl and its analogues have been detected in sewage-impacted streams (10^{-1}−10^2 ng/L).[23] Tramadol is a highly prescribed opioid analgesic due to its less addictive nature[26] and was the second most prescribed opioid (21.1%) in the U.S. in 2016−2017.[27] In streams, tramadol has been measured at a concentration range of 10−10^3 ng/L.[15] The result of this study fills a knowledge gap on the fate and stability of residual drugs in streams.

2. MATERIALS AND METHODS

2.1. Chemicals and Reagents. Isotopically labeled opioid standards (buprenorphine, codeine, fentanyl, and tramadol; 100 ug/mL in methanol) were purchased from Sigma-Aldrich (St. Louis, MO). High-purity reagents were purchased from Thermo Fisher: methanol, formic acid, ammonium hydroxide, ethyl acetate, and isopropanol. Ultrapure water was prepared on-site as needed (Barnstead E-pure, Thermo Scientific).

2.2. River Water, Biofilm, and Sediment Sampling. Grab river water samples were obtained during two sampling events from a conservation area in Holderness, New Hampshire, and transported to our laboratory in prewashed carboys in coolers. This location is part of a tributary to the main river channel and was selected to minimize background drug levels (subsequently confirmed to be negligible, <LOD). The first water sample was used to grow the biofilms for the river microcosms. The second water sample was used in subsequent degradation experiments. In each sampling event, the water sample was immediately processed in the laboratory within 4 h from sampling.

Seed river biofilm was obtained from the main river channel downstream of the conservation area and adjacent to our laboratory. This location was selected after noting negligible biofilm growing on rocks at the conservation area. Pebbles (diameter <5 cm) with attached biofilm were obtained approximately 10 cm below the water surface of the riverbank. The pebbles were washed with DI water and then rinsed twice with river water (from the conservation).

Sediments were obtained via grab sampling from a small shallow creek in a conservation area approximately 15 miles from our laboratory. This location was selected in consideration of crew safety. The Holderness conservation area had fewer floating debris (leaves and twigs) but was deeper. Sediments were taken from the top 10 cm of the sediment bed, placed in covered glass jars, and transported in coolers to our laboratory. In the lab, the sediments were triple-washed with distilled water to remove large debris and then stored at 4 °C until use. Three days before the degradation experiments, the sediments were washed with methanol to remove background drugs (if any), washed with ultrapure water to remove residual methanol, then oven-dried at 105 °C, screened to retain 1−2 μm particles, and then added to the microcosms. A separate subsequent analysis indicated no detectable background drug concentrations in the sediments.

2.3. River Microcosm Experiments. The river microcosm experiments comprised a microbial growth phase for the river biofilm (in a 20 L rectangular plastic container) and a drug degradation phase (in 200 mL glass jars).

2.3.1. Biofilm Growth Phase. For the biofilm growth phase, 10 L of river water was transferred to a sterile 20 L plastic container at room temperature. Ten pieces of washed pebbles (with biofilm) were placed at the bottom of the container. Precleaned and sterilized 2 cm flat glass beads were added as additional surfaces for biofilm growth[30] and were laid farther apart in the container to ensure uniform biofilm growth on the exposed surfaces. Water was dosed with supplemental nutrients (40 μg/L NO_3^- and 2.5 μg/L of PO_4^{-3}) to promote the biofilm growth,[31] covered loosely with transparent plastic, and placed near a window under natural light. The water temperature was maintained at 25 ± 5 °C. A separate preliminary test indicated that maximum biofilm growth rate

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ACS Omega 2024, 9, 26355−26362

was achieved in 3 weeks post-seeding; hence, biofilm growth phase was carried out accordingly while monitoring the optical density (750 nm, DR6000 UC-vis spectrophotometer)[32] of water. Each week, water was dosed with additional 40 μg/L of NO_3^- and 2.5 μg/L of PO_4^{-3} to promote the biofilm growth, and filtered river water was added to maintain a 10 L volume. The beads with the attached biofilm were transferred to the river microcosms at the start of the biodegradation experiments.

2.3.2. Degradation Experiments. Batch degradation experiments were carried out over 6 days in the dark in a temperature-controlled shaker bath (30 °C and 100 rpm). The experiments were run at a slightly higher temperature than other similar degradation studies for pharmaceuticals.[33] River water may exceed 30 °C during warmer weather,[34] with some estimates anticipating even higher future surface water temperatures.[35] A total of 48 river microcosms were set up in parallel in 200 mL glass jars to distinguish among different processes: abiotic chemical degradation, biodegradation, and sorption (Figure 1). Each microcosm contained 150 mL of river water spiked with an in-sample concentration of 500 ng/L d-labeled target analytes at the onset of experiment and covered with air-permeable seals. Setup 1 consisted of autoclaved and filtered (1 μm GFC, Pall) river water to evaluate abiotic degradation. Setup 2 consisted of filtered river water to evaluate the combined effects of abiotic degradation and biodegradation. Setup 3 contained filtered river water, 5 g of river sediments (dry weight), and six glass beads with attached biofilm to examine the additional effect of sorption (vs Setup 2). Control setup consisted of autoclaved ultrapure water spiked with 500 ng/L d-labeled drugs to track pure water hydrolysis. A separate chemical analysis did not find detectable levels of background drugs (i.e., < LOD) in river water. A microcosm containing washed sediments and filtered autoclaved river water was initially considered but subsequently dropped due to equipment space limitations and initial tests showing negligible sediment sorption, which is consistent with previous studies indicating negligible drug removal via sediment sorption in river water.[36] Duplicate microcosm samples were removed and analyzed for aqueous drug concentrations at six time points: 0, 1.5, 6, 21, 72, and 144 h. Water quality parameters were measured throughout the degradation experiments.

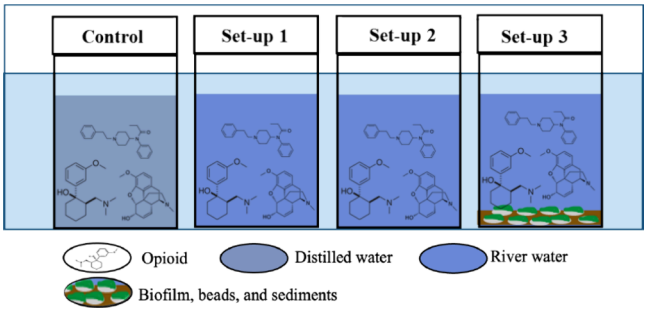

Figure 1. Microcosm setup for degradation studies. 150 mL aqueous samples spiked with opioids were placed in 200 mL glass jars covered with air-permeable seals. Jars were kept in the dark at constant temperature in a shaker bath (30 °C and 100 rpm) for the duration of the degradation tests.

2.4. Sample Processing and Chemical Analysis. *2.4.1. Water Quality Parameters.* The following water quality parameters were measured: pH, dissolved oxygen (YSI 5100 probe), nitrate (cadmium reduction method, 8039) and phosphate (ascorbic acid method, 8048), and solids (total, total suspended and dissolved, ash free dry mass; EPA Method 1684[37]).

2.4.2. Drug Analytes. Aqueous drug concentrations in the microcosms were analyzed following a modified previous method.[38] Briefly, water samples (150 mL) were filtered (1 mm GF, Pall) and passed through solid-phase extraction using Phenomenex Strata-X cartridges (200 mg/cm^3). The cartridges were preconditioned with 10 mL of methanol, followed by 10 mL of ultrapure water and then loaded with filtered samples at a rate of 2 mL/min. After sample loading, the cartridges were washed with 10% methanol in ultrapure water and vacuum-dried for 30 min. The extracted analytes were eluted serially with 5 mL of 2% (v/v) formic acid in methanol, 3 mL of 5% (v/v) ammonium hydroxide in methanol, and 2 mL of ethyl acetate in isopropanol (85:15). Extracts were dried to dryness in a vacuum oven, reconstituted in 0.5 mL of 10% (v/v) methanol in ultrapure water, and analyzed for target opioids in a liquid chromatograph tandem mass spectrometer (Acquity UPLC with Quattro Premier XE, Waters) under positive electrospray ionization (see Supporting Information, SI Table S1). Chromatographic separation was achieved in a C18 column (Hypersil Gold, 1.9 mm × 100 mm × 2.1 mm) using a gradient program of an aqueous mobile phase and an organic mobile phase (0.1% v/v formic acid in methanol). Detection limits for target analytes ranged from 0.01 ng/L (tramadol) to 0.15 ng/L (buprenorphine); method recoveries ranged from 92% (fentanyl) to 105% (tramadol) (SI Table S2). Analyte quantification was performed in MassLynx (version 4.2).

2.5. Modeling of Degradation Kinetics. A preliminary screening analysis indicated that first-order kinetics best described our opioid degradation data. On the assumption of additive effects of degradation processes,[18] the first-order degradation kinetics can be modeled as

$$C(t)_i = C_{0,i}\exp^{-(k_h+k_{ab}+k_b+k_s)t} \quad (1)$$

where $C(t)_i$ is the opioid i concentration at time t, $C_{0,i}$ is its initial concentration, k_h is the hydrolysis rate constant, k_{ab} is the abiotic degradation rate constant, k_b is the biodegradation rate constant, and k_s is the sorption rate constant. A linearized plot of eq 1 yields a line with a slope corresponding to the rate constants. For the control setup, the slope corresponds to k_h. For Setup 1, the slope corresponds to combined k_h and k_{ab}, with the latter constant determined by the difference. For Setup 2, the slope corresponds to combined k_h, k_{ab}, and k_b, with k_b calculated by the difference. Finally, Setup 3 adds the effect of sorption (k_s).

3. RESULTS AND DISCUSSION

3.1. Water Characteristics. The measured water quality parameters are summarized and plotted in Figure S1 (Supporting Information). Nitrate (0.30−1.98 mg/L) and phosphate (0.01−0.18 mg/L) levels and total solids (228−306 mg/L) in the microcosms were typical of freshwater systems.[39] The pH levels indicated slightly acidic to neutral conditions. DO levels indicated that aerobic conditions were maintained throughout the degradation study.

3.2. Drug Stabilities in River Water. Figure 2 shows the normalized remaining drug concentrations in the aqueous phase of each river microcosm over time. All four opioids

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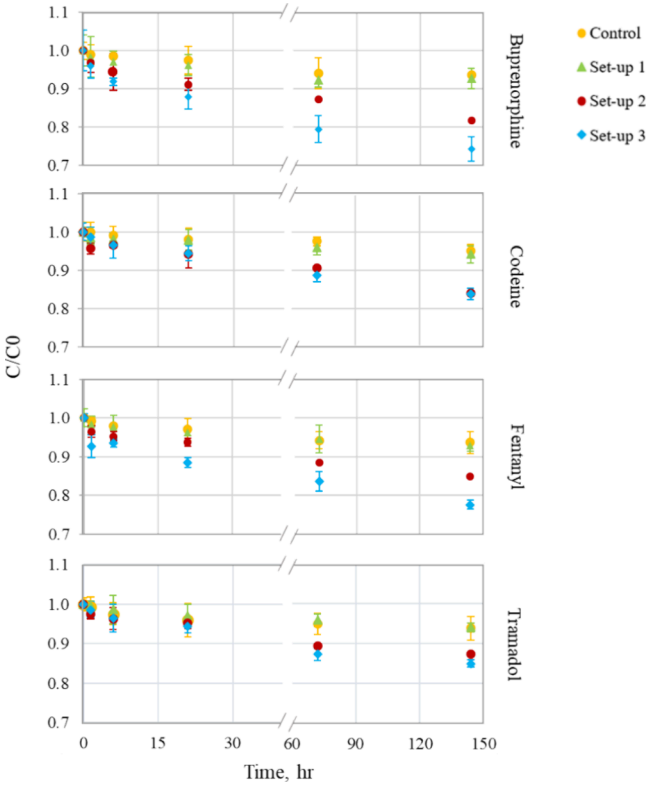

Figure 2. Plots of the normalized drug concentration over time. Markers represent average values, and vertical bars represent minimum−maximum range of duplicate samples.

exhibited relatively high stability in river water. Of the four, buprenorphine was found to be the least stable, with 26% removed after 6 days. Biodegradation played a major role in its degradation, contributing about 11% to buprenorphine removal, followed by hydrolysis and sorption, with each contributing about 7% removal. Abiotic degradation had the least effect on buprenorphine removal (0.8%). We did not find prior studies on the stability of buprenorphine in river water nor in wastewater with which to compare our results, though a recent report noted some degree of degradation for buprenorphine in biosolids after 2 weeks for biosolid samples kept at refrigerator (1 °C and −10 °C) and room (23 °C) temperatures.[40]

Fentanyl was the second least stable opioid after buprenorphine, with 22.5% of fentanyl degraded after 6 days. As with buprenorphine, abiotic degradation made the least contribution (0.7%) to fentanyl degradation. In contrast, hydrolysis, biodegradation, and sorption had relatively similar contributions to fentanyl degradation: 6.3% was due to hydrolysis, 8% was due to biodegradation, and 7.3% was due to sorption. We also did not find prior studies on fentanyl degradation in river water; however, Pagsuyoin et al. (2022) and McCall et al. (2016) reported that fentanyl is prone to sorption in the wastewater matrix, mainly due to the presence of biofilm and organic particulates.

Codeine was the third least stable opioid, exhibiting 16% removal in river water after 6 days, mainly due to biodegradation (11%). These findings are consistent with the results from a prior study by Lin et al. which reported that codeine hydrolysis in river water was not observed even after 30 days, whereas 25% removal via biodegradation occurred after 14 days.[41]

Tramadol was the most stable of the four opioids, exhibiting only 15% removal after 6 days, mainly attributed to biodegradation (6.5%) and hydrolysis (6.1%). Sorption accounted for only 2.5% of tramadol removal. Rua-Gomez and Putman (2013) also previously reported very slow biotic degradation for tramadol in surface water (half-life below 0.00029 h^{-1}) in experiments held under laboratory conditions and in field tests.

3.3. Effects of Degradation Processes on Opioid Stability. First-order rate constants for each degradation process and the corresponding degradation half-lives were calculated[42] (Table 2) from the fitted first-order degradation models (Figure 3). Overall, hydrolysis had a comparatively lower effect on drug degradation compared to biodegradation, with k_h values ranging from 0.008 to 0.011 d^{-1}. The lower effect of hydrolysis is expected given that the pK_a values of the four studied opioids (see Table 1) are higher than the near-neutral pH conditions of the microcosms, i.e., species tend to be mainly present in their unprotonated form in water.[18] Furthermore, except for fentanyl, the opioids also generally lack the functional groups that promote hydrolysis, e.g., amides and esters.[43] However, we note that the microcosm temperatures (30 °C) were slightly higher than the standard temperature (25 °C) for which the pK_a values in Table 1 were determined. pK_a decreases with increasing temperatures;[29] thus, some degree of protonation may happen even at neutral pH.

Abiotic degradation also had a negligible influence on opioid degradation, with the calculated half-lives ranging from 852 d (codeine) to 2,863 d (tramadol) (with calculated k values near zero in Table 2). Similar trends were noted for other pharmaceuticals, where no degradation due to abiotic processes was observed in degradation studies carried out in the dark.[33] Rua-Gomez and Puttman (2013) noted that the presence of nitrates and dissolved organic matter in river water promotes drug degradation via indirect and direct photolysis (i.e., via the formation of reactive hydroxyl radicals), although they also did not find significant abiotic degradation for tramadol (and other opioids) when degradation studies in river water were carried out in the dark.

The effect of sorption was most pronounced in buprenorphine (43 d half-life) and fentanyl (62 d), followed distantly in tramadol (118 d) and codeine (212 d). This trend is consistent

Table 2. First-Order Rate Constants for Different Degradation Processes

	degradation rate constant, d^{-1}(Half-life, d)			
opioid	k_h	k_{ab}	k_b	k_s
buprenorphine	0.011 ± 0.002 (64 ± 13)	0.0006 ± 0.004 (1132 ± 7515)	0.018 ± 0.006 (39 ± 13)	0.016 ± 0.009 (44 ± 26)
codeine	0.008 ± 0.001 (91 ± 14)	0.0008 ± 0.002 (852 ± 1859)	0.016 ± 0.003 (43 ± 9)	0.003 ± 0.004 (212 ± 288)
fentanyl	0.010 ± 0.002 (68 ± 16)	0.0003 ± 0.003 (2102 ± 20252)	0.013 ± 0.004 (52 ± 18)	0.011 ± 0.008 (61 ± 42)
tramadol	0.009 ± 0.003 (75 ± 22)	0.0002 ± 0.003 (2863 ± 37411)	0.011 ± 0.004 (62 ± 23)	0.006 ± 0.006 (119 ± 118)

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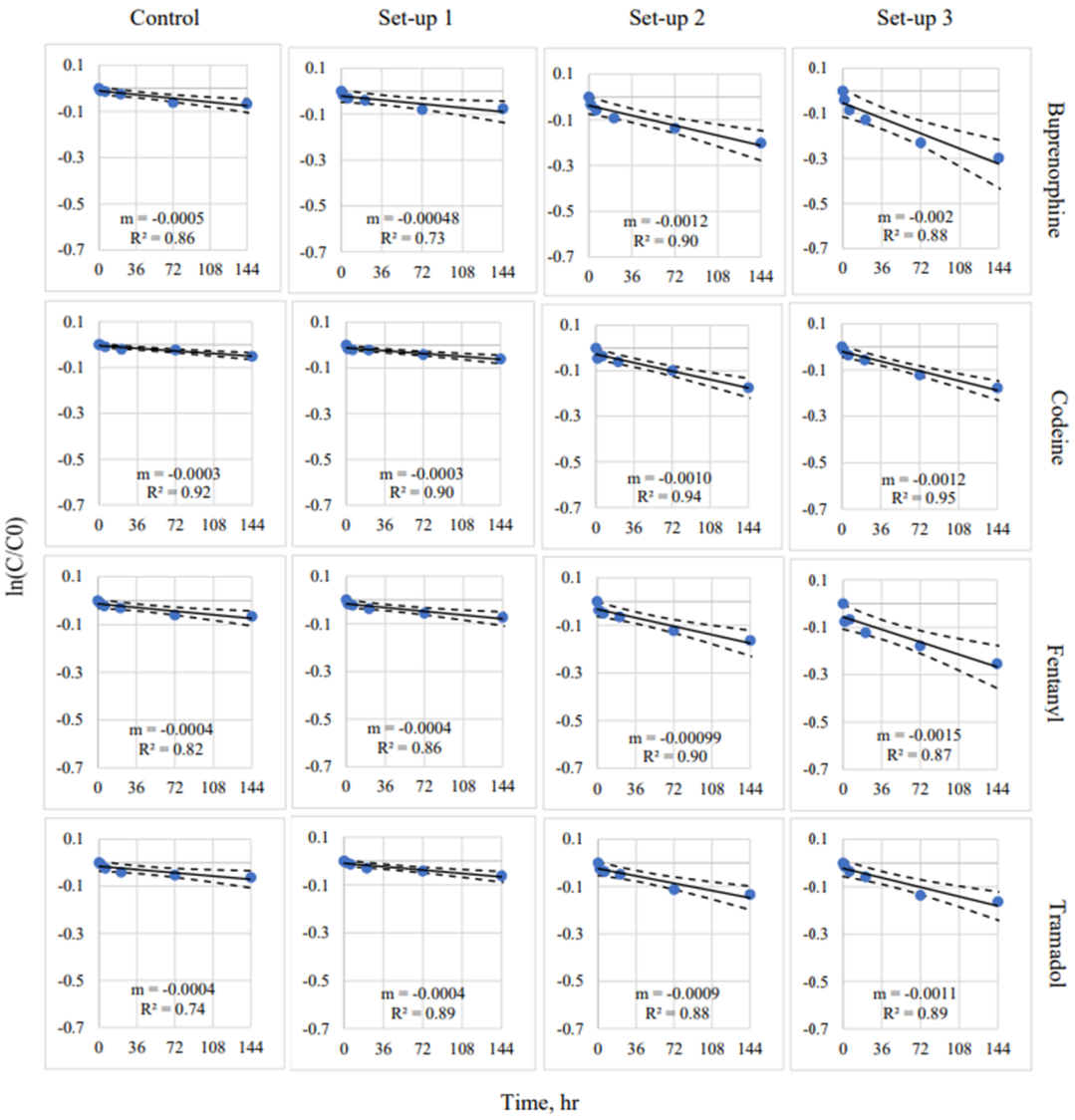

Figure 3. Degradation data are fitted to first-order models. Dashed lines represent 95% confidence intervals, and the solid lines represent model fits. Dots represent normalized remaining concentration (C/C_0) of opioids in water. m is the slope of the model fit, and R^2 is the goodness of fit.

with the expected affinities of the four opioids to organic carbon based on their log K_{ow} values (>4 for buprenorphine and fentanyl and <3 for tramadol and codeine). In this study, the organic carbon content of the microcosm was attributed mainly to the organic particulates in water and the biofilm in the sediments/beads (Setup 3, 49−94 mg/L as AFDM measured over 6 days, Figure S1). Previously, it has been reported that aqueous fentanyl was removed faster in unfiltered wastewater compared to filtered wastewater due to sorption to suspended particulate matter.[44]

Biodegradation had the most significant contribution to opioid degradation in river water, with half-lives ranging from 39 d (buprenorphine) to 62 d (tramadol). Biodegradation has also been noted as an important attenuation process for other pharmaceuticals like acetaminophen in river water.[45] Furthermore, biodegradation tends to have greater effect in wastewater than in river water due to the presence of higher organic matter and microorganisms in the former.[46] Indeed, some biodegradation may have occurred in the sediment biofilm (Setup 3) and amplified the effect of sorption. However, we were not able to distinguish the individual effects of sorption and biofilm-mediated biodegradation in the sediment, given the small volume of the microcosms. Nonetheless, we note that the organic carbon content in our microcosms was small in comparison to the net aqueous matrix amounts (49−94 mg/L as AFDM or 0.005−0.01 mass percent in Setup 3, nondetect AFDM in other microcosms). The sediment content in Setup 3 was also small, ∼3% (dry weight) of the microcosm. Biodegradation in biofilms can be a significant sink for organic pollutants, as has been shown for diclofenac in river beds with significant amounts of attached biofilms.[47] Furthermore, filtration with 1 μm filters can remove fine particulates, and it may also exclude the effect of larger organisms such as Bacillus if they are present in natural waters.[48] Some nominal 1 μm filters allow larger microorganism (e.g., Cryptosporidium) to pass through.[49]

3.3.1. Implications to Exposure Risks in Aquatic Organisms. The high consumption, continuous discharge from wastewater treatment facilities, and high environmental stability of psychoactive drugs have compounding effects on their pseudopersistence in streams[11] and, consequently, may exacerbate the exposure risks they pose to aquatic organisms.

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ACS Omega 2024, 9, 26355−26362

Our results show that our studied opioids are relatively very stable in river water, with degradation half-lives 1−4 orders of magnitude higher than the half-life values reported for wastewater systems (Table 3), despite the higher temperature

Table 3. Half-Life of Opioids in Aqueous Matrices

		river water half-life, h	
opioids	wastewater half-life, h	previous studies	this study[a]
buprenorphine	1.1−4.4 (T = 20 °C, pH = 7.5, gravity and rising main)[58]		369.12
codeine	0.5−1.7 (T = 20 °C, pH = 7.5, gravity and rising main)[58]		595.20
fentanyl	17 (T = 25 °C, pH= 7.5)[18]		473.52
tramadol	122 (w/o glucose) 32 (w. glucose) (T = 30 °C)[59]	2887 (T = 23 °C pH = 7.5)[60]	628.80

[a]Overall half-life, i.e., accounting for all degradation processes, calculated from Setup 3. T = 30 ± 0.04 °C and pH = 6.83 ± 0.04. See Figure S1.

of our microcosms. Degradation rates generally increase at higher temperatures; however, drug stability is influenced by other factors such as richness of microbial community[50] and environmental conditions (e.g., biochemical composition of matrix[51]). It is expected that the consumption of these opioids will remain high or rise even further. Buprenorphine is currently included in the World Health Organization's list of essential medicines[52] and is projected to become the most common therapeutic treatment for opioid use disorder in the near future.[53] Public health concern has been raised worldwide over the increasing use and misuse of fentanyl[54] and tramadol[55] in recent years, which have been also associated with increased overdose deaths.[56] Codeine remains as one of the commonly prescribed opioids, including among patients with post-COVID conditions.[57]

Freshwater systems are home to many aquatic organisms. The increasing consumption and persistence of psychoactive drugs in streams merit conducting further studies exploring their acute and chronic exposure effects on aquatic organisms, including the potential synergistic impacts of exposure to drug mixtures at environmentally relevant concentrations. Drugs may bioaccumulate and travel through the food chain. For example, codeine bioaccumulates in crucian carp[61] and was frequently detected in riparian spiders through their consumption of aquatic insect larvae.[7] It is also worthwhile to further examine the effects of biodegradation−sorption mechanisms in other ecosystems (e.g., other watersheds). Microbial community profiles can differ across ecosystems[62] and shift over time even for the same ecosystem.[63] The effects of biodegradation−sorption in other ecosystems may vary from those observed in our work. There is also a need for further studies on how environmental processes, such as photolytic degradation, dilution, and plant uptake, can function as natural attenuation pathways for drug discharges in the environment. Previous studies on pharmaceuticals and estrogens have shown that direct and indirect photolysis (e.g., via enhanced formation of reactive hydroxy radicals in the presence of organic matter and nitrates) can be significant degradation pathways for persistent organics,[60,64] with indirect photolysis tending to have greater effect than direct photolysis.[60] Still, photolytic effects on drug degradation vary. Codeine exhibits absorbance at wavelengths >286 nm and can undergo direct photolysis, whereas amphetamine-type stimulants are not prone to direct photolysis but can still undergo indirect photolysis due to the presence of dissolved organic matter, nitrates, and bicarbonates.[41] Plant uptake can also significantly remove pharmaceuticals from surface waters, which may lead to concerns for potential bioaccumulation effects on organisms in the upper trophic levels of the food web.[65,66]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.4c02486.

LC-MS/MS settings, target drugs and their properties, and DO and temperature of microcosms during degradation runs (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Sheree A. Pagsuyoin − *Department of Civil and Environmental Engineering, University of Massachusetts Lowell, Lowell, Massachusetts 01854, United States;* orcid.org/0000-0003-4090-957X; Email: Sheree_Pagsuyoin@uml.edu

Author

Varsha Niroula − *Department of Civil and Environmental Engineering, University of Massachusetts Lowell, Lowell, Massachusetts 01854, United States*

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.4c02486

Notes

The authors declare no competing financial interest.

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