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Evaluation of wastewater tracers to predict pharmaceutical distributions and behavior in the Long Island Sound estuary

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HIGHLIGHTS

- Sucralose demonstrated conservative behavior when compared to salinity.
- New York Harbor is the major source of pharmaceuticals to the estuary.
- Sucralose proved effective as a tracer of pharmaceuticals.
- Attenuation factors identified varied behavior of pharmaceuticals.

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ABSTRACT

Urban estuaries receive large volumes of effluents from municipal wastewater treatment facilities containing numerous contaminants, such as pharmaceuticals residues. Water was sampled for 16 highly prescribed pharmaceuticals at 17 sites along the Long Island Sound (LIS) estuary located in the Northeastern U.S. Pharmaceutical concentrations were highest in western LIS, ranging from non-detect to 71 ng L^{-1} and declining steadily eastward, while river samples from four major tributaries ranged from non-detect to 83 ng L^{-1}. Two tracers, sucralose and caffeine, accurately predicted pharmaceutical behavior in LIS while only sucralose was effective at the river sites. Sucralose also tracked well with the salinity gradient in LIS, exhibiting conservative behavior along the transect. Attenuation factors were determined for measurable pharmaceuticals and compared against sucralose to estimate the magnitude of decline in concentrations that may be attributable to in situ degradation and partitioning. The results demonstrate sucralose's effectiveness as a tracer of wastewater-borne contaminants under estuarine conditions.

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1. Introduction

The extensive use of pharmaceuticals by human populations has resulted in their widespread distribution throughout the aquatic environment (Hughes et al., 2013). Following use, pharmaceutical residues enter municipal wastewater treatment facilities (WWTF) via sanitary wastewater inputs, where their removal efficiencies are highly variable (Verlicchi et al., 2012). Due to the high volume and continuous use and release of many pharmaceuticals to receiving waters, it is necessary to understand their environmental occurrence, fate and effects.

The concentrations of pharmaceutical residues present in most aquatic systems are generally well below therapeutic dosage levels (Fent et al., 2006). However, numerous pharmaceutical compounds are often present in water bodies at elevated levels, especially downstream of wastewater (WW) discharges (Kay et al., 2017), as well as in and near urbanized areas (Kolpin et al., 2004). By design, pharmaceutical compounds are biologically active and can interact physiologically with organisms, which raises concerns regarding potential biological or adverse effects (Fabbri and Franzellitti, 2016). For most of the pharmaceutical compounds found and measured in the environment, derived effects-based concentrations have not been established, limiting assessment of their overall environmental risk (aus der Beek et al., 2016). As a result, most developed countries have no regulatory standards for pharmaceuticals in ambient receiving waters. In the European Union, several classes of

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pharmaceuticals are included in a watch list developed to determine risk to the aquatic environment and whether EU Environmental Quality Standards should be established.

Coastal waters and estuaries in close proximity to densely populated urban centers are particularly impacted by domestic WWTF discharges and in some cases episodic releases of untreated sewage from combined sewage overflows (CSOs). This is the case with Long Island Sound (LIS), an urban estuary adjacent to New York City, coastal Connecticut, and Long Island, USA (Fig. 1). Numerous WWTFs and CSO discharges are located in nearby greater New York City (NYCDEP, 2012; NYCDEP, 2016). As a result, enormous volumes of treated and untreated WW are released daily, with many of these discharges entering the western LIS. Recent work has shown elevated concentrations of WW associated contaminants, including pharmaceutical residues, to be present in the East River of NY Harbor (Lara-Martin et al., 2014; Cantwell et al., 2018).

Accurately assessing the distribution and fate of pharmaceuticals from WW discharged to a large urban estuary can be complicated by the receiving water body's size, morphology, and other factors (Bayen et al., 2013). The substantial number and volume of pharmaceuticals consumed and likely present in sanitary WW effluent makes measurement and assessment of all but the most highly used or those with the greatest potential for adverse effects impractical. Complicating the assessment of pharmaceuticals in estuarine waters is their diverse physicochemical properties, which influence their partitioning, stability, degradation and transformation—all of which must be accounted for in order to understand their behavior and fate.

Wastewater tracers have been previously proposed and evaluated as tools to identify sources and estimate sanitary WW loadings to surface waters (Nakada et al., 2008). Two compounds, caffeine and sucralose, are both ubiquitous in WW (Buerge et al., 2003; Oppenheimer et al., 2011, 2012) and have been used or proposed as tracers of sanitary wastewater and associated contaminants in surface and groundwater. Ideally, contaminant tracers are stable compounds with low detection limits and are source specific. Sucralose has demonstrated persistence in WWTFs and natural waters (Arbeláez et al., 2015; Labare and Alexander, 1993; Scheurer et al., 2010), while caffeine has exhibited behavior that suggests it is more labile and subject to degradation (Benotti and Brownawell, 2009). When suitable tracers are selected and applied, they have the potential for elucidating the processes controlling the dilution and fate of WW-borne contaminants in large and complex water bodies such as estuaries. Tracers may also be useful for determining the spatial distribution of contaminants and discriminating among WW sources discharging to receiving waters (Cantwell et al., 2018).

The primary objectives of this study were to: (1) measure the occurrence, evaluate the spatial distribution and confirm the major source(s) of 16 highly prescribed pharmaceuticals in the surface waters of the LIS estuary, and (2) refine the assessment of sucralose and caffeine as tracers of WW and micro-contaminants such as pharmaceutical compounds residing in the WW stream. Four major rivers in Connecticut were also sampled to estimate the contribution and impact of pharmaceuticals to LIS.

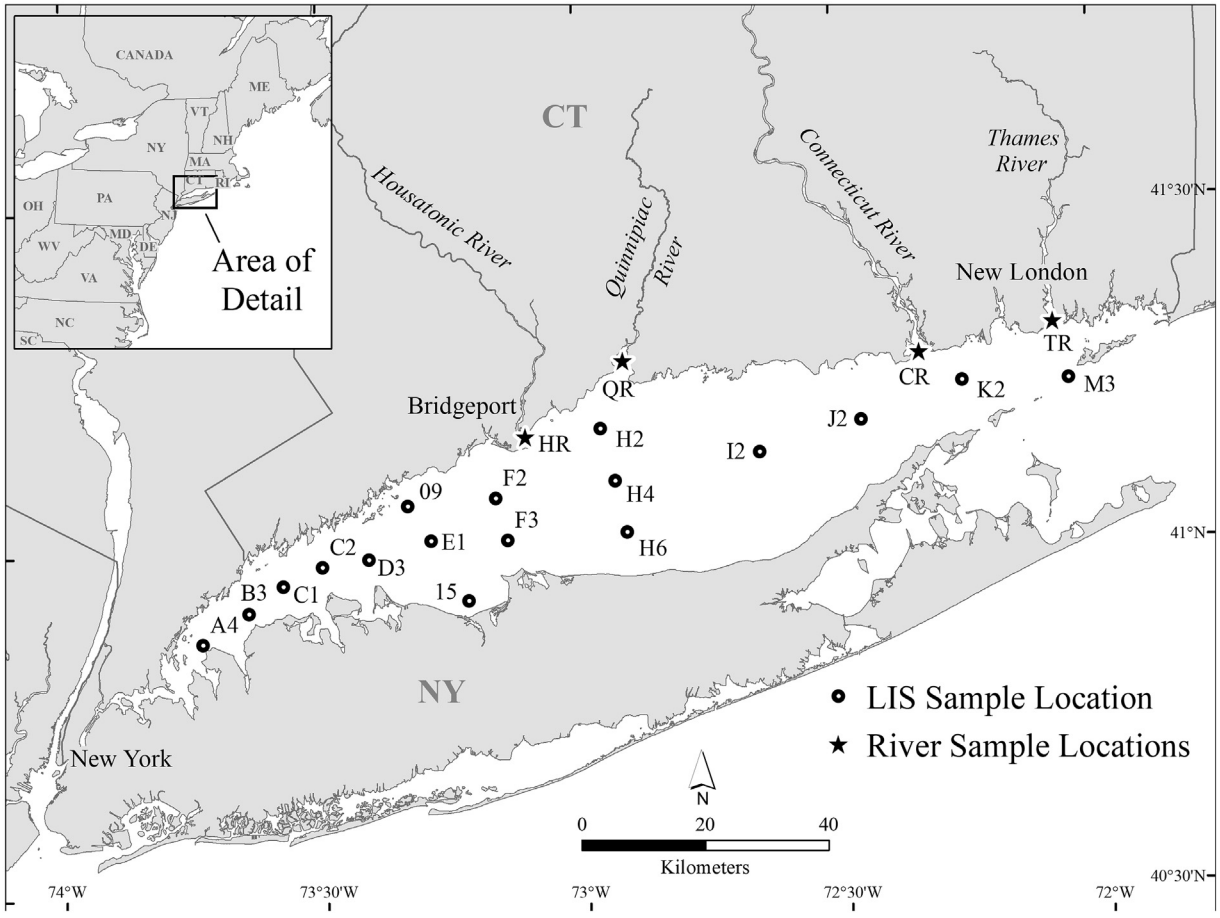

Fig. 1. Map of the study area and site locations.

2. Materials and methods

2.1. Study area

Long Island Sound is an urban estuary located east of New York City, with Connecticut to the north, and the northern shoreline of Long Island to the south (Fig. 1). The overall length of LIS is 177 km (110 miles), starting from the East River in New York City and ending at the entrance of Block Island Sound. The LIS is 34 km (21 miles) at its widest point, with depths ranging from 20 to 70 m. Long Island Sound is a unique estuary in several respects––one is that several major freshwater tributaries (e.g., Thames, Connecticut Rivers) discharge near its connection to the ocean (Gay et al., 2004). Also notable is that a tidal strait, the East River, exists at the head of the estuary, transporting fresh water (including WWTF discharges) from the Hudson River into LIS (O'Donnell et al., 2014).

Water circulation in LIS is quite complex, and there is an incomplete understanding of the mechanisms and processes regulating the flow and movement of water masses. Previous research of the East River (Blumberg and Pritchard, 1997) estimated an eastward flow of surface water at 260 m^3/s and a westward flow of bottom water at 570 m^3/s, resulting in a net westward flow of 310 m^3/s moving towards New York Harbor. Annual mean volume exchange at the eastern edge of LIS is much greater, estimated at 22,700±5000 m^3/s (Codiga and Aurin, 2007).

The impact of long-term high-volume WW discharge has been well documented in LIS, especially issues concerning nutrient loading and associated effects such as hypoxia (Varekamp et al., 2014; Wolfe et al., 1991; Zhao et al., 2011). Approximately 2.7×10^6 m^3/d of WW is discharged into the East River by six WWTFs, accounting for the most concentrated volume of WW discharged to LIS. WW influences along the north shore of LI are minimal, with nine plants discharging approximately 5.7×10^4 m^3/d across a length of 120.4 km. Conversely, the coastline of Connecticut and Westchester county, NY have 19 WWTFs discharging approximately 6.0×10^5 m^3/d along the 162.6 km of coastline. Finally, there are 75 WWTFs within the watersheds of the four major Connecticut rivers sampled for this study that account for 1.1×10^6 m^3/d to LIS.

2.2. Sampling

Sampling was conducted at 17 stations along a 148 km (92 mile) transect from western LIS to its eastern end where it enters Block Island Sound (Fig. 1). Water samples from LIS were collected May 1–4, 2017, during dry weather conditions off the Connecticut Department of Energy and Environmental Protection vessel *John Dempsey*. Grab samples were collected from 0.25 m below the water surface at each site using a rosette multi-Niskin water sampler (Table S1). Samples were kept on ice until returned to the laboratory and stored in the dark at 4 °C until processed. Surface water conditions (e.g., salinity, temperature) were also recorded at each station during sampling with a Hydrolab data sonde. Major riverine inputs were also sampled during dry weather to estimate their relative contribution of pharmaceuticals to LIS. Water was collected from sites at and near the mouths of the Housatonic and Quinnipiac Rivers on May 2, 2017, and from the Thames and Connecticut Rivers on May 3, 2017.

2.3. Water extractions

Extraction protocols followed EPA Method 1694 with slight modifications using Oasis HLB solid phase extraction (SPE) cartridges (6 cc, 500 mg, Waters Corporation). For the extractions, 500-mL river samples and 2.5-L LIS samples were adjusted to pH 2 using hydrochloric acid (6N) and spiked with 100 ng of isotopically labeled internal standards (IS) (Table S2). Cartridges were conditioned with 6 mL of methanol, followed by 6 mL of pH 2 Milli-Q water, and 6 mL of pH 2 filtered artificial seawater. Samples were loaded onto SPEs using a vacuum manifold at a rate of 5–10 mL/min. After loading, the SPEs were rinsed with 12 mL of pH 2 Milli-Q water, dried for 15 min under vacuum and eluted with 12 mL of methanol. Extracts were then evaporated to dryness, reconstituted with 1 mL mobile phase (Milli-Q:methanol, 80:20), vortexed, transferred to vials and stored at 4 °C until analysis. Each set of extractions included a blank, fortified blank, and duplicate.

2.4. Analysis

The pharmaceuticals evaluated were from 7 therapeutic classes: antihypertensives (acebutolol, atenolol, diltiazem, labetalol, losartan, metoprolol, propranolol, valsartan, and verapamil); antibiotics (sulfamethoxazole and trimethoprim); an analgesic (acetaminophen); an anticonvulsant (carbamazepine); a diuretic (furosemide); an antilipemic (gemfibrozil); and an antiulcerative (ranitidine). The 16 pharmaceuticals were quantified using high purity standards (Sigma Aldrich) with isotopically enriched surrogates (deuterated and/or ^{13}C) as an IS (CDN Isotope) (Table S3). Analysis was performed on a Waters Acquity UPLC using a Waters Xevo TQD MS/MS operated in electrospray ionization (ESI) mode. Compounds were detected by MS/MS with ionization conditions of the capillary set to 0.5 kV in ESI+ and 3.5 kV in ESI- (Table S4). Compound specific settings were used for quantification and confirmation multiple reaction monitoring (MRM) transitions (Tables S2). Compounds were calibrated using a 10-point curve ranging from 0.25 ng/mL to 300 ng/mL. Calibration curves had an $r^2 = 0.99$ or better for all compounds. Calibration verification standards were prepared from neat compounds of certified purity and analyzed every 10 samples to confirm instrumental performance over the course of the analytical run. Recoveries for each compound were generally within 10% of their calculated concentrations. Duplicate samples were collected during each sampling trip and the relative percent difference was ≤5% for analytes above the method detection limit. All statistical analyses were performed using Microsoft Excel. Method detection limits were determined for each of the compounds using instrument detection limits defined as a signal to noise ratio >10 and are reported in Supplemental Data, Table S5, along with further information on quality control.

3. Results and discussion

3.1. Long Island Sound

3.1.1. Pharmaceutical concentrations

Of the 16 pharmaceuticals in this study, only 6 were present at 15 or more of the 17 sites within LIS. Concentrations of these 6 pharmaceuticals ranged from non-detect to 71 ng L^{-1}, with mean concentrations declining in the following order: valsartan > losartan > sulfamethoxazole > metoprolol > carbamazepine > trimethoprim (Table 1). Four other pharmaceuticals—acetaminophen, propranolol, atenolol and diltiazem—were present at four or fewer sites, primarily at the western end of the transect, and ranged from non-detect to 29 ng L^{-1}. Six other compounds (acebutolol, furosemide, gemfibrozil, labetalol, ranitidine, verapamil) were not detected at any sites. In LIS, pharmaceutical concentrations showed a consistent trend from west to east along the transect (Fig. 2). Concentrations were the highest at the westernmost site (A4), and declined steeply by approximately 60 percent at the next station (B3), a distance of approximately 9 km. Eastward along the transect,

Table 1
Concentrations (ng/L) of study compounds measured in Long Island Sound and its major tributaries (SUC = sucralose; CAF = caffeine; ACE = acetaminophen; CAR = carbamazepine; SUL = sulfamethoxazole; PRO = propranolol; ATE = atenolol; MET = metoprolol; TRI = trimethoprim; RAN = ranitidine; LAB = labetalol; DIL = diltiazem; LOS = losartan; VAL = valsartan).

Sites	SUC	CAF	ACE	ATE	CAR	DIL	LAB	LOS	MET	PRO	RAN	SUL	TRI	VAL
Long Island Sound														
A4 - Execution Rocks	670	140	29	7.0	9.8	1.5		54	25	0.42		35	5.0	71
B3 - Rye Beach	490	70			5.8	0.60		24	11	0.11		14	3.5	40
C1 - Oyster Bay	400	40			4.9	0.28		10	6.0			9.9	1.6	21
C2 - Stamford	450	41			4.8	0.29		11	6.3			8.8	1.7	24
D3 - Eaton's Neck Point	350	34			4.1			7.7	5.0			7.5	1.2	18
09 - Saugatuck River Entrance	360	31			4.3			6.8	5.0			7.4	1.5	18
E1 - Nissequogue River Entrance	330	27			3.6			5.8	4.0			5.7	1.0	14
15 - Smithtown Bay	260	28			3.3			6.1	3.9	0.10		6.5	1.1	15
F2 - Crane Neck, NY	350	28			3.3			5.5	4.3			5.3	1.1	14
F3 - Crane Neck, NY	390	24			3.6			4.9	4.1			7.8	0.98	14
H2 - New Haven Harbor Entrance	340	16			2.9			3.9	2.9			5.8	0.54	9.0
H4 - New Haven Harbor Entrance	290	19			3.9			4.1	3.5			6.8	0.91	11
H6 - Herod Point	280	16			3.9			3.9	3.1			6.0	0.85	9.6
I2 - Sachem Head	230	16			3.5			3.5	2.6			6.3	0.63	8.1
J2 - Duck Island	180	14			2.7			2.5	2.0			4.2	0.54	6.6
K2 - Plum Gut Harbor	150	14			1.8				1.8			2.6	0.40	4.5
M3 - Silver Eel Pond	120	8.1			1.4				1.3			2.6		3.8
Rivers														
Thames 1 - Can 13	450	15			3.6	0.6		3.7	11				0.82	11
Thames 2 - Coast Guard Marina	460	10			3.6	0.4		3.4	11				0.51	11
Thames 3 - Nautilus Museum	450	13			4.2	0.4		3.8	12	0.18			0.95	12
Connecticut 1 - Lighthouse Point	420	82	7.7	8.1	4.9	1.2	1.6	7.4	16	0.61		7.2	2.2	26
Connecticut 2 - Railroad Bridge	530	97	5.9	6.0	5.3	1.4	1.6	7.9	19	0.66		7.6	2.8	30
Connecticut 3 - Daymark 22	450	91	8.8	6.8	5.7	1.3	1.8	7.5	18	0.54		6.5	2.2	28
Quinnipiac 1 - Sandy Point	840	31		5.5	8.9	2.0		20	24	0.87		17	5.6	69
Quinnipiac 2 - Lighthouse Reach	920	32		7.7	12	2.1		20	29	1.0		40	6.2	51
Quinnipiac 3 - Power Plant	1240	25		13	23	3.3	0.89	32	43	1.6		62	9.1	83
Housatonic 1 - Channel Site 2	660	50		5.6	10	1.3	1.4	13	21	0.50	3.3	13	3.9	44
Housatonic 2 - Stratford Point	360	31		1.5	5.0			5.2	3.8			7.6	0.37	16
Housatonic 3 - Bridge	820	45		5.6	18	1.7	1.9	12	28	1.1	3.7	15	4.4	38

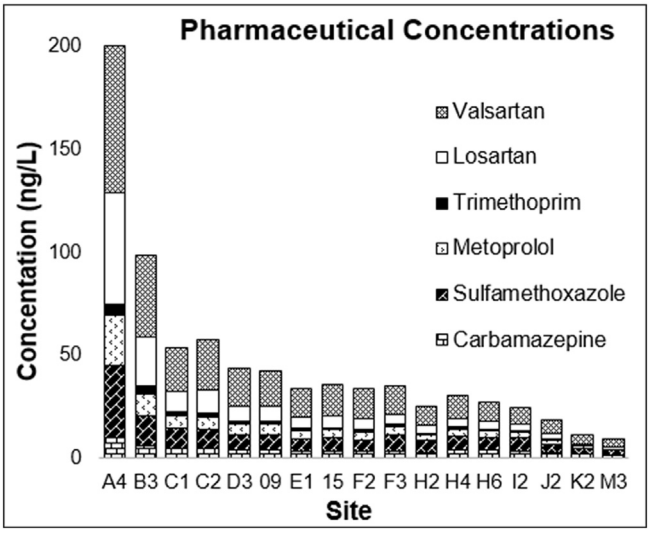

Fig. 2. Concentrations of frequently detected pharmaceuticals in Long Island Sound (ng L^{-1}).

concentrations continued to decline as distance increased, albeit at a slower rate.

Despite being among the most highly prescribed drugs (Batt et al., 2016; Kostich et al., 2014), more than half the studied pharmaceuticals were absent or present at low concentrations. Compared to concentrations measured in other urban estuaries in the Northeastern U.S. (e.g., Jamaica Bay, Benotti and Brownawell, 2009; Narragansett Bay, Cantwell et al., 2017), these were generally lower, except for the westernmost site (A4). Clearly, the transect data identify WWTFs that discharge to the East River as a major source of pharmaceuticals to the LIS estuary, which is substantiated by prior research (Lara-Martin et al., 2014) and WW discharge data (Table S6). Overall, the spatial trends illustrate the importance of physical processes and conditions regulating dilution and influencing contaminant distributions throughout LIS.

3.1.2. Salinity

A well-defined trend in the surface water salinity in LIS was also evident along the transect. Salinity was lowest in western LIS at 26 psμ (site A4), increasing progressively to 29.8 psμ at the easternmost station (site M3) (Table S1). This gradient reflects high salinity water entering LIS to the east from Block Island Sound, and lower salinity water entering LIS from the Hudson River via the East River tidal strait, which also receives wastewater effluents from NYC WWTFs, estimated at 1.0×10^9 m^3 annually (US EPA, 2018). Fresh water also enters LIS from riverine inputs along the Connecticut coast, averaging 2.44×10^{10} m^3 annually based on USGS (2018) gage data. However, direct influence from the rivers on salinity values was not apparent along the transect, despite the elevated river flows normally observed during springtime (USGS, 2018). This may be explained by the siting of the sampling stations, none of which are close to the major rivers entering LIS, as well as the circulation patterns within LIS.

The combination of low salinity water elevated in pharmaceuticals entering the head of the estuary and dilution by high salinity water (low in pharmaceutical concentrations) entering LIS from Block Island Sound played a crucial role in shaping concentrations observed along the transect. Evidence for this classic example of

estuarine circulation lies in the salinity data. Regressing the distance of the stations along the transect (with the westernmost station, A4, as km 0) to their corresponding surface salinity values using a linear model resulted in a r^2 of 0.9. The progressive and relatively uniform increase in surface water salinity from west to east is remarkable and illustrates the role of estuarine morphology and physical processes (e.g., tides and currents) in driving the circulation and mixing of water within LIS. As a result, these processes are a key factor in regulating the concentrations, spatial distribution and dilution of the study pharmaceuticals as well as other WW-borne contaminants.

The salinity data were also used to examine the individual behavior of the 6 ubiquitous pharmaceuticals. Linear regression of salinity values to each of the pharmaceuticals ranged from a low of $r^2 = 0.48$ for sulfamethoxazole to $r^2 = 0.67$ for trimethoprim (Table 2, Fig. S1). The relatively narrow range of r^2 values indicates comparable behavior among the pharmaceuticals along the salinity gradient. Other studies found similar behavior among pharmaceuticals and salinity over several tidal cycles at a single site in the East River (Lara-Martin et al., 2014) and in Jamaica Bay, NY (Benotti and Brownawell, 2007). Stronger relationships however, were found between the same pharmaceuticals in this study and salinity across eight sites in Narragansett Bay, an urbanized New England estuary (Cantwell et al., 2017). The higher r^2 values in Narragansett Bay (e.g., 0.83–0.95), possibly reflect its smaller size and a shorter residence time of water estimated at 26 days (Pilson, 1985). For LIS, the lower r^2 values for the pharmaceuticals is evidence that other variables besides dilution are responsible for the concentrations observed. Despite residence times estimated at six months or more in some areas (Vlahos and Whitney, 2017) and the likely loss by processes other than dilution (e.g., degradation) of some of the compounds, there is a meaningful relationship between salinity and pharmaceutical concentrations throughout the LIS transect.

3.1.3. Tracer evaluation

The salinity data also provide an approach to evaluate tracer behavior and effectiveness and better understand the spatial distribution of WW contaminants. Regression analysis of sucralose values in LIS versus salinity was performed using a linear model. Sucralose had an r^2 of 0.81, tracking well with the conservative behavior of salinity. The r^2 of sucralose versus salinity was higher than all the pharmaceuticals, reflecting its persistence in marine waters following discharge from WWTFs (Soh et al., 2011; Yang et al., 2017). Similar responses for sucralose versus salinity over a range of 24–30 psμ were found in a high-density sampling study ($n = 67$) in Narragansett Bay, RI, USA ($r^2 = 0.88$) (Cantwell et al., in prep), in the Cape Fear estuary in North Carolina, USA ($r^2 = 0.9$) (Mead et al., 2009), and in the Bay of Cadiz, Spain ($r^2 = 0.92$) (Baena-Nogueras et al., 2018), further documenting its stability and near-conservative behavior in estuarine waters.

The concentration of sucralose present along the transect was examined to assess its efficacy as a tracer of WW-associated contaminants. Sucralose was present at all sites at concentrations ranging from 120 to 670 ng L^{-1}. The concentration of sucralose at the eastern entrance to LIS was a factor of 12 greater than its minimum reporting limit (10 ng L^{-1}), providing a robust response despite substantial dilution along the transect. Regressions using a linear model produced r^2s ranging from 0.73 to 0.86 for each of the pharmaceuticals, showing sucralose predicted their behavior relatively well (Table 2, Fig. S2). Carbamazepine had the highest r^2 (0.86), correlating well with sucralose due to its well-documented resistance to degradation in natural waters (Kahle et al., 2009). Regressing the same data using an exponential model, however, yielded improved r^2 values, except for carbamazepine, ranging from 0.84 to 0.94 (Table 2). The higher r^2s obtained using the exponential model again suggests loss of some of the pharmaceuticals is a factor, due to proportionally greater or non-linear declines in concentration observed relative to sucralose (Table 2). Compared to salinity, sucralose (using either regression model) provided a better prediction of pharmaceutical concentrations. This is principally due to sucralose being a co-constituent along with pharmaceutical residues in WW effluents that are entering estuarine receiving waters. These results demonstrate the value of sucralose as a WW tracer for elucidating spatial trends and for assessing potential impacts of WW effluents and WW-borne contaminants such as pharmaceuticals following discharge to a large and complex water body such as LIS.

The performance of caffeine as a tracer was also evaluated against salinity and the pharmaceuticals. Compared to sucralose's relationship with salinity (0.81), the r^2 of caffeine was appreciably lower at 0.55, reflecting its lability in ambient waters (Benotti and Brownawell, 2009). The r^2 of caffeine versus salinity was mid-range to those between the pharmaceuticals and salinity (0.48–0.67) (Table 2), showing similar behavior and suggesting degradation or sorption. Benotti and Brownawell (2007) measured caffeine and pharmaceuticals in the Jamaica Bay estuary of NY during dry weather and found a similar correlation between caffeine and salinity ($r^2 = 0.57$). In contrast, caffeine did not correlate well with salinity ($r^2 = 0.10$) in a recent study of Narragansett Bay (Cantwell et al., 2017).

Like sucralose, caffeine was present at all locations in LIS, but at lower concentrations (8–140 ng L^{-1}). Regressing concentrations of the 6 frequently detected pharmaceuticals to caffeine using a linear model resulted in r^2s ranging from 0.91 to 0.99 for all compounds (Fig. S3), while an exponential model resulted in reduced r^2 values (Table 2). The trends between caffeine and the pharmaceuticals observed with the linear model suggest highly similar behavior in LIS.

Comparing the two tracers, caffeine is labile, as are most of the study pharmaceuticals apart from carbamazepine, which trends closely with the stable behavior of sucralose. For the 6 pharmaceuticals present throughout LIS, the linear r^2s for caffeine slightly

Table 2
Coefficients of determination (r^2) in Long Island Sound derived by linear and exponential regression.

Compound	Salinity		Sucralose		Caffeine	
	Linear	Exponential	Linear	Exponential	Linear	Exponential
Sucralose	0.81	0.89				
Caffeine	0.55	0.83	0.77	0.89		
Carbamazepine	0.66	0.81	0.86	0.84	0.91	0.66
Losartan	0.65	0.82	0.78	0.88	0.99	0.90
Metoprolol	0.51	0.84	0.75	0.94	0.99	0.84
Sulfamethoxazole	0.48	0.74	0.73	0.90	0.96	0.81
Trimethoprim	0.67	0.81	0.80	0.84	0.96	0.78
Valsartan	0.58	0.87	0.81	0.92	0.99	0.75

exceeded the exponential r^2s generated with sucralose, providing evidence for this observation. The use of sucralose and caffeine as pharmaceutical tracers were also evaluated at 65 sites in the Hudson River Estuary (Cantwell et al., 2018). The r^2 of the same 6 pharmaceuticals averaged 0.85 (0.77–0.97) when regressed linearly with sucralose, whereas caffeine showed much lower correlations, averaging $r^2 < 0.20$ (<0.01–0.59) for the same compounds. Evaluation of the same pharmaceuticals in Narragansett Bay also revealed poor correspondence with caffeine under similar conditions (M. Cantwell, unpublished results).

Caffeine's behavior and performance as a tracer in LIS when compared to salinity or pharmaceutical compounds are remarkably different from those observed in other estuaries (e.g., Narragansett Bay, Hudson River). Calculated half-lives of caffeine in estuarine waters were found to range from 5.9 to >100 days (Benotti and Brownawell, 2009), with shorter half-lives reported from areas that were highly impacted by effluent and the longer half-lives from offshore coastal waters. It was postulated that in waters not significantly impacted by WW effluents, caffeine degradation rates decline as bacterial abundance decreases, with its persistence increasing as water is transported offshore (Benotti and Brownawell, 2009). Spatial variability in the degradation rate of caffeine, along with other variables such as hydraulic residence time of the respective water bodies, may explain its inconsistent performance across estuarine systems.

While caffeine's responses in LIS and in other estuaries is variable and does not meet the strict definition of a tracer (i.e., persistence), its correlation with the study compounds here provides insight into its behavior. The high level of correspondence between caffeine and the measured pharmaceuticals here in LIS indicates that degradation may be occurring at a similar rate for some of these compounds.

Aside from tracking pharmaceuticals well, using both sucralose and caffeine as tracers provided multiple yet contrasting lines of evidence for predicting the behavior of WW-borne contaminants in LIS. Sucralose and other WW tracers such as x-ray contrast media, however, are not metabolized in the body and do not degrade appreciably in natural waters, which in many cases makes them superior to labile compounds like caffeine. Overall, this study provides further evidence of the effectiveness of sucralose as a tracer of hydrophilic contaminants associated with sanitary WW effluents such as pharmaceuticals under a broad range of conditions in large and complex urban estuaries.

3.1.4. Attenuation factors

In LIS, it is likely that some level of degradation is occurring, with biotic and abiotic processes (e.g., microbial and photolytic) potentially reducing concentrations and transforming the structural state of pharmaceuticals (Baena-Nogueras et al., 2017). In this study, metabolites of the pharmaceuticals were not measured, limiting assessment of their degradation pathways and fate. Any degradation observed would likely be influenced to some extent by the residence time of water in LIS, which is highly variable with estimates ranging from 71 days (Gay and O'Donnell, 2009) to more than six months (Vlahos and Whitney, 2017), depending on freshwater flows to LIS.

Evidence for degradation of the study pharmaceuticals lies in the concentration trends of the compounds along the transect. Dividing the concentration of each compound at each site by their initial values at site A4 (the westernmost and highest concentration site) and correcting for dilution using salinity values determines their relative decline over distance in LIS. Operationally, this decline includes factors regulating concentration, including sorption to particles and degradation. Plotting these "attenuation factors" from west to east illustrates individual compound behavior along the transect (Fig. 3). Note that sucralose has the lowest attenuation factor (with a terminal value of 4.7), followed next by carbamazepine (6.2). Despite the well-documented persistence of both these compounds (Huntscha et al., 2012), there is some observable attenuation, especially at the sites in the eastern LIS. In contrast, caffeine and the other pharmaceuticals present show attenuation more than double that of the conservative behaving tracer sucralose by the end of the transect. Subtracting the attenuation factor of sucralose from the other compounds provides an estimate of their respective losses and is an approach that could estimate the magnitude of partitioning and degradation of WW-derived contaminants under field conditions.

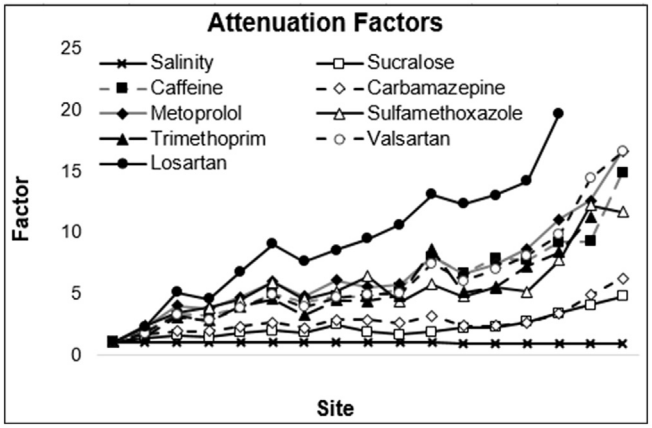

Fig. 3. Attenuation factors along Long Island Sound.

The log K_{ow} values of these compounds provide an indication of their potential for solid phase partitioning, although other factors are important in regulating partitioning (e.g., pH, ionic effects). All compounds except for valsartan have published log K_{ow}s below 3, indicating limiting partitioning potential. Several of the compounds (e.g., trimethoprim, carbamazepine and metoprolol) have field derived K_d values of less than 2.0 from estuarine waters (Cantwell et al., 2016), indicating a limited likelihood for removal by sorption processes. Similar findings were reported for sorption experiments on many of the same pharmaceuticals in this study (Benotti and Brownawell, 2009). Combined, these findings support microbial degradation as the likely factor influencing the concentrations of caffeine and potentially, for some of the pharmaceuticals in LIS.

3.2. CT rivers

Each of the four major CT rivers were sampled at 3 locations near their respective river mouths to estimate their contributions of pharmaceuticals to LIS. Concentrations were variable, with the highest levels of most pharmaceuticals found in the Quinnipiac River, followed by the Housatonic, although the frequency of occurrence was highest in the Connecticut (Table 1). The Thames had both the lowest concentrations and frequency of occurrence. As in LIS, valsartan, losartan, carbamazepine, metoprolol and trimethoprim were detectable at all sites. Additionally, pharmaceuticals that were not measurable at many sites in LIS—such as atenolol, propranolol and diltiazem—occurred at greater frequency in the rivers. Overall, the range in concentrations (non-detect to 83 ng L^{-1}) was similar to that of LIS.

The differing morphology of the rivers, size of their respective watersheds, and volume of WW discharged all played substantial roles in the concentrations at the river mouths. Using flow data from each of the rivers on their sampling date, flux estimates were calculated for the study compounds (Table S7). The largest fluxes

were observed in the Connecticut River, followed by the Housatonic, Quinnipiac and Thames. The magnitude of fluxes were driven mainly by river flow, with the Connecticut's flow substantially larger than the others, resulting in a flux approximately a factor of 5 greater than the Housatonic. While the Quinnipiac had the highest overall pharmaceutical concentrations of all rivers, its low flow resulted in fluxes that were near to (or in some cases lower than) the Thames, which had the lowest overall concentrations. Combining the river flux data provides a rough estimate of the pharmaceuticals emanating from Connecticut watersheds and entering LIS. For the tracers, the daily fluxes of sucralose and caffeine were more than 4600 and 800 g/d, respectively. For the pharmaceuticals, only metoprolol and valsartan had fluxes greater than 100 g/d, with the rest remaining below 68 g/d.

Data were pooled across the four rivers to examine how well sucralose and caffeine predicted concentrations of the study pharmaceuticals. Sucralose and caffeine were measurable at all sites, with concentrations ranging from 360 to 1240 ng L^{-1} and 10–97 ng L^{-1}, respectively. Regression analysis of pharmaceuticals present at all sites was performed with sucralose and caffeine as independent variables using a linear model which provided the best fits. For sucralose, r^2s for each of the pharmaceuticals ranged from 0.81 to 0.94 (except for atenolol at 0.43), showing excellent correspondence. Conversely, caffeine and sulfamethoxazole had an r^2 of 0.36 while the other pharmaceuticals showed no relationship greater than 0.07 (Table 3). With exception of the Connecticut River, which is relatively undeveloped at the mouth, the other three river mouths are highly urbanized harbors with WWTFs discharging to the immediate sampling areas. All four rivers, however, have WWTFs that discharge along their length and in their respective watersheds (Table S6). Despite each of the rivers having widely varying watershed characteristics and morphologies, sucralose again has demonstrated an excellent predictive capability of WW derived pharmaceutical concentrations. Caffeine's poor predictive ability of highly prescribed pharmaceuticals was also observed in the Hudson River, with no significant correlation with the same compounds (Cantwell et al., 2018). As discussed earlier, spatial variability in the rate of caffeine degradation due to bacterial abundances may be responsible for the poor correlation of caffeine with the pharmaceuticals at the river sites.

4. Conclusions

In this study, 16 high volume use pharmaceuticals were measured in order to understand their occurrence, behavior and fate in LIS. Less than half of the pharmaceuticals were consistently present in the waters of LIS, with concentrations dropping rapidly from west to east as the distance from NYC increased, confirming WWTFs along the East River as a major source of WW to LIS. Dilution was a key factor in regulating concentration, though degradation likely played a role as well, as demonstrated by the attenuation factors. At the river sites, fluxes to LIS were variable with no discernible impact observed at the sampling sites in the Sound. In LIS, both sucralose and caffeine proved effective as tracers of WW-derived pharmaceuticals, yet exhibited contrasting behavior, as demonstrated by the results of the different regression models. Sucralose tracked well with salinity, demonstrating both conservative behavior and predictable changes in concentrations due to dilution effects. Sucralose levels also correlated well with pharmaceutical concentrations at the river sites while caffeine did not. These findings agree with other recent studies, which show sucralose as a consistently effective tracer of pharmaceuticals in large, urban estuaries. Further, the tracer and pharmaceutical data illustrate the critical role that estuarine morphology and circulation play in regulating the fate and transport of WW-derived contaminants in LIS. Further work is recommended to continue the evaluation of sucralose as a tracer of other contaminants associated with WW effluents.

Table 3
Coefficients of determination (r^2) in the four rivers derived by linear regression.

Compound	Sucralose	Caffeine
Caffeine	0.04	
Trimethoprim	0.94	0.0002
Losartan	0.91	0.01
Metoprolol	0.90	0.002
Diltiazem	0.86	0.004
Carbamazepine	0.84	0.01
Valsartan	0.84	0.0002
Propranolol	0.83	0.07
Sulfamethoxazole	0.81	0.4
Atenolol	0.48	0.004

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2018.12.171.

References

Arbeláez, P., Borrull, F., Pocurull, E., Marcé, R.M., 2015. Determination of high-intensity sweeteners in river water and wastewater by solid-phase extraction and liquid chromatography-tandem mass spectrometry. J. Chromatogr. A 1393, 106–114. http://doi.org/10.1016/j.chroma.2015.03.035.

aus der Beek, T., Weber, F., Bergmann, A., Hickmann, S., Ebert, I., Hein, A., Küster, A., 2016. Pharmaceuticals in the environment—global occurrences and perspectives. Environ. Toxicol. Chem. 35, 823–835. http://doi.org/10.1002/etc.3339.

Baena-Nogueras, R.M., González-Mazo, E., Lara-Martín, P.A., 2017. Degradation kinetics of pharmaceuticals and personal care products in surface waters: photolysis vs biodegradation. Sci. Total Environ. 590–591, 643–654. http://doi.org/10.1016/j.scitotenv.2017.03.015.

Baena-Nogueras, R.M., González-Mazo, E., Fernandez, C.C., Lara-Martín, P.A., 2018. Occurrence, distribution and environmental risk of pharmaceutically active compounds (PhACs) in coastal and ocean waters from the Gulf of Cadiz (SW Spain). Sci. Total Environ. 612, 649–659. https://doi.org/10.1016/j.scitotenv.2017.08.279.

Batt, A.L., Kincaid, T.M., Kostich, M.S., Lazorchak, J.M., Olsen, A.R., 2016. Evaluating the extent of pharmaceuticals in surface waters of the United States using a national-scale rivers and streams assessment survey. Environ. Toxicol. Chem. 35 (4), 874–881. https://doi.org/10.1002/etc.3161.

Bayen, S., Zhang, H., Desai, M.M., Ooi, S.K., Kelly, B.C., 2013. Occurrence and distribution of pharmaceutically active and endocrine disrupting compounds in Singapore's marine environment: influence of hydrodynamics and physical–chemical properties. Environ. Pollut. 182, 1–8. http://doi.org/10.1016/j.envpol.2013.06.028.

Benotti, M.J., Brownawell, B.J., 2007. Distributions of pharmaceuticals in an urban estuary during both dry-and wet-weather conditions. Environ. Sci. Technol. 41 (16), 5795–5802. http://doi.org/10.1021/es0629965.

Benotti, M.J., Brownawell, B.J., 2009. Microbial degradation of pharmaceuticals in estuarine and coastal seawater. Environ. Pollut. 157 (3), 994–1002. http://doi.org/10.1016/j.envpol.2008.10.009.

Blumberg, A.F., Pritchard, D.W., 1997. Estimates of the transport through the east river, New York. J. Geophys. Res.: Oceans 102 (C3), 5685–5703. http://doi.org/10.1029/96JC03416.

Buerge, I.J., Poiger, T., Müller, M.D., Buser, H.R., 2003. Caffeine, an anthropogenic marker for wastewater contamination of surface waters. Environ. Sci. Technol.

37 (4), 691–700. http://doi.org/10.1021/es020125z.
Cantwell, M.G., Katz, D.R., Sullivan, J.C., Ho, K., Burgess, R.M., Cashman, M., 2016. Selected pharmaceuticals entering an estuary: concentrations, temporal trends, partitioning, and fluxes. Environ. Toxicol. Chem. 35 (11), 2665–2673. http://doi.org/10.1002/etc.3452.
Cantwell, M.G., Katz, D.R., Sullivan, J.C., Ho, K., Burgess, R.M., 2017. Temporal and spatial behavior of pharmaceuticals in Narragansett Bay, Rhode Island, United States. Environ. Toxicol. Chem. 36 (7), 1846–1855. http://doi.org/10.1002/etc.3710.
Cantwell, M.G., Katz, D.R., Sullivan, J.C., Shapley, D., Lipscomb, J., Epstein, J., Juhl, A.R., Knudson, C., O'Mullan, G.D., 2018. Spatial patterns of pharmaceuticals and wastewater tracers in the Hudson River Estuary. Water Res. 137, 335–343. http://doi.org/10.1016/j.watres.2017.12.044.
Codiga, D.L., Aurin, D.A., 2007. Residual circulation in eastern Long Island Sound: observed transverse-vertical structure and exchange transport. Cont. Shelf Res. 27 (1), 103–116. http://doi.org/10.1016/j.csr.2006.09.001.
Fabbri, E., Franzellitti, S., 2016. Human pharmaceuticals in the marine environment: focus on exposure and biological effects in animal species. Environ. Toxicol. Chem. 35 (4), 799–812. http://doi.org/10.1002/etc.3131.
Fent, K., Weston, A.A., Caminada, D., 2006. Ecotoxicology of human pharmaceuticals. Aquat. Toxicol. 76 (2), 122–159. http://doi.org/10.1016/j.aquatox.2005.09.009.
Gay, P., O'Donnell, J., Edwards, C., 2004. Exchange between Long Island Sound and adjacent waters. J. Geophys. Res. 109. http://doi.org/10.1029/2004JC002319. C06017.
Gay, P., O'Donnell, J., 2009. Comparison of the salinity structure of the Chesapeake Bay, the Delaware Bay and Long Island Sound using a linearly tapered advection-dispersion model. Estuar. Coast 32 (1), 68–87. http://doi.org/10.1007/s12237-008-9101-4.
Hughes, S.R., Kay, P., Brown, L.E., 2013. Global synthesis and critical evaluation of pharmaceutical data sets collected from river systems. Environ. Sci. Technol. 47 (2), 661–677. https://doi.org/10.1021/es3030148.
Huntscha, S., Singer, H.P., McArdell, C.S., Frank, C.E., Hollender, J., 2012. Multiresidue analysis of 88 polar organic micropollutants in ground, surface and wastewater using online mixed-bed multilayer solid-phase extraction coupled to high performance liquid chromatography–tandem mass spectrometry. J. Chromatogr. A 1268, 74–83. http://doi.org/10.1016/j.chroma.2012.10.032.
Kahle, M., Buerge, I.J., Müller, M.D., Poiger, T., 2009. Hydrophilic anthropogenic markers for quantification of wastewater contamination in ground- and surface water. Environ. Toxicol. Chem. 28 (12), 2528–2536. http://doi.org/10.1897/08-606.1.
Kay, P., Hughes, S.R., Ault, J.R., Ashcroft, A.E., Brown, L.E., 2017. Widespread, routine occurrence of pharmaceuticals in sewage effluent, combined sewer overflows and receiving waters. Environ. Pollut. 220, 1447–1455. https://doi.org/10.1016/j.envpol.2016.10.087.
Kolpin, D.W., Skopec, M., Meyer, M.T., Furlong, E.T., Zaugg, S.D., 2004. Urban contribution of pharmaceuticals and other organic wastewater contaminants to streams during differing flow conditions. Sci. Total Environ. 328 (1–3), 119–130. https://doi.org/10.1016/j.scitotenv.2004.01.015.
Kostich, M.S., Batt, A.L., Lazorchak, J.M., 2014. Concentrations of prioritized pharmaceuticals in effluents from 50 large wastewater treatment plants in the US and implications for risk estimation. Environ. Pollut. 184, 354–359. http://doi.org/10.1016/j.envpol.2013.09.013.
Labare, M.P., Alexander, M., 1993. Biodegradation of sucralose, a chlorinated carbohydrate, in samples of natural environments. Environ. Toxicol. Chem. 12 (5), 797–804. http://doi.org/10.1002/etc.5620120502.
Lara-Martín, P.A., González-Mazo, E., Petrovic, M., Barceló, D., Brownawell, B.J., 2014. Occurrence, distribution and partitioning of nonionic surfactants and pharmaceuticals in the urbanized Long Island Sound Estuary (NY). Mar. Pollut. Bull. 85 (2), 710–719. https://doi.org/10.1016/j.marpolbul.2014.01.022.
Mead, R.N., Morgan, J.B., Avery, G.B., Kieber, R.J., Kirk, A.M., Skrabal, S.A., Willey, J.D., 2009. Occurrence of the artificial sweetener sucralose in coastal and marine waters of the United States. Mar. Chem. 116 (1), 13–17. http://doi.org/10.1016/j.marchem.2009.09.005.
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. http://doi.org/10.1021/es7030856.
NYCDEP, 2012. The State of the Harbor. Retrieved from. http://www.nyc.gov/html/dep/pdf/hwqs2012.pdf.
NYCDEP, 2016. Green Infrastructure Performance Metrics Report. Retrieved from. http://www.nyc.gov/html/dep/pdf/green_infrastructure/gi-performance-metrics-report-2016.pdf.
O'Donnell, J., Wilson, R.E., Lwiza, K., Whitney, M., Bohlen, W.F., Codiga, D., Fribance, D., Fake, T., Bowman, M., Varekamp, J., 2014. The physical oceanography of Long Island Sound. In: Latimer, J., Tedesco, M., Swanson, R., Yarish, C., Stacey, P., Garza, C. (Eds.), Long Island Sound Prospects for the Urban Sea. Springer-Verlag, New York, NY, pp. 79–158. http://doi.org/10.1007/978-1-4614-6126-5_3.
Oppenheimer, J.A., Badruzzaman, M., Jacangelo, J.G., 2012. Differentiating sources of anthropogenic loading to impaired water bodies utilizing ratios of sucralose and other microconstituents. Water Res. 46 (18), 5904–5916. http://doi.org/10.1016/j.watres.2012.07.060.
Oppenheimer, J., Eaton, A., Badruzzaman, M., Haghani, A.W., Jacangelo, J.G., 2011. Occurrence and suitability of sucralose as an indicator compound of wastewater loading to surface waters in urbanized regions. Water Res. 45 (13), 4019–4027. http://doi.org/10.1016/j.watres.2011.05.014.
Pilson, M., 1985. On the residence time of water in Narragansett Bay. Estuaries 8 (1), 2–14. http://doi.org/10.2307/1352116.
Scheurer, M., Storck, F.R., Brauch, H.J., Lange, F.T., 2010. Performance of conventional multi-barrier drinking water treatment plants for the removal of four artificial sweeteners. Water Res. 44 (12), 3573–3584. http://doi.org/10.1016/j.watres.2010.04.005.
Soh, L., Connors, K.A., Brooks, B.W., Zimmerman, J., 2011. Fate of sucralose through environmental and water treatment processes and impact on plant indicator species. Environ. Sci. Technol. 45 (4), 1363–1369. http://doi.org/10.1021/es102719d.
USEPA, 2018. Enforcement and Compliance History Online. https://echo.epa.gov/ (Accessed 30 January 2018).
USGS, 2018. National Water Information System. http://waterdata.usgs.gov/nwis (Accessed 31 January 2018).
Varekamp, J.C., McElroy, A.E., Mullaney, J.R., Breslin, V.T., 2014. Metals, organic compounds, and nutrients in long Island sound: sources, magnitudes, trends, and impacts. In: Latimer, J., Tedesco, M., Swanson, R., Yarish, C., Stacey, P., Garza, C. (Eds.), Long Island Sound Prospects for the Urban Sea. Springer-Verlag, New York, NY, pp. 203–283. http://doi.org/10.1007/978-1-4614-6126-5_5.
Verlicchi, P., Al Aukidy, M., Zambello, E., 2012. Occurrence of pharmaceutical compounds in urban wastewater: removal, mass load and environmental risk after a secondary treatment—a review. Sci. Total Environ. 429, 123–155. http://doi.org/10.1016/j.scitotenv.2012.04.028.
Vlahos, P., Whitney, M.M., 2017. Organic carbon patterns and budgets in the Long Island Sound estuary. Limnol. Oceanogr. 62, S46–S47. http://doi.org/10.1002/lno.10638.
Wolfe, D.A., Monahan, R., Stacey, P.E., Farrow, D.R.G., Robertson, A., 1991. Environmental quality of long Island sound: assessment and management issues. Estuar. Coast 14 (3), 224–236. http://doi.org/10.2307/1351658.
Yang, Y.Y., Liu, W.R., Liu, Y.S., Zhao, J.L., Zhang, Q.Q., Zhang, M., Zhang, J.N., Jiang, Y.X., Zhang, L.J., Ying, G.G., 2017. Suitability of pharmaceuticals and personal care products (PPCPs) and artificial sweeteners (ASs) as wastewater indicators in the Pearl River Delta, South China. Sci. Total Environ. 590–591, 611–619. http://doi.org/10.1016/j.scitotenv.2017.03.001.
Zhao, S., Zhang, P., Crusius, J., Kroeger, K.D., Bratton, J.F., 2011. Use of pharmaceuticals and pesticides to constrain nutrient sources in coastal groundwater of northwestern Long Island, New York, USA. J. Environ. Monit. 13 (5), 1337–1343. http://doi.org/10.1039/c1em10039d.