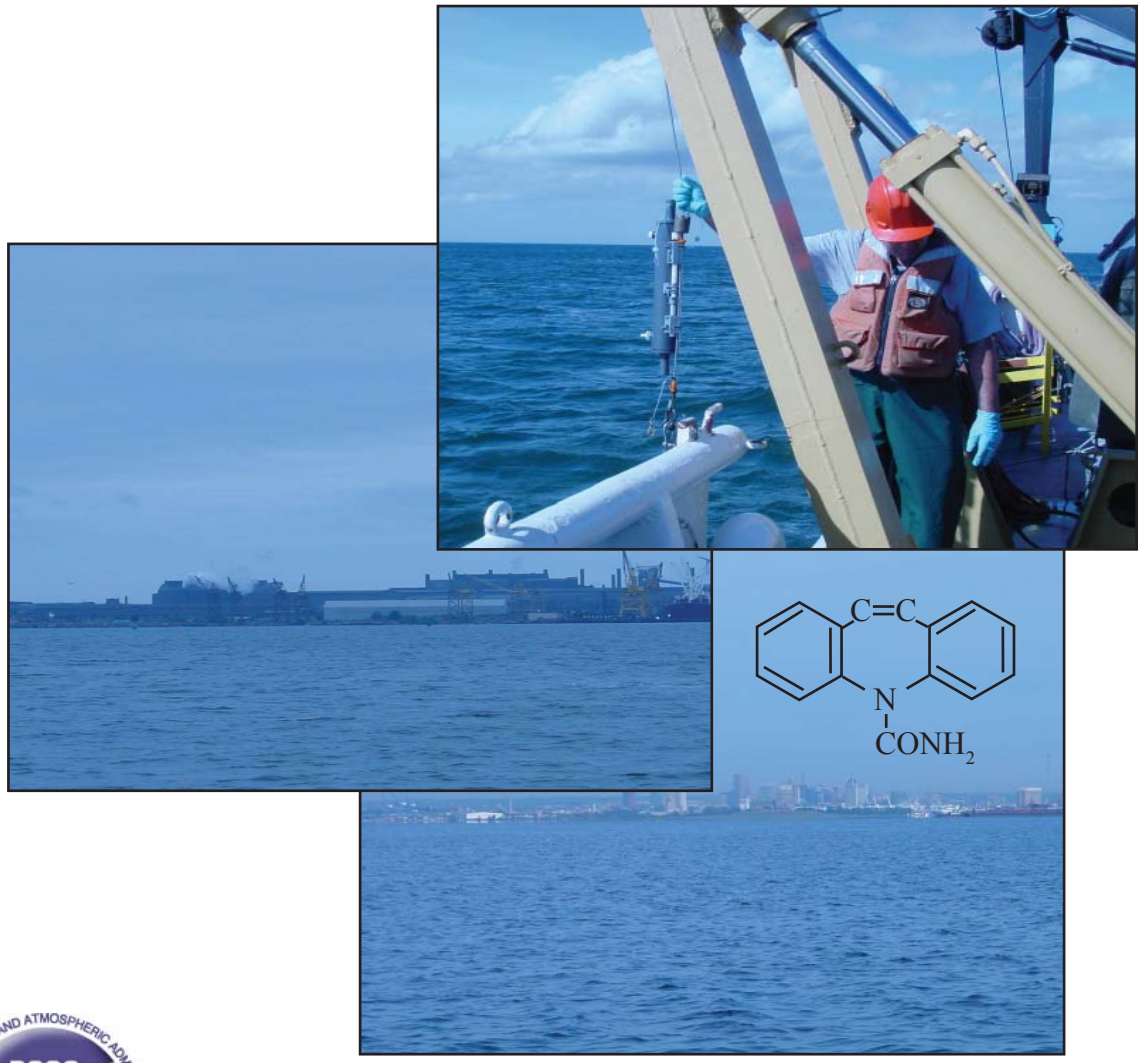
Human Use Pharmaceuticals in the Estuarine Environment: A Survey of the Chesapeake Bay, Biscayne Bay and Gulf of the Farallones



NOAA Technical Memorandum NOS NCCOS 7

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Human Use Pharmaceuticals in the Estuarine Environment: A Survey of the Chesapeake Bay, Biscayne Bay and Gulf of the Farallones

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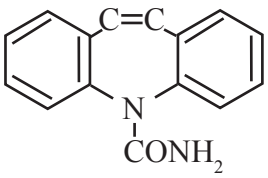
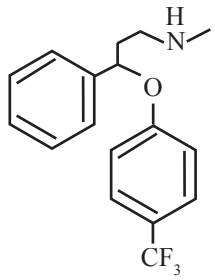
Introduction

The assessment of emerging risks in the aquatic environment is a major concern and focus of environmental science (Daughton and Ternes, 1999). One significant class of chemicals that has received relatively little attention until recently are the human use pharmaceuticals.

In 2004, an estimated 2.6 billion prescriptions were written for the top 300 pharmaceuticals in the U.S. (RxList, 2005). Mellon *et al.* (2001) estimated that 1.4 million kg of antimicrobials are used in human medicine every year. The use of pharmaceuticals is also estimated to be on par with agrochemicals (Daughton and Ternes, 1999). Unlike agrochemicals (*e.g.*, pesticides) which tend to be delivered to the environment in seasonal pulses, pharmaceuticals are continuously released through the use/excretion and disposal of these chemicals, which may produce the same exposure potential as truly persistent pollutants.



Carbamazepine



Fluoxetine

Molecular structures of two compounds included in this study, the antiepileptic carbamazepine, and fluoxetine or Prozac®, an antidepressant.

Human use pharmaceuticals can enter the aquatic environment through a number of pathways, although the main one is thought to be via ingestion and subsequent excretion by humans (Thomas and Hilton, 2004). Unused pharmaceuticals are typically flushed down the drain or wind up in landfills (Jones *et al.* 2001).

In wastewater treatment plants (WWTPs), a number of pharmaceuticals are only partly removed by conventional biological treatments, resulting in their discharge to surface waters (Andreozzi *et al.*, 2002). There have also been reports of pharmaceuticals occurring in groundwater, typically as a result of their disposal in landfills (Jones *et al.*, 2001).

Halling-Sørensen *et al.* (1998) noted that pharmaceuticals are developed with the intention of having a biological effect, and often have physico/chemical properties (*e.g.*, ability to pass through membranes, persistence) chosen to avoid their inactivation prior to having a curative effect. Brain *et al.* (2004) concluded that while the concentrations of individual compounds in the environment are low, the combination of a variety of pharmaceuticals in natural waters could prove toxicologically significant. In addition, there is also the possibility that pharmaceuticals could interact with other pollutant classes (*e.g.*, pesticides or polycyclic aromatic hydrocarbons (PAHs)) within the environment in unanticipated ways.

The effects of pharmaceuticals in the aquatic environment are just beginning to be investigated. Some pharmaceutical types such as lipid regulators or antidepressants could, for example, interfere with an aquatic organism's basic metabolism (*e.g.*, energy transfer) or put it at a competitive disadvantage (*e.g.*, behavioral effects). Boyd and Furlong (2002) noted that potential impacts of pharmaceuticals in the environment include abnormal physiological effects, impaired reproduction, increased cancer rates, and disruption of bacterial beds used to treat wastewater in many treatment plants. There is also concern that the continuous addition of antibiotics to the aquatic environment could result in

the emergence of antibiotic-resistant, disease causing strains of bacteria (Yang and Carlson, 2004).

Andreozzi *et al.* (2003) concluded that detection of pharmaceutical residues in the environment raises questions about the impacts they may be having, and highlighted the need for data on exposure in the aquatic environment. To assess exposure, information is needed on the occurrence and concentration of these chemicals. One strategy is to first look for pharmaceuticals in waters adjacent or downstream of likely points of discharge, such as WWTPs. These areas would likely have higher concentrations of human use pharmaceuticals, and perhaps detectable impacts in aquatic organisms.

Currently, the Environmental Protection Agency (EPA) and the U.S. Geological Survey (USGS) are investing significant resources to assess the contamination of freshwater systems with prescription and nonprescription pharmaceuticals (Daughton and Ternes, 1999; Kolpin, *et al.*, 2002). To understand the implications in the coastal aquatic environment, NOAA's National Status and Trends (NS&T) Program, of the Center for Coastal Monitoring and Assessment, conducted a pilot study to assess the presence of a suite of human use pharmaceuticals at selected sites in the Chesapeake Bay, Biscayne Bay, and the Gulf of the Farallones.

NOAA ship Ferrell used to collect water samples in the Chesapeake Bay.

The NS&T Program has monitored organic and inorganic contaminants and their effects in the Nation's estuaries and coastal waters for over 20 years (NOAA, 1998). As part of this effort, NS&T also investigates the occurrence of what have become known as "emerging contaminants of concern", previously unknown or unidentified classes of contaminants that may be impacting the environment. Pharmaceutical compounds fall within this category. The goal of this pilot project was to assess the presence of a number of commonly prescribed human use pharmaceuticals in three coastal areas of the U.S.

Materials and Methods

Water samples were collected in conjunction with three NOAA monitoring/research projects to assess sediment contamination, macrobenthic infaunal communities, and bioeffects in the Chesapeake Bay, Biscayne Bay, and the Gulf of the Farallones. The primary sampling area for the pharmaceuticals pilot project was the Chesapeake Bay. All samples were collected in 2002. A description of sample collection and handling protocols follows. Ancillary data collected at each site is shown in Table 1.

Chesapeake Bay. Water samples from the Chesapeake Bay and tributaries were collected in September 2002. Sampling sites were primarily located adjacent to WWTP outfalls. The rationale for using this approach was to create the best opportunity for detecting the pharmaceuticals of interest. If there were no detections at these sites, it would be unlikely they would be detected in the estuarine environment in general.

Water samples were collected from the NOAA ship *Ferrell,* or from its launch in shallow water. Water samples were collected using a PVC Niskin-type, 2 liter sampler rinsed with acetone and distilled water just prior to deployment. Composite (near surface and bottom) water samples were collected from 14 sites in the northern and southern portions of the Bay. Water samples from the Niskin sampler were emptied into certified clean 4 liter amber glass jugs, and the samples were kept on ice until they were extracted at the University of Maryland, within two weeks of sample collection.

Eight of the 14 sites sampled in the Chesapeake were adjacent to WWTPs, and included Back River,

Table 1. Ancillary water quality data collected at pharmaceutical sampling sites.

Sample date	Water sample type	Location	Station	Map ID	Latitude (DD)	Longitude (DD)	Depth (m)	Secchi depth (m)	Surface measurements Temperature (ºC)	Surface measurements Salinity (ppt)	Surface measurements Dissolved Oxygen	Surface measurements pH	Bottom measurements Temperature (ºC)	Bottom measurements Salinity (ppt)	Bottom measurements Dissolved Oxygen (mg/L)
Chesapeake Bay															
9/26/2002	composite	Back River	Back River WWTP outfall	BR	39.2936	-76.4786	3.4	0.5	24.0	2.9	7.8		23.0	5.5	4.2
9/26/2002	composite	Back River	Back WWTP, 1 km downstream	BR1	39.2885	-76.4635	1.7	0.5	22.1	5.7	11.6		22.1	5.9	10.7
9/26/2002	composite	Back River	Back WWTP, 5 km downstream	BR5	39.2629	-76.4444	2.3	0.5	22.1	8.8	10.5		22.4	8.7	1.1
9/26/2002	composite	Back River	Back WWTP, 10 km downstream	BR10	39.2423	-76.4035	3.7	1	22.0	10.7	9.5		22.1	10.8	7.7
9/25/2002	composite	Patapsco River	Patapsco River WWTP outfall	PR	39.2283	-76.5324	6.1	3.3	24.1	14.2	5.7		24.3	14.6	3.6
9/25/2002	composite	Patapsco River	Patapsco WWTP, 1 km downstream	PR1	39.2351	-76.5473	15.0		23.6	15.5			24.4	16.7	
9/25/2002	composite	Patapsco River	Patapsco WWTP, 5 km downstream	PR5	39.2087	-76.5194	17.0		23.7	15.2			24.2	16.6	
9/25/2002	composite	Patapsco River	Patapsco WWTP, 10 km downstream	PR10	39.1912	-76.4782	17.0		23.6	15.0			24.0	16.6	
9/25/2002	composite	Patapsco River	Cox Creek WWTP outfall	CC	39.1859	-76.5196	3.7		23.9	14.3	7.7		23.8	14.3	0.1
9/24/2002	composite	Annapolis	Annapolis WWTP outfall	AN	38.9635	-76.4599	18.0	3	24.2	16.0	10.8		24.7	16.7	7.4
9/27/2002	composite	Norfolk	Chesapeake-Elizabeth WWTP outfall	CEP	36.9399	-76.1752	9.2	2.5							
9/23/2002	composite	Hampton Roads	Nansemond WWTP outfall	NTP	36.9319	-76.3970	51.0	2.5	25.4	23.4	8.7		25.5	23.3	8.3
9/23/2002	composite	Norfolk	Virginia Initiative WWTP outfall	VIP	36.8800	-76.3300	52.0	2.1	25.7	22.0	7.9		25.7	22.2	7.6
9/28/2002	composite	Virginia Beach	Atlantic WWTP outfall	AST	36.7834	-75.9287	11.5	1.5		30.3					
Biscayne Bay															
3/6/2002	surface	Site #1	Princeton Canal mouth	PCM	25.5190	-80.3306	10.0		21.7	4.5	6.1	7.9			
3/6/2002	surface	Site #2	Military Canal	MIC	25.4897	-80.3386	10.0		19.4	16.7	8.1	7.9			
3/7/2002	surface	Site #3	Mowry Canal	MC	25.4696	-80.3399	10.0		21.8	1.5	7.8	8.1			
3/4/2002	surface	Site #4	North Canal mouth	NCM	25.4631	-80.3341	7.0		24.4	27.3		7.6			
3/7/2002	surface	Site #5	Florida City Canal, E of mouth	FC	25.4490	-80.3290	2.0		17.8	21.6	7.2	8.0			
3/5/2002	surface	Site #8	Channel leading to North Canal	NCC	25.4575	-80.3150	5.6		19.4	30.9	6.8	7.9			
3/5/2002	surface	Site #9	Turkey Point	TP	25.4356	-80.3051	5.5		19.4	32.5	7.0	7.9			
3/5/2002	surface	Site #12	South of Turkey Point	STP	25.4236	-80.2938	4.1		19.2	34.8	6.7	8.0			
3/5/2002	surface	Site #16	SE of Pelican Bank	PB	25.4180	-80.2706	6.0		19.4	36.4	6.5	7.9			
3/5/2002	surface	Site #20	South of Featherbed Bank	FB	25.4798	-80.2146	10.0		20.1	37.7	6.9	8.1			
3/6/2002	surface	Site #31	Black Point	BP	25.5345	-80.3246	8.2		20.5	7.5	5.6	8.3			
Gulf of the Farallones															
3/4/2002	composite	San Francisco Coast	North of WWTP outfall	SF1	37.7060	-122.5683	10.9		12.2	31.4	8.7		11.9	31.9	8.8
3/4/2002	composite	San Francisco Coast	South of WWTP outfall	SF2	37.6968	-122.5711	10.9		12.0	31.7	8.8		11.2	33.0	8.9

Abbreviations: WWTP, wastewater treatment plant; km, kilometers; DD, decimal degrees; m, meters; ºC, degrees Celsius; ppt, parts per thousand; mg/L, milligrams/liter

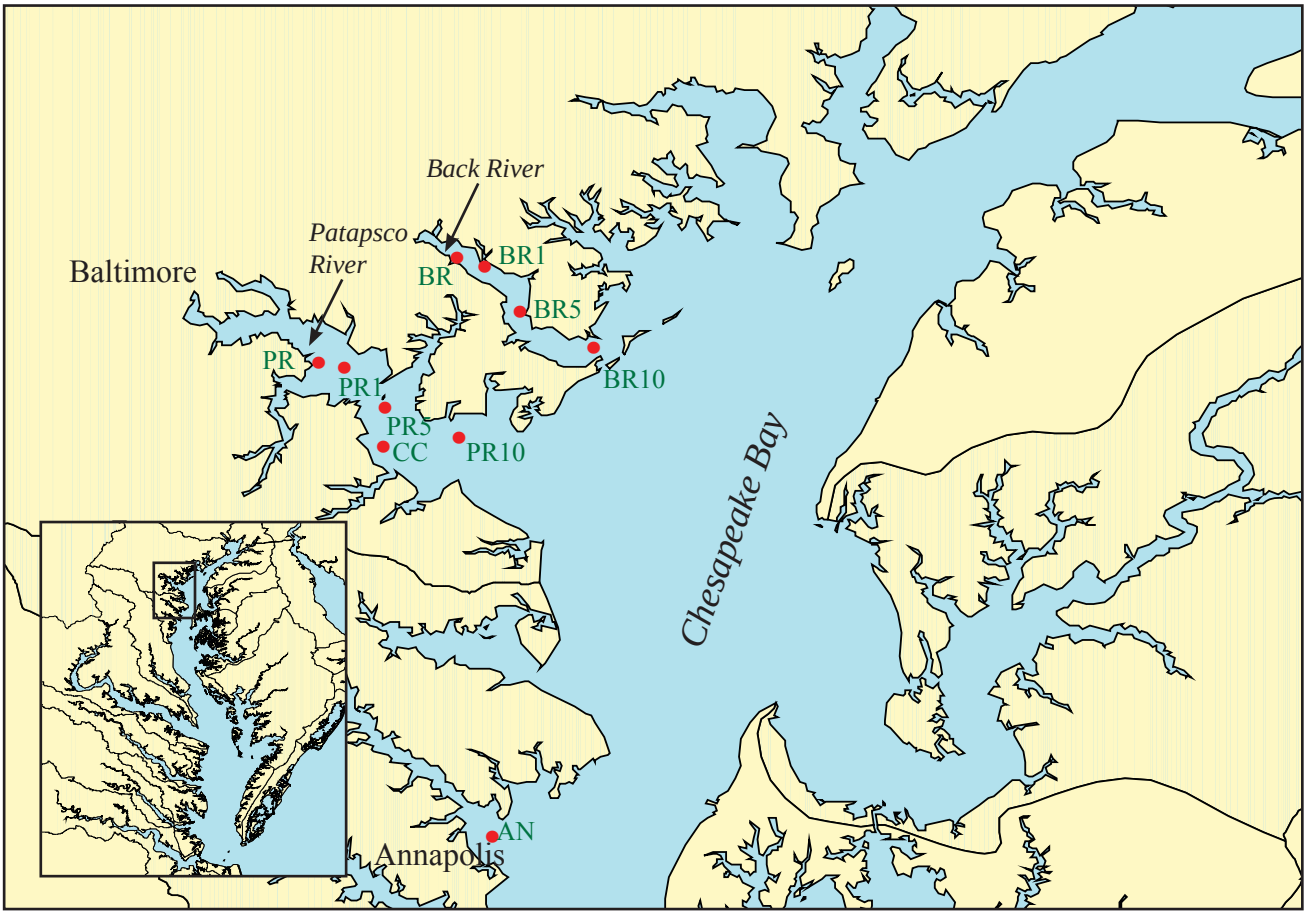


Figure 1. Sampling sites in the northern Chesapeake Bay (see Table 1 for site code descriptions).

Patapsco River, Cox Point and Annapolis in the northern part of the Bay (Figure 1), and near the Virginia Initiative, Atlantic, Chesapeake-Elizabeth, and Nansemond WWTPs in the southern portion (Figure 2). Water samples taken at these sites were collected as close as possible to the point of discharge.

For the Back River (BR) site, locating the exact discharge point for the WWTP was fairly straightforward, as the outfall is an above water concrete conduit. At the Patapsco River WWTP, even though the diffuser is on the bottom of the river at a depth of approximately 7 meters, the effluent plume was clearly visible on the surface of the water. However, for the remaining five facilities sampled in the Chesapeake Bay, the point of discharge had to be estimated from latitude and longitude coordinates for the pipe, obtained from EPA's online Permit and Compliance System (EPA, 2005) or from NOAA navigational charts.

In addition to sampling adjacent to the WWTP discharge points in the Back River and Patapsco River, water samples were also collected 1, 5, and 10 km (*e.g.*, BR1, BR5, BR10) downstream of these WWTP facilities (Figure 1). The goal was to assess how dilution and other physical or biological processes might affect downstream concentrations of the pharmaceuticals.

Biscayne Bay. The second area sampled for this pilot project was Biscayne Bay. Eleven sites in and around the western shore of the Bay were selected (Figure 3 and Table 1). Sampling sites were located at the mouth of drainage canals (*e.g.*, Mowry Canal) or in areas further offshore where groundwater discharges to Biscayne Bay may be present. Long *et al.* (1999) reported a number of sites in Biscayne Bay to be toxic to benthic infauna using one or more bioassays.

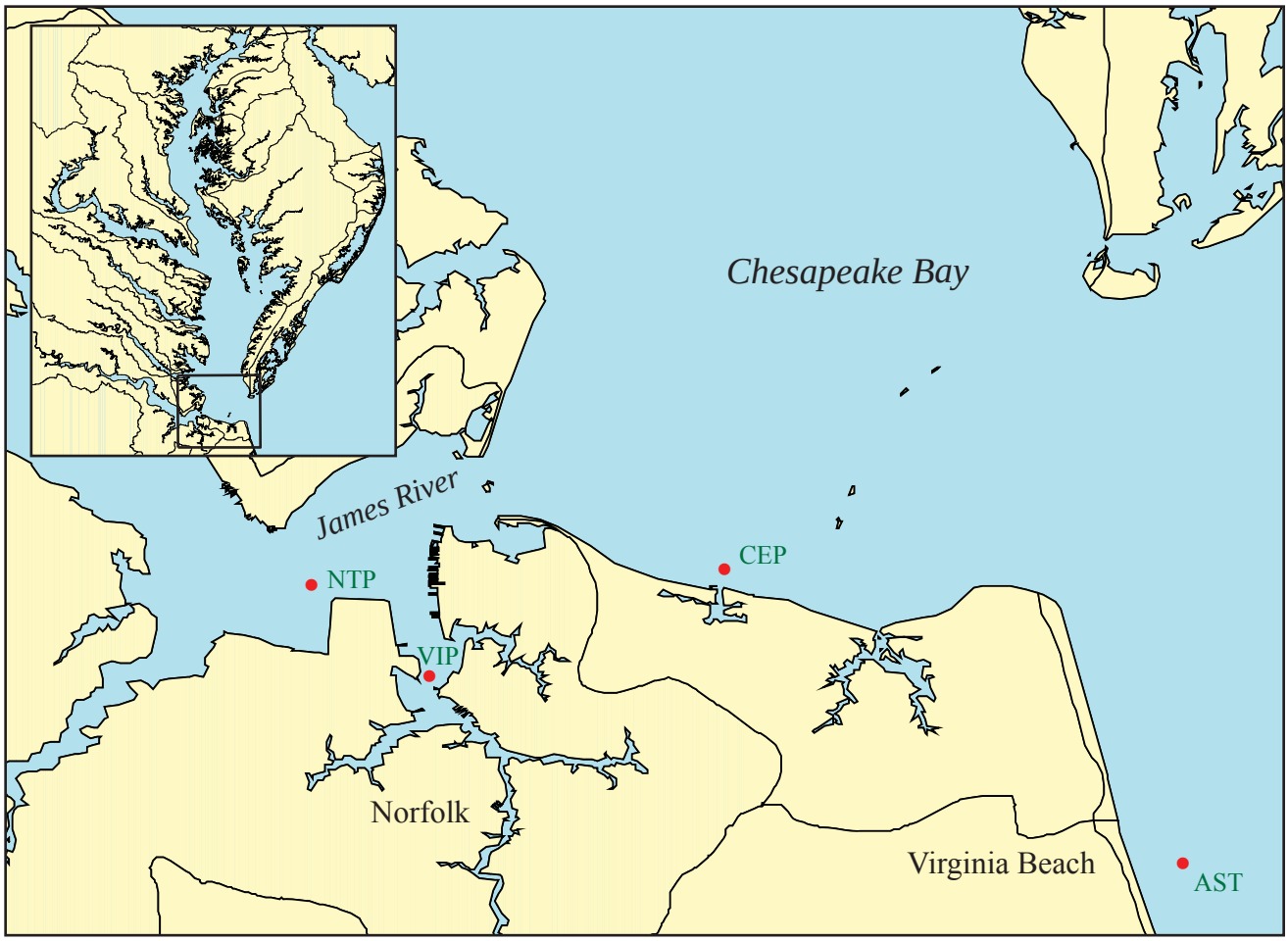


Figure 2. Sampling sites in the southern Chesapeake Bay (see Table 1 for site code descriptions).

All samples collected from Biscayne Bay were near-surface water samples. Water samples were collected by directly submerging a 4 liter certified clean amber jug beneath the surface of the water, capping the container, and then placing it on ice in a cooler.

As in the other locations for this study, the presence of human use pharmaceuticals could be used as an indicator of sewage-related inputs (WWTP or septic) and in Biscayne Bay, could conceivably be contributing to the observed sediment toxicity in the area (Long *et al.*, 1999).

Gulf of the Farallones. The final collection area for this pilot project was the Gulf of the Farallones in the Pacific Ocean, off the coast of San Francisco (Figure 4). As in the Chesapeake and Biscayne Bays, samples were taken in conjunction with a NOAA project to assess the presence of contaminants and toxicity to benthic infauna. Samples were collected aboard the NOAA ship *McArthur I*. The first sample site (SF1) was 0.6 km north of the location of the outfall for the Oceanside WWTP, as reported in EPA's online Permit and Compliance System (EPA, 2005) and as shown on the NOAA nautical chart. The diffuser pipe is located approximately 6 km offshore at a depth of 24 meters. The second location was 0.6 km south of this location. Composite (near surface and bottom) water samples were taken using a rosette-type Niskin sampler at both sites. The water samples were emptied into certified clean 4 liter amber glass jugs, and kept on ice until they were filtered and extracted at the University of Maryland.

Sample Processing. All samples received were kept at 4°C, prior to filtration and extraction. The proto-

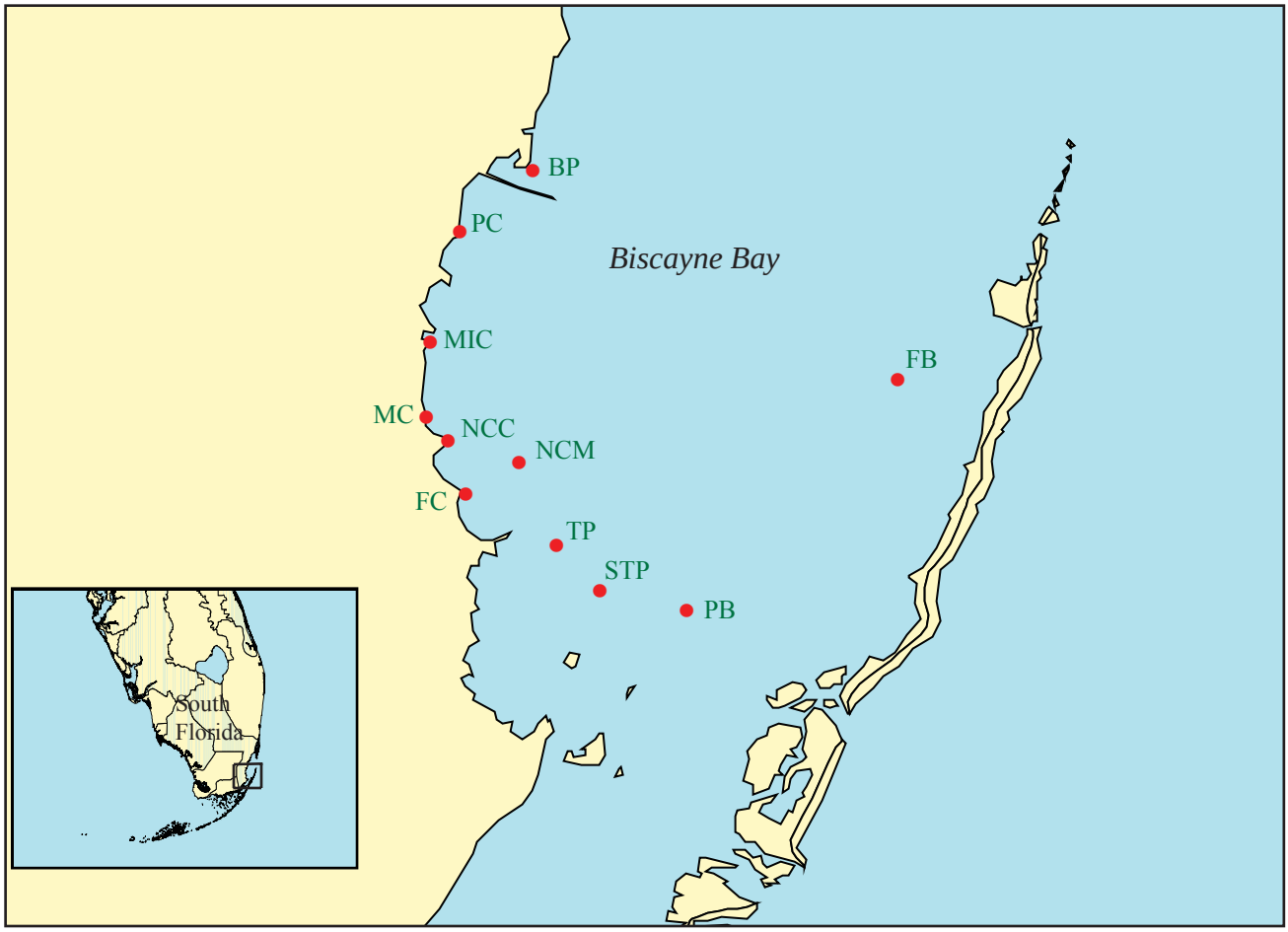


Figure 3. Sampling sites in Biscayne Bay (see Table 1 for site code descriptions).

cols used for the extraction were those of Cahill *et al*. (2004). A brief description follows.

Samples were first filtered through a 0.7 µm Whatman glass fiber filter to remove particulate material. Each filtered water sample received 1 µg/L of phenacetin-1-ethoxy ^{13}C as a surrogate analyte. One liter of the water sample was then passed through a conditioned Waters® Oasis HLB SPE cartridge at a rate of 15 ml/min. The cartridge was then eluted using 2 ml aliquots of methanol and acidified methanol.

The methanol extracts were stored for an extended period of time (approximately 6 months) at -20°C at the University of Maryland prior to shipment to the U.S. Geological Survey (USGS) for analysis. Samples sent to the USGS were shipped overnight on dry ice.

Sample Analysis. All sample analyses were carried out by the National Water Quality Laboratory of the USGS in Denver, Colorado. Below is a summary of the analytical protocols provided by USGS (Werner, pers. comm. and Cahill *et al*., 2004).

The sample methanol extracts were transferred to borosilicate glass test tubes, and 100 µl of reagent water was then added. The methanol was removed from the samples using a Zymark® TurboVap sample concentrator with a water bath set at 40°C and nitrogen flow at 5 PSI. Samples were reduced to approximately 100 µl final volume and reconstituted with 850 µl of formate buffer solution and 50 µl of an internal standard solution in methanol.

The samples were analyzed by High-Performance Liquid Chromatography/Mass Spectroscopy (HPLC/

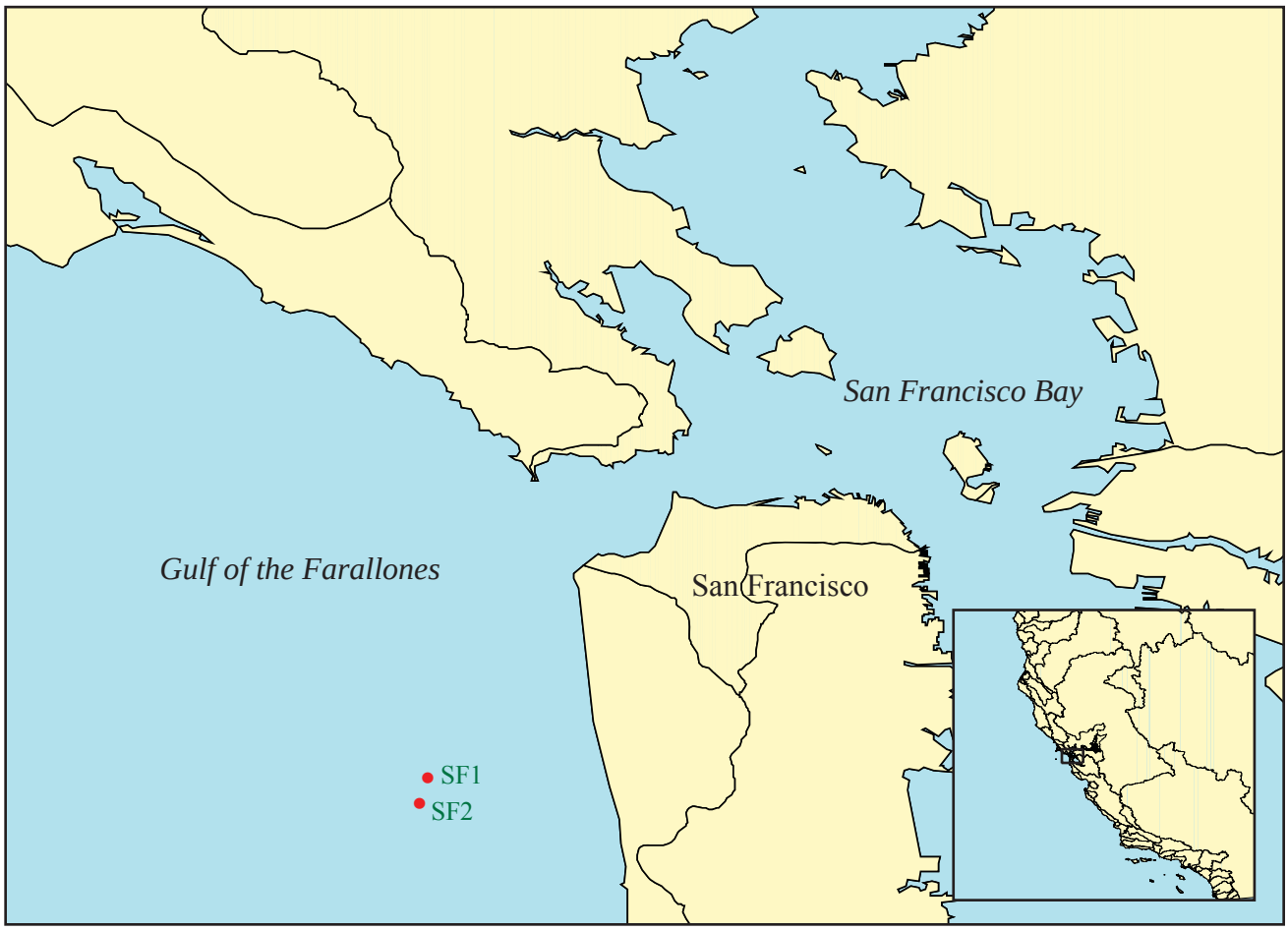


Figure 4. Sampling sites in the Gulf of the Farallones (see Table 1 for site code descriptions).

MS) using positive mode electrospray ionization (ESI) and selective ion monitoring to detect selected analytes.

HPLC separation of analytes was achieved using a reverse-phase analytical column with a C_{18} stationary phase. The chromatographic eluents used consisted of a 10 mM formate buffer in reagent water and acetonitrile. A multi-step gradient profile was used to achieve an optimized separation of analytes.

The HPLC column was coupled to a mass spectrometer using ESI for detection and quantitation of individual separated analytes. ESI is used for these polar organic compounds because it will efficiently produce a charged ion (a protonated molecular ion) with relatively little fragmentation. This results in high sensitivity. To improve selectivity, the ESI source is operated so that in-source, collisionally-induced molecular dissociation occurs, producing characteristic patterns of fragment ions used to specifically identify the compound of interest. Measured ratios of ion abundances of these fragments and of the molecular ions are used to either confirm an analyte detection or to discount matrix interferences.

Addition of the internal standard (D_4 nicotinamide) immediately prior to analysis was used to correct for variations in final extract volume when quantifying analyte results and calculating sample concentrations.

Compounds Analyzed. Selected properties of the 24 human use pharmaceuticals and related compounds included in this pilot project, along with their molecular structures are shown in Table 2. The pharmaceuti-

cals include a number of antibiotics, analgesics, lipid regulators and antidepressants. Selection of the compounds was based on a variety of factors including number of prescriptions, persistence and the possibility of having an environmental impact, probability of being able to develop sensitive analytical protocols for water samples, and the availability of analytical standards.

Twenty-one of the compounds in Table 2 (excluding caffeine, 1,7-dimethylxanthine, and cotinine) are dispensed through a doctor's prescription. A number of the compounds such as caffeine and cotinine have been used as traditional markers of human sewage. Table 2 also includes a number of metabolites. Dehydronifedipine is a metabolite of the antianginal medication nifedipine. A metabolite of the antidepressant paroxetine was also included. Similarly, the presence of 1,7-dimethylxanthine, a metabolite of caffeine was characterized as well.

Launch from the NOAA ship Ferrell used to collect water samples from shallow areas.

Of the human use pharmaceuticals listed in Table 2, eight (asterisked) were among the top 100 prescribed medications, accounting for nearly 180 million prescriptions in the U.S. annually (RxList, 2005).

Four antibiotics, including azithromycin, erythromycin-H_2O (erythromycin degradate), sulfamethoxazole, and trimethoprim were included. Erythromycin and azithromycin belong to a class of antibiotics known as macrolides, used to treat a wide variety of infections. In the U.S. in 2004, an estimated 2.5 million prescriptions were written for erythromycin, which is produced by *Streptomyces erythraeus,* a strain of filamentous bacteria.

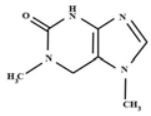
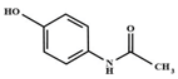
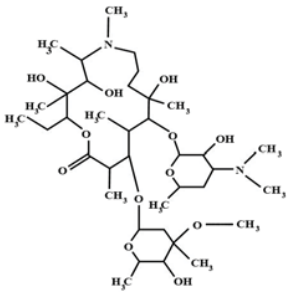
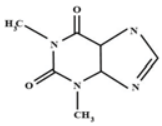
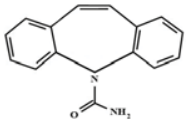
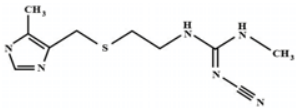
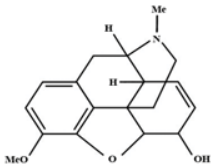
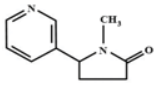
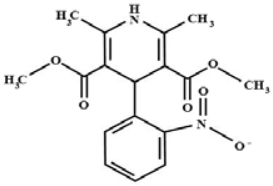
In this document, detections of erythromycin-H_2O are reported rather than concentrations. Because of the low recovery levels of erythromycin-H_2O from water samples (typically around 10%), and the possibility of interferences (similar ion fragments) from other sources (Furlong, pers. comm.), quantification of erythromycin-H_2O was not possible.

Sulfamethoxazole belongs to another large group of antibiotics known as sulfonamides or sulfa medicines. Trimethoprim is a synthetic antibacterial. Sulfamethoxazole and trimethoprim, often used in combination are especially effective in treating infections in urinary and digestive tracts, along with sinus and bronchial infections. There is concern regarding the possible overuse of antibiotics leading to increased antibiotic resistant, possibly pathogenic strains of bacteria, in humans and in the environment.

Fluoxetine and paroxetine are two widely used antidepressants, both belonging to a class of compounds known as selective serotonin reuptake inhibitors. An estimated 35 million prescriptions were written for these two pharmaceuticals in 2004 (RxList, 2005). Low levels of serotonin have been linked to depression, and both fluoxetine and paroxetine work to elevate levels of this neurotransmitter. In addition, fluoxetine (Prozac®) also has a strong energizing effect, helping in the treatment of clinical depression cases involving a lack of energy. Anxiety disorders can also lead to low levels of serotonin, needed to metabolize stress hormones, and fluoxetine can be beneficial by making more serotonin available.

Paroxetine is also a widely prescribed selective serotonin reuptake inhibitor. Recently, however, there has been concern regarding the use of these and other antidepressants, related to possible increases in suicidal behavior.

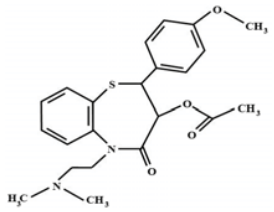
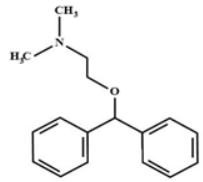
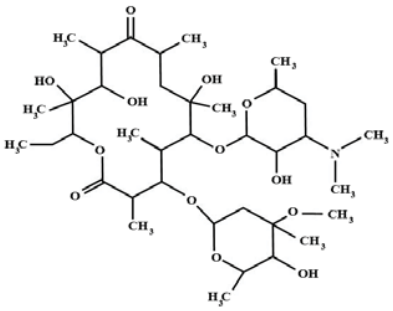
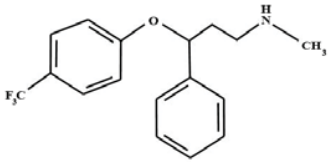
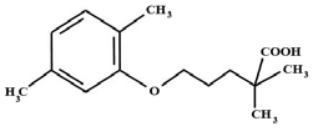
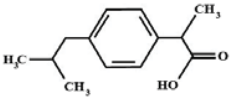
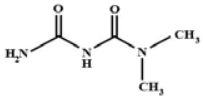
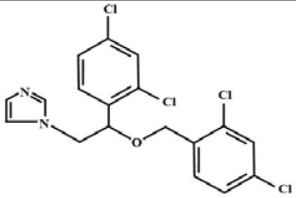
Table 2. Selected properties of the pharmaceuticals analyzed.

Compound	Structure	Use	Brand/Common Name	MW	CAS
1,7-dimethylxanthine		Caffeine metabolite	Paraxanthine	180.16	611-59-6
*Acetaminophen		Analgesic and antipyretic	Tylenol®	151.17	103-90-2
*Azithromycin		Antibiotic	Zithromax®	748.88	83905-01-5
Caffeine		Stimulant	Caffeine	194.19	58-08-2
Carbamazepine		Antiepileptic, antidepressant	Tegretol®	236.27	298-46-4
Cimetidine		Antacid	Pepcid®	252.34	51481-61-9
Codeine		Analgesic	Codeine	299.36	76-57-3
Cotinine		Nicotine metabolite	Cotinine	176.22	486-56-6
Dehydronifedipine	 Nifedipine (parent of dehydronifedipine)	Antianginal	Procardia® metabolite	344.32	67035-22-7

Abbreviations: CAS, Chemical Abstract Service; MW, molecular weight; ®, Registered trademark

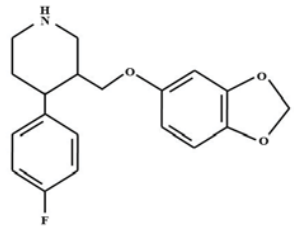
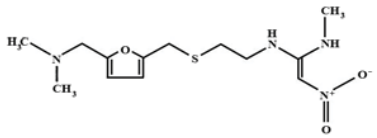
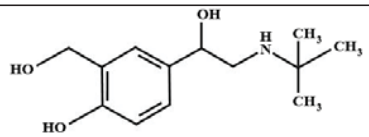
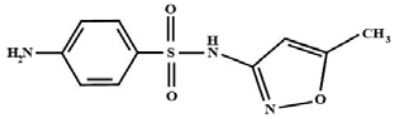
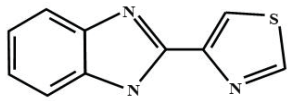
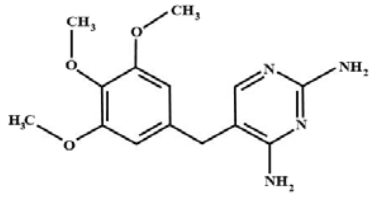
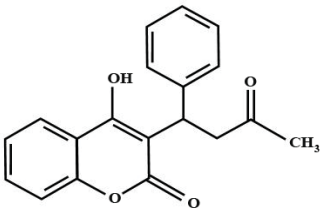
*Top 100 prescribed pharmaceutical according to RxList (2005)

Table 2. Selected properties of the pharmaceuticals analyzed (continued).

Compound	Structure	Use	Brand/Common Name	MW	CAS
*Diltiazem		Antianginal	Cardizem®	450.98	33286-22-5
Diphenhydramine		Antihistamine	Benadryl®	291.82	147-24-0
Erythromycin-H_2O		Antibiotic	E-mycin®	733.93	114-07-8
*Fluoxetine		Antidepressant	Prozac®	345.8	54910-89-3
Gemfibrozil		Lipid regulator	Lopid®	250.35	25812-30-0
*Ibuprofen		Analgesic and antipyretic	Motrin®	351.83	15687-27-1
*Metformin		Antidiabetic	Glucophage®	129.17	657-24-9
Miconazole		Antifungal	Micatin®	416.12	22916-47-8

Abbreviations: CAS, Chemical Abstract Service; MW, molecular weight; ®, Registered trademark
*Top 100 prescribed pharmaceutical according to RxList (2005)

Table 2. Selected properties of the pharmaceuticals analyzed (continued).

Compound	Structure	Use	Brand/Common Name	MW	CAS
*Paroxetine metabolite	 Paroxetine (parent compound)	Antidepressant	Paxil® metabolite	-	-
Ranitidine		Antacid	Zantac®	350.87	66357-35-5
Salbutamol		Antiasthmatic	Proventil®	239.3	51022-70-9
Sulfamethoxazole		Antibiotic	Bactrim®	253.28	723-46-6
Thiabendazole		Anthelmintic	Mintezol®	201.26	148-79-8
Trimethoprim		Antibiotic	Proloprim®	290.3	738-70-5
*Warfarin		Anticoagulant	Coumadin®	308.33	129-06-6

Abbreviations: CAS, Chemical Abstract Service; MW, molecular weight; ®, Registered trademark
*Top 100 prescribed pharmaceutical according to RxList (2005)

Two antianginal medications, diltiazem and a metabolite of nifedipine, were included in the pilot project. Approximately 12 million prescriptions were written for diltiazem and nifedipine in 2004 (RxList, 2005). Both drugs are known as calcium channel blockers and are used in the treatment of hypertension, or angina (chest pain due to a lack of oxygen to the heart muscle). Calcium channel blockers act to slow down the force of the contraction of the heart, lowering blood pressure.

In 2004, approximately 6 million prescriptions were written for the lipid regulator gemfibrozil (RxList, 2005), used to lower triglycerides (fats) and cho-

lesterol in the blood. Gemfibrozil acts to increase the activity of the peroxisome proliferator-activated receptor-alpha, involved in the metabolism of fats and carbohydrates. Use of this pharmaceutical is thought to decrease the amount of fat produced by the liver.

The antidiabetic drug metformin (over 25 million prescriptions in 2004) is used to treat type 2 (noninsulin-dependant) diabetes. Insulin is a polypeptide hormone that helps regulate the metabolism of carbohydrates. The mechanism of action of metformin is unclear, but it may reduce the rate of hepatic gluconeogenesis and also improve the peripheral uptake and utilization of glucose in the body. Cimetidine belongs to a group of antacid medications known as H_2-receptor antagonists, which block the action of histamine on the parietal cells of the stomach, decreasing the amount of acid produced by these cells.

Carbamazepine is used in the treatment of epilepsy and sometimes for bipolar disorders. The mechanism of carbamazepine is not well understood, but appears to act primarily through inhibition of sodium channels, important in the process of muscle contraction and nerve impulse conduction. As will be seen, this compound appears to be fairly persistent in the aquatic environment.

Finally, three analgesics, acetaminophen, ibuprofen and codeine were included. Analgesics or pain killers, are a diverse group of drugs. The term analgesic comes from the Greek term for "without pain". Ibuprofen is a commonly prescribed pain medication (25 million prescriptions in the U.S.), and is also available as an over the counter medication in lower strengths. Ibuprofen is known as a COX-2 inhibitor. This class of pharmaceuticals selectively blocks the action of the COX-2 enzyme involved in the production of prostaglandins, which have a role in pain and fever responses in the body. Acetaminophen (16 million U.S. prescriptions in 2004 and also available in over the counter preparations) is believed to reduce pain by reducing the production of prostaglandins.

Codeine, the methylated form of morphine, is available in the U.S. by prescription. In the body, only about 10% of codeine is converted into morphine, producing a less potent effect than morphine itself. Codeine, like morphine, works directly on the central nervous system to relieve pain, and in particular at the synapses of the arcuate nucleus, located in the hypothalamus.

Results and Discussion

The results of the pharmaceutical analyses are shown in Table 3 (Chesapeake Bay) and Table 4 (Biscayne Bay and Gulf of the Farallones). Most often, chemicals were below quantifiable detection; those that were detected were in the low ng/L range. In the Chesapeake Bay, 13 of the 24 compounds (54%) analyzed were found at least once. In Biscayne Bay, only three compounds were detected; in the Gulf of the Farallones two were found. In their reconnaissance of wastewater contaminants in 139 streams in the U.S., the USGS detected 84% of these same pharmaceuticals (Kolpin *et al.*, 2002). In Germany, Ternes (1998) detected over 80% of a variety of pharmaceuticals in WWTP effluents, and roughly 60% in surface waters.

Chesapeake Bay. The primary study area for this pilot project was the Chesapeake Bay, which is also where most of the detections of the pharmaceuticals occurred. The four WWTPs in the northern part of the estuary (Figure 1) had a greater average number of detected compounds (6.5) per WWTP site compared to the southern Bay (1.7). One explanation for this is that the effluent plumes from the WWTPs near Baltimore were typically more visible and therefore samples were known to be taken in proximity of the discharge. In the southern part of the Chesapeake, there was no indication of the effluent plume, and the location of the outfalls had to be estimated using latitude and longitude coordinates. At the Annapolis sampling site in the northern part of the Bay, the effluent plume was also not visible, and may have been one reason only two compounds were detected, similar to the number of detections at the WWTPs in the southern portion of the Bay.

From Table 3, a number of patterns emerge. The most frequently detected pharmaceutical was carbamazepine, found at all sites in the northern Bay, and at one site in the southern Bay. The maximum concentration of carbamazepine was 0.030 µg/L (Table 3) at the outfall of the Back River WWTP.

Table 3. Pharmaceuticals detected at the Chesapeake Bay sites.

Compound	Concentration (µg/L)													
	Back River	Back River 1km	Back River 5km	Back River 10km	Patapsco River	Patapsco River (1km)	Patapsco River (5km)	Patapsco River (10km)	Cox Creek	Annapolis	Chesapeake-Elizabeth	Nansemond	Virginia Initiative	Atlantic Sewage
1,7-dimethylxanthine	<LRL	<LRL	<LRL	<LRL	0.21	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Acetaminophen	<LRL	<LRL	<LRL	<LRL	0.0022	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Azithromycin	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Caffeine	<LRL	<LRL	<LRL	<LRL	0.24	0.0091	0.0045	<LRL	0.016	<LRL	0.0050	<LRL	<LRL	<LRL
Carbamazepine	0.030	0.023	0.012	0.0056	0.010	0.0021	0.0021	0.0021	0.0067	0.0013	<LRL	0.0011	<LRL	<LRL
Cimetidine	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Codeine	<LRL	<LRL	<LRL	<LRL	0.0089	<LRL	<LRL	<LRL	0.0014	<LRL	<LRL	<LRL	<LRL	<LRL
Cotinine	0.0097	0.013	0.0087	0.0052	0.020	0.0039	0.0037	0.0037	0.0052	0.0024	0.0026	0.0025	0.0014	√
Dehydronifedipine	0.0027	0.0018	√	√	<LRL	<LRL	<LRL	<LRL	√	<LRL	<LRL	<LRL	<LRL	<LRL
Diltiazem	<LRL	<LRL	<LRL	<LRL	0.0032	<LRL	<LRL	<LRL	0.0018	<LRL	<LRL	<LRL	<LRL	<LRL
Diphenhydramine	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Erythromycin-H_2O	√	√	√	√	√	<LRL	<LRL	√	√	<LRL	<LRL	<LRL	<LRL	<LRL
Fluoxetine	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	0.0026	<LRL
Gemfibrozil	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Ibuprofen	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Metformin	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Miconazole	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Paroxetine metabolite	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Ranitidine	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Salbutamol	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Sulfamethoxazole	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	0.011	<LRL	<LRL	<LRL	<LRL	<LRL
Thiabendazole	<LRL	<LRL	<LRL	<LRL	0.0038	<LRL	<LRL	<LRL	√	<LRL	<LRL	<LRL	<LRL	<LRL
Trimethoprim	<LRL	<LRL	<LRL	<LRL	√	<LRL	<LRL	<LRL	0.0014	<LRL	<LRL	<LRL	<LRL	<LRL
Warfarin	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL

Note: Table entries with the symbol √ refer to samples where the compound was detected, but due to either low recoveries (i.e., erythromycin-H_2O) or lower analyte concentration, could not be quantified.
Abbreviations: km, kilometers downstream of wastewater treatment plant outfall; µg/L, micrograms/liter; <LRL, below laboratory reporting level.

Table 4. Pharmaceuticals detected at the Biscayne Bay and Gulf of the Farallones sites.

	Concentration (µg/L)												
	Biscayne Bay											Gulf of the Farallones	
Compound	Princeton Canal	Military Canal	Mowry Canal	North Canal Mouth	Florida City Canal	Channel to North Canal	Turkey Point	South of Turkey Point	SE of Pelican Bank	South of Featherbed Bank	Black Point	114A	SW-00
1,7-dimethylxanthine	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Acetaminophen	<LRL	<LRL	0.0033	<LRL	0.0019	<LRL	<LRL	<LRL	<LRL	<LRL	0.0029	<LRL	<LRL
Azithromycin	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Caffeine	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Carbamazepine	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Cimetidine	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Codeine	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Cotinine	<LRL	<LRL	<LRL	<LRL	<LRL	√	√	<LRL	<LRL	√	<LRL	√	<LRL
Dehydronifedipine	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	√	<LRL
Diltiazem	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Diphenhydramine	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Erythromycin-H_2O	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Fluoxetine	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Gemfibrozil	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Ibuprofen	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Metformin	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Miconazole	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Paroxetine metabolite	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Ranitidine	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Salbutamol	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Sulfamethoxazole	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Thiabendazole	<LRL	<LRL	√	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Trimethoprim	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL
Warfarin	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL	<LRL

Note: Table entries with the symbol √ refer to samples where the compound was detected, but due to lower analyte concentration, could not be quantified.
Abbreviations: km, kilometers downstream of wastewater treatment plant outfall; µg/L, micrograms/liter; <LRL, below laboratory reporting level.

A number of other studies have also detected this pharmaceutical in surface waters. Boyd and Furlong (2002) found carbamazepine to be one of the most frequently detected pharmaceuticals in the Las Vegas Wash, an urban river which drains the city of Las Vegas and empties into Lake Mead. Ternes (1998) concluded this compound was ubiquitously present in rivers and streams in Germany. In 2004, approximately 2.7 million prescriptions were written for carbamazepine in the U.S. (RxList, 2005). Yet, there are many other compounds such as azithromycin (37 million) and metformin (25 million) that were not detected, but have a far greater number of prescriptions written.

Studies have shown carbamazepine to be fairly persistent in the environment. Heberer (2002) found that less than 10% of carbamazepine is typically degraded during the sewage treatment process. Lam *et al.* (2004) calculated a mean half-life for carbamazepine in outdoor field microcosms of 82 days, over four times higher than any of the other compounds (acetaminophen, atorvastatin, caffeine, levofloxacin, sertraline, sulfamethoxazole, and trimethoprim) in that study. Andreozzi *et al.* (2003) calculated a half-life approaching 100 days for exposures in northern latitudes.

Collection of water samples aboard the NOAA ship Ferrell.

There has not been much work to date to assess the toxicity of carbamazepine to aquatic organisms. The information generated to date appears to indicate that acute toxicity to a number of species of bacteria, green algae, diatoms, rotifers and a few crustaceans is on the order of mg/L, at least an order of magnitude higher than typical environmental concentrations (Ferrari *et al.*, 2004). A chronic toxicity study, however, indicated a 7-day no effect concentration on reproduction in the crustacean *Ceriodaphnia dubia* as low as 25 µg/L (Ferrari *et al.*, 2004). Carbamazepine has a reported bioconcentration factor of approximately 15 (Jones *et al.*, 2002) in daphnia, indicating it is not strongly accumulated from water column exposures in this organism.

The antibiotic degradate erythromycin-H_2O was detected at 50% of the sites sampled in the Chesapeake Bay, including all those in the northern portion. In their assessment of pharmaceuticals and other organic contaminants in U.S. streams, Kolpin *et al.* (2002) found erythromycin-H_2O in over 21% of the water samples taken, the second highest of any antibiotic included in their inventory. Boyd and Furlong (2002) also found erythromycin in samples from the Las Vegas Wash, but not Lake Mead. Ashton *et al.* (2004) found erythromycin in 44% of final WWTP effluent samples, and 38% of downstream samples in the U.K. Erythromycin was below the limit of detection in samples in five U.K. estuaries (Thomas and Hilton, 2004).

There does not appear to be much data generated yet on the aquatic toxicity of erythromycin. Jones *et al.* (2002) modeled a predicted environmental concentration (PEC of 0.81 µg/L), compared that with a predicted no effects concentration (PNEC) for fish and invertebrates, and calculated a PEC: PNEC ratio of 0.01. Ratios greater than one indicate the predicted environmental concentration would be above the no-effects concentration, and using this approach, would be cause for greater concern. Brain *et al.* (2004), found no significant phytotoxicity in the duckweed *Lemna gibba* (EC50 > 1,000 µg/L). However, Jones *et al.* (2002) calculated a bioconcentration factor for erythromycin of approximately 45, and suggested this pharmaceutical could accumulate, at least to some degree in aquatic biota.

In the Chesapeake Bay, dehydronifedipine, a metabolite of the antianginal medication nifedipine, was found in five water samples, mainly from the Back River sites, at a maximum concentration of 0.003 µg/L. In their study of U.S. streams, Kolpin *et al.* (2002) found dehydronifedipine in approximately 14% of the samples. Boyd and Furlong (2002) also found dehydronifedipine in water samples from the Las Vegas Wash, but not from Lake Mead. No information was located on the aquatic toxicity of nifedipine or dehydronifedipine.

The antibiotic trimethoprim was found twice (Patapsco River and Cox Creek) in the Chesapeake Bay samples, at a maximum concentration of 0.001 µg/L. Ashton *et al.* (2004) detected trimethoprim in 65% of WWTP effluent water samples, and 38% of downstream samples in five rivers in the U.K. In Germany, Hirsch *et al.* (1999) detected trimethoprim in approximately 90% of the WWTP effluents and 20% of samples from streams and rivers. Kolpin *et al.* (2002) detected trimethoprim in 27% of samples from streams in the U.S., the highest of any antibiotic included in their study. In microcosm experiments, Lam *et al.* (2004) calculated an average half-life of 5.7 days. Brain *et al.* (2004) reported no significant phytotoxicity in *L. gibba*.

Sulfamethoxazole was detected at one sampling location, Cox Creek, at a concentration of 0.011 µg/L. Kolpin *et al.* (2002) detected this antibiotic in 19% of stream samples. Boyd and Furlong (2002) detected sulfamethoxazole in both the Las Vegas Wash and in Lake Mead. In Germany, Hirsch *et al.* (1999) found this compound in all 10 WWTP effluents sampled, and in 50% of downstream samples. Ashton *et al.* (2004) detected sulfamethoxazole in 9% of WWTP effluents, but it was undetectable downstream in the U.K. Thomas and Hilton (2004) did not detect this compound in U.K. estuaries.

In their microcosm studies, Lam *et al.* (2004) found that sulfamethoxazole was one of the more persistent compounds tested, with a half-life of 19 days. In addition, Brain *et al.* (2004) found that sulfamethoxazole was the most phytotoxic antibiotic tested, significantly reducing the weight of *L. gibba* (EC50 of 81 µg/L).

The antianginal medication diltiazem was found twice in the Chesapeake Bay, with a maximum concentration of 0.003 µg/L. Kolpin *et al.* (2002) detected this pharmaceutical in approximately 14% of their water samples. Jones *et al.* (2002) calculated a PEC:PNEC of 0.34.

Fluoxetine was detected once in the southern portion of the Chesapeake Bay at a concentration of 0.003 µg/L. Kolpin *et al.* (2002) detected fluoxetine in 1% of their samples. In Louisiana, Boyd *et al.* (2003) did not detect fluoxetine in any surface water samples. Brooks *et al.* (2003) investigated the acute and sublethal toxicity of fluoxetine on a number of fish and invertebrates, with the results indicating that effects concentrations were an order of magnitude higher than the highest reported municipal effluent concentration.

The analgesic acetaminophen was detected at the Patapsco River site at a concentration of 0.002 µg/L. Ibuprofen was not detected at any of the sites in the Chesapeake Bay, although it was detected in approximately 10% of the streams sampled by Kolpin *et al.* (2002).

The pharmaceuticals detected in the Chesapeake Bay water samples (excluding caffeine and the caffeine metabolite 1,7-dimethylxanthine) are plotted by site in Figure 5. Carbamazepine was the most frequently detected pharmaceutical followed by the erythromycin degradate, erythromycin-H_2O. Cotinine, the metabolite of the stimulant nicotine (commonly associated with tobacco), was detected in all water samples.

Figure 5 also provides some evidence of a downstream (1, 5, and 10 km) gradient or transport. Carbamazepine, erythromycin-H_2O and dehydronifdipine were detectable in water samples 10 km downstream of the Back River. In the Patapsco River, a downstream gradient was not apparent. Interestingly, there was a detection of erythromycin-H_2O at the 10 km Patapsco River, but not at the 1 or 5 km sites (Figure 5). The reason for this is unknown, but could be related to discharges from the Cox Creek WWTP, which had a detection of erythromycin-H_2O, and is adjacent and somewhat upstream of the Patapsco River 10 km site (Figure 1).

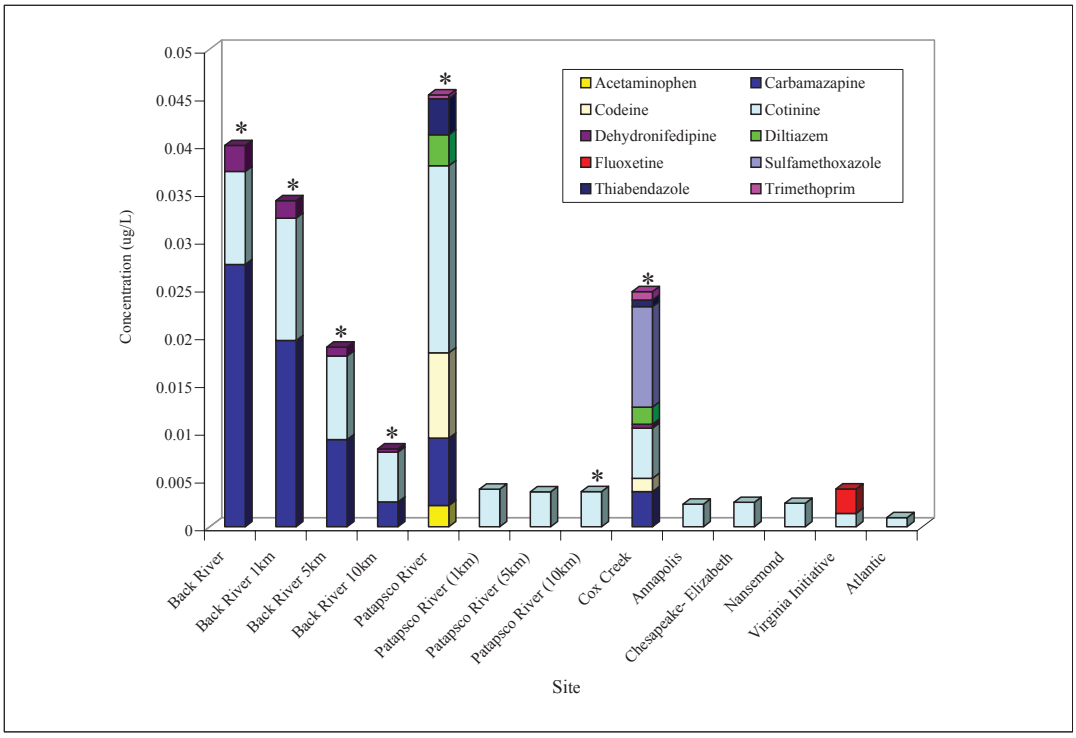


Figure 5. Concentration of compounds detected (excluding caffeine) in Chesapeake Bay water samples. *Erythromcyin-H_2O detected in these samples but not quantified.

Biscayne Bay. Three compounds were detected at the sites in Biscayne Bay: cotinine, acetaminophen, and the anthelmintic thiabendazole. The maximum acetaminophen concentration (0.003 µg/L) in Biscayne Bay (Table 4) was similar to that found at the Patapsco River site (Table 3).

Fewer detections of pharmaceuticals at the Biscayne Bay sites compared with Chesapeake Bay is perhaps not surprising, as the sites in Biscayne Bay were not adjacent to WWTPs, but located near drainage canals which receive inputs from a variety of sources. There was speculation that sediment toxicity observed in an earlier study in Biscayne Bay (Cantillo and Lauenstein, 2004) could have been related to the presence of pharmaceuticals entering the Bay from wastewater or groundwater discharges. The results from this pilot project, however, would appear to make this less likely.

Gulf of the Farallones. There were only two compounds detected in the samples collected in the Gulf of the Farallones, cotinine (the metabolite of nicotine), and dehydronifedipine, a metabolite of the anti-anginal medication nifedipine. The low detections in the Gulf of the Farallones site were likely due in part, to the difficulty in identifying the effluent plume from the Oceanside WWTP, along with strong currents in the area. The diffuser heads are located 7 km offshore at a depth of 24 m.

Comparison with Other Work. Table 5 contains published values for the detection of a number of the pharmaceuticals included in this study. In general, the concentrations found in the pilot project are somewhat lower than that reported elsewhere. The reason for this may be related to the amount of time that elapsed between the extraction of the water samples and the actual analysis, roughly 6 months. Although the extracts were kept at -20°C, it is likely that some

Table 5. Reported detections of selected human use pharmaceuticals in the aquatic environment.

Compound	Conditions	Concentration (ug/l)	Frequency (%)	Reference
Carbamazepine	WWTP effluent	BDL	0	Weigel et al. (2004)
Carbamazepine	WWTP effluent	BDL	0	Weigel et al. (2004)
Carbamazepine	WWTP effluent	0.3 - 1.03	NA	Andreozzi et al. (2003)
Carbamazepine	surface waters	0.008-0.263	57-83	Kolpin et al. (2004)
Carbamazepine	surface waters	0.14	NA	Boyd and Furlong (2002)
Dehydronifedipine	surface waters	0.0003-0.002	10	Kolpin et al. (2004)
Dehydronifedipine	surface waters	0.03	14	Kolpin et al. (2002)
Diltiazem	surface waters	0.002-0.106	20	Kolpin et al. (2004)
Diltiazem	surface waters	0.049	13	Kolpin et al. (2002)
Fluoxetine	surface waters	BDL	0	Kolpin et al. (2004)
Fluoxetine	surface waters	BDL	0	Boyd et al. (2003)
Fluoxetine	surface waters	0.012	1	Kolpin et al. (2002)
Sulfamethoxazole	WWTP effluent	BDL - 0.09	NA	Andreozzi et al. (2003)
Sulfamethoxazole	WWTP effluent	0.18	NA	Yang and Carlson (2004)
Sulfamethoxazole	surface waters	BDL-0.063	7	Kolpin et al. (2004)
Sulfamethoxazole	surface waters	0.07 (max.)	NA	Kolpin et al. (2004)
Sulfamethoxazole	surface waters	0.52	19	Kolpin et al. (2002)
Trimethoprim	WWTP effluent	0.66 (max.)	NA	Hirsch et al. (1999)
Trimethoprim	surface waters	BDL-0.035	NA	Kolpin et al. (2004)
Trimethoprim	surface waters	BDL - 0.569	NA	Thomas and Hilton (2004)
Trimethoprim	surface waters	0.042 (max.)	38	Ashton et al. (2004)
Trimethoprim	surface waters	0.30	NA	Kolpin et al. (2002)

Abbreviations: WWTP, wastewater treatment plant; BDL, below detection level; NA, not available; max., maximum concentration detected; %, frequency of detection for the pharmaceutical

degradation of the pharmaceuticals present in the extracts had taken place. As a result, the concentrations reported for the Chesapeake Bay, Biscayne Bay, and the two sites in the Gulf of the Farallones, can be viewed as conservative estimates of the concentrations originally present in the water samples.

Summary and Conclusions

The goal of this pilot project was to assess the presence of 24 human use pharmaceuticals and associated chemicals in selected estuarine and coastal waters. In the Chesapeake Bay, samples were collected adjacent to and downstream of wastewater treatment plants (WWTPs). In Biscayne Bay, samples were collected at the mouth of drainage canals and offshore areas that might be affected by inputs from the drainage canals or possibly groundwater discharges. In the Gulf of the Farallones, two sites were sampled near the reported location of a WWTP outfall discharging to the Pacific Ocean.

Analysis of the Chesapeake water samples revealed the presence of 13 of the 24 compounds. In Biscayne Bay, three compounds were detected; in the Gulf of the Farallones, two were found. In the Chesapeake Bay on the Back River there was evidence of a downstream gradient; two pharmaceuticals (carbamazepine and erythromycin-H_2O (erythromycin degradate)) were detected 1, 5, and 10 km downstream of the WWTP.

The antiepileptic medication carbamazepine was detected in 11 of the 14 sites in the Chesapeake Bay. The published literature has documented the pres-

ence and persistence of carbamazepine in the aquatic environment. Erythromycin-H_2O was detected, but not quantified at seven sites. Fewer detections of pharmaceuticals in Biscayne Bay was not surprising as none of the sites sampled were adjacent to WWTP outfalls.

The effects of the pharmaceuticals in estuarine and coastal waters is currently unknown. An important first step is to document which compounds are present and in what concentrations, so that the appropriate studies (laboratory and field) can be designed to assess possible impacts.

Future work, particularly in the Chesapeake Bay is recommended to assess pharmaceuticals in both the water column and sediments. In the Chesapeake Bay, the western shore has a higher human population, while the eastern shore is home to significant poultry CAFO (concentrated animal feeding operations) activity. A study to assess the differences in the types (human versus animal use) and concentrations of pharmaceuticals present, and a concurrent assessment of antibiotic resistant populations of bacteria in both the western and eastern shores of the Chesapeake Bay would provide information needed to begin assessing the impacts (both human and environmental) of pharmaceuticals in estuarine and coastal environments.

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