Pharmaceutical Residues in the Auckland Estuarine Environment

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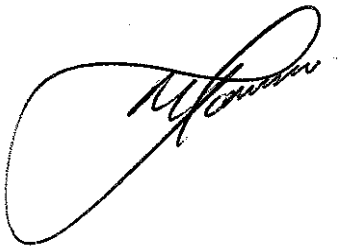

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Pharmaceutical Residues in the Auckland Estuarine Environment

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Executive summary

A knowledge gap exists around environmental concentrations of pharmaceuticals within New Zealand. Pharmaceuticals are designed to be potently bioactive against certain human and animal biological processes. However, they also have the potential to be persistent and bioaccumulative and display adverse toxicity on other (non-target) organisms (Ahrens 2008). With continuous inputs into the environment and only partial removal by wastewater treatment plants, some pharmaceuticals will likely end up in the marine receiving environment and there is a need to obtain some measure of these environmental concentrations and effects.

This report describes a preliminary study of the quantitation of a range of pharmaceuticals in estuarine sediments from the Auckland region, by advanced mass spectrometry techniques. Archived estuarine samples from an earlier study (Stewart*, et al.* 2009) were analysed at the Institute of Environmental Assessment and Water Research, Barcelona, Spain facilitated by an International Science and Technology (ISAT) linkages fund.

The analytical method enabled the quantitation of 46 pharmaceuticals in two separate analyses. Generally the method performed well, with limits of quantitation (LOQ) ranging from 0.1 - 11.3 ngg^{-1} (median 0.6 ng g^{-1}) and limits of detection (LOD) ranging from 0.02 - 3.4 ng g^{-1} (median 0.2 ng g^{-1}). Although these 46 compounds are a European Union (EU) pharmaceutical suite, they are considered relevant to New Zealand as 33 (72%) are listed in the New Zealand Pharmaceutical Management Agency (Pharmac) 2007 schedule (Pharmac 2007).

Of the 46 pharmaceuticals analysed in estuarine sediments, 21 were quantified at one or more sites. The maximum concentration at any one site was 10.79 ng g^{-1} (acetaminophen; Halfmoon Bay Marina). Average sediment concentrations across all sites ranged from 7.66 ng g^{-1} (acetaminophen) down to 0.16 ng g^{-1} (Bezafibrate). Of the 21 pharmaceuticals quantified, 18 were in the Pharmac 2007 schedule.

Approximately half (25) of the pharmaceuticals analysed in Auckland sediments were below the limits of quantitation (LOQ). Eleven of these were detected at one or more sites, and 14 were not detected at any site. Fifteen of the 25 pharmaceuticals not quantified were listed in the Pharmac 2007 schedule.

This study is the first of its kind in New Zealand; however, the multi-residue approach used had some limitations. Such a large suite of analytes (46) makes a “one size fits all” analytical approach unfeasible because the method was not optimal for all pharmaceuticals.

Furthermore, pharmaceuticals have a wide range of physico-chemical properties and many do not partition strongly to sediment. As such, it was not possible to correlate sediment concentrations with potential inputs into the environment as water phase data were not available.

Recommendations for the future follow a tiered approach:

1. Carry out pharmaceutical concentration studies into inputs - both liquid and solid phase - in the major WWTPs around Auckland:
    a. Initially use a multi-residue analysis - such as in this current study - to give broad coverage of pharmaceutical classes. These data will most likely have to be provided by international collaboration. Note: limitations in the methodology described in this report are minimised as WWTP input concentrations will be considerably higher than environmental concentrations (Stewart, unpublished data).
    b. Analyses should be “time averaged” to avoid potential short-term variations in concentrations.
2. Development of domestic capability in the analysis of pharmaceuticals:
    a. With capability within the country, future studies can concentrate on pharmaceuticals relevant to New Zealand.
    b. This list should be created using a consultative procedure based on information from point 1 and further considerations such as toxicological profiles and breakdown products (described in section 4.4).
3. Carry out future analytical and toxicological studies with a ‘New Zealand relevant’ suite of pharmaceuticals - on solid and liquid phases - including:
    a. WWTP inputs and outputs;
    b. The marine receiving environment;
    c. Effects on New Zealand relevant biota.
4. Benchmark results to international studies, including:
    a. WWTP influent and effluent concentrations;
    b. Environmental water and sediment concentrations;
    c. Toxicological effects on biota.

These recommendations provide a broad framework for addressing current knowledge gaps around pharmaceuticals in the Auckland marine receiving environment.

1 Introduction

A recent study of emerging chemicals of concern (ECCs) - including surfactants, flame retardants, plasticisers, estrogens, antifouling agents and pesticides - in Auckland marine receiving environments revealed that in certain locations the sediment concentrations of many of these, as yet unregulated, chemicals were comparable to those reported internationally (Stewart*, et al.* 2009). Sites were selected to broadly cover the region and include a range of land uses/potential inputs; sewage, marina, landfill, urban/industrial, agricultural/horticultural.

One class of contaminant that was not included in the study were pharmaceuticals and personal care products (PPCPs). These comprise a very large number of chemicals with varying therapeutic uses, for example, analgesic, antibiotic, lipid regulation, beta blockers and antacids. Pharmaceuticals are designed to be potently bioactive against certain human and animal biological processes, however they also have the potential to be persistent and bioaccumulative and display adverse toxicity on other (non-target) organisms (Ahrens 2008). Of concern is that there is a continuous input of pharmaceuticals into the environment due to their constant (and increasing) use and only partial removal by wastewater treatment plants (WWTPs) (e.g., Ternes *et al.*(2004)).

Research in New Zealand into pharmaceuticals in wastewaters and the aquatic environment is sparse. A 2006 study of estrogens in sewage treatment plant (STP) and animal waste effluents around the Waikato was not aimed at pharmaceuticals, however included the human oral contraceptive pill active ingredient 17α-ethynylestradiol. This was detected at only one STP at trace levels (Sarmah*, et al.* 2006b). A PhD project at the University of Canterbury assessed 12 commonly used pharmaceuticals from various therapeutic classes in sewage effluent, biosolids and porewater and assessed removal efficiencies of three different treatment options (Gielen 2007). This study included both analytical measurements and toxicological assessments. A survey into disposal practices of pharmaceuticals in New Zealand has been undertaken (Braund*, et al.* 2009) and suggests that "*a significant percentage of unwanted medications are disposed of via routes that have the potential to adversely affect the environment*".

Within New Zealand, no research has been undertaken into the fate of pharmaceuticals entering the marine receiving environment. This is partly due to the lack of capability and experience in analysing pharmaceuticals in this country. To address this knowledge gap, - and facilitated by an International Science and Technology (ISAT) linkages fund - sediment samples were analysed at the research group of Professor Mira Petrović, at the Institute of Environmental Assessment and Water Research, in Barcelona, Spain. Professor Petrović's group are very active in developing methods for quantifying emerging contaminants (including PPCPs) in environmental matrices. This collaboration allowed for the analysis of a large set of pharmaceuticals in archived sediment samples collected from around the Auckland region.

This report describes the methodology and results of this initial investigation of pharmaceuticals in Auckland aquatic receiving environment sediments and makes recommendations for future follow-up work on this important subset of emerging contaminants.

2 Methods

2.1 Laboratory chemicals

All laboratory chemicals used and their sources are as described in Jelić *et al.*(2009). In brief, all standards were of high purity grade (>90%) and all solvents used were of high performance liquid chromatography (HPLC) grade, or better.

Isotopically labelled compounds - used as internal standards - are described in Table 2.

2.2 Sediment collection and processing

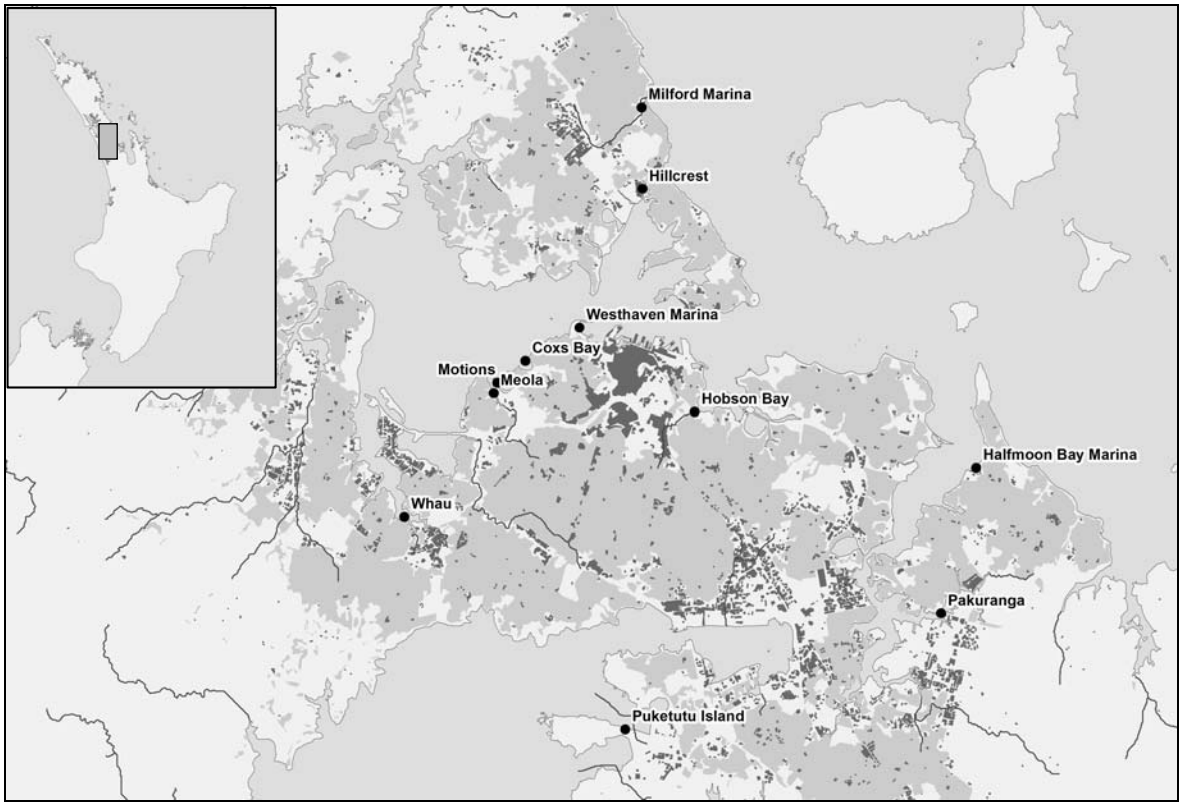
Sediments were sampled in March 2008 at 13 estuarine locations around Auckland, including sites in both the Waitemata and Manukau Harbours. The 11 central Auckland sites are illustrated in Figure 1. Full details of site selection and sediment collection are provided in Stewart, *et al.*(2009). However, briefly, sediments were collected as follows: with the exception of the marinas, each site was marked with a quadrat of 50 x 50 cm and two replicate samples taken randomly within that quadrat. Only the top 3 cm of the sediment (surface sediment) was collected and transferred immediately into clean solvent rinsed glass jars and chilled, on ice.

Three different protocols of sampling were used. Where sediment could hold its form without collapsing, cleaned and rinsed polypropylene housings were used to take sediment samples. The top 3 cm was extruded through the corer. For sites that had either sediment that was sloppy and would not hold its form, or a high density of mangroves, a corer was not feasible. In this situation, a plastic scoop was used to scrape off the top 3 cm. For sampling subtidal sediments inside marinas, a Jenkins corer was used to collect sediment. By using this method, it was possible to sample the top 3 cm of sediment without disturbing the sediment. In all cases, the total wet weight of sediment sampled for each replicate was ca. 2 kg.

Sediments were stored at 4º C until processing. Each replicate sample was transferred to a large foil tray and combined to form a homogenised mixture. Large debris (stones, shellfish, plant material) were removed. Once a homogenised sample was obtained, sediments were freeze-dried using a sample shelf temperature of -10ºC. Dried sediments were couriered to the laboratories of Professor Petrović, in Barcelona for extraction and analysis.

Figure 1

Sample Sites for the 11 central Auckland sites[a,b].



[a] Mahurangi (Warkworth) and Taihiki River (near Pukekohe) are outside this map area and are not shown.
[b]Inset is North Island of New Zealand with study area shown by a box.

2.3 Extraction and clean-up

All freeze-dried sediment samples (1 g; Table 1) were extracted by accelerated solvent extraction using a Dionex ASE 200, with the following conditions: H_2O:MeOH (2:1), pressure 1500 psi, temperature 100 °C, heat time 5 min, static time 5 min, 3 cycles. Extracts were all made up to a volume of 500 mL with H_2O.

Oasis HLB solid phase extraction (SPE) cartridges (Waters, 500 mg, 6 mL) were conditioned with MeOH (5 mL) and H_2O (5 mL). Extracts were eluted through the SPE with a flow of 10 $mLmin^{-1}$. The SPE was then washed with H_2O (5 mL) and dried under vacuum for 15-20 min. Each SPE cartridge was eluted with MeOH (2x4 mL) and the extract dried under N_2 gas.

Sediment extracts were re-dissolved in H_2O:MeOH (3:1, 490 μL) and internal standard mix (1 ppm, 10 μL) added.

Table 1.

Code	Sample type	Site
OA133/1	Sediment	Coxs - Replicate1
OA133/2	Sediment	Coxs - Replicate2
OA133/3	Sediment	Meola - Replicate1
OA133/4	Sediment	Meola - Replicate2
OA133/5	Sediment	Motions - Replicate1
OA133/6	Sediment	Motions - Replicate2
OA133/7	Sediment	Milford Marina - Replicate1
OA133/8	Sediment	Milford Marina - Replicate2
OA133/9	Sediment	Westhaven Marina - Replicate1
OA133/10	Sediment	Westhaven Marina - Replicate2
OA133/11	Sediment	Hobson Bay - Replicate1
OA133/12	Sediment	Hobson Bay - Replicate2
OA133/13	Sediment	Shoal Bay Hillcrest - Replicate1
OA133/14	Sediment	Shoal Bay Hillcrest - Replicate2
OA133/15	Sediment	Halfmoon Bay Marina - Replicate1
OA133/16	Sediment	Halfmoon Bay Marina - Replicate2
OA133/17	Sediment	Pakuranga - Replicate1
OA133/18	Sediment	Pakuranga - Replicate2
OA133/19	Sediment	Whau - Replicate1
OA133/20	Sediment	Whau - Replicate2
OA133/21	Sediment	Taihiki River - Replicate1
OA133/22	Sediment	Taihiki River - Replicate2
OA133/23	Sediment	Mahurangi - Replicate1
OA133/24	Sediment	Mahurangi - Replicate2
OA133/25	Sediment	Puketutu Island - Replicate1
OA133/26	Sediment	Puketutu Island - Replicate2
OA133/5SR	Spiked sediment	Motions - Replicate1

2.3.1 Spike recoveries

Three replicate representative samples of sediment (OA133/5, Motions replicate 1; Table 1) were spiked with a pharmaceutical standard mix (1 ppm; 50 µL), thoroughly

mixed and left overnight at -20 °C. Spiked samples were extracted and cleaned-up as described in Section 2.3.

2.4 LC/MS/MS analysis

Methodology for Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS)analysis was based on that of Jelić *et al.*(2009), and modified where necessary to reflect changes since publication, including new analytes of interest, different LC columns and updated selected reaction monitoring (SRM) transitions (Table 2).

High Pressure Liquid Chromatography (HPLC) analysis was performed using a Symbiosis^{TM} Pico HPLC equipped with an autosampler and connected in series to an AB Sciex 4000 QTRAP hybrid quadrupole-linear ion trap mass spectrometer, equipped with a Turbo Ion Spray source.

The suite of 46 pharmaceuticals analysed in sediments was chosen from those that are known to survive wastewater treatment plant processing and so have a greater chance of being found in the receiving environment (Petrović pers. comm.). It is difficult to gauge the numbers of pharmaceuticals used worldwide. It has been estimated that in the EU 3000 different substances are used in human medicine and many more in veterinary medicine (Fent*, et al.* 2006). In New Zealand around 1800 medicines are subsidised through the Pharmaceutical Schedule(Pharmac 2011). As such, it is important to emphasise that the suite of pharmaceuticals analysed in this study is only a very small proportion of those used. However, the 46 pharmaceuticals have been chosen to reflect different therapeutic classes and for which authentic standards are available (Jelic*, et al.* 2009).

Pharmaceuticals were analysed in this study in two separate analyses; one analysis with positive mode ionisation and one analysis with negative mode ionisation. Due to varying physico-chemical properties of each pharmaceutical, it is necessary to run both polarities of analysis. Positive mode ionisation afforded the pseudo-molecular ion $[M+H]^+$ for all pharmaceuticals analysed, while negative mode ionisation afforded the pseudo-molecular ion $[M-H]^-$ for all pharmaceuticals analysed. Separation was achieved on a Hypersil GOLD PFP (50x2.1 mm, 3 μm) HPLC column from Thermo Scientific. Positive mode: flow 0.3 $mLmin^{-1}$, Solvent A: H_2O 0.1% HCOOH (pH 2.5), Solvent B: MeCN, 0 min (95%A-5%B), 0-10 min (50%A-50%B), 10-11 min (100%B), 11-13 min (100%B), 13-14 min (95%A-5%B), 14-17 min (95%A-5%B), TOTAL RUN: 17min. Negative mode: flow 0.4 $mLmin^{-1}$ Solvent A: H_2O 10mM ammonium formate, Solvent B: MeCN/MeOH (1:1, v/v), 0 min (85%A-15%B), 0-9 min (20%A-80%B), 9-10 min (10%A-90%B), 10-10.3 min (85%A-15%B), 10.3-12 min (85%A-15%B) TOTAL RUN: 12 min. Twenty nine (29) pharmaceuticals were analysed under positive mode ionisation, while 17 were analysed under negative mode ionization (Table 2).

Data acquisition was performed in selective reaction monitoring (SRM) mode. For most compounds, two SRM transitions between the precursor ion and two of the most abundant fragment ions were monitored (Table 2). The use of two SRM transitions

allows a broad accomplishment of the requirements set by the EU regulations related to identification and confirmation of pharmaceuticals in LC/MS/MS analysis (EC 2002).

Quantitation, based on peak areas, was performed by internal standard calibration. The internal standard used for each analyte is presented in Table 2. The internal standard was usually a deuterated and/or ^{13}C analogue of the analyte of interest, however when this was not available, a suitable secondary internal standard was used. This was either of the same compound class or, if not available, one that eluted close to the analyte of interest.

Table 2.

Pharmaceuticals analysed by LC/MS/MS with internal standard used for quantitation and MS/MS method parameters.

Compound	Internal standard	precursor ion (*m/z*)	pseudo-molecular ion	SRM1	SRM2	SRM ratio (SRM1/SRM2)
Analgesics and NSAIDS						
Acetaminophen	Acetominophen-d_4	149.8	$[M-H]^-$	107.1	-	-
Ketoprofen	Ketoprofen-^{13}C-d_3	253.0	$[M-H]^-$	209.0	197.0	57.1
Naproxen	Naproxen-d_3	229.0	$[M-H]^-$	169.0	185.0	0.8
Ibuprofen	Ibuprofen-d_3	205.0	$[M-H]^-$	161.0	-	-
Diclofenac	Diclofenac-d_4	294.0	$[M-H]^-$	250.0	214.0	20.9
Indomethacin	Indomethacin-d_4	356.0	$[M-H]^-$	312.0	297.0	4.5
Mefenamic acid	Mefenamic acid-d_3	240.0	$[M-H]^-$	196.0	180.0	17.0
Phenazone	Albuterol-d_3	189.0	$[M+H]^+$	56.0	147.0	2.1
Lipid Regulators and Statins						
Atorvastatin	Atorvastatin-d_5	559.0	$[M+H]^+$	440.0	250.0	0.9
Mevastatin	Atorvastatin-d_5	391.0	$[M+H]^+$	185.0	159.0	0.8
Pravastatin	Furosemide-d_5	422.9	$[M-H]^-$	321.0	303.0	1.7
Clofibric acid	Clofibric acid-d_4	213.0	$[M-H]^-$	127.0	85.0	3.6
Fenofibrate	Atorvastatin-d_5	361.0	$[M+H]^+$	139.0	-	-
Bezafibrate	Bezafibrate-d_4	360.0	$[M-H]^-$	274.0	154.0	4.1
Gemfibrozil	Gemfibrozil-d_6	248.9	$[M-H]^-$	120.9	127.0	16.0
Psychiatric Drugs						
Carbamazepine	Carbamazepine-d_{10}	237.0	$[M+H]^+$	194.0	-	-
Lorazepam	Diazepam-d_5	323.0	$[M+H]^+$	277.0	229.0	2.2
Diazepam	Diazepam-d_5	285.0	$[M+H]^+$	193.0	154.0	1.5
Antacids						
Famotidine	Famotidine-$^{13}C_3$	338.0	$[M+H]^+$	189.0	259.0	1.3
Ranitidine	Ranitidine-d_6	315.0	$[M+H]^+$	176.0	130.0	2.0
Cimetidine	Cimetidine-d_3	253.0	$[M+H]^+$	159.0	95.0	1.0

Compound	Internal standard	precursor ion (*m/z*)	pseudo-molecular ion	SRM1	SRM2	SRM ratio (SRM1/SRM2)
Macrolide antibiotics						
Josamycin	Clarithromycin-*N*-Me-d_3	828.0	$[M+H]^+$	174.0	600.0	11.6
Erythromycin	Erythromycin-^{13}C-d_3	734.0	$[M+H]^+$	158.0	576.0	5.7
Clarithromycin	Clarithromycin-*N*-Me-d_3	748.0	$[M+H]^+$	158.0	591.0	68.5
Roxythromycin	Clarithromycin-*N*-Me-d_3	838.0	[M+H]+	158.0	679.0	11.8
Tylosin	Erythromycin-^{13}C-d_3	916.0	[M+H]+	174.0	773.0	110.4
Other antibiotics						
Metronidazole	Hydroxy-metronidazole-d_2	172.0	[M+H]+	128.0	82.0	1.8
Trimethoprim	Hydroxy-metronidazole-d_2	291.0	[M+H]+	230.0	261.0	1.7
Sulfamethazine	Sulfamethazine-d_4	279.0	[M+H]+	186.0	124.0	0.7
Chloramphenicol	Furosemide-d_5	323.0	[M-H]-	152.0	194.0	5.4
Nifuroxazide	Enrofloxacin-d_5	276.0	[M+H]+	121.0	65.0	1.3
Beta blockers						
Atenolol	Atenolol-d_7	267.0	[M+H]+	145.0	190.0	2.6
Sotalol	Sotalol-d_6	273.0	[M+H]+	213.0	255.0	1.0
Nadolol	Atenolol-d_7	310.0	[M+H]+	254.0	201.0	1.1
Pindolol	Atenolol-d_7	249.0	[M+H]+	116.0	98.0	6.7
Timolol	*rac*-Timolol-d_5	317.0	[M+H]+	261.0	244.0	1.0
Metoprolol	Metoprolol-d_7	268.0	[M+H]+	133.0	121.0	1.1
Beta agonists						
Salbutamol	Albuterol-d_3	240.0	[M+H]+	148.0	166.0	3.0
Clenbuterol	Clenbuterol-d_9	277.0	[M+H]+	203.0	132.0	3.2
Barbiturates						
Phenobarbital	Phenobarbital-d_5	231.0	[M-H]-	188.0	-	-
Butalbital	Phenobarbital-d_5	223.0	[M-H]-	180.0	85.0	5.6
Pentobarbital	Phenobarbital-d_5	225.0	[M-H]-	182.0	85.0	9.3
Antihypertensives						
Enalapril	Diazepam-d_5	377.0	[M+H]+	234.0	203.0	9.9
Diuretics						
Hydrochlorothiazide	Hydrochlorothiazide-d_2	295.8	[M-H]-	268.8	204.8	1.0
Furosemide	Furosemide-d_5	329.0	[M-H]-	284.6	205.0	1.0

Compound	Internal standard	precursor ion (*m/z*)	pseudo-molecular ion	SRM1	SRM2	SRM ratio (SRM1/SRM2)
Antidiabetics						
Glibenclamide	Glibenclamide-d_3	494.0	[M+H]+	369.0	169.0	2.1

3 Results

3.1 Method performance data

Method performance data for the 46 pharmaceuticals is presented in Table 3and includes the limit of quantitation (LOQ), limit of detection (LOD), % recovery of spiked standards from a sediment sample and relative standard deviation (% RSD, n=3) of the spike recovery data. The LOQ and LOD are determined as the minimum detectable amount of analyte with a signal-to-noise of 10 and 3, respectively. The LOQ ranged from 0.1 - 11.3 ngg^{-1}, with an average of 1.9 $ngg^{-1}$and median of 0.6 ngg^{-1}. The LOD ranged from 0.02 - 3.4 ngg^{-1} with an average of 0.6 ngg^{-1}, and a median of 0.2 ngg^{-1}. Percentage recovery of spiked standards ranged between 11 and 222%, with an average of 68% and median of 65%. The % RSD ranged from 1 - 98% with an average of 13% and median of 9% (Table 3).

Generally, the method performed well. Median LOQ and LOD values were markedly lower than average values, suggesting less influence of high value outliers in the data in a relatively small dataset.

Median recoveries of 65% (average 68%) are generally considered acceptable for environmental matrices, bearing in mind that the varying physico-chemical properties of the pharmaceuticals being analysed prevent a universal optimised method. A median %RSD of 9% between three replicate spikes suggests low analytical variability.

However, some pharmaceutical classes had poor recoveries or variability between replicate spikes. Macrolide antibiotics (n=5) were especially problematic with percent recoveries of between 16 and 48% and %RSD of between 14 and 98%, suggesting the method was poorly optimised for this class. Macrolide antibiotics are generally moderately lipophilic with $LogK_{ow}$ values in the range of 2.8-3.3 (Le-Minh*, et al.* 2010). As such the extraction solvent (33% methanol in water) was potentially too polar to maximise extraction of these compounds. The barbiturates (n=3) had good recoveries (74 - 113%) but high analytical variability with %RSD of 15 - 21%.

All results are recovery corrected, so a very low recovery can lead to a greater chance of inaccuracies in the reported concentration. This is a limitation of analysing a large suite of vastly different compounds using one methodology.

Table 3.

Method performance parameters for the analysis of pharmaceuticals in Auckland

Compound	LOQ (ngg^{-1})	LOD (ngg^{-1})	Spike Recovery, %	RSD, % (n=3)
Analgesics and NSAIDS				
Acetaminophen	6.1	1.8	20	9
Ketoprofen	5.2	1.6	81	9
Naproxen	4.8	1.4	101	5
Ibuprofen	4.2	1.3	69	8
Diclofenac	1.2	0.4	116	4
Indomethacin	1.3	0.4	69	9
Mefenamic Acid	0.7	0.2	222	6
Phenazone	0.2	0.1	74	6
Lipid Regulators and Statins				
Atorvastatin	1.1	0.3	11	22
Mevastatin	11.3	3.4	89	13
Pravastatin	2.9	0.9	60	3
Clofibric Acid	0.6	0.2	51	14
Fenofibrate	1.3	0.4	97	7
Bezafibrate	0.1	0.04	72	4
Gemfibrozil	0.6	0.2	91	4
Psychiatric Drugs				
Carbamazepine	0.2	0.1	62	6
Lorazepam	2.6	0.8	84	2
Diazepam	0.6	0.2	84	6
Antacids				
Famotidine	0.4	0.1	45	17
Ranitidine	0.3	0.1	11	13
Cimetidine	0.3	0.1	34	18
Macrolide Antibiotics				
Josamycin	2.1	0.6	48	21
Erythromycin	4	1.2	16	98
Tylosin	4.8	1.4	43	23
Clarithromycin	0.5	0.1	16	16
Roxythromycin	0.5	0.1	28	14

Compound	LOQ (ngg^{-1})	LOD (ngg^{-1})	Spike Recovery, %	RSD, % (n=3)
Other Antibiotics				
Metronidazole	0.4	0.1	20	13
Trimethoprim	0.1	0.02	45	16
Sulfamethazine	0.3	0.1	61	13
Chloramphenicol	0.5	0.1	127	9
Nifuroxazide	2.4	0.7	103	33
Beta Blockers				
Atenolol	0.5	0.2	62	9
Sotalol	0.6	0.2	58	1
Nadolol	0.2	0.05	75	8
Pindolol	0.1	0.02	45	22
Timolol	0.4	0.1	72	10
Metoprolol	0.8	0.2	55	8
Beta Agonists				
Salbutamol	0.1	0.04	57	7
Clenbuterol	0.2	0.1	62	3
Barbiturates				
Phenobarbital	5.6	1.7	74	21
Butalbital	3.7	1.1	93	17
Pentobarbital	10.1	3	113	15
Antihypertensives				
Enalapril	0.4	0.1	84	7
Diuretics				
Hydrochlorothiazide	0.1	0.04	54	11
Furosemide	1.2	0.4	73	25
Antidiabetics				
Glibenclamide	0.2	0.1	78	6
Minimum	0.1	0.02	11	1
Maximum	11.3	3.4	222	98
Average	1.9	0.6	68	13
Median	0.6	0.2	65	9

LOQ = limit of quantitation; LOD = limit of detection; RSD = relative standard deviation; spike recovery is based on an average of three spiked replicates

3.2 Sediment concentrations

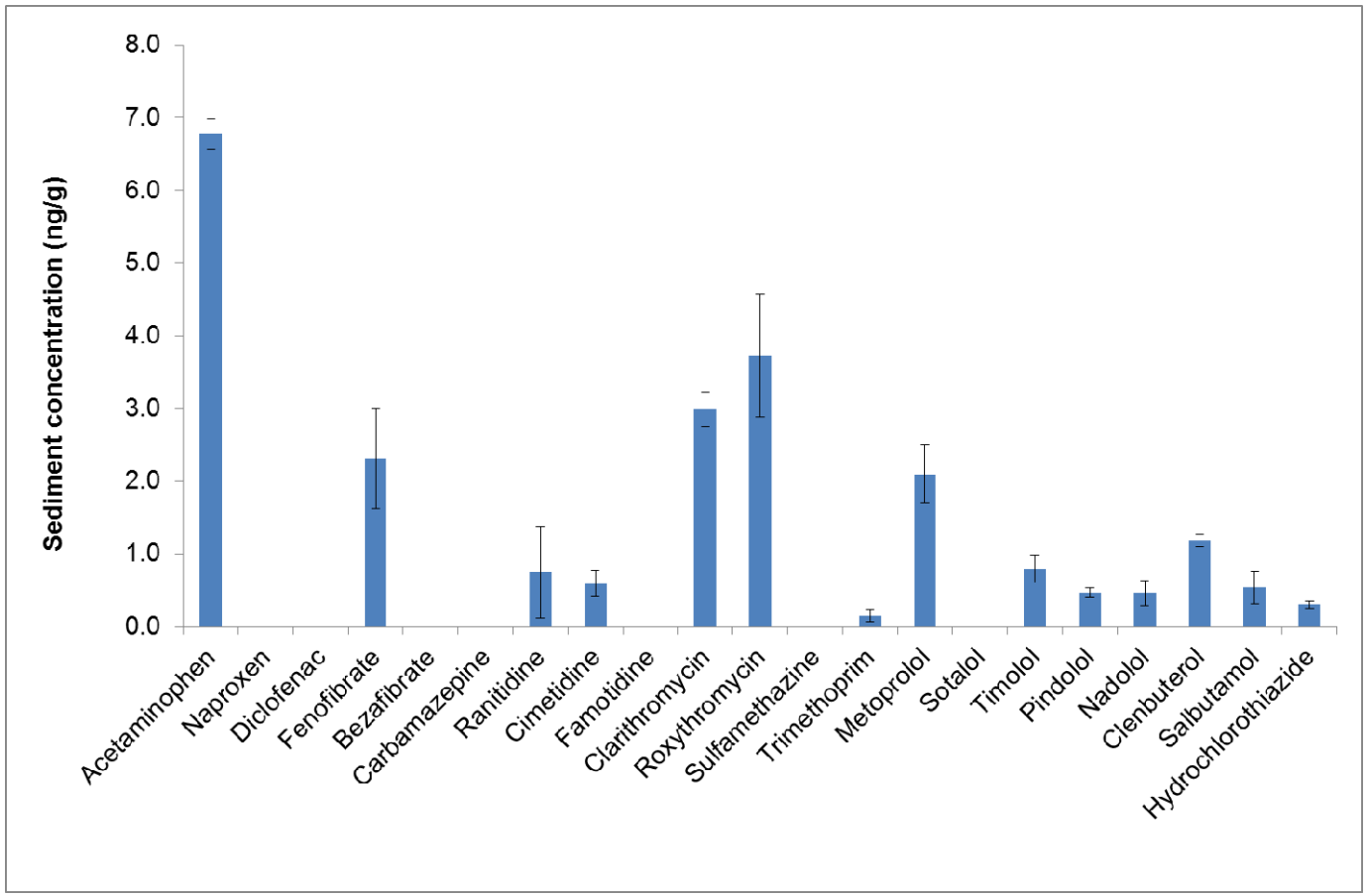
Twenty-one pharmaceuticals were quantified in this study (>LOQ), with graphical concentrations at each site presented in Figure to Figure 14.

A table of concentrations by site is contained in Appendix 1.

Of the 25 pharmaceuticals not quantified, 11 were detected at one or more sites, i.e., their observed concentration were below the LOQ but above the LOD. The remaining 14 pharmaceuticals were not detected at any site (<LOD).

Figure 2

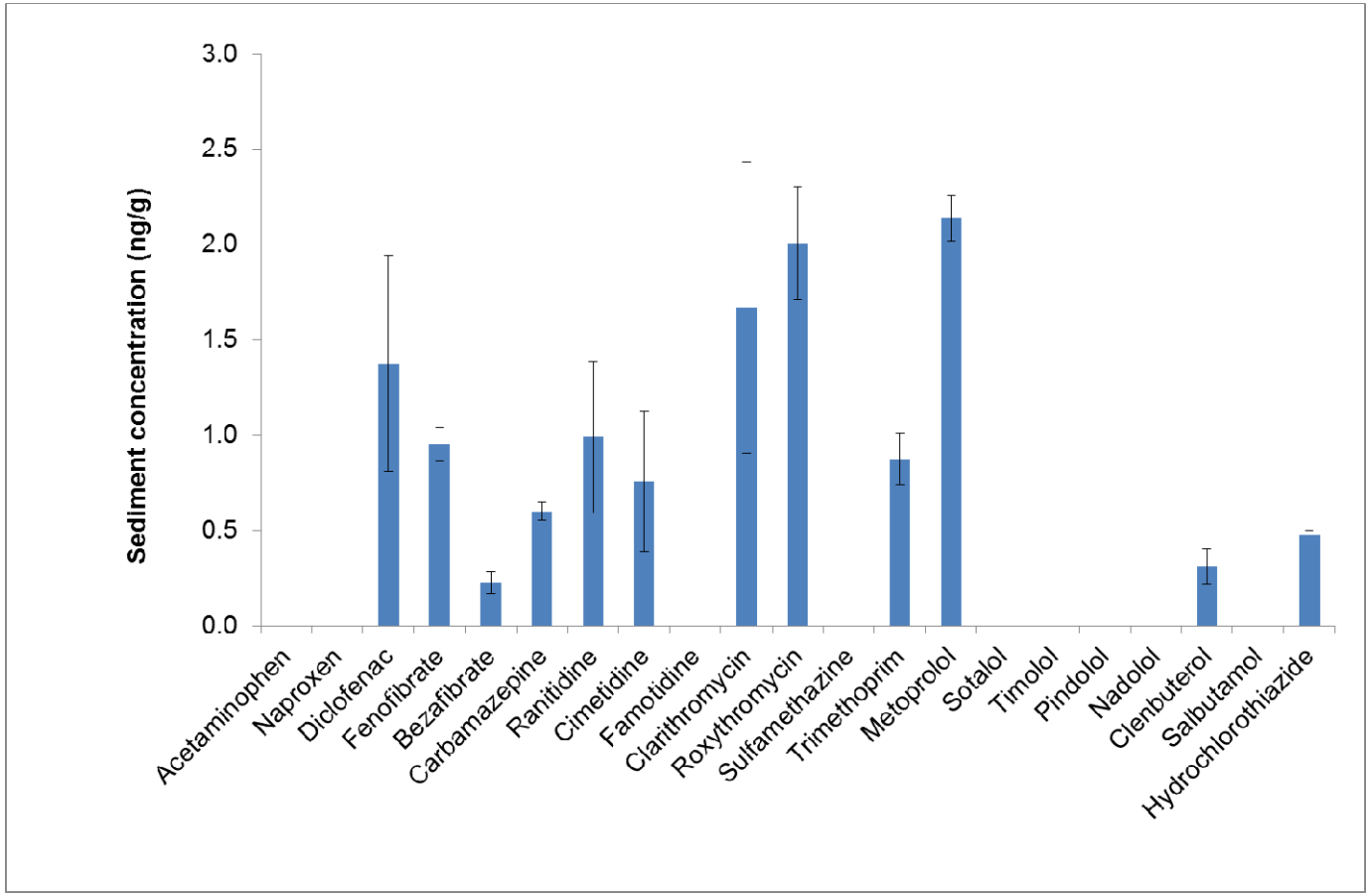
Average sediment concentrations of pharmaceuticals from Coxs Bay



Average concentrations and standard error based on two replicates; only pharmaceuticals above limit of quantitation presented

Figure 3

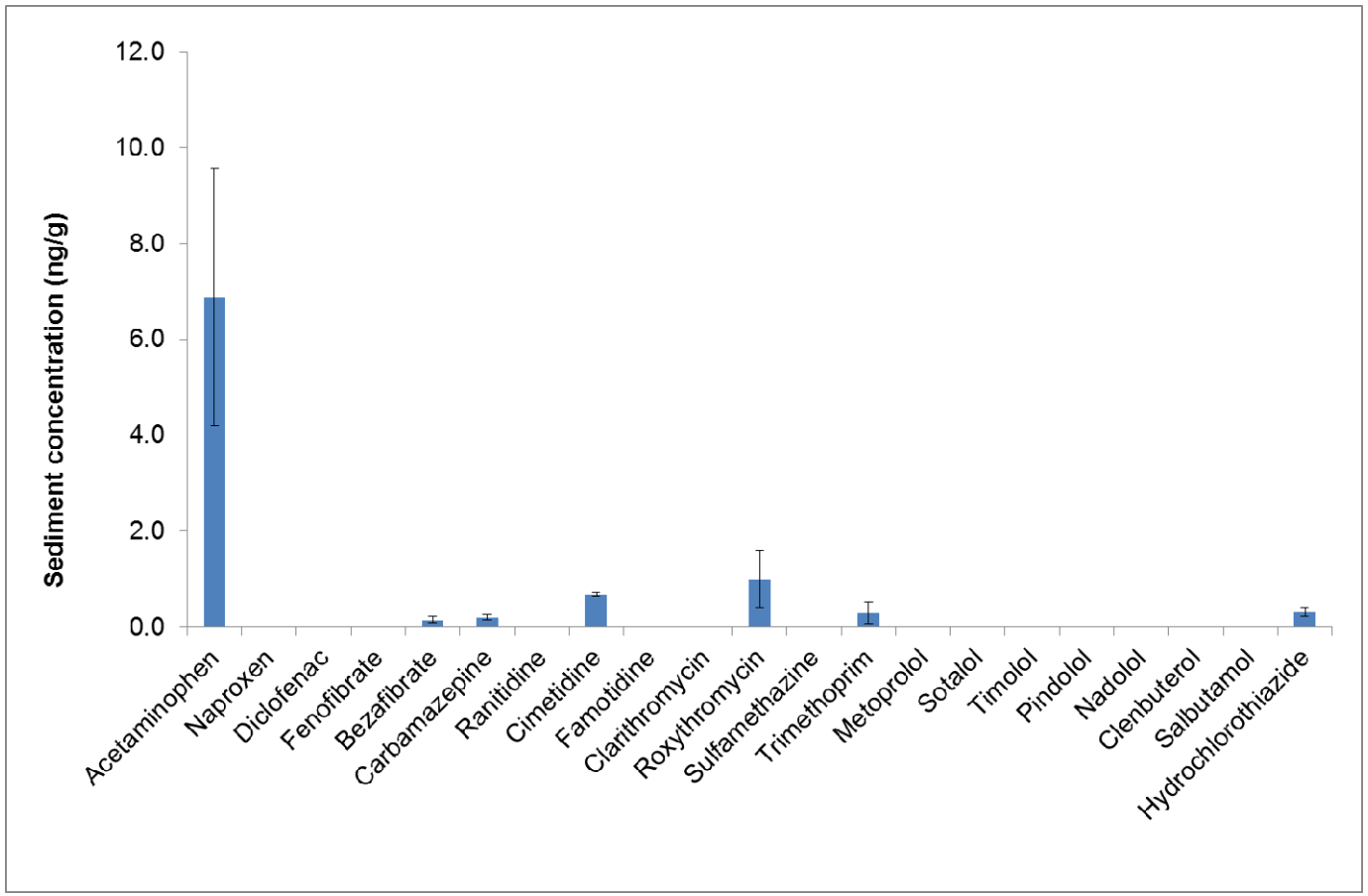
Sediment concentrations of pharmaceuticals from Meola.



Average concentrations and standard error based on two replicates; only pharmaceuticals above limit of quantitation presented

Figure 4

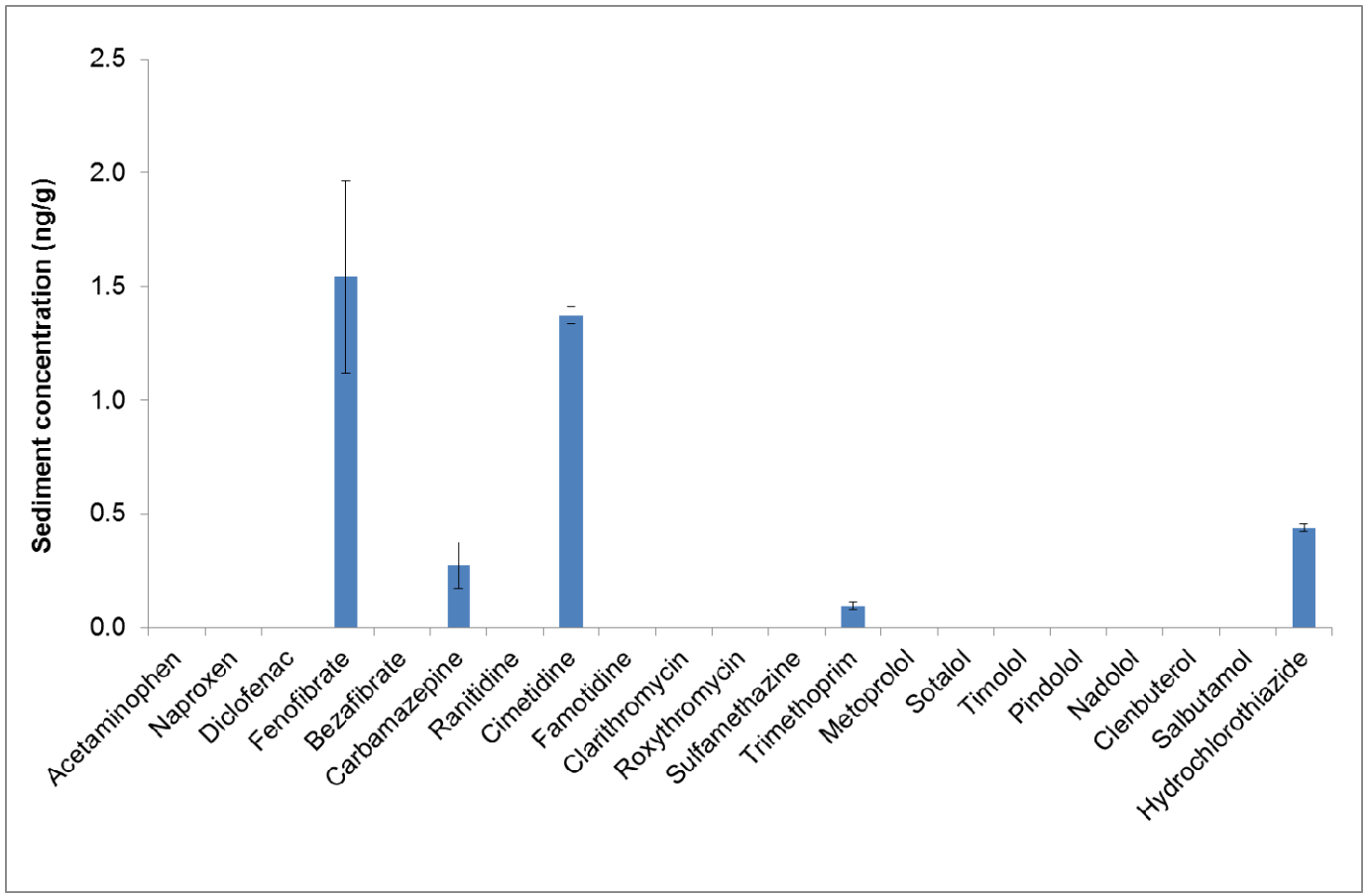
Sediment concentrations of pharmaceuticals from Motions.



Average concentrations and standard error based on two replicates; only pharmaceuticals above limit of quantitation presented

Figure5

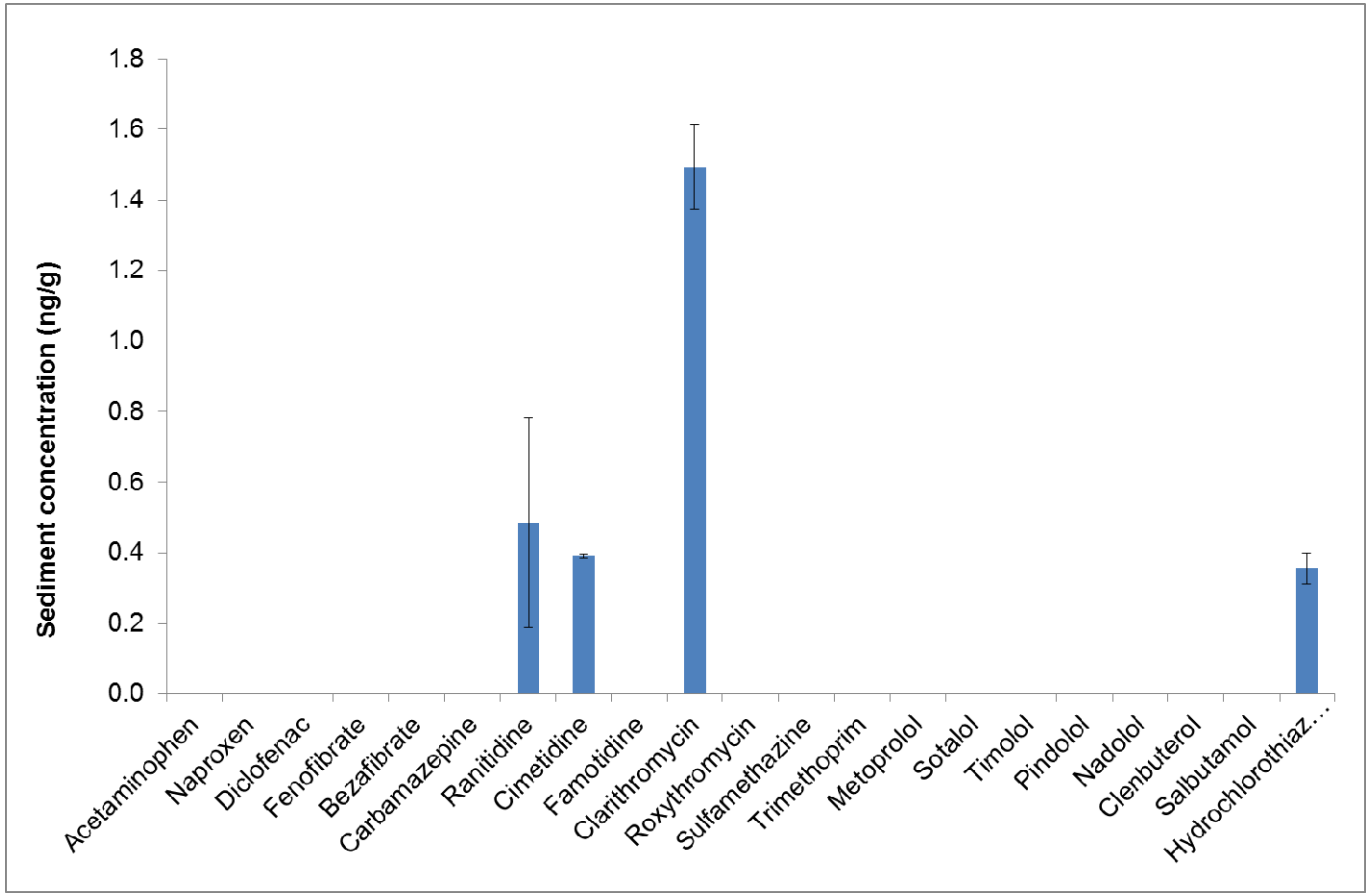
Sediment concentrations of pharmaceuticals from Milford Marina.



Average concentrations and standard error based on two replicates; only pharmaceuticals above limit of quantitation presented

Figure 6

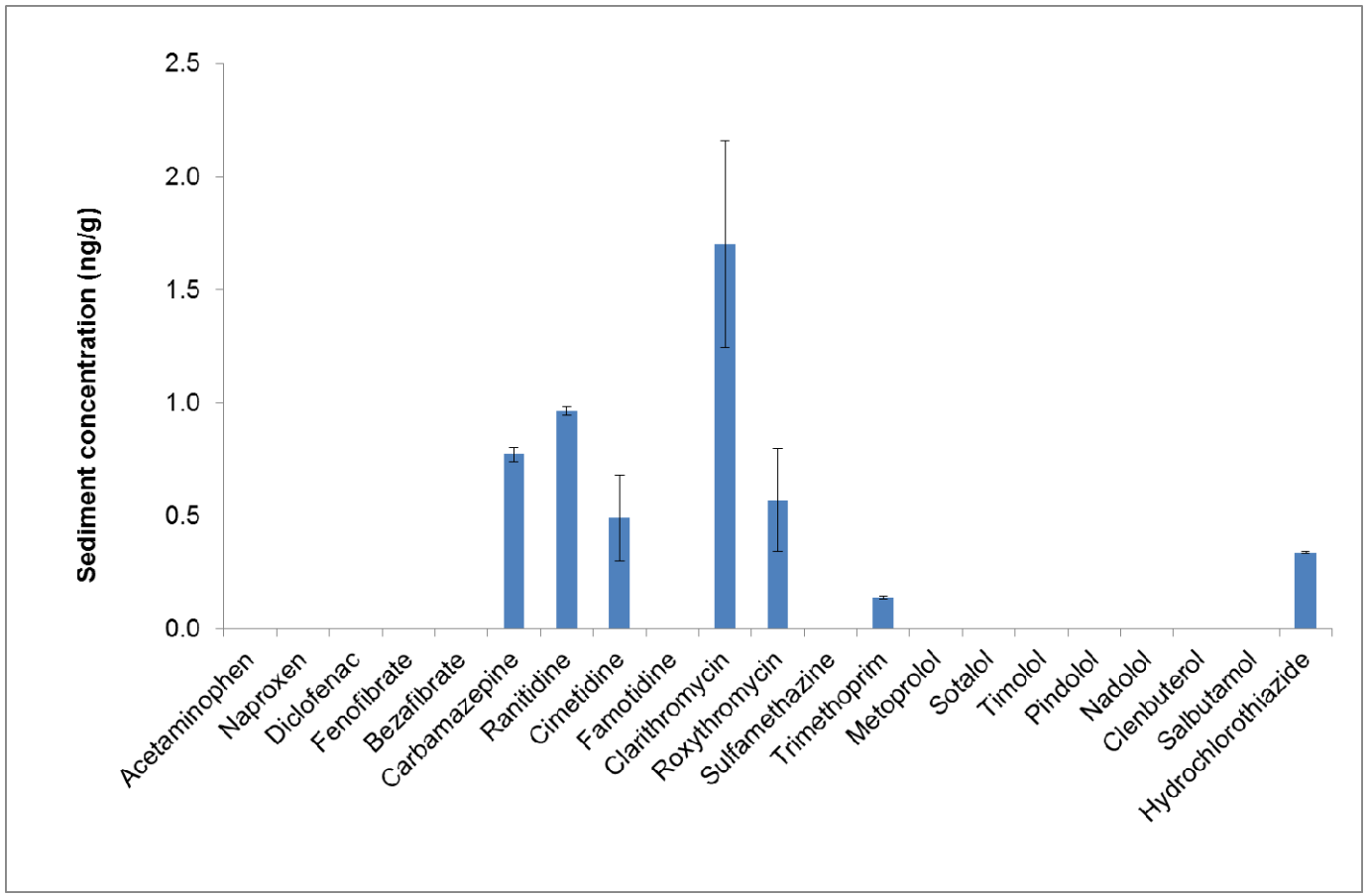
Sediment concentrations of pharmaceuticals from Westhaven Marina.



Average concentrations and standard error based on two replicates; only pharmaceuticals above limit of quantitation presented

Figure 7

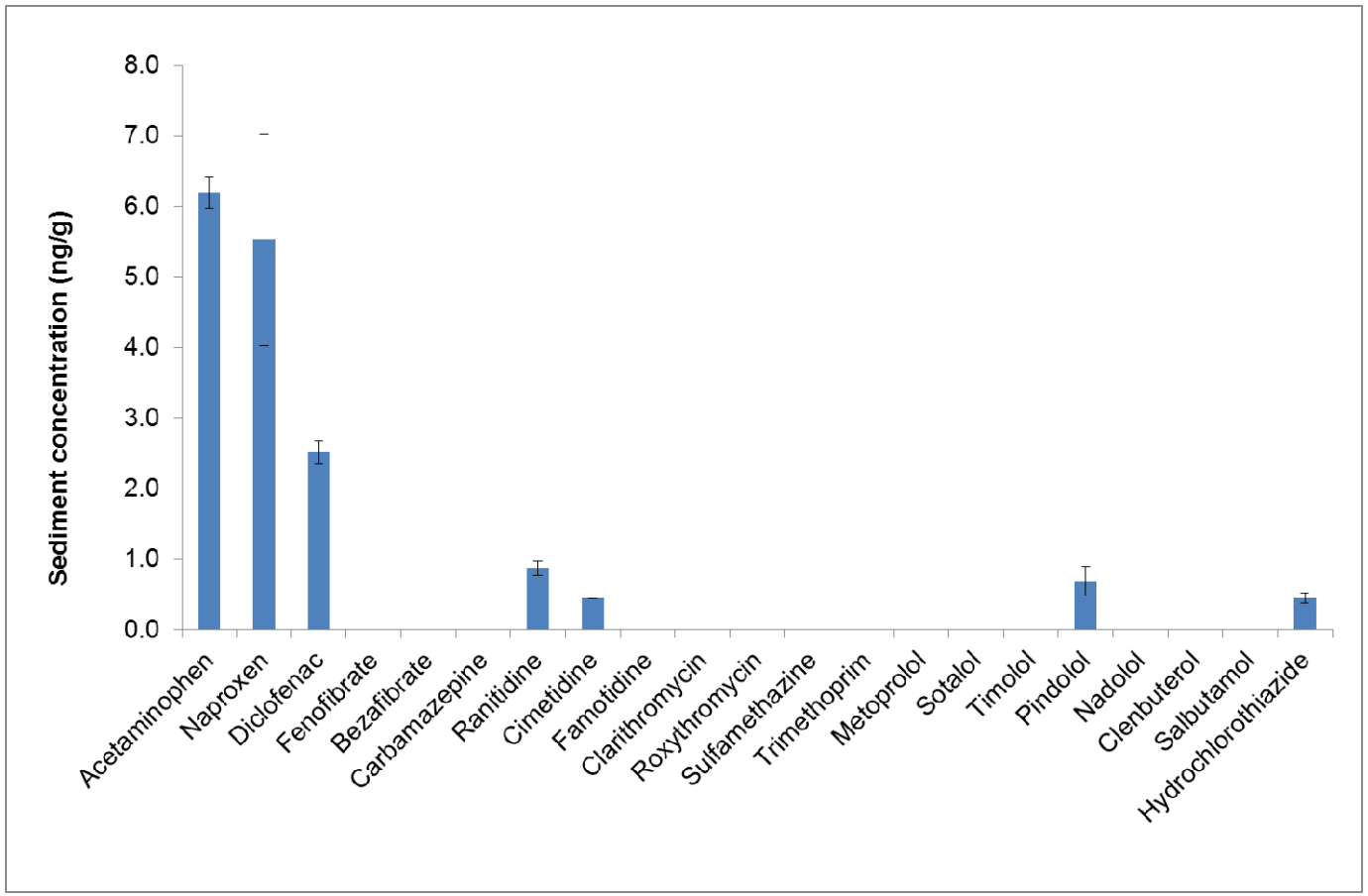
Sediment concentrations of pharmaceuticals from Hobson Bay.



Average concentrations and standard error based on two replicates; only pharmaceuticals above limit of quantitation presented

Figure 8

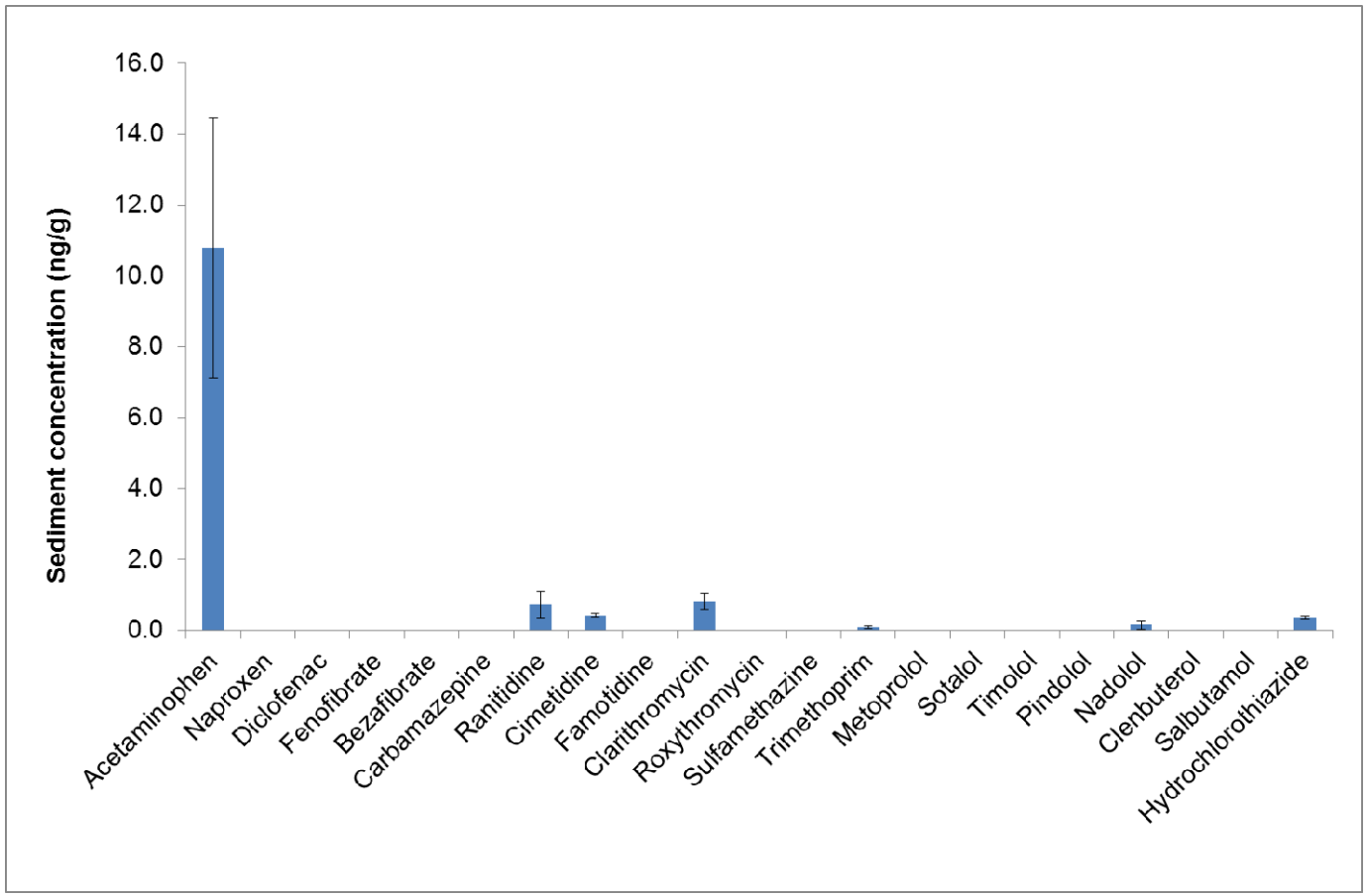
Sediment concentrations of pharmaceuticals from Shoal Bay Hillcrest.



Average concentrations and standard error based on two replicates; only pharmaceuticals above limit of quantitation presented

Figure 9

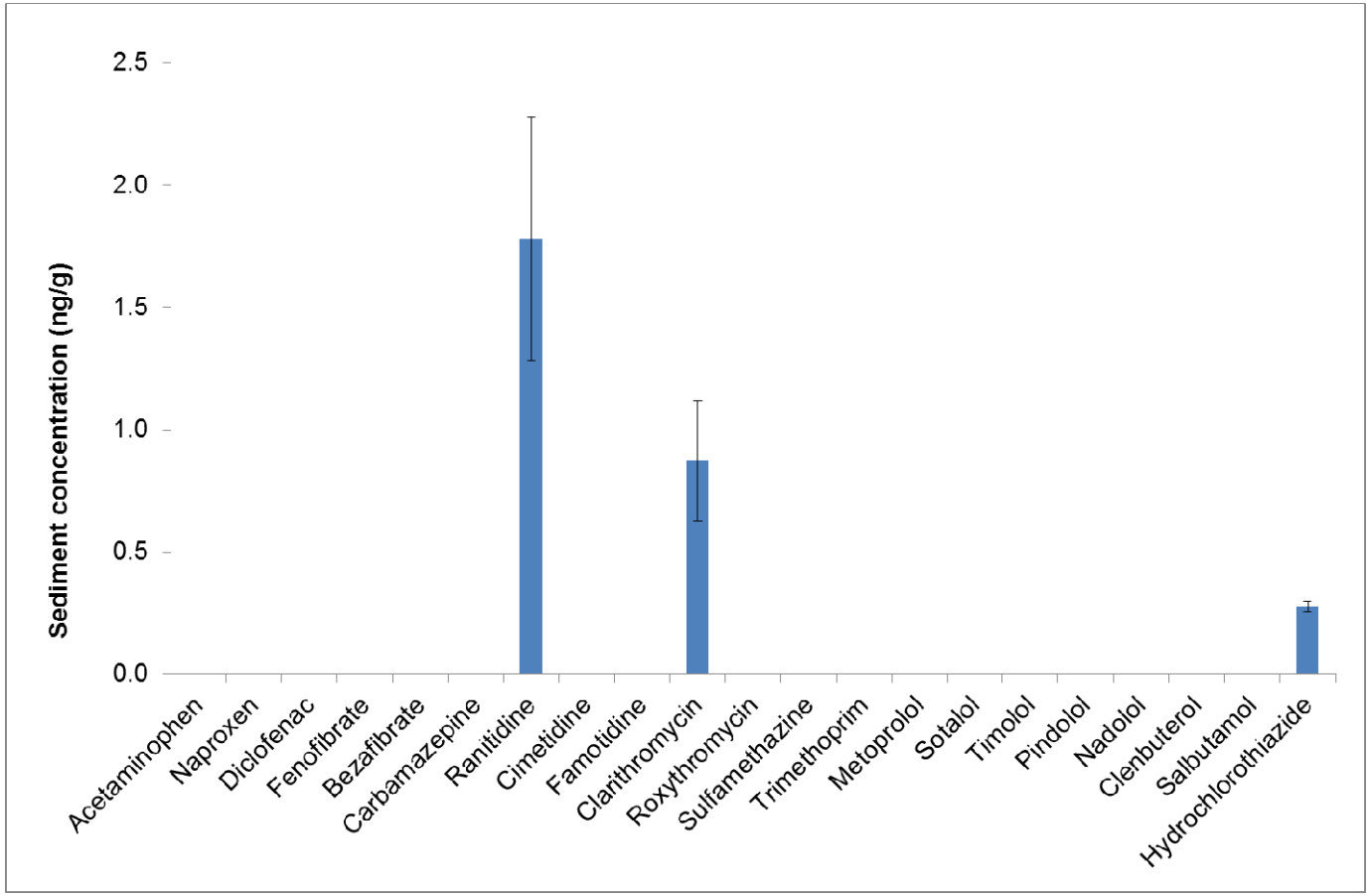
Sediment concentrations of pharmaceuticals from Halfmoon Bay Marina.



Average concentrations and standard error based on two replicates; only pharmaceuticals above limit of quantitation presented

Figure 10

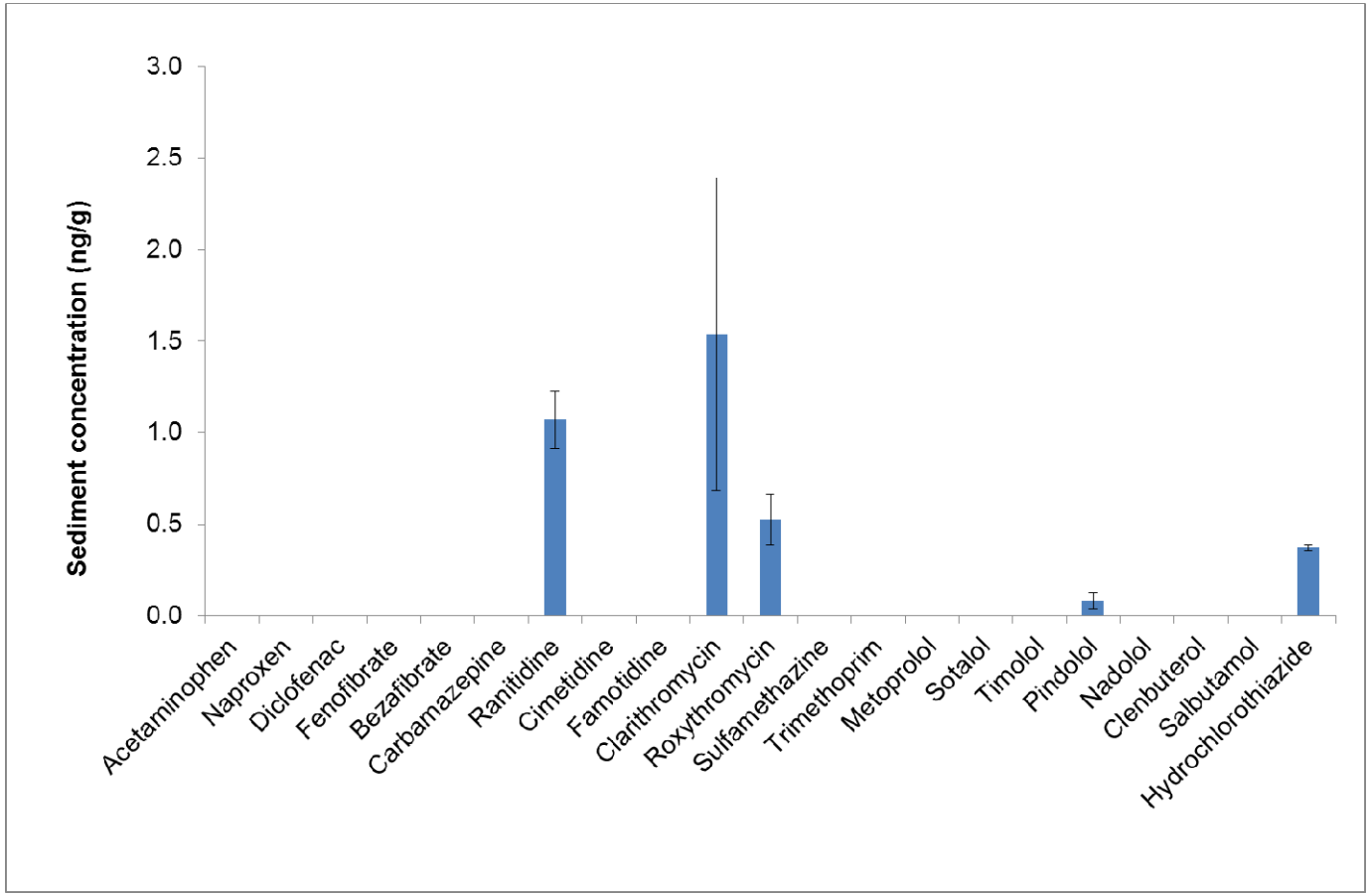
Sediment concentrations of pharmaceuticals from Pakuranga.



Average concentrations and standard error based on two replicates; only pharmaceuticals above limit of quantitation presented

Figure 11

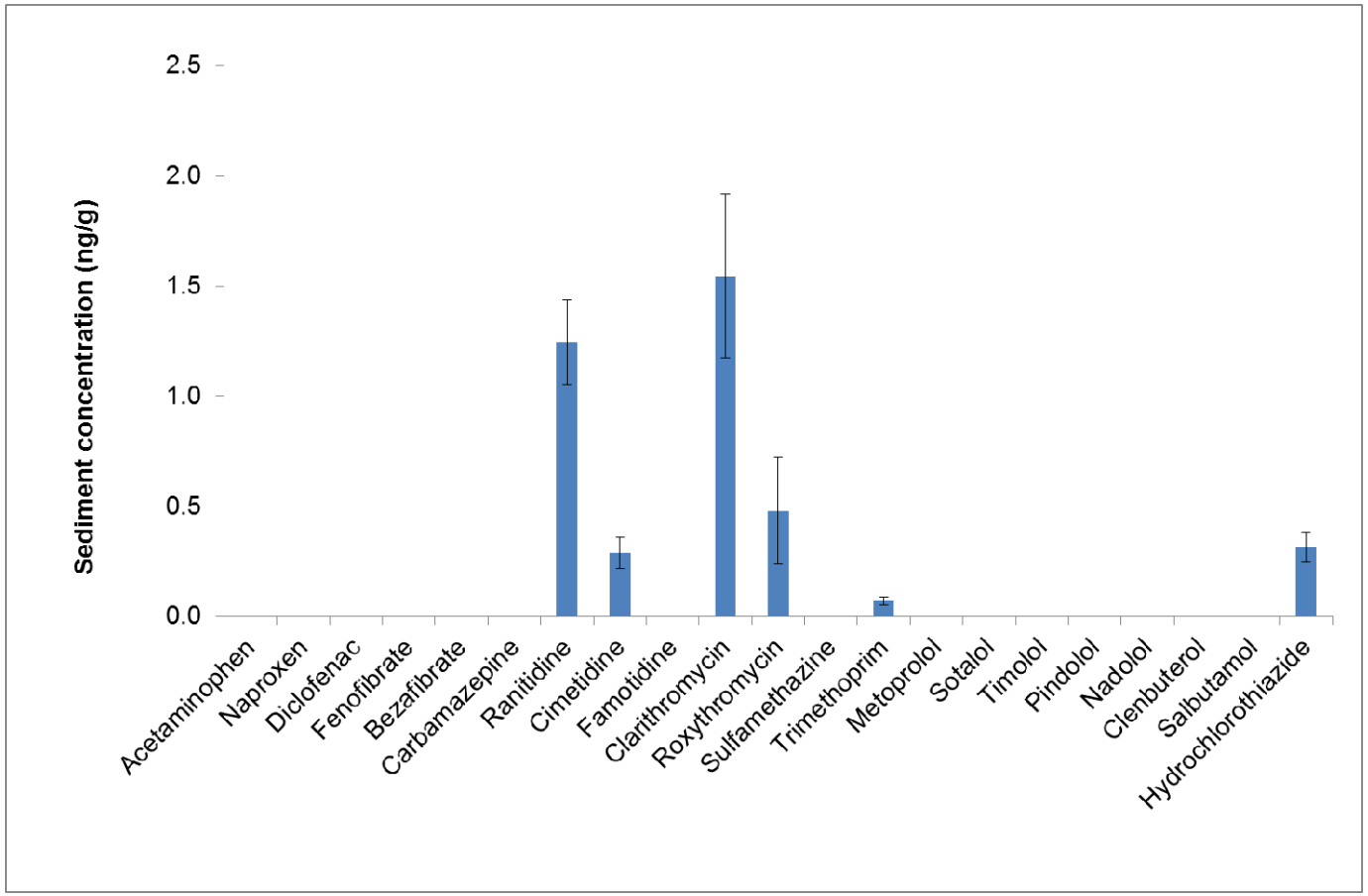
Sediment concentrations of pharmaceuticals from Whau.



Average concentrations and standard error based on two replicates; only pharmaceuticals above limit of quantitation presented

Figure 12

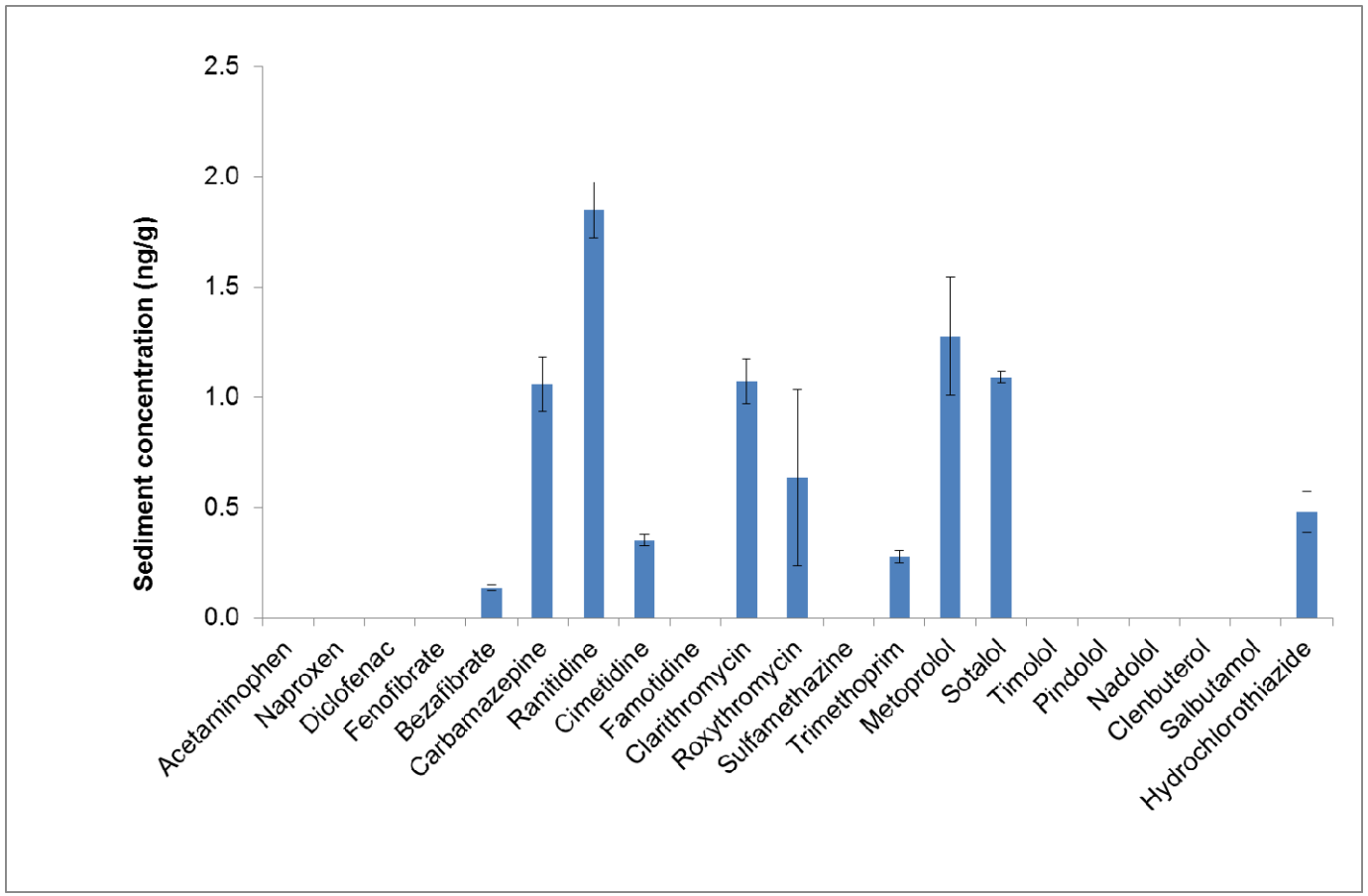
Sediment concentrations of pharmaceuticals from Taihiki River.



Average concentrations and standard error based on two replicates; only pharmaceuticals above limit of quantitation presented

Figure 13

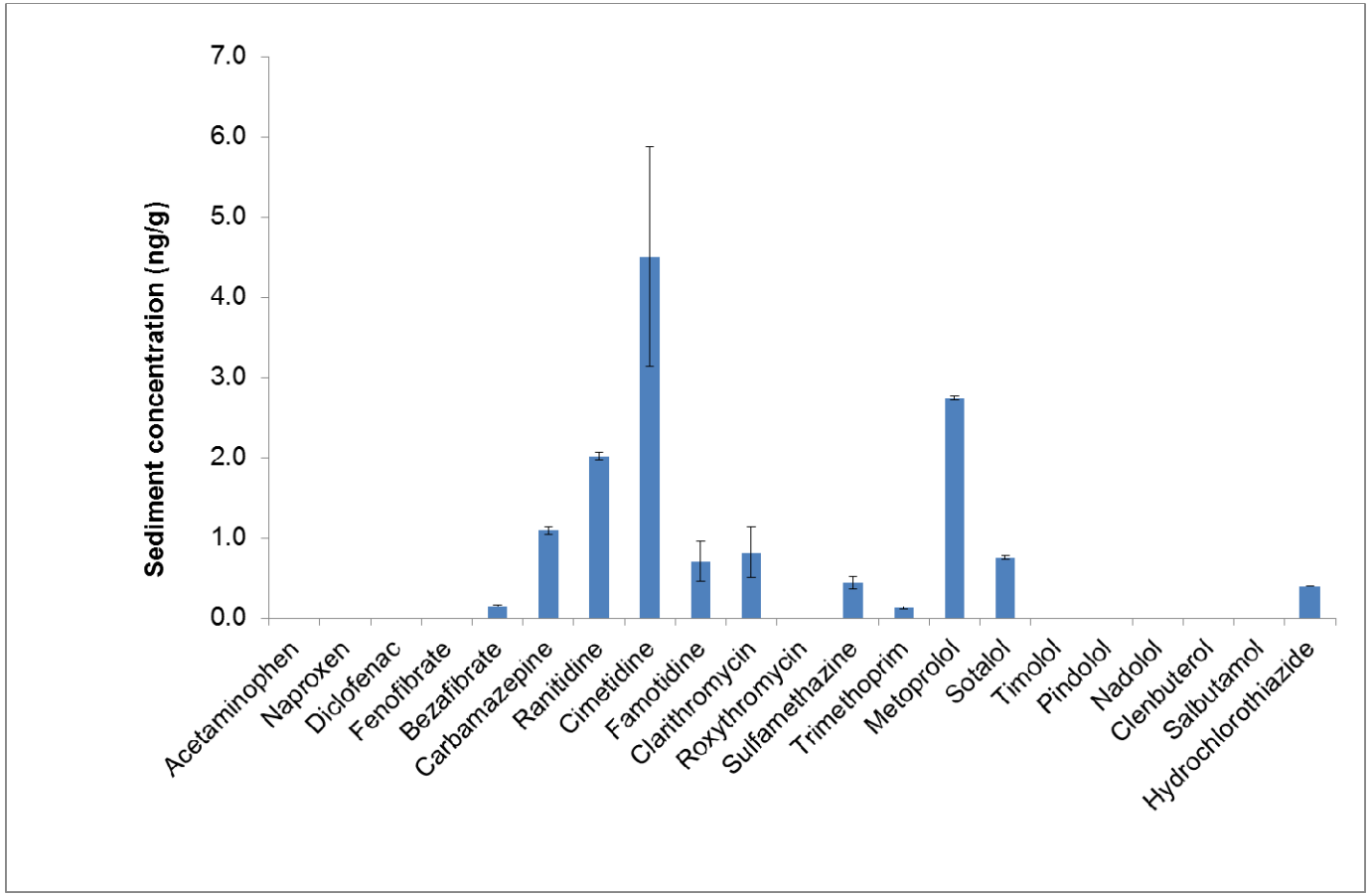
Sediment concentrations of pharmaceuticals from Mahurangi.



Average concentrations and standard error based on two replicates; only pharmaceuticals above limit of quantitation presented

Figure 14

Sediment concentrations of pharmaceuticals from Puketutu Island.



Average concentrations and standard error based on two replicates; only pharmaceuticals above limit of quantitation presented

Average sediment concentrations across all sites (for pharmaceuticals above LOQ) are presented in Table 4 with a graphical representation in Figure 15. Five of these - namely naproxen, salbutamol, sulfamethazine, timolol and famotidine - were not an average as they were only measured at one site. Average concentrations ranged from 0.16 ngg^{-1} to 7.66 ngg^{-1}.

For all pharmaceuticals quantified, the average concentration was 1.4 ngg^{-1}. The average acetaminophen concentration (7.7 ngg^{-1}) and the single naproxen concentration (5.5 ngg^{-1}) above LOQ are markedly higher than the average (Figure 15), suggesting that these are two of the most abundant pharmaceuticals that partition to the sediment compartment of the marine receiving environment. Their relatively high LOQ prevents more accurate determination of average concentrations across the region.

Table 4.

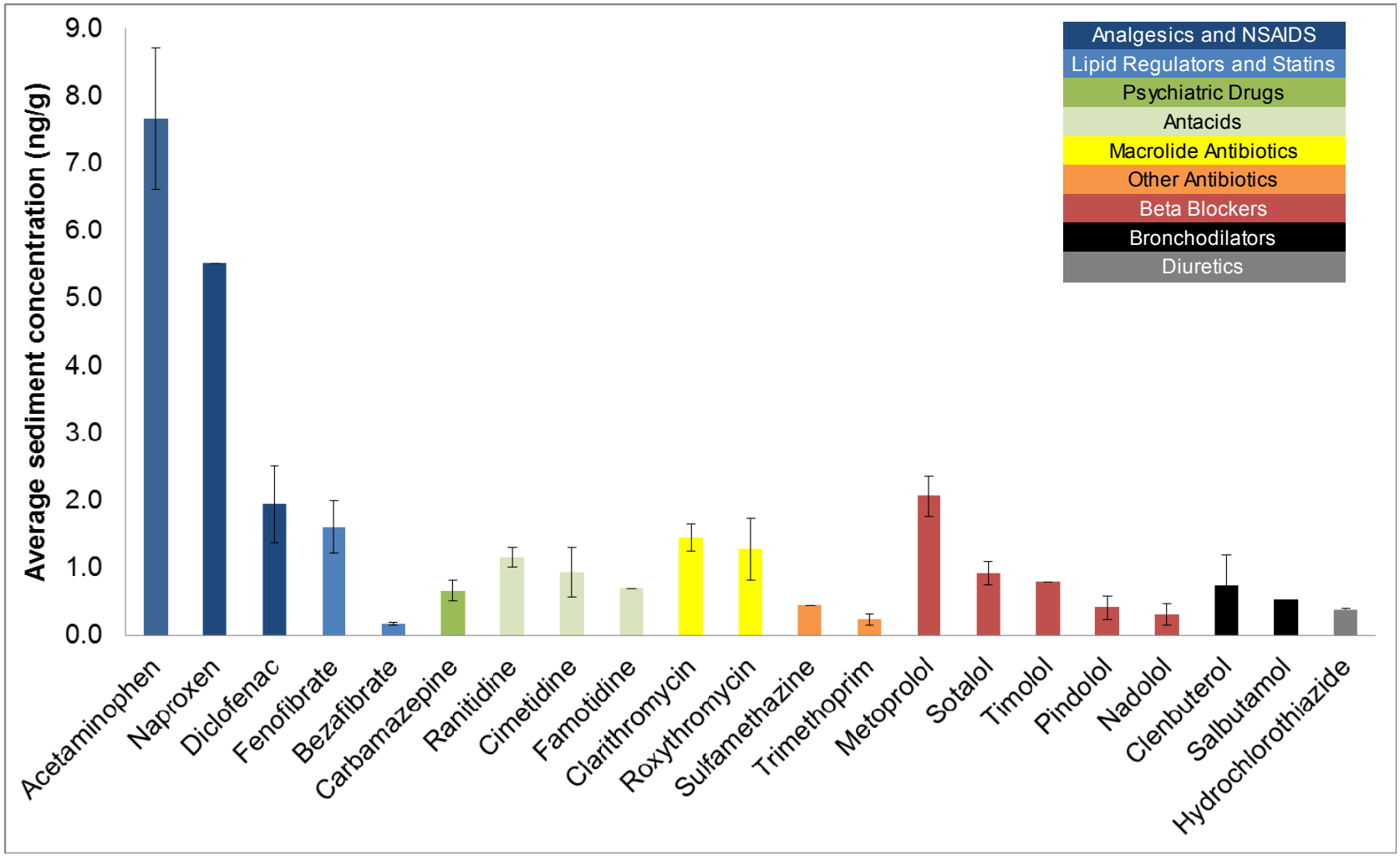
Average sediment concentration of pharmaceuticals above LOQ[a]

Pharmaceutical	Average Sediment Concentration (ngg^{-1})	Standard error	LOQ (ngg^{-1})	Number of sites pharmaceutical quantified
Acetaminophen	7.66	1.05	6.1	4
Naproxen	5.53	-	4.8	1
Metoprolol	2.06	0.30	0.8	4
Diclofenac	1.95	0.57	1.2	2
Clarithromycin	1.45	0.39	1.3	3
Fenofibrate	1.38	0.20	0.5	10
Roxythromycin	1.28	0.46	0.5	7
Ranitidine	1.16	0.15	0.3	11
Cimetidine	0.94	0.37	0.3	11
Sotalol	0.92	0.17	0.6	2
Timolol	0.80	-	0.4	1
Clenbuterol	0.75	0.44	0.2	2
Famotidine	0.70	-	0.4	1
Carbamazepine	0.67	0.15	0.2	6
Salbutamol	0.53	-	0.1	1
Sulfamethazine	0.44	-	0.3	1
Pindolol	0.41	0.18	0.1	3
Hydrochlorothiazide	0.38	0.02	0.1	13
Nadolol	0.31	0.15	0.2	2
Trimethoprim	0.23	0.08	0.1	9
Bezafibrate	0.16	0.02	0.1	4

[a]Naproxen, salbutamol, sulfamethazine, timolol and famotidine are not an average but single concentration.

Figure 15

Average concentration of pharmaceuticals in Auckland estuarine sediment that were above limit of quantitation[a,b]



Pharmaceuticals are colour coded by therapeutic class; error bars are ±1 standard error with the exception of naproxen, salbutamol, sulfamethazine, timolol and famotidine which are a single concentration

4 Discussion

4.1 International context

The environmental fate of pharmaceuticals has barely been studied in sediments, with most research to date concentrating on sewage sludge and effluent and the environmental water phase. With a wide variety of physico-chemical properties, pharmaceuticals will adsorb to sediment in differing degrees (Löffler*, et al.* 2005), so it is important to study both solid phase and water phase samples.

To our knowledge, reports of pharmaceuticals in estuarine sediments are only just emerging. The multi-residue method development paper that the methodology of this report is based on (Jelic*, et al.* 2009) analysed river sediments,from the middle course of the Ebro river, Spain and even with average and median detection limits of 1.29 ngg^{-1} and 0.36 ngg^{-1}, respectively, did not detect any pharmaceuticals.

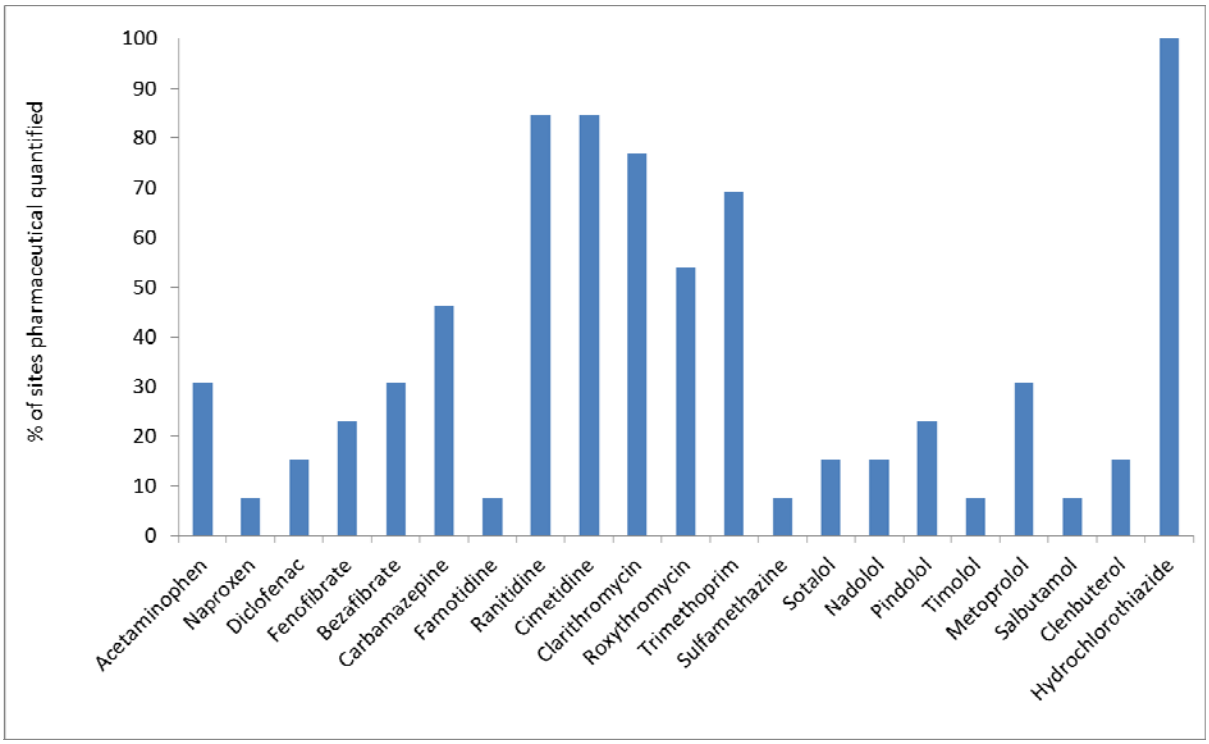
The recent study of Yang *et al.*(2011) described the occurrence and phase distribution of eight pharmaceuticals in the Yangtze Estuary, China. Although individual concentrations were not available for all compounds, concentrations ranged from approximately 10 ng g^{-1} (propranolol, sulfamethoxazole and carbamazepine) up to 431 ng g^{-1} (tamoxifen), 415 ng g^{-1} (mebeverine) and 164 ng g^{-1} (indomethacine). Maximum concentrations in the Chinese study were markedly higher than the current study.

4.2 Frequency of detection

Of the 46 pharmaceuticals analysed, 21 (46%) were quantified in one or more estuarine sediments (Figure 16). Hydrochlorothiazide was quantified at all 13 sites, with ranitidine, cimetidine, clarithromycin, roxythromycin and trimethoprim all quantified at over half the sites (Figure 16).

Figure 16

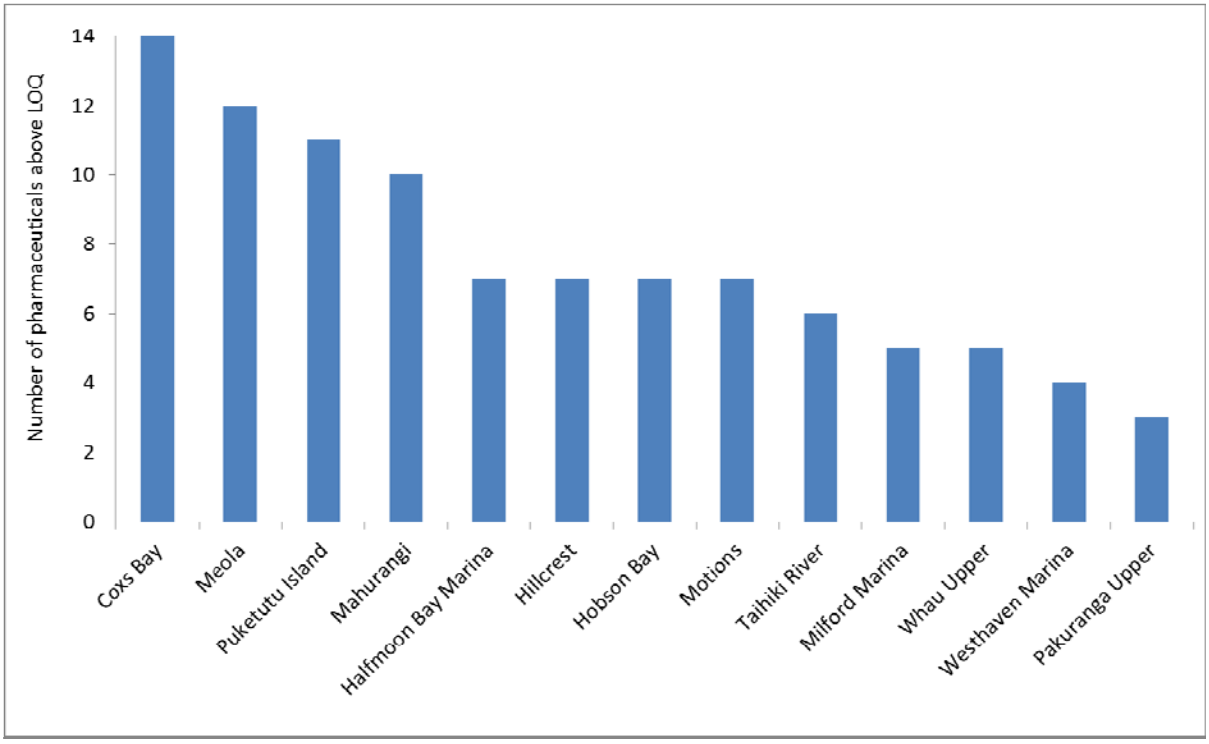
Pharmaceuticals quantified in estuarine sediments and percentage of sites where individual pharmaceuticals found.



The maximum number of pharmaceuticals quantified at one site was 14, from Coxs Bay (Figure 17) (see Figure 2 to Figure 14 for individual pharmaceuticals quantified at each site). Meola (12), Puketutu Island (11) and Mahurangi (10) were the sites with the next highest numbers quantified. Coxs Bay and Meola are presumably influenced by wastewater overflows as they are far removed from WWTP. The Puketutu Island site is the old disused oxidation ponds for Mangere Waste Water Treatment Plant (WWTP), so higher numbers of pharmaceuticals quantified from this site suggest high stability of these compounds, or recent input. The Mahurangi site was situated downstream from the Warkworth sewage treatment plant so could explain higher numbers of pharmaceuticals quantified.

Figure 17

Number of pharmaceuticals quantified at each site.



The sediment concentrations of 25 of the 46 pharmaceuticals analysed were below LOQ for all sites in this study. Reasons for this are manifold and may include a combination of:

1. High individual LOQs for some pharmaceuticals (Table 3);
2. Affinity to sediment based on physico-chemical properties of each pharmaceutical;
3. The suite of pharmaceuticals analysed were chosen to reflect drugs that are commonly used in the EU, which may be different to the usage patterns in New Zealand;
4. Very low concentrations - or zero concentrations (see point 3) - of some pharmaceuticals.

High individual LOQs for some pharmaceuticals are a result of using a multi-residue approach. This method will not be optimised for every chemical due to the differing physico-chemical properties of such a large suite. This can potentially be addressed in the future if a smaller, more focussed, suite of pharmaceuticals is analysed.

The concentration of pharmaceuticals at each of the sites and frequency of detection in sediments across the region is not necessarily a reflection of input into the environment. Many pharmaceuticals will not partition strongly to sediment and will be predominantly in the water phase (Löffler*, et al.* 2005). As such, to obtain a more

comprehensive idea of what the environmental concentrations are, both solid and water phases need to be analysed.

4.3 Relevance to New Zealand

The relevance of the EU suite of pharmaceuticals analysed in this study to New Zealand can be assessed by comparing the suite with the pharmaceutical schedule provided by the New Zealand Pharmaceutical Management Agency (Pharmac). The schedule is updated periodically, however the one released 1st December 2007 (Pharmac 2007) is relevant to this study, with samples collected March 2008.

Of the 46 pharmaceuticals analysed, 33 (72%) are listed in the Pharmac schedule of December 2007, suggesting the suite of pharmaceuticals analysed is mostly relevant to New Zealand. Those that are not included in the schedule are phenazone, mevastatin, fenofibrate, clofibric acid, gemfibrozil, josamycin, tylosin, sulfamethazine, clenbuterol, phenobarbital, butalbital, pentobarbital, and nifuroxazide. Of note, from the above list only gemfibrozil has been added to the most recent Pharmac schedule of April 2012 (Pharmac 2012).

Interestingly, of the 21 pharmaceuticals quantified in estuarine sediments around Auckland (Figure 15), three are not contained in the Pharmac schedule (2007 *or* 2012), namely fenofibrate, sulfamethazine and clenbuterol. Fenofibrate was found at Coxs Bay, Meola and Milford Marina at concentrations of 2.31, 0.95 and 1.54 ngg^{-1} respectively. Although not in the Pharmac schedule (and so not subsidised), fenofibrate (a cholesterol lowering drug) was used in a major trial in New Zealand from 2000-2005 (FIELD) and is available through online pharmacies - two examples are www.inhousedrugstore.biz and rxmedicine247.com/index.php. However, even with online access to fenofibrate, such high relative concentrations at three sites is surprising. Sulfamethazine was quantified at only one site, Puketutu Island, at a concentration of 0.44 ngg^{-1}. Sulfamethazine is a veterinary antibiotic used primarily in pigs (Sarmah*, et al.* 2006a) so its presence at Puketutu only may be due to trade waste sources into the WWTP. Clenbuterol was quantified at two sites, Coxs Bay and Meola, at concentrations of 1.19 and 0.31 ngg^{-1}, respectively. Clenbuterol is a controversial fat burning diet pill used by some bodybuilders, athletes and celebrities and has been prohibited by the world anti-doping agency (WADA) (2011).

The suite of pharmaceuticals analysed in this study is mostly relevant to New Zealand, and would be acceptable to use in future studies. However, it could be improved upon by tailoring the suite to New Zealand prescription numbers. The Pharmac list of top 20 prescribed drugs for year ending June 2010 is shown in Table 5. Of the top 20 prescribed drugs, only five were included in this current study, which suggests the suite analysed may not be a close fit to high use prescriptions.

Of course, some of these numbers will be further inflated by over the counter sales. From Table 5, paracetamol, aspirin, ibuprofen and diclofenac (as lower doses and gels) are available without prescription.

Table 5.

Top 20 medicines by prescription numbers (Pharmac 2011)[a]

Rank	Chemical	Treats	Prescription numbers[b]
1	*Paracetamol*	*Pain*	*2,260,000*
2	Aspirin	CV risk	1,380,000
3	Simvastatin	Raised cholesterol	1,280,000
4	Omeprazole	Reflux	1,080,000
5	Amoxycillin	Bacterial infection	1,040,000
6	*Metoprolol succinate*	*Heart disease*	*920,000*
7	*Salbutamol*	*Asthma*	*840,000*
8	Amoxycillin clauvulanate	Bacterial infection	820,000
9	*Ibuprofen*	*Pain*	*630,000*
10	Cilazapril	Heart disease	620,000
11	*Diclofenac sodium*	*Pain*	*600,000*
12	Prednisone	Steroid	560,000
13	Zopliclone	Insomnia	550,000
14	Flucloxacillin sodium	Bacterial infections	530,000
15	Cholecalciferol	Osteoporosis	520,000
16	Metformin hydrochloride	Diabetes	440,000
17	Levothyroxine	Thyroid gland deficiency	430,000
18	Felodipine	Heart disease	430,000
19	Quinapril	Heart disease	430,000
20	Bendrofluazide	Asthma	410,000

[a] Pharmaceuticals italicized were analysed in this study
[b] year ending June 2010

4.4 Further considerations

Around 1800 medicines are subsidised in New Zealand through the pharmaceutical schedule (Pharmac 2011). The true number of chemicals with potentially harmful toxicological properties is increased even further when conjugates and breakdown products - many of which are unknown - are included. As such, the assessment of inputs of these medicines into the waste stream and potentially the environment is even more complicated than the initial 1800 number suggests. In addition, while toxicological data may exist for the parent active ingredient (in the human target at least), there is little information on toxicology of these conjugates and breakdown products.

In addition, there is a knowledge gap in the literature about what concentrations of pharmaceuticals are potentially harmful to aquatic species, particularly estuarine species. This is beginning to be addressed, to some extent, by the establishment of an ecotoxicological database, Wikipharma (Molander*, et al.* 2009), a risk assessment database, PEIAR (Pharmaceuticals in the Environment, Information for Assessing Risk) (Cooper*, et al.* 2008) and strategies to prioritise active pharmaceutical ingredients (APIs) for ecotoxicity testing and environmental monitoring (Roos*, et al.* 2012).

WWTP effluents are presumably the highest input of pharmaceuticals into the environment, due to incomplete removal of many pharmaceuticals during the WWTP process. However, other inputs may be significant at some sites such as waste water overflows and groundwater leachates in the vicinity of landfill sites. With respect to waste water overflows, this appears to be the case in sites such as Coxs Bay and Meola, which are established catchments far removed from WWTP, but had the highest frequency of pharmaceuticals detected in the region, with 14 and 12, respectively.

Furthermore, WWTP outputs are divided into solid and liquid, with solid material transferred to landfill and liquid effluent released into the marine receiving environment. The solid landfill material may be a cause for future leaching into groundwater. Analysis of both solid and liquid phases is desirable, at least in the short term, to gauge the distribution of target pharmaceuticals in these compartments.

5 Recommendations

This was a preliminary study with limited replication, varying (and sometimes high) quantitation limits, and a European relevant pharmaceutical suite. Nevertheless, results have shown that many pharmaceuticals are entering the marine receiving environment around Auckland. However, there are still large knowledge gaps that need to be addressed. These include:

- The extent to which pharmaceuticals are partitioning between solid and liquid phases is unknown;
- The input of pharmaceuticals into the environment from WWTP, wastewater overflows and landfill leachates is unknown;
- The loads of pharmaceuticals into WWTPs are largely unknown;
- The environmental effects of these contaminants.

Recommendations for the future follow a tiered approach:

1. Carry out pharmaceutical concentration studies into inputs - both liquid and solid phase - in the major WWTPs around Auckland:
    a. Initially use a multi-residue analysis - such as in this current study - to give broad coverage of pharmaceutical classes. These data will most likely have to be provided by international collaboration. Note: limitations in the methodology described in this report are minimised as WWTP input concentrations will be considerably higher than environmental concentrations (Stewart, unpublished data)
    b. Analyses should be “time averaged” to avoid potential short term variations in concentrations.
2. Development of domestic capability in the analysis of pharmaceuticals:
    a. With capability within the country, future studies can concentrate on pharmaceuticals relevant to New Zealand;
    b. This list should be created using a consultative procedure based on information from point 1 and further considerations such as toxicological profiles and breakdown products (described in section 4.4).
3. Carry out future analytical and toxicological studies with a ‘New Zealand relevant’ suite of pharmaceuticals - on solid and liquid phases - including:
    a. WWTP inputs and outputs;
    b. The marine receiving environment;
    c. Effects on New Zealand relevant biota.
4. Benchmark results to international studies, including:
    a. WWTP influent and effluent concentrations;

b. Environmental water and sediment concentrations;

c. Toxicological effects on biota.

These recommendations provide a broad framework for addressing current knowledge gaps around pharmaceuticals in the Auckland marine receiving environment.

6 Acknowledgements

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7 Glossary of abbreviations and terms

ASE	Accelerated Solvent Extraction
ECCs	Emerging Chemicals of Concern
HPLC	High Pressure Liquid Chromatography
H_2O	Water
LC	Liquid Chromatography
LC/MS/MS	Liquid Chromatography/Tandem Mass Spectrometry
LOD	Limit of Detection
$LogK_{ow}$	Octanol-water partition coefficient
LOQ	Limit of Quantitation
MeCN	Acetonitrile
MeOH	Methanol
MS	Mass Spectrometer
NSAID	Non-Steroidal Anti-Inflammatory Drug
Pharmac	New Zealand Pharmaceutical Management Agency
POCIS	Polar Organic Chemical Integrative Sampler
PPCPs	Pharmaceuticals and Personal Care Products
QqLIT	Quadrupole Linear Ion Trap
SPE	Solid Phase Extraction
SRM	Selective Reaction Monitoring
STP	Sewage Treatment Plant
WWTP	Wastewater Treatment Plant

8 References

Ahrens, M (2008). *Review of organic chemicals of potential environmental concern in use in Auckland*. Prepared by NIWA for Auckland Regional Council. Auckland Regional Council technical report, TR2008/028

Braund, R *et al* (2009). Disposal practices for unused medications in New Zealand. *Environment International,* 35(6), 952-955

Cooper, E R *et al* (2008). Preliminary risk assessment database and risk ranking of pharmaceuticals in the environment. *Science of the Total Environment*, 398(1-3), 26-33

EC (2002). Commission Decision (2002/657/EC) of 12 August 2002 implementing Council directive 96/23/EC concerning the performance of analytical methods and the interpretation of results, *Official Journal of the European Communities* L221, 8–36

Fent, K *et al* (2006). Ecotoxicology of human pharmaceuticals. *Aquatic Toxicology*, 76(2), 122-159

FIELD. Fenofibrate Intervention and Event Lowering in Diabetes [online]. Available from: www.thefieldtrial.org

Gielen, G J H P (2007). *The fate and effects of sewage-derived pharmaceuticals in soil*. University of Canterbury

Jelic, A *et al* (2009). Multi-residue method for trace level determination of pharmaceuticals in solid samples using pressurized liquid extraction followed by liquid chromatography/quadrupole-linear ion trap mass spectrometry. *Talanta*, 80(1), 363-371

Le-Minh, N *et al* (2010). Fate of antibiotics during municipal water recycling treatment processes. *Water Research*, 44(15), 4295-4323

Löffler, D *et al* (2005). Environmental fate of pharmaceuticals in water/sediment systems. *Environmental Science and Technology*, 39(14), 5209-5218

Molander, L *et al* (2009). WikiPharma - A freely available, easily accessible, interactive and comprehensive database for environmental effect data for pharmaceuticals. *Regulatory Toxicology and Pharmacology*, 55(3), 367-371

Pharmac (2007). Pharmaceutical Schedule, effective 1 December 2007

Pharmac (2011). Pharmaceutical Management Agency. Annual Review 2011

Pharmac (2012). Pharmaceutical Schedule, April 2012

Roos, V *et al* (2012). Prioritising pharmaceuticals for environmental risk assessment: Towards adequate and feasible first-tier selection. *Science of the Total Environment*, 421–422(0), 102-110

Sarmah, A K *et al* (2006a). A global perspective on the use, sales, exposure pathways, occurrence, fate and effects of veterinary antibiotics (VAs) in the environment. *Chemosphere*, 65(5), 725-759

Sarmah, A K *et al* (2006b). A survey of endocrine disrupting chemicals (EDCs) in municipal sewage and animal waste effluents in the Waikato region of New Zealand. *Science of the Total Environment*, 355(1-3), 135-144

Stewart, M *et al* (2009). Field Analysis of Chemicals of Emerging Environmental Concern in Auckland's Aquatic Sediments. Prepared by NIWA for Auckland Regional Council. Auckland Regional Council technical report, TR2009/021

Ternes, T A *et al* (2004). Scrutinizing pharmaceuticals and personal care products in wastewater treatment. *Environmental Science and Technology*, 38(20), 392A-399A

Yang, Y *et al* (2011). Occurrence and phase distribution of selected pharmaceuticals in the Yangtze Estuary and its coastal zone. *Journal of Hazardous Materials*, 190(1-3), 588-596

9 Appendix 1: Table of individual pharmaceutical sediment concentrations by site

Table Appendix 1

Individual pharmaceutical concentrations in sediments from sites around Auckland.

Site	Pharmaceutical[a]	Sediment Concentration (ngg^{-1})[b]	Standard error
Coxs Bay	Acetaminophen	6.78	0.21
	Hydrochlorothiazide	0.30	0.05
	Salbutamol	0.53	0.22
	Ranitidine	0.74	0.63
	Cimetidine	0.59	0.18
	Nadolol	0.46	0.17
	Trimethoprim	0.15	0.08
	Pindolol	0.47	0.07
	Timolol	0.80	0.19
	Metoprolol	2.09	0.40
	Clenbuterol	1.19	0.08
	Clarithromycin	2.98	0.24
	Roxythromycin	3.73	0.84
	Fenofibrate	2.31	0.69
Meola	Hydrochlorothiazide	0.48	0.02
	Bezafibrate	0.22	0.06
	Diclofenac	1.38	0.57
	Ranitidine	0.99	0.40
	Cimetidine	0.76	0.37
	Trimethoprim	0.88	0.13
	Metoprolol	2.14	0.12
	Clenbuterol	0.31	0.09
	Carbamazepine	0.60	0.05
	Clarithromycin	1.67	0.77
	Roxythromycin	2.01	0.30
	Fenofibrate	0.95	0.09
Motions	Acetaminophen	6.89	2.69
	Hydrochlorothiazide	0.32	0.09
	Bezafibrate	0.15	0.08
	Cimetidine	0.68	0.04
	Trimethoprim	0.29	0.23
	Carbamazepine	0.21	0.05
	Roxythromycin	1.00	0.59

Site	Pharmaceutical[a]	Sediment Concentration (ngg^{-1})[b]	Standard error
Milford Marina	Hydrochlorothiazide	0.44	0.02
	Cimetidine	1.37	0.04
	Trimethoprim	0.10	0.02
	Carbamazepine	0.27	0.10
	Fenofibrate	1.54	0.42
Westhaven Marina	Hydrochlorothiazide	0.35	0.05
	Ranitidine	0.49	0.30
	Cimetidine	0.39	0.01
	Clarithromycin	1.49	0.12
Hobson Bay	Hydrochlorothiazide	0.34	0.00
	Ranitidine	0.96	0.02
	Cimetidine	0.49	0.19
	Trimethoprim	0.14	0.01
	Carbamazepine	0.77	0.03
	Clarithromycin	1.70	0.46
	Roxythromycin	0.57	0.23
Shoal Bay Hillcrest	Acetaminophen	6.20	0.22
	Hydrochlorothiazide	0.45	0.07
	Naproxen	5.53	1.50
	Diclofenac	2.52	0.16
	Ranitidine	0.88	0.10
	Cimetidine	0.45	0.00
	Pindolol	0.69	0.21
Halfmoon Bay Marina	Acetaminophen	10.79	3.65
	Hydrochlorothiazide	0.36	0.04
	Ranitidine	0.74	0.38
	Cimetidine	0.42	0.04
	Nadolol	0.16	0.13
	Trimethoprim	0.09	0.03
	Clarithromycin	0.81	0.25
Pakuranga Upper	Hydrochlorothiazide	0.28	0.02
	Ranitidine	1.78	0.50
	Clarithromycin	0.87	0.25

Site	Pharmaceutical[a]	Sediment Concentration (ngg^{-1})[b]	Standard error
Whau Upper	Hydrochlorothiazide	0.37	0.01
	Ranitidine	1.07	0.16
	Pindolol	0.08	0.05
	Clarithromycin	1.54	0.85
	Roxythromycin	0.53	0.14
Taihiki River	Hydrochlorothiazide	0.31	0.07
	Ranitidine	1.25	0.19
	Cimetidine	0.29	0.07
	Trimethoprim	0.07	0.02
	Clarithromycin	1.55	0.37
	Roxythromycin	0.48	0.24
Mahurangi	Hydrochlorothiazide	0.48	0.09
	Bezafibrate	0.13	0.01
	Sotalol	1.09	0.03
	Ranitidine	1.85	0.13
	Cimetidine	0.35	0.02
	Trimethoprim	0.28	0.03
	Metoprolol	1.28	0.27
	Carbamazepine	1.06	0.12
	Clarithromycin	1.07	0.10
	Roxythromycin	0.64	0.40
Puketutu Island	Hydrochlorothiazide	0.39	0.00
	Bezafibrate	0.15	0.01
	Famotidine	0.70	0.25
	Sotalol	0.75	0.02
	Ranitidine	2.01	0.05
	Cimetidine	4.50	1.37
	Trimethoprim	0.13	0.01
	Sulfamethazine	0.44	0.08
	Metoprolol	2.74	0.02
	Carbamazepine	1.09	0.04
	Clarithromycin	0.82	0.31

[a] Only those with LOQ > 0 included
[b] Average of 2 replicates