Seasonal and Diurnal Fluctuations in the Concentrations of Pharmaceuticals and Personal Care Products (PPCPs) in Residential Sewage Water

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Seasonal and diurnal fluctuations in pharmaceuticals and personal care products (PPCPs) concentrations in residential sewage water were ascertained in an area with no businesses industry (*e.g.*, plants or offices) upstream. PPCPs with high detection rates included ibuprofen, acetaminophen and indomethacin (antipyretic analgesics), atenolol and disopyramide (antiarrhythmics), clarithromycin (antibiotic), levofloxacin (synthetic antimicrobial agent) and triclosan (disinfectant). In summer, the concentration of triclosan was the highest, while in winter, the concentrations of ibuprofen and acetaminophen were higher than the others. Moreover, three types of diurnal fluctuations were observed: no marked diurnal changes (triclosan), high daytime concentrations (disopyramide) and high nighttime concentrations (acetaminophen).

Key words——pharmaceuticals, personal care products, sewage water

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INTRODUCTION

In recent years, many reports have documented minute amounts of pharmaceuticals and personal care products (PPCPs) in river water[1,2] and water discharged from sewage plants,[2–7] however, the effects of these PPCPs in the environment, on wildlife and humans have not been fully elucidated. Since PPCPs are chemical compounds that are commercially developed for their effects on the human body, it is possible that they also affect wildlife to some degree. Most studies that measured PPCPs concentrations before and after sewage treatment used composite samples that were collected based on an average flow rate (average daily flow rate).[2,5,8] Therefore, few data have been available regarding diurnal fluctuations in PPCPs concentrations. Drugs vary in the time of day they are taken, the dosage spacing, and the excretion rate. Moreover, ointments and creams are washed away during bathing. In this manner, diurnal fluctuations in PPCPs concentrations in sewage water are believed to be marked. Hence, in the present study, residential sewage water was monitored for 24 hr to ascertain the diurnal fluctuations in PPCPs concentrations. In addition, because cold medications are more frequently used in winter, seasonal changes in PPCPs concentrations were also analyzed.

In the past, many studies sampled sewage water in urban areas,[2–5,9] but such sewage water also contains sewage from industrial plants and hospitals. Hence, in this present study, sewage water samples were collected at a sewage manhole where there were no businesses upstream.

MATERIALS AND METHODS

Target Compounds—— The following PPCPs were measured: ibuprofen, mefenamic acid, indomethacin, acetaminophen (antipyretic analgesics), carbamazepine (antiepileptic), propranolol, atenolol, disopyramide (antiarrhythmics), ifenprodil (agent to improve cerebral circulation and metabolism), fluconazole (antifungal agent), erythromycin, clarithromycin (antibiotics), levofloxacin (synthetic antibacterial agent) and triclosan (disinfectant). Previous studies have demonstrated that these compounds were frequently used, and detected in the water environment in Japan.[1–3] In addition, it is known that these PPCPs show relatively higher ratio of Predicted Environmental Con-

Table 1. Target Compounds and Measurement Conditions of HPLC/MS-MS

Compound	M. W.	Ionization mode	Precursor ion (m/z)	Product ion (m/z)	Cone voltage (V)	Collision Energy (eV)	Mobile phase[a)]	LOD[b)] (μg/l)	LOQ[b)] (μg/l)
ibuprofen	206.3	ESI−	205.4	161.3	15	10	A1	5	15
mefenamic acid	241.3	ESI+	242.1	224.0	15	20	A2	10	30
indomethacin	357.8	ESI+	358.2	139.1	25	25	A1	1	4
acetaminophen	151.2	ESI+	152.3	110.1	25	15	A2	20	60
carbamazepine	236.3	ESI+	237.1	194.1	15	20	A1	1	5
propranolol	259.3	ESI+	260.4	155.3	30	30	A2	10	30
atenolol	266.3	ESI+	267.0	145.0	30	25	A1	30	105
disopyramide	339.5	ESI+	340.4	239.3	20	20	A1	0.5	1
ifenprodil	325.4	ESI+	326.4	308.3	30	20	A2	0.5	1
erythromycin	733.9	ESI+	734.6	158.4	25	30	A2	1	5
clarithromycin	747.9	ESI+	749.0	158.0	25	35	A2	1	5
levofloxacin	361.4	ESI+	362.4	318.3	30	15	A2	5	20
fluconazole	306.3	ESI+	307.3	169.2	23	20	A2	5	15
triclosan	289.5	ESI−	287.1	35.0	15	12	A1	10	40

a) A1: 0.2 mM acetic acid/ammonium acetate in water, A2: 0.1 vol% formic acid in water. *b*) LOD: limit of detection, LOQ: limit of quantification.

centration (PEC) to Predicted No-Effect Environmental Concentration (PNEC).[3–5)] Therefore these targeted PPCPs were selected in the present study. All solvents used in the present study were used HPLC grade or residual pesticide test grade.

Sampling Site and Time and Sample Preparation —— Sewage water samples were collected directly from a manhole in Nagasaki city above a sewage pipe draining approximately 300 homes but no businesses. Samples were collected at the following times: 9:00, 10:00, 12:00, 20:00 and 23:00 in April 2005; 9:00, 11:00, 13:00, 15:00, 17:00, 19:00, 22:00, 1:00, 4:00 and 7:00 in August 2005, and 18:00, 23:00, 3:00, 7:00, 10:00 and 14:00 in December 2005. Each sample was immediately transported to the laboratory, and about 200 ml was passed through an Empore Disk (SDB-XD, 3 M Inc., St. Paul, MN, U.S.A.). Extraction was carried out three times using 5 ml of methanol solution. The eluate was concentrated using nitrogen gas and dissolved in 1 ml of water and methanol (1 : 1) solution and analyzed by HPLC/MS-MS. Recovery tests using Empore Disks showed that recovery was markedly low at pHs of about 2–3, but recovery percentages were stably high at pH of about 7. Since the pH of all sewage water samples in this study was 7–8, solid-phase extraction was carried out without adjusting pH.

Equipment —— HPLC was performed using Alliance 2695 (Waters, Milford, MA, U.S.A.) and Sun Fire C18 (2.1 × 50 mm, Waters) columns. As mobile phases, methanol and 0.2 mM acetic acid + ammonium acetate solution (A1) or 0.1% formic acid solution (A2) were used. Mobile phase selection was based on the detection sensitivity of target compounds. Flow rate of the mobile phase was set at 0.2 ml/min, and the injection volume was 3 μl. The linear gradient was held at 0% methanol for 3 min, increased to 50% over 5 min, increased to 90% over 5 min, and held for 5 min. Mass spectrometry was conducted using a Quattro micro tandem mass spectrometer (Micromass, Milford, MA,

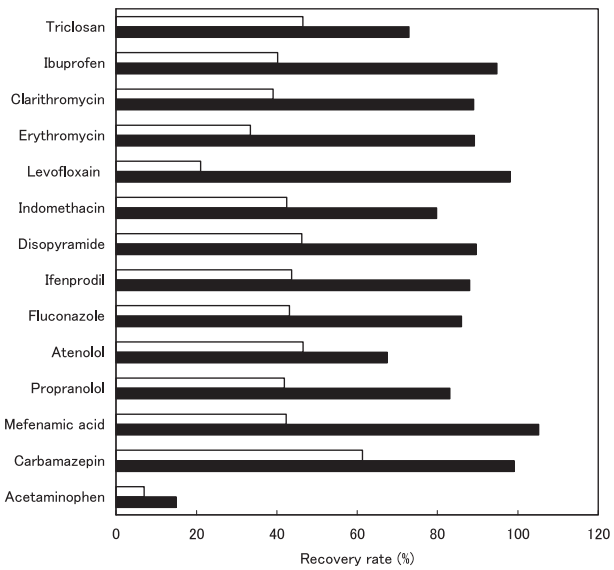

Fig. 1. Results of a Recovery Test Added with 10 μg of Each Compound

The white and black bars indicate the recovery rates to sewage water and pure water, respectively.

Table 2. Concentrations of PPCPs in Sewage Water Over Three Seasons Determined by HPLC/MS-MS

Compound	Concentrations of PPCPs (ng/l)										
	in April 2005					in December 2005					
	9:00	10:00	12:00	20:00	23:00	7:00	10:00	14:00	18:00	23:00	3:00
ibuprofen	27.9	23.8	53.8	14.8	5.95	668	1070	117	28.8	64.8	94.3
mefenamic acid	LOD	162	167	LOD	LOD	33.0	LOQ	LOQ	LOQ	LOD	175
indomethacin	207	22.5	7.73	9.38	8.6	197	84.9	136	21.4	42.5	32.9
acetaminophen	27.4	21.0	25.9	1.51	11.5	402	1080	603	140	256	7370
carbamazepine	90.7	91.4	11.7	11.8	6.82	61.7	353	LOQ	42.0	60.0	20.2
propranolol	LOD	LOD	LOD	LOD	LOD	LOD	LOD	LOD	LOD	LOD	LOD
atenolol	8.27	395	28.4	192	9.93	74.4	20.6	70.5	62.8	LOQ	79.7
disopyramide	11.6	265	LOD	22.2	4.17	129	99.3	178	55.8	51.9	24.4
ifenprodil	6.12	9.13	LOD	LOD	LOD	LOD	LOD	LOD	LOD	LOD	LOD
fluconazole	136	275	LOD	LOD	LOD	LOD	LOD	LOD	LOD	LOD	529
erythromycin	8.42	67.9	LOD	LOD	LOD	LOD	LOD	90.9	LOD	LOD	LOD
clarithromycin	2520	3090	79.6	585	285	1980	171	186	43.8	46.8	279
levofloxacin	101	452	360	617	406	3090	LOQ	LOQ	4260	508	1050
triclosan	1990	2280	1040	645	771	952	670	803	497	902	1350

Compound	Concentrations of PPCPs (ng/l)									
	in August 2005									
	7:00	9:00	11:00	13:00	15:00	17:00	19:00	22:00	1:00	4:00
ibuprofen	192	77.3	50.4	21.5	13.6	9.97	14.5	48.9	149	345
mefenamic acid	248	LOD	25.1	1.2	LOD	LOD	7.82	27.6	74.2	64.9
indomethacin	22.4	12.9	7.4	82.0	LOQ	10.1	275	33.8	91.9	31.9
acetaminophen	42.0	139	87.8	57.0	105	256	84.7	643	705	500
carbamazepine	10.8	LOQ	22.6	17.8	LOQ	LOQ	166	20.1	12.8	LOQ
propranolol	LOD	LOD	26.6	LOD	LOD	LOD	23.3	LOD	LOQ	LOQ
atenolol	596	15.6	26.5	26.1	28.2	11.3	37.5	112	133	88.0
disopyramide	29.1	304	886	569	62.7	196	15.7	86.5	90.2	47.3
ifenprodil	LOD	LOD	1.45	6.32	LOD	LOD	1.78	LOQ	LOD	LOD
fluconazole	LOD	LOD	LOD	73.4	LOD	236	120	LOD	255	2860
erythromycin	122	LOQ	29.8	34.0	LOQ	LOQ	58.9	LOD	LOD	7.92
clarithromycin	687	695	311	178	1430	687	1910	243	1100	248
levofloxacin	519	192	250	300	412	365	256	244	3800	994
triclosan	6920	6890	6660	4610	5410	4120	2780	3340	5240	3830

LOD: limit of detection, LOQ: limit of quantification.

U.S.A.). Table 1 shows the target compounds and measurement conditions. The limit of detection (LOD) and limit of quantification (LOQ) for the entire method were determined as signal-to-noise ratios (S/N) of 3 and 10, respectively. The S/N values were calculated by correlation with the sample concentration determined by standard addition.

RESULTS AND DISCUSSION

Figure 1 shows the results of a recovery test in which 10 μg of each target compound was added to pure water (n = 1) or sewage water (n = 1). For both water, the recovery rate for acetaminophen was very low, but the recovery rate for the other compounds in pure water was 88 ± 10% (mean ± S.D.). However, in sewage water, the recovery rate for all compounds except acetaminophen was about half at 42 ± 9%. Recovery rates have also been low in most previous studies[1,6,7] on PPCPs concentrations in sewage. This can be explained by matrix suppression. Previous studies have reported the matrix suppression with the analysis of PPCPs in water samples.[1,6,7] In addition, this is thought to be because sewage water contains various contaminants, and most PPCPs are amphoteric compounds, but details are unknown. However, in the present study, it was necessary to ascertain the concentration order of PPCPs in sewage water, and as a result, instead of measuring the recovery rate for each compound, the concentration of each compound was calculated

by the absolute calibration curve method.

Table 2 summarizes the concentrations of PPCPs in sewage water over three seasons. As shown in the table, detection rates were high for ibuprofen, indomethacin, acetaminophen, atenolol, disopyramide, clarithromycin, levofloxacin, and triclosan. In terms of diurnal changes, there were marked concentration changes at different times of day for most compounds. However, the concentration of triclosan decreased slightly during daytime hours due to higher flow rates; otherwise it mostly remained constant. The concentration of disopyramide fluctuated somewhat but tended to be higher during daytime hours. This might reflect times of dosage and excretion, but the details could not be clarified. In terms of seasonal changes, the concentration of triclosan was several times higher in summer when compared to the other seasons. This might reflect the use of products such as hand soap. In contrast, the concentrations of antipyretic analgesics such as ibuprofen and acetaminophen were several times higher in winter when compared to the other seasons, possibly because these drugs are used more frequently for cold in winter.

In conclusions, in order to gather basic data on the quantities of PPCPs in sewage water, samples were obtained from a sewage manhole collecting sewage from a purely residential area with a population of approximately 300 people, at different times of the day in three different seasons. Concentrations of PPCPs were measured by HPLC/MS-MS. With the exception of triclosan, marked diurnal fluctuations were apparent. For compounds such as disopyramide, nighttime concentrations were higher. Moreover, in terms of seasonal changes, the concentration of triclosan was higher in summer, and the concentrations of antipyretic analgesics were higher in winter. In the future, when analyzing the effects of PPCPs on wildlife, it will be important to consider seasonal changes in their concentrations.

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