Occurrence of Pharmaceutical and Personal Care Products (PPCPs) in Surface Water from Mankyung River, South Korea

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The present study demonstrates the occurrence of pharmaceuticals and personal care products (PPCPs) in surface water from the Mankyung River, South Korea. Samples collected at 5 Sites along the Mankyung River were assayed using a liquid chromatograph coupled with a tandem mass spectrometer (LC/MS/MS) for 13 PPCPs. Overall, 11 out of the 13 selected PPCPs, which span a range of therapeutic classes and one personal care product, were detected in surface water samples collected from the Mankyung River. The most prevalent contaminants were ibuprofen, with average concentrations ranging from not detected (ND) to 414 ng/l, followed by carbamazepine (ND-595 ng/l), atenolol (ND-690 ng/l), clarithromycin (ND-443 ng/l), mefenamic acid (ND-326 ng/l), erythromycin (ND-137 ng/l), fluconazole (ND-111 ng/l), levofloxacin (ND-87.4 ng/l), indomethacin (ND-33.5 ng/l), propranolol (ND-40.1 ng/l), ifenprodil (ND-35.4 ng/l), disopyramide (ND) and triclosan (ND). PPCP concentrations were highest in surface water samples collected downstream from a sewage treatment plant (STP), implying possibly insufficient removal efficiency of the PPCPs in the STP. Contamination by PPCPs such as ibuprofen, carbamazepine, atenolol, mefenamic acid and clarithromycin was high in the Mankyung River compared to concentrations in other countries.

Key words —— pharmaceuticals and personal care products, water pollution, Mankyung River

INTRODUCTION

Pollution of aquatic environments by pharmaceuticals and personal care products (PPCPs) is of great concern worldwide.[1–4] A wide variety of pharmaceutical pollutants have been investigated in previous studies, including antiepileptic, hormones, painkillers, contraceptives, anti-neoplastics, tranquilizers, lipid regulators, anti-inflammatories, antibiotics, contrast media, β-blockers, anticancer drugs, other cytotoxic compounds, antiphlogistics, and compounds responsible for regulating blood pressure.[5–11] These compounds are used as pharmaceutical ingredients in approximately 3000 different products licensed in the European Union (EU) to date.[9] Han *et al.*[12] reported concentrations of various pharmaceuticals in wastewater treatment plants (WWTP) influents and effluents from South Korea during their 2004 survey. For example, diclofenac (mean 2.59 μg/l), ibuprofen (mean 0.30 μg/l), carbamazepine (mean 1.84 μg/l) and salicylic acid (mean 23.92 μg/l) were detected at high concentrations in WWTP influents.

PPCPs are used in a wide variety of products for humans, veterinary medicine, agriculture and aquaculture,[13] and enter the environment via sewage treatment plants (STPs) and untreated domestic wastewater.[1,2] Recent studies have reported the occurrence of various PPCPs in surface, drinking and ground water, as well as soils and sediments, ranging in concentration from ng/l to μg/l in STP effluent and the aquatic environment.[2,3,8,9,12–16] Kolpin *et al.*[3] reported that tests for PPCPs conducted in 1999 and 2000 by the U.S. Geological Survey (USGS) in 139 streams of 30 states showed

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that PPCPs were found in 80% of the streams sampled. Although PPCPs have been developed to target specific metabolic pathways in humans and livestock, their mode of action in aquatic organisms, even at low concentrations, is still unknown in terms of the potential outcomes and effects.[1,17,18] Several studies have demonstrated that certain PPCPs are produced and used in such large quantities that the potential for affecting aquatic organisms is very high.[13] For example, our previous study has demonstrated that triclosan, an antibacterial agent, is quite highly toxic to aquatic animals (such as microalga, crustacean, and fish) and is particularly highly toxic (IC_{25} = 3.4 μg/l triclosan) to the green alga (*Selenastrum capricornutum*) used as a test organism.[19]

Most studies on the occurrence and fate of PPCPs have been conducted in Europe or the United States.[3,20] Although a previous study has demonstrated the occurrence of PPCPs in the Youngsan River[7] and WWTP of South Korea,[12] little is known about the current status of PPCP contamination in the aquatic environments of South Korea. Consequently, this study focused on the PPCP contamination in the aquatic environment of Saemangeum estuarine, South Korea.

The Saemangeum reclamation lies at the mouths of the Dongjin and Mankyung Rivers, on the coast of Jeollabuk-do. Construction of a 33 km long seawall has allowed the large-scale reclamation of the entire Saemangeum tidal flat (40100 ha) near Gunsan City, Iksan City, and Jeonju City. After the first plan of the Saemangeum reclamation was presented in 1989, building of the seawall was completed in April 2006, and according to the governmental plan the next stage of the landfill process will continue until 2011. The purpose of the Saemangeum project is to create croplands (28300 ha) and freshwater lakes (11800 ha). The area supports 158 species of fish, or 76.9 percent of all fish species in the Yellow Sea, with over 300 aquatic and plant species. In addition, it is a major stopover point for 20000 birds that annually migrate from Australia and New Zealand to East Asia. During any given year more than 500000 birds may be found there, including 30 species of waterbirds more than any other Site in Korea.

The Saemangeum tidal flat is relatively polluted by industrial wastes, livestock wastes, sewage and runoff from the Dongjin and Mankyung Rivers. The Mankyung River is, in particular, more heavily polluted by heavy metals, nitrogen and phosphorus than the Dongjin River.[21,22] In the Mankyung River, the various streams receive untreated municipal, industrial, livestock wastewaters and is a nonpoint pollution source from the Jeonju City, Wanju Gun and Iksan City. Therefore, it is an important area for studying the distribution characteristics of PPCPs in the aquatic environment. As part of a large effort to characterize the impact on the Mankyung River, the objective of our study was therefore to assess concentrations of 13 PPCPs in the surface waters at five different Sites along this, South Korean river. This work reports a comprehensive survey of PPCPs in the surface waters of the Mankyung River. The information on the distribution of PPCPs will be useful for managing pollutants, and evaluating and remediating the aquatic environment of South Korea.

MATERIALS AND METHODS

Study Area —— The Mankyung River is located in the province of Jeollabuk-do of South Korea (35°5′–35°56′N and longitude 126°35′–126°50′E; Fig. 1). Its total length is 77.4 km and the basin area is 1527 km.[2,22] The river has the Gosan stream as its origin, which is joined by the tributaries of the Jeonju and Iksan streams before it empties into the Yellow Sea. The annual average flow of Mankyung River is 780.5 million m^3/year, which is 31.4% of 2488 million m^3/year in Jeollabuk-do. Water usage in the river is divided between domestic water (17.9%), industrial water (11.1%), agricultural water (63%), and water used for environmental maintenance of the river (8%).[22–24] Generally, water quality in the Mankyung River is relatively good in the upper stream reaches, deteriorating markedly as the river flows through Jeonju City, Iksan City and Wanju Gun where the water becomes progressively more contaminated by influents containing industrial, agricultural and livestock wastewater. Site 1 is located downstream of municipal STP which is connected to a sewage system servicing Jeonju City (population: 0.65 million) on Jeonju stream. Site 2, which is surrounded by extensive agricultural land, the annual average flow rate of the Gosan stream is 259200 m^3/d. Site 3 is located downstream of the confluence of the tributaries on which Sites 1 and 2 are located. Site 4 is located downstream of a livestock wastewater treatment plant (LWTP), and Site 5 is located on the Mankyung River below the confluence of all of the rivers and has the additional

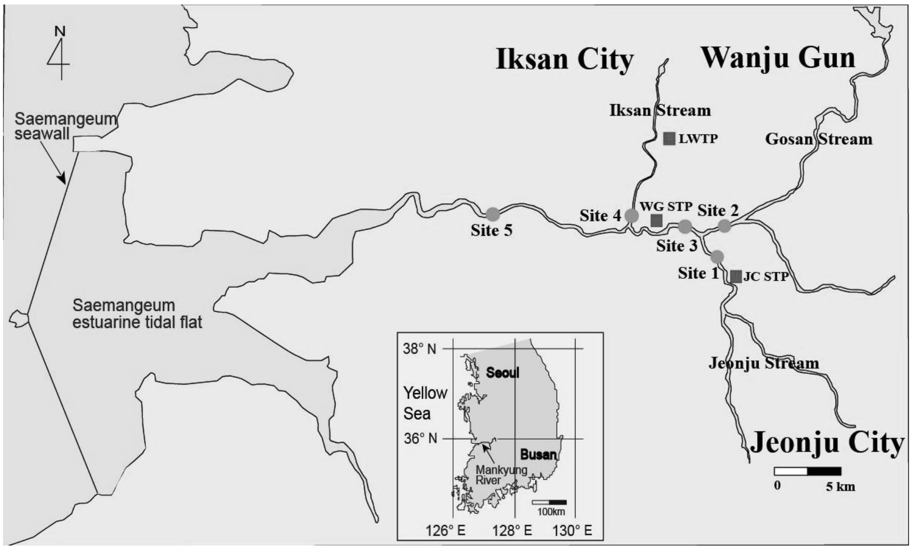

Fig. 1. Sampling Locations along the Mankyung River and Its Tributaries in South Korea

Table 1. CAS Number, Therapeutic Class, pKa, and LogK_{ow} for the Target PPCPs Selected for this Study

PPCP	CAS number	Therapeutic class	pKa[a]	LogK_{ow}
Ibuprofen	15687-27-1	Antipyretic analgesics	4.41	3.97[25]
Mefenamic acid	61-68-7	Antipyretic analgesics	3.73	5.12[25]
Indomethacin	53-86-1	Antipyretic analgesics	3.96	4.27[25]
Carbamazepine	298-46-4	Antiepileptic	13.94	2.47[25]
Propranolol	525-66-6	Antiarrhythmics	13.84	3.48[25]
Atenolol	29122-68-7	Antiarrhythmics	13.88	0.16[25]
Disopyramide	3737-09-5	Antiarrhythmics	15.40	0.66[26]
Ifenprodil	245-491-4	Agent to improve cerebral circulation and metabolism	9.99	4.25[a]
Fluconazole	86386-73-4	Antifungal agent	11.01	0.5[27]
Erythromycin	114-07-8	Antibiotics	13.09	3.06[25]
Clarithromycin	81103-11-9	Antibiotics	13.08	3.16[28]
Levofloxacin	100986-85-4	Synthetic antibacterial agent	5.23	0.28[29]
Triclosan	3380-34-5	Disinfectant	7.80	4.76[30]

CAS number, therapeutic class, pKa and LogK_{ow} of selected PPCPs were gleaned from the literature. *a*) Value calculated using Advanced Chemistry Development software.

impact of the STP at Wanju Gun.

Chemicals, Reagents and Apparatus —— Standard solutions for atenolol, fluconazole, ifenprodil, disopyramide, levofloxacin and clarithromycin were purchased from Wako Pure Chemical Industries, Co., Ltd., Tokyo, Japan. Propranolol, indomethacin, erythromycin and ibuprofen were purchased from Nacalai Tesque, Co., Ltd., Tokyo, Japan. Carbamazepine and triclosan were purchased from Tokyo Chemical Industry, Co., Ltd., Tokyo, Japan and mefenamic acid was purchased from Sigma-Aldrich, St. Louis, MO, U.S.A. The Chemical Abstracts Service (CAS) number, therapeutic class, pKa, and LogK_{ow} for the target PPCPs selected in this study are shown in Table 1. Empore™ High Performance Extraction Disks (SDB-XD) were purchased from 3 M Empore, Co., Ltd., St. Paul, MN, U.S.A. and glass fiber filters (GF/F, 0.47 mm) were purchased from Whatman, Maidstone, U.K.

Sample Analysis —— Water samples from the Mankyung River were collected in November of 2006. Samples were taken from 1 m below the surface and stored below 4°C until analysis. The samples were adjusted to pH 7 before storage because recovery percentages of each PPCP were stably high at pH of about 7, and analyzed for a variety of water quality parameters, including temperature, potential of hydrogen (pH), dissolved oxygen (DO; using Winkler method), chemical oxygen demand (COD; using $KMnO_4$ method), ammonium-nitrogen (NH_4^+-N; using indophenol blue method), nitrite-nitrogen (NO_2^--N; using diazotization method), nitrate-nitrogen (NO_3^--N; using Cd-Cu column reduction method), total nitrogen (TN; using semimicro Kjeldhal method), phosphate-phosphorus (PO_4^{3-}-P; using molybdenum blue method), total phosphate (TP; using potassium peroxydisulfate method), total suspended solids (TSS; using gravimetric method), volatile suspended solids (VSS; using gravimetric method), fixed suspended solids (FSS; using gravimetric method), chlorophyll-a (Chl-a; using acetone extraction and extinction method) were determined according to American Public Health Association (APHA, 1995) techniques.[31]

The concentrations of PPCPs in surface water were analyzed following the method described by Arizono and Takao.[5] Water samples were extracted by solid-phase extraction (SPE) using SDB-XD and GF/F preconditioned under vacuum using 5 ml methanol followed by 15 ml Milli-Q water to avoid dryness. Sample volumes of 1 l were percolated under vacuum at a flow rate of between 10–15 ml/min. The GF/F and SDB-XD were rinsed with 10 ml ultrapure water and dried by vacuum for 15 min to remove as much water as possible before extraction was performed five times using 5 ml of 100% methanol solution. After elution, the extract was transferred to 50 ml vials and evaporated to a final volume of 1 ml under a stream of nitrogen. Thirteen PPCPs were analyzed for all samples using liquid chromatography-tandem mass spectrometry (LC/MS/MS).

LC/MS/MS Instrumentation —— The LC/MS/MS system consisted of an integrated Waters high performance liquid chromatography (HPLC) system and a Micromass Quattro micro tandem mass spectrometer (Waters Corporation, Milford, MA, U.S.A.). Solid phase extraction of the samples was followed by LC/MS/MS analysis of the analytes performed using an electrospray (ESI) interface.

The HPLC system consisted of a Waters Alliance 2695 quarternary solvent delivery system (Waters Corporation), and included a vacuum degasser, a binary pump, a thermostatted autosampler and column oven compartment. A Waters SunFire™ C_{18} column (2.1×50 mm) with a 3.5 µm particle size was used with an injection volume of 3 µl. The mobile phase was 0.2 mM acetic acid/ammonium acetate in water (A1; for determining ibuprofen, indomethacin, carbamazepine, atenolol, disopyramide and triclosan) or 0.1% formic acid in water (A2; for determining mefenamic acid, propranolol, ifenprodil, fluconazole, erythromycin, clarithromycin and levofloxacin) starting with 10% methanol at a flow rate of 0.2 ml/min. The gradient was held at 10% methanol for 3 min, increased to 50% over 5 min, increased to 90% over 5 min, and held for 5 min.

LC/MS/MS conditions were as follows: 3.0 kV capillary voltage with source block and desolvation temperatures at 120 and 350°C, respectively. Desolvation and cone gas (N_2) flows were 350 1/hr and 50 1/hr, respectively, and the argon pressure in the collision gas was 4.5×10^{-3} mbar. The cone voltage and the collision energy parameters were optimized in the continuous flow mode for each PPCP.

Method Performance: Recovery —— Recovery of PPCPs in water samples was determined using different volumes of PPCP (0.5, 1, and 2 µg) spiked replicates ($n = 5$ as shown in Table 2) in 1 l samples of distilled or river water. The spiked volumes were 0.5 µg for mefenamic acid, disopyramide, ifenprodil, fluconazole, clarithromycin, levofloxacin and triclosan, 1.0 µg for indomethacin, atenolol and erythromycin, and 2.0 µg for ibuprofen, carbamazepine and propranolol. The limit of detection (LOD) and limit of quantification (LOQ) for the entire method was determined as signal-to-noise ratio (S/N) of 3 and 10, respectively. The S/N values were calculated by correlation with the sample concentration determined by standard addition. The recovery rates in distilled water ranged from 64 to 145% (mean 87.1%), while average recovery rates for all compounds in surface water was approximately 69.4% (range 32.1–110%, Table 2). This can be explained by matrix suppression. In addition, this is thought to be because river water contains various contaminants and most PPCPs are amphoteric compounds, although details are unknown. Recovery rates (ranging from 4.2 to 123%) in most previous studies on PPCP concentrations are low.[6,32]

RESULTS

Characteristics of Water Quality Parameters

A summary of the physical and chemical properties of the water quality parameters in the Mankyung River is shown in Table 3. The pH of all water samples was close to neutral, ranging from

Table 2. Limits of Detection (LOD) and Quantification (LOQ) and Recovery Rate (%) of PPCPs

PPCP	LOD (ng/l)	LOQ (ng/l)	Selected ions for MS quantification		Recovery (%)
			Precursor Ion (m/z)	Product Ion (m/z)	Surface water ($n = 5$)
Ibuprofen	5	15	205.4	161.3	78.1 ± 10.9
Mefenamic acid	10	30	241.3	224.0	74.5 ± 10.3
Indomethacin	1	4	358.2	139.11	35.7 ± 24.5
Carbamazepine	1	4	237.1	194.1	78.0 ± 5.3
Propranolol	10	30	260.4	155.3	73.1 ± 10.1
Atenolol	30	100	267.0	145.0	78.9 ± 15.5
Disopyramide	0.5	2	307.2	220.2	109.8 ± 12.7
Ifenprodil	0.5	2	326.4	308.3	71.4 ± 9.7
Fluconazole	5	15	307.3	169.2	78.9 ± 9.4
Erythromycin	1	4	734.6	158.4	79.7 ± 13.3
Clarithromycin	1	4	749.0	158.0	72.3 ± 10.7
Levofloxacin	5	15	362.4	318.3	32.1 ± 8.9
Triclosan	10	30	287.1	35.0	37.8 ± 27.2

Table 3. Surface Water Quality Parameters from the Mankyung River

Parameter	Site 1	Site 2	Site 3	Site 4	Site 5
Temperature (°C)	15.2	8.90	12.9	8.80	11.5
pH	6.89	7.02	6.98	7.14	6.98
DO (mg/l)	6.50	10.8	8.30	5.37	8.74
COD (mg/l)	16.1	3.23	9.18	12.4	8.41
NH_4^+-N (mg/l)	8.26	0.04	2.99	11.4	3.17
NO_2^--N (mg/l)	0.09	0.01	0.09	0.05	0.12
NO_3^--N (mg/l)	1.32	0.66	1.24	1.71	1.06
DIN (mg/l)	9.68	0.71	4.32	13.1	4.34
TN (mg/l)	28.7	6.98	7.34	40.1	13.5
PO_4^{3-}-P (mg/l)	0.31	0.01	0.38	0.26	0.20
TP (mg/l)	0.64	0.03	0.48	1.49	0.26
TSS (mg/l)	7.00	4.60	7.60	31.0	20.2
VSS (mg/l)	6.20	3.20	6.40	17.7	7.60
FSS (mg/l)	0.80	1.40	1.20	13.3	12.6
Chl-a (μg/l)	7.74	4.44	5.77	14.7	9.14

NH_4^+-N; ammonium-nitrogen, NO_2^--N; nitrite-nitrogen, NO_3^--N; nitrate-nitrogen, DIN: dissolved inorganic nitrogen (NH_4^+-N+NO_2^--N+NO_3^--N), PO_4^{3-}-P; phosphate-phosphorus.

pH 6.89 to 7.14. The DO concentrations ranged from 5.37 to 10.84 mg/l, with relatively low concentrations observed at Sites 1 and 4. The COD values ranged from 3.23 to 16.1 mg/l, with the COD at Site 1 being higher than at any other along the Mankyung River. The variations of the dissolved inorganic nitrogen (DIN) such as the summation of NH_4^+-N, NO_2^--N and NO_3^--N (0.71–13.1 mg/l) and TN (6.98–40.1 mg/l) concentrations in the river were generally similar, because these parameters depend on the nitrogen concentration. The mean DIN for all sample Sites along the Mankyung River, except at Site 2, was 78.5% NH_4^+-N, 1.50% NO_2^--N, and 20.00% NO_3^--N; that is, the main component of DIN was ammonium. The extremely high concentrations of NH_4^+-N in Sites 1 and 4 suggest possible contamination by untreated livestock or household wastewater. These Sites have severe eutrophication (algal growth) problems as is also shown by the high Chl-a concentrations. The PO_4^{3-}-P and TP concentrations ranged from 0.01 to 0.38 mg/l, and 0.03 to 1.49 mg/l, respectively, with the variation in TN and TP concentrations generally being similar.[24,31] Chl-a concentrations ranged from 4.44 to 14.7 mg/l and the Chl-a at Site 4 was higher than it was at all other Sites. Based on the findings of this research, the most significant contribution of pollution in the Mankyung River appears

Table 4. Concentrations of PPCPs in Surface Water

PPCP	Concentration (ng/l)				
	Site 1	Site 2	Site 3	Site 4	Site 5
Ibuprofen	336 ± 21	ND	160 ± 17	132 ± 15	414 ± 13
Mefenamic acid	326 ± 21	ND	174 ± 18	ND	89 ± 11
Indomethacin	33.5 ± 8	ND	20.7 ± 4	ND	18.0 ± 3
Carbamazepine	595 ± 14	ND	174 ± 25	29.9 ± 4	103 ± 7
Propranolol	40.1 ± 3	ND	22.5 ± 5	ND	ND
Atenolol	690 ± 26	ND	160 ± 19	ND	ND
Disopyramide	ND	ND	ND	ND	ND
Ifenprodil	ND	ND	35.4 ± 16	ND	ND
Fluconazole	111 ± 13	ND	61.7 ± 8	16.0 ± 2	42.1 ± 5
Erythromycin	137 ± 15	ND	75.6 ± 10	7.40 ± 2	39.4 ± 7
Clarithromycin	443 ± 14	ND	115 ± 7	ND	49.2 ± 5
Levofloxacin	87.4 ± 13	ND	52.0 ± 11	ND	ND
Triclosan	ND	ND	ND	ND	ND

ND: Not detectable (below the LOQ).

to be that of livestock wastewater from the Iksan stream.[23,33]

Concentrations of PPCPs

The concentrations of 13 PPCPs in surface water samples collected at 5 Sites along the Mankyung River in South Korea are presented in Table 4. Among the PPCPs analyzed, the concentrations of ibuprofen (< 15–414 ng/l; ND: not detectable; below the LOQ) were the highest, followed by carbamazepine (< 4–595 ng/l) and atenolol (< 100–690 ng/l). While most of the other PPCPs assayed were detected at various concentrations, disopyramid and triclosan were not detected at any of the Sites sampled. Of the 5 Sites sampled, the concentrations of PPCPs in the surface water below Site 1 located downstream of an STP on the Jeonju stream were the highest (Table 4).

DISCUSSION

We clarified the occurrence and potential sources of PPCP contaminants in the Mankyung River. Together with the contribution of the Iksan stream, this river flows into the Yellow Sea after the confluence of the Jeonju and Gosan streams. At Site 1 on the Jeonju stream (flow rate 293760 m^3/d), the high concentration of PPCPs and nutritive salts can be explained by contamination by domestic wastewater from 0.65 million people and STP effluent. A previous study has demonstrated that the flow rate to the Jeonju City STP was about 303000 m^3/d, and the plant served a population of 650000 inhabitants.[34] In addition to these high sewage services, the highest concentration of PPCPs detected in Site 1 may also be related to the removal efficiency of the PPCPs in the STP. Further research is required to clarify the concentrations of PPCPs in the STP influent and effluent. At Site 2 on the Gosan stream, the concentrations of nutritive salts and PPCPs were the lowest among the research Sites assayed. The water quality of Site 2 is assumed to be almost the same as the surface water on the upstream STP of Jeonju stream. At Site 3, immediately below the confluence of the Jeonju and Gosan streams, PPCPs and nutritive salts were diluted by the relatively clean water of the Gosan stream, decreasing the concentrations of these substances. At Site 4 on the Iksan stream, at a Site that was markedly influenced by water contaminated by livestock wastewater, the concentration of nutritive salts was the highest among those assayed. Since the PPCPs selected for this research are mainly used for humans, their concentrations are relatively low. At Site 5, which is influenced by STP effluents from Wanju Gun and is located below all of the other tributaries, the concentration of PPCPs and nutritive salts was high. The Jeonju City and Wanju Gun STPs, activated sludge, have a quite similar treatment process and discharge into the Jeonju stream and Mankyung River. Effluents consist of about 84% domestic wastewater, 15% industrial wastewater, and 1% livestock wastewater. The flow rate to the Jeonju City STP was about 303000 m^3/d, and the plant served a population of 650000 inhabitants.[34] The flow rate to the Wanju Gun STP was about

Table 5. Comparison of PPCP Concentrations (ng/l) Detected in Aquatic Environments Globally

Location	IBU	MEF	INDO	CBZ	PRO	AT	DISOP
Surface water in Korea	ND[a)]–414	ND–326	ND–33.5	ND–595	ND–40.1	ND–690	ND
Surface water in Korea[7)]	11–38	—	—	4.5–6.1	—	—	—
Surface water in UK[6)]	< 20–5044	< 50–366	—	—	< 10–215	—	—
Surface water in Romania[8)]	LOQ–115.2	—	—	LOQ[c)]–75.1	—	—	—
Surface water in Italy[4)]	20.0	—	—	175.3	—	241.1	—
Surface water in Italy[4)]	17.4	—	—	34.2	—	41.7	—
STP influent in Japan[5)]	339	157	45.1	9.17	1.93	17.9	78.5
STP influent in Germany[9)]	3400 ± 1700	—	—	2000 ± 1300	510 ± 350	2300 ± 2000	—
WWTP effluent in USA[10)]	250	—	—	—	—	—	—
WWTP effluent in Korea[7)]	10–137	—	—	73–729	—	—	—
STP effluent in Japan[5)]	36.1	75.3	102	NA	ND	18.9	298
STP effluent in Germany[9)]	130 ± 60	—	—	2100 ± 700	180 ± 20	360 ± 20	—
STP effluent in Italy[4)]	121.2	—	—	291.1	—	466.0	—
Location	**IFN**	**FCZ**	**EM**	**CAM**	**LVFX**	**TCS**	
Surface water in Korea	ND–35.4	ND–111	ND–137	ND–443	ND–87.4	ND	
Surface water in Korea[7)]	—	—	1.8–4.8	—	—	NA[b)]	
Surface water in UK[6)]	—	—	< 10–1022	—	—	—	
Surface water in Romania[8)]	—	—	—	—	—	LOQ–56.7	
Surface water in Italy[4)]	—	—	4.5	8.3	—	—	
Surface water in Italy[4)]	—	—	15.9	20.3	—	—	
STP influent in Japan[5)]	ND	NA	NA	206	186	254	
STP influent in Germany[9)]	—	—	830 ± 270	460 ± 100	—	—	
WWTP effluent in USA[10)]	—	—	—	—	—	250	
WWTP effluent in Korea[7)]	—	—	8.9–294	—	—	1.3–32	
STP effluent in Japan[5)]	ND	155	47.5	232	62.4	ND	
STP effluent in Germany[9)]	—	—	620 ± 440	210 ± 40	—	—	
STP effluent in Italy[4)]	—	—	47.4	18.1	—	—	

Note: IBU: Ibuprofen, MEF: Mefenamic acid, INDO: Indomethacin, CBZ: Carbamazepine, PRO: Propranolol, AT: Atenolol, DISOP: Disopyramide, IFN: Ifenprodil, FCZ: Fluconazole, EM: Erythromycin, CAM: Clarithromycin, LVFX: Levofloxacin, TCS: Triclosan, —: Not determined. *a*) ND: Not detectable. *b*) NA: Not applicable. *c*) LOQ: Limit of quantification.

32000 m^3/d, and the plant served a population of 80000 inhabitants.[34)] LWTP in Iksan City treats approximately 3100 m^3/d of livestock wastewater.[34)] Our findings indicate that PPCP contaminants can be explained by domestic wastewater and a non-point pollution source in Jeonju City and Wanju Gun.

These concentrations of PPCPs are comparable with previously reported data for surface water STP and WWTP samples (Table 5). Ibuprofen, mefenamic acid and indomethacin are well-known non-steroid anti-inflammatory drugs (NSAIDs) that are used in the treatment of headaches and pain, and that also exhibit anticarcinogenic effects on colon cancer.[35)] Koutsouba *et al.*[36)] reported that the annual production of ibuprofen is estimated at hundreds of tons worldwide. We do not have enough information to discuss whether the pollution of NSAIDs is related to the volume of consumption or sales of NSAIDs in South Korea. In addition, ibuprofen is also considered to be representative of the antirheumatic group of medicaments, and has previously been found in the Youngsan River in South Korea, sewage treatment work (STW) effluents, rivers in the U.K., and WWTP influents and effluents in Moenchaltorf, Uster and Maur in Switzerland.[6–8, 37)] In this study, ibuprofen was detected in the range from ND to 414.3 ng/l, which is similar to those reported by Yu *et al.*[10)] from the Back River wastewater treatment plant (BRWWTP) effluent in Baltimore, MD in the U.S.A. Similarly, ibuprofen has been detected in STP influent in Nagasaki City in Japan.[5)] Interestingly, a maximum ibuprofen concentration of 414 ng/l was observed at Site 5 in this study, which could be attributed to STP effluents from Wanju Gun and a non-point pollution source in the Mankyung River.

The PPCPs can be classified into two categories: whether or not chemicals are easily eliminated by treatment of STP. The elimination ability of PPCPs at their removal plant processes may be complicated; thus, the hydrolysis, oxidation, biodegradation and sorption ability is different for each STP for each treatment process employed. The nature of PPCPs is also considered to be an important factor. In the case of hydrophilic PPCPs such as ibuprofen, up to 90% of this compound is apparently removed.[2] Biodegradation of ibuprofen is predominant as compared with sorption. In addition, Bendz *et al.*[38] showed that removal rates of diclofenac, naproxen and triclosan were 22, 93 and 58%, respectively. Although there is no STP or WWTP around Site 5 in the Mankyung River, the concentration of ibuprofen on this Site is higher than the other research Sites. In a future study, it will be important to search for the unknown sewage point and/or hot spot of the high level of ibuprofen around Site 5. In addition, propranolol is excreted as the parent compound or as its metabolite.[39] The elimination rate for propranolol has been reported to be 96% and 32%, indicating that differences exist in the elimination efficiencies of STP (domestic wastewater) and WWTP (industrial wastewater) treatment plants.[2,39] Carbamazepine and its metabolites may be typical persistent compounds which are not degraded and adsorbed during wastewater treatment.[2] Some metabolites of PPCPs that are more stable than parent compounds may be produced during biotransformation. Miao *et al.*[40] reported that carbamazepine and all five metabolites were detected in STP influent and effluent samples. Only carbamazepine and 10,11-dihydro-10,11-dihydroxycarbamazepine were detected in the surface water sample. Notably, 10,11-dihydro-10,11-dihydroxycarbamazepine was detected at approximately 3 times higher concentrations than the parent drug, carbamazepine, in all of the aqueous samples. These metabolites can differ from the parent compound in terms of toxicology and environmental impact. It is reported that the amount of PPCPs in the effluent of the treatment processes can sometimes be higher than the amount in the influent.[41] For example, natural estrogens mainly occur in their conjugated form in urine, which, however, can be transformed back into the parent substances by microorganisms and enzymes in sewage plants. The enzymatic cleavage of the glucronide of carbamazepine increases the release of the parent compound in the treatment plant.[40] Therefore, regeneration of the metabolites into the original compounds during the treatment is suggested as one of the reasons for the higher metabolites.

To our knowledge, this is the first study on PPCP contamination in the Mankyung River, South Korea. The results of this study may provide useful information for the management of the aquatic environment of this river. Future studies are needed to clarify and identify metabolized PPCPs and their elimination efficiency of STP and LWTP in this area.

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REFERENCES

1) Hirsch, R., Ternes, T., Haberer, K. and Kratz, K. L. (1999) Occurrence of antibiotics in the aquatic environment. *Sci. Total Environ.*, **225**, 109–118.
2) Ternes, T. A. (1998) Occurrence of drugs in German sewage treatment plants and rivers. *Water Res.*, **32**, 3245–3260.
3) Kolpin, D. W., Furlong, E. T., Meyer, M. T., Thurman, E. M., Zaugg, S. D., Barber, L. B. and Buxton, H. T. (2002) Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999–2000: A national reconnaissance. *Environ. Sci. Technol.*, **36**, 1202–1211.
4) Zuccato, E., Calamari, D., Natangelo, M. and Fanelli, R. (2000) Presence of therapeutic drugs in the environment. *Lancet*, **355**, 1789–1790.
5) Arizono, K. and Takao, Y. (2006) The environmental pollution of pharmaceuticals and its ecotoxicological impacts. *Journal of Japan Society on Water Environment*, **29**, 16–20.
6) Ashton, D., Hilton, H. and Thomas, K. V. (2004) Investigation the environmental transport of human pharmaceuticals to streams in the United Kingdom. *Sci. Total Environ.*, **333**, 167–184.
7) Kim, S. D., Cho, J. W., Kim, I. S., Vanderford, B. J. and Snyder, S. A. (2007) Occurrence and removal of pharmaceuticals and endocrine disruptors in South Korean surface, drinking, and waste waters. *Water Res.*, **41**, 1013–1021.
8) Moldovan, Z. (2006) Occurrences of pharmaceutical and personal care products as micropollutants in rivers from Romania. *Chemosphere*, **64**, 1808–1817.
9) Ternes, T. A., Bonerz, M., Herrmann, N., Teiser, B. and Andersen, H. R. (2007) Irrigation of treated watewater in Braunschweig, Germany: An option to remove pharmaceuticals and musk fragrances. *Chemosphere*, **66**, 894–904.
10) Yu, J. T., Bouwer, E. J. and Coelhan, M. (2006) Occurrence and biodegradability studies of selected pharmaceuticals and personal care products

in sewage effluent. *Agricultural Water Management*, **86**, 72–80.

11) Zuccato, E., Castiglioni, S. and Fanelli, R. (2005) Identification of the pharmaceuticals for human use contamination the Italian aquatic environment. *J. Hazard. Mater.*, **122**, 205–209.

12) Han, G. H., Hur, H. G. and Kim, S. D. (2006) Ecotoxicological risk of pharmaceuticals from wastewater treatment plants in Korea: Occurrence and toxicity to *Daphnia magna. Environ. Toxicol. Chem.*, **25**, 265–271.

13) Laville, N., Aït-Aïssa, S., Gomez, E., Casellas, C. and Porcher, J. M. (2004) Effects of human pharmaceuticals on cytotoxicity, EROD activity and ROS production in fish hepatocytes. *Toxicology*, **196**, 41–55.

14) Lissemore, L., Hao, C., Yang, P., Sibley, P. K., Mabury, S. and Solomon, K. R. (2006) An exposure assessment for selected pharmaceuticals within a watershed in Southern Ontario. *Chemosphere*, **64**, 717–729.

15) Nakada, N., Komori, K., Suzuki, Y., Konishi, C., Houwa, I. and Tanaka, H. (2007) Occurrence of 70 pharmaceutical and personal care products in Tone River Basin in Japan. *Proc. 5th IWA Spec. Conf. Assess. Control Micropollut./Hazard. Subst. Water*: MICROPOL & ECOHAZARD; DECHEMA e. V., Frankfurt/Main, Germany, 57–62.

16) Stumpf, M., Ternes, T. A., Wilken, R. D., Rodrigues, S. V. and Baumann, W. (1999) Polar drug residues in sewage and natural waters in the state of Rio de Janeiro, Brazil. *Sci. Total Environ.*, **225**, 135–141.

17) Daughton, C. G. and Ternes, T. A. (1999) Pharmaceuticals and personal care products in the environment: agents of subtle change. *Environ. Health Perspect.*, **107**, 907–938.

18) Radi, A., ElRies, M. A. and Kandil, S. (2003) Electrochemical study of the interaction of levofloxacin with DNA. *Anal. Chim. Acta*, **495**, 61–67.

19) Tatarazako, N., Ishibashi, H., Teshima, K., Kishi, K. and Arizono, K. (2004) Effects of triclosan on various aquatic organisms. *Environ. Sci.*, **11**, 133–140.

20) Castiglioni, S., Bagnati, R., Fanelli, R., Pomati, F., Calamari, D. and Zuccato, E. (2006) Removal of pharmaceuticals in sewage treatment plants in Italy. *Environ. Sci. Tenchnol.*, **40**, 357–363.

21) Kim, J. G., You, S. J., Cho, E. I. and Ahn, W. S. (2003) Distribution characteristics of heavy metals for tidal flat sediments in the Saemankeum area. *Journal of the Korean Fisheries Society*, **36**, 55–61.

22) Yun, S. G., Lee, J. S., Jung, G. B., Kim, M. K., Kim, S. J., Koh, M. H. and Eom, K. C. (2002) Evaluation of water quality characteristics on tributaries of Mankyeong river. *Korean Journal of Environmental Agriculture*, **21**, 237–242.

23) Kim, J. G. and Kim, J. W. (2004) Evaluation of algal growth potential in the Mankyung River by MBOD method. *Journal of the Environmental Sciences*, **13**, 807–817.

24) Lee, K. B., Lee, D. B., Lee, S. B. and Kim, J. D. (1999) Change in agricultural irrigation water quality in Mankyeong river. *Korean Journal of Environmental Agriculture*, **18**, 6–10.

25) Gros, M., Petrović, M. and Barceló, D. (2006): Development of a multi-residue analytical methodology based on liquid chromatography-tandem mass spectrometry (LC-MS/MS) for screening and trace level determination of pharmaceuticals in surface and wastewaters. *Talanta*, **70**, 678–690.

26) Wakaumi, M., Tsuruoka, S., Sakamoto, K., Shigal, T. and Fujimura, A. (2005) Pilsicainide in breast milk from a mother: comparison with disopyramide and propafenone. *Br. J. Clin. Pharmacol.*, **59**, 120–122.

27) Jezequel, S. G. (1994) Fluconazole: Interspecies scaling and allometric relationship of pharmacokinetic properties. *J. Pharm. Pharmacol.*, **46**, 196–199.

28) McFarland, J. W., Berger, C. M., Froshauer, S. A., Hayashi, S. F., Hecker, S. J., Jaynes, B. H., Jefson, M. R., Kamicker, B. J., Lipinski, C. A., Lundy, K. M., Reese, C. P. and Vu, C. B. (1997) Quantitative structure-activity relationships among macrolide antibacterial agents: In vitro and in vivo potency against Pasteurella multocida. *J. Med. Chem.*, **40**, 1340–1346.

29) Ross, D. L., Elkinton, S. K. and Riley, C. M. (1992) Physicochemical properties of the fluoroquinolone antimicrobials. III. 1-Octanol/water partition coefficients and their relationships to structure. *Int. J. Pharm.*, **88**, 379–389.

30) Yoon, Y., Westerhoff, P., Snyder, S. A., Wert, E. C. and Yoon, J. (2007) Removal of endocrine disrupting compounds and pharmaceuticals by nanofiltration and ultrafiltration membranes. *Desalination*, **202**, 16–23.

31) APHA (American Public Health Association) (1995) *Standard methods for the examination of water and wastewater*, In: Eaton, A. D., Clesceri, L. S. Greenberg, A. E., editors. 19th ed., Washington, D.C., USA: APHA-AWWA-WEF.

32) Seino, A., Furusho, S. and Masunaga, S. (2004) Occurrence of pharmaceuticals used in human and veterinary medicine in aquatic environments in Japan. *Journal of Japan Society on Water Environment*, **27**,

685–691.
33) Moon, Y. H., Park, J. M., Son, J. G. and Kim, K. H. (2001) Change in water quality on upper stream of Mankyeong river. *Korean Journal of Environmental Agriculture*, **20**, 252–257.
34) Semangeum Ecology Information System (SEIS) (2003). Available from: http://www.smgeco.net
35) Logan, R. F., Little, J., Hawtin, P. G., Hardcastle, J. D. (1993) Effect of aspirin and nonsteroidal anti-inflammatory drugs on colorectal adenomas: case-control study of subjects participating in the Nottingham faecal occult blood screening programme. *BMJ*, **307**, 285–289.
36) Koutsouba, V., Heberer, T., Fuhrmann, B., Schmidt-Baumler, K., Tsipi, D. and Hiskia, A. (2003) Determination of polar pharmaceuticals in sewage water of Greece by gas chromatography-mass spectrometry. *Chemosphere*, **51**, 69–75.
37) Tixier, C., Singer, H. P., Oellers, S. and Müller, S. R. (2003) Occurrence and fate of carbamazepine, clofibric acid, diclofenac, ibuprofen, ketoprofen, and naproxen in surface waters. *Environ. Sci. Technol.*, **37**, 1061–1068.
38) Bendz, D., Paxéus, N. A., Ginn, T. R. and Loge, F. J. (2005) Occurrence and fate of pharmaceutically active compounds in the environment, a case study: Höje River in Sweden. *J. Hazard. Mater.*, **122**, 195–204.
39) Walle, T., Walle, U. K. and Olanoff, L. S. (1985) Quantitative account of propranolol metabolism in urine of normal man. *Drug Metab. Dispos.*, **13**, 204–209.
40) Miao, X.-S., Yang J.-J. and Metcalfe, C. D. (2005) Carbamazepine and its metabolites in wastewater and in biosolids in a municipal wastewater treatment plant. *Environ. Sci. Technol.*, **39**, 7469–7475.
41) Baronti, C., Curini, R., D'Ascenzo, G., Corcia, A. D., Centili, A. and Samperi, R. (2000) Monitoring natural and synthetic estrogen at activated sludge treatment plants and in a receiving river water. *Environ. Sci, Technol.*, **34**, 5059–5066.