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Removal and transformation of pharmaceuticals in wastewater treatment plants and constructed wetlands

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Abstract

Since trace organic compounds such as pharmaceuticals in surface water have been a relevant threat to drinking water supplies, in this study the removal of pharmaceuticals and transformation of pharmaceuticals into metabolites were investigated in the main sources of micropollutants such as wastewater treatment plants (WWTPs) and engineered constructed wetlands. Pharmaceuticals were effectively removed by different WWTP processes and wetlands. Pharmaceutical metabolites with relatively low log *D* value resulted in the low removal efficiencies compared to parent compounds with relatively high log *D* value, indicating the stability of metabolites. And the constructed wetlands fed with wastewater effluent were encouraged to prevent direct release of micropollutants into surface waters. Among various pharmaceuticals, different transformation pattern of ibuprofen was observed with significant formation of 1-hydroxy-ibuprofen during biological treatment in WWTP, indicating preferential biotransformation of ibuprofen. Lastly, transformation of pharmaceuticals depending on their structural position was investigated in terms of electron density, and the electron rich $C_1 = C_2$ bond of carbamazepine was revealed as an initial transformation position.

1 Introduction

For several decades, pharmaceuticals and personal care products (PPCPs) have been noticed as emerging problematic compounds (Ternes et al., 1998; Snyder et al., 2003). In order to reduce residual concentrations of PPCPs, various advance treatments have been studied by many research groups (Lee et al., 2010; Rosal et al., 2010 and many others). However, high levels of PPCPs are still detected in wastewater effluent, surface waters, and drinking waters (Kim et al., 2007; Lee et al., 2012; Yoon et al., 2010; Benotti et al., 2009). Since those trace organic compounds have been detected even in treated drinking waters by Benotti et al. (2009), control of micropollutants has been important

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especially in wastewater treatment plants, the main source of the micropollutants in the aquatic environments.

Meanwhile, constructed wetlands have been introduced as an alternative to wastewater treatment for micropollutant removal (Matamoros et al., 2006); furthermore, there have been a few reports focused on the relationship between log D and removal of PPCPs in wetland systems. In a previous study (Lee et al., 2011), removal efficiency in constructed wetlands was investigated using corresponding octanol-water partitioning coefficients of pharmaceuticals.

And few studies have been reported with regarding to behaviors of pharmaceutical metabolites in various environments (Stumpf et al., 1998; Quintana et al., 2005). The potential ecotoxicological effect of pharmaceutical metabolites is still not known, thus there is necessity to further study the fate of pharmaceutical metabolites in various wastewater treatment processes.

In this study, removal and transformation of pharmaceuticals has been investigated with regarding to physicochemical and structural properties of pharmaceuticals and their metabolites in various environments such as WWTPs and constructed wetlands receiving wastewater effluent.

2 Materials and methods

2.1 Target compounds

Various micropollutant compounds, including 9 pharmaceuticals, 11 selected metabolites, and 1 personal care product, were selected in this study. Acetaminophen (ACT), atenolol (ATN), carbamazepine (CBZ), diclofenac (DCF), glimepiride (GMP), ibuprofen (IBU), naproxen (NPX), O-desmethyl-naproxen (O-desmethyl-NPX), sulfamethoxazole (SMX), and tri(2-chloroethyl) phosphate (TCEP) were obtained from Sigma-Aldrich (St. Louis, MO, US). Caffeine (CAF) was purchased via Fluka Chemie GmbH (Buchs, Switzerland). 1-hydroxy ibuprofen (IBU-1OH), 2-hydroxy ibuprofen

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(IBU-2OH), ibuprofen carboxylic acid (IBU-CA), iopromide (IOP), and N-acetyl-sulfamethoxazole (N-acetyl-SMX), paraxanthine, paraxanthine-1-methyl-d3, 4-hydroxy diclofenac were purchased via Toronto Research Inc (Toronto, Canada). Authentic carbamazepine metabolites 10, 11-dihydro-10, 11-epoxy-carbamazepine (CBZ-EP), 2-hydroxy-carbamazepine (CBZ-2OH), 3-hydroxy-carbamazepine (CBZ-3OH), and 10, 11-dihydro-10-hydroxy-carbamazepine (CBZ-10OH) were provided from Norvatis Pharma AG (Basel, Switzerland). Carbamazepine-d_{10} and $^{13}C_1$-naproxen-d_3 were purchased from Cambridge Isotope Laboratories (Andover, MA, US). Atenolol-d_7 and diclofenac-d_4 were obtained from C/D/N Isotopes (Pointe-Claire, Canada). Ibuprofen-d_3, N^4-acetyl sulfamethoxazole-d_4, and sulfamethoxazole-d_4 were obtained from Toronto Research Inc (Toronto, Canada). HPLC grade methanol was obtained from J.T. Baker (Phillipsburg, NJ, US). Methyl *tert*-butyl ether (MTBE) and formic acid were obtained from Sigma-Aldrich (St. Louis, MO, US). Information of target compounds and their metabolites is listed in Table 1. The log K_{ow}, log D_{ow}, and pK_a for investigated compounds were calculated based on the molecular structures using ChemAxon Marvin Calulater Plugin. The log D_{ow} is a pH dependent log K_{ow} value and in this study log D at pH 7 was used.

2.2 Sample collection

In June 2010, water samples were collected from each process (influent and effluent of the various unit operations) in three different wastewater treatment plant. One is Gwangju primary municipal wastewater treatment plant, which is operated with the nitrogen and phosphorus removal treatment system (600 000 m^3 day^{-1}). Second sampling site was the Gwangju secondary municipal wastewater treatment plant, which had two different treatment trains (Conventional Activated Sludge and Modified Ludzack-Ettinger (MLE) process), having total capacity up to 120 000 m^3 day^{-1}. Additionally, water samples from both Damyang wastewater treatment plant and Damyang constructed wetlands were collected and studied. Damyang constructed wetlands connected to Damyang wastewater treatment plant is a free surface flow constructed wetland, which

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has two different ponds consisting of the *Aporus* pond followed by the *Typha* pond. The hydraulic retention time of wetlands is approximately 6 h and flow rate is 1800 m^3 day^{-1}. Every sample was spiked with a biocide sodium azide and ascorbic acids to quench any residual oxidant in the field.

2.3 SPE and LC-MS/MS analysis

After filtration using a glass fiber membrane filter, all analytes were extracted using an AutoTrace automated solid phase extraction (SPE) system (Caliper Corporation, Hopkington, MA), as depicted by Vanderford et al. (2006). Briefly, the 6 mL, 500 mg hydrophilic-lipophilic balance (HLB) glass cartridges (Waters Corporation, Milford, MA) were preconditioned in the following order: 5 mL of MTBE, 5 mL of methanol, and 5 mL of deionized water. In all, 500 mL of samples, spiked with the addition of standards for internal calibration, were loaded onto the cartridges at 15 mL min^{-1} in duplicate, after which the cartridges were rinsed with 5 mL of deionized pure water, and then dried with a steam of air for 50 min. The cartridges were eluted with 5 mL of methanol, followed by 5 mL of 1/9 (v/v) methanol/MTBE. The eluted solution was concentrated in a water bath at 40 °C with a gentle stream of air to a final volume of 500 µL, which was a concentration factor of 1000. The levels of pharmaceuticals and their metabolites were then measured using a Water 2695 Separations Module (Waters, Milford, MA, US) coupled with a Micromass Quattro Micro triple quadrupole tandem mass spectrometer (Micromass, Manchester, UK) in electrospray ionization mode (ESI). A 20 µL sample loop and 150 mm ×2.1 mm SunFire C18 column with a particle size of 3.5 µm (Waters, Milford, MA, US) was employed for analyte separation. A binary gradient, consisting of 0.1 % formic acid (eluent A) and 100 % acetonitrile (eluent B), was used at a flow rate of 0.2 ml min^{-1}. Selected PPCPs and their metabolites were analyzed using two different gradients. The gradient used for the PPCPs and most of the metabolites was as follows: gradient with 15 % of B was held for 4 min, increased linearly to 80 % for 6 min, held for 3 min with 80 % of B and then linearly increased to 100 % for 7 min. The gradient used for the carbamazepine metabolites was as follows: gradient with 10 % of

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B increased linearly to 40 % for 15 min, increased linearly to 90 % for 10 min, and held until 30 min (Kang et al., 2008). A 5 min equilibration step with gradient of 10 % B was used at the beginning of each run. Detail LC-MS/MS analysis condition and analytical parameters of target compounds are shown in Table 2.

2.4 Molecular orbital calculations

Molecular orbital were calculated as single determinant (Hartree–Fock) for optimization bearing the minimum energy obtained at the AM1 level. All semi-empirical calculations to obtain the point charge and electron density for pharmaceuticals and metabolites were performed in MO-G with a SCIGRESS package version 7.7 (Fujitsu Co. Ltd.) (Watanabe et al., 2003).

3 Results and discussion

3.1 Removal of pharmaceuticals and personal care products in WWTPs and wetlands

Removal of PPCPs in municipal wastewater treatment plants and constructed wetlands were investigated and summarized in Table 3. Gwangju WWTP is a major source, releasing tons of micropollutants into the Yeongsan River, and the concentrations of PPCPs in Gwangju WWTPs ($\sim \mu g\,L^{-1}$) were generally much higher than in Damyang WWTP ($\sim ng\,L^{-1}$), presumably resulting from the dense population in the Gwangju area.

Particularly, high concentrations of caffeine and acetaminophen in WWTP influents reflect frequent use and ingestion of those compounds in this urban area. Most of PPCPs exhibited high removal efficiency (> 90 %) during the WWTPs processes, except for carbamazepine removal in Gwangju secondary WWTP (removal efficiency at 74 %). After discharge of WWTP effluent into connected constructed wetlands, levels of some PPCPs (carbamazepine, sulfamethoxaolze, diclofenac, and TCEP) decreased

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slightly. This result indicates that operation of wastewater stabilization ponds or wetlands would be helpful to prevent the release of micropollutants into surface water. Our research group has previously studied the Damyang constructed wetlands with respect to the control of organic micropollutants, and reported the efficiency of wetland treatments depending on the wetland characteristics and properties of micropollutants (Park et al., 2009). Many other studies have also supported the necessity of additional wetland treatments for micropollutants control (Matamoros and Bayona, 2006; Conkle et al., 2008).

3.2 Transformation of pharmaceuticals and formation of metabolites in WWTPs

Table 4 shows occurrence of parent pharmaceuticals and their metabolites in WWTPs and wetlands system. In the WWTPs influent, most metabolites were detected at high levels of concentration with a range of 100–10 000 ng L^{-1} compared to WWTP effluents, indicating a dominant transformation pathway of metabolite resulting from human rather than microbial transformation. However, after passing the WWTPs, concentrations of most metabolites were observed higher than that of parent compounds, indicating the structural stability of the metabolites during the WWTP process relative to their parent compounds. The stability of metabolites may be related to the difference of the log D value between parent pharmaceutical compounds and pharmaceutical metabolites. As pharmaceuticals transformed into their metabolites, their log D value at pH 7 slightly decreased (Table 1). Considering the dominant removal mechanism of micropollutants in the WWTP process (i.e., sorption and biodegradation), the decrease of log D may result in the reduction of sorption of pharmaceutical metabolites on the sludge surface. Consequently, pharmaceutical metabolites would be detected at higher levels than parent compounds in WWTP effluents.

In the case of sulfamethoxazole metabolite – even though the concentrations of N-acetyl-sulfamethoxazole were low enough in wastewater effluents – by considering retransformation of acetylated metabolite back into its parent compound, the N-acetyl-sulfamethoxazole should be assumed to be a pharmaceutically active

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parent compound (Göbel et al., 2005). And based on this, monitoring of N-acetyl-sulfamethoxazole is important and necessary for the effective control of micropollutants in an aquatic environment.

During the engineered constructed wetland treatments, there was no specific change of pharmaceutical metabolites in exception with ibuprofen metabolites. As can be seen in Fig. 1, ibuprofen was differently transformed depending on the treatment process. In WWTPs influent, 2-hydroxy ibuprofen, the well-known human metabolite of ibuprofen, was dominant, whereas after the activated sludge treatment, concentrations of 1-hydroxy ibuprofen indicate the highest level in all WWTPs and wetlands. Significant formation of 1-hydroxy ibuprofen in WWTPs might be possibly explained by preferential microbial metabolism in the activated sludge treatment process. In the additional experimental results conducted in river waters, a completely different composition of ibuprofen metabolites was observed. Over all, 2-hydroxy-ibuprofen was found to be dominant in both river waters, Yeongsan River and Seomjin River (data are not shown). This might infer that 2-hydroxy ibuprofen is much more persistent and stable than 1-hydroxy ibuprofen and even than parent compound, ibuprofen, as previously mentioned by Weigel et al. (2004).

In contrast, carbamazepine did not exhibit any change in transformation behavior during WWTPs and wetland treatments (Fig. 2). All the selected carbamazepine metabolites, 10,11-epoxy-carbamazepine, 2-hydroxy-carbamazepine, 3-hydroxy-carbamazepine and 10-hydroxy-carbamazepine was detected in influents, effluents of WWTPs and wetlands. Even though the levels of 10,11-epoxy-carbamazepine was low, the eco-toxicological effect of CBZ-EP on the environment is worthy of further examination due to its pharmaceutically active property like its parent compound, carbamazepine. The most dominant carbamazepine metabolite was 10-hydroxy-carbamazepine. The predominant formation of CBZ-10OH might be due to the different distribution of electron density of atoms in carbamazepine.

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3.3 Effect of electron density on transformation of carbamazepine into metabolites

In previous studies, electron density distribution of chemicals has been used to find the initial positions of OH radical attack in oxidation (Watanabe et al., 2003; Jung et al., 2010; Heimstad et al., 2009). A higher electron density indicates more electrons in the bonds, resulting in electrophilic reaction (Horikoshi et al., 2004; Kaneco et al., 2006). In this study, the electron density of pharmaceuticals was examined to find the initial transformation position in various transformation mechanisms including biological process and photochemical oxidations. In a previous study, Park et al. (2009) suggested that the hydrolysis reaction at the amide and urea functional groups may lead to the biological transformation of carbamazepine. Frontier electron density of carbamazepine calculated by MOPAC, Scigress software is shown in Table 5. Radical frontier density, the averaged value of nucleophilic frontier density and electrophilic frontier density, are used in this study. Based on the electron density of carbamazepine, the carbaon bonds between C_1 and C_2 showed the largest frontier electron density (0.208 and 0.214, respectively). This electron rich carbon bond of the olefin structure may provide the initial position of oxidation. Prevalent occurrence of specific carbamazepine metabolites such as CBZ-EP, CBZ-10OH, and CBZ-DiOH in environment are presumably related with this oxidation pathway. Unfortunately, with other metabolites it was difficult to find a relationship between transformation and electron density. However, electron density of chemicals is still believed to be a key parameter to elucidate unknown pathway in various processes, especially in the oxidation process.

4 Conclusions

Removal and transformation of pharmaceuticals in WWTPs and constructed wetlands were extensively investigated in this study. Pharmaceuticals were effectively removed by different WWTP processes and wetlands. From this study, the additional operation

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of wastewater management wetlands was encouraged to prevent direct discharge of micropollutants into surface waters. And additionally, pharmaceutical metabolites were found to be more stable than the parent compounds during WWTP processes due to the lower log *D* value of metabolites than in parent compounds. Different transformation patterns of pharmaceuticals were also observed, especially in transformation of ibuprofen. Furthermore, 1-hydroxy ibuprofen was dominantly formed during biological treatment in WWTP, indicating preferential biotransformation of ibuprofen. Lastly, the electron density of carbamazepine was examined to elucidate the transformation pathway. The electron rich $C_1 = C_2$ bond in olefin structure of carbamazepine was revealed as an initial transformation position.

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Table 1. Tested parent compounds and metabolites.

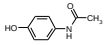
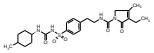
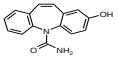
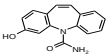
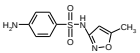
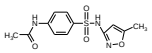
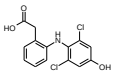
Analytes	Uses	Structure	pK_a [a]	$logK_{ow}$ [a]	logD [a] at pH7
Acetaminophen	Analgesic		9.46	0.91	0.91
Glimepiride	Anticholesterol		4.32	3.12	2.18
tri(2-chloroethyl) phosphate (TCEP)	Flame retardant		N.E	2.11	2.11
Carbamazepine (CBZ)	Anticonvulsant		N.E	2.77	2.77
CBZ-EP	Carbamazepine metabolite		N.E.	1.97	1.97
CBZ-2OH	Carbamazepine metabolite		9.3	2.66	2.66
CBZ-3OH	Carbamazepine metabolite		9.46	2.66	2.66
CBZ-10OH	Carbamazepine metabolite		14.1	1.73	1.73
Sulfamethoxazole	Antibiotic		6.16	0.79	0.14
N^4-acetylsulfamethoxazole	Sulfamethoxazole metabolite		5.88	0.86	0.1
Diclofenac	Analgesic		4.00	4.26	0.96
4-hydroxyl-diclofenac	Diclofenac metabolite		3.76, 8.61	3.96	0.89

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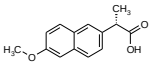
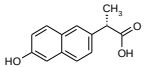
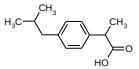
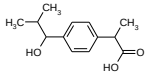
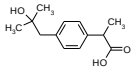
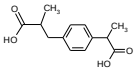
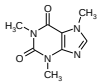
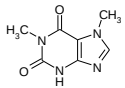
Table 1. Continued.

Naproxen	Analgesic		4.19	2.99	0.25
O-desmethyl-naproxen	Naproxen metabolite		4.34, 9.78	3.9	0.23
Ibuprofen	Analgesic		4.85	3.84	1.71
1-hydroxyl-ibuprofen	Ibuprofen metabolite		4.90	2.85	0.77
2-hydroxyl-ibuprofen	Ibuprofen metabolite		4.63	2.08	0.03
Ibuprofen carboxylic acid	Ibuprofen metabolite		3.97, 4.77	2.78	-2.36
Caffeine	Stimulant		N.E	-0.55	-0.55
Paraxanthine	Caffeine metabolite		10.76	0.24	0.24

[a] log P, log D, and pK_a value were calculated from the Software Calculator Plugins.
[b] N.E: nonexistent at pH range 1–14.

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Table 2. Analytical parameters of selected compounds (MDL: method detection limit; RL: reporting limit).

Compound	Retention time (min)	Cone voltage (V)	Collision energy (eV)	Parent ion (m/z)	Daughter ion (m/z)	MDL ($ng\,L^{-1}$)	RL ($ng\,L^{-1}$)
ESI negative							
Diclofenac	15.53	15	10	294	249	1.3	3.9
Diclofenac-d_4	11.23	15	12	298	254		
4-OH-DCF	13.70	20	12	310	266	5.1	15.3
Ibuprofen	15.70	15	8	205	161	1.2	3.6
Ibuprofen-d_3	11.63	15	8	208	164		
IBU-1OH	12.87	15	7	221	177	5.8	17.5
IBU-2OH	12.23	17	7	221	177	0.9	2.7
IBU-CA	12.27	12	5	235	191	2.3	6.8
Naproxen	9.84	10	8	229	185	3.3	10.0
Naproxen-d_3	9.83	10	6	233	189		
O-desmethyl-NPX	8.10	15	12	215	171	1.2	3.5
N-acetyl-SMZ	7.71	30	13	294	198	0.9	2.7
TCEP	9.12	30	16	285	161	7.9	23.8
ESI positive							
Acetaminophen	3.98	28	17	152	110	0.5	1.5
Acetaminophen-d_4	3.98	28	17	156	114		
Glimepiride	11.34	28	13	491	352	1.5	4.6
Sulfamethoxazole	7.83	30	18	254	156	0.6	1.7
Sulfamethoxazole-d_4	7.80	25	15	258	160		
Caffeine	6.11	35	20	195	138	1.5	4.6
Paraxanthine	2.72	30	22	181	124	9.3	27.9
Paraxanthine-d_3	2.72	30	22	184	124		
Carbamazepine	19.31	35	18	237	194	0.7	2.1
Carbamazepine-d_{10}	8.74	35	18	247	204		
CBZ-EP	15.64	28	24	253	180	1.2	3.6
CBZ-2OH	14.34	35	20	253	210	13.0	3.9
CBZ-3OH	15.78	35	20	253	210	1.5	4.5
CBZ-10OH	13.63	30	20	255	194	0.2	0.5

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Table 3. Concentrations of selected PPCPs in WWTPs and wetlands.

PPCPs	Gwangju Primary WWTP		Gwangju Secondary WWTP		Damyang WWTP and Constructed wetlands				
	WWTP influent ($ng\,L^{-1}$)	WWTP effluent ($ng\,L^{-1}$)	WWTP influent ($ng\,L^{-1}$)	WWTP effluent ($ng\,L^{-1}$)	WWTP influent ($ng\,L^{-1}$)	WWTP effluent ($ng\,L^{-1}$)	Acorus wetland ($ng\,L^{-1}$)	Typha wetland ($ng\,L^{-1}$)	Wetland effluent ($ng\,L^{-1}$)
Caffeine	72 471.2	< 4.6	45 457.0	1857.8	36 880.6	< 4.6	< 4.6	47.0	< 4.6
Carbamazepine	2085.4	108.3	1668.8	362.8	844.5	417.2	387.1	161.4	268.3
Sulfamethoxazole	6048.6	88.8	8092.9	70.7	409.7	27.4	17.9	7.4	17.4
Acetaminophen	162 159.9	1705.8	227 705.4	180.5	194 586.8	189.7	354.8	549.5	349.6
Ibuprofen	2626.0	< 3.6	4576.5	166.6	1645.3	17.9	43.2	52.9	47.2
Naproxen	1140.5	< 10.0	1778.5	10.7	203.5	< 10.0	11.4	< 10.0	< 10.0
Diclofenac	2673.5	111.7	2702.8	< 3.8	150.5	19.8	20.15	< 3.8	8.9
Glimepiride	18 895.3	197.4	40 338.6	86.6	36.8	12.3	11.3	< 4.6	14.4
TCEP	6011.8	320.3	4774.7	< 23.8	2608	340.6	277.85	186.35	268.4

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Table 4. Concentrations of parent pharmaceuticals and their metabolites in WWTPs and wetlands.

Parent compounds and their metabolites	Gwangju Primary WWTP		Gwangju Secondary WWTP		Damyang WWTP and Constructed wetlands				
	WWTP influent ($ng\,L^{-1}$)	WWTP effluent ($ng\,L^{-1}$)	WWTP influent ($ng\,L^{-1}$)	WWTP effluent ($ng\,L^{-1}$)	WWTP influent ($ng\,L^{-1}$)	WWTP effluent ($ng\,L^{-1}$)	Acorus wetland ($ng\,L^{-1}$)	Typha wetland ($ng\,L^{-1}$)	Wetland effluent ($ng\,L^{-1}$)
Caffeine	72 471.2	< 4.6	45 457.0	< 4.6	36 880.6	< 4.6	< 4.6	47.0	< 4.6
Paraxanthine	8215.3	33.9	10 442.1	< 27.9	3222.3	< 27.9	< 27.9	< 27.9	< 27.9
Sulfamethoxazole	6048.6	88.8	8092.9	166.6	409.7	27.4	17.9	7.4	17.4
N-acetyl-SMZ	5224.8	64.5	6224.2	72.4	152.6	4.9	< 2.7	< 2.7	5.3
Naproxen	1140.5	< 10.0	1778.5	10.7	203.5	< 10.0	11.4	< 10.0	< 10.0
O-desmethyl-NPX	191.5	31.7	125.0	31.1	245.0	9.3	< 3.5	< 3.5	7.75
Diclofenac	2673.5	111.7	2702.8	86.6	150.5	19.8	20.15	< 3.8	8.9
4-OH-DCF	530.6	582.1	396.0	504.6	212.0	40.2	21.15	< 15.3	< 15.3

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Table 5. Calculations of frontier electron density for carbamazepine.

Atom List	HOMO Density	Nucleophilic Frontier Density	Electrophilic Frontier Density	Radical Frontier Density	LUMO Density
C_1	0.148	0.202	0.215	0.208	0.131
C_2	0.119	0.252	0.175	0.214	0.169
C_3	0.064	0.222	0.108	0.165	0.136
C_4	0.118	0.113	0.184	0.148	0.057
C_5	0.046	0.201	0.088	0.145	0.090
C_6	0.067	0.113	0.136	0.124	0.049
N_7	0.074	0.003	0.211	0.107	0.000
C_8	0.039	0.141	0.080	0.111	0.054
C_9	0.010	0.117	0.036	0.076	0.030
C_{10}	0.068	0.214	0.111	0.163	0.133
C_{11}	0.012	0.088	0.044	0.066	0.013
C_{12}	0.046	0.094	0.117	0.105	0.047
C_{13}	0.024	0.048	0.076	0.062	0.007
C_{14}	0.111	0.129	0.173	0.151	0.072
C_{15}	0.016	0.043	0.078	0.060	0.010
C_{16}	0.012	0.010	0.021	0.016	0.000
N_{17}	0.007	0.002	0.072	0.037	0.000
O_{18}	0.018	0.002	0.064	0.033	0.000
H_{19}	0.000	0.001	0.001	0.001	0.000
H_{20}	0.000	0.000	0.001	0.001	0.000
H_{21}	0.001	0.002	0.002	0.002	0.001
H_{22}	0.002	0.001	0.003	0.002	0.000

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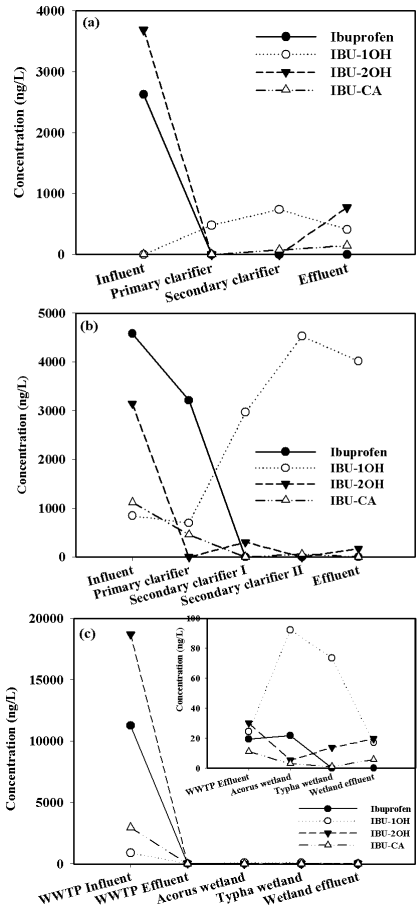

Fig. 1. Transformation of ibuprofen in different WWTPs system: **(a)** Gwangju primary WWTP, **(b)** Gwangju secondary WWTP, **(c)** Damyang WWTP and constructed wetlands.

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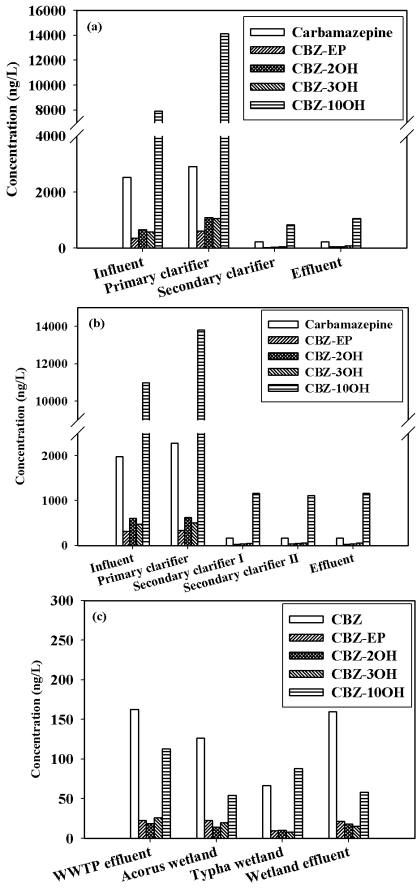

Fig. 2. Distribution of carbamazepine metabolites in different WWTPs system: **(a)** Gwangju primary WWTP, **(b)** Gwangju secondary WWTP, **(c)** Damyang WWTP and constructed wetlands.

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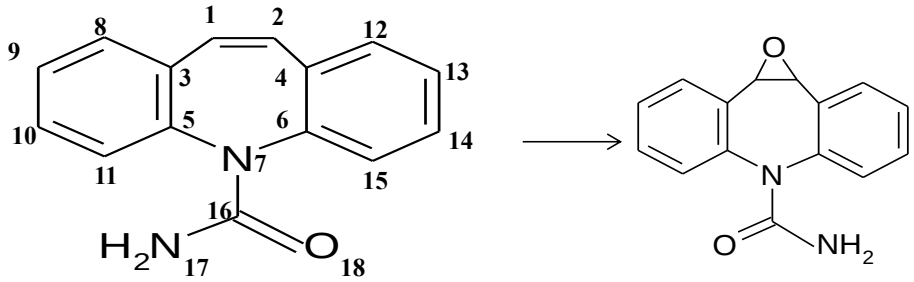

Fig. 3. Structure of carbamazepine.

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