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Occurrence Assessment of Pharmaceuticals in Various Sewage Treatment Plants and Effluent-Receiving Streams in Korea

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Abstract: The occurrence of micropollutants, including pharmaceuticals, personal care products, pesticides, and hormones in various aquatic ecosystems is a matter of grave concern due to their possible repercussions on human and wildlife endocrine systems. The wastewater containing pharmaceuticals from various sites is usually introduced to sewage treatment plants (STPs); therefore, monitoring of pharmaceuticals in STPs is crucial. In this study, we determined the occurrence of 58 pharmaceuticals in the influent and effluent of 13 STPs based on regional and linked wastewater differences and investigated their removal rates. Furthermore, we assessed the contribution rates of some STP effluents on pharmaceutical concentration in the upstream and downstream areas of the discharge source. Different kinds of pharmaceuticals were measured in the STPs. The top five pharmaceuticals with high concentrations in the influent of each STP were similar due to the dominance of domestic sewage in the influent. The average concentration of acetaminophen, caffeine, acetylsalicylic acid, naproxen, and ibuprofen in the influent of the STPs was higher than that of other pharmaceuticals, and their removal was 94–100%. In contrast, iopamidol, cimetidine, diphenhydramine, and carbamazepine showed a high average concentration in the effluent. The monitoring results of nine streams near STPs indicated that the effluent could contribute to the increase in the types of pharmaceuticals in the receiving streams. The detected pharmaceuticals' types were 9–29 and 17–33 in the upstream and downstream areas, respectively, of STP discharge channels. Based on flowrate data, the contribution rate of the STP effluent on the stream was −69–326%.

Keywords: pharmaceutical; wastewater treatment plant; effect assessment; receiving streams

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1. Introduction

The occurrence of micropollutants in various aquatic ecosystems is a matter of grave concern due to their possible repercussions on human and wildlife endocrine systems. With the growing interest in their effects on the human body and ecosystems, their occurrence and behavior in various water environments are being investigated [1,2]. The micropollutants include household chemical products, such as pharmaceuticals, cosmetics, antimicrobials, pesticides, and hormones [3].

Among them, the production and consumption of pharmaceuticals used for the treatment of various diseases and the prevention of waterborne diseases are increasing globally. They are usually introduced to sewage treatment plants (STPs) through various discharge sources, including households, hospitals, and industries. Because pharmaceuticals have a wide range of applications, regional variation in pharmaceuticals' occurrence patterns can be observed. For instance, pharmaceuticals such as acetaminophen, caffeine, and ibuprofen are frequently detected with a higher concentration in the influent of STPs in North America, Europe, and Asia. In contrast, a higher concentration of naproxen and triclosan in North America [4–6] ciprofloxacin and gemfibrozil in Europe [7,8] cetylsalicylic acid, chlortetracycline, cimetidine, and iopromide in Asia [9–12] were also reported, respectively.

Meanwhile, some pharmaceuticals having complex chemical structures and physicochemical properties may be discharged from STPs without being treated [13]. The untreated pharmaceuticals can be a trigger for the proliferation of pharmaceutical-resistant bacteria which pose a potential risk to mankind [14,15]. Furthermore, residual pharmaceuticals detected in aquatic environments are mainly caused by STP effluents [16,17]. Therefore, it is necessary to identify the pollution status and establish management measures through the continuous monitoring of STPs' effluents and effluent-receiving streams.

In this study, we investigated the occurrence of 58 pharmaceuticals in the influents and effluents of 13 full-scale STPs. Moreover, we also assessed the pharmaceuticals' occurrence in receiving streams located nearby the discharge sources of the STPs.

2. Materials and Methods

2.1. Description of Target STPs

To assess the occurrence of pharmaceuticals in influent, linked wastewater, effluent, upstream, and downstream of STPs, we selected 13 full-scale STPs. The 5 full-scale STPs and the other 7 STPs were selected for the regional feature effect and for linked wastewater effects on pharmaceuticals' concentrations, respectively. The STPs were located in the Chungcheongnam-do, Chungcheongbuk-do, Gyeonggi-do, Gyeongsangbuk-do, and Jeollabuk-do provinces in Korea. The specifications of the STPs are summarized in Table 1. We conducted four sampling campaigns (spring [April], summer [July], autumn [September], and winter [November]) using a grab sampling method. We collected 250 mL of each sample (domestic sewage, linked wastewater, mixture of sewage and linked wastewater, and effluent) with a stainless bowl. The collected samples were transferred immediately into amber bottles and stored at 4 °C.

Table 1. Specifications of selected sewage treatment plants (STPs).

STP	Capacity (m^3/d)	Process	Regional Feature	Linked Wastewater		
				Flowrate (m^3/d)	Percentage (%)	Wastewater Type
1	22,000	HDF [1]	Urban and rural complex area	-	-	-
2	17,000	HDF [1]	Urban and rural complex area	-	-	-
3	47,000	Bio-SAC	Urban	-	-	-
4	1500	SMMIAR [2]	-	124.6	14.7	Industrial
5	25,000	Activated sludge, DNR [3]	-	1916.6	8.9	Industrial
6	12,900	HDF [1]	-	163.7	1.3	Livestock
7	10,000	NPR [4]	-	315.7	4.0	Livestock
8	30,000	SDPR [5]	-	296	1.1	Leachate
9	2000	DeNiPho	-	59.6	2.8	Leachate
10	16,000	CSBR [6]	-	209.9	2.3	Food waste
11	3000	DeNiPho	-	68.2	2.5	Food waste
12	200	KSBNR [7]	Rural	-	-	-
13	300	CF-SBR [8]	Rural	-	-	-

Notes: 1: Hanwha dynamic flow. 2: Submerged moving media intermittent aeration reactor. 3: Daewoo nutrient removal. 4: Nitrogen and phosphorus removal (with moving media). 5: SK denitrifying phosphorus removal. 6: Constant level and continuous flow sequencing batch reactor. 7: Kist Shinwon biological nutrient removal. 8: Continuous feeding sequencing batch reactor.

2.2. Target Pharmaceuticals and Chemical Reagents

We selected 58 pharmaceuticals classified as analgesics or non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics, antiarrhythmic agents, antihistamines, contrast agents, hormones, stimulants, and "others" based on at least one of the following conditions: (1) widespread occurrence; (2) high maximum concentration (exceeding 10,000 ng/L) in municipal wastewater influents of Asia [3,10,12,18–26]; and (3) availability of analytical techniques. The physicochemical properties of the target pharmaceuticals are summarized in Table 2.

Table 2. Physicochemical properties of target pharmaceuticals.

No.	Pharmaceuticals	CAS No.	Molecular Formula	Molecular Weight (g/mol)	pKa	Water Solubility (mg/mL)	log K_{ow}
	Analgesics/Non-Steroidal Anti-Inflammatory Drugs						
1	Acetaminophen	103-90-2	$C_8H_9NO_2$	151.165	9.38	14 (at 20 °C)	0.46
2	Acetylsalicylic acid	50-78-2	$C_9H_8O_4$	180.159	3.49	3.3 (at 20 °C)	1.19
3	Diclofenac	15307-86-5	$C_{14}H_{11}Cl_2NO_2$	296.147	4.15	2.37×10^{-3} (at 25 °C)	4.51
4	Ibuprofen	15687-27-1	$C_{13}H_{18}O_2$	206.285	5.3	2.1×10^{-2} (at 25 °C)	3.97
5	Ketoprofen	22071-15-4	$C_{16}H_{14}O_3$	254.28	4.45	5.1×10^{-2} (at 25 °C)	3.12
6	Naproxen	22204-53-1	$C_{14}H_{14}O_3$	230.263	4.15	15.9×10^{-3} (at 25 °C)	3.18
	Antibiotics						
7	Amoxicillin	26787-78-0	$C_{16}H_{19}N_3O_5S$	365.404	3.23 * 7.43 **	3.43 (at 25 °C)	0.87
8	Cefalexin	15686-71-2	$C_{16}H_{17}N_3O_4S$	347.389	3.26 * 7.23 **	10	0.65
9	Cefradine	38821-53-3	$C_{16}H_{19}N_3O_4S$	349.4	3.46 * 7.6 **	21.3	−1.5
10	Chlortetracycline	57-62-5	$C_{22}H_{23}ClN_2O_8$	478.882	2.99 * 9.04 **	0.259 ***	−0.62
11	Ciprofloxacin	85721-33-1	$C_{17}H_{18}FN_3O_3$	331.4	6.09	<1	0.28
12	Clarithromycin	81103-11-9	$C_{38}H_{69}NO_{13}$	747.964	8.99	0.33×10^{-3}	3.16
13	Cloxacillin	61-72-3	$C_{19}H_{18}ClN_3O_5S$	435.9	2.78	13.9×10^{-3}	2.48
14	Demeclocycline	127-33-3	$C_{21}H_{21}ClN_2O_8$	464.9	−2.6 * 8.23 **	1.52 (at 21 °C)	0.2
15	Erythromycin	114-07-8	$C_{37}H_{67}NO_{13}$	733.937	8.88	2	3.06
16	Florfenicol	73231-34-2	$C_{12}H_{14}Cl_2FNO_4S$	358.2	8.49 * −3.4 **	0.219 ***	
17	Flumequine	42835-25-6	$C_{14}H_{12}FNO_3$	261.25	6.5	2.19 *** (at 25 °C)	1.6
18	Lincomycin	154-21-2	$C_{18}H_{34}N_2O_6S$	406.5	7.6	0.927 *** (at 25 °C)	0.29
19	Ofloxacin	82419-36-1	$C_{18}H_{20}FN_3O_4$	361.373	5.45 * 6.2 **	28.3	−0.39
20	Oseltamivir	196618-13-0	$C_{16}H_{28}N_2O_4$	312.4	14.03 * 9.31 **	1.6 *** (at 25 °C)	1
21	Oseltamivir acid	187227-45-8	$C_{14}H_{24}N_2O_4$	284.35	4.19 * 9.33 **	0.686***	0.95
22	Oxytetracycline	79-57-2	$C_{22}H_{24}N_2O_9$	460.439	3.27	0.313 (at 25 °C)	−0.90
23	Pefloxacin	70458-92-3	$C_{17}H_{20}FN_3O_3$	333.36	5.66 * 6.47 **	11.4 (at 25 °C)	0.27
24	Penicillin G	61-33-6	$C_{16}H_{18}N_2O_4S$	334.4	2.74	0.21	1.83
25	Penicillin V	87-08-1	$C_{16}H_{18}N_2O_5S$	350.4	2.79	<1	2.09
26	Roxithromycin	80214-83-1	$C_{41}H_{76}N_2O_{15}$	837.058	12.45 * 9.08 **	0.187	1.7
27	Sulfachlorpyridazine	80-32-0	$C_{10}H_9ClN_4O_2S$	284.72	6.6 * 2.02 **	0.035	0.31
28	Sulfadimethoxine	122-11-2	$C_{12}H_{14}N_4O_4S$	310.3	6.91 * 1.95 **	0.343	1.63

Table 2. *Cont.*

No.	Pharmaceuticals	CAS No.	Molecular Formula	Molecular Weight (g/mol)	pKa	Water Solubility (mg/mL)	log K_{ow}
29	Sulfamethazine	57-68-1	$C_{12}H_{14}N_4O_2S$	278.330	7.59	1.5 (at 29 °C)	0.89
30	Sulfamethoxazole	723-46-6	$C_{10}H_{11}N_3O_3S$	253.276	6.16 * 1.97 **	0.61 (at 37 °C)	0.89
31	Sulfathiazole	72-14-0	$C_9H_9N_3O_2S_2$	255.310	7.2	0.373 (at 25 °C)	0.05
32	Tetracycline	60-54-8	$C_{19}H_{28}O_2$	288.4	3.3	0.231 (at 25 °C)	−1.3
33	Triclosan	3380-34-5	$C_{22}H_{24}N_2O_8$	444.440	7.9	0.01 (at 20 °C)	4.76
34	Trimethoprim	738-70-5	$C_{14}H_{18}N_4O_3$	290.3	7.12	0.4 (at 25 °C)	0.91
35	Tylosin	1401-69-0	$C_{46}H_{77}NO17$	916.1	7.73	5 (at 25 °C)	1.63
36	Vancomycin	1404-90-6	$C_{66}H_{75}Cl_2N_9O_{24}$	1449.2	2.99 * 9.93 **	0.225	−3.1
	Antiarrhythmic Agents						
37	Atenolol	29122-68-7	$C_{14}H_{22}N_2O_3$	266.341	9.6	13.3 (at 25 °C)	0.16
38	Metoprolol	51384-51-1	$C_{15}H_{25}NO_3$	267.369	9.7	0.402 ***	1.88
39	Propranolol	525-66-6	$C_{16}H_{21}NO_2$	259.349	9.42	0.0617 (at 25 °C)	3.48
	Antihistamines						
40	Chlorpheniramine	132-22-9	$C_{16}H_{19}ClN_2$	274.79	9.13	160 (at 25 °C)	3.38
41	Cimetidine	51481-61-9	$C_{10}H_{16}N_6S$	252.340	6.8	9.38 (at 25 °C)	0.40
42	Diphenhydramine	58-73-1	$C_{17}H_{21}NO$	255.35	8.98	3.06 (at 37 °C)	3.27
43	Ranitidine	66357-35-5	$C_{13}H_{22}N_4O_3S$	314.404	7.8 **	0.0795 ***	1.93
	Contrast Agents						
44	Iopamidol	60166-93-0	$C_{17}H_{22}I_3N_3O_8$	777.1	11 * −2.8 **	120 *** (at 20 °C)	−2.42
45	Iopromide	73334-07-3	$C_{18}H_{24}I_3N_3O_8$	791.1	11.09 * −1.7 **	0.336 ***	−2.05
	Hormones						
46	Androstenedione	63-05-8	$C_{19}H_{26}O_2$	286.409	19.03 * −4.8 **	0.0578 (at 25 °C)	2.75
47	Testosterone	58-22-0	$C_{19}H_{28}O_2$	288.4	18.52 * −0.88 **	0.0234 (at 25 °C)	3.32
	Stimulant						
48	Caffeine	58-08-2	$C_8H_{10}N_4O_2$	194.19	14	21.7	−0.07
	Others						
49	Aripiprazole	129722-12-9	$C_{23}H_{27}Cl_2N_3O_2$	448.4	7.6	0.00777	5.3
50	Benzophenone	119-61-9	$C_{13}H_{10}O$	182.22	−7.5 **	0.137 (at 25 °C)	3.18
51	Carbamazepine	298-46-4	$C_{15}H_{12}N_2O$	236.274	15.96 * −3.8 **	0.152 ***	2.45
52	Fluoxetine	54910-89-3	$C_{17}H_{18}F_3NO$	309.3	10.1	0.0017 ***	4.05
53	Gemfibrozil	25812-30-0	$C_{15}H_{22}O_3$	250.338	4.42 * −4.8 **	0.0278 ***	4.387
54	Mefenamic acid	61-68-7	$C_{15}H_{15}NO_2$	241.28	4.2	0.02 (at 25 °C)	5.12
55	Quetiapine	111974-69-7	$C_{21}H_{25}N_3O_2S$	383.51	7.06	0.0403	2.81

Table 2. *Cont.*

No.	Pharmaceuticals	CAS No.	Molecular Formula	Molecular Weight (g/mol)	pKa	Water Solubility (mg/mL)	log K_{ow}
56	Sildenafil	139755-83-2	$C_{22}H_{30}N_6O_4S$	474.6	11.14 * 5.99 **	3.5	2.75
57	Tadalafil	171596-29-5	$C_{22}H_{19}N_3O_4$	389.4	15.17 * −4.2 **	0.25 ***	1.7
58	Warfarin	81-81-2	$C_{19}H_{16}O_4$	308.333	5	0.017 (at 20 °C)	2.70

Notes: * Strongest acidic. ** Strongest basic. *** Estimated or predicted value.

All target pharmaceuticals, solvents, and chemical reagents were purchased from Sigma-Aldrich (Saint Louis, MO, USA) and Fluka (Seelze, Germany) with high-purity grade (≥98%). The isotopically labeled standards were purchased from Sigma-Aldrich and Toronto Research Chemicals (Toronto, ON, Canada). Based on dissolution characteristics, a standard solution (10 mg/L) of each pharmaceutical was prepared using an appropriate solvent (methanol, water, and 0.1 N HCl) and stored at 4 °C.

2.3. Target Pharmaceutical Analysis

For analysis, 5 mL of each sample was filtered using a 0.2 µm polyvinylidene fluoride filter. A filtered sample quantity of 1350 µL was transferred into amber auto-sampler vials and mixed with 150 µL of 1% formic acid in methanol, 10 µL of 40 mg/mL ethylenediaminetetraacetic acid disodium salt dihydrate, and 10 µL of 500 µg/L isotopically labeled standards in methanol.

A pretreated sample (900 µL) was analyzed using liquid chromatography-tandem mass spectrometry (LC-MS/MS) [Nexera X2 (LC), LCMS-8050 (MS), Shimadzu, Co., Kyoto, Japan] coupled with online solid phase extraction (SPE), which is commonly applied for interference clean-up in the original matrix. The advanced chromatography experts 5 C18 pentafluorophenyl [ACE® 5 C18-PFP (150 × 2.1 mm)] and Shim-pack MAYI-ODS(G) (2.0 × 10 mm) [Shimadzu, Co. Kyoto, Japan] columns were used for LC and online SPE, respectively. The operating conditions of the online SPE LC-MS/MS are presented in Table 3. In particular, acetylsalicylic acid, diclofenac, florfenicol, gemfibrozil, ibuprofen, triclosan, and warfarin were analyzed in negative electrospray ionization mode in MS operation.

Table 3. Operating conditions of online solid phase extraction liquid chromatography-tandem mass spectrometry.

Parameters	Condition
Mobile phase A, C	0.1% formic acid in water
Mobile phase B	Methanol
Mobile phase D	Acetonitrile:methanol:IPA:water (1:1:1:1)
Gradient elution	10% B pump (0–5 min)—100% B pump (5–20 min)—10% B pump (20 min–)
Injection volume	900 µL
Flow rate	1.5 mL/min
Ionization mode	ESI * negative, positive
Gas temperature	270 °C
Gas flow	12 L/min
Nebulizer	40 psi
Sheath gas heater	375 °C
Sheath gas flow	11 L/min
Capillary voltage	(−)3500, (+)3500

Note: * ESI, electrospray ionization.

2.4. Quality Control

To confirm the analysis method, linearity, limit of detection (LOD), limit of quantification (LOQ), accuracy, and precision tests of the target pharmaceuticals were performed.

The LOD and LOQ were determined from fortified water samples with a signal-to-noise (S/N) ratio of 3 and 10 on the chromatogram, respectively. The accuracies of the target pharmaceuticals were determined by spiking the mixed standard solutions of 58 pharmaceuticals to concentration ranges of 10–200 (low level), 500–1000 (middle level), and 1000–5000 ng/L (high level). In linearity assessment, the coefficient of determination (R2) of the calibration curve for 58 pharmaceuticals was higher than 0.99. The LOD and LOQ were in the ranges 1.3–24.9 and 4.2–79.2 ng/L, respectively. Furthermore, we confirmed the reliability of the analysis method with high accuracies: 93.3–115.2% (low level), 92.8–108.0% (middle level), and 93.8–113.4% (high level). The linearity, LOD, LOQ, and accuracy of the target pharmaceuticals are summarized in Table S1.

2.5. Organic Carbon Analysis

In order to confirm the steady-state conditions of target STPs, the total organic carbon (TOC) and dissolved organic carbon (DOC) concentration of the influents and effluents of each STPs were analyzed using a total organic carbon analyzer (Shimadzu, Co., Kyoto, Japan). For DOC analysis, each sample was filtered with a 0.45 μm polytetrafluoroethylene membrane filter.

3. Results and Discussion

3.1. Organic Carbon Removal of Selected STPs

To identify the steady-state conditions of 13 STPs, the total organic carbon (TOC) and dissolved organic carbon (DOC) concentrations of the influent and effluent of each STP were analyzed. The average TOC and DOC concentrations in the influent were 33–137 and 24–120 mg/L, respectively, while those in the effluent were 6–15 and 3–10 mg/L, respectively. The average TOC and DOC removal rates of the target STPs were 62–95% and 61–96%, respectively, which were the lowest removal rates among those of STPs in rural areas. Moreover, the average TOC and DOC concentrations in the effluent of the target STPs were low, as they were 15 and 10 mg/L, respectively (Figure 1), confirming the steady-state operation of the STPs regardless of the linked treatment and the properties of the linked wastewater.

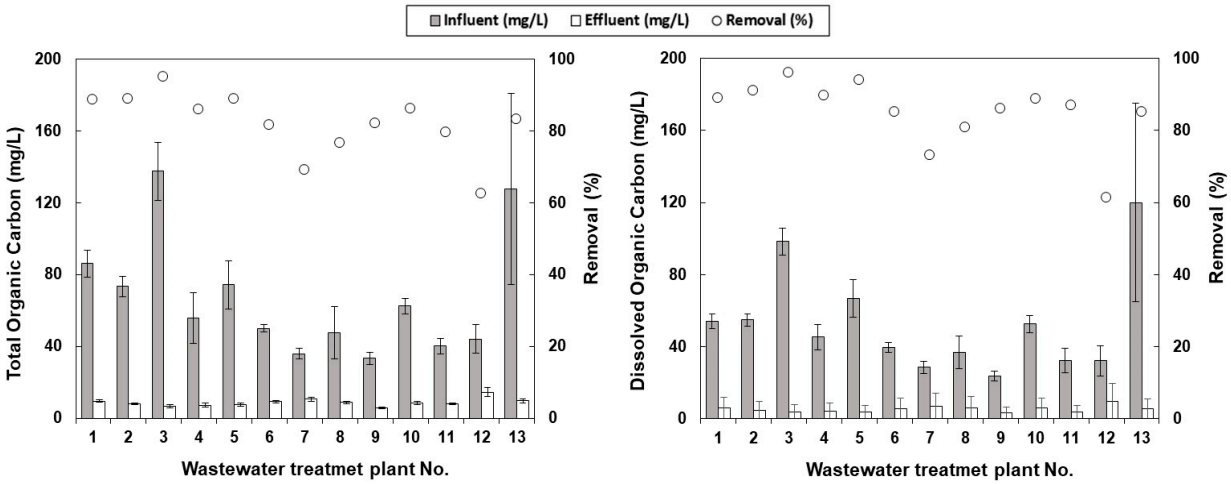

Figure 1. Removal of total organic carbon and dissolved organic carbon in 13 sewage treatment plants.

3.2. Occurrence and Fate of Target Pharmaceuticals in Each STP

The types of micropollutants detected in the influent and effluent of the target STPs varied depending on the regional features and linked treatment conditions. Among the 58 pharmaceuticals, 30–38 and 29–37 pharmaceuticals were detected in the influent and effluent, respectively. Fourteen pharmaceuticals (amoxicillin, aripiprazole, chlortetracycline, cloxacillin, demeclocycline, flumequine, oseltamivir acid, pefloxacin, penicillin G, penicillin V, testosterone, triclosan, tylosin, and warfarin) were not detected in any of the influent or effluent samples.

Among the 13 micropollutants from analgesics/NSAIDs, antiarrhythmic agents, and antihistamines, 11–13 items were detected in the influent and effluent. Among the 30 antibiotics investigated, 9–14 and 8–16 items were detected in the influent and effluent, respectively.

The investigation of micropollutants whose concentrations exceeded the LOQ in the influent and effluent of the 13 STPs revealed that the top five micropollutants with the highest average concentration in the influent were acetaminophen (28,586 ng/L), caffeine (25,470 ng/L), acetylsalicylic acid (13,551 ng/L), naproxen (5720 ng/L), and ibuprofen (4318 ng/L), while the top five micropollutants in the effluent were iopamidol (3648 ng/L), cimetidine (1589 ng/L), caffeine (434 ng/L), diphenhydramine (278 ng/L), and carbamazepine (265 ng/L). Moreover, when the average removal rate for each micropollutant in the target STPs was calculated, acetaminophen, acetylsalicylic acid, androstenedione, caffeine, cefalexin, cefradine, ibuprofen, and naproxen showed an average removal rate of $\geq$90%. The average concentrations of carbamazepine, chlorpheniramine, diclofenac, diphenhydramine, iopamidol, iopromide, lincomycin, metoprolol, propranolol, sildenafil, and sulfamethazine were found to be higher in the effluent than in the influent of the STPs (Figure 2).

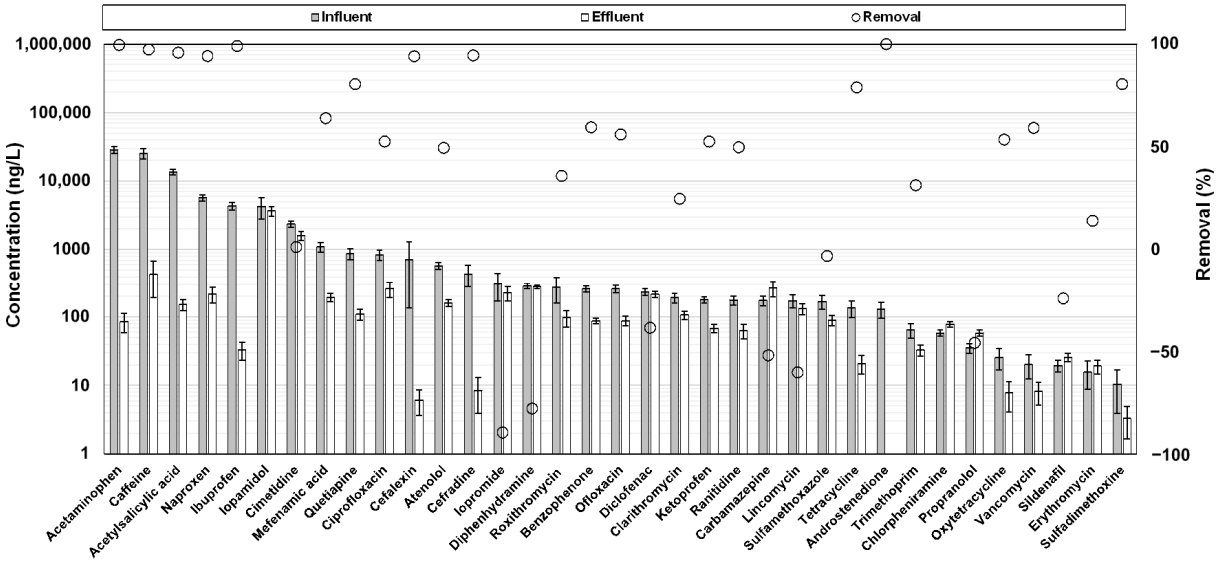

Figure 2. Occurrence and removal of target pharmaceuticals in 13 sewage treatment plants.

Despite the differences in process configuration, regional feature, and linked wastewater, the removals of pharmaceuticals including acetaminophen, acetylsalicylic acid, androstenedione, caffeine, cefalexin, cefradine, ibuprofen, and naproxen were as high as 90%. The contribution of biological wastewater treatment in the removal of these pharmaceuticals is widely known [6,23–25,27–29]. In contrast, a negative removal of carbamazepine, chlorpheniramine, diclofenac, diphenhydramine, iopamidol, iopromide, lincomycin, metoprolol, propranolol, sulfamethazine, and sulfathiazole in each STP was verified. They have resistance to biological wastewater treatment [30–33]. Research on the removal of pharmaceuticals having resistance to biological wastewater treatment emphasized tertiary

treatment including activated carbon, UV/H_2O_2, Fenton oxidation, and ozonation [34–36]. However, the mitigation of pharmaceuticals in effluent is limited as only a few countries have regulations for pharmaceuticals in the effluent from STPs; moreover, tertiary treatment is not mandatory.

3.3. Occurrence of Target Pharmaceuticals in STPs Based on Regional Differences

3.3.1. Urban Area

The investigation of the concentrations of micropollutants in the influent and effluent of an STP (STP_3) showed that the top five micropollutants with the highest average concentration in the influent were caffeine (109,175 ng/L), acetaminophen (40,182 ng/L), acetylsalicylic acid (24,420 ng/L), naproxen (8697 ng/L), and ibuprofen (5497 ng/L), while the top five micropollutants in the effluent were iopamidol (3634 ng/L), cimetidine (546 ng/L), roxithromycin (396 ng/L), diphenhydramine (225 ng/L), and acetylsalicylic acid (216 ng/L) (Tables S2 and S3). In particular, the concentration of caffeine in the influent was 5.1–9.5 times higher than those in the STPs in urban and rural complex and rural areas. During the treatment process, $\geq$99% of the top five micropollutants in the influent of the STP were removed. Six items (androstenedione, cefalexin, ciprofloxacin, mefenamic acid, ranitidine, and tetracycline) exhibited a removal rate of more than 70%. However, the concentrations of some micropollutants (such as clarithromycin, diphenhydramine, iopamidol, iopromide, lincomycin, and roxithromycin) were higher in the effluent than in the influent, revealing that they were not treated in the STP.

3.3.2. Urban and Rural Complex Area

The investigation of the concentrations of micropollutants in the influent and effluent of two STPs (STP_1 and STP_2) revealed that the top five micropollutants with the highest average concentration in the influent were caffeine (25,425 ng/L), acetaminophen (24,907 ng/L), acetylsalicylic acid (12,982 ng/L), iopamidol (9486 ng/L), and naproxen (5051 ng/L), while the top five micropollutants in the effluent were iopamidol (5099 ng/L), cimetidine (1140 ng/L), ciprofloxacin (798 ng/L), iopromide (395 ng/L), and diphenhydramine (279 ng/L) (Tables S2 and S3). The average removal rate was found to be more than 97% for caffeine, acetaminophen, acetylsalicylic acid, naproxen, and ibuprofen. The removal of some micropollutants (such as chlorpheniramine, diclofenac, iopamidol, and propranolol) was not observed.

3.3.3. Rural Area

The investigation of the concentrations of micropollutants in the influent and effluent of two STPs (STP_12 and STP_13) showed that the top five micropollutants with the highest average concentration in the influent were acetaminophen (34,371 ng/L), acetylsalicylic acid (12,434 ng/L), caffeine (11,013 ng/L), ibuprofen (5770 ng/L), and naproxen (4795 ng/L), while the top five micropollutants in the effluent were cimetidine (3971 ng/L), iopamidol (3256 ng/L), caffeine (2322 ng/L), carbamazepine (745 ng/L), and naproxen (655 ng/L) (Tables S2 and S3). The top five micropollutants in the influent were similar to those in the influent of the urban STP; however, the removal rates of caffeine and naproxen, which showed high removal rates in the STPs in urban and urban-rural complex areas, were found to be relatively low. This may be due to the large fluctuations in the influent load of small-scale STPs in rural areas.

The removal rates of acetaminophen, acetylsalicylic acid, ibuprofen, cefalexin, cefradine, and androstenedione were more than 90%, while those of caffeine, naproxen, quetiapine, and trimethoprim were 50–90%. Some substances (such as atenolol, cimetidine, sulfamethoxazole, iopamidol, and diclofenac) were not removed in the treatment facilities.

3.4. Occurrence of Target Pharmaceuticals in STPs Based on Linked Wastewater Differences

3.4.1. Industrial

In the two STPs (STP_4 and STP_5) linked with industrial wastewater, it was not possible to collect domestic sewage influent because wastewater was directly introduced through the sewer from the wastewater discharge facilities. The investigation of the concentrations of micropollutants in the linked wastewater, mixed water, and effluent of the STPs showed that the top five micropollutants with the highest average concentration in the linked wastewater were caffeine (7722 ng/L), acetaminophen (6745 ng/L), iopamidol (2726 ng/L), naproxen (2657 ng/L), and acetylsalicylic acid (1915 ng/L), while the top five micropollutants in the mixed water were acetaminophen (25,410 ng/L), iopamidol (13,140 ng/L), acetylsalicylic acid (13,094 ng/L), caffeine (12,731 ng/L), and naproxen (4876 ng/L) (Tables S2 and S3). The top five micropollutants in the mixed water showed different concentrations from those in the influent of the STPs in urban and rural complex areas; however, the micropollutant types were similar. This appears to be because of the low ratio of the linked wastewater to the total treatment volume in the entire treatment facility.

3.4.2. Livestock

The investigation of the concentrations of micropollutants in the influent, linked wastewater, mixed water, and effluent of the two STPs (STP_6 and STP_7) linked with livestock wastewater revealed that the top five micropollutants with the highest average concentration in the influent were acetaminophen (24,747 ng/L), caffeine (19,611 ng/L), acetylsalicylic acid (13,009 ng/L), naproxen (5994 ng/L), and ibuprofen (3112 ng/L), while the top five micropollutants in the linked wastewater were lincomycin (3723 ng/L), mefenamic acid (1568 ng/L), acetylsalicylic acid (615 ng/L), sulfamethazine (528 ng/L), and naproxen (504 ng/L). The top five micropollutants in the mixed water were acetaminophen (22,878 ng/L), caffeine (15,266 ng/L), acetylsalicylic acid (7167 ng/L), naproxen (6198 ng/L), and ibuprofen (3040 ng/L) (Tables S2 and S3). Although the types of the top five micropollutants in the linked wastewater were different from those of the facilities investigated above, the top five micropollutants in the mixed water were the same as those in the influent. The micropollutant load introduced into the STPs linked with livestock wastewater was mainly affected by those in domestic sewage.

3.4.3. Leachate

The investigation of the concentrations of micropollutants in the influent, linked wastewater, mixed water, and effluent of the two STPs (STP_8 and STP_9) linked with leachate showed that the top five micropollutants with the highest average concentration in the influent were acetaminophen (23,629 ng/L), caffeine (11,953 ng/L), acetylsalicylic acid (10,908 ng/L), naproxen (5539 ng/L), and ibuprofen (3156 ng/L), while the top five micropollutants in the linked wastewater were ibuprofen (13,185 ng/L), mefenamic acid (6148 ng/L), ketoprofen (3802 ng/L), caffeine (2505 ng/L), and naproxen (2497 ng/L). The top five micropollutants in the mixed water were acetaminophen (22,916 ng/L), acetylsalicylic acid (18,115 ng/L), caffeine (11,335 ng/L), naproxen (6709 ng/L), and cimetidine (5353 ng/L) (Tables S2 and S3). The top five micropollutants in the leachate were NSAIDs, and the concentration of ketoprofen was relatively higher than those in other linked wastewater. This may be because ketoprofen is released into leachate during the waste treatment process as it is an anti-inflammatory analgesic commonly found in commercial medical products, such as pain relief patches, and disposed of in a solid form.

3.4.4. Food Wastewater

The investigation of the micropollutants in the influent, linked wastewater, mixed water, and effluent of the two STPs (STP_10 and STP_11) linked with food wastewater revealed that the top five micropollutants with the highest average concentration in the influent were acetaminophen (33,234 ng/L), caffeine (30,914 ng/L), acetylsalicylic acid (13,428 ng/L), ibuprofen (7778 ng/L), and naproxen (6702 ng/L). The top five micropollutants in the linked

wastewater were caffeine (1154 ng/L), mefenamic acid (820 ng/L), diclofenac (576 ng/L), iopamidol (556 ng/L), and ibuprofen (427 ng/L), while the top five micropollutants in the mixed water were caffeine (26,789 ng/L), acetaminophen (26,433 ng/L), acetylsalicylic acid (13,624 ng/L), naproxen (6104 ng/L), and ibuprofen (5111 ng/L) (Tables S2 and S3).

3.5. Occurrence of Pharmaceuticals in Effluent-Receiving Streams

In 9 of the 13 STP effluent receiving streams, 9–29 and 17–33 pharmaceuticals were detected in the upstream and downstream areas, respectively, of the discharge channel, confirming that the STPs contributed to the increase in the number of detected micropollutants in the downstream area. Eighteen pharmaceuticals, including amoxicillin, androstenedione, aripiprazole, chlortetracycline, cloxacillin, demeclocycline, flumequine, metoprolol, oseltamivir acid, pefloxacin, penicillin G, penicillin V, sulfathiazole, tadalafil, testosterone, triclosan, tylosin, and warfarin were not detected (Figure 3a). To evaluate the effect of STPs on receiving streams, the following 10 items were selected from the 58 residual pharmaceuticals: acetaminophen and diclofenac (anti-inflammatory analgesics), ciprofloxacin and lincomycin (antibiotics), cimetidine (antihistamine), atenolol (antiarrhythmic agent), caffeine (stimulant), carbamazepine (antiepileptic), iopamidol (contrast agent), and mefenamic acid (anticoagulant). The substances that can be treated in the STPs, such as acetaminophen and caffeine, did not affect the concentrations of micropollutants in the receiving stream; however, substances such as carbamazepine, diclofenac, and lincomycin contributed to the increase in their concentrations in the receiving stream (Figure 3b). Moreover, atenolol, ciprofloxacin, and mefenamic acid, which exhibited removal rates of 40–60% in the STPs, contributed to the increase in micropollutant concentrations in the effluent-receiving stream.

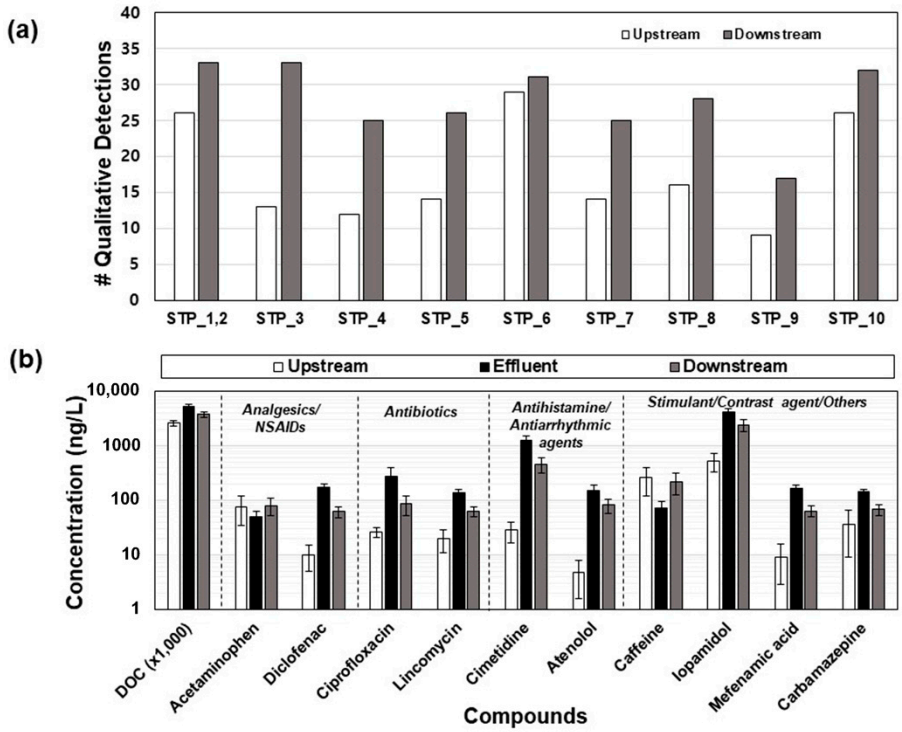

Figure 3. (**a**) Detection of target pharmaceuticals in the stream near sewage treatment plants (STPs). (**b**) Occurrence of selected pharmaceuticals in the stream near STPs. DOC, dissolved organic carbon.

To investigate the effect of STP effluent on the concentrations of micropollutants in the receiving stream, the contribution rates of STP effluent on four receiving streams that provide flow measurement network data, including the W stream (STP_4), B stream (STP_5), S stream (STP_7), and J stream (STP_9), were calculated. The ratios of STP effluent flow to the stream flow of the W, B, S, and J streams were 0.9%, 30%, 2%, and 0.06%, respectively.

The pollutant load was calculated using the average concentration of each micropollutant in the effluent and the upstream and downstream areas of the discharge channel, effluent flow of the four facilities, and stream flow. The contribution rate was analyzed using the following equation:

$$\text{Contribution rate (\%)} = M_{Effluent}/(M_{Downstream} - M_{Upstream}) \times 100 \quad (1)$$

where $M_{Effluent}$ = mass loading of pharmaceuticals in the STP effluent (g/d); $M_{Downstream}$ = mass loading of pharmaceuticals downstream; $M_{Upstream}$ = mass loading of pharmaceuticals upstream.

The investigation of the ten items showed that the contribution rates of STP effluent on the receiving streams were 0.5–59% for the W stream, −69–326% for the B stream, −9.4–41% for the S stream, and 0.2–13% for the J stream (Figure 4).

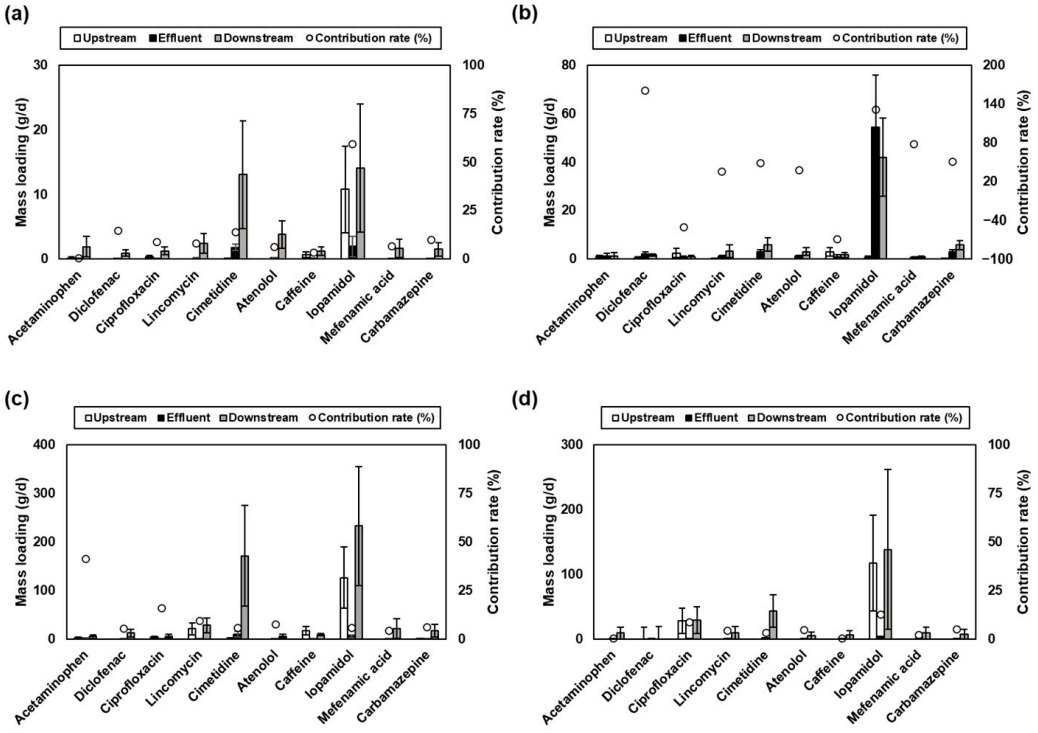

Figure 4. Contribution rate of sewage treatment plant (STP) effluent to the stream located near STPs. (**a**) W stream (STP_4), (**b**) B stream (STP_5), (**c**) S stream (STP_7), and (**d**) J stream (STP_9).

In the W stream, acetaminophen showed the lowest contribution rate (0.5%) among the selected substances. In the case of carbamazepine and diclofenac, which are difficult to treat in the STPs, the contribution rates of STP effluent on the receiving stream were found to be 9.9% and 14.6%, respectively, which were relatively higher than those of other selected substances. Iopamidol exhibited the highest contribution rate (59.4%) among the selected substances. This appears to be because the iopamidol load in the upstream area was 14–150-times higher than those of other selected substances. In the B stream, the ratio of STP effluent flow to the stream flow was 30%, and thus the influence of the STP effluent was highest among the target receiving streams. In particular, the contribution rates of STP_5 effluent on carbamazepine and diclofenac in the stream were found to be 50% and 161%, respectively. The contribution rate of caffeine in the C stream was a negative value, indicating that the effluent of the STP reduced the concentration of the substance in the receiving stream. The contribution rate of ciprofloxacin (15.9%) was found to be higher than that of other STPs. In the J stream, the ratio of STP effluent flow to the stream flow was low, and thus no substantial change in the concentrations of micropollutants in the stream was observed. However, iopamidol was accumulated in the upstream area. For

iopamidol, an X-ray contrast agent, the contribution rate of STP effluent in the downstream areas of the four streams ranged from 6% to 131%. It appears that iopamidol was detected in higher concentrations than the other micropollutants due to its accumulation in these streams. Furthermore, iopamidol is discharged from STPs without being properly removed; therefore, its continuous monitoring and management are required.

4. Conclusions

In this study, 13 STPs were selected based on regional and linked wastewater differences. The pharmaceuticals' concentration in the influent and effluent and their occurrence in effluent-receiving streams were also investigated.

A significant difference in pharmaceuticals' type in the STP influent by regional feature was not observed. The concentration of caffeine, was the highest in the STP influent from urban and rural complex areas, while that of acetaminophen was the highest in the STP influent from rural areas. In the STPs in rural areas, caffeine and naproxen, which exhibited high removal rates in residential, commercial, and urban and rural complex areas, showed relatively low removal rates. This appears to be due to large fluctuations in the influent load for small-scale STPs in rural areas and insufficient maintenance.

The occurrence characteristics of pharmaceuticals in the influent of STPs, which treat linked wastewater, were not remarkably different. This appears to be because of the low ratio of the linked wastewater to the total influent volume. Lincomycin, mefenamic acid, and sulfamethazine exhibited high concentrations in linked livestock wastewater, while mefenamic acid and ketoprofen were high in linked leachate. Therefore, intensive monitoring is required for treating these micropollutants in STPs having a high ratio of linked treatment.

In the nine effluent-receiving streams, 9–29 and 17–33 pharmaceuticals were detected in the upstream and downstream, respectively. It confirmed that the number of pharmaceuticals detected in the effluent-receiving streams was increased by the STP effluent. The contribution rate of the STP effluent on the streams was found to range from −69–326%. The STPs were not designed for the mitigation of pharmaceuticals but for the treatment of conventional water quality criteria items such as organics, nitrogen, and phosphorus. Therefore, investigation of pharmaceuticals in STP influent and effluent and effluent-receiving streams should be performed to meet the future water quality level and to establish the management measures.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/w15223897/s1, Table S1: Linearity, limit of detection (LOD), limit of quantification (LOQ), accuracy, and precision of target pharmaceuticals analysis; Table S2: Concentration of target pharmaceuticals in influents; Table S3: Concentration of target pharmaceuticals in effluents.

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References

1. Gogoi, A.; Mazumder, P.; Tyagi, V.K.; Tushara Chaminda, G.G.; An, A.K.; Kumar, M. Occurrence and Fate of Emerging Contaminants in Water Environment: A Review. *Groundw. Sustain. Dev.* **2018**, *6*, 169–180. [CrossRef]
2. Tijani, J.O.; Fatoba, O.O.; Babajide, O.O.; Petrik, L.F. Pharmaceuticals, Endocrine Disruptors, Personal Care Products, Nanomaterials and Perfluorinated Pollutants: A Review. *Environ. Chem. Lett.* **2016**, *14*, 27–49. [CrossRef]
3. Yang, Y.; Ok, Y.S.; Kim, K.H.; Kwon, E.E.; Tsang, Y.F. Occurrences and Removal of Pharmaceuticals and Personal Care Products (PPCPs) in Drinking Water and Water/Sewage Treatment Plants: A Review. *Sci. Total Environ.* **2017**, *596–597*, 303–320. [CrossRef]
4. Blair, B.D.; Crago, J.P.; Hedman, C.J.; Treguer, R.J.F.; Magruder, C.; Royer, L.S.; Klaper, R.D. Evaluation of a Model for the Removal of Pharmaceuticals, Personal Care Products, and Hormones from Wastewater. *Sci. Total Environ.* **2013**, *444*, 515–521. [CrossRef]
5. Hedgespeth, M.L.; Sapozhnikova, Y.; Pennington, P.; Clum, A.; Fairey, A.; Wirth, E. Pharmaceuticals and Personal Care Products (PPCPs) in Treated Wastewater Discharges into Charleston Harbor, South Carolina. *Sci. Total Environ.* **2012**, *437*, 1–9. [CrossRef] [PubMed]
6. Yu, Y.; Wu, L.; Chang, A.C. Seasonal Variation of Endocrine Disrupting Compounds, Pharmaceuticals and Personal Care Products in Wastewater Treatment Plants. *Sci. Total Environ.* **2013**, *442*, 310–316. [CrossRef]
7. Aydin, S.; Aydin, M.E.; Ulvi, A.; Kilic, H. Antibiotics in Hospital Effluents: Occurrence, Contribution to Urban Wastewater, Removal in a Wastewater Treatment Plant, and Environmental Risk Assessment. *Environ. Sci. Pollut. Res.* **2019**, *26*, 544–558. [CrossRef] [PubMed]
8. Rosal, R.; Rodríguez, A.; Perdigón-Melón, J.A.; Petre, A.; García-Calvo, E.; Gómez, M.J.; Agüera, A.; Fernández-Alba, A.R. Occurrence of Emerging Pollutants in Urban Wastewater and Their Removal through Biological Treatment Followed by Ozonation. *Water Res.* **2010**, *44*, 578–588. [CrossRef] [PubMed]
9. Choi, K.J.; Kim, S.G.; Kim, S.H. Removal of Antibiotics by Coagulation and Granular Activated Carbon Filtration. *J. Hazard. Mater.* **2008**, *151*, 38–43. [CrossRef]
10. Tewari, S.; Jindal, R.; Kho, Y.L.; Eo, S.; Choi, K. Major Pharmaceutical Residues in Wastewater Treatment Plants and Receiving Waters in Bangkok, Thailand, and Associated Ecological Risks. *Chemosphere* **2013**, *91*, 697–704. [CrossRef]
11. Tran, N.H.; Reinhard, M.; Gin, K.Y.H. Occurrence and Fate of Emerging Contaminants in Municipal Wastewater Treatment Plants from Different Geographical Regions-a Review. *Water Res.* **2018**, *133*, 182–207. [CrossRef]
12. Tran, N.H.; Chen, H.; Reinhard, M.; Mao, F.; Gin, K.Y.H. Occurrence and Removal of Multiple Classes of Antibiotics and Antimicrobial Agents in Biological Wastewater Treatment Processes. *Water Res.* **2016**, *104*, 461–472. [CrossRef]
13. Wilkinson, J.; Hooda, P.S.; Barker, J.; Barton, S.; Swinden, J. Occurrence, Fate and Transformation of Emerging Contaminants in Water: An Overarching Review of the Field. *Environ. Pollut.* **2017**, *231*, 954–970. [CrossRef] [PubMed]
14. Le, T.H.; Ng, C.; Tran, N.H.; Chen, H.; Gin, K.Y.H. Removal of Antibiotic Residues, Antibiotic Resistant Bacteria and Antibiotic Resistance Genes in Municipal Wastewater by Membrane Bioreactor Systems. *Water Res.* **2018**, *145*, 498–508. [CrossRef] [PubMed]
15. WHO. Integrated Surveillance of Antimicrobial Resistance in Foodborne Bacteria: Application of a One Health Approach. Available online: https://iris.who.int/bitstream/handle/10665/255747/9789241512411-eng.pdf?sequence=1 (accessed on 31 October 2023).
16. Luo, Y.; Guo, W.; Ngo, H.H.; Nghiem, L.D.; Hai, F.I.; Zhang, J.; Liang, S.; Wang, X.C. A Review on the Occurrence of Micropollutants in the Aquatic Environment and Their Fate and Removal during Wastewater Treatment. *Sci. Total Environ.* **2014**, *473–474*, 619–641. [CrossRef]
17. Vieno, N.; Tuhkanen, T.; Kronberg, L. Elimination of Pharmaceuticals in Sewage Treatment Plants in Finland. *Water Res.* **2007**, *41*, 1001–1012. [CrossRef] [PubMed]
18. Behera, S.K.; Kim, H.W.; Oh, J.E.; Park, H.S. Occurrence and Removal of Antibiotics, Hormones and Several Other Pharmaceuticals in Wastewater Treatment Plants of the Largest Industrial City of Korea. *Sci. Total Environ.* **2011**, *409*, 4351–4360. [CrossRef] [PubMed]
19. Choi, K.; Kim, Y.; Park, J.; Park, C.K.; Kim, M.Y.; Kim, H.S.; Kim, P. Seasonal Variations of Several Pharmaceutical Residues in Surface Water and Sewage Treatment Plants of Han River, Korea. *Sci. Total Environ.* **2008**, *405*, 120–128. [CrossRef]
20. Ghosh, G.C.; Nakada, N.; Yamashita, N.; Tanaka, H. Occurrence and Fate of Oseltamivir Carboxylate (Tamiflu) and Amantadine in Sewage Treatment Plants. *Chemosphere* **2010**, *81*, 13–17. [CrossRef]
21. Li, B.; Zhang, T. Mass Flows and Removal of Antibiotics in Two Municipal Wastewater Treatment Plants. *Chemosphere* **2011**, *83*, 1284–1289. [CrossRef]
22. Sim, W.J.; Lee, J.W.; Lee, E.S.; Shin, S.K.; Hwang, S.R.; Oh, J.E. Occurrence and Distribution of Pharmaceuticals in Wastewater from Households, Livestock Farms, Hospitals and Pharmaceutical Manufactures. *Chemosphere* **2011**, *82*, 179–186. [CrossRef] [PubMed]
23. Subedi, B.; Balakrishna, K.; Joshua, D.I.; Kannan, K. Mass Loading and Removal of Pharmaceuticals and Personal Care Products Including Psychoactives, Antihypertensives, and Antibiotics in Two Sewage Treatment Plants in Southern India. *Chemosphere* **2017**, *167*, 429–437. [CrossRef]
24. Sun, Q.; Li, M.; Ma, C.; Chen, X.; Xie, X.; Yu, C.P. Seasonal and Spatial Variations of PPCP Occurrence, Removal and Mass Loading in Three Wastewater Treatment Plants Located in Different Urbanization Areas in Xiamen, China. *Environ. Pollut.* **2016**, *208*, 371–381. [CrossRef]

25. Tran, N.H.; Gin, K.Y.H. Occurrence and Removal of Pharmaceuticals, Hormones, Personal Care Products, and Endocrine Disrupters in a Full-Scale Water Reclamation Plant. *Sci. Total Environ.* **2017**, *599–600*, 1503–1516. [CrossRef]
26. Zhang, X.; Zhao, H.; Du, J.; Qu, Y.; Shen, C.; Tan, F.; Chen, J.; Quan, X. Occurrence, Removal, and Risk Assessment of Antibiotics in 12 Wastewater Treatment Plants from Dalian, China. *Environ. Sci. Pollut. Res.* **2017**, *24*, 16478–16487. [CrossRef]
27. Guerra, P.; Kim, M.; Shah, A.; Alaee, M.; Smyth, S.A. Occurrence and Fate of Antibiotic, Analgesic/Anti-Inflammatory, and Antifungal Compounds in Five Wastewater Treatment Processes. *Sci. Total Environ.* **2014**, *473–474*, 235–243. [CrossRef] [PubMed]
28. Mailler, R.; Gasperi, J.; Coquet, Y.; Buleté, A.; Vulliet, E.; Deshayes, S.; Zedek, S.; Mirande-Bret, C.; Eudes, V.; Bressy, A.; et al. Removal of a Wide Range of Emerging Pollutants from Wastewater Treatment Plant Discharges by Micro-Grain Activated Carbon in Fluidized Bed as Tertiary Treatment at Large Pilot Scale. *Sci. Total Environ.* **2016**, *542*, 983–996. [CrossRef]
29. Thiebault, T.; Boussafir, M.; Le Milbeau, C. Occurrence and Removal Efficiency of Pharmaceuticals in an Urban Wastewater Treatment Plant: Mass Balance, Fate and Consumption Assessment. *J. Environ. Chem. Eng.* **2017**, *5*, 2894–2902. [CrossRef]
30. de Franco, M.A.E.; de Carvalho, C.B.; Bonetto, M.M.; de Pelegrini Soares, R.; Féris, L.A. Diclofenac Removal from Water by Adsorption Using Activated Carbon in Batch Mode and Fixed-Bed Column: Isotherms, Thermodynamic Study and Breakthrough Curves Modeling. *J. Clean. Prod.* **2018**, *181*, 145–154. [CrossRef]
31. Gardner, M.; Jones, V.; Comber, S.; Scrimshaw, M.D.; Coello-Garcia, T.; Cartmell, E.; Lester, J.; Ellor, B. Performance of UK Wastewater Treatment Works with Respect to Trace Contaminants. *Sci. Total Environ.* **2013**, *456–457*, 359–369. [CrossRef] [PubMed]
32. Keen, O.S.; Baik, S.; Linden, K.G.; Aga, D.S.; Love, N.G. Enhanced Biodegradation of Carbamazepine after UV/H2O 2 Advanced Oxidation. *Environ. Sci. Technol.* **2012**, *46*, 6222–6227. [CrossRef] [PubMed]
33. Long, Y.; Feng, Y.; Li, X.; Suo, N.; Chen, H.; Wang, Z.; Yu, Y. Removal of Diclofenac by Three-Dimensional Electro-Fenton-Persulfate (3D Electro-Fenton-PS). *Chemosphere* **2019**, *219*, 1024–1031. [CrossRef] [PubMed]
34. Baghdadi, M.; Ghaffari, E.; Aminzadeh, B. Removal of Carbamazepine from Municipal Wastewater Effluent Using Optimally Synthesized Magnetic Activated Carbon: Adsorption and Sedimentation Kinetic Studies. *J. Environ. Chem. Eng.* **2016**, *4*, 3309–3321. [CrossRef]
35. Hama Aziz, K.H.; Miessner, H.; Mueller, S.; Kalass, D.; Moeller, D.; Khorshid, I.; Rashid, M.A.M. Degradation of Pharmaceutical Diclofenac and Ibuprofen in Aqueous Solution, a Direct Comparison of Ozonation, Photocatalysis, and Non-Thermal Plasma. *Chem. Eng. J.* **2017**, *313*, 1033–1041. [CrossRef]
36. Komtchou, S.; Dirany, A.; Drogui, P.; Bermond, A. Removal of Carbamazepine from Spiked Municipal Wastewater Using Electro-Fenton Process. *Environ. Sci. Pollut. Res.* **2015**, *22*, 11513–11525. [CrossRef] [PubMed]