# Supplementary Information

## Manuscript title:

Distribution, mass load and environmental impact of multiple-class pharmaceuticals in conventional and upgraded municipal wastewater treatment plants in East China

## Authors:

Xiangjuan Yuan, Zhimin Qiang*, Weiwei Ben, Bing Zhu, Jiuhui Qu

*Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences, 18 Shuang-qing Road, Beijing 100085, China*

**List of supplementary materials:**

# Text S1 Sample pretreatment, extraction and analysis

## 1. Sample pretreatment

Wastewater samples were centrifuged at 7000 rpm (J2-HS, Beckmann Coulter, USA) for 15 min. The supernatant was vacuum-filtered through glass microfiber filters (GF/F, Whatman, UK), acidified to pH 2.5–3.0 with 40% (v/v) $H_2SO_4$ solution, added with 0.1 g $Na_2EDTA$ to complex potential interfering metals and improve the extraction efficiency of target pharmaceuticals. After pretreatment, the wastewater samples were stored in the dark at 4 $^oC$ and extracted by solid phase extraction (SPE) within 24 h.

Sludge samples were also centrifuged at 7000 rpm for 15 min. The sediment was collected, freeze-dried under vacuum (FD-1-50, Boyikang, China) for at least 48 h, homogenized with a mortar and pestle, sieved to obtain desired particles (diameter ≤ 0.5 mm), and stored at –20 $^oC$.

## 2. Sample extraction

For wastewater samples, the target pharmaceuticals were extracted by SPE using Oasis HLB cartridges (6 mL, 500 mg, Waters). The cartridge was preconditioned sequentially with 5 mL each of methanol (MeOH), HCl (0.5 M) and Milli-Q water. Each sample (400 mL for the effluent and 200 mL for the influent) was spiked with a mixture of four internal standards (ISs) (i.e., 100 ng SMN-$^{13}C_6$ for SAs, 100 ng OLF-$D_3$ for FQs, 100 ng DMC for TCs, and 100 ng CAF-$^{13}C_3$ for Others), and extracted by the HLB cartridge at a flow rate of approximately 3 mL $min^{-1}$. Afterwards, the cartridge was rinsed sequentially with 5 mL each of 5% methanol aqueous solution and Milli-Q water, dried under vacuum, and then eluted with 10 mL MeOH. The eluate was collected in a 10 mL glass vial, dried under a gentle stream of $N_2$, and dissolved with a mixture of 400 μL MeOH and 600 μL Milli-Q water. The resulting extract was centrifuged at 10000 rpm for 6 min (Centrifuge 5418, Eppendorf, Germany), and the supernatant was filtered through 0.2 μm PES filters (PALL, USA) for UPLC-MS/MS analysis.

For sludge samples, 0.5 g of the freeze-dried solid particles was accurately weighed into a 30 mL glass centrifuge tube, spiked with a mixture of four ISs (i.e., 100 ng SMN-$^{13}C_6$ for SAs, 500 ng OLF-$D_3$ for FQs, 500 ng DMC for TCs, and 100 ng CAF-$^{13}C_3$ for Others), and vibrated intensively. A mixture of MeOH (5 mL) and 0.2 M citric acid (pH 4.4, 5 mL) was added to the tube, vortexed for 30 s, ultrasonicated for 10 min, centrifuged at 5000 rpm for another 10 min, and the extracted for three times. The extracts were combined together and diluted to 300 mL with Milli-Q water, so that the MeOH content was below 5%. Subsequently, the resulting solution was purified and enriched by SPE using the same procedures as for the wastewater samples above.

### 3. UPLC-MS/MS analysis

The chromatographic separation of target pharmaceuticals was performed on an Agilent 1290 UPLC system equipped with an Agilent Zorbax SB-C18 column (100 mm × 2.1 mm, 1.8 μm). The column was maintained at 30 $^{o}$C and the injection volume was 5 μL. Milli-Q water containing 0.2% formic acid (v/v) (A) and acetonitrile (B) were used as the mobile phases at a flow rate of 0.3 mL $min^{-1}$. The gradient elution program (time in min, % mobile phase B) was set as follows: (0, 5), (2, 5), (5, 13), (8, 15), (13, 20), (18, 30), (25, 60), (27, 100), (30, 100), (30.1, 5), and (33, 5).

An Agilent 6420 Triple Quad LC/MS, equipped with an electrospray ionization (ESI) source and operated in the positive ion mode, was employed to analyze the target pharmaceuticals. The MS system was operated under the following conditions: capillary voltage 4.0 kV, drying gas temperature 300 $^{o}$C, drying gas flow rate 12 L/min, and nebulizing gas pressure 40 psi. For each compound, the fragmentor voltage, collision energy (CE), and multiple reaction monitoring (MRM) transitions were optimized (Table S4). Data were acquired under time-segmented conditions based on the chromatographic separation of target pharmaceuticals to maximize the detection sensitivity. MassHunter Workstation Software (B.04.00, Agilent) was employed for both instrument control and data acquisition/analysis.

## 4. Quantification and method performance

The target pharmaceuticals were quantified by the internal standard method. Calibration curves were established with mixed pharmaceutical standards and ISs prepared in Milli-Q water. New calibration was established every time when analyzing different batches of wastewater and sludge samples. The UPLC-MS/MS was check-tuned every month to ensure the stability of the instrument. For each pharmaceutical, its recovery was calculated as the detected concentration of a spiked sample minus that of a non-spiked sample in comparison to the initial spiked concentration. Four mixed ISs were spiked into the sample prior to the entire analytical procedure, so as to compensate for the loss of target pharmaceuticals and minimize the matrix interference during the sample pretreatment and detection processes. Recoveries were determined by triplicate samples at each concentration level, and the precisions were assessed by the relative standard deviation (RSD).

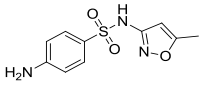
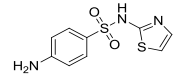
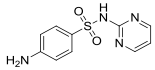
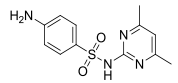
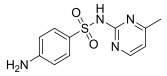
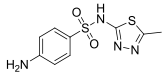
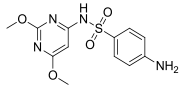
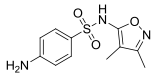
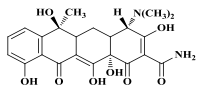
The percent matrix effect (%ME) for each pharmaceutical was determined experimentally according to the following equation:

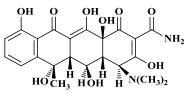
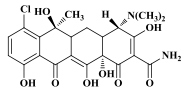
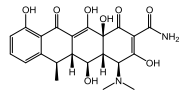
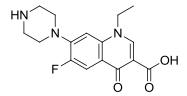
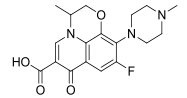
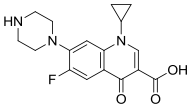
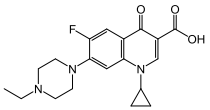
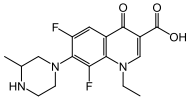
$$\%\mathrm{ME} = \frac{\text{signal response of the spiked post-extracted reference matrix sample}}{\text{signal response of the spiked Milli-Q water sample}} \times 100 \qquad \text{(S1)}$$

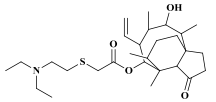
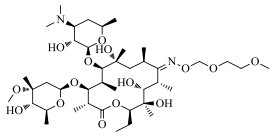
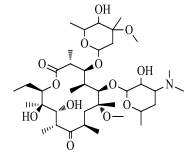
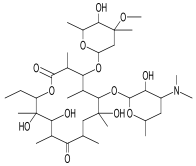
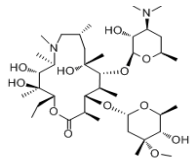
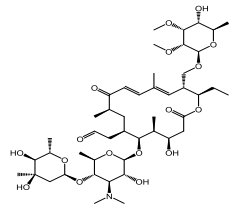
It is seen that 100%ME means no matrix interference; otherwise, a %ME value of greater (or less) than 100 denotes signal enhancement (or suppression).

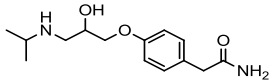
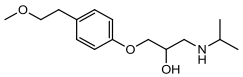
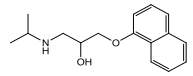
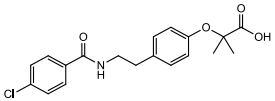
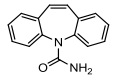
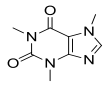
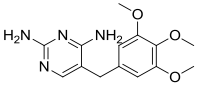
The limit of quantification (LOQ) of target pharmaceuticals was determined for both wastewater and sludge samples, representing the minimum concentration that gave a signal-to-noise ratio of 10. The calibration linear range, recovery, percent matrix effect and limit of quantification of target pharmaceuticals are listed in Table S5.

**Table S1** Major physicochemical properties of target pharmaceuticals and internal standards

| Class | Compound | Acronym | CAS NO. | Formula | MW | p$K_a$ [a] | log$K_{ow}$ [a] | Structure |
|---|---|---|---|---|---|---|---|---|
| Sulfonamides (SAs) | Sulfamethoxazole | SMX | 723-46-6 | $C_{10}H_{11}N_3O_3S$ | 253.28 | 1.85 ± 0.30<br>5.60 ± 0.04 | 0.89 |  |
| | Sulfathiazole | STZ | 72-14-0 | $C_9H_9N_3O_2S_2$ | 255.32 | 2.01 ± 0.30<br>7.11 ± 0.09 | 0.05 |  |
| | Sulfadiazine | SDZ | 68-35-9 | $C_{10}H_{10}N_4O_2S$ | 250.30 | 1.57 ± 0.10<br>6.50 ± 0.30 | –0.12 |  |
| | Sulfamethazine | SMN | 57-68-1 | $C_{12}H_{14}N_4O_2S$ | 278.33 | 2.07 ± 0.30<br>7.49 ± 0.13 | 0.80 |  |
| | Sulfamerazine | SMR | 127-79-7 | $C_{11}H_{12}N_4O_2S$ | 264.30 | 2.82 ± 0.31<br>6.84 ± 0.30 | 0.34 |  |
| | Sulfamethizole | SML | 144-82-1 | $C_9H_{10}N_4O_2S_2$ | 270.33 | 1.86 ± 0.30<br>5.29 ± 0.04 | 0.51 |  |
| | Sulfadimethoxine | SDM | 122-11-2 | $C_{12}H_{14}N_4O_4S$ | 310.33 | 2.13 ± 0.30<br>6.08 ± 0.09 | 1.48 |  |
| | Sulfisoxazole | SFX | 127-69-5 | $C_{11}H_{13}N_3O_3S$ | 267.30 | 1.52 ± 0.10<br>4.83 ± 0.50 | 1.01 |  |
| Tetracyclines (TCs) | Tetracycline | TCN | 60-54-8 | $C_{22}H_{24}N_2O_8$ | 444.44 | 3.30 ± 0.10<br>7.70 ± 0.15<br>9.50 ± 0.15 | –1.47 |  |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Oxytetracycline | OTC | 79-57-2 | $C_{22}H_{24}N_2O_9$ | 460.43 | 3.27 ± 0.10<br>7.32 ± 0.04<br>9.11 ± 0.10 | –1.5 |  |
| | Chlortetracycline | CTC | 64-72-2 | $C_{22}H_{23}ClN_2O_8$ | 478.9 | 3.30 ± 0.40<br>7.40 ± 0.13<br>9.27 ± 0.50 | –0.33 |  |
| | Doxycycline | DOX | 564-25-0 | $C_{22}H_{24}N_2O_8$ | 444.43 | 3.02±0.30<br>7.97±0.15<br>9.15±0.30 | –0.72 |  |
| Fluoroquinolones (FQs) | Norfloxacin | NOR | 70458-96-7 | $C_{16}H_{18}FN_3O_3$ | 319.33 | 3.59 ± 0.70<br>8.38 ± 0.25 | 1.48 |  |
| | Ofloxacin | OLF | 82419-36-1 | $C_{18}H_{20}FN_3O_4$ | 362.15 | 2.27 ± 0.40<br>6.41 ± 0.30 | 1.41 |  |
| | Ciprofloxacin | CIP | 85721-33-1 | $C_{17}H_{18}FN_3O_3$ | 331.34 | 2.68 ± 0.20<br>8.38 ± 0.25 | 1.31 |  |
| | Enrofloxacin | ENR | 93106-60-6 | $C_{19}H_{22}FN_3O_3$ | 359.4 | 3.85 ± 0.30<br>6.19 ± 0.18 | NA [b] |  |
| | Lomefloxacin | LOM | 98079-51-7 | $C_{17}H_{19}F_2N_3O_3$ | 351.35 | 5.64<br>8.47 | –0.39 |  |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Macrolides (MLs) | Tiamulin | TIA | 55297-95-5 | $C_{28}H_{47}NO_4S$ | 493.82 | 7.60 | 6.43 |  |
| | Roxithromycin | ROX | 80214-83-1 | $C_{41}H_{76}N_2O_{15}$ | 837.53 | 9.17 ± 0.30 | 3.73 |  |
| | Clarithromycin | CLA | 81103-11-9 | $C_{38}H_{69}NO_{13}$ | 747.95 | 7.25 | 3.16 |  |
| | Erythromycin | ERY | 114-07-8 | $C_{37}H_{67}NO_{13}$ | 733.93 | 8.90 ± 0.15 | 2.83 |  |
| | Azithromycin | AZN | 83905-01-5 | $C_{38}H_{72}N_2O_{12}$ | 748.98 | 7.34 | 4.02 |  |
| | Tylosin | TYL | 1401-69-0 | $C_{46}H_{77}NO_{17}$ | 916.1 | 3.31 ± 0.30<br>7.50 ± 0.13 | NA |  |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| β-blockers | Atenolol | ATE | 29122-68-7 | $C_{14}H_{22}N_2O_3$ | 266.34 | 9.17 ± 0.38 | 0.10 |  |
| | Metoprolol | MET | 37350-58-6 | $C_{15}H_{25}NO_3$ | 267.36 | 9.18 ± 0.38 | 1.79 |  |
| | Propranolol | PROP | 525-66-6 | $C_{16}H_{21}NO_2$ | 259.35 | 9.45 ± 0.03 | 3.10 |  |
| Lipid regulators | Bezafibrate | BF | 41859-67-0 | $C_{19}H_{20}ClNO_4$ | 361.82 | 3.29 ± 0.10 | 3.46 |  |
| Antiepileptics | Carbamazepine | CBZ | 298-46-4 | $C_{15}H_{12}N_2O$ | 236.27 | 13.94 ± 0.20 | 2.67 |  |
| Stimulants | Caffeine | CAF | 58-08-2 | $C_8H_{10}N_4O_2$ | 194.19 | 10.40 | –0.13 |  |
| Dihydrofolate reductase inhibitors | Trimethoprim | TMP | 738-70-5 | $C_{14}H_{18}N_4O_3$ | 290.32 | 7.20 ± 0.17 | 0.79 |  |
| Internal standards (ISs) | Demeclocycline | DMC | 127-33-3 | $C_{21}H_{21}ClN_2O_8$ | 464.85 | | | |
| | Sulfamethazine -$^{13}C_6$ | SMN-$^{13}C_6$ | 1189426-16-1 | $C_6{}^{13}C_6H_{14}N_4O_2S$ | 293.30 | | | |
| | Ofloxacin-$D_3$ | OLF-$D_3$ | 1173147-91-5 | $C_{18}H_{17}D_3FN_3O_4$ | 364.39 | | | |
| | Caffeine-$^{13}C_3$ | CAF-$^{13}C_3$ | 78072-66-9 | $^{13}C_3C_5H_{10}N_4O_2$ | 197.19 | | | |

[a] Calculated by ACD/Labs software; [b] NA: not available.

**Table S2** Operation parameters of two studied WWTPs

| WWTP | Secondary treatment | Tertiary treatment | HRT [b] (h) | SRT [c] (d) | Designed treatment capacity ($m^3$ $d^{-1}$) | Average flow ($m^3$ $d^{-1}$) | Population equivalent | Sludge treatment/disposal | Sludge yield (t $yr^{-1}$) |
|---|---|---|---|---|---|---|---|---|---|
| Plant A | A/A/O-MBBR | RFSD [a] | 18 | 18–20 | 300,000 | 200,000 | 820,000 | drying/landfill | 69,000 |
| Plant B | C-Orbal OD | UV–RFSD | 20 | 15 | 200,000 | 150,000 | 660,000 | drying/landfill | 59,000 |

[a] RFDS: rotary disc filter; [b] HRT: hydraulic retention time; [c] SRT: sludge retention time.

**Table S3** Characteristics of wastewater and sludge in two studied WWTPs

| WWTP | Process | Flow rate ($m^3\ d^{-1}$) | SS [a] ($mg\ L^{-1}$) | COD [b] ($mg\ L^{-1}$) | $BOD_5$ [c] ($mg\ L^{-1}$) | TP [d] ($mg\ L^{-1}$) | TN [e] ($mg\ L^{-1}$) | $NH_4$-N ($mg\ L^{-1}$) | pH |
|---|---|---|---|---|---|---|---|---|---|
| Plant A | Influent | 200000 | 322 | 220 | 128 | 6.9 | 38 | 25 | 7.4–7.6 |
| | Primary clarifier | 200000 | 150 | | | | | | |
| | Anoxic | 300000 | 3600 | | | | | | |
| | Anaerobic | 300000 | 3500 | | | | | | |
| | Oxic | 500000 | 3600 | | | | | | |
| | MBBR | 500000 | 4000 | | | | | | |
| | Secondary clarifier | 200000 | 15 | | | | | | |
| | Final effluent | 200000 | 7 | 31 | 5.7 | 0.4 | 13 | 1.1 | 6.8–7.0 |
| | Return sludge | 100000 | 8600 | | | | | | |
| | Excess sludge | 4000 | 8600 | | | | | | |
| Plant B | Influent | 150000 | 274 | 344 | 100 | 4.2 | 35 | 18 | 7.2–7.8 |
| | Grit chamber | 150000 | 120 | | | | | | |
| | Oxidation ditch | 300000 | 3000 | | | | | | |
| | Secondary clarifier | 150000 | 20 | | | | | | |
| | Final effluent | 150000 | 10 | 29 | 3.5 | 0.2 | 14 | 0.3 | 7.4–7.6 |
| | Return sludge | 120000 | 6700 | | | | | | |
| | Excess sludge | 3000 | 6700 | | | | | | |

[a] SS: suspended solids; [b] COD: chemical oxygen demand; [c] $BOD_5$: 5-d biochemical oxygen demand; [d] TP: total phosphorus; [e] TN: total nitrogen.

**Table S4** Optimized operational parameters of MS/MS for target pharmaceuticals

| Compound | Precursor ion (m/z) | Product ions (m/z) (CE, eV) | Fragmentor (V) | Segment period (min) |
|---|---|---|---|---|
| ATE | 267.3 | 145.0 (28); 74.1 (30) | 100 | 0–5.5 |
| SDZ | 251.2 | 156.0 (12); 92.1 (25) | 105 | 0–5.5 |
| STZ | 256.3 | 92.1 (25); 156.1 (10) | 100 | 5.5–7.2 |
| SMR | 265.3 | 92 (40); 156 (15) | 110 | 5.5–7.2 |
| CAF | 195.1 | 138.0 (20); 110.1 (30) | 110 | 5.5–7.2 |
| CAF-$^{13}C_3$ (IS) | 198.1 | 140.0 (20) | 105 | 5.5–7.2 |
| TMP | 291.3 | 230.1 (20); 123.1 (40) | 135 | 7.2–10.5 |
| SMN | 279.3 | 186 (10); 92 (35) | 115 | 7.2–10.5 |
| SMN-$^{13}C_6$ (IS) | 285.1 | 186.1 (15) | 105 | 7.2–10.5 |
| OTC | 461.3 | 426.2 (15); 442.9 (10) | 135 | 7.2–10.5 |
| SML | 271.3 | 155.9 (10); 92.2 (30) | 100 | 7.2–10.5 |
| OLF | 362.3 | 318 (20); 261.2 (35) | 135 | 7.2–10.5 |
| LOM | 352.2 | 308.1(15); 265.1(25) | 125 | 7.2–10.5 |
| NOR | 320.2 | 233.1 (30); 275.9 (15) | 135 | 7.2–10.5 |
| OLF-$D_3$ (IS) | 365.2 | 321.1 (15); 261.1 (30) | 120 | 7.2–10.5 |
| CIP | 332.2 | 288.1 (15); 188.9 (30) | 135 | 7.2–10.5 |
| TCN | 445.3 | 410.2 (15); 154 (25) | 120 | 7.2–10.5 |
| MET | 268.3 | 56.2 (35); 116.1 (25) | 115 | 10.5–13 |
| DMC (IS) | 465.1 | 154.4 (28) | 125 | 10.5–13 |
| ENR | 360.1 | 342.2(18); 316.2(15) | 140 | 10.5–13 |
| SMX | 254.3 | 91.9 (25); 156.0 (15) | 105 | 10.5–13 |
| SFX | 268.3 | 156.1 (10); 91.9 (30) | 105 | 13–15 |
| CTC | 479.2 | 154 (20); 444 (10) | 130 | 13–15 |
| DOX | 445.2 | 428.1(15);154(32) | 125 | 15-19 |
| AZN | 749.6 | 591.5(30); 158(40) | 160 | 15-19 |
| SDM | 311.0 | 92 (30); 156 (20) | 110 | 15–19 |
| PROP | 260.3 | 116.2 (18); 74.2 (25) | 105 | 15–19 |
| TYL | 916.5 | 772.4(25); 174.1(38) | 170 | 19-25 |
| CBZ | 237.2 | 194.2 (20); 179.0 (35) | 110 | 19-25 |
| ERY-$H_2O$ | 716.4 | 558.2 (15); 158 (35) | 160 | 19–25 |
| TIA | 494.4 | 192.2 (15); 119.1 (35) | 145 | 19–25 |
| CLA | 748.6 | 158.2 (35); 590.2 (15) | 165 | 19–25 |
| ROX | 837.6 | 679.3 (12); 158.2 (30) | 160 | 19–25 |
| BF | 362.2 | 316.2 (10); 139.1 (30) | 110 | 19–25 |

**Table S5** Calibration linear range, recovery, percent matrix effect and limit of quantification of target pharmaceuticals

| Compound | Internal standard | $r^2$ | Linear range | Recovery (RSD) (%) | | %ME | | LOQ | |
|---|---|---|---|---|---|---|---|---|---|
| | | | (μg $L^{-1}$) | Wastewater [a] | Sludge [b] | Wastewater | Sludge | Wastewater (ng $L^{-1}$) | Sludge (μg $kg^{-1}$) |
| SDZ | SMN-$^{13}C_6$ | 0.999 | 0.5–700 | 97 (9) | 112 (0) | 108 | 94 | 0.28 | 1.00 |
| STZ | SMN-$^{13}C_6$ | 0.999 | 0.5–700 | 96 (5) | 130 (5) | 118 | 96 | 0.21 | 0.25 |
| SMR | SMN-$^{13}C_6$ | 0.999 | 0.5–700 | 100 (4) | 105 (5) | 117 | 99 | 0.21 | 0.20 |
| SMN | SMN-$^{13}C_6$ | 0.999 | 0.5–700 | 110 (2) | 114 (2) | 113 | 105 | 0.09 | 0.05 |
| SML | SMN-$^{13}C_6$ | 0.999 | 0.5–700 | 106 (0) | 82 (0) | 116 | 74 | 0.17 | 0.05 |
| SMX | SMN-$^{13}C_6$ | 0.999 | 0.5–700 | 107 (13) | 103 (2) | 117 | 89 | 0.43 | 0.40 |
| SFX | SMN-$^{13}C_6$ | 0.999 | 0.5–700 | 126 (4) | 115 (1) | 117 | 107 | 0.43 | 0.20 |
| SDM | SMN-$^{13}C_6$ | 0.999 | 0.5–700 | 121 (4) | 108 (1) | 118 | 115 | 0.25 | 0.05 |
| NOR | OLF-$D_3$ | 0.995 | 0.5–1000 | 131 (3) | 89 (7) | 98 | 124 | 0.21 | 0.20 |
| OLF | OLF-$D_3$ | 0.995 | 0.5–1000 | 99 (8) | 107 (8) | 107 | 109 | 0.02 | 0.15 |
| CIP | OLF-$D_3$ | 0.998 | 0.5–1000 | 112 (3) | 61 (2) | 96 | 144 | 0.21 | 0.20 |
| ENR | OLF-$D_3$ | 0.997 | 0.5–700 | 129 (4) | 85 (5) | 90 | 105 | 0.36 | 0.50 |
| LOM | OLF-$D_3$ | 0.997 | 0.5–700 | 115 (5) | 128 (1) | 93 | 119 | 0.43 | 0.50 |
| TCN | DMC | 0.997 | 0.5–700 | 108 (1) | 100 (7) | 87 | 115 | 0.29 | 0.50 |
| OTC | DMC | 0.996 | 0.5–700 | 120 (6) | 105 (10) | 111 | 99 | 0.27 | 0.80 |
| CTC | DMC | 0.998 | 0.5–700 | 93 (5) | 82 (5) | 92 | 114 | 0.54 | 1.00 |
| DOX | DMC | 0.998 | 0.5–700 | 125 (3) | 118 (6) | 106 | 109 | 0.45 | 0.80 |
| ERY-$H_2O$ | – [c] | 0.999 | 0.5–700 | 73 (5) | 70 (6) | 115 | 82 | 0.07 | 0.05 |
| TIA | – | 0.999 | 0.5–700 | 81 (2) | 80 (3) | 109 | 85 | 0.05 | 0.03 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| CLA | – | 0.999 | 0.5–1000 | 73 (4) | 82 (2) | 107 | 82 | 0.02 | 0.05 |
| ROX | – | 0.999 | 0.5–1000 | 71 (7) | 90 (3) | 115 | 75 | 0.02 | 0.03 |
| TYL | – | 0.998 | 0.5–700 | 109 (2) | 96 (3) | 106 | 80 | 0.05 | 0.10 |
| AZN | – | 0.997 | 0.5–1000 | 127 (2) | 106 (1) | 110 | 95 | 0.10 | 0.20 |
| ATE | CAF-$^{13}C_3$ | 0.998 | 0.5–700 | 69 (0) | 58 (2) | 108 | 139 | 0.28 | 1.00 |
| MET | CAF-$^{13}C_3$ | 0.999 | 0.5–1000 | 90 (4) | 92 (2) | 113 | 105 | 0.44 | 0.15 |
| PROP | CAF-$^{13}C_3$ | 0.998 | 0.5–1000 | 102 (3) | 81 (2) | 113 | 96 | 0.26 | 0.20 |
| CAF | CAF-$^{13}C_3$ | 0.999 | 0.5–1000 | 107 (4) | 115 (3) | 110 | 116 | 0.73 | 0.80 |
| CBZ | CAF-$^{13}C_3$ | 0.997 | 0.5–700 | 91 (1) | 86 (3) | 117 | 87 | 0.17 | 0.20 |
| BF | CAF-$^{13}C_3$ | 0.999 | 0.5–700 | 88 (3) | 86 (2) | 115 | 105 | 0.17 | 0.20 |
| TMP | – | 0.995 | 0.5–700 | 72 (0) | 89 (0) | 112 | 96 | 0.04 | 0.02 |

[a] Spiked concentration: 0.5 μg $L^{-1}$, except CAF (10 μg $L^{-1}$) because of its high concentration in the influent; [b] Spiked concentrations: 0.2 mg $kg^{-1}$ for SAs, MLs and Others, and 1.0 mg $kg^{-1}$ for TCs and FQs; [c] –: no IS used.

**Table S6** Pharmaceutical concentrations in wastewater (ng $L^{-1}$) in different treatment units of Plant A (mean (SD), $n$ = 3)

| Compound | Influent | Primary clarifier | Anaerobic | Anoxic | Oxic | MBBR | Secondary clarifier | Return sludge supernatant | Final effluent |
|---|---|---|---|---|---|---|---|---|---|
| SDZ | 3.28 (0.13) | 2.80 (0.29) | 1.87 (0.03) | 1.74 (0.31) | 2.01 (0.13) | 1.35 (0.20) | 1.29 (0.22) | 0.80 (0.07) | 0.98 (0.31) |
| STZ | 3.25 (1.11) | 2.00 (0.68) | 1.13 (0.54) | 0.94 (0.57) | 1.35 (0.16) | 0.76 (0.31) | 0.29 (0.07) | 0.29 (0.19) | <LOQ [a] |
| SMN | 3.94 (0.50) | 4.75 (1.55) | 4.77 (0.92) | 4.64 (0.20) | 6.33 (1.28) | 9.44 (5.74) | 4.32 (0.45) | 3.51 (0.06) | 4.31 (1.01) |
| SMX | 222.4 (18.1) | 207.5 (4.49) | 139.7 (5.46) | 148.6 (2.60) | 147.6 (3.75) | 98.55 (4.07) | 73.16 (0.58) | 61.56 (0.07) | 53.82 (2.25) |
| NOR | 138.7 (8.59) | 113.4 (2.74) | 41.91 (7.16) | 40.55 (4.34) | 43.32 (1.90) | 39.18 (3.94) | 29.06 (2.00) | 32.16 (3.64) | 28.50 (0.11) |
| OLF | 684.5 (19.1) | 527.3 (18.9) | 185.4 (15.3) | 177.6 (15.1) | 177.5 (16.5) | 180.0 (29.5) | 103.6 (2.80) | 105.7 (4.77) | 111.4 (6.57) |
| CIP | 90.6 (4.50) | 73.33 (0.72) | 24.72 (1.42) | 25.37 (1.74) | 27.08 (0.92) | 26.50 (3.48) | 17.81 (2.47) | 20.67 (2.24) | 19.94 (2.81) |
| LOM | 3.33 (0.79) | 4.20 (0.49) | 1.22 (0.24) | 1.87 (0.22) | 1.49 (0.63) | 0.67 (0.47) | 0.72 (0.48) | 3.29 (0.80) | 1.42 (0.30) |
| TCN | 2.95 (0.28) | 1.23 (0.61) | 1.35 (0.66) | 1.73 (0.75) | 1.18 (0.67) | 0.70 (0.13) | 0.62 (0.19) | <LOQ | 0.90 (0.25) |
| CTC | 0.97 (0.12) | 0.67 (0.51) | 0.54 (0.05) | 0.58 (0.05) | <LOQ | 1.34 (0.54) | <LOQ | <LOQ | <LOQ |
| OTC | 23.51 (0.70) | 19.07 (3.59) | 5.52 (0.46) | 2.58 (1.27) | 19.66 (1.23) | 2.29 (0.43) | 1.45 (0.25) | 1.35 (0.29) | 1.62 (0.03) |
| DOX | 1.52 (0.68) | 1.12 (0.63) | 0.53 (0.25) | <LOQ | 0.54 (0.03) | <LOQ | 0.65 (0.33) | <LOQ | <LOQ |
| CLA | 228.7 (2.66) | 220.4 (4.25) | 101.3 (0.23) | 97.21 (2.51) | 101.4 (1.87) | 104.3 (1.73) | 91.71 (1.12) | 84.86 (3.60) | 77.29 (4.41) |
| ERY-$H_2O$ | 6.28 (0.62) | 5.46 (1.87) | 5.11 (1.13) | 5.18 (1.24) | 7.40 (1.67) | 6.01 (1.87) | 2.46 (0.13) | 1.13 (0.65) | 1.52 (0.25) |
| ROX | 564.9 (5.55) | 488.1 (5.37) | 256.9 (4.92) | 241.5 (3.08) | 249.5 (8.18) | 265.5 (7.30) | 261.6 (0.77) | 266.2 (3.04) | 224.0 (14.2) |
| AZN | 478.4(3.50) | 394.6 (1.63) | 151.5 (3.93) | 148.0 (12.5) | 146.3 (12.9) | 121.9 (8.87) | 113.7 (0.69) | 111.9 (4.60) | 138.69 (2.76) |
| ATE | 29.69 (0.22) | 20.71 (1.04) | 7.90 (0.37) | 10.03 (1.29) | 8.49 (2.46) | 7.73 (1.56) | 5.00 (1.56) | 3.58 (0.56) | 3.01 (0.61) |
| MET | 271.2 (5.77) | 252.7 (3.68) | 221.8 (3.60) | 226.2 (2.38) | 235.5 (6.48) | 239.0 (4.85) | 266.7 (0.81) | 290.3 (6.49) | 259.69 (0.12) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| PROP | 2.27 (0.12) | 1.24 (0.14) | 1.90 (0.16) | 1.90 (0.09) | 2.09 (0.32) | 2.25 (0.22) | 1.72 (0.18) | 2.96 (0.50) | 1.87 (0.54) |
| CBZ | 21.03 (0.81) | 21.90 (0.92) | 23.86 (0.67) | 25.29 (0.79) | 25.83 (0.37) | 27.85 (0.84) | 31.42 (0.47) | 34.86 (0.35) | 30.25 (1.11) |
| BF | 9.52 (0.37) | 7.40 (0.85) | 8.21 (0.84) | 7.65 (1.09) | 8.40 (0.82) | 7.29 (0.88) | 6.40 (0.36) | 3.99 (0.33) | 6.17 (0.07) |
| CAF | 14929.1 (513) | 11160.6 (133) | 5472.3 (260) | 4443.6 (140) | 2924.6 (105) | 388.2 (95.3) | 15.59 (0.95) | 57.70 (18.7) | 15.31 (0.44) |
| TMP | 46.58 (0.27) | 25.69 (0.71) | 29.29 (1.00) | 31.85 (0.43) | 33.72 (0.49) | 33.34 (0.92) | 33.14 (0.05) | 34.09 (1.73) | 35.41 (3.32) |
| ∑ SAs | 232.8 | 217.1 | 147.5 | 155.9 | 157.3 | 110.1 | 79.05 | 66.15 | 59.30 |
| ∑ FQs | 917.1 | 718.2 | 253.2 | 245.3 | 249.4 | 246.4 | 151.2 | 161.8 | 161.2 |
| ∑ TCs | 28.95 | 22.09 | 7.93 | 5.23 | 21.71 | 4.62 | 3.19 | 2.00 | 3.24 |
| ∑ MLs | 1278.3 | 1108.6 | 514.9 | 491.9 | 504.5 | 497.7 | 469.5 | 464.1 | 441.5 |
| ∑ Others | 15309.4 | 11490.3 | 5765.3 | 4746.5 | 3238.6 | 705.6 | 360.0 | 427.4 | 351.7 |

[a] LOQ: limit of quantification (S/N = 10).

**Table S7** Pharmaceutical concentrations in wastewater (ng $L^{-1}$) in different treatment units of Plant B (mean (SD), $n$ = 3)

| Compound | Influent | Primary clarifier | OD-external | OD-internal | Secondary clarifier | Return sludge supernatant | Final effluent |
|---|---|---|---|---|---|---|---|
| SDZ | 5.60 (0.35) | 5.47 (0.45) | 1.23 (0.24) | 0.97 (0.13) | 1.28 (0.10) | 1.01 (0.19) | 1.60 (0.29) |
| SMN | 12.10 (0.65) | 11.51 (1.28) | 8.64 (0.98) | 7.08 (1.03) | 6.39 (0.55) | 5.87 (0.51) | 4.99 (3.12) |
| SMX | 246.9 (20.9) | 234.1 (9.40) | 129.9 (9.16) | 76.60 (4.36) | 87.53 (3.95) | 80.15 (2.80) | 120.6 (3.90) |
| NOR | 169.3 (4.83) | 128.1 (9.04) | 69.54 (2.16) | 66.40 (9.17) | 48.24 (2.79) | 50.20 (1.68) | 50.23 (7.69) |
| OLF | 722.0 (7.67) | 628.6 (14.0) | 420.5 (9.29) | 296.8 (17.5) | 326.06 (9.95) | 322.6 (25.2) | 341.4 (26.0) |
| CIP | 69.71 (3.01) | 59.93 (3.38) | 42.10 (5.96) | 34.26 (3.62) | 14.66 (8.24) | 22.38 (2.29) | 14.99 (3.92) |
| LOM | 36.39 (3.95) | 22.66 (1.61) | 5.18 (0.18) | 18.94 (1.61) | 1.96 (0.37) | 9.21 (1.35) | 4.22 (0.40) |
| TCN | 1.65 (0.44) | 1.15 (0.63) | 1.20 (0.48) | 0.96 (0.56) | 0.89 (0.77) | <LOQ | 0.67 (0.28) |
| CTC | 1.66 (0.14) | 1.33 (0.95) | 2.13 (1.01) | 1.50 (0.79) | 0.58 (0.22) | 0.68 (0.25) | 0.88 (0.56) |
| OTC | 34.45 (7.29) | 31.04 (6.45) | 9.04 (5.14) | 22.95 (3.51) | 6.45 (0.37) | 8.30 (0.92) | 8.96 (1.54) |
| DOX | 5.33 (1.01) | 3.52 (1.25) | 2.02 (1.21) | 1.16 (0.16) | 0.83 (0.28) | 0.99 (0.25) | 0.96 (0.44) |
| CLA | 125.1 (3.92) | 123.6 (2.89) | 44.08 (2.11) | 12.39 (0.55) | 16.36 (0.43) | 9.64 (0.81) | 18.55 (0.31) |
| ERY-$H_2O$ | 5.51 (0.52) | 5.68 (0.44) | 4.95 (1.46) | 2.45 (0.37) | 2.61 (0.59) | 2.45 (0.42) | 2.54 (1.10) |
| ROX | 572.4 (12.6) | 584.7 (1.64) | 559.9 (13.7) | 429.1 (3.11) | 453.1 (5.90) | 494.7 (9.58) | 412.5 (3.82) |
| AZN | 897.9 (19.6) | 859.1 (15.1) | 847.2 (16.5) | 625.8 (18.9) | 631.4 (11.3) | 710.1 (15.8) | 603.2 (25.8) |
| ATE | 47.34 (1.77) | 42.83 (3.60) | 13.32 (0.36) | 2.19 (0.42) | 7.69 (0.45) | 3.98 (1.97) | 2.68 (0.36) |
| MET | 187.2 (3.20) | 182.7 (2.62) | 202.3 (6.44) | 226.8 (1.87) | 180.4 (0.76) | 181.1 (3.07) | 177.1 (8.47) |
| PROP | 3.30 (0.07) | 3.14 (0.12) | 2.82 (0.28) | 2.87 (0.09) | 3.27 (0.07) | 2.85 (0.25) | 2.82 (0.39) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| CBZ | 12.06 (0.38) | 13.13 (0.37) | 21.82 (0.52) | 24.01 (0.57) | 21.75 (0.49) | 20.33 (0.60) | 20.48 (1.07) |
| BF | 2.15 (0.58) | 2.96 (0.90) | 0.86 (0.44) | 0.58 (0.27) | 0.42 (0.30) | 0.53 (0.48) | 0.66 (0.40) |
| CAF | 8600.6 (91.0) | 8298.4 (409.1) | 535.5 (22.5) | 64.57 (2.78) | 6.51 (0.54) | 71.20 (4.72) | 9.55 (0.76) |
| TMP | 41.10 (0.52) | 40.15 (1.99) | 37.89 (1.78) | 36.47(1.20) | 34.98 (1.90) | 28.65 (0.66) | 33.48 (1.06) |
| ∑SAs | 264.7 | 251.0 | 139.8 | 84.64 | 95.20 | 87.02 | 127.2 |
| ∑FQs | 997.4 | 839.3 | 537.3 | 416.4 | 390.9 | 404.4 | 410.9 |
| ∑TCs | 43.09 | 37.04 | 14.39 | 26.56 | 8.75 | 10.23 | 11.47 |
| ∑MLs | 1600.9 | 1548.2 | 1456.1 | 1069.8 | 1103.4 | 1216.9 | 1036.7 |
| ∑Others | 8893.7 | 8583.3 | 814.5 | 357.5 | 255.1 | 308.7 | 246.8 |

**Table S8** Pharmaceutical concentrations in sludge (μg $kg^{-1}$) in different treatment units of two studied WWTPs (mean (SD), $n$ = 3)

| Compound | Plant A | | | | | Plant B | | |
|---|---|---|---|---|---|---|---|---|
| | Anaerobic | Anoxic | Oxic | MBBR | Return sludge | OD-external | OD-internal | Return sludge |
| STZ | 2.60 (0.30) | 4.30 (1.22) | 2.92 (0.36) | 3.18 (0.12) | 4.13 (0.11) | 2.75 (0.78) | 1.69 (0.29) | 2.86 (0.42) |
| SMN | 1.29 (0.20) | 0.52 (0.32) | 0.92 (0.10) | 1.02 (0.16) | 1.05 (0.05) | 3.11 (0.35) | 1.16 (0.20) | 1.04 (0.58) |
| SMX | 65.88 (3.00) | 17.61 (0.67) | 17.72 (1.15) | 26.00 (1.58) | 20.64 (0.20) | 19.62 (0.60) | 18.75 (0.96) | 18.11 (0.47) |
| NOR | 3146.5 (36.5) | 2503.9 (2.62) | 2667.8(88.6) | 2958.7 (5.70) | 3147.7 (31.5) | 2357.6 (12.9) | 2380.0 (78.1) | 2138.8 (37.5) |
| OLF | 10747.1 (109) | 9314.4 (17.3) | 11231.3 (98.8) | 10317.4 (81.3) | 11348.1 (131) | 7274.6 (36.8) | 6915.7 (55.2) | 7704.9 (44.9) |
| CIP | 865.5 (6.90) | 693.9 (9.97) | 729.92 (27.3) | 788.9 (18.6) | 876.9 (10.6) | 528.4 (3.08) | 575.5 (14.1) | 555.8 (21.5) |
| LOM | 310.6 (8.81) | 284.6 (3.39) | 319.0 (26.3) | 292.5 (3.62) | 353.8 (7.64) | 348.1 (7.24) | 342.7 (1.60) | 352.5 (11.0) |
| TCN | 48.09 (0.83) | 38.38 (1.47) | 48.29 (1.55) | 48.14 (0.70) | 44.20 (2.23) | 36.83 (1.41) | 38.00 (0.78) | 43.54 (0.21) |
| CTC | 13.93 (0.42) | 10.90 (0.81) | 13.31 (2.08) | 10.34 (2.05) | 13.22 (0.84) | 80.29 (0.22) | 81.74 (0.38) | 92.00 (2.61) |
| OTC | 350.4 (1.64) | 259.7 (1.29) | 341.7 (12.9) | 335.6 (7.36) | 340.2 (4.65) | 408.2 (10.5) | 390.4 (3.96) | 454.5 (14.8) |
| DOX | 13.12 (0.44) | 10.12 (0.10) | 12.98 (0.35) | 11.58 (0.54) | 12.13 (0.30) | 14.40 (0.25) | 14.61 (0.37) | 18.06 (0.40) |
| CLA | 64.01 (0.74) | 65.60 (1.05) | 67.35 (0.82) | 48.18 (0.47) | 42.81 (0.58) | 15.24 (0.58) | 13.03 (0.48) | 14.75 (0.94) |
| ERY-$H_2O$ | 3.06 (0.12) | 2.80 (0.13) | 3.63 (0.11) | 2.23 (0.22) | 2.29 (0.08) | 3.18 (0.26) | 3.43 (0.60) | 3.21 (0.27) |
| ROX | 58.97 (1.08) | 51.59 (0.24) | 56.90 (1.41) | 50.74 (0.47) | 43.33 (0.56) | 73.59 (1.13) | 68.11 (1.82) | 50.22 (0.94) |
| AZN | 4990.4 (60.6) | 2683.4 (48.4) | 4441.1 (51.8) | 5764.7 (76.2) | 6026.8 (8.49) | 8468.1 (10.5) | 7983.6 (28.5) | 6148.9 (18.1) |
| MET | 10.99 (0.51) | 8.84 (0.14) | 10.38 (0.09) | 8.63 (0.41) | 8.49 (0.16) | 5.09 (0.16) | 6.13 (0.22) | 5.90 (0.17) |
| PROP | 0.99 (0.04) | 0.93 (0.05) | 1.03 (0.07) | 0.99 (0.03) | 1.17 (0.03) | 1.66 (0.10) | 1.45 (0.08) | 1.17 (0.12) |
| CAF | 50.96 (0.79) | 53.38 (1.19) | 33.43 (0.50) | 23.2 (0.41) | 20.72 (0.26) | 12.83 (0.87) | 11.00 (0.44) | 9.51 (1.38) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| TMP | 7.56 (0.24) | 6.59 (0.27) | 7.55 (0.36) | 6.51 (0.13) | 8.03 (0.12) | 6.66 (0.47) | 5.82 (0.15) | 5.74 (0.13) |
| ∑ SAs | 69.77 | 22.43 | 21.57 | 30.20 | 25.82 | 25.49 | 21.60 | 22.00 |
| ∑ FQs | 15079.8 | 12803.1 | 14957.4 | 14367.0 | 15736.6 | 10537.2 | 10239.5 | 10778.7 |
| ∑ TCs | 425.6 | 319.1 | 416.3 | 405.7 | 409.8 | 539.7 | 524.7 | 608.1 |
| ∑ MLs | 5116.4 | 2803.4 | 4569.0 | 5864.8 | 6115.3 | 8560.1 | 8068.2 | 6217.1 |
| ∑ Others | 70.50 | 69.74 | 52.39 | 39.35 | 38.41 | 26.24 | 24.40 | 22.31 |

**Table S9** Effluent and sludge RQ values for target pharmaceuticals in two studied WWTPs

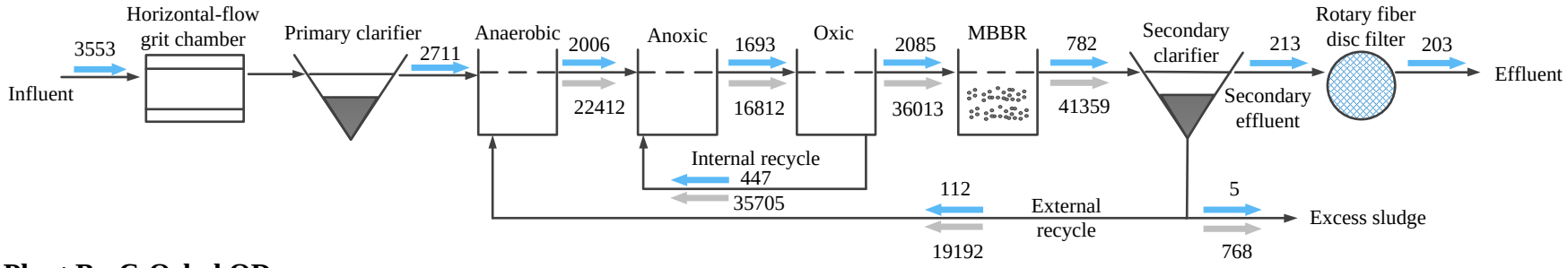
| Compound | L(E)C50 [a] (mg $L^{-1}$) | | | Max. conc. in effluent (ng $L^{-1}$) | Effluent RQ | | | Max. conc. in sludge (µg $kg^{-1}$) | Sludge RQ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Algae | Invertebrates | Fish | | Algae | Invertebrates | Fish | | Algae | Invertebrates | Fish |
| | | | | | | Plant A | | | | | |
| SDZ | 0.135 | 6.923 | 596.385 | 1.72 | 1.27E-02 | 2.48E-04 | 2.88E-06 | <LOQ | NA | NA | NA |
| STZ | NA | 85.4 | >500 | 0.49 | NA | 5.78E-06 | 9.87E-07 | 11.03 | NA | 1.05E-06 | 1.80E-07 |
| SMN | 1.358 | 4.66 | 178.574 | 7.38 | 5.44E-03 | 1.58E-03 | 4.13E-05 | 2.83 | 8.10E-04 | 2.36E-04 | 6.16E-06 |
| SMX | 0.027 | 4.5 [b] | 562.5 | 59.21 | 2.19E+00 [c] | 1.32E-02 | 1.05E-04 | 30.25 | 3.89E-01 [c] | 2.33E-03 | 1.87E-05 |
| NOR | 2 | 29.88 | 344.261 | 103.45 | 5.17E-02 | 3.46E-03 | 3.00E-04 | 3661.39 | 2.17E-03 | 1.46E-04 | 1.26E-05 |
| OLF | 0.016 [b] | 30 [b] | 10 [b] | 287.32 | 1.80E+01 | 9.58E-03 | 2.87E-02 | 12127.22 | 8.21E-01 | 4.38E-04 | 1.31E-03 |
| CIP | 0.005 | >60 | >100 | 45.24 | 9.05E+00 | 7.54E-04 | 4.52E-04 | 999.73 | 5.48E-01 | 4.57E-05 | 2.74E-05 |
| LOM | 0.106 | 10 | 10 | 3.43 | 3.23E-02 | 3.43E-04 | 3.43E-04 | 390.70 | 3.98E-03 | 4.22E-05 | 4.22E-05 |
| TCN | 0.09 | 44.8 | 220 | 6.06 | 6.74E-02 | 1.35E-04 | 2.76E-05 | 44.20 | 2.43E-04 | 4.88E-07 | 9.95E-08 |
| CTC | 0.05 | 225 | 78.9 | 6.32 | 1.26E-01 | 2.81E-05 | 8.01E-05 | 14.03 | 7.90E-04 | 1.76E-07 | 5.00E-07 |
| OTC | 0.17 | 0.18 | 110.1 | 15.82 | 9.30E-02 | 8.79E-02 | 1.58E-05 | 340.20 | 9.26E-04 | 8.74E-04 | 1.57E-07 |
| DOX | NA | 0.3 | NA | 2.71 | NA | 9.03E-03 | NA | 12.13 | NA | 5.47E-05 | NA |
| CLA | 0.07 | 20 | >100 | 88.70 | 1.27E+00 | 4.44E-03 | 8.87E-04 | 47.07 | 1.55E-01 | 5.42E-04 | 1.08E-04 |
| ERY-$H_2O$ | 0.02 | 0.22 | 61 [b] | 3.52 | 1.76E-01 | 1.60E-02 | 5.77E-05 | 4.22 | 1.21E-02 | 1.10E-03 | 3.97E-06 |
| ROX | 4 [b] | 6 [b] | 50 [b] | 312.72 | 7.82E-02 | 5.21E-02 | 6.25E-03 | 48.14 | 8.60E-03 | 5.73E-03 | 6.88E-04 |
| AZN | 1.971 | 3.066 | 19.827 | 239.86 | 1.22E-01 | 7.82E-02 | 1.21E-02 | 7149.00 | 7.83E-03 | 5.04E-03 | 7.79E-04 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ATE | NA | 30 | >100 | 7.85 | NA | 2.62E-04 | 7.85E-05 | <LOQ | NA | NA | NA |
| MET | 7.9 | 8.8 | >100 | 259.69 | 3.29E-02 | 2.95E-02 | 2.60E-03 | 8.49 | 4.27E-03 | 3.84E-03 | 3.38E-04 |
| PROP | 0.244 | 0.8 | 11.4 | 2.04 | 8.36E-03 | 2.55E-03 | 1.79E-04 | 1.17 | 1.41E-03 | 4.31E-04 | 3.02E-05 |
| CBZ | 25.5 | 13.8 | 35.4 | 30.25 | 1.19E-03 | 2.19E-03 | 8.55E-04 | <LOQ | NA | NA | NA |
| BF | 1.873 | 25 | 3.452 | 6.17 | 3.30E-03 | 2.47E-04 | 1.79E-03 | <LOQ | NA | NA | NA |
| CAF | 805 [b] | 46 [b] | 46 [b] | 15.31 | 1.90E-05 | 3.33E-04 | 3.33E-04 | 27.89 | 1.12E-05 | 1.96E-04 | 1.96E-04 |
| TMP | 2.6 [b] | 4.8 [b] | 100 | 35.41 | 1.36E-02 | 7.38E-03 | 3.54E-04 | 8.03 | 1.52E-03 | 8.26E-04 | 3.96E-05 |
| | | | | $RQ_{tot}$ | 3.13E+01 | 3.19E-01 | 5.56E-02 | | 1.96E+00 | 2.19E-02 | 3.60E-03 |
| | | | | | Plant B | | | | | | |
| SDZ | 0.135 | 6.923 | 596.385 | 1.60 | 1.18E-02 | 2.31E-04 | 2.68E-06 | <LOQ | NA | NA | NA |
| SMN | 1.358 | 4.66 | 178.574 | 6.72 | 4.95E-03 | 1.44E-03 | 3.76E-05 | 7.28 | 4.53E-03 | 1.32E-03 | 3.44E-05 |
| SMX | 0.027 | 4.5 [b] | 562.5 | 143.92 | 5.33E+00 | 3.20E-02 | 2.56E-04 | 21.42 | 5.24E-01 | 3.14E-03 | 2.52E-05 |
| NOR | 2 | 29.88 | 344.261 | 117.29 | 5.86E-02 | 3.93E-03 | 3.41E-04 | 2414.63 | 4.23E-03 | 2.83E-04 | 2.46E-05 |
| OLF | 0.016 [b] | 30 [b] | 10 [b] | 401.63 | 2.51E+01 | 1.34E-02 | 4.02E-02 | 7704.89 | 3.01E+00 | 1.60E-03 | 4.81E-03 |
| CIP | 0.005 | >60 | >100 | 52.01 | 1.04E+01 | 8.67E-04 | 5.20E-04 | 563.19 | 6.77E-01 | 5.64E-05 | 3.38E-05 |
| LOM | 0.106 | 10 | 10 | 18.08 | 1.71E-01 | 1.81E-03 | 1.81E-03 | 357.06 | 1.31E-02 | 1.39E-04 | 1.39E-04 |
| TCN | 0.09 | 44.8 | 220 | 2.73 | 3.03E-02 | 6.10E-05 | 1.24E-05 | 46.54 | 4.46E-04 | 8.96E-07 | 1.82E-07 |
| CTC | 0.05 | 225 | 78.9 | 5.62 | 1.12E-01 | 2.50E-05 | 7.13E-05 | 92.00 | 2.04E-03 | 4.54E-07 | 1.29E-06 |
| OTC | 0.17 | 0.18 | 110.1 | 37.17 | 2.19E-01 | 2.07E-01 | 3.38E-04 | 454.53 | 7.29E-03 | 6.89E-03 | 1.13E-05 |
| DOX | NA | 0.3 | NA | 3.67 | NA | 1.22E-02 | NA | 18.06 | NA | 4.94E-04 | NA |
| CLA | 0.07 | 20 | >100 | 18.55 | 2.65E-01 | 9.28E-04 | 1.86E-04 | 14.75 | 2.06E-02 | 7.20E-05 | 1.44E-05 |
| ERY-$H_2O$ | 0.02 | 0.22 | 61 [b] | 2.66 | 1.33E-01 | 1.21E-02 | 4.36E-05 | 3.41 | 1.94E-02 | 1.77E-03 | 6.37E-06 |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ROX | 4 [b] | 6 [b] | 50 [b] | 412.46 | 1.03E-01 | 6.87E-02 | 8.25E-03 | 61.50 | 2.26E-02 | 1.51E-02 | 1.81E-03 |
| AZN | 1.971 | 3.066 | 19.827 | 615.51 | 3.12E-01 | 2.01E-01 | 3.10E-02 | 8466.35 | 7.40E-02 | 4.76E-02 | 7.36E-03 |
| ATE | NA | 30 | >100 | 2.68 | NA | 8.95E-05 | 2.68E-05 | <LOQ | NA | NA | NA |
| MET | 7.9 | 8.8 | >100 | 177.10 | 2.24E-02 | 2.01E-02 | 1.77E-03 | 5.90 | 3.42E-03 | 3.07E-03 | 2.70E-04 |
| PROP | 0.244 | 0.8 | 11.4 | 2.82 | 1.15E-02 | 3.52E-03 | 2.47E-04 | 9.64 | 1.44E-02 | 4.38E-03 | 3.07E-04 |
| CBZ | 25.5 | 13.8 | 35.4 | 23.44 | 9.19E-04 | 1.70E-03 | 6.62E-04 | <LOQ | NA | NA | NA |
| BF | 1.873 | 25 | 3.452 | 0.92 | 4.93E-04 | 3.69E-05 | 2.67E-04 | <LOQ | NA | NA | NA |
| CAF | 805 [b] | 46 [b] | 46 [b] | 13.11 | 1.63E-05 | 2.85E-04 | 2.85E-04 | 15.07 | 2.09E-05 | 3.66E-04 | 3.66E-04 |
| TMP | 2.6 [b] | 4.8 [b] | 100 | 33.48 | 1.29E-02 | 6.98E-03 | 3.35E-04 | 5.74 | 1.64E-03 | 8.91E-04 | 4.28E-05 |
| | | | | $RQ_{tot}$ | 4.23E+01 | 5.88E-01 | 8.67E-02 | | 4.40E+00 | 8.71E-02 | 1.53E-02 |

[a] LC50 = half lethal concentration, EC50 = half effective concentration; [b] These data are from ECOSAR (U.S. EPA), all other data are from literature[1-16]; [c] Red and yellow shades indicate high and medium risks, respectively.

**Plant A: A/A/O-MBBR**




**Plant B: C-Orbal OD**

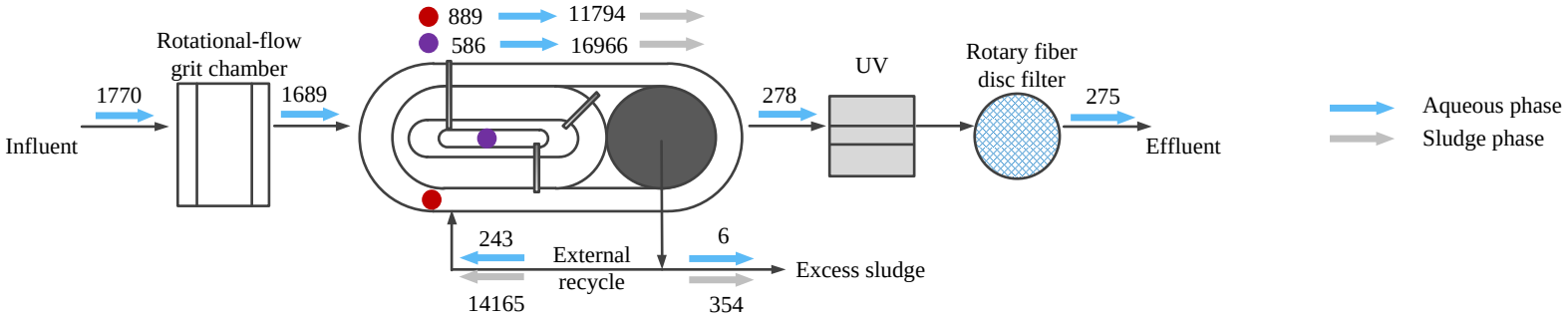



**Fig. S1** Total mass flows (g $d^{-1}$) of target pharmaceuticals along the treatment processes in two studied WWTPs.

## References:


1. K. Choi, Y. Kim, J. Jung, M. H. Kim, C. S. Kim, N. H. Kim and J. Park, *Environ. Toxicol. Chem.*, 2008, **27**, 711–719.
2. M. Cleuvers, *Toxicol. Lett.*, 2003, **142**, 185–194.
3. B. Ferrari, R. Mons, B. Vollat, B. Fraysse, N. Paxeus, R. Lo Giudice, A. Pollio and J. Garric, *Environ. Toxicol. Chem.*, 2004, **23**, 1344–1354.
4. M. Grung, T. Kallqvist, S. Sakshaug, S. Skurtveit and K. V. Thomas, *Ecotox. Environ. Safe.*, 2008, **71**, 328–340.
5. M. D. Hernando, A. Aguera and A. R. Fernandez-Alba, *Anal. Bioanal. Chem.*, 2007, **387**, 1269-1285.
6. M. Isidori, M. Lavorgna, A. Nardelli, L. Pascarella and A. Parrella, *Sci. Total Environ.*, 2005, **346**, 87–98.
7. J. W. Kim, H. Ishibashi, R. Yamauchi, N. Ichikawa, Y. Takao, M. Hirano, M. Koga and K. Arizono, *J. Toxicol. Sci.*, 2009, **34**, 227–232.
8. Y. J. Lee, S. E. Lee, D. S. Lee and Y. H. Kim, *Environ. Toxicol. Phar.*, 2008, **26**, 216–221.
9. W. H. Li, Y. L. Shi, L. H. Gao, J. M. Liu and Y. Q. Cai, *Chemosphere*, 2013, **92**, 435–444.
10. H. Sanderson, D. J. Johnson, C. J. Wilson, R. A. Brain and K. R. Solomon, *Toxicol. Lett.*, 2003, **144**, 383–395.
11. Q. Sui, B. Wang, W. T. Zhao, J. Huang, G. Yu, S. B. Deng, Z. F. Qiu and S. G. Lu, *Chemosphere*, 2012, **89**, 280–286.
12. L. Wollenberger, B. Halling-Sorensen and K. O. Kusk, *Chemosphere*, 2000, **40**, 723–730.
13. Q. Yan, X. Gao, Y. P. Chen, X. Y. Peng, Y. X. Zhang, X. M. Gan, C. F. Zi and J. S. Guo, *Sci. Total Environ.*, 2014, **470**, 618–630.
14. L. H. Yang, G. G. Ying, H. C. Su, J. L. Stauber, M. S. Adams and M. T. Binet, *Environ. Toxicol. Chem.*, 2008, **27**, 1201–1208.
15. L. H. M. L. M. Santos, A. N. Araujo; A. Fachini, A. Pena, C. Delerue-Matos and M. C. B. S. M. Montenegro, *J. Hazard. Mater.*, 2010, **175**, 45–95.
16. P. Verlicchi, M. Al Aukidy and E. Zambello, *Sci. Total Environ.*, 2012, **429**, 123–155.