***SUPPLEMENTARY INFORMATION***

**The fate of pharmaceuticals and personal care products (PPCPs), endocrine disrupting contaminants (EDCs), metabolites and illicit drugs in a WWTW and environmental waters**

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**Figure S1:** Layout of the treatment processes at the WWTW in the current study. The plant has a capacity of 55 megaliters per day, and receives wastewater from both domestic and industrial sources (estimated ratio of 60:40 respectively). Wastewater treatment consists of four biological nutrient removal (BNR) modules, with the first three modules being a 3-stage treatment process developed by the University of Cape Town **(A)**, and a fourth module consisting of a modified Ludzack-Ettinger (MLE) treatment process **(B)**.

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**Figure S2:** Liquid chromatography-Mass spectrometry (UPLC/TQD-MS) methods for acidic and basic compound detection.

**Table S1:** List of corrected recoveries of target ECs within WWTW influent/effluent and river water upstream and downstream samples.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Chemical Class | Chemical | Corrected recovery (%) | | | |
| WWTW | | River water | |
| Effluent | Influent | Upstream | Downstream |
| UV filters | Benzophenone-1 | 45.7 | 39.3 | 63.4 | 64.5 |
| Benzophenone-3 | 164.6 | 41.9 | 92.7 | 98.3 |
| Benzophenone-4 | 145.7 | 121.9 | 136.2 | 128.1 |
| Parabens | Methylparaben | 97.1 | 83.9 | 94.2 | 93.5 |
| Ethylparaben | 62.8 | 50.6 | 56.9 | 60.6 |
| Propylparaben | 106.1 | 83.7 | 149.1 | 170.7 |
| Butylparaben | 95.1 | 81.8 | 135.6 | 156.9 |
| Plasticizer | Bisphenol-A | 119.5 | 87.7 | 125.8 | 119.0 |
| Antibiotics | Sulfasalazine | 118.9 | 177.6 | 165.5 | 140.1 |
| Clarithromycin | 158.2 | 56.2 | 97.6 | 104.8 |
| Azithromycin | 51.3 | 30.6 | 59.6 | 76.5 |
| Trimethoprim | 158.2 | 165.2 | 149.3 | 164.1 |
| Sulfamethoxazole | 135.4 | 130.7 | 107.0 | 110.0 |
| H2 receptor agonists | Ranitidine | 66.5 | 57.3 | 63.7 | 68.7 |
| Cimetidine | 73.7 | 93.8 | 117.8 | 119.5 |
| NSAIDs | Ketoprofen | 107.6 | 113.7 | 108.5 | 110.8 |
| Ibuprofen | 87.1 | 81.9 | 110.4 | 110.3 |
| Naproxen | 85.5 | 86.8 | 101.9 | 103.6 |
| Diclofenac | 191.8 | 208.7 | 190.9 | 176.5 |
| Acetaminophen | 120.7 | 122.6 | 104.8 | 103.2 |
| Lipid regulators | Bezafibrate | 90.4 | 95.2 | 102.6 | 106.5 |
| Atorvastatin | 229.4 | 270.2 | 159.2 | 116.8 |
| Anti-depressants and metabolites | Venlafaxine | 71.1 | 50.5 | 85.2 | 76.5 |
| Desvenlafaxine | 88.0 | 88.5 | 107.1 | 101.9 |
| Fluoxetine | 107.5 | 108.3 | 117.1 | 120.7 |
| Desmethylcitalopram | 95.6 | 114.4 | 88.2 | 79.6 |
| Antihistamines | Fexofenadine | 66.1 | 73.7 | 61.1 | 47.4 |
| Anti-cancer | Azathioprine | 145.8 | 165.3 | 104.1 | 104.1 |
| Anti-epileptic and metabolites | Carbamazepine | 95.5 | 100.6 | 99.0 | 100.2 |
| Carbamazepine10,11-epoxide | 128.9 | 139.2 | 126.8 | 135.2 |
| 10,11-Dihydro-10-hydroxycarbamazepine | 131.9 | 154.3 | 115.8 | 124.1 |
| Diabetes | Metformin | 113.6 | 122.6 | 123.0 | 118.1 |
| Gliclazide | 125.5 | 56.5 | 101.5 | 93.7 |
| Hypertension | Valsartan | 185.0 | 195.6 | 165.7 | 145.1 |
| Irbesartan | 143.6 | 137.9 | 195.4 | 203.0 |
| Lisinopril | 67.0 | 47.9 | 39.4 | 37.1 |
| X-ray contrast media | Iopromide | 137.8 | 147.0 | 167.6 | 174.5 |
| Beta-blocker | Atenolol | 91.7 | 86.8 | 97.4 | 102.4 |
| Analgaesics and metabolites | Morphine | 91.4 | 111.3 | 104.6 | 102.3 |
| Normorphine | 94.6 | 106.5 | 93.5 | 94.6 |
| Codeine | 100.6 | 80.0 | 103.7 | 98.0 |
| Tramadol | 83.5 | 83.6 | 100.2 | 94.1 |
| N-desmethyltramadol | 67.6 | 67.0 | 74.8 | 74.9 |
| O-desmethyltramadol | 101.2 | 118.1 | 104.4 | 99.4 |
| Drug precursor and metabolite | Ephedrine/pseudoephedrine | 69.0 | 60.9 | 77.5 | 87.0 |
| Stimulants and metabolites | Amphetamine | 106.1 | 103.3 | 101.1 | 106.3 |
| Methamphetamine | 98.1 | 107.8 | 93.4 | 92.2 |
| Cocaine | 102.8 | 101.8 | 100.9 | 102.0 |
| Benzoylecgonine | 121.6 | 116.9 | 112.8 | 119.9 |
| Cocaethylene | 101.8 | 103.8 | 103.6 | 101.4 |
| Mephedrone | 99.9 | 103.3 | 105.3 | 99.9 |
| Human indicators and metabolites | Creatinine | 67.3 | 82.2 | 71.0 | 66.8 |
| Nicotine | 80.2 | 108.3 | 77.6 | 82.4 |
| Caffeine | 132.0 | 124.4 | 92.7 | 90.3 |
| Cotinine | 98.9 | 83.1 | 100.7 | 100.5 |
| 1,7 dimethylxantine | 122.2 | 114.6 | 67.3 | 60.7 |

| **Table S2**: Quantitative concentrations (ng.L-1) of the detected ECs in samples obtained from influent and effluent WWTW, and river water samples located upstream and downstream of the plant. Abbreviations: *DMX*- 1,7-dimethylxantine; *NDT* – N-desmethyltramadol; *ODT* – O-desmethyltramadol; *CBZ-ep* – carbamazepine epoxide; *dh-h-CBZ* – 10,11-dihydro-10-hydroxycarbamazepine; *d-venlafaxine* – desvenlafaxine; *dm-citalopram* – desmethylcitalopram. | | | | | | | | | | | | | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Concentration (ng.L-1, ± stdev) | | | | | | | | | | | | | | | | | | | |
| 06/07/2015 | | | | 07/07/2015 | | | | 08/07/2015 | | | | 09/07/2015 | | | | 10/07/2015 | | | |
| US | Inf. | Eff. | DS | US | Inf. | Eff. | DS | US | Inf. | Eff. | DS | US | Inf. | Eff. | DS | US | Inf. | Eff. | DS |
| *Chemicals in ESI- mode* | | | | | | | | | | | | | | | | | | | | |
| Atorvostatin | 82 ±0.4 | 278 ±8.6 | 206 ±13.4 | 76 ±4.4 | 77 ±0.7 | 570 ±5.3 | 175 ±4.7 | 146 ±4.9 | 71 ±0.4 | 635 ±3.2 | 184 ±1.6 | 152 ±13.2 | 70 ±0.1 | 447 ±8.6 | 233 ±6.6 | 233 ±8.5 | 71 ±0.8 | 1101 ±12.3 | 252 ±4.9 | 146 ±1.8 |
| Benzophenone-1 | - | 4552 ±2909.2 | - | - | - | 172 ±2.1 | - | - | - | 67 ±4.9 | - | - | - | 183 ±1.7 | - | - | - | 121 ±1.7 | - | - |
| Benzophenone-4 | 443 ±8.5 | 9085 ±49.5 | 2869 ±9.5 | 498 ±1.4 | 411 ±2.6 | 7280 ±70.7 | 2549 ±3.1 | 1584 ±0.9 | 448 ±7.4 | 7505 ±233.4 | 1978 ±3.3 | 1022 ±5.2 | 475 ±4.2 | 9710 ±70.7 | 1961 ±5.3 | 1184 ±7.8 | 429 ±0.6 | 9440 ±113.1 | 1904 ±4.4 | 1094 ±8.6 |
| Bezafibrate | 46 ±1.3 | 1611 ±3.6 | 540 ±12.0 | 133 ±8.6 | 47 ±3.3 | 1952 ±5.6 | 664 ±3.7 | 427 ±2.5 | 56 ±4.9 | 1403 ±8.6 | 463 ±6.2 | 249 ±0.1 | 66 ±5.0 | 2998 ±10.3 | 405 ±2.1 | 206 ±1.1 | 59 ±0.9 | 1999 ±5.7 | 317 ±5.2 | 157 ±0.4 |
| Bisphenol A | 167 ±0.1 | 944 ±39.5 | 301 ±0.8 | 614 ±95.5 | 360 ±184.9 | 4043 ±273.9 | 223 ±7.4 | 616 ±452.3 | 213 ±3.1 | 1567 ±23.8 | 148 ±0.6 | 167 ±42.4 | 233 ±41.9 | 1640 ±121.1 | 225 ±0.6 | 338 ±18.9 | 223 ±8.7 | 1742 ±7.6 | 337 ±67.5 | 247 ±39.6 |
| Butylparaben | - | - | - | - | - | - | - | - | - | 39 ±2.3 | - | - | - | 165 ±1.6 | - | - | - | 173 ±4.5 | - | - |
| Diclofenac | 280 ±6.1 | 5579 ±231.5 | 2525 ±3.1 | 758 ±58.9 | 647 ±388.3 | 4130 ±314.8 | 2285 ±4.3 | 2182 ±233.3 | 354 ±4.9 | 2734 ±9.5 | 2152 ±2.0 | 1570 ±161.6 | 393 ±0.1 | 2910 ±1.3 | 2283 ±8.8 | 1424 ±9.5 | 663 ±1.6 | 5647 ±0.5 | 2385 ±106.1 | 1374 ±83.5 |
| Ethylparaben | - | 885 ±5.9 | - | - | - | 4649 ±9.3 | - | - | - | 1983 ±7.9 | - | - | - | 3279 ±17.1 | - | - | - | 2291 ±14.6 | - | - |
| Fexofenadine | 413 ±3.4 | - | 1384 ±2.1 | 591 ±14.9 | 347 ±2.5 | 0.8 ±1.1 | 1198 ±10.4 | 1025 ±3.4 | 351 ±1.3 | 4114 ±63.2 | 1314 ±7.3 | 959 ±11.7 | 402 ±8.1 | 156 ±220.4 | 1216 ±3.1 | 891 ±6.8 | 330 ±5.4 | 3331 ±28.7 | 1613 ±6.9 | 968 ±0.8 |
| Ibuprofen | 129 ±3.8 | 15780 ±410.1 | 1151 ±1.8 | 233 ±2.0 | 175 ±0.4 | 9055 ±7.1 | 1031 ±3.0 | 608 ±1.6 | 213 ±1.6 | 10865 ±431.3 | 444 ±4.8 | 145 ±0.7 | 125 ±1.5 | 14810 ±155.6 | 375 ±4.3 | 436 ±3.5 | 125 ±0.6 | 15250 ±240.4 | 304 ±0.5 | 138 ±1.5 |
| Irbesartan | 305 ±4.1 | 1224 ±6.8 | 872 ±7.4 | 489 ±2.3 | 347 ±98.3 | 1133 ±2.2 | 908 ±2.8 | 759 ±45.8 | 273 ±2.8 | 897 ±1.6 | 772 ±3.5 | 563 ±2.2 | 299 ±10.7 | 1333 ±9.3 | 737 ±4.5 | 498 ±3.1 | 332 ±3.5 | 837 ±2.3 | 823 ±28.7 | 463 ±4.2 |
| Ketoprofen | - | 353 ±19.1 | 296 ±4.9 | 12 ±16.8 | - | 353 ±4.5 | 244 ±3.9 | - | - | 500 ±6.9 | 394 ±3.4 | 341 ±1.5 | - | 1490 ±2.9 | 435 ±2.7 | 205 ±5.5 | 642 ±1.9 | 5586 ±4.1 | 665 ±4.5 | 764 ±2.9 |
| Methylparaben | 26 ±0.3 | 6110 ±551.5 | 44 ±2.5 | 61 ±0.4 | 38 ±9.8 | 30050 ±480.8 | 46 ±4.5 | 41 ±0.9 | 65 ±1.3 | 14455 ±49.5 | 132 ±48.9 | 117 ±49.7 | 102 ±0.2 | 12030 ±806.1 | 252 ±4.0 | 295 ±20.5 | 62 ±3.2 | 12800 ±961.7 | 76 ±10.7 | 216 ±18.0 |
| Naproxen | 209 ±2.1 | 3675 ±21.2 | 2882 ±0.3 | 471 ±9.1 | 184 ±0.8 | 2925 ±21.2 | 2799 ±8.4 | 1899 ±64.9 | 221 ±10.1 | 3205 ±21.2 | 2058 ±2.7 | 1070 ±10.7 | 243 ±4.9 | 5455 ±21.2 | 1993 ±7.3 | 1199 ±2.2 | 265 ±2.3 | 5295 ±49.5 | 1751 ±12.9 | 924 ±3.7 |
| Propylparaben | - | - | - | - | 14 ±19.4 | 10950 ±509.1 | - | - | 21 ±0.2 | 15830 ±56.6 | 72 ±49.9 | 96 ±64.6 | 51 ±9.1 | 2835 ±162.6 | 144 ±19.9 | 225 ±13.9 | 41 ±51.1 | 1305 ±431.3 | 22 ±27.4 | 89 ±0.7 |
| Sulfasalazine | 38 ±1.9 | 3330 ±0.0 | 163 ±1.4 | 36 ±1.8 | 43 ±11.5 | 3330 ±14.1 | 131 ±16.2 | 44 ±5.2 | 37 ±3.0 | 3335 ±7.1 | 67 ±15.2 | 67 ±23.7 | 35 ±1.8 | 3350 ±14.1 | 122 ±3.6 | 63 ±37.9 | 35 ±0.5 | 3440 ±99.0 | 79 ±22.5 | 55 ±28.9 |
| Valsartan | 233 ±5.7 | 19660 ±919.2 | 2692 ±4.0 | 674 ±6.5 | 253 ±7.7 | 17535 ±728.3 | 2834 ±3.0 | 1768 ±2.5 | 300 ±6.2 | 15620 ±452.6 | 1630 ±3.4 | 605 ±5.8 | 264 ±0.2 | 17510 ±664.7 | 1338 ±3.1 | 1020 ±6.9 | 269 ±2.1 | 17825 ±558.6 | 1131 ±4.7 | 556 ±0.8 |
| *Chemicals in ESI+ mode* | | | | | | | | | | | | | | | | | | | | |
| Acetaminophen | - | 232760 ±11229 | 61 ±5.4 | 27 ±4.0 | 24 ±2.4 | 282675 ±8619 | 44 ±8.7 | 39 ±3.6 | 26 ±0.6 | 343620 ±25343 | 41 ±4.1 | 26 ±10.0 | 17 ±3.0 | 228893 ±15737 | 216 ±23.7 | 200 ±11.6 | 17 ±2.6 | 136887 ±680 | 123 ±10.8 | 27 ±1.6 |
| Amphetamine | 18 ±0.3 | 1110 ±290.1 | 60 ±0.1 | 76 ±8.1 | 20 ±3.0 | 2591 ±332.6 | 184 ±2.5 | 38 ±4.8 | 67 ±2.3 | 535 ±74.2 | 94 ±2.4 | 29 ±6.7 | 17 ±2.8 | 760 ±61.2 | 73 ±2.7 | 21 ±2.0 | 14 ±0.1 | 256 ±12.0 | 54 ±5.8 | 22 ±2.8 |
| Atenolol | 202 ±0.5 | 2541 ±13.1 | 392 ±26.0 | 193 ±10.0 | 158 ±15.5 | 1593 ±18.1 | 712 ±70.5 | 544 ±6.1 | 161 ±5.1 | 1745 ±18.6 | 537 ±17.8 | 241 ±22.6 | 155 ±7.9 | 1839 ±110.4 | 457 ±19.9 | 216 ±11.2 | 105 ±2.1 | 1627 ±101.5 | 364 ±12.1 | 166 ±1.4 |
| Azathioprine | - | 89 ±2.2 | - | - | - | 65 ±2.4 | - | - | - | 57 ±7.4 | - | - | - | 83 ±3.8 | - | - | - | 65 ±0.9 | - | - |
| Azithromycin | - | 32 ±2.8 | 157 ±12.1 | 3 ±1.0 | - | 23 ±1.8 | 173 ±3.5 | 7 ±2.5 | 25 ±0.6 | 139 ±15.6 | 213 ±7.2 | 11 ±1.8 | - | 65 ±4.5 | 178 ±1.5 | 5 ±1.1 | - | 45 ±3.3 | 138 ±24.5 | - |
|  | Concentration (ng.L-1, ± stdev) | | | | | | | | | | | | | | | | | | | |
| 06/07/2015 | | | | 07/07/2015 | | | | 08/07/2015 | | | | 09/07/2015 | | | | 10/07/2015 | | | |
| US | Inf. | Eff. | DS | US | Inf. | Eff. | DS | US | Inf. | Eff. | DS | US | Inf. | Eff. | DS | US | Inf. | Eff. | DS |
| Benzophenone-3 | 54 ±0.5 | 173 ±9.3 | 79 ±0.2 | 58 ±1.8 | 55 ±0.4 | 211 ±3.7 | 75 ±3.5 | 62 ±6.4 | 57 ±0.1 | 103 ±8.1 | 87 ±9.5 | 60 ±5.9 | 59 ±0.5 | 137 ±1.3 | 77 ±3.3 | 71 ±3.8 | 56 ±1.3 | 63 ±4.1 | 76 ±6.7 | 70 ±5.2 |
| Benzoylecgonine | - | 514 ±0.9 | 7 ±0.8 | - | - | 478 ±10.8 | - | - | - | 298 ±8.7 | - | - | - | 276 ±12.2 | - | - | - | 380 ±29.4 | - | - |
| Carbamazepine | 172 ±8.3 | 403 ±6.2 | 426 ±20.2 | 241 ±23.3 | 153 ±10.3 | 459 ±9.5 | 411 ±18.3 | 304 ±14.9 | 152 ±3.1 | 332 ±7.7 | 390 ±13.9 | 281 ±16.8 | 165 ±4.8 | 458 ±20.0 | 422 ±14.5 | 294 ±6.2 | 144 ±7.0 | 610 ±24.8 | 414 ±3.5 | 277 ±5.7 |
| CBZ-ep | 421 ±3.3 | 1119 ±26.2 | 1239 ±20.0 | 647 ±37.4 | 367 ±24.7 | 1183 ±44.3 | 1363 ±1.8 | 834 ±40.0 | 398 ±11.6 | 1094 ±60.7 | 1159 ±9.6 | 733 ±26.5 | 432 ±10.1 | 1666 ±82.4 | 1235 ±4.2 | 765 ±21.4 | 376 ±8.9 | 1269 ±12.2 | 1184 ±30.6 | 783 ±20.9 |
| Caffeine | 573 ±171.6 | 15125 ±559.3 | 799 ±60.9 | 1039 ±77.8 | 784 ±117.9 | 5094 ±61.9 | 470 ±22.8 | 356 ±62.1 | 950 ±77.9 | 347155 ±30568.0 | 718 ±97.5 | 787 ±268.6 | 862 ±97.7 | 1214375 ±21291.0 | 3824 ±102.9 | 6646 ±122.1 | 891 ±257.6 | 389460 ±29090.0 | 2557 ±26.1 | 1559 ±41.3 |
| Cimetidine | - | 731 ±3.8 | - | - | - | 499 ±2.3 | - | - | - | 1337 ±86.3 | - | - | - | 454 ±23.5 | - | - | - | 1378 ±8.1 | - | - |
| Clarithromycin | 91 ±0.5 | 491 ±6.3 | 488 ±0.2 | 126 ±3.0 | 59 ±4.1 | 497 ±12.9 | 516 ±5.9 | 265 ±2.0 | 87 ±2.5 | 1541 ±2.4 | 603 ±0.4 | 235 ±5.0 | 67 ±4.7 | 953 ±2.1 | 495 ±5.7 | 250 ±2.7 | 78 ±0.2 | 260 ±39.9 | 579 ±0.1 | 302 ±8.2 |
| Cocaethylene | - | 225.5 ±4.5 | - | - | - | 186.0 ±39.1 | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Cocaine | - | 28 ±0.1 | - | - | - | 147 ±31.0 | - | - | - | 125 ±4.4 | - | - | - | 97 ±8.8 | - | - | - | 40 ±2.1 | - | - |
| Codeine | 1 ±0.4 | 1550 ±2.1 | 516 ±6.2 | 34 ±3.3 | - | 1011 ±4.8 | 401 ±3.0 | 216 ±1.8 | 15 ±2.8 | 1737 ±4.5 | 289 ±6.9 | 138 ±3.0 | 15 ±3.8 | 947 ±45.9 | 286 ±15.2 | 144 ±4.0 | 13 ±1.2 | 1070 ±22.1 | 235 ±4.1 | 112 ±1.1 |
| Cotinine | 21 ±0.9 | 4892 ±3.8 | 32 ±0.1 | 35 ±0.0 | 23 ±1.3 | 3333 ±21.6 | 25 ±0.9 | 17 ±0.4 | 27 ±0.9 | 4493 ±19.2 | 23 ±0.9 | 23 ±4.2 | 27 ±2.6 | 4147 ±13.9 | 25 ±2.0 | 36 ±0.3 | 29 ±6.0 | 4266 ±0.8 | 35 ±2.2 | 47 ±1.8 |
| Creatinine | - | 2849 ±33.2 | - | - | - | 2939 ±9.5 | - | - | - | - | - | - | - | 4900 ±339.4 | - | - | - | 12625 ±374.8 | - | - |
| dh-h-CBZ | 23 ±2.5 | 33 ±0.5 | 110 ±1.7 | 41 ±5.6 | 21 ±1.6 | 55 ±3.6 | 110 ±2.1 | 62 ±2.0 | 21 ±1.0 | 42 ±3.7 | 99 ±3.5 | 60 ±2.5 | 24 ±1.0 | 137 ±1.6 | 103 ±0.8 | 61 ±3.0 | 24 ±1.5 | 196 ±4.8 | 98 ±4.5 | 60 ±0.2 |
| dm-citalopram | - | - | 6 ±0.4 | - | - | - | 1 ±1.6 | - | - | - | 11 ±5.4 | - | - | - | 3 ±0.3 | - | - | - | 6 ±0.1 | - |
| DMX | 262 ±96.0 | 237345 | 22 ±31.5 | 471 ±551.8 | 24 ±33.2 | 163613 | - | 216 ±305.1 | 901 ±37.5 | 16765 | 716 ±1012.8 | 630 ±426.9 | 452 ±579.0 | 110975 | 3705 | 1641 ±1879.1 | 759 ±962.0 | 147445 | 1216 | 1830 ±2260.5 |
| d-venlafaxine | 60 ±0.9 | - | 297 ±11.0 | 80 ±6.9 | 43 ±9.7 | 171 ±21.9 | 287 ±10.0 | 191 ±6.4 | 44 ±1.6 | 206 ±2.0 | 317 ±3.7 | 192 ±13.8 | 56 ±4.1 | 245 ±15.1 | 337 ±1.3 | 200 ±18.4 | 47 ±1.3 | 323 ±43.6 | 334 ±1.8 | 212 ±15.9 |
| Gliclazide | 46 ±0.3 | 671 ±219.1 | 79 ±2.3 | 19 ±26.7 | 43 ±1.1 | 169 ±2.5 | 58 ±1.3 | 60 ±8.8 | 41 ±0.4 | 258 ±34.9 | 48 ±0.8 | 47 ±1.1 | 41 ±0.1 | 304 ±0.5 | 68 ±5.6 | 75 ±4.4 | 45 ±0.6 | 135 ±7.1 | 71 ±1.3 | 69 ±2.7 |
| Iopromide | 271 ±4.4 | 386 ±3.5 | 944 ±3.5 | 256 ±3.4 | 247 ±7.2 | 622 ±18.2 | 1218 ±37.4 | 808 ±10.5 | 265 ±5.5 | 1029 ±23.2 | 1049 ±44.5 | 484 ±14.8 | 275 ±3.1 | 2762 ±232.6 | 1113 ±15.5 | 814 ±4.1 | 271 ±4.2 | 1172 ±56.8 | 978 ±100.9 | 629 ±24.4 |
| Lisinopril | - | - | - | - | - | - | - | - | - | 196 ±5.2 | - | - | - | 200 ±1.6 | - | - | - | - | - | - |
| Mephedrone | - | - | - | - | - | - | - | - | - | 56 ±12.8 | - | - | - | 121 ±0.7 | - | - | - | 36 ±0.5 | - | - |
| Metformin | 75 ±0.1 | 9228 ±280.0 | 499 ±7.8 | 126 ±0.9 | 67 ±0.6 | 4799 ±122.9 | 566 ±30.6 | 316 ±43.1 | 78 ±0.6 | 3585 ±89.0 | 378 ±13.1 | 160 ±0.9 | 81 ±0.4 | 4723 ±14.1 | 295 ±37.2 | 161 ±0.9 | 65 ±0.9 | 4740 ±7.0 | 167 ±1.9 | 111 ±1.0 |
| Methamphetamine | - | 450 ±6.7 | 0.2 ±0.3 | - | - | 420 ±42.9 | 25 ±1.5 | 25 ±1.6 | - | 271 ±40.2 | 13 ±1.6 | - | - | 315 ±15.1 | 4 ±1.8 | - | - | 316 ±27.4 | 3 ±1.3 | - |
| Morphine | - | 687 ±30.6 | - | - | - | 414 ±5.4 | - | - | - | 391 ±4.4 | - | - | - | 474 ±40.8 | - | - | - | 457 ±25.2 | - | - |
| NDT | 7 ±1.3 | - | 111 ±1.8 | 65 ±5.1 | 8 ±0.6 | 145 ±12.9 | 95 ±5.7 | 69 ±4.2 | 29 ±4.8 | 149 ±11.9 | 121 ±10.0 | 84 ±21.1 | 24 ±12.4 | - | 115 ±3.0 | 72 ±8.3 | 12 ±5.8 | 33 ±2.8 | 126 ±0.4 | 81 ±2.8 |
| Nicotine | 95 ±4.9 | 4874 ±95.0 | 182 ±1.3 | 268 ±1.9 | 108 ±21.5 | 11866 ±138.5 | 175 ±4.7 | 182 ±0.2 | 239 ±23.9 | 11866 ±141.4 | 174 ±4.8 | 232 ±4.5 | 241 ±38.0 | 10365 ±35.4 | 217 ±2.8 | 350 ±3.0 | 89 ±16.8 | 8625 ±190.9 | 169 ±7.3 | 195 ±6.4 |
| Norephedrine | - | 2914 ±890.7 | - | - | - | 1950 ±265.7 | - | - | - | 1107 ±357.7 | - | - | - | 852 ±20.8 | - | - | - | 772 ±34.1 | - | - |
| Normorphine | - | - | - | - | - | 111 ±6.6 | - | - | - | 144 ±65.5 | - | - | - | 128 ±12.6 | - | - | - | 185 ±8.6 | - | - |
| ODT | 199 ±9.8 | - | 1469 ±57.8 | 319 ±26.3 | 182 ±16.5 | 214 ±303.0 | 1330 ±71.6 | 691 ±47.7 | 254 ±10.0 | 1283 ±33.16 | 1139 ±33.3 | 594 ±54.2 | 227 ±10.0 | - | 1136 ±16.0 | 671 ±29.3 | 177 ±16.3 | - | 1056 ±55.1 | 612 ±14.1 |
| (Pseudo)ephedrine | 35 ±3.7 | 4885 ±77.8 | 177 ±3.6 | 61 ±1.5 | 30 ±4.6 | 4080 ±70.7 | 167 ±7.9 | 85 ±5.9 | 44 ±2.1 | 5720 ±254.6 | 109 ±0.7 | 43 ±8.6 | 50 ±1.8 | - | 113 ±14.9 | 102 ±1.5 | 36 ±3.8 | 16640 ±2152 | 138 ±7.8 | 111 ±5.6 |
| Ranitidine | - | 240 ±16.2 | - | - | - | 143 ±0.7 | - | - | - | 50 ±19.7 | - | - | - | 52 ±12.8 | - | - | - | 103 ±18.0 | - | - |
|  | Concentration (ng.L-1, ± stdev) | | | | | | | | | | | | | | | | | | | |
| 06/07/2015 | | | | 07/07/2015 | | | | 08/07/2015 | | | | 09/07/2015 | | | | 10/07/2015 | | | |
| US | Inf. | Eff. | DS | US | Inf. | Eff. | DS | US | Inf. | Eff. | DS | US | Inf. | Eff. | DS | US | Inf. | Eff. | DS |
| Sulfamethoxazole | 859 ±7.3 | 2589 ±3.2 | 1560 ±18.6 | 711 ±6.3 | 749 ±29.7 | 554 ±16.5 | 1229 ±2.1 | 1283 ±69.7 | 745 ±15.4 | 1339 ±6.0 | 1473 ±81.9 | 1351 ±43.1 | 801 ±56.9 | 806 ±4.8 | 1289 ±0.1 | 962 ±35.9 | 634 ±19.4 | 2521 ±46.1 | 1173 ±42.4 | 758 ±19.4 |
| Tramadol | 101 ±2.3 | - | 549 ±0.9 | 169 ±0.8 | 87 ±5.2 | 480 ±0.6 | 495 ±4.0 | 337 ±0.4 | 92 ±3.1 | 411 ±4.4 | 514 ±4.6 | 324 ±0.1 | 116 ±1.2 | 503 ±4.5 | 514 ±43.5 | 332 ±3.2 | 94 ±0.1 | 493 ±9.6 | 540 ±18.5 | 337 ±0.9 |
| Trimethoprim | 410 ±0.3 | 6249 ±34.8 | 1490 ±6.0 | 381 ±10.0 | 318 ±20.6 | 11136 ±981.5 | 1117 ±4.0 | 879 ±1.8 | 419 ±4.1 | 7250 ±53.0 | 1446 ±11.2 | 1045 ±60.8 | 404 ±9.9 | 4537 ±296.4 | 1501 ±7.3 | 1067 ±31.5 | 363 ±3.7 | 4502 ±908.1 | 1676 ±24.1 | 1121 ±24.4 |
| Venlafaxine | 34 ±0.4 | - | 148 ±5.3 | 60 ±3.2 | 36 ±2.2 | 461 ±22.0 | 126 ±1.0 | 102 ±0.6 | 34 ±1.3 | 335 ±21.2 | 143 ±3.2 | 107 ±4.7 | 42 ±0.0 | 270 ±0.0 | 140 ±4.5 | 101 ±6.3 | 32 ±1.1 | 275 ±21.2 | 155 ±3.6 | 104 ±0.0 |

**Table S3**: Average mass loads (g.day-1) determined for the ECs at influent and final effluent water in the WWTW.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Chemical Class | Compound Name | Mass Load (g.day-1, average ± stdev) | | Removal (%) |
| Influent | Effluent |
| UV Filters | Benzophenone-1 | 43.3 ±83.7 | - | 100 |
|  | Benzophenone-3 | 5.9 ±2.5 | 3.2 ±0.2 | 46 |
|  | Benzophenone-4 | 370.4 ±52.1 | 92.0 ±17.3 | 75 |
| Parabens | Methylparaben | 650.8 ±389.8 | 4.5 ±3.7 | 99 |
|  | Ethylparaben | 113.3 ±62.8 | - | 100 |
|  | Propylparaben | 331.2 ±289.8 | 3.3 ±2.6 | 99 |
|  | Butylparaben | 5.4 ±3.3 | - | 100 |
| Plastisizer | Bisphenol A | 85.8 ±52.1 | 10.1 ±3.0 | 88 |
| Antibiotics | Azithromycin | 2.6 ±2.0 | 7.0 ±1.1 | -170 |
|  | Sulfasalazine | 144.4 ±3.6 | 4.6 ±1.6 | 97 |
|  | Clarithromycin | 32.2 ±21.6 | 21.9 ±1.9 | 32 |
|  | Sulfamethoxazole | 66.7 ±40.0 | 54.9 ±6.2 | 18 |
|  | Sulfasalazine | 144.4 ±3.6 | 4.6 ±1.6 | 97 |
|  | Trimethoprim | 289.6 ±118.1 | 59.1 ±8.2 | 80 |
| Hypertensions | Irbesartan | 46.8 ±9.9 | 33.6 ±2.8 | 28 |
|  | Lisinopril | 8.6 ±0.4 | - | 100 |
|  | Valsartan | 758.4 ±63.3 | 78.6 ±32.0 | 90 |
| H2 receptor agonists | Cimetidine | 37.6 ±18.7 | - | 100 |
|  | Ranitidine | 5.0 ±3.3 | - | 100 |
| NSAIDs | Ibuprofen | 565.8 ±130.1 | 27.0 ±16.1 | 95 |
|  | Ketoprofen | 71.1 ±95.7 | 16.6 ±6.6 | 77 |
|  | Naproxen | 177.3 ±53.3 | 93.8 ±20.7 | 47 |
|  | Diclofenac | 180.2 ±58.3 | 95.1 ±5.6 | 47 |
|  | Acetaminophen | 10530.2 ±3216.0 | 4.0 ±3.2 | 100 |
| Lipid Regulators | Bezafibrate | 86.1 ±28.6 | 19.5 ±5.4 | 77 |
|  | Atorvostatin | 26.0 ±13.0 | 8.6 ±1.4 | 67 |
| Diabetes | Metformin | 232.6 ±92.0 | 15.6 ±6.5 | 93 |
|  | Gliclazide | 13.2 ±9.0 | 2.6 ±0.5 | 80 |
| Beta-blockers | Atenolol | 80.3 ±16.2 | 20.1 ±5.8 | 75 |
| X-ray contrast media | Iopromide | 51.9 ±41.8 | 43.4 ±5.1 | 16 |
| Anti-depressants & metabolites | Venlafaxine | 14.5 ±3.8 | 5.8 ±0.4 | 60 |
|  | Desvenlafaxine | 10.2 ±2.8 | 12.9 ±1.0 | -26 |
|  | Fluoxetine | - | 1.1 ±0.9 | - |
|  | Desmethylcitalopram | - | 0.2 ±0.1 | - |
| Anti-epileptics & metabolites | Carbamazepine | 19.5 ±4.4 | 16.9 ±0.8 | 13 |
|  | 10,11-dihydro-10-hydroxycarbamazepine | 4.0 ±3.1 | 4.2 ±0.3 | -6 |
|  | Carbamazepine-10,11-epoxide | 54.6 ±11.4 | 50.5 ±3.9 | 7 |
| Antihistamine | Fexofenadine | 107.5 ±88.5 | 54.9 ±6.2 | 49 |
| Anti-cancer | Azathioprine | 3.1 ±0.6 | - | 100 |
| Analgaesics & metabolites | Tramadol | 15.7 ±9.3 | 21.3 ±0.8 | -36 |
|  | N-desmethyltramadol | 4.7 ±2.8 | 4.6 ±0.5 | 1 |
|  | O-desmethyltramadol | 21.1 ±28.9 | 50.1 ±6.8 | -58 |
|  | EDDP | 0.6 ±0.0 | 0.6 ±0.0 | 5 |
|  | Codeine | 54.1 ±14.3 | 14.1 ±4.5 | 74 |
|  | Morphine | 20.8 ±5.0 | 0.2 ± - | 99 |
|  | Normorphine | 6.1 ±1.3 | - | 100 |
| Drug precursor  Stimulants & metabolites | (Pseudo)ephedrine | 269.4 ±260.9 | 5.7 ±1.2 | 98 |
| Amphetamine | 45.4 ±39.9 | 3.8 ±2.2 | 92 |
| Cocaine | 3.8 ±2.3 | 0.4 ±0.0 | 90 |
| Benzoylecgonine | 16.7 ±4.5 | 0.3 ± - | 98 |
| Cocaethylene | 8.8 ±1.1 | - | 100 |
| Methamphetamine | 15.2 ±3.3 | 0.4 ±0.4 | 98 |
| Norephedrine | 65.1 ±38.5 | - | 100 |
| Mephedrone | 3.1 ±2.0 | - | 100 |
| Human indicators & metabolites | Cotinine | 181.6 ±22.9 | 1.1 ±0.2 | 99 |
|  | Nicotine | 410.2 ±127.5 | 7.5 ±1.0 | 98 |
|  | 1,7-dimethylxantine | 5818.9 ±3420.3 | 48.7 ±63.2 | 99 |
|  | Caffeine | 17224.1 ±21941.2 | 69.1 ±61.7 | 100 |
|  | Creatinine | 251.1 ±196.2 | - | 100 |

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**Figure S3:** Percentage change of the detected ECs between final effluent water samples and river samples located downstream of the plant. Standard deviation shows variation between sampling days.

**Table S4**: Environmental risk calculation of the detected ECs based on conventional environmental risk assessment (ERA) and modulation of molecular initiating events (MIEs) and key events (KEs). Abbreviations: MEC – measured environmental concentration (based on concentrations in the current study); PNEC – predicted no-effect concentration (acute or chronic lethal toxicity outcomes); RQ – risk quotient (MEC.PNEC-1 or MEC.AOP conc.-1). An RQ > 1 is indicated in bold and reflects that the EC is of environmental concern. # Concentration of river water is a combination of both upstream and downstream water samples.

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | MEC (ug.L-1) | | Environmental Risk Assessment (ERA) | | | |  | Molecular Initiating Events (MIEs) and Key Events (KEs) | | | | |
| Compound | Effluent | River Water# | PNEC (µg.L-1) | Reference | RQeff | RQrw |  | Event | Conc.  (µg.L-1) | Reference | RQeff | RQrw |
| Diclofenac | 2.31 | 0.96 | 0.10 | Bergmann et al., 2011 | **23.1** | **10.0** |  | Increased VTG gene expression in fish (MIE) | 1.0 | Hong et al., 2007; Gröner et al., 2017 | **2.31** | **0.96** |
|  |  |  |  |  |  |  |  | Decreased thyroid hormone levels in fish (KE) | 1.0 | Saravanan et al., 2014 | **2.31** | **0.96** |
| Ibuprofen | 0.66 | 0.23 | 7.10 | Carlsson et al., 2006a | 0.13 | 0.04 |  | Lower thyroid-mediated mRNA transcripts in tadpoles (MIE) | 1.5 | Veldhoen et al., 2014 | 0.44 | 0.15 |
|  |  |  |  |  |  |  |  | Decreased egg fertilisation in fish (KE) | 0.1 | Nesbitt, 2011 | **6.60** | **2.30** |
| Naproxen | 2.30 | 0.67 | 3.30 | Bergmann et al., 2011 | 0.7 | 0.2 |  | Decreased egg fertilisation in fish (KE) | 0.1 | Nesbitt, 2011 | **23.0** | **6.7** |
| Carbamazepine | 0.41 | 0.22 | 2.50 | Ferrari et al., 2003 | 0.16 | 0.09 |  | Lower keto-testosterone hormone levels in fish (KE) | 0.5 | Galus et al., 2013 | 0.82 | 0.4 |
| Azithromycin | 0.17 | 0.015 | 4.80 | Bergmann et al., 2011 | 0.04 | 0.003 |  |  |  |  |  |  |
| Iopromide | 1.06 | 0.43 | 6800.0 | Bergmann et al., 2011 | 0.001 | 0.001 |  |  |  |  |  |  |
| Sulfamethoxazole | 1.34 | 0.89 | 0.59 | Bergmann et al., 2011 | **2.27** | **1.51** |  | Induction of VTG in fish | 1000.0 | Kang et al., 2006 | 0.001 | 0.001 |
| Acetaminophen | 0.10 | 0.04 | 0.24 | Bergmann et al., 2011 | 0.42 | 0.17 |  |  |  |  |  |  |
| Clarithromycin | 0.54 | 0.16 | 0.2 | Bergmann et al., 2011 | **2.7** | 0.8 |  |  |  |  |  |  |
| Irbesartan | 0.82 | 0.43 | 100.0 | Minguez et al.,2016 | 0.01 | 0.004 |  |  |  |  |  |  |
| Valsartan | 1.93 | 0.59 | 100.0 | Minguez et al.,2016 | 0.02 | 0.006 |  |  |  |  |  |  |
| Ketoprofen | 0.41 | 0.39 | 3.10 | Bergmann et al., 2011 | 0.13 | 0.13 |  |  |  |  |  |  |
| Bezafibrate | 0.48 | 0.14 | 1.20 | Bergmann et al., 2011 | 0.4 | 0.12 |  |  |  |  |  |  |
| Tramadol | 0.52 | 0.20 | 0.96 | ECOSAR | 0.54 | 0.21 |  |  |  |  |  |  |
| Venlafaxine | 0.14 | 0.07 | 47.60 | Minguez et al.,2016 | 0.003 | 0.001 |  |  |  |  |  |  |
| Methamphetamine | 0.009 | - | 2.30 | ECOSAR | 0.004 | - |  |  |  |  |  |  |
| Morphine |  |  | 32.0 | ECOSAR |  |  |  |  |  |  |  |  |
| Cocaine | 0.009 | - | 4.90 | ECOSAR | 0.002 | - |  |  |  |  |  |  |
| Benzoylecgonine |  |  | 4.90 | ECOSAR |  |  |  |  |  |  |  |  |
| Codeine | 0.35 | 0.08 | 0.06 | ECOSAR | **5.83** | **1.33** |  |  |  |  |  |  |
| Benzophenone\* | 1.16 | 0.41 | 6.00 | ECOSAR | 0.19 | 0.07 |  |  |  |  |  |  |
| Methylparaben | 0.11 | 0.11 | 11.2 | Carlsson et al., 2006b | 0.01 | 0.01 |  | Increase VTG and lower GSI in fish | 8400.0 | Barse et al., 2010 | 0.001 | 0.001 |
| Propylparaben | 0.08 | 0.08 |  |  |  |  |  | Increased VTG in fish | 9.0 | Scott, 2014 | 0.009 | 0.009 |
| Chloramphenicol |  |  | 0.019 | Bergmann et al., 2011 |  |  |  |  |  |  |  |  |
| Amphetamine | 0.09 | 0.03 | 0.98 | Bergmann et al., 2011 | 0.09 | 0.03 |  |  |  |  |  |  |
| Bisphenol A | 0.25 | 0.32 | 1.0 | ECOSAR | 0.25 | 0.32 |  | Induction of VTG in fish | 10.0 | Villeneuve et al., 2011 | 0.03 | 0.03 |
| Atenolol | 0.49 | 0.21 | 100.0 | Minguez et al.,2016 | 0.005 | 0.002 |  |  |  |  |  |  |
| Trimethoprim | 1.45 | 0.64 | 20.0 | Bergmann et al., 2011 | 0.07 | 0.03 |  |  |  |  |  |  |
| Nicotine | 0.18 | 0.20 | 0.014 | Bergmann et al., 2011 | **12.86** | **14.29** |  |  |  |  |  |  |

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