**Determination and Risk Assessment of Pharmaceutical Residues in the Urban Water Cycle**

Zarimah Mohd Hanafiah1, Wan Hanna Melini Wan Mohtar1, Teh Sabariah Abd Manan2,3, Nur Aina Bachi'1, Nurfaizah Abu Tahrim4, Haris Hafizal Abd Hamid5, Abdulnoor A. J. Ghanim6, Amirrudin Ahmad2,7, Nadiah Wan Rasdi2,8, Hamidi Abdul Aziz3

1Department of Civil Engineering, Faculty of Engineering and Built Environment, Universiti Kebangsaan Malaysia, 43600 UKM Bangi, Selangor Darul Ehsan, Malaysia.

2Institute of Tropical Biodiversity and Sustainable Development, Universiti Malaysia Terengganu, 21030 Kuala Nerus, Terengganu Darul Iman, Malaysia.

3School of Civil Engineering, Universiti Sains Malaysia, 14300 Nibong Tebal, Pulau Pinang, Malaysia.

4Department of Chemical Sciences, Faculty of Science and Technology, Universiti Kebangsaan, 43600 UKM Bangi, Selangor Darul Ehsan, Malaysia.

5Department of Earth Sciences and Environment, Faculty of Science and Technology, Universiti Kebangsaan Malaysia, 43600 UKM Bangi, Selangor Darul Ehsan, Malaysia.

6Department of Civil Engineering, College of Engineering, Najran University, Najran 61441, KSA.

7Faculty of Science and Marine Environment, Universiti Malaysia Terengganu, 21030 Kuala Nerus, Terengganu Darul Iman, Malaysia.

8Faculty of Fisheries and Food Science, Universiti Malaysia Terengganu, 21030 Kuala Nerus, Terengganu Darul Iman, Malaysia.

Corresponding Author:

Wan Hanna Melini Wan Mohtar1

Department of Civil Engineering, Faculty of Engineering and Built Environment, Universiti Kebangsaan Malaysia, 43600 UKM Bangi, Selangor Darul Ehsan, Malaysia.

Email address: hanna@ukm.edu.my

**Table S-1 Chemical structure and molecular formula of targeted compounds**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Targeted compounds | Chemical Structure | Molecular formula | CAS number | Molecular Weight (g/mol) | LogKow |
| Ibuprofen (IBU) |  | C13H18O2 | 15687-27-1 | 206.28 | 3.97 |
| Naproxen (NAP) |  | C14H14O3 | 22204-53-1 | 230.26 | 3.18 |
| Ketoprofen (KET) |  | C16H14O3 | 22071-15-4 | 254.28 | 2.66 |
| Diazepam (DIA) |  | C16H13ClN2O | 439-14-5 | 284.74 | 2.85 |
| Diclofenac (DIC) |  | C14H11Cl2NO2 | 15307-86-5 | 296.15 | 1.90 |

**Table S-2 Recovery and quality standard for targeted analyte**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Analyte | Retentiontime (min) | Recovery (%) | Linearity from response | Coefficient of determination (*R2*) from a response | Coefficient of variation (σ/mean)(%) | Standard deviation of response (σ) | Slope of the calibration curve(s) | LOD (x105 ng/L)3.3\*(σ/s) | LOQ(x106 ng/L)10\*(σ/s) |
| IBU | 9.05 | 99.1 | y=53977x-21811 | 0.9844 | 15.14 | 7093.08 | 53977 | 4.337 | 1.314 |
| NAP | 12.0 | 97.7 | y=4331.4x+6382.8 | 0.9607 | 5.32 | 505.919 | 4331.4 | 3.854 | 1.168 |
| KET | 12.8 | 111.7 | y=106608x+65246 | 0.9889 | 16.30 | 21820.06 | 106608 | 6.754 | 2.046 |
| DIA | 14.9 | 74.86 | y=144164x+162864 | 0.9755 | 17.59 | 29990.55 | 144164 | 6.865 | 2.080 |
| DIC | 13.0 | 69.1 | y=48855x+6961.8 | 0.9992 | 9.36 | 5241.51 | 48855 | 3.540 | 1.072 |

**Table S-3 The pharmaceutical residue (IBU, NAP, KET, DIA, DIC) in the urban water**

|  |  |  |  |
| --- | --- | --- | --- |
| **Country** | **Water cycle** | **Pharmaceuticals** | **Ref.** |
| Sweden | STP | IBU, NAP, KET, DIC | (Larsson et al., 2014) |
| Canada | STP | IBU, NAP | (Guerra et al., 2014) |
| South Africa | STP | IBU, NAP, DIC | (Madikizela and Chimuka, 2017) |
| Spain | STP | IBU, NAP, KET, DIC | (Gracia-Lor et al., 2017) |
| Spain | Surface water | IBU, KET, DIC | (Jurado et al., 2021) \*Groundwater |
| Spain | Treated water | IBU, NAP, DIC | (Carmona et al., 2014) |
| India | STP | DIA | (Subedi et al., 2017) |
| Beijing, China | STP | DIA | (Wang et al., 2017) |
| United Kingdom | STP | DIA | (Baker and Kasprzyk-Hordern, 2013) |
| Thailand | Surface water | IBU, NAP, DIC | (Tewari et al., 2013) |
| Italy | Surface water | IBU, NAP, KET, DIC | (Marchese et al., 2003) |
| Italy | Surface water | DIA | (Zuccato et al., 2000) |
| Serbia | Treated water | KET | (Petrović et al., 2014) |
| France | Treated water | IBU, NAP, DIC | (Togola and Budzinski, 2008) |
| Algeria | Treated water | KET | (Kermia et al., 2016) |
| Johor, Malaysia | STP | IBU, NAP | (Yacob et al., 2017) |
| Selangor, Malaysia | Surface water | KET | (Abu Tahrim et al., 2018) |
| Putrajaya, Malaysia | Treated water | DIC | (Wee et al., 2020) |
| Selangor, Malaysia | STP, Surface water, Treated water | IBU, NAP, KET, DIA, DIC | Current Study |

**cycle (STP, surface water, and treated water).**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Model No.**  | **ANOVA Model** | **Sum of Squares** | **df** | **Mean Square** | **F** | **Sig. F Change** |
| 1. | Influent Vs. Effluent | SSW | 1888825833 | 1 | 1888825833 | 235.671 | 0.001 |
| SSB | 24043967.36 | 3 | 8014655.785 |  |  |
| SST | 1912869800 | 4 |  |  |  |
| a Dependent Variable: Effluent |  |  |  |  |
| b Predictors: (Constant), Influent |  |  |  |  |
| 2. | Effluent Vs. Surface Water | SSW | 484.843 | 1 | 484.843 | 16.746 | 0.026 |
| SSB | 86.856 | 3 | 28.952 |  |  |
| SST | 571.699 | 4 |  |  |  |
| a Dependent Variable: Water |  |  |  |  |
| b Predictors: (Constant), Effluent |  |  |  |  |
| 3. | Surface Water Vs. Treated Water | SSW | 244.891 | 1 | 244.891 | 11.223 | 0.044 |
| SSB | 65.464 | 3 | 21.821 |  |  |
| SST | 310.354 | 4 |  |  |  |
| a Dependent Variable: Treated water |  |  |  |  |
| b Predictors: (Constant), River water |  |  |  |  |

**Table S-4 ANOVA analysis on NSAIDs in the urban water cycle.**

**Table S-5 The Pearson correlation on NSAIDs in the urban water cycle**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Pearson Correlation** | **Influent** | **Effluent** | **Surface Water** | **Treated Water** |
| Influent | 1.000 | - | - | - |
| Effluent | 0.994\*\* | 1.000 | - | - |
| Surface Water | 0.950\* | 0.921 | 1.000 | - |
| Treated Water | 0.982\*\* | 0.992\*\* | 0.888\* | 1.000 |
| \*\* Correlation is significant at the 0.01 level (2-tailed).\* Correlation is significant at the 0.05 level (2-tailed). |