

Supplementary information

# Environmental Persistence of the Antidepressant Fluoxetine and Its Pharmaceutical Alternative: Kinetics of Oxidation and Mathematical Simulations

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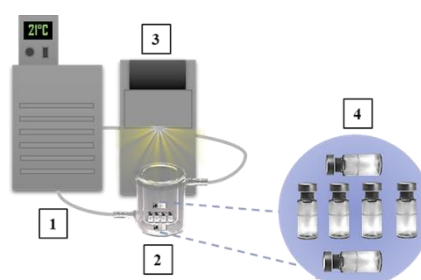
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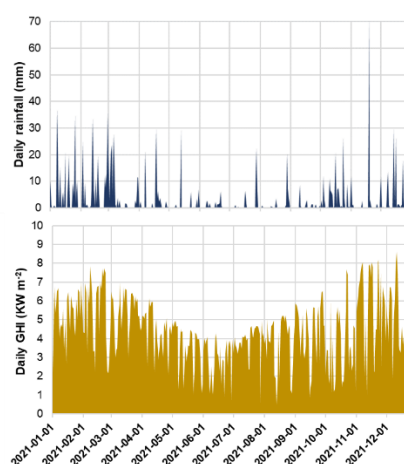
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## 1. Supplementary figures

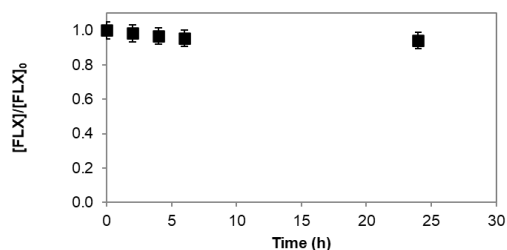


**Figure S1.** Experimental setup used to study the photodegradation of antidepressants under simulated sunlight. (1) Thermostatic bath; (2) jacketed beaker; (3) Irradiation source; (4) distribution arrangement of vials in the beaker.

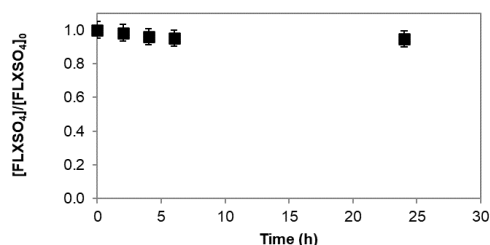


**Figure S2.** Pluviometric and radiometric data of the site studied for the simulation period (2021). Daily rainfall and radiometric data were collected from the automatic weather station in the vicinity of the Guarapiranga reservoir, maintained by the Instituto Nacional de Meteor-

ologia (INMET). Original data are provided as total global horizontal irradiance per hour. The data were integrated over the hours to evaluate the total daily irradiance.



**Figure S3.** Hydrolysis of FLX in pure water. Conditions:  $[\text{FLX}]_0 = (10.22 \pm 0.25) \text{ mg L}^{-1}$ ; natural pH ( $\sim 6.7$ ).



**Figure S4.** Hydrolysis of FLXSO<sub>4</sub> in pure water. Conditions:  $[\text{FLXSO}_4]_0 = (10.34 \pm 0.30) \text{ mg L}^{-1}$ ; natural pH ( $\sim 6.3$ ).

## 2. Supplementary tables

**Table S1.** Physicochemical parameters of the Guarapiranga Reservoir water. Point GUAR00100 (23°45'15"S, 46°43'37"W). Samples collected on 30 May 2022.

Parameter	Value
pH	7.2
Temperature (°C)	26.7
Escherichia coli** (UFC mL <sup>-1</sup> )	4,000.0
Total suspended solids (mg L <sup>-1</sup> )	100
Dissolved aluminum (mg L <sup>-1</sup> )	0.11
Dissolved copper (mg L <sup>-1</sup> )	0.01
Total calcium (mg L <sup>-1</sup> )	12.0
Total magnesium (mg L <sup>-1</sup> )	2.01
Conductivity (μS cm <sup>-1</sup> )	140
Turbidity (UNT)	9.60
Nitrates (mg L <sup>-1</sup> )	0.03
Nitrites (mg L <sup>-1</sup> )	0.10
Dissolved oxygen (mg L <sup>-1</sup> )	7.18
Total fluoride (mg L <sup>-1</sup> )	0.12
Total dissolved solids (mg L <sup>-1</sup> )	100
Total solids (mg L <sup>-1</sup> )	100
Hardness (mg L <sup>-1</sup> )	38.3
Sodium (mg L <sup>-1</sup> )	11.1

Total sulfate (mg L <sup>-1</sup> )	4.21
Total chloride (mg L <sup>-1</sup> )	10.5
Potassium (mg L <sup>-1</sup> )	4.00
Total chromium (mg L <sup>-1</sup> )	0.02
Total manganese (mg L <sup>-1</sup> )	0.13
Total iron (mg L <sup>-1</sup> )	0.83
Dissolved iron (mg L <sup>-1</sup> )	0.11
Total nickel (mg L <sup>-1</sup> )	0.02
Total copper (mg L <sup>-1</sup> )	0.01
Total zinc (mg L <sup>-1</sup> )	0.02
Total barium (mg L <sup>-1</sup> )	0.03
Total lead (mg L <sup>-1</sup> )	0.01
Color	Green
Chlorophyll-a (µg L <sup>-1</sup> )	111
Pheophytin-a (µg L <sup>-1</sup> )	20.15
Number of cyanobacterial cells (No. Cells mL <sup>-1</sup> )	124952
Total organic carbon (mg L <sup>-1</sup> )	9.75

**Table S2.** Retention times (RT), limits of detection (LOD), and limits of quantification (LOQ) of the compounds used in the study.

Compound	RT (min)	LOD (mg L <sup>-1</sup> )	LOQ (mg L <sup>-1</sup> )
FLX	11.0	0.245	0.743
FLXSO <sub>4</sub>	10.5	0.127	0.385
pCBA	8.3	0.120	0.380
FFA	3.9	0.070	0.220
TMP	10.4	0.090	0.280

### 3. Changes incorporated into the APEX code

The original APEX code [19] is based on the solution of simplified mass balances to assess the phototransformation kinetics of compounds that occur in sunlit surface water. Although this model presents remarkable flexibility to address various environmental concerns, some points were not considered in the original version. Therefore, our previous work [27] sought to add some contributions, such as the assessment of the effects of geographic location and seasonal changes, as well as some additional terms to account for the phenomena of eutrophication.

In this work, we proposed to add some modifications to the latest version of the photochemical model. The first is based on calculating the depth of the water. In this version, an average distance for the compounds to react with light was considered to be more realistic, which was previously evaluated as if the compounds were just at the bottom of the water body ( $h_{max}$ ). To consider the exponential behavior of the attenuation along the water column [46], a logarithmic mean was considered for the calculation of the optical path ( $h$ ). For this, one  $h_{min}$  (considered as 0.1 m), which refers to the surface of the water body, was counted in the calculation. Therefore, the  $h$  value used was based on Equation S1:

$$h = \frac{h_{max} - h_{min}}{\ln\left(\frac{h_{max}}{h_{min}}\right)} \quad (\text{S1})$$

Furthermore, the bromide concentration from the chloride concentration [47] was considered in the calculations.

$$M_{Br} = \frac{(2.57 \times 10^{-3} \times M_{Cl} - 9.8x \times 10^{-3}) \times 10^{-1}}{79.904} \quad (S2)$$

The other modification was the consideration of the phenomenon of the adsorption of pollutants in the suspended solids. This phenomenon is important to consider because it causes a change in the concentration of the pollutant in the liquid phase, which has significant importance in modeling the removal of pollutants in aquatic environments. Initially, it is necessary to consider the distribution of pollutants between the solid and liquid phases. Thus, the concept of distribution coefficient (solid/liquid) ( $K_d$ ) was considered, which relates the concentration of the species that is adsorbed on the solids with the concentration of the species that remains in the water, as shown in **Equation S3**:

$$K_d = \frac{C_{X,solid}}{C_{X,water}} \quad (S3)$$

However, the model used the organic carbon distribution coefficient ( $K_{oc}$ ) and the fraction of organic carbon in solids ( $f_{oc}$ ) to calculate  $K_d$ , according to the following equation.

$$K_d = f_{oc} \times K_{oc} \quad (S4)$$

The value of  $K_{oc}$  was obtained using a program already developed for the determination of property values for several compounds, the Open Quantitative Structure–Activity Relationship Application (OPERA). This program allows the use of models to calculate property values from the CAS number and SMILES code of a compound. The model for the adsorption coefficient on organic carbon is based on PaDEL descriptors, used to classify molecules into different groups and thus obtain property estimates from machine learning algorithms and the structure of each of the compounds [48].

With the value of  $K_{oc}$  and, therefore, the value of  $K_d$ , a balance was developed, considering that adsorption on solids is always in equilibrium. In this sense, it was possible to calculate the concentration of the pollutant that is in the water and the concentration of the pollutant that is in the solids, as can be seen in **Equations S5–S8**:

$$C_{X,tot} \times V = C_{X,w} \times V + C_{X,s} \times S \quad (S5)$$

$$K_d = \frac{C_{X,s}}{C_{X,w}} \quad (S6)$$

$$C_{X,w} = C_{X,tot} \times \left( \frac{V}{V + K_d \times S} \right) \quad (S7)$$

$$C_{X,s} = K_d \times C_{X,w} \quad (S8)$$

Therefore, it was possible to consider the real concentration of antidepressants in the aqueous phase in the modeling because of the adsorption processes.

The last modification was the implementation of pollutant biodegradation. In this mechanism, the concentration of the pollutant is reduced by its consumption as a substrate of the microorganisms present in the medium. These reactions are responsible for much of the degradation of organic compounds present in natural waters [42]. Despite the complexity of this type of phenomenon, a more simplified form was approached in the modeling.

The OPERA program was used again to obtain the biodegradation half-life as the main mechanism, similar to the  $K_{oc}$  value obtained in the adsorption modeling. However, this simplification has some limitations in relation to the use of the OPERA program for two reasons: (i) the program is designed to feed hydrocarbon molecules but allows any

compound as an input; (ii) the half-life data used for training come from different conditions.

Equations S9-S11 summarize the development used to implement the biological degradation of pharmaceutical contaminants.

$$\frac{dN_x}{dt} = -k_{X,biodeg} \times N_x \quad (S9)$$

$$k_{X,biodeg} = \frac{\ln(2)}{t_{1/2,degrad}} \quad (S10)$$

$$r_{X,biodeg} = k_{X,biodeg} \times [X] \quad (S11)$$

## References

19. Bodrato, M.; Vione, D. APEX (Aqueous Photochemistry of Environmentally occurring Xenobiotics): Free software tool to predict the kinetics of photochemical processes in surface waters. *Environ. Sci. Process Impacts*, **2014**, *16*, 732–740. <https://doi.org/10.1039/c3em00541k>
27. Souza, L.P.; Sanches-Neto, F.O.; Junior, G. M. Y.; Ramos, B.; Lastre-Acosta, A. M.; Carvalho-Silva, V. H.; Teixeira, A.C.S.C. Photochemical environmental persistence of venlafaxine in an urban water reservoir: A combined experimental and computational investigation, *Process Saf. Environ. Prot.*, **2022**, *166*, 478-490. <https://doi.org/10.1016/j.psep.2022.08.049>
46. Liu, W. C.; Hsu, M. H.; Chen, S. Y.; Wu, C. R.; Kuo, A. Y. Water column light attenuation in Danshuei river estuary, Taiwan. *J Am Water Resour Assoc*, **2005**, *41*, 425-436. <https://doi.org/10.1111/j.1752-1688.2005.tb03746.x>
47. Magazinovic, R. S.; Nicholson, B. C.; Mulcahy, D. E.; Davey, D. E. Bromide levels in natural waters: its relationship to levels of both chloride and total dissolved solids and the implications for water treatment. *Chemosphere*, **2004**, *57*, 329-335. <https://doi.org/10.1016/j.chemosphere.2004.04.056>
48. Mansouri, K.; Grulke, C. M.; Judson, R. S.; Williams, A. J. OPERA models for predicting physicochemical properties and environmental fate endpoints. *Journal of Cheminformatics*, **2018**, *10*. <https://doi.org/10.1186/s13321-018-0263-1>
42. Schwarzenbach, R. P.; Gschwend, P. M.; Imboden, D. M. *Environmental Organic Chemistry*. 2nd edition. New Jersey: John Wiley & Sons, Inc, 2003.