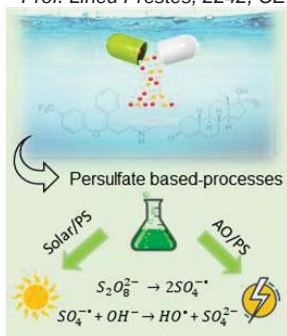


Investigation of Persulfate-Based AOPs to Decontaminate Water with a Mixture of Fluoxetine and Levonorgestrel

L. P. Souza¹, J. M. S. Jesus¹, F. K. Tominaga², B. Ramos¹, S. I. Borrelly² and A. C. S. C. Teixeira¹. (1) Research Group in Advanced Oxidation Processes (AdOx), Department of Chemical Engineering, Escola Politécnica, University of São Paulo, Avenida Prof. Luciano Gualberto, tr. 3, 380, São Paulo, Brazil, larissapdesouza@usp.br. (2) Nuclear and Energy Research Institute-IPEN-CNEN/SP, São Paulo, Brazil, Av. Prof. Lineu Prestes, 2242, CEP 05508-000, São Paulo, SP, Brazil.



This work reports a study on two forms of persulfate activation (solar irradiation and anodic oxidation-AO) for the degradation of active pharmaceutical ingredients (APIs). A solution containing a mixture of levonorgestrel and fluoxetine ($[LNG]_0 = 0.29 \pm 0.03 \text{ mg L}^{-1}$; $[FLX]_0 = 5.02 \pm 0.34 \text{ mg L}^{-1}$) was treated with persulfate ($[PS]_0 = 0.07 \text{ mol L}^{-1}$) and irradiated or electrolyzed for 60 min under similar conditions. The results revealed similar decays of APIs in the two activation forms studied, solar/PS ($k_{LNG} = 6.6 \times 10^{-2} \text{ min}^{-1}$; $k_{FLX} = 7.7 \times 10^{-2} \text{ min}^{-1}$) and AO/PS ($k_{LNG} = 7.8 \times 10^{-2} \text{ min}^{-1}$; $k_{FLX} = 9.7 \times 10^{-2} \text{ min}^{-1}$), with slightly better results for the electrochemical process. However, acute toxicity assessed with *Daphnia similis* indicated that AO/PS provided a three-fold increase in the values of toxic units.

Introduction

The occurrence and fate of active pharmaceutical ingredients (APIs) in the environment have been a worldwide concern [1]. Among emerging APIs increasingly present in urban waters, fluoxetine (FLX), used in the treatment of psychotropic diseases such as depression, anxiety, and bulimia [1]; and levonorgestrel (LNG), a synthetic steroid widely used as an emergency contraceptive pill in Brazil [2], are already being detected in the aquatic environment at concentrations of 2-140 ng L⁻¹ (FLX) [1] and 0.9-17.9 ng L⁻¹ (LNG) [2]. Moreover, LNG and FLX are classified as priority agents based on the Toxicity Priority Index (ToxPi), occupying the 5th and 25th positions in the ranking, respectively [3]. In view of the potential effects of APIs in natural waters, advanced oxidation processes (AOPs) have been studied to avoid their release [4,5]. Persulfate-based processes are posed as a promising technology: in comparison with HO[•], SO₄^{•-} radicals have a higher redox potential (2.5-3.1V vs. 1.8-2.7V), higher selectivity, and longer half-life (30-40 μs) [6]. In addition, persulfate can be generated by a wider range of driving forces, such as UVA/UVB photons and electron current [7]. In this direction, this work aims to investigate persulfate activation via UVA and anodic oxidation for the degradation of the APIs mixture.

Material and Methods

Reagents. Levonorgestrel (LNG, C₂₁H₂₈O₂, ≥ 98.0%) was purchased from Zhejiang Xianju Pharmaceutical Co. Ltd. Fluoxetine (FLX, C₁₇H₁₈F₃NO ≥ 98.0%) was supplied by Campos Manipulação. The oxidizing agent sodium persulfate (≥ 98%, Na₂S₂O₈, PS) was purchased from Sigma-Aldrich. Methanol (HPLC grade, Sigma Aldrich), acetic acid (LabSynth), and trifluoroacetic acid (Sigma Aldrich) were used to prepare the mobile phases used in liquid chromatography. Deionized water (18.2 MΩ cm) was

obtained from a Milli-Q Direct-Q system (Millipore).

Degradation experiments. The photodegradation experiments were performed using a mercury iodide lamp (Master HPI-T Plus, Philips Co.), providing 1.94 mW cm⁻² in the 290-800 nm. A boron-doped diamond electrode (BDD, Boromond Co.) and stainless steel 304 were used as anode and cathode in the electrochemical process, respectively. The active electrode area was 20 cm² and the gap distance was kept at 13 mm. A 30 V/5 A-power supply (MPS 300-5B MINIPA) was used as a constant current source. The samples were contained in a 250-mL Pyrex beaker and flowed through the reactors (photochemical or electrochemical) using a peristaltic pump (Provitec, AWM 5000-AX-D) (Figure 1). The samples were collected (0, 5, 10, 15, 30, 45, 60 min) and separated for HPLC analysis.

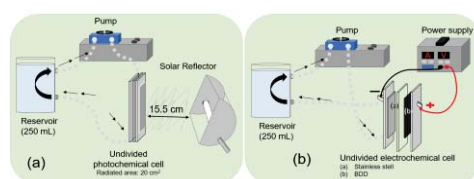


Figure 1. Experimental setup for solar/PS (a) and AO/PS (b).

Analytical methods. The concentrations of LNG and FLX were monitored by ultra-fast liquid chromatography, as described elsewhere [8,9]. The acute toxicity was evaluated using *Daphnia similis* according to the Brazilian Association of Technical Standards (NBR 12713/04) [10].

Results and Discussion

Table 1 presents the removal efficiency and k_{obs} after 60 minutes of treatment, indicating a higher removal efficiency in AO/PS for both APIs. Control

experiments under solar irradiation showed that LNG undergoes a significant photolytic degradation, unlike FLX. Conversely, in control experiments using only PS, FLX removal (77.1%) was higher than LNG (45.2%), indicating a possible selectivity of sulfate radicals ($\text{SO}_4^{\cdot-}$) for the former. Comparing the activated persulfate processes, AO/PS provided the highest removal of both LNG and FLX. **Figure 2** presents the values of TU (toxic units) of the treated solution for *D. similis*, and shows that AO/PS promoted a three-fold increase in comparison to solar/PS. This suggests that different reaction mechanisms are taking place [7], stressing the need for a detailed investigation of the by-products generated in AO/PS

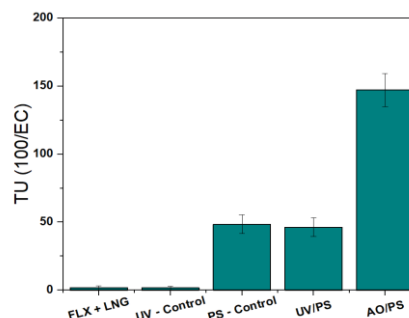


Figure 2. Acute toxicity (in toxic units, $\text{TU} = 100/\text{EC}_{50}$) assessed using *D. similis*. $[\text{LNG}]_0 = 0.29 \pm 0.03 \text{ mg L}^{-1}$; $[\text{FLX}]_0 = 5.02 \pm 0.34 \text{ mg L}^{-1}$; $[\text{PS}]_0 = 0.07 \text{ mol L}^{-1}$; $j = 37.5 \text{ mA cm}^{-2}$.

Table 1. Values of k_{obs} and removal rate for LNG and FLX in the 60 min of applied persulfate-based process. $[\text{LNG}]_0 = 0.29 \pm 0.03 \text{ mg L}^{-1}$; $[\text{FLX}]_0 = 5.02 \pm 0.34 \text{ mg L}^{-1}$; $[\text{PS}]_0 = 0.07 \text{ mol L}^{-1}$; $j = 37.5 \text{ mA cm}^{-2}$.

Treatment	LNG			FLX		
	$k_{\text{obs}} (\text{min}^{-1})$	R^2	Removal60' (%)	$k_{\text{obs}} (\text{min}^{-1})$	R^2	Removal60' (%)
Sunlight	9.7×10^{-3}	0.9877	44.0	1.3×10^{-3}	0.8954	6.2
PS	1.3×10^{-2}	0.9387	45.2	2.0×10^{-2}	0.9710	77.1
Solar/PS	6.6×10^{-2}	0.8984	96.7	7.7×10^{-2}	0.9843	< LOD
AO/PS	7.8×10^{-2}	0.9916	< LOD	9.7×10^{-2}	0.9939	< LOD

Conclusions

The results obtained showed that both sunlight and anodic oxidation can efficiently activate persulfate anions and achieve 100% removal of both APIs in the mixture within 60 min. AO/PS seems to be the best process to decompose a mixture of pharmaceuticals such as LNG and FLX, although acute toxicity assays allowed to observe that the AO/PS process provided an increase in initial toxicity. The application of a coupled process using both forms of persulfate activation will be further investigated to mitigate the generation of hazardous by-products.

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