Degradation of COVID-19 pharmaceutical by Solar Photo-Fenton process: Evaluation of experimental conditions and identification of transformation products.

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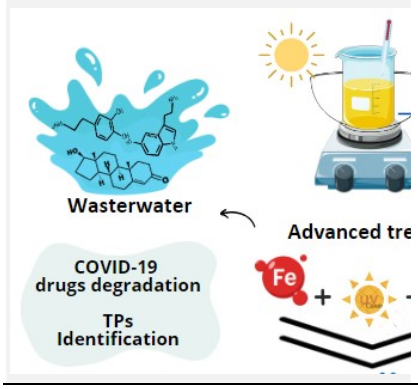

During COVID-19 pandemic, high consumption of antivirals, antibiotics and antiparasitics, resulted in an increase in the variety and quantities of these compounds in wastewater (WW) even after treatment, generating concern about their release to the environment. The present study investigated the degradation of six pharmaceuticals, used for COVID-19 treatment (some of them with off label use), by Solar Photo-Fenton (SPF) process under different experimental conditions. The transformation products (TPs) generated were also identified using a purpose-built data base. The degradation rates obtained were higher than 80% in all conditions, but they led to different TPs. In pH 2.8 was possible to identify 27 TPs while in pH 5.0 29 TPs were generated.

Introduction

The presence of pharmaceuticals in WW is one of main sources of water pollution. During the COVID-19 pandemic this scenario was worsened, as several pharmaceuticals were used in an attempt to treat the disease symptoms, some of them with off label use. Azithromicyn (AZT), Dexamethasone Acetate (DEX), Dipyrone (DIP), Hydroxychloroquine (HCQ), Nitazoxanide (NTZ) and Paracetamol (PCT), are a few examples of drugs widely used that eventually ended up in the environment[1]. SPF process offers a low cost and environmental friendly solution; however, the pH under which SPF is applied is one of the main focuses of study these days[2]. Thus, the goal of this study was to investigate the SPF process for the degradation of COVID-19 pharmaceuticals using classical and near-neutral SPF and to identify the TPs generated under each condition tested, using a purpose-built data base.

Material and Methods

SPF experiments were performed in a 1L photoreactor, with a stirrer, at room temperature. 1L of DW spiked with 1.5 mgL^{-1} of AZT, DEX DIP, HCQ, NTZ and PCT was added to the photoreactor. 50 mg of H_2O_2 (35% w/v) was added at the initial treatment time, sample aliquots were collected at varied times (0-120 min) and 200 µL of $NaHSO_3$ (28% w/v) was added to each sample, to quench the residual H_2O_2 and stop the degradation. Samples were analyzed by LC-QTOF MS to monitor the degradation of the MIX solution and TPs formation. The SPF process was investigated in three experimental conditions: i) pH 2.8 (classical) and ii) pH 5.0 (near-neutral), both with single addition (SA) of iron (5 mgL^{-1}) at 0 min; iii) pH 5.0 with multiple additions (MA) of iron, at 0 min (5 mgL^{-1}) and at 20 min (5 mgL^{-1}). The identification of TPs was accessed using a purpose-built data base containing 140 TPs of the "parent" pharmaceuticals.

Results and Discussion

The SFP process achieved degradation rates higher than 80% in all conditions, although it was possible to see some important differences **(Fig. 1)**. As expected, pH 2.8 demonstrated faster degradation for all compounds, since this is the optimum pH to perform SPF treatment. In this pH, the maximum removal for all compounds were observed at t_{30W} = 29 min and after that lower degradation rates or insignificant degradation were observed. The degradation experiment at pH 2.8 resulted in different kinetics. PCT, AZT and HCQ followed biphasic degradation, with a first stage (up to t_{30W} = 29 min) defined as a pseudo-first order kinetic and in the second stage insignificant or no degradation was observed. The recalcitrant fraction corresponded to less than 20% for all pharmaceuticals and can be explained by the lack of H_2O_2 in the solution as it was completely consumed even with extra addition. For NTZ and DEX the degradation followed a pseudo first order kinetics. The obtained parameters are presented in **Table 1**. Under this pH it was possible to identify 27 TPs. Considering the experiments performed at pH 5.0 with SA and MA of Iron (Fe^{2+}), both presented very similar results with exception of AZT, the degradation was faster with MA of iron but was almost complete with SA of iron. This result showed lack of efficacy of the MA approach, since the expectation was to achieve results similar to pH 2.8, as described by other authors[3,4]. Both conditions using pH 5.0 resulted in different kinetics for each pharmaceutical, these results are also presented in **Table 1**. For DIP, it was not possible to determine the kinetic values due to the

fast elimination in all approaches performed. Under these conditions it was possible to identify 29 TPs. The TPs of DIP and PCT were the only ones affected by the pH, as different compounds were identified under different pHs. For DIP this can be explained by the generation of the metabolite Acetylaminoantipirina (AAA) in pH 5.0. This metabolite generated other four TPs that were not detected in pH 2.8. It is important to highlight that different TPs have different characteristics and therefore this can impact the environmental risk associated. For the other pharmaceuticals the same TPs were identified in both conditions tested (pH 2.8 and pH 5.0 SA and MA). Additionally, it was also possible to observe the generation of TPs with a sulfonic group attached due to reactions between TPs and $NaHSO_3$, used to quench residual H_2O_2. These reactions were evidenced by the appearance of two peaks with the same *m/z* in the chromatogram, after thorough analysis of MS spectra (bbCID) it was possible to attribute one of these peaks to the TP (matching the data base) and one to the same TP with a sulfonic group attached

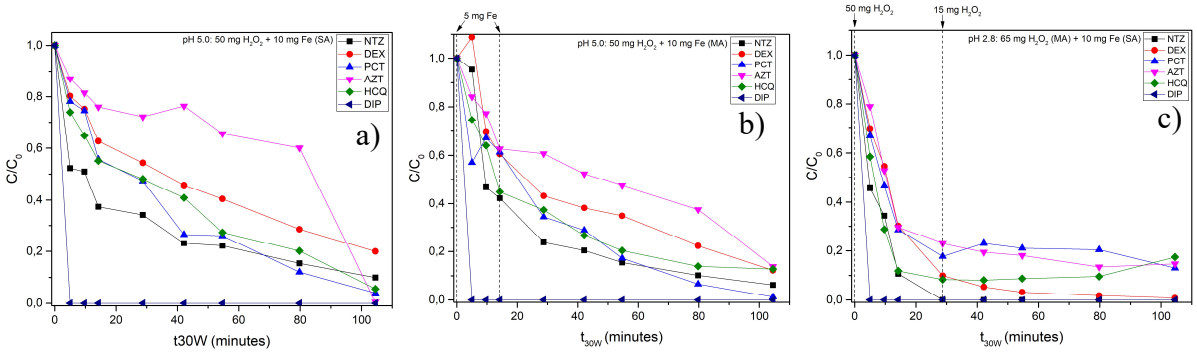

Figure 1. Pharmaceuticals degradation under different SPF conditions: a) pH 5.0 SA; b) pH 5.0 MA; c) pH 2.8.

Table 1. Kinetc parameters obtained for the pharmaceuticals under different SPF conditions.

pH		DEX	NTZ	PCT	AZT	HCQ
2.8	Kinetic model	p. 1st order	p. 1st order	p. 1st order + RF	p. 1st order + RF	p. 1st order + RF
	k_{obs1}/min^{-1}	0.09318	0.1357	0.1517	0.1173	0.1997
	y_0	-	-	0.1827	0.1561	0.0948
	r^2	0.9944	0.9895	0.9857	0.9801	0.9809
5.0 MA	Kinetic model	p. 1st order + RF	2-step p. 1st order	p. 1st order	2-step p. 1st order	p. 1st order + RF
	k_{obs1}/min^{-1}	0.0448	0.1069	0.0633	0.2741	0.0709
	k_{obs2}/min^{-1}	-	0.0114	-	0.0039	-
	y_0	0.1803	-	-	-	0.1601
	r^2	0.9741	0.9506	0.9357	0.9571	0.9823
5.0 SA	Kinetic model	p. 1st order + RF	2-step p. 1st order	p. 1st order	2-step p. 1st order	p. 1st order + RF
	k_{obs1}/min^{-1}	0.0344	0.5822	0.0322	0.2741	0.0328
	k_{obs2}/min^{-1}	-	0.0184	-	0.0039	-
	y_0	0.2160	-	-	-	0.8715
	r^2	0.9719	0.9719	0.9882	0.9751	0.9435

[a]: p. first order = pseudo first order kinetics; [b]: RF = Recalcitrant Fraction.

Conclusions

The SPF degradation of some pharmaceuticals tested achieved primary elimination rates above 80% in all conditions evaluated, indicating that both pHs, 2.8 and 5.0, are suitable to promote efficient degradation. In this way, the pH 2.8 resulted in faster degradation and can be used to reduce the treatment time. While, pH 5.0 is near to neutral and can be considered as more environmental friendly. Under pH 2.8 27 TPs were identified while under pH 5.0 29 TPs were identified. Although pH 2.8 generated less TPs is also important to predict the environment risk associated with these TPs, in order to have more information.

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