Degradation of Losartan Potassium and Furosemide by UV and UV/H$_2$O$_2$ processes

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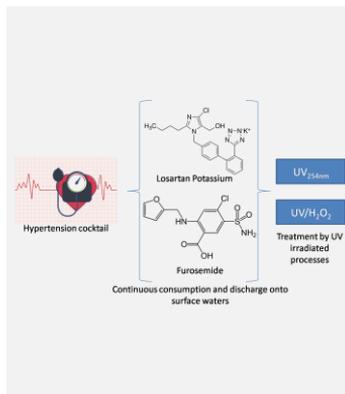
Losartan Potassium (LP) and Furosemide (FRSM) are consumed mainly by hypertensive patients. Their consumption is predicted to increase in the next years, and thus their discharge onto surface waters. Therefore, it is important to establish effective treatment technologies for the removal of these compounds in water treatment plants (WTP). In the present work, quantum yields (Φ_{254nm}) were calculated for LP and FRSM at different pH values (3, 6 and 9), in order to analyze their photo-liability. Then, UV and UV/H$_2$O$_2$ treatments were compared for the degradation of LP and FRSM. Values obtained for quantum-yields varied from 0.01 to 0.04 for LP, and from 0.03 and 0.10 for FRSM. In our conditions, both UV and UV/H$_2$O$_2$ processes were effective for the removal of LP and FRSM. Although, TOC degradation was reduced (6 and 8%), indicating accumulation of degradation products.

Introduction

Life expectancy has increased in many countries due to medical advances. As a consequence of population aging, the consumption of pharmaceuticals has also raised, especially for drugs related to the cardiovascular system, such as β-blockers, angiotensin inhibitors and receptor antagonists, and diuretics. It is estimated that 1.5 billion people will suffer from hypertension by 2020.

Thereafter, the disposal of these drugs to surface waters (SW) through public sewage discharge will also continuously increase in the next years. The presence of some pharmaceuticals in surface waters may lead to impacts on human health and on the life cycle of aquatic species [1]. In this context, it is important to establish and implement effective treatment technologies for the removal of these compounds.

The occurrence of some β-blockers and their treatment through various technologies has been previously reported [2]. However, reduced attention is given to angiotensin II receptor antagonists, such as sartans [3]. Losartan potassium (LP) is part of the group of the angiotensin II receptor antagonists and was the most consumed drug in Brazil in 2015. Moreover, if submitted to chlorination, which is a process used in most of the Water Treatment Plants (WTP) in Brazil, cyanide, a poison that may threaten human health, may be formed and remain in drinking water [4]. Furosemide (FRSM) is a diuretic that is usually taken by patients in parallel to sartans as part of the cocktail for the high blood pressure treatment. In addition, diuretics are highly consumed in Brazil for weight loss purposes through illegal market. Both of these compounds have been detected in SW worldwide [5].

The aims of this work were to analyse the photo-liability under UV irradiation (254 nm) of LP and FRSM and to evaluate their degradation by UV and UV/H$_2$O$_2$ treatments. These two treatments were chosen due to their simplicity of operation and because UV light has already been applied for disinfection purposes in water and wastewater Treatment Plants (WTP and WWTP).

Material and Methods

LP and FRSM were purchased from Sigma-Aldrich. Liquid chromatography equipped with a UV detector has been used for the quantification of pharmaceuticals (Agilent 1260 Infinity II series, DAD detector equipped with a 60 mm high sensitivity cell). The separation has been performed on Poroshell 120 EC-C18 3 x 50 mm, 2.7µm) C18 columns (Poroshell HPH-C18 4.6 x 150 mm 2.7 um and 120 EC-C18 3 x 50 mm, 2.7µm). Ultra-pure water (40%) and MeOH (60%) both containing 0.1% Formic Acid were used as mobile phase. Flow was set at 0.5 mL.min^{-1} and the UV detector was set at 240 nm.

Experiments performed for the determination of quantum yields (Φ) were conducted in a UV reactor (Lamp: LIGHTENNINGCURE™ C8 HAMAMATSU, vol: 3.5 mL) under constant agitation. A filter (254 nm; Semrock Maxlamp™) was placed at light source. The incident photonic flux ($I_0 = 1,6 \times 10^{-8}$ Einstens.s^{-1}) was determined by actinometry experiments using H$_2$O$_2$ and confirmed with Atrazine [6, 7]. Initial concentrations of each of the compounds were equivalent to 2.17 µM and 3 µM for LP and FRSM respectively, which corresponds to 1 mg.L^{-1} for each compound. Quantum yields were calculated for acidic (pH = 3), without modification (6 for LP and 5.5 for FRSM) and basic pH (9). pH was adjusted by using solution of HCl and NaOH (0.1 M and 0.01 M).

UV/H$_2$O$_2$ and UV degradation treatments were performed in a 2 L cylindrical bench photo-reactor equipped with a low-pressure mercury vapour lamp emitting a monochromatic radiation at 253.7 nm (Heraeus GPH212T5L/4, 10 W) in axial position. The incident photonic flux ($I_0 = 3,1 \times 10^{-6}$ Einstens.s^{-1}) was determined by actinometry analyses as

described above [6, 7]. Optical pathway (3.14 cm) was calculated as according to Beltran *et al.*, 1995 [8]. Temperature was kept constant at 20°C. Samples were withdrawn during reactions for quantification of LP, FRSM, H_2O_2 [9], and TOC (TOC-V_{CSH} Total Carbon Analyzer Shimadzu). Initial concentrations of LP and FRSM were equivalent to 50 µM in order to enable TOC analyses (theoretical values 13.2 and 7 mgC.L^{-1} of TOC for LP and FRSM respectively). H_2O_2 initial concentration was 10^{-3} M for all the UV/H_2O_2 reactions (molar ratio H_2O_2/target molecule 20:1).

Results and Discussion

UV irradiation treatment has been employed in many WTP as tertiary treatment, mainly for disinfection. In addition to disinfection, this process may also lead to photolysis of some compounds. During UV irradiation, the excitation of a molecule does not necessarily culminate on photolysis and the quantum yield (Φ) of a compound will influence its photolysis rate [10]. Table 1 shows LP and FRSM quantum yields values on pH 3, natural and 9.

Table 1. LP and FRSM quantum-yields and absorption coefficients (ϵ_{254nm}) at different pH

pH	Φ_{254nm}			$\epsilon_{254\,nm}\,(10^3)$		
	3	6	9	3	6	9
LP	0.01± 0.002	0.04± 0.006	0.03± 0.002	10,4	11,2	11,7
FRSM	0.10± 0.003	0.03± 0.007	0.03± 0.002	4,1	3,7	3,9

LP photo-stability in medical formulation has already been reported previously [11]. However, this is the first report on pure LP quantum yield. Values of LP quantum yields (Table 1) vary from 0.01 to 0.03 and are 3 to 4 times lower at acidic pH compared to basic and neutral pH, respectively. Regarding FRSM, the quantum-yield value determined at pH 3 is in agreement with previously reported value (0.02) [12]. Acidic pH increases the quantum-yields and ϵ values for this compound, which explains higher photolysis rate of FRSM at pH 3. It is known that the pK_a for FRSM is 3.9, which means that it is in its anion form at neutral pH. Also, photo-instability of FRSM in its unionized form has been previously reported [13]. Quantum yield values calculated for target compounds are 100 to 1000 times higher than that of caffeine (0.0003 at pH 7) [10] which is considered a photo-stable compound.

When submitted to UV irradiation, H_2O_2 is cleaved to produce hydroxyl radicals (•OH): extremely reactive and non-selective oxidants that react with recalcitrant compounds. Advanced Oxidation Processes (AOP) such as UV/H_2O_2 have been considered promising alternatives for the removal of contaminants of emerging concern on WTP and WWTP. Under ideal conditions, AOPs may lead to total mineralization to CO_2 and H_2O. When compared to other AOPs, UV/H_2O_2 process is of simple operation, once no pH adjustment is

needed prior to reaction, thus reducing costs and use of chemical reagents.

Target compounds were submitted to UV and UV/H_2O_2 processes and results for compound degradation and TOC removal are presented in Figure 1. Regarding LP, degradation using UV only was around 48% ($k_{d,\,UV}$ = 0.01 $M^{-1}\cdot s^{-1}$) after 60 min of irradiation (pH 7), while for UV/H_2O_2 degradation rate increased to 95% ($k_{d,\,UV/H2O2}$ = 0.05 $M^{-1}\cdot s^{-1}$).
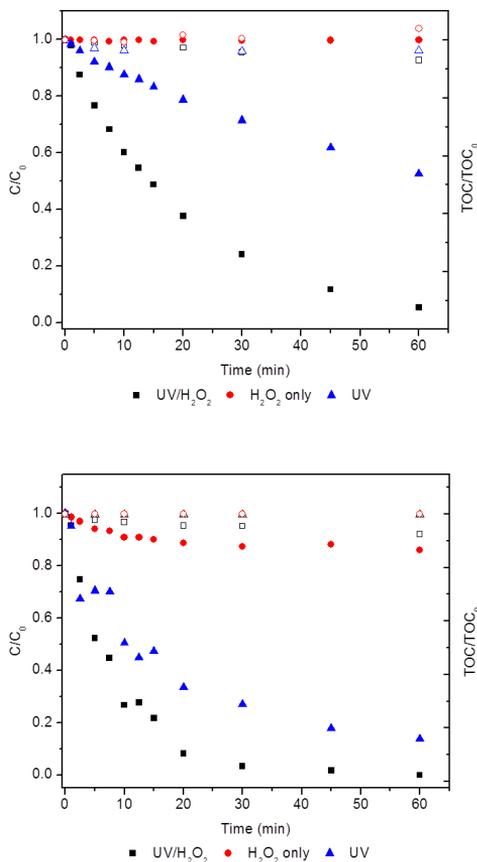
Figure 1. UV and UV/H_2O_2 degradation of LP (top) and FRSM (bottom) and TOC removals. Unfilled symbols correspond to TOC results, pH 8.

Also, while no TOC removal was observed for LP UV photolysis, 6% TOC removal was achieved by UV/H_2O_2. These results indicate that most of the transformation products formed from LP degradation remained in solution for both processes. In addition, two main transformation products were formed after photolysis, while four could be observed after UV/H_2O_2. Considering the separation apparatus used in this work (C_{18} column), we may conclude that transformation products are more polar than LP, since they sorted earlier than target compound. This may suggest a change of chemical functions based on LP chemical structure.

Degradation of FRSM through UV and UV/H_2O_2 showed, respectively, 87% ($k_{d, UV}$ = 0.04 s^{-1}) and 98% ($k_{d, UV/H2O2}$ = 0.11 s^{-1}) removal of FRSM after 60 minutes of reaction. TOC removal was equivalent to 8% and was observed only for UV/H_2O_2 reaction. Although still transluscent, visual aspect of solutions changed during reaction and samples of FRSM after UV and UV/H_2O_2 processes showed, respectively, slightly red and yellow colours after 60 minutes of irradiation. Also, the analyses of chromatograms show that two similar main transformation products are formed during both reactions, while only one of them remains after UV/H_2O_2. The first degradation product was detectable after 15 min of UV irradiation and accumulates in the system. However, during UV/H_2O_2 process, degradation goes further and this product is formed and degraded throughout reaction with the formation of a second product. It has been reported that FRSM undergoes dechlorination when exposed to light. Also, it may initiate free radical reactions and excited-state energy transfer under irradiation, thus elucidating the fact that UV irradiation alone was nearly as effective for the degradation of FRSM as UV/H_2O_2 [13].

Further analysis by LC/MS will be performed in order to investigate intermediates formed during each of the reactions for LP and FRSM degradation and clarify degradation pathway. Taking that mineralization rates were reduced, it is also important to investigate what are the characteristics (chemical properties, toxicity, estrogenicity, etc) of the compounds that remained in solution after the application of UV irradiation as tertiary treatment.

Conclusions

LP and FRSM quantum yields were calculated in different pH conditions and indicate that these compounds are slightly photo-liable under UV$_{254nm}$ irradiation. Results obtained for UV$_{254nm}$ and UV/H_2O_2 treatment processes show that both processes are effective for the degradation of these compounds, and that UV/H_2O_2 degradation rates were higher than those obtained after UV$_{254nm}$ alone for both pharmaceuticals. However, TOC removals were reduced, thus indicating that degradation products remained in solution. Therefore, if present in SW and submitted to UV irradiation, a process which is commonly applied as a disinfection step in treatment plants, these pharmaceuticals will probably be removed with the formation of recalcitrant by-products. Further investigation on the nature of degradation products is needed.

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