Photochemical mineralization of Ibuprofen medicinal product by means of UV, hydrogen peroxide, titanium dioxide and iron

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ABSTRACT

Pharmaceutical compounds contribute to the emerging pollutants in water and in many cases, they are not efficiently mineralized by conventional treatment methods. At the same time, landfills remain the main final destination of discarded drugs. In the present study, the mineralization of the Ibuprofen medicinal commercial product (Algofren®) in aqueous solutions using UV irradiation, hydrogen peroxide, titanium dioxide and ferric ions was examined. All experiments were conducted in a batch photoreactor operated for 120–150 min. The main target was to select the most effective operating conditions for the mineralization of the solutions treated. Single photolysis or TiO₂ photocatalysis were proved inefficient in eliminating the total organic carbon (TOC). By adjusting the initial amounts of Ibuprofen product and hydrogen peroxide, 81% TOC removal was achieved after 120 min. Adding iron in the solution led to a higher mineralization degree, especially during the first 30 min of the process. Iron was shown also to decrease the environmental footprint of the process as expressed via the electric energy per order, $E_{Ed}$.

Key words | Algofren, Fe(III), H₂O₂, photo-Fenton

INTRODUCTION

There has been increasing interest in relation to the presence of pharmaceutical compounds in water over the last 20 years due to their potential negative effect on aquatic organisms (Méndez-Arriaga et al. 2010). Pharmaceuticals can infiltrate water bodies and eventually drinking water sources through various pathways: excretion from patients, hospital waste, and disposal of unused drugs down household drains. Due to pharmaceuticals’ positive impact on human health, the study of the fate and impact of pharmaceuticals on the environment has not been a priority until recently.

Ibuprofen (IB) belongs to the non-steroidal anti-inflammatory drugs (NSAIDs), which are medicinal products commonly prescribed to mitigate pain and inflammation, especially among seniors. These drugs constitute 5%–10% of prescribed medications worldwide every year (Wongrakpanich et al. 2018). IB has been suggested to be added to the list of priority pollutants of the EU Water Framework Directive 2000/60/EC. It was among the main compounds detected in the River Elbe in 1998 at concentrations between 20 and 140 ng/L as well as being among the most frequently detected pharmaceuticals in both African and European continents (Fekadu et al. 2019). IB is considered to pose a threat for aquatic populations although its effect on natural organisms has not been fully investigated. It has been shown to have adverse impacts on the survival and reproduction of planktonic rotifer species, Brachionus calyciflorus and Brachionus havanensis (González-Pérez et al. 2016).

Compared with other target compounds like phenol that have been included in hundreds of works, studies regarding the photochemical degradation and mineralization of IB in water using advanced oxidation processes are relatively recent; they include its heterogeneous photocatalytic treatment in ultrapure water (Jiménez-Salcedo et al. 2019; Lin et al. 2019), heterogeneous Fenton oxidation in wastewater using Fe-ZSM5 catalyst (Adityosulindro et al. 2018), photo-Fenton in water (Méndez-Arriaga et al. 2010), ultraviolet light in aqueous solutions (Chianese et al. 2016), catalytic ozonation (Betancur-Corredor et al. 2016), UV/chlorine advanced oxidation process (Xiang et al. 2016), UV/H₂O₂ and UV/S₂O₅²⁻ treatment (Kwon et al. 2015), sono-photocatalysis in aqueous matrices (Michael et al. 2014), homogeneous photocatalysis (Loaiza-Ambuludi et al. 2014), classic Fenton,
photo-assisted Fenton, UV/H₂O₂ and peroxymonosulphate oxidation (Scheers et al. 2012), ozonation, UV photolysis and Fenton (Epold et al. 2012), sonolysis, photocatalysis and sono-photocatalysis in the presence of Fe³⁺ and TiO₂ (Madhavan et al. 2010), electro-Fenton and UVA photoelectro-Fenton in aqueous medium (Skoumal et al. 2009), and UV/H₂O₂ (Yuan et al. 2009). Felis & Miksch (2009) studied also the UV/H₂O₂ degradation of Ibuprofen, among other analgesics, in water with/without adding urea as a representative compound of urine.

In most degradation and kinetic studies, Ibuprofen concentration has been monitored in pure water or in synthetic solutions. This limits the application of AOPs for treating commercial pharmaceuticals that have expired or been left unused. Specifically, medicinal products, including the commercial one for IB, contain other compounds besides the active substance, namely excipients for long-term stabilization, flavor, solubility etc., and it is known that advanced oxidation processes can be adversely affected by the presence of other compounds in solutions that may act as radical scavengers. The disposal of drugs in households has attracted a lot of interest lately as drugs are still improperly disposed of in garbage or flushed into the sewage system in many countries. Municipal landfills remain the main destination for discarded drugs (Tischler et al. 2013) and thus, alternative treatment options should be sought.

In the present work, the mineralization of Ibuprofen in its medicinal product (commercial name Algofren®) was studied by UV photolysis, UV/H₂O₂ photochemical treatment, heterogeneous photocatalysis and photo-Fenton.

**MATERIALS AND METHODS**

**Chemicals and reagents**

All reagents were used as received without any further purification. Pharmaceutical solutions were prepared from the commercial drug: Algofren®, 150 mL syrup, 100 mg/5 mL, active substance Ibuprofen (Figure 1), excipients: xanthan gum, carboxymethyl cellulose sodium, glycerox, sorbitol, sodium benzoate, aroma strawberry, citric acid, sodium saccharin, polysorbate 80, ponceau 4R E124, microcrystalline cellulose, disodium EDTA, purified water. The stock solution was prepared with diluting 150 mL of Algofren® in deionized water to a volume of 1,000 mL under continuous magnetic stirring. IB was responsible for 7.7% of the total organic carbon in the solution. Titanium dioxide (TiO₂, Degussa P-25, 21 nm, 50 m²/g) was used as heterogeneous photocatalyst. Hydrogen peroxide solution (H₂O₂, 50% w/w, ρ = 1.11 g/mL) was used as oxidant. Iron(III) chloride (FeCl₃) was used to provide ferric ions in the solution. Only deionized water was used.

**Experimental procedure and analysis**

All experiments were conducted in a batch photoreactor (Heraeus Noblelight UV-RS-3) equipped with a low-pressure mercury lamp with 15 W power, which produced ultraviolet light of 253.4 nm. The lamp was immersed in the center of a glass cylindrical vessel of 1,000 mL maximum volume. The pharmaceutical solution with volume 800 mL was first introduced in the reactor under continuous magnetic stirring and then the oxidant and/or the catalyst was added. Time zero corresponded to the moment that the UV-lamp was switched on. A WTW-pH90 pH-meter was used to measure the solution pH. Samples were withdrawn from the reactor and sent for analysis at specific time intervals. Total organic carbon (TOC) in samples was quantified using SHIMADZU TOC-VCSH and Ibuprofen concentration was attended by means of HP GC 6890–MSD 5973 (HP5-MS column). Each experiment lasted 120 minutes unless otherwise stated.

TOC removal efficiency and IB conversion were calculated using the following formulas:

\[
\text{TOC removal efficiency} = \frac{[\text{TOC}]_0 - [\text{TOC}]_{120 \text{ min}}}{[\text{TOC}]_0} \times 100\% \quad (1)
\]

\[
\text{IB conversion} = \frac{[\text{IB}]_0 - [\text{IB}]_{120 \text{ min}}}{[\text{IBP}]_0} \times 100\% \quad (2)
\]

For clarity reasons, it is highlighted that wherever the term ‘IB solution’ is mentioned hereinafter, it refers to the aqueous solution of the medicinal product Algofren®, namely the active compound Ibuprofen together with its excipients in water.

Figure 1 | Ibuprofen molecule.
RESULTS AND DISCUSSION

UV photolysis

The direct photolysis of IB solutions under UV irradiation was initially studied in the absence of any oxidant or catalyst. The initial concentration of Ibuprofen was in the range 5–100 mg/L corresponding to 53–965 mg/L of carbon. It is obvious in Figure 2 that the removal efficiencies observed were low. Specifically, only for IB initial concentration 5 mg/L was the TOC removal observed of practical significance (27.6%).

For complex solutions, UV alone is usually not enough to achieve complete mineralization. Loaiza-Ambuludi et al. (2014) studied the UV-C degradation of 0.2 mM Ibuprofen in water (without excipients) and reported a higher TOC removal of 53% but only after 8 hours of irradiation.

UV/H₂O₂

The effect of the initial concentration of hydrogen peroxide in the range of 19.6–78.4 mmol/L was studied keeping the same initial TOC concentration of 178.3 ± 5.3 mg/L, which corresponded to 20 mg/L IB. It is clear from Figure 3 that the increase in H₂O₂ initial concentration was beneficial up to 39.2 mmol/L, leading to 81% TOC removal. For concentrations of hydrogen peroxide higher than this value, the process efficiency was not improved.

This trend can be attributed to the fact that excessive H₂O₂ may act as a hydroxyl radical scavenger to form perhydroxyl radicals, decreasing thus the OH concentration according to the following reaction:

\[ \text{H}_2\text{O}_2 + \text{HO}^* \rightarrow \text{HO}_2^- + \text{H}_2\text{O} \]  (3)

The effect of the initial TOC concentration was then studied using the same initial ratio of [H₂O₂] to [IB] (=66.6 mg/L H₂O₂/mg/L IB) that was shown to be the most beneficial in the previous set of experimental runs. It is clear in Figure 4 that both TOC removals and IB conversions were strongly affected by the initial carbon concentration, which can be attributed to the fact that more photons were available to species to react at low concentrations or to the different reaction pathways followed in each case (Philippopoulos & Poulopoulos 2005). This is also depicted in the reaction rate coefficients considering pseudo-first-order kinetics for IB conversion (Table 1).

UV/TiO₂

The photocatalytic mineralization of IB was also studied using titanium dioxide as photocatalyst at concentrations
The TOC removals achieved were too low to be of practical significance (Figure 5). The addition of hydrogen peroxide also did not lead to any synergistic effect as the same TOC removals were measured when using only H2O2.

Jiménez-Salcedo et al. (2019) studied the adsorption and photodegradation of IB (5 mg/L) in water by means of UV and TiO2 (2.7 g/L) and they reported that Ibuprofen was completely degraded in 10 min in acidic conditions; however, some by-products remained in the solution even after seven hours. Lin et al. (2019) also achieved almost complete degradation of Ibuprofen (5 mg/L) in water using TiO2 nanofibers under 2 h exposure to UV light. Again, the carbon removal observed was only 25%. It was shown that although Ibuprofen was effectively oxidized at fast rates, substantially longer time was required for the organic intermediates to be mineralized. The results of this study are in agreement with the above-mentioned works. The photocatalytic treatment of IB solutions using TiO2 under UV light is not capable of achieving high degrees of mineralization within two hours, especially when considerable amounts of additional carbon are present due to excipients.

UV/H2O2/Fe

Iron is well known to act as a homogeneous photocatalyst in UV/H2O2 systems by enhancing considerably the decomposition of hydrogen peroxide into hydroxyl radicals (Anipsitakis & Dionysiou 2007). When ferrous ions are used, the process is called photo-Fenton, while when ferric ions are added to the solution, the process is called photo-Fenton-‘like’. The effect of ferric ion addition in the range of 2.2–86 ppm on TOC removal was examined for IB solutions with initial TOC 178.3 mg/L and initial hydrogen peroxide 39.2 mmol/L. Experiments were extended to 150 min. The results obtained are shown in Figure 6. It is apparent that the concentration of iron had a significant effect on TOC removal only during the first 60 min, and particularly during the first 15 min of operation. After 150 min, the TOC values measured were practically the same. So, when 86 ppm of iron were used, 47% of TOC removal was achieved in only 15 min. In contrast, when no iron was added, the TOC achieved in 15 min was less than 8%. This observation becomes important if the operating cost of the UV lamp is considered. After 60 min of operation, all TOC removals gradually converged. In the case of iron concentrations higher than 5 ppm, further treatment for iron removal is required to meet the concentration limit of 5 mg/L for safe disposal (Lemley et al. 1999).

Considering the TOC removals achieved at 30 min and the concentration limit for iron disposal, the concentration of 8.6 ppm for Fe(III) was selected for the next experiments. Specifically, it was tested whether the results obtained could be extended to different initial IB and TOC concentrations keeping constant the initial ratios [H2O2]o/[IB]o (=66.6 mg/L H2O2/mg/L IB) and [H2O2]o/[Fe(III)]o (=154.9 mg/L H2O2/mg/L Fe(III)). The main differences among the TOC removals achieved were observed during the first 30 min. After that point, the TOC removal trend was similar for all initial concentrations used (Figure 7). The superior performance of photo-Fenton against the other treatment processes tested in terms of TOC removal is shown in Figure 8.
Another way to compare different technologies is through the electric energy per order, namely the energy required for 90% degradation of a pollutant per m$^3$ of contaminated water, $E_{EO}$ (kWh/m$^3$/order), which in the case of a batch reactor is given by (Bolton et al. 2001):

$$E_{EO} = \frac{P \cdot t \cdot 1000}{V \cdot 60 \cdot \log(C_o/C_f)}$$

(4)

where:
- $P$ = electrical power of the UV lamp, kW
- $t$ = irradiation time, min
- $V$ = the volume of the treated wastewater, L
- $C_o$ = the initial concentration of the pollutant, mg L$^{-1}$
- $C_f$ = the final concentration of the pollutant, mg L$^{-1}$

The electric energy per order was estimated using TOC values and for the UV/H$_2$O$_2$ and UV/H$_2$O$_2$/Fe experiments. The values obtained were in the range of 2.5–4.0 kWh/m$^3$/order and are shown in Table 2. These values are similar to the ones found in the literature for UVC/H$_2$O$_2$ systems.

Table 2 | The electric energy per order for UV/H$_2$O$_2$ and UV/H$_2$O$_2$/Fe treatment

<table>
<thead>
<tr>
<th>Fe(III) (ppm)</th>
<th>$E_{EO}$ (kWh/m$^3$/order)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4.0</td>
</tr>
<tr>
<td>2.2</td>
<td>3.8</td>
</tr>
<tr>
<td>8.6</td>
<td>2.9</td>
</tr>
<tr>
<td>17</td>
<td>3.4</td>
</tr>
<tr>
<td>86</td>
<td>2.5</td>
</tr>
</tbody>
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There is a great dependence of energy consumption on the process applied, while adding small amounts of iron decreased the environmental footprint (Foteinis et al. 2018).

CONCLUSIONS

The mineralization of Ibuprofen using its medicinal product with the commercial name Algofren® in aqueous solutions was studied by UV photolysis, UV/H$_2$O$_2$ photochemical treatment, heterogeneous photocatalysis and photo-Fenton. The main target was to select the most favorable conditions to treat such medicinal products (active substance together with excipients) taking into account the total organic carbon removal achieved, the limits for iron disposal and the electric energy per order for each option. The main conclusions are as follows:

(a) UV photolysis or heterogeneous photocatalysis with titanium dioxide did not lead to TOC removals of practical value.

(b) In UV/H$_2$O$_2$ treatment, the increase in hydrogen peroxide initial concentration was beneficial up to 39.2 mmol/L leading to 81% TOC removal. For higher concentrations, the TOC removals achieved were not increased.

(c) The concentration of iron during the photo-Fenton treatment affected considerably the TOC removals observed only during the first 60 min. At the end of the process, namely after 150 min, the TOC values measured were practically independent of initial iron concentration.

(d) The electric energy per order was estimated using TOC values in the case of UV/H$_2$O$_2$ and UV/H$_2$O$_2$/Fe treatment. The values obtained were in the range of 2.5–4.0 kWh/m$^3$/order.

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