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Photocatalytic treatment of metoprolol and propranolol

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ABSTRACT

The aim of this study was to investigate and compare the effect of an advanced oxidation process, the photocatalysis, on the removal of two emerging contaminants in water; the pharmaceuticals metoprolol tartrate salt (MET) and propranolol hydrochloride (PRO). The analyzed parameters were pharmaceutical removal, total organic carbon (TOC), specific UV absorbance (SUVA), chemical oxygen demand (COD), biochemical oxygen demand (BOD_5), toxicity and formed intermediates. Besides, the optimal photocatalyst concentration was determined. Afterwards, photocatalytic experiments were carried out with 0.4 g L^{-1} of TiO_2 as suspended catalyst and a Xenon lamp (Philips XOP 15-OF, 1000 W) as irradiation source. According to the results, after 240 min of irradiation, a removal near to 94% was obtained for both compounds. After 360 min of treatment, a mineralization degree in the vicinity of 55% was observed. Biodegradability index (BOD_5/COD) improved from values close to zero (raw solution) up to 0.4 and 0.6 for MET and PRO. The acute toxicity measured by the inhibition percentage of bioluminescence from *Vibro fischeri* indicates that the photocatalytic treatment of this kind of compounds promotes toxicity reduction. According to the experimental results, photocatalysis appears as a useful technique for the degradation of both β-blockers.

1. Introduction

Environmental problems represent an increasing concern in our society and the treatment of different pollutants receives more and more attention. In this way, the emerging pollutants imply a new challenge. Among them, pharmaceuticals are an increasing problem, because, nowadays, they appear at low concentrations in surface waters. However, their increasing consumption [1] due to the increase of the world population and its age means that they can appear at high concentrations in a few years, if measures are not taken. Drugs in waters come from hospitals, pharmaceutical industry or from domestic waters, by rejected drugs not used or by human excretions, because they are partially metabolized by the body and excreted [2].

Once in the sewage treatment plants, the complete removal of these pharmaceuticals cannot be assured by conventional water treatment methods because of the recalcitrant nature of many of these compounds. In addition, the amount of these compounds is continuously increasing and they can arrive to be ecotoxicological important [2], because of their biological activity, causing potential environmental impact. Ecotoxicological studies show that aquatic organisms are sensitive to these substances.

Metoprolol tartrate salt (MET) and propranolol hydrochloride (PRO) are two β-blockers which may be considered as emerging contaminants, which have not been deeply studied yet. Both are used for several diseases such as hypertension, angina pectoris, cardiovascular system and lately chronic heart failure [3–6]. Propranolol has the highest acute and chronic toxicity within the class of the β-blockers, followed by metoprolol [7–9]. These two β-blockers have been detected in surface waters [10–12] and, in addition, this kind of compounds appear in sewage treatment plants, and they cannot be totally eliminated [7,12–17]. Due to the potential environmental effects of the target compounds, alternative treatments should be tested. Advanced oxidation processes (AOPs) appear as a good alternative. Some references report the treatment of these drugs by different oxidation processes. Metoprolol can be degraded by UV/H_2O_2 [18,19], photo-Fenton [5,18], ozonation [20], UV/O_3, O_3/H_2O_2 [19] and photocatalysis [5,6]. On the other hand, the AOPs used to treat propranolol which have been studied are: ozonation [21,22], photodegradation [23,24], UV/H_2O_2 [22,25], UV/O_3 [25], O_3/H_2O_2 [25], photocatalysis [6,22].

Previous reports, which have studied the effect of photocatalysis on metoprolol and propranolol, provided data of degradation, kinetics, effect of the pH, intermediates and degradation pathways [6]. Besides, toxicity tests (*Synechococcus leopoliensis* and *Brachyonus calyciflorus*) have also been studied [22]. Although previous works attempted to investigate the degradation of MET and PRO by photocatalysis, this work contributes with experiments carried

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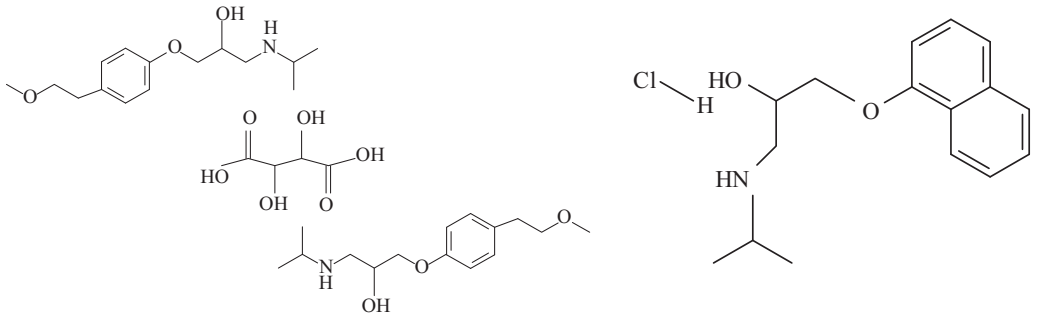


a MET molecular structure b PRO molecular structure

Fig. 1. β-Blockers molecular structures.

out with simulated solar light (Xe lamp) as well as investigates the biodegradability, organic matter oxidation and acute ecotoxicity (*Vibro fischeri*) of the formed intermediates along the reaction time.

The aim of this work is to test the possibilities of a photocatalytic treatment of MET and PRO by using TiO_2 in suspension as catalyst for their removal. In addition, the effect of the TiO_2 loading, the evolution of some lumped parameters as TOC, COD, BOD, SUVA and the toxicity will give important information about the degradation of the main pollutants and their reaction.

2. Materials and methods

2.1. Chemicals

Aqueous pharmaceutical solutions were prepared in Milli Q water with MET [56392–17–7] and PRO [318–98–9], which were purchased from Sigma–Aldrich Chemical Co. (Spain). Synthetic amorphous titanium dioxide (Degussa P-25, Spain) was used as received. Fig. 1 shows the structure of the target pharmaceuticals, in order to facilitate the understanding of the reaction between •OH radicals and the pharmaceuticals.

2.2. Analytical procedures

The target compounds concentrations were monitored by a high-performance liquid chromatograph (HPLC) from Waters using a *SEA18* 5 μm 15 × 0.46 Teknokroma column, and a Waters 996 photodiode array detector using the Empower Pro software 2002 Water Co. The mobile phases were composed by water and acetonitrile (MET 20:80 and PRO 50:50), injected with a flow-rate of 0.85 and 0.80 mL min^{-1} and detected at maximum UV absorbance set at wavelengths of 221.9 and 213.7 for MET and PRO, respectively. In order to remove the catalyst, before the HPLC analysis, samples were filtered with a polyethersulfone membrane filter of 0.45 μm.

Total organic carbon (TOC) was measured in a Shimadzu TOC-V CNS instrument. Spectrophotometric measurements to obtain MET and PRO absorption spectrum were carried out in a PerkinElmer UV/vis Lambda 20 (220–700 nm range) spectrophotometer. Biochemical oxygen demand (BOD_5) determinations were carried out according to the Standard Methods (5120) by the OxiTop® procedure. To analyze the chemical oxygen demand (COD), the Standard Methods (5220D) procedures were followed. The specific UV absorbance ($SUVA_{254\,nm}$) values were calculated dividing the $UV_{254\,nm}$ absorbances by COD ($SUVA = (UV_{254}/COD) \times 100$). pH was measured by a Crison GLP 22 instrument. The ecotoxicity of the samples were measured by the acute toxicity using Microtox tests, where the inhibition of *Vibrio fischeri* bioluminescence at 15 min of incubation was determined. For the intermediates identification, samples were analyzed by the electrospray ionization/mass spectrometry using an electrospray (ion spray) ESI-MS, and a LC-MSD-TOF (2006) mass spectrometer [26,27].

2.3. Photoreactor

A stirred reservoir tank (1.0 L) was filled with the pharmaceutical-TiO_2 (suspended) aqueous solution. The aqueous suspension was continuously pumped (peristaltic pump Ecoline VC-280 II, Ismatec) into the Solarbox (Co.fo.me.gra 220 V 50 Hz) and recirculated to the reservoir tank with a flow of 0.65 L min^{-1}. In the Solarbox, the Duran tubular photoreactor (0.078 L) was irradiated by a Xe-OP lamp (Phillips 1 kW) with a photon flux equal to 3.34×10^{-5} Einstein s^{-1} (290–400 nm), determined by uranyl oxalate actinometry [28]. In order to keep the solution at 25 °C, the jacket temperature of the stirred tank was controlled with an ultra-thermostat bath (Haake K10). All connections and pipes employed were made of Teflon and/or glass material to avoid losses by adsorption.

3. Results and discussion

As shown in Fig. 1, pharmaceutical solutions were not prepared with the pure compound. The salt present in the MET commercial form has influence on analytical measurements, and this fact has to be taken into account in the assessment of MET photocatalytic degradation.

As a first step, blank experiments were carried out to verify the influence of secondary source of errors in the results. Blank experiments of photolysis, adsorption and stripping were performed, accomplishing a maximum error of 4.7% for MET, and 9.0% for PRO.

Reproducibility experiments were carried out as well, obtaining a standard deviation average of 0.33 on the pharmaceutical removal for MET, and 2.24 for PRO.

3.1. MET and PRO removal

The initial pharmaceutical concentration solution chosen was 50 mg L^{-1}. Experiments with pharmaceuticals concentration close to the range detected in real water samples were not possible due to analytical limitations. Before carrying out the assessment of the pharmaceuticals removal, the determination of the best catalyst concentration for our system was attempted.

3.1.1. Influence of TiO_2 concentration

A scanning of TiO_2-catalyst concentration was performed for both compounds. Fig. 2 shows the pharmaceuticals removal after

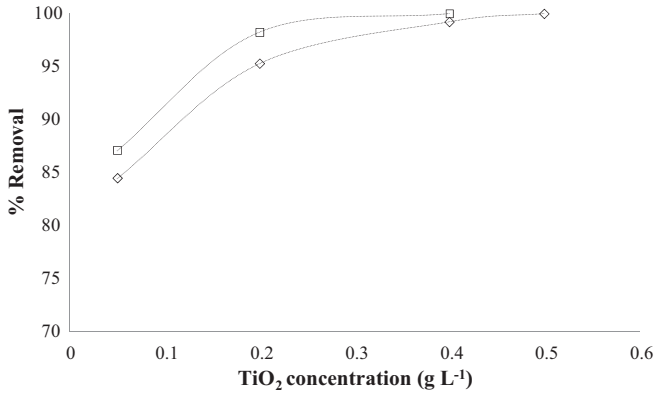


Fig. 2. MET and PRO scan TiO_2-catalyst concentration at 6 h of experiment. ◊: PRO; □: MET.

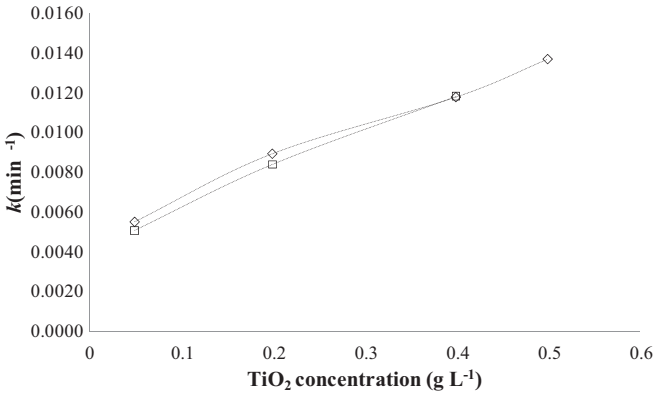


Fig. 4. MET and PRO kinetic constants (300 min). □: MET; ◊: PRO.

360 min of treatment vs. TiO_2 concentration. The experiment lasted about 360 min to ensure the total pharmaceutical removal from the solution. TiO_2 ranged from 0.05 and 0.5 g L^{-1}, which were chosen as the most used concentrations find on the literature surveillance. For both compounds, the final removal increased when the catalyst concentration also increased. Although the highest catalyst concentration (0.5 g L^{-1}) achieved the best result, the concentration of 0.4 g L^{-1} appeared to be the best condition investigated, because catalyst deposition in the reactor can appear when working at higher concentrations.

3.1.2. Compounds removal and kinetics

Working with 0.4 g TiO_2 L^{-1}, the two compounds removal was followed during the photocatalytic process (Fig. 3). The treatment was able to completely remove MET and PRO after 300 and 360 min of irradiation, respectively.

In order to quantify the β-blockers removal rate, the pseudo-first order kinetic constant (k) was calculated for each TiO_2 concentration (see Fig. 4). k values could be obtained from the regression curves slopes representing $-\ln(C/Co)$ vs. time, within the period of 300 min, for each TiO_2 concentration. Constant values for 0.4 g TiO_2 L^{-1} obtained were $0.0113 \pm 5 \times 10^{-4}$ min^{-1} for MET and $0.0118 \pm 3 \times 10^{-4}$ min^{-1} for PRO. Thus, it can be assumed that the studied compounds have similar degradation behavior when treated by photocatalysis. The pH of the treated samples decreased slowly during the reaction time, standing at acidic condition during all the reaction. Although the main structural difference between the studied compounds is in the aromatic rings, the results indicate that their removal rates are similar. On the other hand, the organic salt present in MET commercial formulation should be taken into account since it would compete with MET molecules for the reaction with •OH radicals.

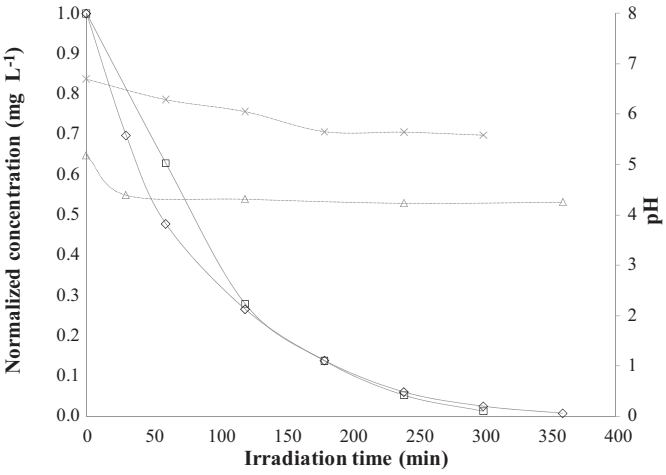


Fig. 3. MET and PRO photocatalysis removal, using 0.4 g TiO_2 L^{-1}. □: MET; ◊: PRO; x: pH_{MET}; △: pH_{PRO}.

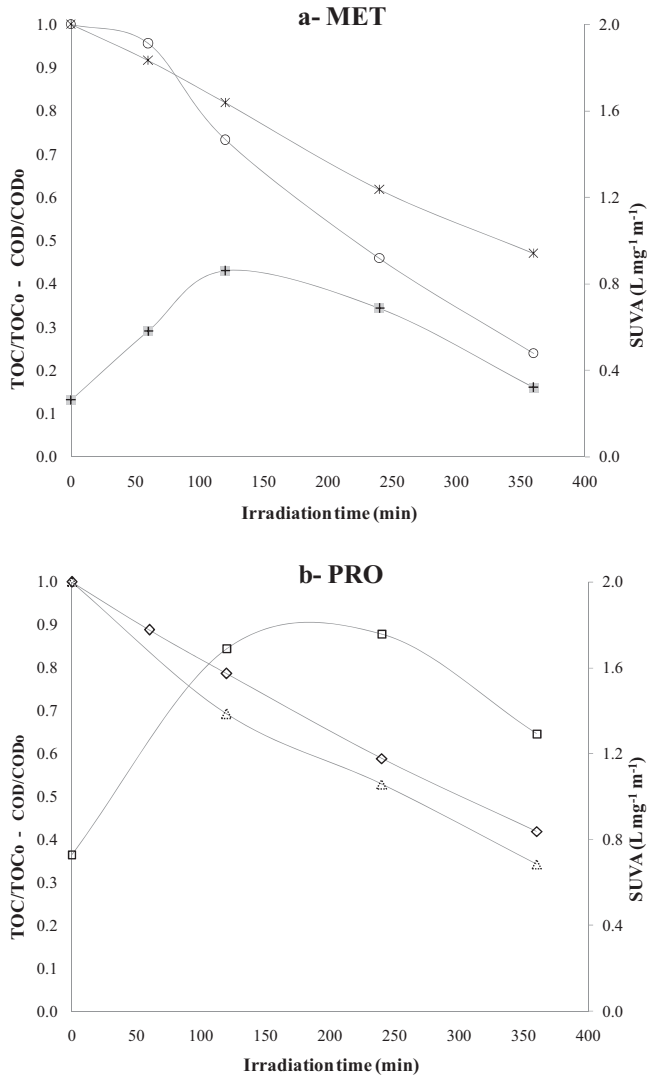
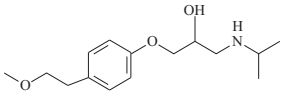
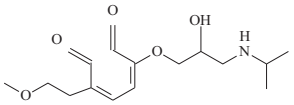
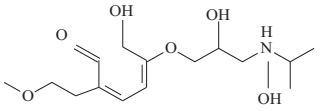
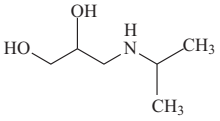
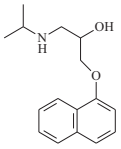
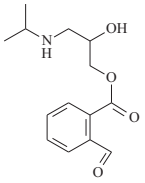
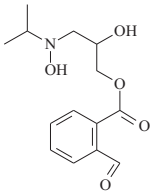
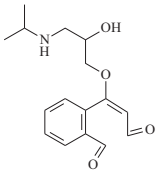
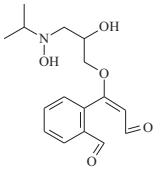


Fig. 5. TOC/TOCo, COD/CODo and SUVA for MET and PRO photocatalysis, using 0.4 g TiO_2 L^{-1}. *: $TOC/TOCo_{MET}$; o: $COD/CODo_{MET}$; +: $SUVA_{MET}$; ◊: $TOC/TOCo_{PRO}$; △: $COD/CODo_{PRO}$; □: $SUVA_{PRO}$.

Table 1
Intermediates proposed structures for the photocatalytic degradation of MET and PRO.

Compound	*m*/*z* (+)	Molecular formula	Proposed Structure
Metoprolol	268	C15H25NO3	
A	300	C15H25NO5	
B	318	C15H27NO6	
C	134	C6H15NO2	
Propranolol	260	C16H21NO2	
A′	266	C14H19NO4	
B′	282	C14H19NO5	
C′	292	C16H21NO4	
D′	308	C16H21NO5	

3.2. Intermediates oxidation and identification

3.2.1. Mineralization, oxidation and aromaticity

Fig. 5 represents the normalized TOC and COD concentration during the photocatalytic process. The mineralization and oxidation profile, represented as the TOC and COD removal, decreased significantly during the irradiation time, achieving values near to 55% after 360 min. It is remarkable that TOC and COD removal reached high values, indicating that the oxidation of intermediates promoted a continuous cleavage of the initial organic structures. Aromaticity, represented by SUVA, which is a measure that indicates the DOC aromatic content, was determined. SUVA is calculated by measuring the DOC and the UV absorbance at 254 nm of a 0.45 μm filtered water sample. Unexpectedly, a global increase of aromaticity appeared. While scanning it during the experiment, it could be seen how it increased in the first hours (Fig. 5). Finally, there is a decrease of it at six hours of irradiation, where the value goes down, but still being higher than the initial one.

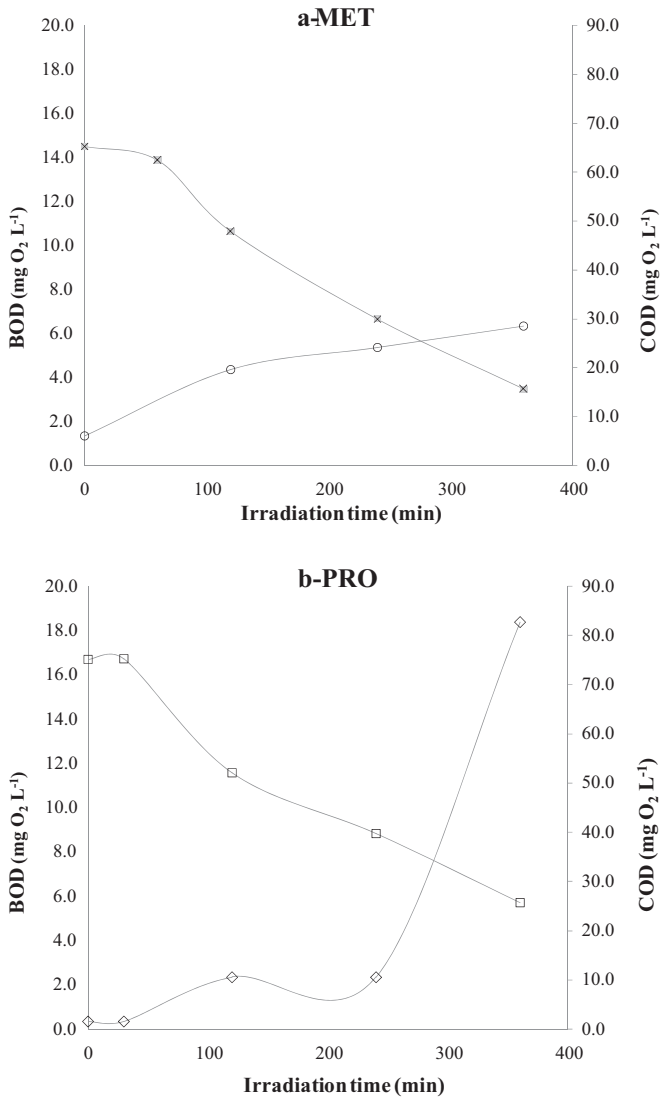


Fig. 6. BOD and COD for MET and PRO photocatalysis, using 0.4 g TiO_2 L^{-1}. o: BOD_{MET}; x: COD_{MET}; ◊: BOD_{PRO}; □: COD_{PRO}.

3.2.2. Intermediates identification

Intermediates identification was carried out in samples collected in the range of 180-360 min of treatment, where intermediates' chromatographic picks had high intensity. Several ions masses were identified during the β-blockers photocatalytic degradation. The *m*/*z* (mass-to-charge ratio) is shown in Table 1.

According to the proposed structures, the oxidation of PRO takes place mainly by the cleavage of the naphthalene ring. However, before this step of oxidation, the continuous hydroxylation of the aromatic ring should occur. Although, the intermediate B′ and D′ would be formed due to an additional •OH attack on the amino group, this pathway of oxidation is not favored in the experimental conditions used. The intermediate D′ was already found in a great extent by the ozonation of PRO at pH 8, where the presence of •OH radical is noticeable [21]. As the pKa of PRO is about 9.42 [23], the reactivity of the amino group is very weak. The step of oxidation on the amino group could be considered as a secondary reaction pathway, occurring only when the oxidized naphthalene ring became less reactive. Concerning the MET oxidation, a similar degradation pathway is proposed. Hydroxyl radical supposed to attack the aromatic ring in first place. Afterwards an additional hydroxylation would happen. As already commented, some intermediates would come from the •OH attack on the amino group as a secondary reaction center, which was the case of the proposed intermediate B. Intermediate C, would be in a more advanced oxidation state, when the aromatic ring is completely oxidized. The formation of intermediate C is in agreement with a degradation pathway proposed in a previous work [6].

3.3. Biodegradability and toxicity assessment

In order to evaluate the suitability of the photocatalytic treatment in waters containing β-blockers, the biodegradability and toxicity tests were performed along the reaction time. For both compounds, the biodegradability (BOD_5/COD) of the un-treated solution was near zero, indicating that the target compounds solutions are not biodegradable. Nevertheless, the continuous compounds oxidation promoted by the reaction with hydroxyl radicals favored the formation of more biodegradable compounds.

Fig. 6 performances BOD and the COD for both compounds during the treatment, showing an increase on the BOD while the COD decreases during the irradiation time.

With the aim of illustrating the biodegradability profile of the formed intermediates during the photocatalytic process, Fig. 7

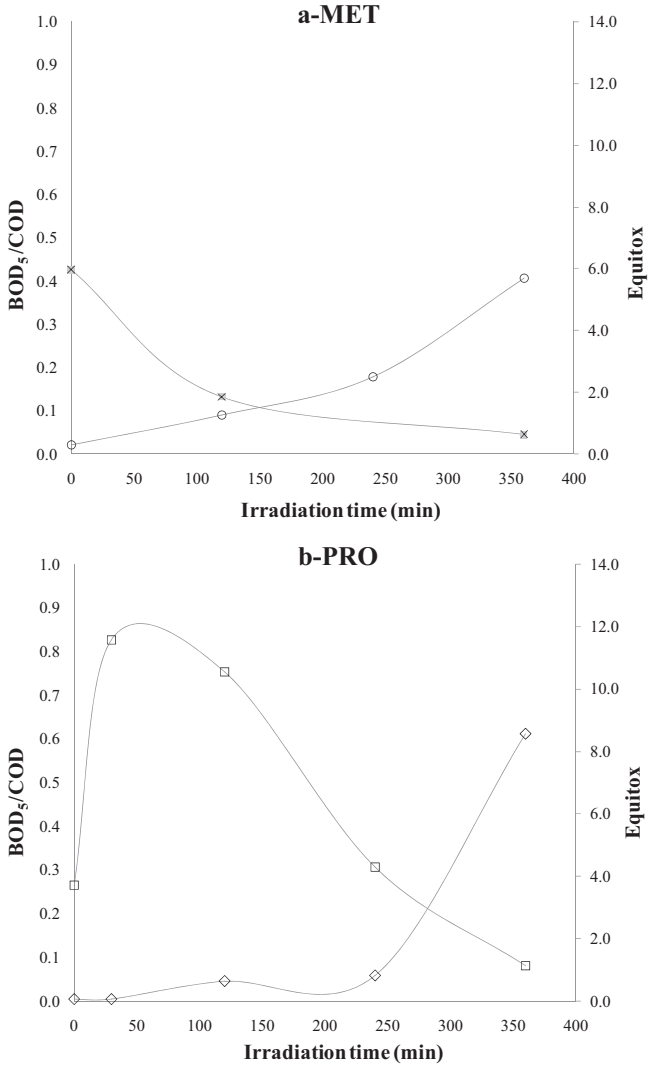


Fig. 7. BOD_5/COD and equitox for MET and PRO photocatalysis, using 0.4 g TiO_2 L^{-1}. o: BOD_5/COD_{MET}; x: $Equitox_{MET}$ ◊: BOD_5/COD_{PRO}; □: $Equitox_{PRO}$.

depicts the biodegradability indicator value (BOD_5/COD) during the reaction time. MET oxidation leaded to a gradual formation of more biodegradable compounds since the first minutes of reaction, achieving at the end of irradiation time a biodegradability indicator value higher than 0.4. In the case of PRO, the biodegradability improvement was not observed until 250 min of treatment. At the end of the experiment (360 min), the formation of high biodegradability products was observed. Therefore, treatment time is an important factor to improve the biodegradability of the effluent in waters polluted with PRO. To complement the information about the hazardousness of a treated effluent to the environment, the toxicity assessment was also carried out. The toxicity of the treated samples presented different trends. Fig. 7a shows that the oxidation of MET promoted the overall toxicity reduction of the sample since the beginning of the treatment. On the other hand, PRO photocatalytic treatment (Fig. 7b) induced a first step of oxidation where the formed intermediates are more toxic than the primary compound. Then, after 30 min of irradiation, the toxicity decreases constantly, achieving a lower toxicity value after 360 min. Consequently, this behavior confirms the importance of the reaction time in the case of the treatment of waters containing PRO. The overall toxicity reduction caused by the oxidation of the target compounds shown in this work is in agreement with previous investigation carried out with other toxicity methods [22].

4. Conclusions

- At the used experimental conditions, photocatalytic treatment was proved to be an effective method to achieve mineralization degrees in the vicinity of 55% for waters containing β-blockers MET and PRO.
- The tested compounds presented similar removal rate by photocatalysis. After 360 min of treatment, with 0.4 g L^{-1} of catalyst, both compounds were totally removed.
- The oxidation of MET and PRO is accomplished mainly due to the •OH attack on the aromatic rings with the posterior cleavage of the naphthalene group in the case of PRO and formation of aliphatic compounds after MET oxidation.
- Biodegradability of the samples increased with time. However, in the case of PRO, biodegradability starts to increase only after 4 h of treatment, implying that the irradiation time is an important factor.
- 360 min of irradiation promoted the decrease of the overall toxicity of the samples. Nevertheless, a toxicity peak is observed in the first minutes of reaction of the PRO solution.

Acknowledgements

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