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Direct UV photolysis of propranolol and metronidazole in aqueous solution

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ABSTRACT

The aim of this work was to study the direct photolysis of two pharmaceuticals: propranolol (PRO) and metronidazole (MET) promoted by ultra violet radiation (UV). For this purpose, 50 and 100 mg L^{-1} aqueous solutions of PRO and MET were irradiated by two different UV sources: a UV-254 germicidal lamp (UV-C) and a UV-365 black light lamp (UV-A). After 8 h of irradiation, direct UV photolysis promoted substantial pharmaceuticals removal, especially with the use of UV-C radiation (near 50%). However, on average only 12% of the organic matter content was photodegraded. The photo-transformation of both compounds promoted the formation of more biodegradable byproducts. Nevertheless, PRO direct UV-C photolysis produced byproducts with less toxic character while MET irradiation promoted a slight increase of toxicity. Direct photolysis of PRO using solar radiation was proved to be as effective as those runs carried out with the UV-C device. Kinetic constants based on time and UV-C fluency were in a magnitude order of 10^{-2} h^{-1} and 10^{-5} cm^2 mJ^{-1}, respectively.

1. Introduction

In the last decades, the presence of emerging contaminants in different types of water appeared as a new environmental threat which needs to be faced by several governments around the word [1,2]. Among the emerging contaminants found in waters, the class of pharmaceuticals has been detected in surface water and sewage wastewater treatment plants (SWTP) effluents [3–5].

Generally, pharmaceuticals reach waterways through the discharge of wastewaters and effluents on environment, which often are not properly treated. On the other hand, it was proved that when pharmaceuticals reach SWTP, they are not completely removed [6]. This circumstance leads to the development of new water treatment technologies, which should be properly tested in order to face this new type of contamination [7].

Propranolol (hydrochloride, 1-(isopropylamino)-3-(1-napthyloxy)-2-propanol hydrochloride), is a β-adrenergic antagonist that is widely used for the treatment of angina pectoris, arrhythmia, and hypertension [8]. It may be both a photosensitizing agent and light-unstable, similar to other drugs that have chromophoric structures containing a naphthalene skeleton [9]. Metronidazole (2-(2-methyl-5-nitro-1H-imidazol-1-yl)ethanol), is an antibiotic used in the treatment of infections caused by a wide range of anaerobic bacteria, protozoa and bacteroides, including trichomoniasis, amoebiasis, vaginosis and gingivitis [10,11]. Besides, MET manifests its activity against both anaerobic Gram-negative and anaerobic spore-forming Gram-positive bacilli [12]. PRO and MET concentration in the range of ng L^{-1} has been found in surface waters and SWTP [13–16].

Nowadays, water treatment by means of ultraviolet irradiation is an established method for drinking-water disinfection [17] and has received recognition as a promising method for wastewater purification in the last years [18,19]. It is important to remark that even when UV is combined with other oxidants, such as ozone or hydrogen peroxide, the photolysis pathways play an important role on the final organic compound removal. Even when UV radiation is used for water treatment (e.g. for water disinfection), UV can degrade organic compounds by direct photolysis of photolabile compounds as a consequence of light adsorption. Moreover, in photocatalytic studies is very important to know the extension of the photolysis in the process in order to control this interference and evaluate the efficacy of the catalyst.

Pharmaceuticals can undergo abiotic transformations in surface waters via hydrolysis and photolysis. As the majority of pharmaceuticals designed for oral intake are resistant to hydrolysis, the photolysis appears as the primary pathway for their abiotic transformation in surface waters [20]. Hence, the investigation of the level of photo-transformation achieved by artificial UV and solar light would help to understand their effects on environment.

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The aim of this work was to study the direct photolysis of 50 and 100 mg L^{-1} of PRO and MET aqueous solutions by means of UV-C and UV-A radiation. Complementary runs with the use of solar light were also carried out. COD, UV_{254} absorbance and pharmaceuticals concentration analysis were carried out in order to monitor the degradation of pharmaceuticals along the irradiation time. BOD_5/COD was used as biodegradability indicator and the toxicity of formed intermediates was monitored along the runs. Time and fluency based kinetic constants for PRO and MET direct UV-C photolysis were also calculated.

2. Materials and methods

Metronidazole and propranolol, both with 99% of purity were obtained from the "Laboratório Farmacêutico do Estado de Pernambuco" (Pharmaceutical Laboratory of the State of Pernambuco) LAFEPE (Recife, Brazil). The solutions were prepared with deionized water.

Direct photolysis experiments were carried out in Petri dishes with surface area of 63.6 cm^2 placed into UV lamps devices. The UV devices were equipped with three UV lamps placed on the reactors lid. Each reactor was provided of three lamps and had the capacity to irradiate four Petri dishes. Thus, in order to ensure reproducibility direct photolysis runs were performed in duplicate. Petri dishes were filled with 150 mL of 50 or 100 mg L^{-1} MET or PRO solution and then irradiated for a period that varied between 30 min and 24 h. After the irradiation time, samples were withdrawn from the Petri dishes and quickly analyzed.

The UV lamps used in this work were a UV-254 mercury lamp (UV-C, Ecolume, 30W) and a UV-365 black light mercury lamp (UV-A, Higuchi, F20T10 20W). The measurement of the UV-C and UV-A incident intensity was performed, respectively, by a MRUR-203 and MRU-201 UV light meters, both from Instrutherm Ltda (São Paulo, Brazil).

PRO and MET concentration was quantified by an Aquamate V4.60 UV spectrophotometer (Thermo Scientific, USA) using for the quantification the wavelengths of 289.5 and 318.5 nm, respectively. To monitor the samples biodegradability during irradiation, the biological oxygen demand (BOD_5) (Standard method, 5210 B) was measured. The organic matter content was measured by the chemical oxygen demand (COD) (Standard method, 5220 B).

The toxicity test was carried out using the *Allium* test [21], which is based on the inhibition of the *Allium* root growing caused by toxic substances. According to the standard procedure, the toxicity can be indirectly determined by the comparison between the root growing exposed to the sample for a period of 72 h and those not exposed. Therefore, the effect can be quantified by the percentage of root growing inhibition caused by the root contact with different logarithmic serial dilutions of the sample (100, 10, 1, 0.1 and 0.01 mg L^{-1}). Once the percentage of inhibition is calculated, a graphic that relates the sample concentration in function of the percentage of inhibition is plotted and thus the inhibitory concentration (IC_{50}) can be easily calculated. The IC_{50} is the half maximal inhibitory concentration that express the effectiveness of a compound in inhibiting biological or biochemical function, which in this case is the root growing.

3. Results and discussion

3.1. Removal of PRO and MET by direct UV photolysis

In order to assist the assessment of the pharmaceuticals direct UV photolysis and as well to avoid unnecessary experimental work, the comparison of the absorbance spectra of the target compounds with the emission spectra of the UV lamps was performed. This strategy assists the understanding of the behavior of a compound in front of the lamp radiation [22]. In Fig. 1, the emission spectra of the two used UV lamps were plotted along with the absorption spectra of PRO and MET.

A preliminary analysis of Fig. 1 reveals that the target compounds should undergo direct UV photolysis mainly with the use of the UV-C lamp. Besides, Fig. 1(b) indicates that MET should have better UV absorption than PRO on the wavelength range near 254 nm, hence having a better photolysis rate with the employment

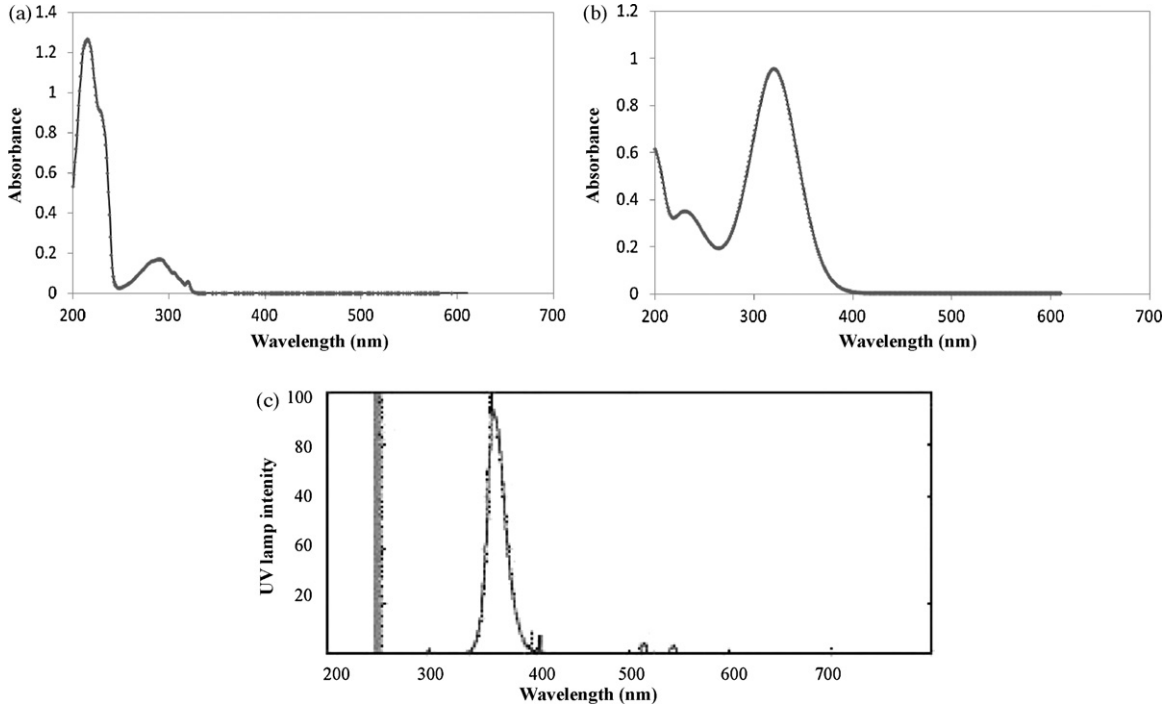

Fig. 1. Comparison between UV lamps emission spectra and compounds absorption spectra. (a) absorption spectrum of PRO; (b) absorption spectrum of MET; (c) emission spectra of UV-C (main peak in 254 nm) and UV-A (main peak in 365 nm) lamps.

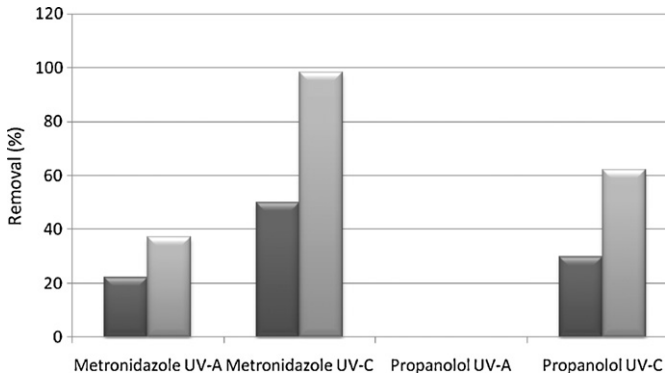

Fig. 2. MET and PRO removal after 8 (dark bars) and 24 h (light bars) of UV irradiation. Initial concentration = 100 mg L^{-1}; pH without adjustment.

of UV-C radiation. Regarding the black light lamp irradiation, Fig. 1 shows that its main peak (365 nm) coincides only with the MET absorption spectrum. Comparing Fig. 1(a) and (c), it can be seen that the UV-A peak does not coincide with the PRO absorption spectra. Therefore, no PRO photo-transformation by irradiation with the UV-A device was expected.

In order to ensure that volatilization of pharmaceuticals did not take place during experimentation, the pharmaceutical solutions were left 8 and 24 h at 60 °C. The pharmaceuticals concentration measurement after the cited time revealed that the target compounds did not undergo volatilization during the runs.

The photodegradation of 100 mg L^{-1} solutions of MET and PRO is presented in Fig. 2. The graphic illustrates MET and PRO removals achieved by UV-A and UV-C irradiation. Measurements of pharmaceuticals concentration after 8 and 24 h of irradiation show a high difference between the removal levels reached by the two tested UV sources. According to the results, after 8 h of irradiation, a MET removal near 50% could be achieved by UV-C irradiation, while runs performed with UV-A lamp were able to achieve a removal near 23%. Concerning the PRO removal, UV-C irradiation reached almost 30% of degradation, while, as expected, runs carried out with the UV-A device did not promote any photo-transformation of PRO structure. Although the difference on the degradation rate can be attributed to the better UV absorption of pharmaceuticals structure in the wavelength near 254 nm (peak emitted by the UV-C lamp), the difference on the lamps power (light intensity) can also contribute to the variation on the degradation level. In this study, the UV-C device is on average 50% more powerful than the UV-A device (UV-C = 90 W; UV-A = 60 W).

Once it was observed that 8 h of irradiation was not able to reach the total removal of the target compounds, the irradiation time was extended to 24 h (Fig. 2). It was observed that 24 h of UV-C irradiation was able to achieve almost the total MET removal and more than 60% of PRO removal.

Comparing the pharmaceuticals photolysis rate, it can be observed that MET showed to be more susceptible to direct UV-C photolysis than PRO as it can be seen in Fig. 2. In the case of runs carried out with the UV-A device, the results cannot be compared due to the absence of PRO UV-A photolysis. However, UV-A irradiation could achieve MET removals near 22 and 37% after 8 and 24 h, respectively.

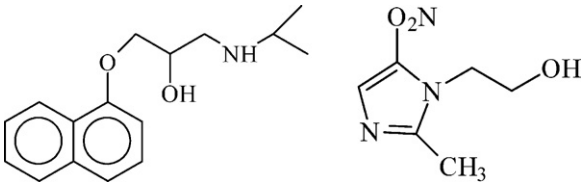

Fig. 3. Molecular structures of propranolol (a) pKa = 9.14 [29] and metronidazole (b) pKa = 2.55 [28].

The next part of this section deals with PRO and MET mineralization induced by UV radiation. Table 1 presents the mineralization degree achieved by the photolysis of 100 mg L^{-1} MET and PRO solutions after 8 h of irradiation. COD measurements demonstrate that both UV sources were able to produce MET mineralization at the used experimental conditions. Besides, PRO undergoes mineralization under UV-C irradiation. Both compounds showed similar mineralization profile, obtaining on average a mineralization degree in the vicinity of 13% with the use of UV-C or UV-A device. Nevertheless, a slight increase of MET mineralization with the use of UV-C radiation was observed. This trend coincides with the pharmaceuticals removal profile previously presented.

3.2. Direct UV photolysis on MET and PRO structures

It is well known that compounds presenting in their structures chromophore structures such as unsaturated bonds and aromatic rings have the capacity of selective light absorption. In Fig. 3, the molecular structure of MET and PRO is presented along with their pKa. Observing the pharmaceuticals structure, it can be suggested that at the wavelength range used in this work, the rings and functional groups seem to be the sites where the UV light absorption can be expected in higher intensity. Although it is known that often the pH of real water samples is a near neutral pH, the addition of buffer solution was avoided in order to prevent its interference on the photolysis mechanism [23]. Thus, the pH of the solutions was not adjusted before irradiation, standing around 3.9 and 5.5 for PRO and MET solutions, respectively. Hence, according to the pKa of the target compounds, PRO undergo photolysis on its protonated state while MET was dissociated, which could increase reactivity.

With the aim of monitoring qualitatively the content of aromatic intermediates along the irradiation time, the UV_{254} absorbance, which can be used as indicator of the aromatic content present in waters [24] was measured. In Table 1, the UV_{254} absorbance removal and the nitrate content are presented. The UV_{254} absorbance decrease after 8 h of irradiation indicates that MET direct UV photolysis reduces the quantity of aromatic intermediates in the medium, indicating the cleavage of the ring (Fig. 3b). In addition, the nitrate measurement reveals that after the cleavage of the ring, the photolysis continues and promotes the nitrate releasing in the medium. Thus, it may be suggested that the first photodegradation step of MET is accomplished with the cleavage of the ring. Afterwards, the functional groups containing nitrogen seem to be the secondary absorption centers.

Table 1
COD, decrease in UV_{254} absorbance and nitrate release promoted by 8 h of UV irradiation. Initial concentration = 100 mg L^{-1}; pH without adjustment.

Compound	UV source	COD removal (%)	UV_{254} removal (%)	NO_3^- (mg L^{-1})
Metronidazole	UV-A	13.2	3.78	5.91
	UV-C	14.3	17.55	6.19
Propranolol	UV-A	–	–	–
	UV-C	11.6	0	0.57

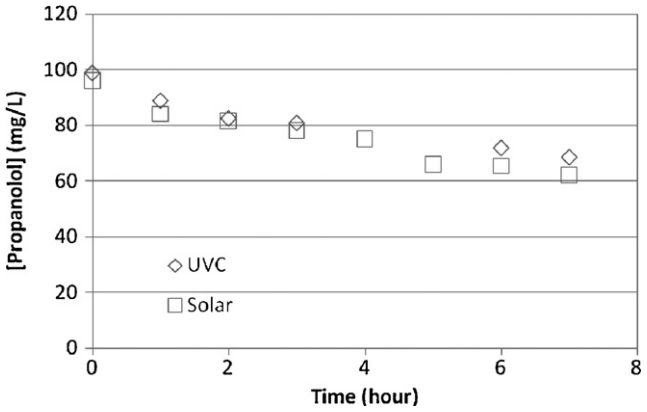

Fig. 4. Direct photolysis of 100 mg L^{-1} of PRO solution by artificial UV-C and solar radiation.

Regarding the PRO direct UV-C photolysis, the UV_{254} absorbance removal equal to zero (Table 1) indicates that 8 h of UV irradiation was not able to promote the naphthalene ring cleavage. Besides, the small nitrate release detected in the irradiated solution should come from the UV photolysis of the amino group, which in this structure seems to be the priority reaction center (Fig. 3a).

3.3. Direct photolysis by solar radiation

Solar radiation is widely used on photocatalytic devices as well as promotes natural photolysis of photolabile organic compounds presents mainly in surface waters. Thus, in order to assess the sunlight capability to promote the direct photolysis of the target compounds, direct photolysis experiments with the use of solar radiation were carried out. Sunlight experiments were performed during autumn in Recife-Brazil (8°S–34°W), where the average of the global solar radiation is about 17 MJ m^{-2} [25]. Then, 100 mg L^{-1} of PRO solution was irradiated with sunlight during 7 h and then PRO concentration was measured along the irradiation time. Fig. 4 presents the PRO photodegradation profile along the time. In this graphic, the sunlight result is compared with a run performed at the UV-C device. According to Fig. 4, direct solar photolysis was proved to be relatively effective to promote PRO photo-transformation, showing to be as effective as the UV-C device used in this work. It should be remarked that as PRO structure is not able to absorb light at wavelength higher that 330 nm as presented in Fig. 1(a), it could be stated that PRO solar direct photolysis is promoted mainly by the UV-BC radiation and not by the visible light. Therefore, the results suggest that the PRO photo-transformation caused by solar light in surface waters cannot be ignored.

3.4. Biodegradability and toxicity of direct photolysis byproducts

This section attempts to carry out the assessment of the formed intermediates biodegradability and toxicity in the course of direct UV photolysis experiments. This information is important due to during some water treatment methods (based on pollutants oxidation) more toxic intermediates may be formed, which can have potential toxicity to environment [26,27]. Therefore, to measure the biodegradability of formed intermediates, BOD_5 and COD values were measured before and after UV irradiation and the rate BOD_5/COD was used as biodegradability indicator. The analysis carried out at the end of the irradiation time showed that after 8 h of treatment, biodegradability increased, in some cases, more than four times, thus indicating a good conversion of the pharmaceuticals to more biodegradable products. Table 2 presents the biodegradability values before and after 8 h of irradiation.

To verify the toxicity evolution of the irradiated samples, a toxicity method based on the inhibition of the *Allium* roots growing was used. To perform the analysis, onions roots were placed in contact with different dilution of raw and irradiated pharmaceutical solutions and afterwards the inhibition of the growing root was measured by measurement of the root length after contact. With the recorded data the IC_{50} was calculated (inhibition concentration) that represents the concentration which promotes the inhibition of 50% of onions root growing. It is important to remark that the IC_{50} increasing is inversely proportional to toxicity augment. Because of experimental problems, the toxicity test was carried out only for runs performed with the UV-C device. With this toxicity method it was not possible to obtain a suitable curve (MET concentration vs. inhibition percentage) for runs carried out with the UV-A device. Toxicity results are presented in Table 2. The toxicity profile showed that direct UV-C photolysis of MET promoted a small decrease on the IC_{50} absolute value, indicating an increase of toxicity for *Allium* roots growing. On the other hand, PRO direct UV-C photolysis promoted the reduction of more than 50% of initial toxicity. In the case of MET UV-C irradiation, it is possible that the increase of irradiation time can promote the degradation of these more toxic byproducts and reduce the toxicity.

3.5. Kinetics

The last part of this work deals with the kinetic constants calculation for the direct photolysis of PRO and MET promoted by UV-C irradiation. To calculate the kinetic constants, 50 mg L^{-1} solution was irradiated for a period of 12 h and the pharmaceuticals concentration was monitored along the irradiation time. The incident irradiance was also recorded and used to calculate the fluency based kinetic constant. Thus, the time and fluency based kinetic constants were calculated. The lamps presented irradiance equal to 476 and 1920 μW cm^{-2} for the UV-A and UV-C devices, respectively. In order to carry out the kinetic constants calculation, a graphic ln([pharmaceutical/pharmaceutical$_0$]) versus UV incident irradiance or time was built. Therefore, the graphic gave a straight line passing through the origin and which slope gave the fluency or time based rate constant. The results are summarized in Table 3. Although during literature survey no calculated kinetic constant under the same experimental conditions was found for the PRO direct UV photolysis, the kinetic constants presented in this work for MET photolysis are in the same order of magnitude

Table 2
Biodegradability and toxicity evolution achieved by 8 h of UV irradiation. Initial concentration = 100 mg L^{-1}; pH without adjustment.

Compound	UV source	BOD_5/COD[a]	BOD_5/COD[b]	IC_{50}[a] (mg L^{-1})	IC_{50}[b] (mg L^{-1})
MET	UV-A	0.02	0.07	–	–
	UV-C	0.02	0.10	102.5	86.7
PRO	UV-A	–	–	–	–
	UV-C	0.01	0.08	39.8	83.5

[a] Raw solution.
[b] Irradiated solution.

Table 3
Kinetic constants for the direct UV-C photolysis of PRO and MET solutions. Initial concentration 50 mg L^{-1}; pH without adjustment.

Compound	UV source	K (h^{-1})[a]	K ($\times 10^{-3}$ cm^2 mJ^{-1})[b]	Φ (mol $Einsteins^{-1}$)[c]
Propanolol	UV-C	4×10^{-2}	0.01	0.07
Metronidazole	UV-C	26×10^{-2}	0.05	0.09

[a] Time based rate constant.
[b] Fluency based rate constant.
[c] Quantum yield.

of that presented by Shemer et al. [28]. Besides, according to the calculated kinetic constants, MET presents higher removal rate when compared with PRO. Thus, the kinetic constant calculation is in agreement with the trend previously presented in this work. Finally, the data of removal rate and light absorption of the studied compounds were used to estimate the apparent quantum yield [30], which are also presented in Table 3.

4. Conclusions

- The direct UV photolysis was proved to be able to promote the removal of PRO and MET in water.
- An increase of the biodegradability indicator (BOD_5/COD) in some cases to more than four times after 8 h of UV irradiation was observed. Regarding the toxicity profile, the trend of the IC_{50} values along UV-C irradiation indicates that the MET photo-transformation favors the formation of intermediates with higher toxicity than the MET raw solution. On the other hand, PRO direct UV-C photolysis promoted the reduction of more than 50% of initial toxicity.
- The direct UV photolysis on the MET molecule probably occurs first on the ring with posterior attack of functional groups containing nitrogen. The PRO molecule seems to undergo UV photolysis on the amino group.
- Direct photolysis with the use of sunlight was comparable with runs carried out with the UV-C device, demonstrating that the photo-transformation of PRO in surface waters by sunlight cannot be ignored.
- The kinetic constants calculated for the direct UV-C photolysis were in an order of magnitude of 10^{-2} h^{-1} and 10^{-1} cm^2 mJ^{-1} for the time and fluency based kinetic constants, respectively.

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