

Photocatalytic degradation efficiency of hazardous macrolide compounds using an external UV-light irradiation slurry reactor

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ABSTRACT

The current work investigates the removal of two hazardous macrolide molecules, spiramycin and tylosin, by photodegradation under external UV-light irradiation conditions in a slurry photoreactor using titanium dioxide as a catalyst. The kinetics of degradation and effects of main process parameters such as catalyst dosage, initial macrolide concentration, light intensity and stirring rate on the degradation rate of pollutants have been examined in detail in order to obtain the optimum operational conditions. It was found that the process followed a pseudo first-order kinetics according to the Langmuir–Hinshelwood model. The optimum conditions for the degradation of spiramycin and tylosin were low compound concentration, 1 g L^{-1} of catalyst dosage, 100 W m^{-2} light intensity and 560 rpm stirring rate. Then, a maximum removal (more than 90%) was obtained after 300 min of irradiation time. Furthermore, results show that the selection of optimized operational parameters leads to satisfactory total organic carbon removal rate (up to 51%) and biochemical oxygen demand to chemical oxygen demand ratio (~ 1) confirming the good potential of this technique to remove complex macrolides from aqueous solutions.

Key words | kinetics, macrolide, photocatalytic degradation, titanium dioxide, UV light

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HIGHLIGHTS

- New insights on the elimination of hazardous molecules by photocatalytic process.
- Mineralization and biodegradability determination for toxicity assessment.
- Contributes to enhanced photoreactor design.

INTRODUCTION

At present, many residues of pharmaceuticals can be detected in municipal wastewater effluents and surface water (Rizzo *et al.* 2009). These substances and their metabolites are found in the environment due to the improper disposal of unused drugs and their excretion by humans or animals, as well as their low biodegradability by the conventional wastewater treatments plants. The presence of pharmaceuticals, especially macrolide antibiotics, and their accumulation in natural water is an emerging pollution leading to the disruption of ecosystems and increased malfunction of the aquatic species reproduction (Kümmerer *et al.* 2000; Babić *et al.* 2017). Several studies were focused on the contamination of the aquatic environment by these hazardous compounds (Löffler & Ternes 2003; Göbel *et al.*

2004; Zuccato *et al.* 2010; Tong *et al.* 2014; Ribeiro *et al.* 2015; Verlicchi *et al.* 2015; Carvalho & Santos 2016). However, the removal of macrolides from wastewater is one of the most important subjects in pollution control. Conventional biological treatments have proved to be inefficient for the removal of macrolide antibiotics because of their complex molecular structure, high toxicity and poor biodegradability (Kümmerer *et al.* 2000). Indeed, these processes were not designed to eliminate such kinds of pollutants.

In this respect, advanced oxidation technologies and more specifically heterogeneous photocatalysis represent hazardous control options for efficiently treating a wide range of emerging contaminants (Kanakaraju *et al.* 2014; Babić *et al.* 2017). Several studies have been achieved by

using TiO₂ as catalyst in photocatalytic degradation of macrolide pollutants (Doll & Frimmel 2005; Rizzo *et al.* 2009; Elmolla & Chaudhuri 2010; Ounnar *et al.* 2016a, 2016b; Lou *et al.* 2017; Lofrano *et al.* 2018).

The present study focuses on the investigation of the photodegradation of two macrolide antibiotics: spiramycin and tylosin. Their widespread usage and frequent detection in the aquatic environment highlight the need for their removal (Michael *et al.* 2013).

Spiramycin is commercially produced through a fermentation process by using strains of *Streptomyces ambofaciens* (Deng *et al.* 2014). It is an effective antibiotic against gram-positive, some gram-negative and other organisms. It is generally used to treat human (oropharynx, respiratory system, amoebiasis, balantidiasis, malaria, and genito-urinary tract) and veterinary infections (cryptosporidiosis and toxoplasmosis).

Tylosin is a veterinary macrolide antibiotic derived from fermentation of *Streptomyces fradiae*. It is used for disease treatment and animal health protection in many countries of the world (Sarmah *et al.* 2006). It is commonly used as a growth promoter in calves, cattle and poultry feed (Yin *et al.* 2016).

The information dealing with the removal of these two macrolides by heterogeneous photocatalysis is still scarce. In spite of few studies reporting on these water pollutants, the elimination of these molecules continues to be a subject of interest (Vaiano *et al.* 2015; Adamek *et al.* 2016; Ounnar *et al.* 2016a, 2016b; Tassalit *et al.* 2016). The present work adds to the general discussion on the role of the advanced oxidation processes for wastewater purification, providing new insight on the influence of the irradiation mode, catalyst type and stirring rate but also on the reduction of the toxicity of these hazardous macrolides in water.

In this paper, the degradation efficiency of spiramycin and tylosin by heterogeneous photocatalysis process was studied using a batch slurry photoreactor with an external UV-light irradiation by using titanium dioxide PC500 as catalyst. The overall aim of this work was to investigate the effects of some key operating parameters on the degradation of target molecules; examine the reaction kinetics; and to assess the mineralization degree and biodegradability of the treated solutions to evaluate the efficiency of the process.

MATERIAL AND METHODS

Chemicals and photocatalyst characteristics

Two macrolide antibiotics were used as pollutant models in this work: spiramycin and tylosin. Spiramycin (SPM, purity

of 98%) was kindly offered by Sanofi-Aventis Company (Algeria). Tylosin tartrate (TYL) was obtained from commercial tylosin produced by Sinochem Corporation. Their chemical structure and properties were given in our previous work (Ounnar *et al.* 2016a). Analytical-grade organic solvents were used for ultra-high-performance liquid chromatography (UHPLC) analysis. All solutions were prepared with ultrapure water produced by an ELGA Option-Q DV 25 water purifier system (18.2 MΩ.cm resistivity at 298 K). The catalyst used was PC500 titanium dioxide powder (TiO₂), supplied by Millenium company (crystalline form; >99% anatase; BET (Brunauer–Emmett–Teller) surface area 317 m² g⁻¹; mean diameter 5–10 nm).

Experimental set-up and procedure

The photocatalytic degradation experiments were carried out using a batch photoreactor system with external UV-light irradiation. It consists of a 3 L cylindrical borosilicate glass with a working volume of 2 L (Figure 1). The macrolide solution containing the appropriate catalyst amount was continuously stirred by a mechanical stirrer to maintain homogeneity. The solution was irradiated by using two UVA lamps (Philips PL-S 9 W/10/4P mercury vapor lamps) placed outside the reactor. According to manufacturer's information, the spectral response of the used lamps is in the range 320–400 nm, with a maximum emission at 365 nm which is suitable for the catalyst activation. The radiation flux was determined with a radiometer, VLX-3 W (Vilbert Lourmat, Marne La Vallee, France).

The experiments were conducted in batch mode at room temperature (about 21 °C) at natural pH (corresponding to the dissolution of macrolide in water, 6.5 ± 0.5). Prior to irradiation, the suspension was stirred in the dark for 30 min

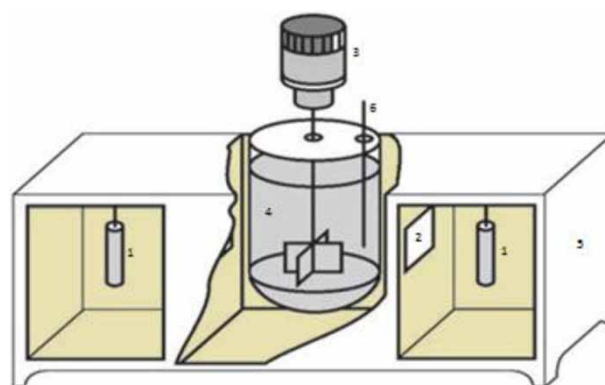


Figure 1 | Schematic representation of the experimental set-up (Favier *et al.* 2019). (1) UV lamp, (2) square opening, (3) stirring module, (4) reactor, (5) box, (6) sampling tube.

in order to achieve the adsorption/desorption equilibrium of macrolide on the semiconductor surface. For all the assays, an irradiation time of 300 min has been used. Moreover, all experiments were carried out in duplicate and the error was less than 5.0%. Favier *et al.* (2015) have presented in their work a detailed description of the experimental device and of the strategy used to modulate the irradiation for the degradation tests.

Analysis

Solution samples were taken over the experiment time and then filtered through a 0.45 μm polytetrafluoroethylene Millipore syringe filter to separate the catalyst. Macrolide residual concentration was monitored by UHPLC (Acquity Hclass: Waters), equipped with a photodiode-array detector. Chromatographic separation was performed with a BEH C18 reversed phase column (100 mm \times 2.1 mm i.d. \times 1.7 μm), at 30 $^{\circ}\text{C}$ and isocratic elution. The mobile phase consisted of 0.1% of aqueous formic acid in acetonitrile/ultra-pure water (20:80 v/v). The injection volume and flow rate were respectively 10 μL and 0.4 mL min^{-1} . Analytes of both SPM and TYL were detected at a λ_{max} of 232 and 290 nm respectively. Total organic carbon (TOC) analyses were carried out with a Shimadzu Analytical 1010 instrument.

Chemical oxygen demand (COD) was determined by means of a NANOCOLOR[®] CSB 150 test from Macherey–Nagel (Düren, Germany) and COD concentration was measured by a NANOCOLOR[®] photometer. The amount of oxygen required for the oxidation of the organic and mineral matter, at 148 $^{\circ}\text{C}$ for 2 h, was quantified after oxidation with $\text{K}_2\text{Cr}_2\text{O}_7$ by heating at acidic pH.

Five-day biological oxygen demand (BOD_5) measurements were carried out using an Oxitop[®] IS6 system (from WTW) in order to check the biodegradability of the macrolide pollutants at 20 $^{\circ}\text{C}$. The procedure as reported by Saidi *et al.* (2013) was applied to inoculate the sample, the blank solution and the control solution with an activated sludge (0.05 g L^{-1}).

RESULTS AND DISCUSSION

The degradation kinetics of the target compounds have been analyzed using a pseudo first-order kinetic model (Gaya & Abdullah 2008), which can be expressed as:

$$\ln\left(\frac{C_0}{C}\right) = k_{\text{ap}} \cdot t \quad (1)$$

C_0 and C (mg L^{-1}) are the concentration of pollutant at $t = 0$ and t respectively. The apparent rate constant (k_{ap} , min^{-1}) is given by the slope of the plot of $\ln(C_0/C)$ versus time (t , min) for the first 30 min of the reaction.

Numerous investigations have demonstrated that heterogeneous photocatalysis of organic substrates could be described by the Langmuir–Hinshelwood (L–H) kinetic model (Gad-Allah *et al.* 2011). If we note r_0 ($\text{mg L}^{-1} \text{min}^{-1}$) the degradation rate, L-H model can be expressed as follows:

$$r_0 = -\frac{dC_0}{dt} = \frac{K_L k_{\text{L-H}} C_0}{1 + K_L C_0} \quad (2)$$

where $k_{\text{L-H}}$ ($\text{mg}^{-1} \text{L min}$) refers to the apparent L-H rate constant and K_L (L mg^{-1}) to the adsorption/desorption equilibrium constant.

Effect of catalyst dosage

The concentration of titanium dioxide is considered as an important parameter in photocatalytic processes operating in suspension. The optimal amount will allow the best performance to be achieved at a low cost. It depends on the nature of the organic compound and the geometry of the reactor (Parra *et al.* 2002).

Experiments were carried out at 20 mg L^{-1} of initial pollutant concentration, a maximal irradiation flux and an average stirring. The TiO_2 concentration was varied from 0 g L^{-1} (photolysis) to 2 g L^{-1} . Figure 2 gives the profile of the calculated rate constants as a function of catalyst dosage for both selected compounds. It is clear that the apparent rate constant is proportional to the catalyst concentration. In the case of SPM, k_{ap} becomes almost constant from a semiconductor concentration value of 0.8 g L^{-1} . On the other hand, the rate constant of the TYL increases continuously as a function of catalyst concentration (Figure 2).

Larger amounts of catalyst favor the degradation. In fact, the increase in active sites leads to formation increase of $\text{O}_2^{\cdot-}$ and/or OH^{\cdot} free radicals. The same result was observed in our previous work in the case of a slurry reactor using internal irradiation (Unnar *et al.* 2016b). However, a maximum degradation rate (over 80%) was obtained for SPM regardless of catalyst concentration, while in the case of TYL it was obtained for TiO_2 concentrations greater than or equal to 0.8 g L^{-1} .

To ensure the reproducibility of obtained results by examining the role of other operating parameters in the reaction patterns and the kinetic features, the optimal catalyst dose was taken equal to 1 g L^{-1} .

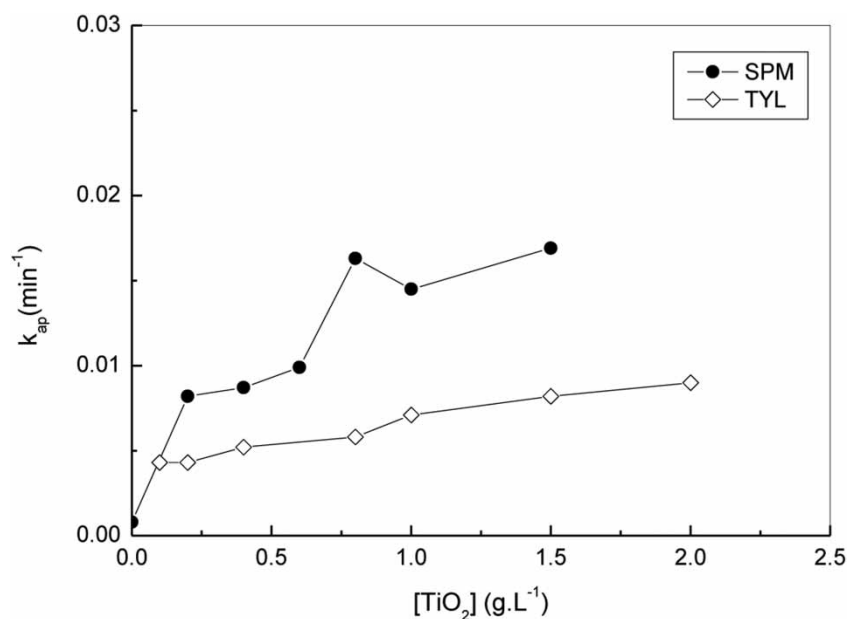


Figure 2 | Effect of the catalyst dosage on the reaction rate constant. $C_0 = 20 \text{ mg L}^{-1}$, irradiation flux = 90 W m^{-2} , natural pH.

According to previous works (Galindo *et al.* 2001; Gad-Allah *et al.* 2011; Ounnar *et al.* 2016b), the relationship between catalyst concentration and degradation kinetics gives rise to the following expressions for each of the two antibiotics studied:

$$k_{\text{ap}}(\text{SPM}) \approx 1.5 \times 10^{-2} [\text{TiO}_2]^{0.3} \quad (3)$$

$$k_{\text{ap}}(\text{TYL}) \approx 0.7 \times 10^{-2} [\text{TiO}_2]^{0.26} \quad (4)$$

The order of the reaction is almost identical for the two molecules studied: 0.30 and 0.26 for SPM and TYL respectively. Similar results (order less than 1) have been reported in previous studies (Galindo *et al.* 2001; Ounnar *et al.* 2016b).

Effect of stirring rate

Figure 3 illustrates the evolution of the apparent rate constant as a function of the stirring rate for the two antibiotics. The k_{ap} constant increases as a function of the

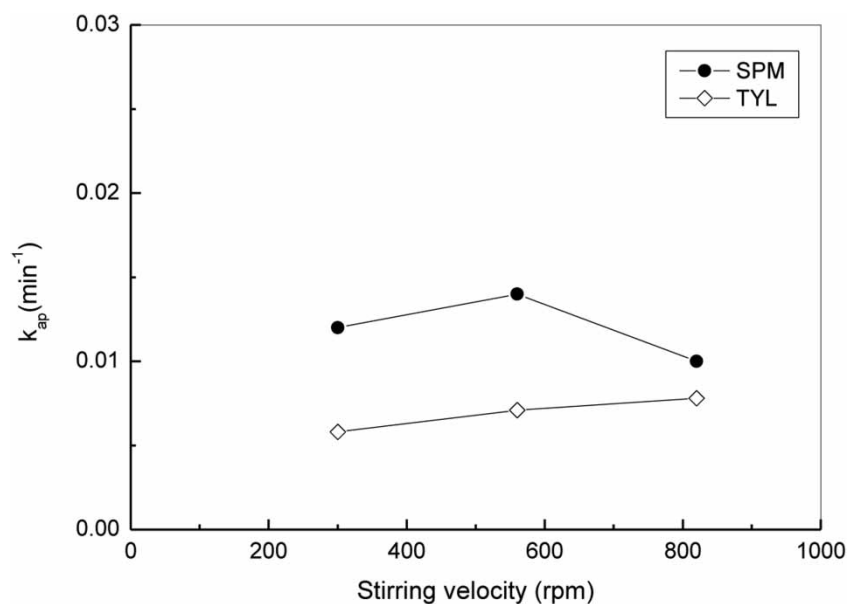


Figure 3 | Effect of stirring rate on reaction rate constant. $C_0 = 20 \text{ mg L}^{-1}$, $[\text{TiO}_2] = 1 \text{ g L}^{-1}$, irradiation flux = 100 W m^{-2} , natural pH.

stirring rate, reaching a maximum value at 560 rpm in the case of SPM. Beyond this value, it decreases. On the other hand, the apparent rate constant for TYL is proportional to the stirring rate.

At low stirring, the reduction in the antibiotic's removal is due to the low interaction between the molecules and catalyst particles in the solution, as well as poor dispersion of the catalyst. Therefore, the increase in stirring rate favors contact by adsorption between TiO_2 and the pollutant molecules. However, this trend is not observed in the case of SPM, since the rate constant decreases above the 560 rpm value. For the reaction system studied, the optimal stirring rate was taken equal to 560 rpm.

Effect of irradiation flux

UV irradiation generates photons required for the transfer of electrons from the valence band to the conduction band of a semiconductor photocatalyst. The energy of a photon is related to its wavelength and the overall energy supply in a photocatalytic process depends on the light intensity. However, the effect of light intensity as well as the wavelength on the removal efficiency of a compound is important (Pareek *et al.* 2008). The relation between this parameter and the photocatalytic degradation rate has been evaluated in several studies for various pollutants (Ahmed *et al.* 2011; Favier *et al.* 2019). It was reported that in water treatment, increasing the incident photon rate would result in an increase in the photocatalytic reaction. In this work,

photocatalytic experiments were conducted at different irradiation flux to evaluate the influence of this parameter on the elimination of the target molecules. Figure 4 represents the profiles of the SPM and TYL apparent rate constant obtained under the investigated conditions. It is clear that the apparent rate constant is proportional to the light intensity. Moreover, the elimination rate of SPM and TYL decreases respectively from 91 to 52% and from 85 to 42% when the light intensity decreases from 100 to 10 W m^{-2} . This is due to the decrease in the number of photons generated with the reduction in intensity. So, the optimal irradiation flux was taken equal to 100 W m^{-2} for the following steps.

However, to achieve a high photocatalytic reaction rate, a relatively high light intensity is required to provide each active site on the catalyst surface with sufficient photon energy (Behnajady *et al.* 2006; Chong *et al.* 2010). Similarly, Mahalakshmi *et al.* (2009) reported that the rate of degradation of propoxur increases with the increase in light intensity. Favier *et al.* (2019) revealed the same behavior for the photocatalytic degradation of clofibric acid.

Effect of initial pollutant concentration

Figures 5 and 6 represent respectively the kinetics and degradation rate constants of the two pollutants according to the value of the initial concentration within the range of $10\text{--}80 \text{ mg L}^{-1}$. The fact that this concentration is higher

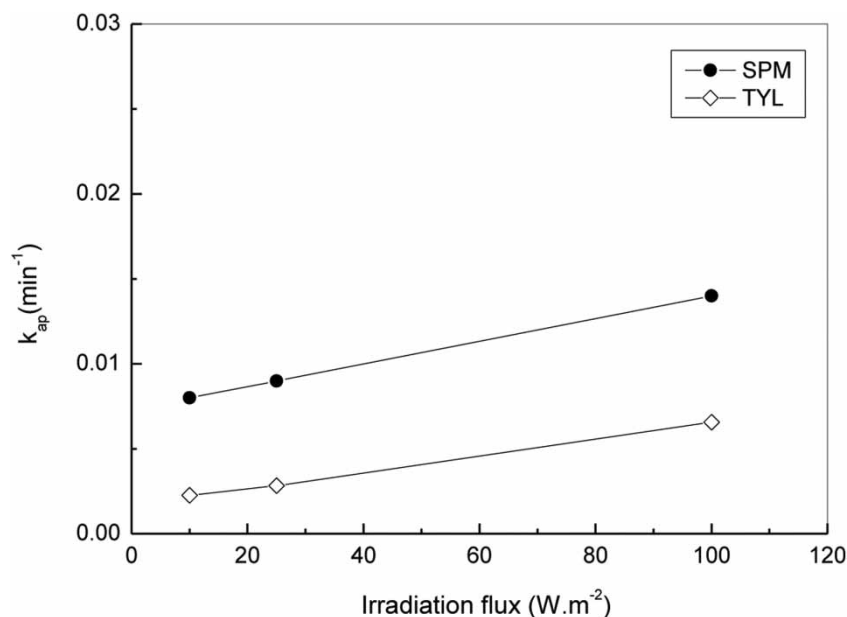


Figure 4 | Effect of irradiation flux on reaction rate constant. Stirring rate = 560 rpm, $C_0 = 20 \text{ mg L}^{-1}$, $[\text{TiO}_2] = 1 \text{ g L}^{-1}$, natural pH.

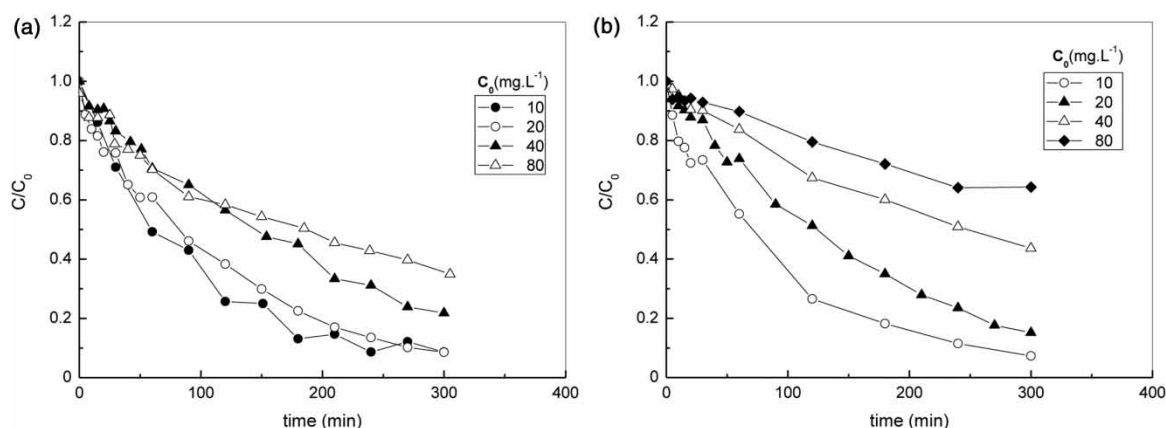


Figure 5 | Effect of initial concentration on the photocatalytic degradation: (a) TYL; (b) SPM. Irradiation flux = 100 W m^{-2} , stirring rate = 560 rpm, $[\text{TiO}_2] = 1 \text{ g L}^{-1}$, natural pH.

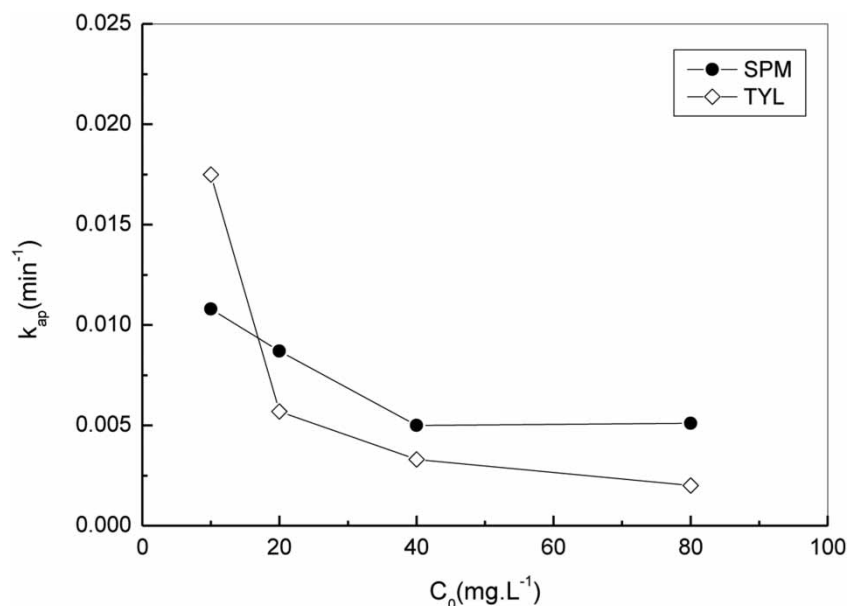


Figure 6 | Effect of initial pollutant concentration on reaction rate constant. Stirring rate = 560 rpm, irradiation flux = 100 W m^{-2} , $[\text{TiO}_2] = 1 \text{ g L}^{-1}$, natural pH.

than typical environmental values would not induce any change in the reaction mechanism, or in the reaction products (Santaballa *et al.* 2006). The experiments were achieved under optimal conditions previously determined, i.e. 1 g L^{-1} TiO_2 , 560 rpm stirring rate and 100 W m^{-2} . It is clear that the time required for maximum degradation depends on the initial concentration C_0 . Indeed, the obtained elimination rate of the two compounds is between 36 and 93% after 300 min of photocatalytic reaction (Figure 5). A maximum value is observed for low concentrations ($\leq 20 \text{ mg L}^{-1}$).

The rate constant varies as a function of C_0 to reach a constant value at high initial concentrations, indicating that first-order kinetics cannot be applied. Consequently,

antibiotic degradation decreases as the initial concentration increases, and the application of the L-H model is suitable to describe such a phenomenon. This model is commonly used to rationalize the mechanisms of reactions occurring on solid surfaces (Kumar *et al.* 2008). The values of reaction constants of the model were determined following the L-H expression (Equation (2)). The obtained values of k_{L-H} (apparent L-H rate constant) and K_L (adsorption/desorption equilibrium constant) for the selected hazardous compounds are given in Table 1. They were of the same order of magnitude as those reported in the literature for the same class of molecules (Gad-Allah *et al.* 2011; Dimitrakopoulou *et al.* 2012). It also appears that SPM degraded faster than

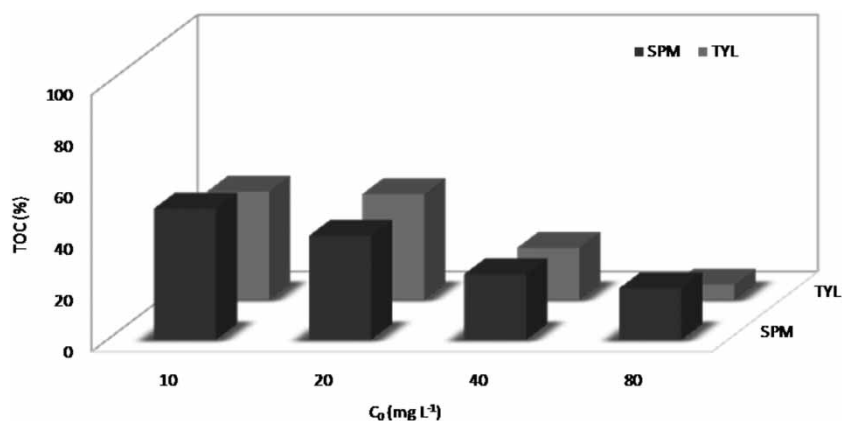
Table 1 | L-H kinetic constants

Compound	k_{L-H} ($\text{mg}^{-1} \text{L min}$)	K_L (mg^{-1})	R^2
Spiramycin	0.306 ± 0.134	0.041 ± 0.005	0.7511
Tylosin	0.122 ± 0.223	0.074 ± 0.004	0.9704

TYL and the kinetic reaction step is considered to be the limiting one.

Mineralization assessment

As for any organic molecule subjected to irradiation in the presence of titanium dioxide, an antibiotic will incur several processing steps leading to the formation of by-products which may be more toxic than the parent compound. Thus, we focused our attention on the mineralization of the target molecules. Figure 7 illustrates the obtained data for mineralization assessment of the two compounds at different initial concentrations. It is clear that the mineralization is weak for high pollutant concentrations, due to the complexity of the selected molecules and their large molar mass. This result leads us to suppose the presence of by-products of the photocatalytic reaction in the case of these hazardous macrolide compounds. It has been observed that even at maximum degradation rate, complete mineralization is not achieved. Nevertheless, the obtained mineralization rate appears to be acceptable over the optimal operating conditions. About 51 and 42% mineralization of SPM and TYL respectively were achieved after 5 hours of irradiation time, for low initial pollutant concentrations (10 mg L^{-1}) and with maximum removal rates around 90%. Supplementary work is needed in order to investigate the by-products identification.

**Figure 7** | Mineralization assessment over initial concentration of compounds. Stirring rate = 560 rpm, irradiation flux = 100 W m^{-2} , $[\text{TiO}_2] = 1 \text{ g L}^{-1}$, natural pH.

Biodegradability enhancement

Several authors use BOD_5/COD ratio to assess the biodegradability of aqueous effluents (Pulgarin *et al.* 1999; Kajitvichyanukul & Suntronvipart 2006). It is commonly accepted that a wastewater is completely biodegradable when that ratio is about 0.4, while a value between 0.3 and 0.4 corresponds to partial biodegradability (Sarría *et al.* 2002). For values below 0.4, the solution is considered non-biodegradable. Thus BOD_5 and COD values were measured at initial concentration of 10 mg L^{-1} and at the end of the photocatalytic reaction in order to know the extent of biodegradability achieved by oxidation. Their determination was performed for duplicate samples for better reproducibility of results.

The COD value of initial solution of SPM and TYL is equal to 15 and 18 mg L^{-1} respectively and their BOD_5 is low, which implies high toxicity to microorganisms in the environment. The results summarized in Table 2 show a BOD_5/COD ratio value equal to 1 for both SPM and TYL after 300 min of degradation time under UV light. The ratio value was higher than 0.4 suggesting that treated solutions are biodegradable. This result is considered as an indication of the positive effect of the applied technique for reducing toxicity of this kind of hazardous macrolide compounds in wastewaters.

Table 2 | Biodegradability of macrolides

Compound	BOD_5/COD (initial)	BOD_5/COD (after 300 min of oxidation)
SPM	0.13	1
TYL	0.16	1.11

CONCLUSION

In this work, the photodegradation efficiency of macrolide antibiotics, namely SPM and TYL, was investigated in batch mode using a slurry reactor with external irradiation. The influence of the main operating parameters (pollutant concentration, catalyst dosage, irradiation flux, stirring) on the degradation kinetic was examined and then optimized. The obtained results confirm the effectiveness of the process for the removal of macrolides, pharmaceutical molecules acknowledged for their persistence in the aquatic environment and for their refractory character through biological elimination. The conclusions based on the experimental results can be summarized as follows.

1. The optimal determined conditions were 1 g L⁻¹ catalyst dosage, average stirring (560 rpm), 100 W m⁻² irradiation flux and low initial pollutant concentration (≤ 20 mg L⁻¹). Thus, a maximum degradation rate (more than 90%) was obtained.
2. Moreover, the reaction kinetics followed the first-order model and was rationalized by the L-H mechanism. The L-H constants have been determined.
3. On the other hand, it was observed that mineralization of both macrolides was not complete even with maximum abatement. This is probably due to the complex structure of the target molecules and the presence of organic intermediates generated during the photocatalytic process.
4. However, a satisfactory biodegradability of the solution was obtained at the end of the reaction suggesting that the photocatalytic oxidation process could be useful as a pre-treatment technique for reducing toxicity of aqueous environments contaminated with such hazardous compounds as macrolides.

DATA AVAILABILITY STATEMENT

All relevant data are included in the paper or its Supplementary Information.

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