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Artigo Original

Photocatalytic oxidation of clozapine using TiO_2 immobilized in polystyrene: effect of operation parameters and artificial neural network modeling

Oxidação fotocatalítica da clozapina empregando TiO_2 imobilizado em poliestireno: efeito dos parâmetros operacionais e modelagem via redes neurais

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Resumo

Nos últimos anos, a fotocatálise heterogênea através de semicondutores demonstrou ser eficiente para o tratamento de águas residuárias contendo poluentes orgânicos, como os fármacos. Dentre alguns fotocatalisadores, o dióxido de titânio (TiO_2) tem sido estudado e aplicado para esta finalidade. À vista disso, neste trabalho investigou-se a degradação fotocatalítica do antipsicótico clozapina sob irradiação ultravioleta, mediante emprego de TiO_2 suspenso e suportado em material de poliestireno. Alguns parâmetros experimentais foram avaliados através de um planejamento fatorial 2^3; verificando-se uma maior taxa de degradação do composto ao utilizar 0,15 g do catalisador imobilizado, [H_2O_2] de 340 mg L^{-1} e pH 9, após 6 h de tratamento. Para tal obteve-se degradações superiores a 93,48% e um modelo de dois estágios foi proposto para descrever a cinética reacional. Uma rede neural artificial foi utilizada para modelar o processo fotocatalítico e determinar a importância das variáveis operacionais. Também ficou estabelecido que o emprego deste tratamento resultou em 78,30% de remoção da demanda química de oxigênio (DQO) nas condições otimizadas. Além disso, a partir de testes de reutilização foi verificada a estabilidade do suporte de TiO_2 após 5 ciclos consecutivos. No entanto, por meio de ensaios toxicológicos com Escherichia coli e Salmonella enteritidis observou-se que os produtos gerados através da reação geram produtos mais tóxicos que o composto original.

Palavras-chave: Ecotoxicidade; Fármaco; Fotocatálise heterogênea; Psicotrópico; Radiação ultravioleta

Abstract

In recent years, heterogeneous photocatalysis using semiconductors has proved to be efficient for the treatment of wastewater containing organic pollutants, such as drugs. Among some photocatalysts, titanium dioxide (TiO_2) has been studied and applied for this purpose. Therefore, this work investigated the photocatalytic degradation of the antipsychotic clozapine under ultraviolet irradiation, using suspended and supported TiO_2 in polystyrene material. Some experimental parameters were evaluated through a factorial design 2^3; a higher degradation rate of the compound was verified using 0.15 g of the immobilized catalyst, [H_2O_2] of 340 mg L^{-1} and pH 9, after 6 h of treatment. It was possible to obtain degradations above 93.48% and a two-stage model was proposed to describe the reaction kinetics. An artificial neural network was used to model the photocatalytic process and to determine the importance of the operational variables. It was also established that the use of this treatment resulted in 78.30% removal of chemical oxygen demand (COD) under optimized conditions. In addition, the stability of TiO_2 support after five consecutive cycles was verified from reuse tests. However, by means of toxicological tests with Escherichia coli and Salmonella enteritidis, it was observed that the products generated by the reaction were more toxic than the original compound.

Keywords: Drug. Ecotoxicity; Heterogeneous photocatalysis; Psychotropic; Ultraviolet radiation

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1 Introduction

The conventional processes used in wastewater treatment plants (WWTP) are not capable to promote the complete removal of refractory pollutants, such as drugs (VILLOTA; LOMAS; CAMARERO, 2018; BOCZKAJ; FERNANDES, 2017). This is due, among other factors, to the low biodegradability of the compounds, which persist after treatment made by the WWTP. In this context, different techniques have been applied as alternatives to fully degrade these products (BOCZKAJ; FERNANDES, 2017; BORGES et al, 2016).

According to Trawinski, Skibinski and Szymanski (2018), the use of techniques such as adsorption, flocculation, sludge stabilization and nitrification have low efficiency in the removal of pharmaceutical products, especially antipsychotics. This fact may be related to the release mechanism of this class of drugs that occurs in a prolonged way. Therefore, they are manufactured to have high stability, mainly in the different types of degradation (acid, basic, thermal and photolytic degradations).

Clozapine is an antipsychotic agent registered since the 1960s, and although other pharmaceuticals have been marketed, this drug is still commonly prescribed (TRAWIŃSKI; SKIBIŃSKI, 2019). Some studies report the detection of this drug at the pharmaceutical WWTP exits (concentration between 9.56 and 14.43 μg L^{-1}) and in river water (8.89 μg L^{-1}) (MATONGO et al, 2015a; MATONGO et al, 2015b), which indicates that the wastewater treatment methods applied in WWTP are ineffective against clozapine. This fact implies in the search for more effective methodologies.

In a study developed by Monsalvo et al. (2014), the application of anaerobic membrane bioreactors was used for the removal of clozapine in synthetic waste water, which reached only 27% efficiency. However, although they have been little evaluated until now, other alternative solutions such as the advanced oxidative processes (AOP) can be successfully used for degradation of this type of drug (COLLADO et al, 2014, NAPOLEÃO et al, 2018).

The AOP are based on the generation and consumption of hydroxyl radicals (·OH), which are highly oxidizing and non-selective chemical species responsible for conducting the oxidation process (BORGES et al, 2016). Among the different types of AOP used, the heterogeneous photocatalysis has deserved prominence, since it has presented good efficiency in the treatment of pharmaceutical products. In this process, the hydroxyl radicals are produced by photochemical tests with ultraviolet (UV) or visible (Vis) radiation combined with a semiconductor (SC) that acts as a photocatalyst. The interaction of the radiation with the surface of the SC causes pairs of electron-hole capable of producing reactive oxygen species, which promote the mineralization of the pollutant.

Among the most used photocatalysts is TiO_2, which presents low cost, low toxicity, high photo-stability and reactivity, besides being insoluble in water (VELÁZQUEZ-MARTÍNEZ et al, 2018). Most of the studies employ this photocatalyst in suspended form, so that the degradation system has a larger surface area and, consequently, leads to a higher rate of reaction (OBLAK et al, 2018). However, the use of the suspended catalyst has some disadvantages, such as: turbidity of the sample, continuous loss of the material, and elevation of the costs related to the process, due to the difficulty of recovering in water (MATILAINEN; SILLANPÄÄ, 2010). In this sense, in order to reduce this loss and even promote the reuse of the photocatalyst, its use in the immobilized form has been investigated (JALLOULI et al, 2018).

The substrate used as carrier must be porous and stable to the oxidant produced during the reaction, in order to provide a higher photocatalyst/pollutant interaction (OBLAK et al, 2018; XING et al, 2018). Polymeric waste from post-consumer plastic materials has been used as a support for photocatalytic reactions (BARROS et al, 2014; SANTOS et al, 2018). Polymers are widely used because they have a relatively low cost of production, besides being light and easy to process (LOSTE et al, 2019). The polymer matrixes most commonly employed to support the TiO_2 film include polyethylene (PE), polystyrene (PS), expanded polystyrene (EPS), polyethylene terephthalate (PET), polypropylene (PP), polyvinyl chloride (PVC), among others (SINGH; MAHALINGAM; SINGH, 2013).

Some studies were carried out applying PS on the photocatalytic degradation of organic pollutants, Yang et al (2006) investigated the photodegradation of the methylene blue dye. This researchers employed titanium dioxide (TiO_2) supported on PS plates under xenon-ultraviolet light was used and 100% discoloration was obtained after 180 min.

TiO_2 can be used in its natural or synthetic form, as well as in its pure state or combined with metals, which in turn contribute to the increase in photocatalytic activity (ZHANG et al, 2013; HAN et al, 2018). In a study carried out by Lin et al (2017), for the drugs ibuprofen, carbamazepine and sulfamethoxazole, higher rates of degradation were observed when using the photocatalyst doped with iron after irradiation with visible light for 6 h. For all the mentioned substances, the photodegradation using TiO_2 in its pure form showed a lower efficiency.

The heterogeneous photocatalysis process, widely used in the degradation of polluting substances, can be modeled to predict the supposed efficiency achieved by influencing the parameters involved in the system (HASSANI et al, 2018). In this sense, artificial neural networks (ANN) are based on biological systems capable of simulating the learning process of neurons in the human brain from experimental data (KHATAEE; KASIRI, 2010; ELMOLLA; CHAUDHURI; ELTOUKHY, 2010). Based on this, Calza et al (2008) used neural network modeling to predict the performance of the photocatalytic process for imipramine antidepressant degradation.

In this context, the present work aims to evaluate the photocatalytic performance of TiO_2 and TiO_2 films deposited in post-consumer polystyrene packaging for the degradation of aqueous solution containing the antipsychotic clozapine. The study also aimed to verify the catalytic activity of iron doped TiO_2, to identify the best working condition for the system with the best results and, from this condition, to carry out an evaluation of the toxicity. It is also proposed to develop an artificial neural network model to evaluate the effect of the operational variables involved in the photocatalysis process.

2 Methodology

2.1 Synthesis of doped TiO_2 and immobilization of the photocatalyst

Based on the methodology by Khan et al (2013), a suspension for doping 1 mol% of Fe^{2+} in TiO_2 was prepared. This solution, was composed of 500 mL of distilled water, containing 79.1 g of TiO_2 and 2.78 g of $FeSO_4 \cdot 7H_2O$. The prepared material was agitated for 6 h in a magnetic stirrer, rested for of 24 h, and then dried in an oven under study for a further 12 h at 100 °C. The obtained Fe-TiO_2 solid was macerated with pestle-mortar and finally calcined at 400 °C for 6 h in a furnace.

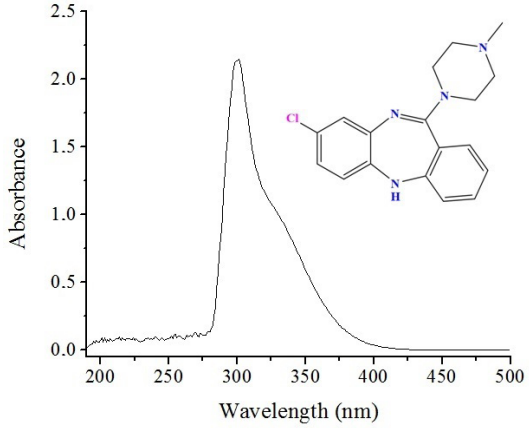
For immobilization of the catalysts, aqueous suspensions of TiO_2 and Fe-TiO_2, both constituted by 5 g of the photocatalyst and 250 mL of distilled water, were initially prepared. The polystyrene (PS) material, obtained from post-consumer yogurt pots, was washed with water and neutral detergent. The immobilization method followed the methodology adapted from Barros et al (2014), in which the suspensions were first acidified with perchloric acid to pH 2.5; then homogenized in a shaker table for 10 min and finally subjected to ultrasonic bath for 30 min. Subsequently, the carriers were submerged in the respective suspension for 10 s and set to dry at room temperature of 27 ± 2 °C for 2 h. Stirring procedures, ultrasonic bath and immersion of the support in the suspension were repeated until the desired mass of catalyst was obtained.

2.2 Photocatalytic degradation of clozapine

Initially, a stock solution containing 100 mg L^{-1} of clozapine (CLZ) was prepared using acetonitrile (Merck) and distilled water (1:9). For its preparation, the active drug was supplied by the Laboratório Farmacêutico do Estado de Pernambuco (LAFEPE), batch 17715 of 2017. The chemical structure of CLZ and its absorbance spectrum are shown in Figure 1.

Figure 1 — Molecular structure and absorbance spectrum of the drug clozapine (dissolved in acetonitrile/water 1:9)

The concentration was determined according to data in the work of Trawinski, Skibinski and Szymanski (2018),



who studied the degradation of the also antipsychotic loxapine. Similarly, to the authors, a 10 mg L^{-1} CLZ concentration was used in this study. Preliminary photocatalytic tests were performed on bench-top reactors UV-C (Zaidan et al, 2017) and artificial sunlight (Santana et al, 2017). The photon emission spectrum of the lamps was measured with radiometer (Emporionet).

In order to select the process that presented the highest degradation efficiency, the following systems were evaluated: TiO_2/radiation, Fe-TiO_2/radiation, TiO_2/radiation/H_2O_2 and Fe-TiO_2/radiation/H_2O_2. For all cases, the catalyst (0.1 g) was used in two forms, in suspension and supported on a polystyrene surface (PS-photocatalyst). It is noteworthy that the deposition process of the catalyst was performed both on the outside and on the inside of the polymer material. When applicable, the concentration of H_2O_2 ($[H_2O_2]$) was equal to 340 mg L^{-1}. It is emphasized that 250 mL of solution of CLZ before being exposed to the radiation were kept in the dark for 30 min in order to achieve the adsorption equilibrium on the surface of the photocatalyst, according Kolsakidou et al (2017). After 60 min of reaction, the post treatment drug concentration was determined in ultraviolet-visible (UV/Vis) spectrophotometer at wavelength (λ) of 294 nm.

2.3 Effect of parameters on the photocatalytic degradation of clozapine

In order to obtain a larger percentage of degradation, it was examined whether the best experimental conditions. For this purpose, face the system identified in a first step, the influence of catalyst mass, $[H_2O_2]$ and the working pH was assessed through factorial design 2^3 (triplicate center point). The minimum, central and maximum levels used for the respective factors were: 0.05, 0.1 and 0.15 g; 170, 255 and 340 mg L^{-1}; and 3, 6 and 9.

2.4 Kinetic evaluation

For the best conditions obtained in the study of factorial design, tests were carried out to investigate the reactional kinetics. To this end, 250 mL of the solution containing the analyte were irradiated, and small aliquots were taken at regular intervals (5, 10, 20, 30, 40, 60, 90, 120, 150, 180, 210, 240, 270, 300, 360 min). From the concentration data obtained at each time, the non-linear model of pseudo-first order proposed by Chan and Chu (2003) was applied (Equation 1).

$$C = C_0 \cdot \left(1 - \frac{t}{\rho + \sigma t}\right) \quad (1)$$

C being the concentration of the dye (mg L^{-1}) after treatment at a reaction time t (min), and C_0 is the initial concentration of the dye (mg L^{-1}). The parameters ρ and σ represent the reactional kinetics (min) and the oxidative capacity of the system (dimensionless), respectively. The values of ρ and σ correspond to the linear and angular coefficients of the line, respectively, obtained from the linearization of Equation 1 (Equation 2).

$$\frac{t}{1-\frac{C_1}{C_0}} = \rho + \sigma t \quad (2)$$

Then, in order to evaluate the organic matter concentration, tests were performed to determine the chemical oxygen demand (COD) in the initial sample of the drug and after submission to the treatment. This analysis was carried out according to the methodology described in the 5220D method of the *Standard methods for the examination of water and wastewater* (APHA, 2012). Before this analysis, the residual concentration of H_2O_2 was determined by using a colorimetric method.

2.5 Mathematical modeling: artificial neural networks

According to Khataee and Kasiri (2010), artificial neural networks (ANN) are efficient to investigate the contribution of the operational parameters during the process of photocatalytic degradation. In this sense, the software Statistica 10.0 (StatSoft, 2010) was used to propose a neural network capable of predicting the degradation percentage of the CLZ, considering the variables studied throughout the process. For this, methodologies with Radial Basis Function (RBF) and Multilayer Perceptron (MLP) configurations were used, which comprised three layers: input, hidden intermediate and output. The transfer functions tested were identity, logistic, hyperbolic tangential, sinusoidal and exponential; while the number of neurons in the hidden layer varied between 3 and 33. The input variables consisted of reaction time (min), mass of TiO_2 (g), $[H_2O_2]$ (mg L^{-1}) and pH. Thus, an analysis of the relevance of each parameter in the percent degradation of the drug was performed. A set of 213 experimental data was used to feed the network, which was divided into training, test and validation subsets, in a proportion of 70, 15 and 15%, respectively. The analyzed variables had their values ranging from: time (5 to 360 min); TiO_2 (0 to 0.15 g); $[H_2O_2]$ (0 to 340 mg L^{-1}) e pH (3 to 9).

2.6 Reactivity tests of the photocatalyst

The stability and reusability of the PS-photocatalyst samples were studied through 5 consecutive cycles. Based on the methodology proposed by Marcelino et al (2019), after each cycle, the carrier was washed thoroughly with distilled water, dried and weighted. The mass loss was insignificant, less than 0.7%. In this case, 250 mL of a new CLZ solution were submitted to the photocatalytic assay, under the same conditions of the kinetic study.

2.7 Ecotoxicity assessment

The toxicity of possible by-products formed during the photocatalytic reaction was investigated by means of acute ecotoxicity tests. These were conducted using the bacteria *Escherichia coli* and *Salmonella enteritidis*, according to methodology presented by Santana et al (2018).

3 Results and discussion

3.1 Photocatalytic degradation of clozapine

In order to determine the photolytic contribution in CLZ degradation, experiments under UV-C and sunlight radiations were performed. In both cases, it was found that the compound's molecule is not photo-stable, since the incidence of light promoted its degradation although not expressively (<10.12%), even after 6 h of treatment. In a study developed by Trawinsk and Skibiński (2019), which evaluated the degradation of this drug (5 mg L^{-1}) by direct photolysis, they also verified the low significance of the process under simulated solar radiation.

The drug was submitted to degradation through a photocatalytic process, evaluating two systems: photocatalyst/radiation and photocatalyst/radiation/H_2O_2. TiO_2 and Fe-TiO_2 photocatalysts were used in suspension and supported on polystyrene polymer material (PS-photocatalyst). The results showed that only the systems TiO_2/radiation/H_2O_2 and Fe-TiO_2/radiation/H_2O_2 through catalyst immobilization promoted degradation of the study drug. In Table 1, the degradation percentages are set for these two systems, employing different radiations.

Table 1 — Results of clozapine degradation from preliminary study

System	Radiation	Catalyst (form)	Degradation (%)
TiO_2/radiation/H_2O_2	UV-C	Suspension	39.20
		Supported	54.10
	Sunlight	Suspension	10.20
		Supported	14.71
Fe-TiO_2/radiation/H_2O_2	UV-C	Suspension	31.89
		Supported	49.81
	Sunlight	Suspension	7.56
		Supported	12.03

Analyzing Table 1, the results show that the TiO_2 (pure) system presented higher efficiency when compared to the Fe-TiO_2 system. Although a difference of about 4.3% was observed between the systems, it does not justify the continuity of the system with the iron impregnated catalyst. It was also found that better results were obtained when using the supported catalyst. Regardless of the suspended system has a larger surface area available for reaction, the suspended particles of the catalyst cause a turbidity, which may have hampered the penetration of the radiation, thus not promoting the degradation of the compound under study (KOLTSAKIDOU et al, 2017). The superiority of the efficiency when adding the H_2O_2 is justified since this reagent

assists not only in the separation of charges when accepting an electron in the conduction band of the TiO_2, but also in the production of the ·OH that has a high oxidizing power (THIND; KUMARI; JOHN, 2018). This fact was also identified by Kolsakidou et al (2017), who found a greater degradation of antineoplastic cytarabine after addition of this reagent. Finally, it was found which systems irradiated by UV-C were more efficient than those that made use of solar radiation.

The low efficiency of the degradation process through solar radiation is related to the inactivation of TiO_2 under visible light, since the band gap width of this semiconductor varies between 3.0 and 3.2 eV (VELÁZQUEZ-MARTÍNEZ et al, 2018). Regarding the doping process, it has been shown that the introduction of iron into TiO_2 could alter the coordination environment of titanium in the crystalline lattice by modifying the structure of the electronic energy band in order to improve the separation and transition of photo-generated loads in the system (SUI et al, 2018). However, it was observed that the performance of the photocatalyst was not optimized as expected. This can be related to the impregnation methodology that was not effective to induce band narrowing or thermal instability of the metal-TiO_2 system, where in some dopant concentrations metal ions exist only as impurities (ADYANI; GHORBANI, 2018).

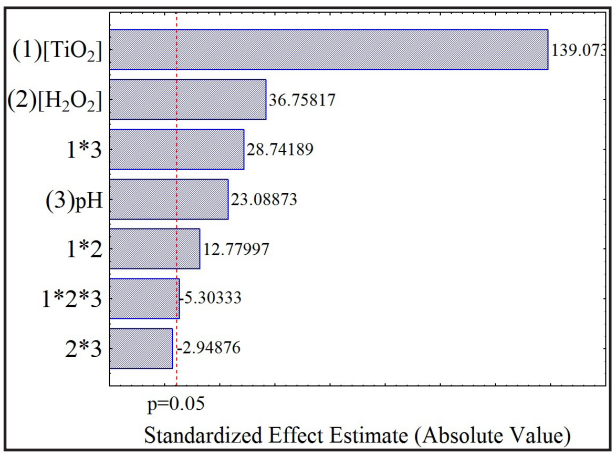
Due to the higher degradation efficiency presented by the use of immobilized TiO_2 in polymer material, scanning electron microscopy (SEM) and Fourier-transform infrared (FT-IR) analyzes of the PS support were performed before and after immobilization (PS-TiO_2). The description of the morphology and the spectrum of its surfaces were previously presented by Santos et al (2018), which is part of the same research group. From the micrographs, the authors observed that unlike the uncoated support, this one when impregnated with 0.1 g of the catalyst presented some irregularities, which were attributed the presence of aggregates of TiO_2 particles. The FT-IR spectra of the carrier were characterized by the presence of bands characteristic of PS bonds: Ar-H (Ar-aromatic), -CH, $-CH_2$ and C=C. For PS-TiO_2 material, it was observed that the PS bands were covered after the impregnation process due to the appearance of the band associated with the O-Ti-O bond. Therefore, the stage of evaluation of the variables involved in the AOP was passed.

3.2 Effect of parameters on the photocatalytic degradation of clozapine

In order to obtain a higher degradation efficiency of the CLZ by heterogeneous photocatalysis, the amount of catalyst was evaluated, $[H_2O_2]$ and pH used in the treatment, using a factorial design 2^3. Therefore, the effect of the individual contribution of the factors, as well as the interaction effect of the factors were determined based on statistical analysis through the Statistica 10.0 (StatSoft, 2010) program. Thus, the Pareto chart was generated for 95% confidence, as can be observed in Figure 2.

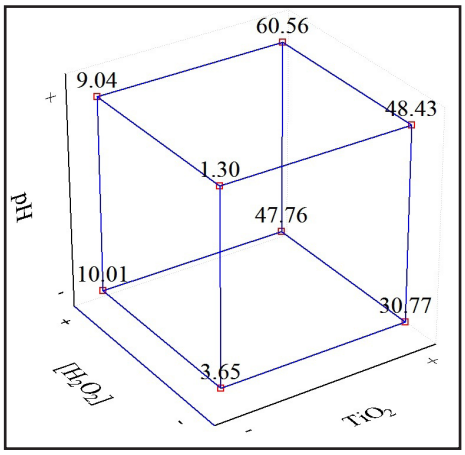
It is suggested after observation of Figure 2 that the main effects TiO_2, $[H_2O_2]$ and pH, as well as the combined effects of TiO_2-$[H_2O_2]$, TiO_2-pH and TiO_2-$[H_2O_2]$-pH significantly improved the photocatalytic degradation of the drug. The factorial analysis also reveals a strong influence of the amount

Figure 2 — Pareto chart for analysis of the variables in the photocatalytic degradation process of clozapine



of TiO_2 in this process. However, since the interaction between the three variables was significant for the TiO_2/UV/H_2O_2 system and that they cannot be analyzed separately, the cube graph was generated (Figure 3).

Figure 3 — Effects of interaction of three variables for photocatalytic degradation efficiency



From Figure 3, it was found that the higher the amount of TiO_2 mass supported, the $[H_2O_2]$ and the pH of the solution to be degraded, the higher the efficiency of the photocatalytic system. The maximum degradability of CLZ obtained in this study after 60 min of treatment was 60.56%, corresponding to the operating conditions of 0.15 g for TiO_2, $[H_2O_2]$ equal to 340 mg L^{-1} and pH equal to 9.

In fact, Kolsakidou et al (2017) state that the increase of the percentage of degradation as a function of the amount of catalyst is attributed to the addition of photo-generated active sites on the TiO_2 surface. These results in the formation of larger amounts of reactive oxygen species. It was also verified that the higher $[H_2O_2]$ studied promoted a better degradability, in agreement with what was predicted by Thind, Kumari and John (2018).

As for the pH value, when it is alkaline there is an increase in the formation of hydroxyl radicals due to the availability of hydroxide ions on the surface of the TiO_2 that can be

easily oxidized (ALALM; TAWFIK; OOKAWARA, 2016). This observation agrees with Dimitrakopoulou et al (2012) that also investigated the effect of pH on the photocatalytic oxidation of the amoxicillin drug using TiO_2 as a photocatalyst and obtained higher degradation in basic media.

3.3 Kinetic evaluation

Considering the experimental conditions determined in the previous step. Thus, the photocatalytic treatment took place over a period of 6 h. The obtained results are presented in Table 3.

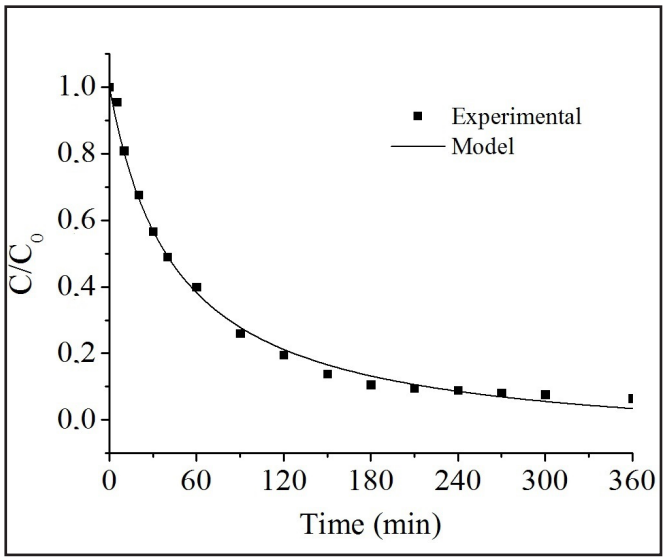
Table 3 — Kinetics data of clozapine degradation

Time (min)	% of degradation	Time (min)	% of degradation	Time (min)	% of degradation
5	4.46	60	60.04	210	90.49
10	19.11	90	73.95	240	91.03
20	32.27	120	80.42	270	91.80
30	43.28	150	86.13	300	92.34
40	51.01	180	89.39	360	93.48

Through this assay, it was found that in the first 3 h the degradation was 89.39%, then a small change in drug concentration over time was observed over the subsequent 3 h. Therefore, after 6 h of photocatalysis, 93.48% efficiency was reached in the treatment when using the proposed system.

The non-linear two-stage kinetic model proposed by Chan and Chu (2003) was used, once the experimental data on the temporal progression of the drug concentration did not follow conventional pseudo-first order kinetics (commonly used in AOP). The kinetic curve obtained from such a model is shown in Figure 4.

Figure 4 — Monitoring of the reaction kinetics with adjustment of the experimental data to the model of Chan and Chu



Through the analysis of Figure 4, it was observed that the experimental data fit the model well, obtaining a significant linear regression coefficient (0.995). In a complementary way, the adjustment proposed by the nonlinear model allowed to calculate the parameters of the investigated process, where ϱ and σ are experimental constants representing, respectively, the reaction kinetics and the oxidative capacity of the system.

Thus, the value of 0.024 min^{-1} obtained for 1/ρ indicates that the reaction mechanism followed the trend of a conventional pseudo-first order kinetics during the first 40 min, where the hydroxyl radical generation and the decay of the drug concentration were extremely fast. In the later stage the reaction may have been limited by the oxidant deficit and the competition of radicals between the analyte and the intermediates. Thus, the reaction stabilized gradually and after 360 min reached its maximum oxidation capacity (1.088).

Since the presence of H_2O_2 exerts a direct influence on COD (TALINLI; ANDERSON, 1992), an evaluation of the residual concentration of hydrogen peroxide was carried out by means of a colorimetric method with MQuant Test Strips (Merck) and it was found a residual value of 15 mg L^{-1}. In this case, considering the correction of the amount of the oxidant (Santana et al., 2018), it was verified that COD had a reduction of 78.30%. Based on this, it is inferred that the non-similarity between the conversion of the organic matter and the decrease of the drug concentration may be associated to the formation of intermediate products (Su et al, 2011; MARTÍNEZ-HUITLE; BRILLAS, 2009). However, the decrease in the COD level is in line with local disposal standards (BRASIL, 2003).

3.4 Mathematical modeling: artificial neural networks

The effect of the variables reaction time (min), mass of TiO_2 (g), $[H_2O_2]$ (mg·L^{-1}) and pH was evaluated in the heterogeneous photocatalysis process for degradation of the CLZ drug under ultraviolet radiation. The experimental data obtained under different operating conditions were modeled using ANN. Among the methodologies analyzed, it was verified that the RBF function was not so precise for describing the data, and, therefore, the best result was achieved when applying the MLP model with topology 4-3-1 and training algorithm back propagation, found in 141 epochs. The network architecture was composed of four neurons in the hidden layer, and the matrix containing the set of neural weights and bias, with sum of squares (SOS) error function, is presented in Table 2. In addition, it was found that the activation function of the hidden and output layers was tangential hyperbolic and logistic, respectively.

Calculations of the relative importance of the input variables in the degradation efficiency value of the CLZ were made through the data contained in Table 2. In this way, it was verified that the reaction time was the most influential factor in the degradation process (80.28%), followed by pH (8.08%), catalyst mass (7.25%) and $[H_2O_2]$

(4.39%). This fact is in agreement with the results obtained in the kinetic study, where it was observed that a higher rate of degradation was reached by extending the reaction time.

Finally, the ANN model developed to predict degradation efficiency was tested for accuracy. In this case, the values predicted by the network were compared with those obtained from the corresponding experiments, as can be observed in Figure 6.

Figures 6(a) to 6(c) represent the comparative analysis between the calculated and experimental values of the drug degradation percentage for the data set distributed between the training, test and validation subsets, respectively. In Figure 6(d) the grouping of the same is contained. From the analysis of these Figures it was verified that the data did not show dispersion tendencies, confirming that the back propagation algorithm as well as the selected topology (4-3-1) were adequate to predict the performance of the catalytic process with based on a neural network model. In view of this, the reliability of this was verified from the correlation coefficients obtained for the output variable, which were higher than 0.9856.

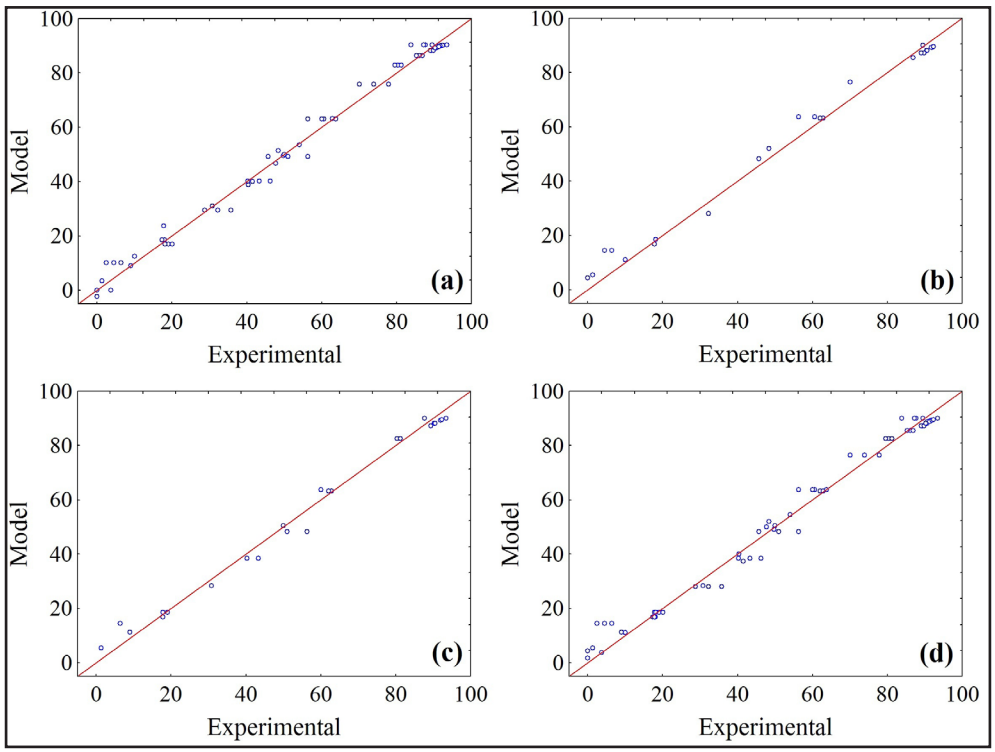
Hassani, Khataee and Karaca (2015) studied the photocatalytic degradation of the drug ciprofloxacin using TiO_2 in the form of nanoparticles. The modeling of the process was done through an ANN with a feed-forward back propagation architecture. The linear transfer function was used in the hidden and output layers, and 14 neurons were sufficient to represent the performance of the model. The input layer was composed of four experimental parameters; initial drug concentration, irradiation time, catalyst dosage and initial pH, which showed significant effects on the degradation efficiency. It was verified the reliability of the model once a correlation coefficient of 0.9864 was obtained for the test subset.

Monteiro et al (2018) also developed a new photo-

Table 2 - Weight matrix of the MLP 4-3-1 ANN

Neuron of hidden layer	Input					Output
	Weight				Bias	(Weight)
	Time	TiO2	[H2O2]	pH	-	-
1	-0.03193	-5.00526	0.23928	1.90290	3.30011	3.86134
2	-2.14163	1.63048	1.30698	0.11394	-0.16485	7.00913
3	0.96722	-0.73174	4.22824	0.30280	-1.57116	5.70832
			Hidden bias			-5.48801

Figure 6 — Parity plots of the models used: (a) training; (b) test; (c) validation and (d) training, testing and validation

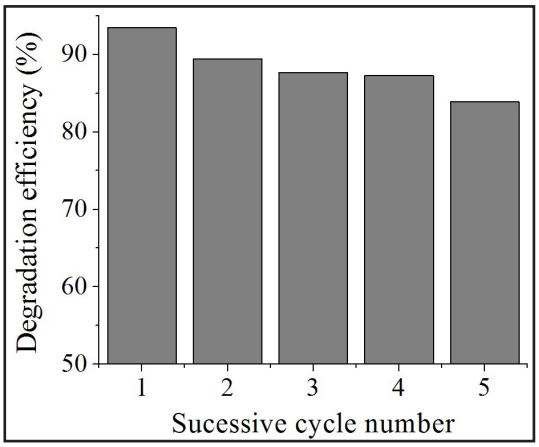


-Fenton process control strategy using ANN model MLP 4-4-1 to treat an aqueous solution containing the mixture of drugs nimesulide and ibuprofen. The experimental results indicated that such a model could accurately predict the conversion of organic matter with correlation coefficients equal to 1 for training, testing and validation. The training algorithm used was the BFGS 4567, the SOS error function, using as an activation function an internal layer Logistic and output Tanh.

3.5 Reactivity tests of the photocatalyst

The ability to reuse PS-TiO_2 support is an important factor, especially from an economic point of view for use on an industrial scale (AREEROB et al, 2018). The stability and reuse of the immobilized catalyst were tested by photocatalytic tests in five consecutive treatments for a period of 360 min each (Figure 5).

Figure 5 — Reuse behavior of PS-TiO2 in the photocatalytic degradation of the CLZ drug



From Figure 5, it was observed that there was no significant decay in the photocatalytic activity of the system after the cycles. Through the obtained data, the stability of the PS-TiO_2 system in the degradation of the drug was also verified, which showed a reduction of only 9.55% during the tests. The decrease in efficiency can be attributed to mass loss after the washing process. However, such a result demonstrates that TiO_2 immobilized on polystyrene material is stable to treatment of the drug.

3.6 Ecotoxicity assessment

The analysis of the toxicity aimed to estimate the toxicological potential of possible reaction intermediates formed during the photocatalytic treatment. The tests were performed with CLZ solution before and after treatment using the bacteria *Escherichia coli* and *Salmonella enteritidis*. The procedure was performed in triplicate, resulting in mean values with relative standard deviation lower than 2.8%.

From the data of growth and cell viability, it was observed that the use of heterogeneous photocatalysis for degradation of the drug in solution caused 100% of cellular inhibition for both organisms studied. In turn, the initial solution presented inhibition values equal to 65.59% and 70.86% for the bacteria *Escherichia coli* and *Salmonella enteritidis*, respectively. The increase in toxicity may be attributed to the formation of by-products, more toxic than the parent compound, or may be due to synergistic effects between the formed substances (ANTONOPOULOU; KONSTANTINOU, 2016). Thus, for a more complete analysis of the formation of new compounds, further studies are needed, since the available data on the acute toxicity of the intermediates are insufficient.

4. Conclusion

It was verified from the study that the PS-TiO_2/UV/H_2O_2 system promoted a higher rate of photodegradation of the drug clozapine. These results confirmed not only the heterogeneous photocatalysis efficiency in the proposed treatment but also revealed the viability of the TiO_2 deposition process in post-consumer polystyrene packages. In addition, the stability of the photocatalytic surface was demonstrated, obtaining reproducible data after five cycles of reuse, thus showing that the supported film can be applied in larger scale processes. The ANN MLP (4-3-1) model with four neurons was successfully employed in modeling the photocatalytic system within the experimental intervals adopted, whereas COD removal indicated that the proposed treatment was able to mineralize the organic compound. Regarding to the toxicological effects of the treatment, more specific and conclusive analyzes should be performed; as the degradation products were found to be more toxic than the organisms studied.

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