Advanced oxidation processes employment for the degradation of lamivudine: kinetic assessment, toxicity study and mathematical modeling

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ABSTRACT

Population growth has led to an increase in the production and use of synthetic compounds such as drugs, whose different classes are being investigated. However, the antiretrovirals are still poorly studied. Since the conventional treatments used in the effluent treatment plants have not been able to degrade these substances, other treatment techniques have been evaluated. Therefore, the objective of this work was to study and optimize the use of advanced oxidative processes (AOPs) in the degradation of lamivudine. It was found, initially, that the photo-peroxidation degraded 69% of the compound after 60 min of exposure to UV-C radiation, and that after evaluating the effect of the $[H_2O_2]$, a degradation of 95% was achieved by using 250 mg L^{-1} of this reagent. The reaction kinetics showed a good fit to the pseudo-first-order model, and the artificial neural network MLP (3-12-1) demonstrated a good accuracy, managing to predict percentages of degradation for the studied AOP. Toxicity tests indicated an increase in the toxic effect on seeds, but the same was not observed in relation to enterobacteria. In general, the appropriateness of the application of AOP in the degradation of the aqueous solution has been demonstrated, with the largest studies regarding the effects of toxicity.

Key words | artificial neural networks, pharmaceutical, photodegradation

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INTRODUCTION

Population growth and industrialization have resulted in an increasing use of natural and synthetic compounds to meet the needs of modern society (Manoli *et al.* 2019). Among the many compounds, pharmaceuticals stand out, with millions of tons being used and produced every day (Coors *et al.* 2018; Kumwimba *et al.* 2018). The pharmaceuticals encompass a large group of human and veterinary medicinal products used throughout the world. Among the most varied classes of pharmaceuticals are the antiretrovirals, which include drugs used in the treatment of herpes, hepatitis, influenza and the human immunodeficiency virus (HIV) (Zhou *et al.* 2016). Due to their application and efficacy in the treatment of HIV, the use of these drugs has grown rapidly around the world (Rwagitinywa *et al.* 2018).

The most commonly used drugs in the class of antiretrovirals are abacavir, nevirapine, stavudine, lamivudine and zidovudine. These drugs are routinely administered as a combination therapy in order to increase their effectiveness in HIV prevention and treatment (Kumari & Singh 2012). The growing use of these products by modern society has generated more and more concern since when not completely metabolized they are excreted via urine and feces,

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following the wastewater collection network to the wastewater treatment plants (WWTPs) (Zhou *et al.* 2016).

In the WWTPs, common physicochemical and biological treatments are not able to completely degrade these compounds, resulting in traces of them been found in the environment (Lindim *et al.* 2016). These substances have already been detected in WWTPs in Europe (Vergeynst *et al.* 2015) and especially in Africa, thanks to the outbreak of AIDS in the continent (Wood *et al.* 2017).

Once verified the presence of pharmaceutical contaminants in the environment and considering the adverse effects they can cause (genotoxicity and endocrine disruption), these compounds are now considered a growing environmental problem (Rodriguez-Narvaez *et al.* 2017). The problem intensifies since the pharmaceutical contaminants are released into the environment constantly, their sources act in an uninterrupted way and their use accompanies the population growth, showing the tendency to be observed in greater concentrations in nature over the years (Ebele *et al.* 2017).

Knowing this and that antiretrovirals are among the most dangerous pharmaceuticals with regard to their toxicity to algae and fish, it is necessary to evaluate the efficiency of treatments that act as an alternative or complement to the conventional ones (Manoli *et al.* 2019). Among the possible treatments to be employed are the electrocoagulation that has been applied as an alternative to replace conventional treatments, since it is able to remove the color of wastewater and decrease the levels of chemical oxygen demand (COD) and biochemical oxygen demand (BOD) (Wang *et al.* 2010) and the advanced oxidation processes (AOPs). This last process involves the production and application of hydroxyl radicals, characterized by being highly reactive, which act by oxidizing complex organic compounds, converting them to carbon dioxide, water and inorganic salts (Brandt *et al.* 2017). Different types of AOP have been used in the treatment of water and effluents, with the photo-peroxidation and the photo-Fenton processes being some of the most common and efficient (Russo *et al.* 2018).

The photo-peroxidation process consists of the addition of hydrogen peroxide (H_2O_2) in the presence of solar or ultraviolet (UV) radiation to promote the generation of hydroxyl radicals (·OH), which are able to oxidize highly complex organic pollutants such as pharmaceutical contaminants. Another important factor in the use of the UV/H_2O_2 process is that UV radiation also acts as a disinfectant, physically inactivating the microorganisms present in the matrix in the study (Ameta & Ameta 2018). The photo-Fenton process involves the reaction between Fe^{2+}/H_2O_2 and Fe^{3+}/H_2O_2, in the presence of UV radiation and/or visible light, with iron ions being the reaction catalysts (Linden & Mohseni 2014).

Studies that evaluated the performance of the application of different types of AOP have shown that photo-peroxidation and photo-Fenton processes are among the most efficient technologies for the degradation of pharmaceutical contaminants present in water and effluents. This area of research has been showing steady growth over the years, being possible to verify publications involving different types of drugs (Expósito *et al.* 2018; Liu *et al.* 2018). An *et al.* (2011) used heterogeneous photocatalysis to degrade lamivudine using TiO_2 at a concentration of 1 g L^{-1} in pH 9. For this, the authors needed 60 min and used a reactor with UV radiation. Yang *et al.* (2016) evaluated the efficiency of the AOPs UV/H_2O_2 and UV/$S_2O_8^{2-}$ for the degradation of reverse osmosis brines in the treatment of wastewater containing five pharmaceutical products, including lamivudine. These researchers found that the AOP can be used as a pre-treatment step in order to reduce the organic load of pharmaceutical contaminants and that the UV/$S_2O_8^{2-}$ process, although resulting in an increase in salinity, may be preferable for the brine treatment than the UV/H_2O_2.

Like any other type of process that involves the presence and use of chemical reactions, the AOP has a reactive kinetics that controls the process and can be modeled (Stefan 2018). In general, the degradation kinetics of organic contaminants using AOPs can be described phenomenologically by rate expressions of pseudo-first-order (C/C_0 versus time relations), with this kinetic behavior also being observed for most pharmaceuticals (Miklos *et al.* 2018).

When working with AOPs for the treatment of persistent organic pollutants, an important factor to be taken into account is that the intermediates and products formed may be more biologically active and consequently more toxic than the parent compounds. For this reason, assessing toxicity is a crucial step after the application of AOP as treatment (Sharma *et al.* 2018). These tests require the use of

organisms with significant ecological representation, sensitivity and availability (Beiras 2018). A wide variety of species can be used in ecotoxicological tests, such as algae, bacteria, vegetables, fish and invertebrates (Priac *et al.* 2017).

Different variables contribute to the efficiency of varying types of existing AOP. Models were executed in order to predict the efficiency of the process. These studies apply mathematical models through artificial neural networks (ANNs) (Jalil *et al.* 2014). Monteiro *et al.* (2018) used the multilayer perceptron (MLP) ANN model to predict and describe the degradation data by AOP of the pharmaceuticals nimesulide and ibuprofen using the photo-Fenton process.

In this context and knowing that treatment processes for the degradation of the pharmaceutical lamivudine are still poorly studied when compared to other classes of drugs (Funke *et al.* 2016), this work aims to promote the degradation of the antiretroviral lamivudine using AOPs. For this, different AOP will be analyzed, as well as the kinetics of degradation and toxicity of the solutions before and after treatment using *Lactuca sativa* and *Eruca sativa* seeds and strains of *E. faecalis*, *E. coli* and *P. mirabilis*.

MATERIALS AND METHODS

Degradation of the aqueous solution of lamivudine: preliminary study

In order to determine the most efficient process for promoting the degradation of the pharmaceutical lamivudine, an aqueous solution containing 5 mg L^{-1} of this compound was subjected to different AOPs in UV-C (Zaidan *et al.* 2017) and sunlight (Santana *et al.* 2017) bench reactors. Initially, the photo-Fenton and photo-peroxidation AOP were tested, as well as the photolysis process for both radiations. To this, 50 mL of the aqueous solution containing the pharmaceutical were irradiated for a period of 60 min, and when applicable, the concentrations of hydrogen peroxide and iron used were, respectively, 100 and 5 mg·L^{-1}. As reagents were used: H_2O_2 (brand: Química Moderna) previously standardized 30%, while the iron used was $FeSO_4{\cdot}7H_2O$ (brand: F. Maia).

The analysis of the pharmaceutical before and after the degradation was performed in a UV/Vis spectrophotometer (ThermoScientific, model Genesys 10S), at a wavelength of 271 nm. The linearity range was 1.0–10.0 mg L^{-1}. It is important to note that the lamivudine active principle used to prepare the solutions was provided by the Laboratório Farmacêutico do Estado de Pernambuco (LAFEPE) (Lot 17774).

Univariate study of the hydrogen peroxide concentration

Knowing the treatment that presented the greater percentage of degradation for the compound under study, the next stage was the optimization of the working conditions. For that, the concentration of hydrogen peroxide was varied in the following values: 80, 100, 150, 200, 250 and 300 mg L^{-1}. The addition of H_2O_2 was done fractionally at the times of 0 and 15 min. Once this study was carried out, it was verified that two of the concentrations presented similar results so that to determine which one should be used in the kinetic study, two more tests were performed with each one. For this, the aqueous solution was exposed to the radiation for periods of 90 and 120 min (with H_2O_2 addition in 0, 10 and 20 min, in order to further improve the efficiency of the process). All assays were performed at a lamivudine concentration of 5 mg L^{-1}.

Kinetic monitoring of the UV/H_2O_2 process and residual H_2O_2 determination

Once the ideal working conditions were defined (the most efficient type of AOP and the ideal concentration of H_2O_2), the kinetic monitoring of the degradation reaction was carried out, with the replacement of the hydrogen peroxide at the times of 0, 10 and 20 min. Starting with the initial concentrations of lamivudine of 5 and 10 mg L^{-1}, 1 L of the solutions containing this drug were subjected to radiation. These were placed in a glass refractory, with aliquots of 3 mL being withdrawn at the times of 5, 10, 15, 20, 25, 30, 40, 50, 60, 70, 80 and 90 min for the evaluation of the lamivudine concentration in a UV–Vis spectrophotometer. The choice of the final kinetics time was made

from the stabilization of the final concentration of the compound under study.

The experimental data obtained during the AOP treatment were adjusted to the first-order, second-order and pseudo-first-order kinetic models; the latter was developed by Chan & Chu (2003). Afterwards, the values of the linear regression coefficients were verified, in order to analyze if there was a good fit to said model.

Artificial neural networks

ANNs were used to verify the influence of the operational parameters used throughout the process of the pharmaceutical degradation. For this, the Statistica 8.0 software was used to propose a neural network capable of predicting the percentage of degradation of lamivudine, taking into account the variables studied throughout the process.

Thus, methodologies with MLP and radial basis function (RBF) configurations were used, comprising three layers: input, hidden intermediate and output. The transfer functions tested were identity, logistic, tanh, sinusoidal and exponential. The input variables consisted of the concentration of hydrogen peroxide [H_2O_2] (mg L^{-1}), reaction time (min) and initial concentration of lamivudine (mg L^{-1}). Then, an analysis of the influence of each parameter on the percentage of degradation of the pharmaceutical studied was done. A set of 96 experimental data to feed the network was used, which was divided into training, test and validation subsets in a proportion of 70, 15 and 15%, respectively.

Toxicity assessment of the lamivudine solution before and after treatment

Once the lamivudine degradation process was understood from the kinetic study, a toxicity analysis of the pharmaceutical solution, before and after the application of the AOP, was started. For this, commercial seeds of *L. sativa* (American lettuce) and *E. sativa* (arugula) were exposed to the before and after treatment solutions (SBT and SPT, in each case) at 100% concentration.

The assays were performed in a Petri dish using qualitative filter paper as the carrier medium. Ten seeds were inoculated into each plate, and then 2 mL of the solutions were added at a temperature of 25 ± 1 °C and protected from light for 5 days. These tests were carried out under the control of positive and negative control samples, adding to the seeds, respectively, distilled water and 3% boric acid, following the same procedure for SAT and SPT. Each test, including the controls, was performed in triplicate. After 5 days, the number of germinated seeds in each plate was evaluated, as well as their root growth. From these data, the relative growth index (RGI) and the germination index (GI), as described by Young *et al.* (2012), were determined.

In addition to the seeds of lettuce and arugula, the bacteriological toxicity was also evaluated in strains of *E. faecalis*, *E. coli* and *P. mirabilis*. These three strains were chosen because they represent microorganisms that are components of the intestinal biota of humans and animals, being consequently present in domestic effluents and conducted to WWTPs.

The toxicity study of the lamivudine solutions, before and after treatment, using these organisms, applied the brain heart infusion agar (BHI) overnight method at 36 °C. The colonies were resuspended in sterile saline solution (0.15 M NaCl) and adjusted turbidimetrically at a wavelength of 600 nm (OD_{600}) to obtain equivalent suspension to 10^5 colony forming units (CFU) per mL. For the assay, the samples were filtered on sterile 13 mm × 0.22 μm PVDF syringe filters. SAT and SPT were diluted to 1:10, 1:100, 1:250, 1:500, 1:750 and 1:1,000 in sterile ultrapure water; 50 μL of the suspensions of *E. faecalis*, *E. coli* and *P. mirabilis* 10^5 UFC mL^{-1} in NaCl 0.15 mol L^{-1} were incubated. Before and after the incubation period, the contents of each treatment were transferred to 96-well microtiter plates for reading at 600 nm (OD_{600}) for determination of growth percentage, compared with the negative control (100% growth). Each assay was done in triplicate and three independent experiments were performed.

RESULTS AND DISCUSSION

Degradation of the aqueous solution of lamivudine: preliminary study

Initially, a spectral scanning analysis of lamivudine was performed (Figure 1), in which the presence of the maximum absorbance is perceived at a wavelength (λ) of 271 nm.

Analyzing Figure 1, it was decided not to take the peak close to 200 nm into account, considering that in the 190–200 nm range, there is a limitation of the equipment used. Considering the maximum λ, the other experiments were conducted only in a quantitative way, without spectral scanning. In the preliminary study, the photolysis and the AOPs photo-Fenton and photo-peroxidation were evaluated as treatments. After performing the tests using sunlight and UV-C radiation, it was found that the photolysis and photo-Fenton processes were inefficient in the degradation of lamivudine at the monitored wavelength (271 nm). The photo-peroxidation process was efficient when using UV-C radiation, reducing the concentration of the drug by 79.8%, a fact that did not occur when using sunlight, which also failed to degrade the study. Therefore, the photo-peroxidation process employing UV-C radiation was considered the best treatment and it was then used in the course of this study.

Univariate study of hydrogen peroxide concentration

At this stage, the drug solution was exposed to radiation under varying concentrations of hydrogen peroxide (80, 100, 150, 200, 250 and 300 mg L^{-1}) added at two times (0 and 15 min). Considering that the results obtained for the concentrations of 250 and 300 mg L^{-1} were similar, it was decided to extend the treatment time in order to safely identify which of the two concentrations would be responsible for promoting a greater efficiency of the process. The values of the degradation percentages obtained for these experiments are shown in Table 1.

The analysis of Table 1 indicates that the tests from 5 to 10 obtained the best percentages of degradation, making it possible to verify that the pairs of experiments 5–8; 6–9 and 7–10 led to similar results. Analyzing the 90 and 120 min data, it was observed that there was no significant difference in the percentage of degradation between the two concentrations studied (250 and 300 mg L^{-1}); therefore, the lowest concentration between these two was chosen for the kinetic study. It was decided to work with this concentration since there is a cost associated with the use of the reagent, and that when used in excess, it acts as a limiting agent of the employed AOP (Mitre *et al.* 2012). In addition, it was found that a triple fractionation of the oxidizing agent led to higher values of degradation when compared to a double fractionation, as described by Lucena (2018).

In order to confirm the obtained results, the data of the variation of the hydrogen peroxide concentration versus the time were evaluated through a simple factorial design 2^2 with a central point in triplicate. The evaluated factors were the [H_2O_2] (with 250, 275 and 300 mg L^{-1} being, respectively, the minimum, central and maximum levels studied) and the time (with 60, 90 and 120 min being the levels studied). Using the Statistica 8.0 software, a Pareto chart was generated for the factorial design data (Figure 1).

When analyzing Figure 2, it is possible to confirm the results for the analysis of the variation of the hydrogen

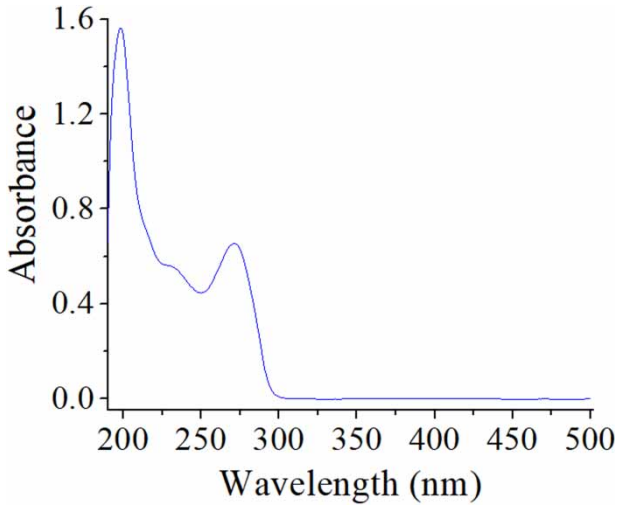

Figure 1 | Scanning analysis of lamivudine in the range of 190 and 500 nm.

Table 1 | Results from the lamivudine degradation by varying the concentration of H_2O_2

Assay	[H_2O_2] (mg L^{-1})	Time (min)	Degradation (%)
1	80	60	55.78
2	100	60	61.10
3	150	60	66.42
4	200	60	68.62
5	250	60	69.36
6		90	94.86
7		120	95.56
8	300	60	69.91
9		90	95.05
10		120	95.56

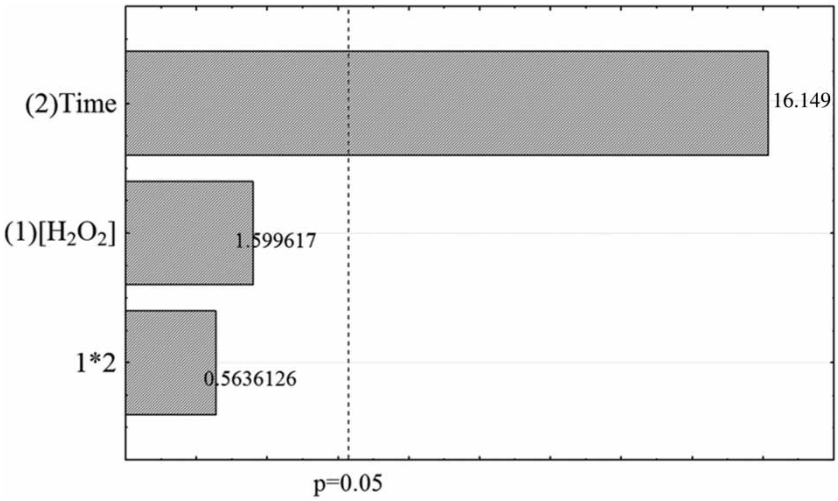

Figure 2 | Pareto chart for evaluation of lamivudine degradation.

peroxide concentration, in which it was found that by increasing the concentration from 250 to 300 mg L^{-1} the process does not suffer more influence from this variable. In this figure, it is also observed that the time variable is significant, which can be better analyzed through kinetic monitoring. Based on the factorial planning data, it was possible to obtain Equation (1) that shows the influence of reaction parameters on the percentage of degradation for the lamivudine:

$$\%\,\text{of degradation} = 614.2962\,\text{Time} + 6.0270\,[H_2O_2] + 0.7482\,\text{Time} \cdot [H_2O_2] \quad (1)$$

Kinetic monitoring of the UV/H_2O_2 process by UV/Vis

After defining the best working conditions for the AOP previously selected and obtaining the ideal H_2O_2 concentration, the next step was the kinetic monitoring of the reaction. For this, the photo-peroxidation/UV-C system was used, applying an $[H_2O_2]$ of 250 mg L^{-1}, at a temperature of 35 ± 1 °C and a pressure of 1 atm. For the study, two initial concentrations of the pharmaceuticals (5 and 10 mg L^{-1}) were evaluated and then, with the percentages of degradation obtained, the adjustment of the experimental data to different models was evaluated. Table 2 shows the results of concentration and percentage of pharmaceutical degradation over time.

Table 2 | Monitoring the degradation of lamivudine solutions

Time (min)	Lamivudine concentration (mg L^{-1})	Degradation (%)	Lamivudine concentration (mg L^{-1})	Degradation (%)
0	5.79	–	10.40	–
5	4.15	28.23	7.97	23.34
10	3.01	48.03	6.19	40.51
15	2.24	61.29	4.94	52.54
20	1.79	69.09	4.13	60.25
25	1.53	73.55	3.72	64.20
30	1.21	79.10	2.80	73.08
40	1.16	79.97	2.34	77.50
50	1.14	80.31	2.13	79.52
60	1.06	81.69	2.11	79.71
70	1.04	82.04	1.93	81.44
80	0.98	83.07	1.91	81.63
90	0.94	83.77	1.89	81.83

When analyzing Table 2, it was noticed that there is a rapid decay of the pharmaceutical concentration in the first 30 min, which can be attributed to the higher generation of highly oxidizing radicals in the first minutes of the reaction, which are available to react and degrade the pollutant more quickly. After this treatment period, as expected,

the decay rate of the degradation decreased, reaching the stability after 90 min. In addition, it was demonstrated that the proposed AOP is efficient to degrade the drug in a slightly higher concentration than that used until then, with a similar efficiency of about 82% after the same treatment period. It was verified, also, that after 90 min of exposure to radiation, approximately 84% of degradation was obtained by degrading 1 L of the aqueous solution of lamivudine, a result lower than that obtained for the same process using a smaller sample volume (50 mL). Based on the data presented in Table 2, different kinetic models could be applied, like: (a) first-order; (b) second-order and (c) nonlinear model proposed by Chan & Chu (2003). Figure 3 shows the kinetics graphs with the respective model adjustments and linear regression coefficients for the three models evaluated.

Analyzing the data from Figure 3, the same kinetic behavior is observed when treating aqueous solutions containing 5 and 10 mg L^{-1} of lamivudine. It was also observed that the experimental data did not present a good fit to the first-order model, for which the values of linear regression coefficients obtained were below 0.82. By verifying the fit of the experimental data, these were better represented by the second-order and nonlinear models

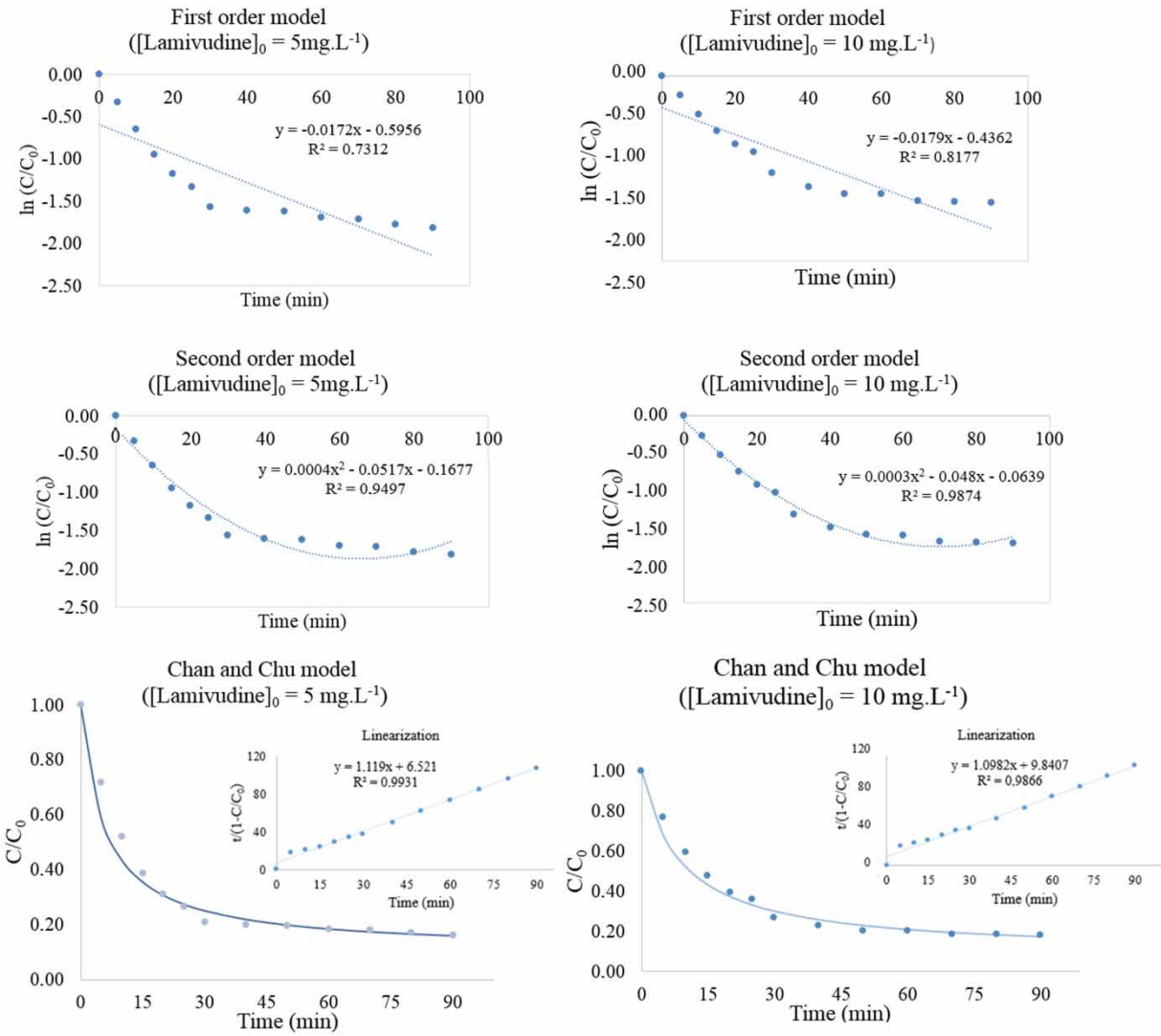

Figure 3 | Kinetic adjustments to first-order, second-order and Chan and Chu models for the degradation of aqueous solutions of lamivudine.

(Chan and Chu). Among these two models, no significant difference was observed for the treatment of 10 mg L^{-1} of the pharmaceutical (both with $R^2 \approx 0.98$); but for 5 mg L^{-1}, there is a greater adequacy to the nonlinear model, reaching a regression of 0.9931. This behavior was expected since the model proposed by Chan and Chu takes into account a high rate of decay of the concentration of the contaminant in the first minutes, a fact that is not observed in a first-order model, where the reaction rate is proportional throughout treatment. It is also due to this finding that the process employed presents a good fit to the second-order model, but inferior to Chan and Chu's nonlinear model since in the final times there is a stabilization of the process, reaching an equilibrium; a fact that is not so well described by the second-order model. Thus, it can be said that the nonlinear model of pseudo-first-order is the one that best describes the treatment via AOP for lamivudine degradation.

Artificial neural networks

From the simulations performed through the Statistica 8.0 software, it was verified that among the models studied, the MLP was more accurate for data analysis. In this case, the best network was composed of 12 neurons in the hidden layer (MLP 3-12-1) and R^2 values equal to 0.984, 0.972, and 0.993 for training, testing and validation, respectively. The activation function of the inside layer and output were Tahn and Exponential, with an SOS error function. The training algorithm was BFGS, found in 109 epoch. This ANN model was tested for accuracy, where the values predicted by the network were compared with those obtained from the corresponding degradation experiments, as can be seen in Figure 4.

From the analysis of Figure 4, to predict the performance of the degradation process based on a neural network model, the suitability of the topology and selected

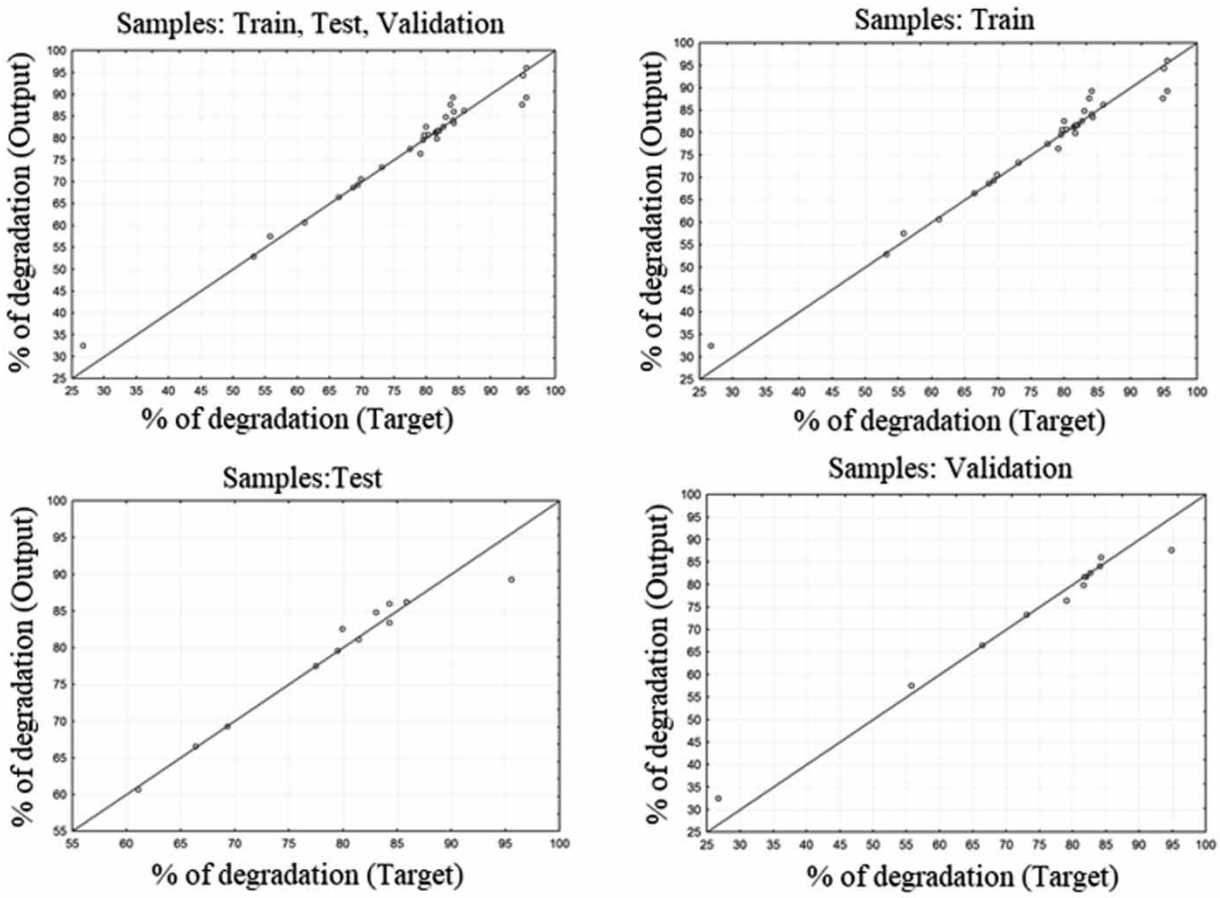

Figure 4 | Model adjustments graphs for training, testing and validation of the ANN.

algorithms was confirmed. The reliability of the model was verified from the correlation coefficients obtained for the output variable, which were higher than 0.972. In addition, Figure 5 shows the architecture diagram for the MLP network 3-12-1.

Thus, it can be said that the ANN MLP 3-12-1 neural network can predict the degradation by AOP, in percentage, of the lamivudine drug by varying the input variables ($[H_2O_2]$, time and initial lamivudine concentration). In this way, different combinations could be tested in order to obtain the desired result.

Toxicity assessment of the lamivudine solution before and after treatment

The seeds of *L. sativa* and *E. sativa* were tested with the pharmaceutical solutions before and after treatment with the AOP, along with negative (NC) and positive controls, respectively, ultrapure water and boric acid 3%. After 5 days of incubation in the dark, it was verified that an average of 8.33 seeds of *L. sativa* germinated in the NC; this number dropped to 5 for the before treatment solution (SBT) and to 3 for the post-treatment solution (SPT). For the seeds of *E. sativa*, an average germination of 9.33, 9 and 9 was observed for NC, SBT and SPT, respectively. This indicates that the germination of *E. sativa* was not influenced by the solutions studied, a fact that did not occur for *L. sativa*, where there was a reduction of more than 50% of the germination for the SPT when compared to the NC.

Considering these data, and in view of the average root growth, the values of the percentage GI and RGI were calculated according to Young *et al.* (2012). The results obtained for the two indices were (a) for *L. sativa* – 1.00 and 100% (water); 0.83 and 49.88% (SBT) and 0.42 and 15.12% (SPT); and (b) *E. sativa* – 1.00 and 100% (water); 0.84 and 80.98% (SBT) and 0.60 and 57.71% (SPT), respectively.

Considering the affirmation of Young *et al.* (2012), that for RGI values lower than 0.8, there is inhibition of root growth, it can be stated that the solution of degraded lamivudine showed inhibition of the growth for both species. This indicates the presence of a toxic effect from the degradation by-products. According to Bedse *et al.* (2009), lamivudine ($C_8H_{11}N_3O_3S$), when subjected to forced degradation tests with oxidative stress, leads to the formation of two by-products with the same molecular formula ($C_8H_{11}N_3O_4S$), and with a theoretical mass of 246.0549 g mol^{-1}. Thus, in order to obtain more information about the toxicity of the intermediates the effects of SBT and SPT were studied in bacteriological strains of three species: *E. faecalis*, *E. coli* and *P. mirabilis*. Figure 6 contains the results of these analyses.

When comparing the percentage of growth of the bacteria for each dilution of the solution before and after treatment (SBT and SPT) with the control used (ultrapure

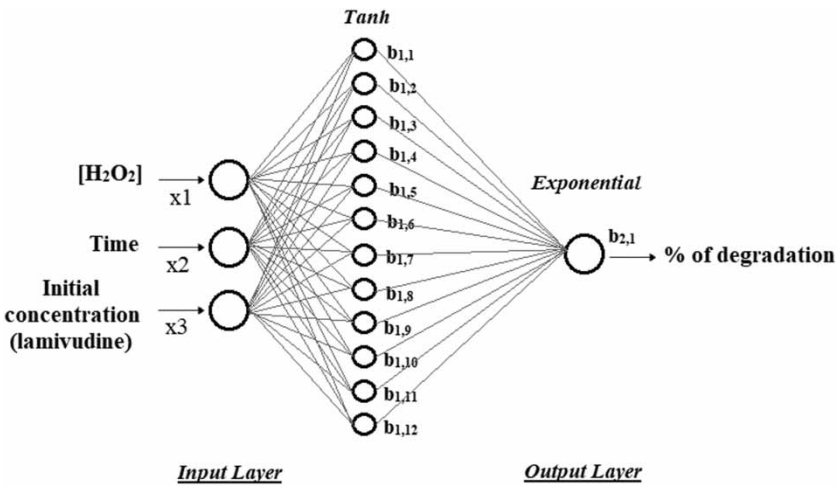

Figure 5 | Architecture diagram of ANN MLP 3-12-1.

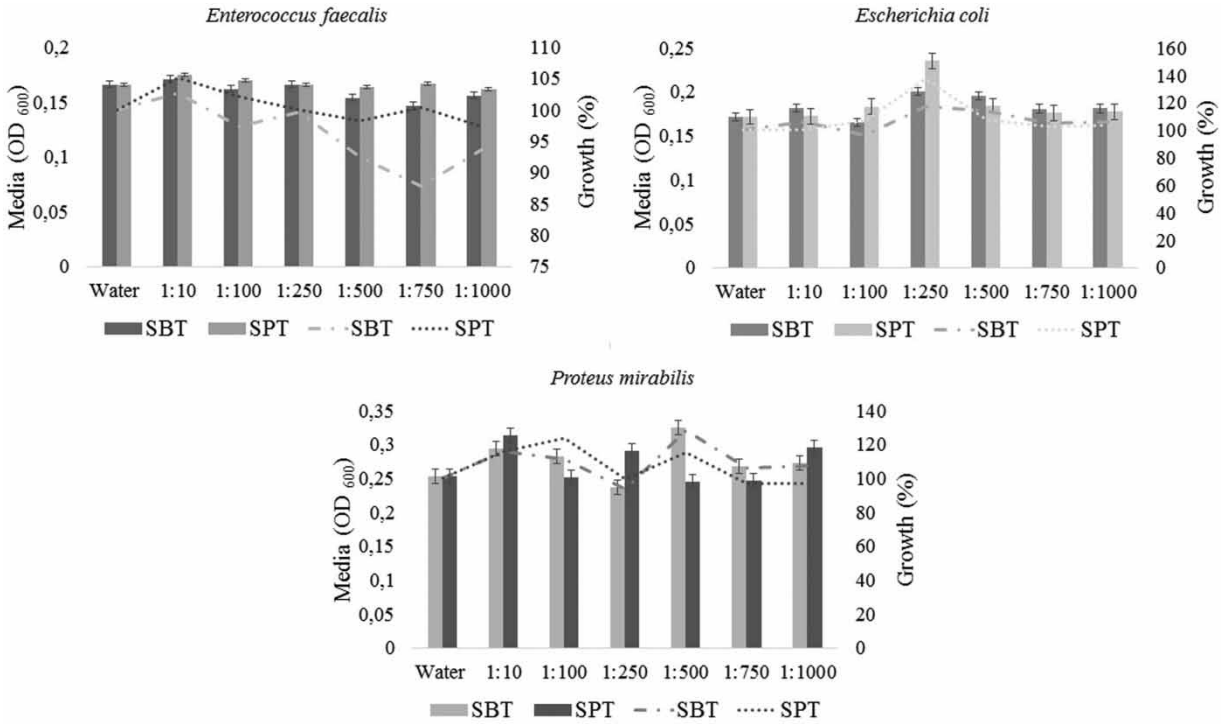

Figure 6 | Bacteriological growth analysis for strains of *E. faecalis*, *E. coli* and *P. mirabilis* against lamivudine solution before and after treatment.

water) (Figure 6), it was verified that there was no significant change. This leads to the conclusion that lamivudine solutions before and after treatment had no toxicological effect on these microorganisms. Thus, there is an indication that there will be no compromise in the composition of domestic sewage and, therefore, in biota. Given the above, no adjustment is required in the treatment conditions with the photo-peroxidation process employed.

CONCLUSIONS

Based on the data generated in this work, it was verified that the photo-peroxidation assisted by UV-C radiation is an efficient process for the degradation of the antiretroviral lamivudine in an aqueous solution. Through optimized working conditions, the process was able to satisfactorily reduce the initial concentration of the pharmaceutical on a bench scale. However, the intermediate compounds formed in the reaction had toxic effects on some species of test organisms; therefore, a more detailed study is necessary to approach the problem. The percent of drug degradation was successfully predicted by applying a three-layer ANN MLP model with 12 neurons in the hidden layer and BFGS training algorithm.

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