

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

3,900

Open access books available

116,000

International authors and editors

120M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Design of Experiments Applied to Antibiotics Degradation by Fenton's Reagent

André Luís de Castro Peixoto,
Ademir Geraldo Cavallari Costalonga,
Mateus Nordi Esperança and
Rodrigo Fernando dos Santos Salazar

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/68097>

Abstract

Advanced oxidation technologies (AOTs) are processes affected by a large number of parameters such as iron (Fe^{2+}) and H_2O_2 concentrations, pH, temperature, light intensity and chemical composition (organics and inorganics). In addition, for different industrial chemical processes, there are different effluents, which greatly vary in chemical composition from each other, not allowing a unique approach for all of them. Thus, it is necessary to adjust AOT parameters to the specific effluent to be treated. In such context, statistical design of experiments (DoE) and response surface methodology (RSM) emerge as important and widely used tools to determine the effects of multiple variables on wastewater treatment processes such as photo-Fenton. A revision of academic studies based on degradation of antibiotics-containing effluents is presented. The chapter also presents commercial cases of AOT and electrical efficiency considerations.

Keywords: design of experiments, planning of experiments, optimization, advanced oxidation technology, Fenton's reagent, pharmaceutical compounds, full scale, figures-of-merit electrical efficiency

1. Introduction

Analgesics, hormones, anaesthetics, mainly antibiotics are pharmaceutical compounds that can lead to damages to the environment and public health when are improperly discarded. The main sources of contamination by compound drugs are due to wastewater, effluent and inadequate disposal by pharmaceutical industries. Many studies related the presence of these

compounds in surface water, groundwater, tap water and urban sewage samples. On the other hand, social and legal demands on the impact of chemical effluents on the environment have driven the development of many procedure and technologies in order to treat wastewater and poisoning water by the presence of these compounds.

By this way, those technologies based on advanced oxidation technologies (AOTs) have been extensively studied for the decomposition of a series of persistent and recalcitrant compounds present in wastewater into less toxic and/or biodegradable substances. In many cases, these technologies result in the formation of CO_2 , H_2O and inorganic compounds of all non-oxygen heteroatom from the oxidation of the organic matter present in the persistent compounds. The AOTs were defined by Glaze et al. [1] as physicochemical processes involving the generation of transient species of high oxidizing power, among which the hydroxyl radical (OH) stands out [1]. This radical has a high oxidizing power ($E_{\text{PH}_{\text{HO}\cdot/\text{HO}}} + 2.8\text{V}$, 25°C) and can be generated by photons (including sunlight) or by other forms of energy, being able to mineralize organic pollutants to non-toxic as CO_2 and H_2O . Some AOTs, such as heterogeneous photocatalysis, radiolysis and other advanced techniques, allow the transformation of toxic contaminants that are not susceptible to oxidation, such as metal ions and halogenated compounds [2]. Among the most studied AOTs, heterogeneous photocatalysis employing semiconductors and/or $\text{H}_2\text{O}_2/\text{UV}/\text{semiconductor}$ has played an important role in relation to emerging technologies for water treatment, due to the large number of investigations on the subject compared to other AOTs studied, which is most extensively presented in the literature [2, 3].

The catalytic oxidation of tartaric acid in the presence of ferrous salts and hydrogen peroxide was reported by Fenton in the mid-1890s. The oxidation of organic compounds under UV irradiation in the presence of ferric ion in acidic media was verified in the 1950s when it was postulated that the electron transfer initiated by the irradiation resulted in the generation of $\cdot\text{OH}$, responsible for the oxidation reactions [4]. Degradation efficiency of different classes of toxic organic compounds has made the photo-Fenton process activated by sunlight quite attractive, investigating the use of AOT based on Fenton processes, Photo-Fenton, as well as derived processes for different applications of environmental interest. In this way, the degree of interest has led to the rapid technological development of this class of AOT. Consequently, it is possible to find these pilot scale systems being tested for the final treatment of water for supply and as tertiary stage of municipal sewage treatment in Canada and Spain [5, 6].

As scientific and technological advances are made involving the use of different advanced oxidative technologies for effluent and wastewater remediation, the need to optimize these processes in order to be commercially available for the mineralization and stabilization of recalcitrant compounds is growing. In this sense, statistical tools based on chemometrics and design of experiments (DoE) have been used to evaluate the figures of merit to extend the range of commercially available systems. Chemometrics is defined as the application of mathematical and statistical models and methods for the solution of chemical problems, in order to maximize the data collection and to allow the extraction of useful information from the obtained data. The development of analytical equipment and chemical processes has led to a need for advances in experimental design methods, with the objective of obtaining secure information in a shorter time span for instrumental calibration and process efficiency analysis [7, 8].

Design of experiments (DoE) is defined as a set of statistical techniques applied to the planning, conduction, analysis and interpretation of controlled tests to find and define factors that influence the values of a parameter or a group of parameters. Its basic principle allows varying all the levels of all the variables, discrete or continuous, in a programmed and rational way, reducing the number of experiments without limiting the number of factors to be analysed. The use of complete factorial design becomes necessary when assessing the influence of variables, without running the risk of excluding factors or interactions that may be important [8]. Although for economical reasons, fractional factorial design is usually applied [7, 8].

However, only a small fraction of the scientific papers related to advanced oxidative technologies makes use of the electrical energy consumption figure-of-merit (EE/O). In our understanding, one of the best response variables that could be used in the study of wastewater degradation (pharmaceuticals or not) would be EE/O. With EE/O as variable response in a design of experiments, not only the main factors associated to the advanced oxidative processes (light source, catalyst, H_2O_2 , O_3 , Fe^{2+} etc.) but also the kinetics of the reaction and the energy cost would be used in an experimental study to reach the objective of the process. There is a gap in the scientific community regarding the use of the EE/O tool that could be explored by researchers in conjunction with the traditional statistical tool design of experiments.

In this sense, the aim of this chapter is to present the use of physicochemical systems based on advanced oxidation technology (AOT) for the effluents remediation containing pharmacological residues. In addition, it is intended to present the state-of-the-art about design of experiments (DoE) and other statistical tools in order to evaluate the figures-of-merit of photochemical reactors for the treatment of pharmaceutical effluent.

2. Basics of DoE

Design of experiments (DoE) is not a set of formulas but a technique used to plan experiments, behind there is a theoretical support with good reasoning math. Basically, it looks good statistical accuracy in response and a lower cost. Therefore, it is a technique of great importance for the industry and its use permits the obtaining of more reliable results and thus saving time and resources.

Design of experiments, in statistics, refers to the whole area of studies that develops technical planning and analysis of experiments. The main techniques of planning experiments are old; however, the great many of these techniques requires a good amount of calculations being essential to use the computational resources.

An experiment is nothing else than a procedure or test in which deliberate alterations are made in input variables of a process to observe, identify and evaluate possible alterations in the response variable, as well as the reasons of such alteration. DoE is a test, or series of tests in which the changes in input variables of a process are known, for then, observe which changes occur in the response variable.

Why plan an experiment? To have a set of rules or way outline to obtain a mathematical model that adequately describes the process investigated, using as few experiments as possible. The planning will let efficiency and economy in the process.

The planning of an experiment investigates potential factors whose variation might impact the response-variable (process output). The planning will be used to obtain valid results and introduce objective conclusions. The planning must maximize the quantity of information that can be obtained for each variation performed. The experimental factor is the variable that is controlled to check its effect in the response; the factors can be classified into two types: qualitative or quantitative. A proper planning has to take into consideration some items: a DOE investigates a list of potential factors whose variation might impact the process output

- Recognition of the problem
- Set experiment objectives
- Define and know the resources
- Optimize resources to meet the objective
- Carry out the experiment and analysis of results

2.1. Recognition of the problem

The Fenton's process consists in the use of $\text{H}_2\text{O}_2/\text{Fe}^{2+}$ and was first observed by Fenton in 1894. In solution, ferrous ions (Fe^{2+}) initiate and catalyze the decomposition of H_2O_2 and lead to the formation of hydroxyl radical ($\cdot\text{OH}$). Mixtures of Fe^{2+} and H_2O_2 are called Fenton reagent. If Fe^{2+} is replaced by Fe^{3+} , it is called Fenton-like reagent.

The efficiency of this process is directly linked or related to other experimental parameters, such as pH, concentration of hydrogen peroxide, iron concentration, concentration of organic matter, intensity of radiation UV-Vis, exposure time and volume of solution.

2.2. Set the experiment objectives

A good problem implies to define the goal of the experiment. This objective must be non-biased, specific, measurable and should lead to a practical result. The aim is to answer the following question: What do you want to investigate? It depends on the operational variables (factors) to be studied, and the way they relate to each other (synergism or antagonism effects) in the process. The DoE allows evaluating synergic and antagonistic effects of the operational variables simultaneously and with a reduced number of experiments. Therefore, one must investigate the changes in the input variables of this process and then observe which changes occur in the response variable. The objective of experimental design is to optimize the experimentation process to obtain as much information as possible.

2.3. Define and know the resources

One must choose and select the variables that are possible to be studied and which probably interfere with the system. In the photo-Fenton process, the variables most studied are pH,

concentration of hydrogen peroxide, the concentration of iron, concentration of organic matter, intensity of radiation (UV-Vis) and time of exposure. The variable response must be chosen with the assurance that the result really supplies useful information about the process under study. One of the possible variables was chosen is the Total Organic Carbon (TOC) removal rate.

The choice of factors and levels must encompass the ranges over which these factors will vary and the specific levels in which each assessment will be carried out. The variables that were not selected must be fixed during the entire experiment. Instruments, equipment, places, people, reagents, time spent and cost of the process are external variables to the process that may influence the application of the method after optimization.

2.4. Optimize resources to meet the objective

Optimization of resources (e.g. chemicals, materials, energy and staff) is a mandatory part of a process. In this step, the sample size should be defined and which and how many levels will be used for each factor should also be known. Only factors that affect the response variable should be selected. Moreover, the way the measures be carried out, the data acquisition method, the equipment or instruments that will be necessary along the experiments should also be defined. Assess whether the parameters involved can be harmed, and evaluate what can go wrong (time, costs, company reputation, etc.). In the optimization of resources step, even in a preliminary way, choose which statistical method will be used to evaluate results. The choice of DoE involves consideration of sample size (number of replications), selection of an appropriate order of experimental runs, formation of experimental blocks or other restrictions involved.

Plan experiments is to define an experimental data acquisition sequence to reach certain objective, among the methods the factorial planning is most useful when the user wants to study the effects of two or more variables, so that in each attempt, or replies, all possible combinations of the levels of each variable are investigated.

2.5. Carry out the experiment and analysis of results

It is necessary to carry out the experiments with rigor—paying attention to minimum details in each run—to ensure that everything is being performed according to the planning. Any errors in the experimental procedure disable the experiment. In data analysis, statistical methods must be used so that the results and conclusions are not an opinion but goals. If the experiment was planned properly and was carried out in agreement to the planning, the application of statistical methods would not be complicated. Excellent statistical packages exist to help in data analysis and graphical methods are the simplest and easiest in data interpretation.

2.5.1. Software

Statistica—developed by Stat Soft—it is one of the systems with an easy-to-use look with a good graphical interface, the software can make correlations, brings several descriptive statistics, a wide range of tables and a variety of graphical analyses. <http://www.statsoft.com/>

SAS—‘Statistical Analysis System’ Developed by SAS—It is one of the best systems used by statisticians. SAS is an integrated system for data analysis applications, consisting of data recovery, file management, statistical analysis, database access, generation of graphs and generation of reports (<http://www.sas.com/>).

MINITAB—developed by Minitab—this is a classic software for statistical purposes. Its interface is similar to a spreadsheet such as Microsoft Excel or Calc of OpenOffice/LibreOffice but with the ability to perform complex statistical analyses. It offers tools of Quality Control, Planning of Experiments (DoE), Reliability Analysis and General Statistics. <http://www.minitab.com/>

ACTION STAT—developed by Estatcamp. Action Stat under R—which is a free software environment for statistical computing and graphics, and one of the most widely used statistical environments. Action Stat connects with Excel to provide a graphical interface for statistical applications (<http://www.portalaction.com.br/>).

DESIGN EXPERT—Developed by Stat-Ease—it is a Windows[®]-based software intended to optimize a product or process. It provides many statistical tools such as: two-level factorial screening designs; general factorial studies; response surface methods (RSM); mixture design techniques; combinations of process factors, mixture components and categorical factors and design and analysis of split plots (<http://www.statease.com>).

3. Design of experiments applied to advanced oxidation technologies

Advanced oxidation technologies are affected by a large number of parameters such as iron (Fe^{2+}) and H_2O_2 concentrations, pH, temperature, light intensity, organic chemical content, among others. In addition, for different industrial chemical processes there are different effluents, which greatly vary in this chemical composition from each other, not allowing a unique approach for all of them. Thus, it is necessary to adjust AOT parameters to the specific effluent to be treated.

This adjustment could be performed using the one-variable-at-a-time (OVAT) approach, but this procedure is time-consuming and less effective due to multiple variable nature of AOT. Statistical design of experiments (DoE) and response surface methodology (RSM) emerge as important and widely used tools to determine the effects of multiple variables on objective functions to be optimized. Different types of DoE used for AOT evaluation include two-level factorial design (2^k FD), central composite design (CCD) and Box-Behnken design (BBD), as can be seen on **Table 1**.

3.1. Two-level factorial design (2^k FD)

Factorial designs are a widely used and efficient way to evaluate the effects of two or more factors and the interactions among them on response variables. When compared to the one-variable-at-a-time (OVAT) experiments, factorial designs exhibit higher relative efficiency, avoid misleading conclusions when interactions are present and allow the effect estimation of

Reference	AOT	Organic matter	DoE	Independent factor: range
Ay and Kargi [9]	Fenton	Amoxicillin	BBD	Amoxicillin concentration: 10–200 mg L ⁻¹ [H ₂ O ₂]: 10–500 mg L ⁻¹ [Fe ²⁺]: 0–50 mg L ⁻¹
Ay and Kargi [10]	Photo-Fenton	Amoxicillin	BBD	Amoxicillin concentration: 10–200 mg L ⁻¹ [H ₂ O ₂]: 10–500 mg L ⁻¹ [Fe ²⁺]: 0–50 mg L ⁻¹
Irani et al. [11]	Coupled adsorption/photo-Fenton	Phenol and paracetamol	BBD	pH: 3–4 Phenol initial concentration: 20–100 mg L ⁻¹ Paracetamol initial concentration: 20–100 mg L ⁻¹ NaX to cobalt ferrite nanoparticles ratio: 0.5–1.5
Diniz [12]	Fenton	Hospital sewage	2 ² FD	[Fe ²⁺]: 0.1–0.5 g L ⁻¹ [H ₂ O ₂]: 0.1–0.5 g L ⁻¹
Marcelino [13]	Ozonation	Amoxicillin and cephalexin	2 ² FD	pH: 5–12 O ₂ flow rate: 0.5–1 Lmin ⁻¹
Marcelino [13]	Fenton	Amoxicillin and cephalexin	2 ² FD	[Fe ²⁺]: 100–500 mg L ⁻¹ [H ₂ O ₂]: 1000–1500 mg L ⁻¹
Marcelino [13]	Photo-Fenton	Amoxicillin and cephalexin	2 ² FD	[Fe ²⁺]: 100–500 mg L ⁻¹ [H ₂ O ₂]: 1000–1500 mg L ⁻¹
Dwivedi et al. [14]	Fenton	Carbamazepine	2 ³ FD	pH: 2–6 [H ₂ O ₂]: 0.5–3 g L ⁻¹ Contact time: 10–30 min
Silva [15]	Photo-Fenton	Amoxicillin	2 ⁴ FD	Amoxicillin concentration: 20–60 mg L ⁻¹ [Fe ²⁺]: 5–15 mg L ⁻¹ [H ₂ O ₂]: 50–150 mg L ⁻¹ UV light intensity: 0–96 W
Dwivedi et al. [14]	Fenton	Carbamazepine	CCD	pH: 1.37–5.62 [H ₂ O ₂]: 0.34–11.65 g L ⁻¹
Pérez-Moya et al. [16]	Photo-Fenton	Sulfamethazine	CCD	[H ₂ O ₂]: 176–1,024 mg L ⁻¹ [Fe ²⁺]: 12–68 mg L ⁻¹
Silva et al. [17]	Photo-Fenton	Phenol	CCD	[NaCl]: 0.04–5,857.86 ppm

Reference	AOT	Organic matter	DoE	Independent factor: range
				[Na ₂ SO ₄]: 0.04–5,857.86 ppm
Affam et al. [18]	Modified Fenton (FeGAC/H ₂ O ₂)	Amoxicilin and cloxacillin	CCD	H ₂ O ₂ /COD molar ratio: 0.32–3.68 [FeGAC]: 1–6 g L ⁻¹ Reaction time: 39.55–140.45 min
Almeida [19]	Photoelectro-Fenton	Paracetamol	CCD	Electric current: 3.5–8.5 A [Fe ²⁺]: 3.30 × 10 ⁻⁴ –1.17 × 10 ⁻³ mol L ⁻¹ pH: 1.37–4.36
Frade [20]	Fenton	Enrofloxacin	CCD	[H ₂ O ₂]: 0.1–0.9 g L ⁻¹ [Fe ²⁺]: 5.0 × 10 ⁻³ –1.2 × 10 ⁻¹ g L ⁻¹ Temperature: 0–40°C
Homem et al. [21]	Fenton	Amoxicillin	CCD	[H ₂ O ₂]: 4.2 × 10 ⁻⁴ –4.28 × 10 ⁻³ g L ⁻¹ [Fe ²⁺]: 3.0 × 10 ⁻⁵ –3.5 × 10 ⁻⁴ g L ⁻¹ Temperature: 20–70°C
Rozas et al. [22]	Fenton and photo-Fenton	Ampicillin	CCD	[Fe ²⁺]: 5.3 × 10 ⁻⁵ –8.7 × 10 ⁻⁵ mol L ⁻¹ [H ₂ O ₂]: 2.3 × 10 ⁻⁴ –5.7 × 10 ⁻⁴ mol L ⁻¹ pH: 2.3–5.7
Sarrai et al. [23]	Photo-Fenton	Tylosin	CCD	[Fe ²⁺]: 6.4 × 10 ⁻⁴ –7.36 × 10 ⁻³ g L ⁻¹ [H ₂ O ₂]: 1.32 × 10 ⁻⁴ –4.68 × 10 ⁻⁴ g L ⁻¹ pH: 1.89–3.9
Zaidan et al. [24]	Photo-Fenton	Phenol	CCD	[Fe ²⁺]: 1.59 × 10 ⁻³ –1.50 × 10 ⁻² mol L ⁻¹ [H ₂ O ₂]: 5.93–21.06 g L ⁻¹ Reaction time: 39.55–140.55 min
Arslan-Alaton et al. [25]	Photo-Fenton-like	Naphthalene sulphonic acid (H-acid)	CCD	Reaction time: 6–30 min [COD]: 0.15–0.75 g L ⁻¹ [H ₂ O ₂]: 1 × 10 ⁻² –5 × 10 ⁻² mol L ⁻¹ [Fe ³⁺]: 5.0 × 10 ⁻⁴ –2.5 × 10 ⁻³ mol L ⁻¹

Reference	AOT	Organic matter	DoE	Independent factor: range
Domínguez et al. [26]	Integrated Fenton/photo-Fenton-like	Carbamazepine	CCD	pH: 2.5–4.5 $[H_2O_2]: 0-1.68 \times 10^{-4} \text{ mol L}^{-1}$ $[Fe^{2+}]: 0-1.68 \times 10^{-5} \text{ mol L}^{-1}$ $[Fe^{3+}]: 0-1.68 \times 10^{-5} \text{ mol L}^{-1}$

Table 1. Studies applying design of experiments for evaluation of advanced oxidation technologies.

a factor at different levels of the other factors. The two-level factorial design with k factors (2^k) is the most important of these special cases. In this methodology, the factors vary from a 'low' level (also designated as -1) to a 'high' level (also designated as $+1$). The 2^k factorial design (2^k FD) is a powerful factor screening tool at initial research stages, since it provides the smallest number of experiments to be run when many factors are investigated [27].

The number of runs in a set of two level factorial design comprises 2^k factorial points and central points. A usual matrix (treatment combinations) for two (2^2) and three (2^3) factors are presented in **Table 2**, in a coded representation.

In **Table 2**, runs 1–4 (for 2 factors, **Table 2a**) and 1–8 (for 3 factors, **Table 2b**) are called factorial points and consists in all 2^k possible combinations for the low and high levels of all factors. Runs 5–7 (for 2 factors, **Table 2a**) and 9–11 (for 3 factors, **Table 2b**) are called central points and are used to obtain an estimate of the error, in order to allow the identification of the significant factors for a defined confidence interval. In general, three to five central points are recommended to obtain a good estimation of response variance. At the central points, the factors assume the mean value between their own low and high levels.

Geometrically, the space delimited by the factors range of variation is represented by a square and a cube, as can be seen in **Figure 1**, for two and three factors, respectively.

The results of 2^k FD can be expressed using a first-order regression model (Eq. (1)):

$$y = \beta_0 + \sum_{j=1}^k \beta_j x_j + \sum_{i < j} \beta_{ij} x_i x_j \quad (1)$$

Where y corresponds to the response variable, x_j (x_i) represents the coded factors, β_0 is the mean value of response variable, β_j 's represent the linear coefficients and β_{ij} 's represent the interaction coefficients. The relationship between the coded (x) and natural (actual) factors (X) is as follows:

$$x = \frac{X - X_0}{\Delta} \quad (2)$$

$$\Delta = \frac{X_{\text{high}} - X_{\text{low}}}{2} \quad (3)$$

		Factor			
		Run	A	B	C
Factor		1	-1	-1	-1
Run	A	2	+1	-1	-1
1	-1	3	-1	+1	-1
2	+1	4	+1	+1	-1
3	-1	5	-1	-1	+1
4	+1	6	+1	-1	+1
5	0	7	-1	+1	+1
6	0	8	+1	+1	+1
7	0	9	0	0	0
		10	0	0	0
		11	0	0	0

Table 2. Two-level factorial designs: (a) two factors; (b) three factors.

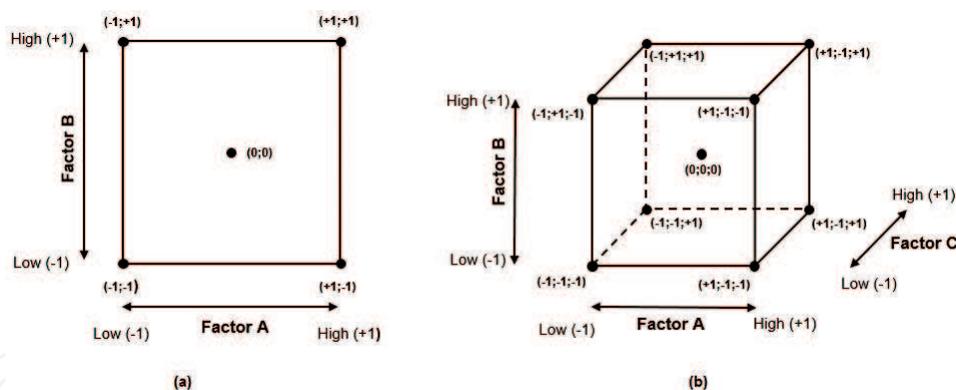


Figure 1. Geometric view of two-level factorial designs: (a) two factors and (b) three factors.

Where X_0 , X_{low} and X_{high} are the value of the natural factor at central point, low level and high level, respectively. For the cases discussed above, Eq. (1) becomes:

$$k = 2\text{factors: } y = \beta_0 + \beta_1x_1 + \beta_2x_2 + \beta_{12}x_1x_2 \tag{4}$$

$$k = 3\text{factors: } y = \beta_0 + \beta_1x_1 + \beta_2x_2 + \beta_3x_3 + \beta_{12}x_1x_2 + \beta_{13}x_1x_3 + \beta_{23}x_2x_3 \tag{5}$$

In Eq. (1), coded variables are preferably used instead of natural factors since coded factors allow an effective evaluation of relative size of factors effects. This means that depending on the ranges and units of natural variables, their relative effects could be masked, leading to erroneous simplification of the model.

The general approach to the statistical analysis of 2^k factorial design consists in the following steps [27]:

- Obtain the generalized model (full model) adjusting the regression model described by Eq. (1) to the experimental data.
- Define a confidence interval and perform an Analysis of Variance (ANOVA) to identify the statistical significant terms of Eq. (1) (single factors and interaction factors).
- Refine the model, excluding the non-significant terms from the model and adding them to the lack of fit, and recalculate the coefficients.
- Verify the model adequacy performing a residual analysis.
- Built response surfaces (or contour plots) to perform the graphical interpretation of the results.

Since Eq. (1) is a first-order model, the response surface described is a plane. Then, it is not possible to affirm that the highest value exhibited corresponds to an optimal value. However, the response surface can be used to obtain a direction of potential improvement using the method of steepest ascent.

3.2. Central composite design (CCD)

The model described by Eq. (1) allows the representation of some curvature on response surface, as the result of twisting of the plane caused by the interaction of factors. However, if there is no curvature with identification of maximum or minimum points in the graph, it is then necessary to provide more information for the mathematical model. For that cases, a second-order model regression may be used [27].

If there is no curvature, then the mean response at the centre point equals the average of the mean response of the factors at their low and high settings (the corners of the design space). Curvature is detected when the average mean response at the centre points is significantly greater or less than the average mean response of the factors at their low and high settings.

$$y = \beta_0 + \sum_{j=1}^k \beta_j x_j + \sum_{i < j} \beta_{ij} x_i x_j + \sum_{j=1}^k \beta_{jj} x_j^2 \quad (6)$$

where β_{jj} 's represent the quadratic term coefficients.

The addition of more coefficients to the model implies the necessity of a higher number of runs to allow a reliable coefficient estimation. This increase is usually done by adding axial points to the factorial design, resulting in the central composite design (CCD). The impact of the axial point addition can be visualized in **Figure 2**, where the study space is larger when compared to the factorial design (**Figure 1**).

The codified α level depends on the number of factors:

$$\alpha = 2^{k/4} \quad (7)$$

For 2 and 3 factors, α becomes equal to 1.41 and 1.68; respectively. The usual treatment combinations are presented in **Table 3**.

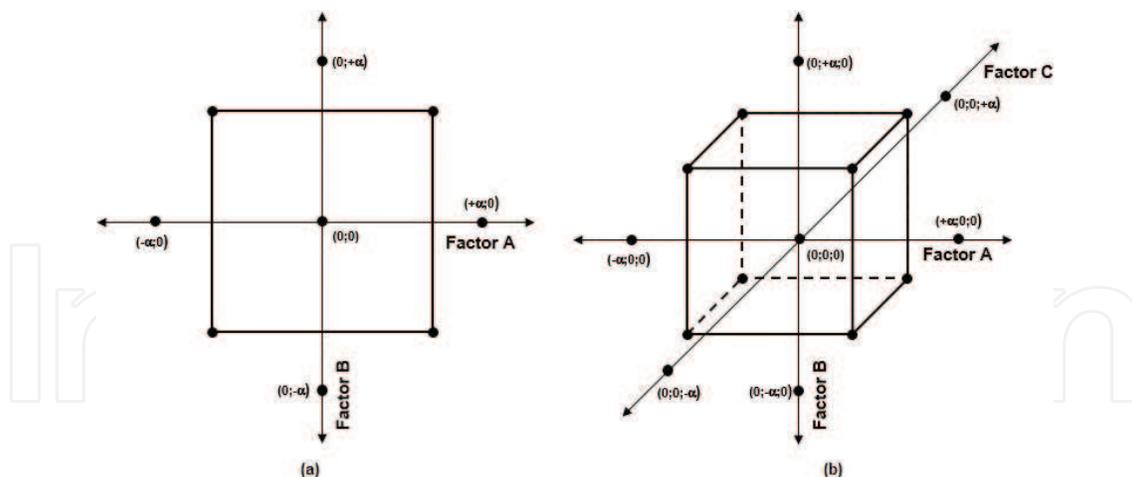


Figure 2. Geometric view of central composite designs: (a) two factors and (b) three factors.

		Factor			
		Run	A	B	C
		1	-1	-1	-1
		2	1	-1	-1
		3	-1	1	-1
		4	1	1	-1
		5	-1	-1	1
		6	1	-1	1
		7	-1	1	1
		8	1	1	1
		9	-1.68	0	0
		10	+1.68	0	0
		11	0	-1.68	0
		12	0	+1.68	0
		13	0	0	-1.68
		14	0	0	+1.68
		15	0	0	0
		16	0	0	0
		17	0	0	0

Table 3. Central composite designs: (a) two factors; (b) three factors.

In **Table 3**, runs 5–8 (for 2 factors, **Table 3a**) and 9–14 (for 3 factors, **Table 3b**) are called axial points. For the cases discussed above, Eq. (6) becomes:

$$k = 2\text{factors: } y = \beta_0 + \beta_1x_1 + \beta_2x_2 + \beta_{12}x_1x_2 + \beta_{11}x_1^2 + \beta_{22}x_2^2 \quad (8)$$

$$k = 3\text{factors: } y = \beta_0 + \beta_1x_1 + \beta_2x_2 + \beta_3x_3 + \beta_{12}x_1x_2 + \beta_{13}x_1x_3 + \beta_{23}x_2x_3 + \beta_{11}x_1^2 + \beta_{22}x_2^2 + \beta_{33}x_3^2 \quad (9)$$

The statistical analysis of central composite design follows the steps presented for the 2^k factorial design, now considering the quadratic terms.

3.3. Box-Behnken design (BBD)

Box-Behnken is a three-level DoE that comprises 2^k factorial points with incomplete block design and is used to fit second-order model regression. For three factors, this methodology corresponds to spherical revolving design, corresponding to a centre point surrounded by the middle points of the edges of a cube circumscribed on a sphere of radius $\sqrt{2}$ [27] (**Figure 3**).

Figure 3 shows that Box-Behnken design do not contain any points at the vertices of the cubic region delimited by the upper and lower levels of each factor (corner points), making this

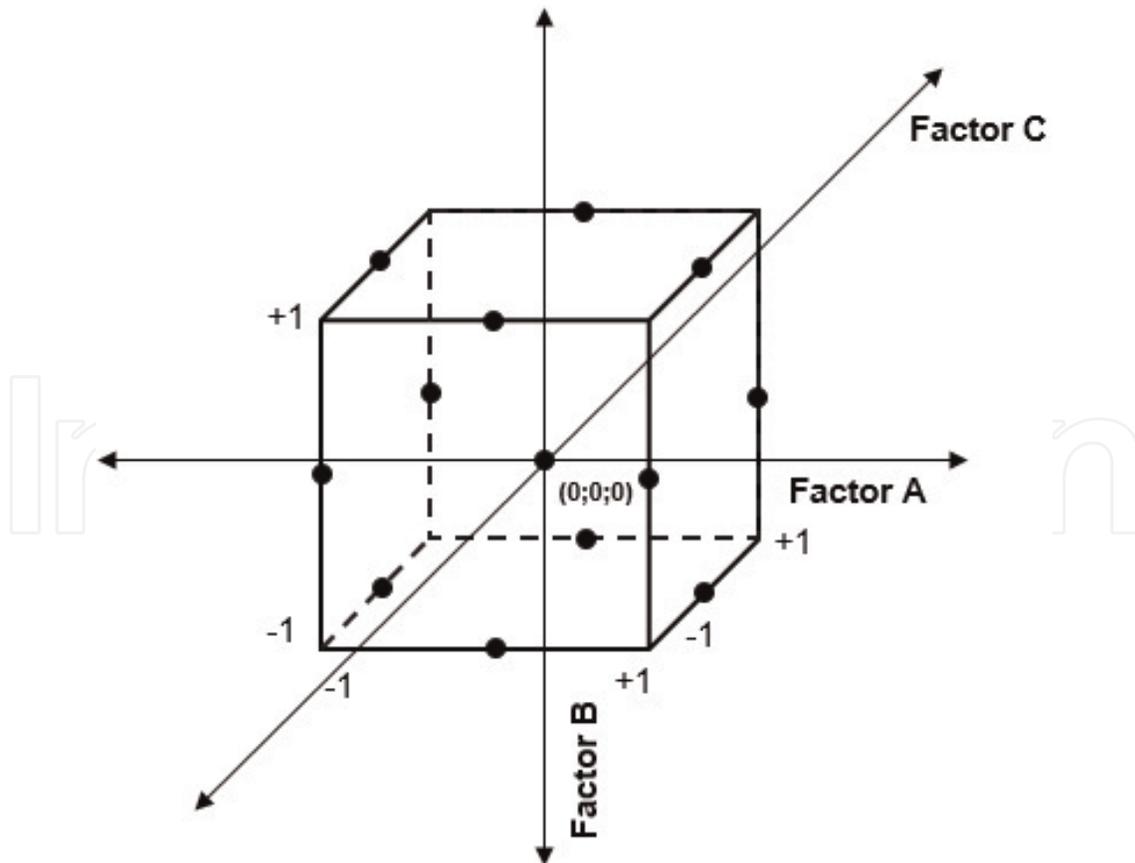


Figure 3. Geometric view of a three-factor Box-Behnken design.

methodology advantageous when these points represent expensive or physically impossible experimental conditions [27]. **Table 4** represents a three factor Box-Behnken design matrix.

3.4. Optimization

Box-Behnken design is also an efficient response surface methodology, since it requires a lower number of runs when compared to central composite design, as can be seen comparing **Tables 3** and **4**.

When a design of experiments is performed, the goal resides in obtaining factor values that optimize (maximize or minimize) the response variables. In general, this objective could be achieved using a sequential strategy, in which a factorial design (2^k FD, for example) followed by a response surface methodology (CCD, for example) are employed in sequence. This procedure is important, since it allows to fit (correct) the factors range of variation and remove non-significant factors from the study.

However, a problem arises when multiple responses are evaluated and need to be optimized simultaneously. This optimization could be performed using several approaches such as to overlay the response surfaces (which is useful for less than three factors); formulation and resolution of constrained optimization problems, using nonlinear programming methods and the desirability functions.

Run	Factor		
	A	B	C
1	-1	-1	0
2	-1	+1	0
3	+1	-1	0
4	+1	+1	0
5	-1	0	-1
6	-1	0	+1
7	+1	0	-1
8	+1	0	+1
9	0	-1	-1
10	0	-1	+1
11	0	+1	-1
12	0	+1	+1
13	0	0	0
14	0	0	0
15	0	0	0

Table 4. Three factor Box-Behnken design.

The use of desirability functions consists in converting all the m response variables (y_i) into individual desirability functions (d_i), making them vary from 0 to 1, which means non-achievement and achievement of the goal, respectively. Thus, the overall desirability function (D) is built according to Eq. (10), and the individual desirability functions are varied in order to optimize D .

$$D = (d_1 \cdot d_2 \dots d_m)^{1/m} \quad (10)$$

4. Advanced oxidation processes: photo-Fenton technology

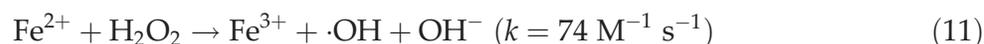
Many organic chemicals discharged into the aquatic environment are not only toxic but also only partly biodegradable and are not easily degraded by conventional biological wastewater treatment plants. That is the reason to develop effective methods aiming degradation of chemical pollutants, either to less noxious transformation products or to their complete mineralization (mainly to CO_2 and H_2O molecules). Throughout the last decades, new methods for water and wastewater cleaning processes, called as advanced oxidation technologies, have received more attention. High rates of pollutant oxidation, flexibility concerning water quality variations and small dimensions of reactors are some advantages of such processes. On the other hand, high operating costs and special safety requirements because of the use of very reactive chemicals (ozone, hydrogen peroxide, etc.) and high-energy sources (UV lamps, electron beams, radioactive sources) are the main negative concerns about AOT.

Advanced oxidation technologies (AOT) imply the use of powerful oxidizing intermediates (the hydroxyl radical OH^\bullet) which can oxidize and degrade primarily organic pollutants from air and water. The term advanced is used because the chemical reactions involved are essentially the same (except billions of times faster) as the reactions that would occur if these pollutants were exposed in a natural environment. The ubiquitous occurrence of hydroxyl radicals (OH^\bullet) in various types of environments that include natural waters, the atmosphere, biological systems and interstellar space is now well established. Hydroxyl radicals were first discovered in 1934 by Haber and Weiss in what is known today as the Fenton reaction [28]. It is now well known that, under most atmospheric conditions, OH^\bullet radicals govern the oxidative capacity of the natural atmosphere. OH^\bullet radicals are composed of a hydrogen atom bonded to an oxygen atom which makes them highly reactive, readily stealing hydrogen atoms from other molecules to form water molecules [29].

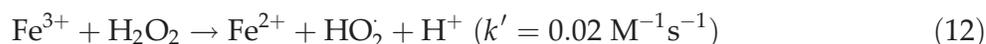
AOTs have been defined by Glaze et al. [1] as 'near ambient temperature and pressure water treatment processes which involve the generation of a very powerful oxidizing agent such as hydroxyl radical (OH^\bullet) in solution in sufficient quantity to effective water purification'. AOTs are applied whenever conventional oxidation techniques are insufficient, when process kinetics becomes very slow, or because contaminants are refractory to chemical oxidation in aqueous medium or partially oxidized yielding stable transformation products showing even greater toxicity than the starting pollutants. However, it must also be taken into consideration that the oxidation ability of most AOT diminishes considerably when treating high organic matter contents ($>5.0 \text{ g L}^{-1}$), thereby requiring the consumption of excessive amounts of expensive reactants that makes the treatment far less cost-affordable.

AOTs oxidize a broad range of contaminants, including those that are not readily removed with other advanced technologies (e.g. reverse osmosis or granular activated carbon). Most of the commercially viable AOT use either ozone or photochemical processes [i.e. ultraviolet (UV) or visible light] to generate OH [30]. In AOT, $\cdot\text{OH}$ radicals are generated usually by coupled chemical and/or physical systems that include $\text{H}_2\text{O}_2/\text{Fe}(\text{II})$ or $\text{H}_2\text{O}_2/\text{Fe}(\text{III})$ (Fenton), $\text{H}_2\text{O}_2/\text{catalyst}$ or peroxide/catalyst (Fenton-like), O_3 (ozonation) and $\text{H}_2\text{O}_2/\text{O}_3$ (peroxone) that are often associated with an irradiation technique, namely vacuum-UV radiation, UV radiation (low-, medium-, or high-pressure lamps), pulse radiolysis or ultrasound [29].

Since its first use [28], until now, the most effective and simple way of generating hydroxyl radicals for organic pollutants degradation is by classical Fenton reaction (Eq. (11)) [31].



However, one of the main inconveniences of Fenton reaction is the rapid consumption of Fe^{2+} (Eq. (11)) and a very slow regeneration of Fe^{2+} by 'Fenton-like' reaction (Eq. (12)). Fenton-based degradation process, therefore, demands a high initial concentration or a continuous dosage of Fe^{2+} . This disadvantage is overcome in photo-Fenton process wherein (UV-Visible irradiation, $\lambda < 550 \text{ nm}$), Fenton/Fenton-like reaction (Eq. (11)) is paired with UV irradiation to regenerate Fe^{2+} (Eq. (13)), thereby minimizing the Fe^{2+} dosage for degradation [31].



Consequently, the photo-Fenton has been recognized as a prospective UV-based AOT for treatment of industrial waste water. In photo-Fenton process, $\text{Fe}(\text{III})$ aqua species, mainly the hydroxo complex $[\text{Fe}(\text{H}_2\text{O})_5\text{OH}]^{2+}$ formed at pH~3 is photoactive and regenerates $\text{Fe}(\text{II})$ upon UV irradiation [31]. In the photo-Fenton process, only iron is catalytic, whereas hydrogen peroxide plays a sacrificial role. The mechanism of the process is very complex and still remains incompletely elucidated; it is widely accepted that hydroxyl radical plays a major role as oxidizing agent, although the involvement of other species, such as high-valence iron, has not been ruled out [32].

When it comes to industrial applications, the scientific literature is scarce and, basically, in the same situation observed by Vogelpohl [33]. There is a lack of published data providing comparisons with bench-scale or pilot-scale data. Moreover, studies developed by companies are often only disclosed internally. As noted by Vogelpohl [33], there are few data on costs, both for installation and for operation, without which there will be a considerable gap between academia and industry. On the other hand, the growing number of patents in the area is a positive factor that indicates that the acceptance of AOTs by the industrial sector is growing each year. By performing a simple search (5 January 2017), through the Google Patents robot, the expression 'advanced oxidation process*' generated a total of 3384 results, the keyword 'fenton' generated 22,977 results, whereas 'wastewater AND pharmaceut* AND fenton' strategy obtained 1379 results. In this bibliographic research, other forms of publication other than patents were excluded.

Despite scarce literature information—compared to academic number of papers—about industrial applications of AOT for water and air remediation, advanced oxidation processes have been successfully commercialized during recent years [34]. Basically, advanced oxidation solutions begin with a wastewater chemical study and a geologic data evaluation (for treatment of contaminated soil and groundwater). A critical step in ensuring the success of a treatment program is the selection of the appropriate chemical reagent and application method. An initial bench-scale is useful to select the appropriate method. Previous information from the scientific literature (reports, academic studies, conference proceedings and papers) is mandatory to the chemical remediation industry. In commercial scale of Fenton's reagent, H₂O₂ dosage of 5–35% (w/w) is applied. The initial weight of H₂O₂ and Fe²⁺ are based on contaminants levels, chemical characteristics, type of soil to be treated, and the specific ratio of H₂O₂:Fe²⁺ determined during the laboratory study (bench scale previous tests). Occasionally, additional reagents may be applied because of heterogeneity of the medium and to diminish H₂O₂ rate of decomposition aiming additional contact time for the contaminants. If the natural pH of the contaminant site is not low enough for efficient hydroxyl radical generation, H₂SO₄ may be added to adjust pH prior to the Fenton's reagent application. Some commercial applications of AOT are shown as follows:

Calgon Carbon Corporation has provided advanced oxidation technologies for disinfection drinking water, municipal wastewater and industrial wastewater with low-pressure and medium-pressure lamps UV reactors (SENTINEL[®], C3 Series[™], and RAYOX[®] systems). According to Calgon Carbon Corp., each Sentinel[®] reactor is able to treat 200 million litres of industrial effluents a day, accommodating pipe size from 12 to 48 inches. On the other hand, Rayox[®] has reactors from lab scale (batch test units with 1 kW, 30 kW, 60 kW and 90 kW) to large applications with patented lamp-cleaning device.

The Geo-Cleanse[®] process is a patented, *in-situ* chemical oxidation technology that utilizes Fenton's reagent and modified-Fenton's reagent to destroy organic compounds from wastewater and soil. As an example of AOT application, Geo-Cleanse International treated groundwater contaminated with high concentrations of perchloroethylene (PCE) and its transformation products at a landfill (25-acre area) located on the Naval Submarine Base, Kings Bay Georgia. The source of PCE contamination was identified on the perimeter of the landfill with concentrations of over 9000 µg L⁻¹. Injection of chemical reagents and catalyst was implemented by the placement of 23 injection wells. The AOT achieved over a 98% destruction of chlorinated hydrocarbons.

Another *in-situ* chemical oxidation solution is provided by CleanOX[®] that is based on the Fenton's reagent. In-Situ Oxidative Technologies Inc. provides ISOTEC's modified Fenton's reagent (MFR), which consists of injecting patented chelated iron catalysts and stabilized hydrogen peroxide into contaminated aquifers (at pH=7).

In-Situ Technieken (The Netherlands) treats contaminated soil also with Fenton's reagent with a process that can be combined (or not) with aerobic/anaerobic biological degradation (BISCO[®]). The Dow Chemical produces raw materials for the polyurethane industry in Delfzijl (The Netherlands). The soil at the site of the sandblasting area was polluted with monochlorobenzene (MCB). The DOW plant in Delfzijl was obliged to submit the principles for a soil remediation plan to the Provincial Government of Groningen. The remediation was

carried out with AOT and in accordance with the Netherlands Directive for Soil Protection (NRB).

On-Contact Remediation Process[®] by Environmental Business Solutions International Inc. (EBSI) is another commercial AOT process. In one of the examples provided by EBSI Inc., *in-situ* remediation was successfully implemented in Boston, Massachusetts. Fuel oil, gasoline and several plasticizer additives, including bis-2-ethylhexyl phthalate (DEHP) were stored in underground storage tanks (UST) outside the facility loading bays. Light Non-Aqueous Phase Liquid, consisting of fuel oil and DEHP, was discovered at the site in the late 1980s and various methods to remove it had been attempted over many years. After three rounds of oxidizer treatment, LNAPL levels were reduced by more than 70% by AOT.

There has been a tendency to quote treatment costs per unit volume for a waste stream and technology (e.g. dollars/1000 gal); however, such notation does not consider the concentration of the contaminant nor the treatment goals. Bolton et al. [35] proposed figures-of-merit that are based on electrical energy consumption within two phenomenological kinetic order regimes: one for high contaminant concentrations and one for low concentrations. A simple understanding of the overall kinetic behaviour of organic destruction in a waste stream (i.e. whether zero or first order) is necessary for describing meaningful electrical efficiencies. These standard figures-of-merit are valuable in that they give a direct link to the electrical efficiency of an advanced oxidation process, independent of the nature of the system and therefore also allow comparison of widely disparate AOT. Such figures-of-merit are necessary not only to compare AOT, but also to provide the requisite data for scale-up and economic analyses for comparison with conventional treatment technologies (e.g. carbon adsorption/regeneration, air stripping and incineration).

There are many important factors in selecting a waste-stream treatment technology including economics, economy of scale, regulations, effluent quality goals, operation (maintenance, control and safety) and robustness (flexibility to change/upsets). Although all these factors are important, economics is often sovereign. A full economic analysis of the net present cost (i.e. amortized investment, installation and operating costs) of implementing a wide range of treatment technologies represents an arduous task and often can be both site- and problem-specific. A simple figure-of-merit based on electrical energy consumption can be very useful and informative for AOT, since these processes are often electrical energy intensive and electrical energy can represent a major fraction of the operating costs. Moreover, electrical energy dosage requirements also dictate the size of the capital equipment needed to generate the requisite dosage, thus investment should also tend to scale with this figure-of-merit [35].

Asaithambi et al. [36] compared the performance of the photo (UV), Fenton, photo-Fenton and ozone-photo-Fenton processes in terms of colour removal and chemical oxygen demand (COD) removal of distillery industrial effluent together with the associated electrical energy per order. The colour and COD removals of industrial effluents were investigated using the pseudo first-order kinetic model. It was observed from the experimental results that $O_3/UV/Fe^{2+}/H_2O_2$ process yielded a 100% colour and 95.50% COD removals with electrical energy per order of 0.015 kWhm^{-3} compared to all other combinations of AOT.

Lin et al. [37] investigated the degradation of ofloxacin antibiotics by UV/H₂O₂ process in a large photoreactor, and the effects of UV wavelength, H₂O₂ dosage and pH on this process. The degradation of ofloxacin proceeded more rapidly under UV-254 nm than under UV-365 nm. The degradation of ofloxacin by the UV/H₂O₂ process followed pseudo-first-order kinetics. At pH 3 and an H₂O₂ dosage of 0.27 g L⁻¹, 97% of ofloxacin was degraded under UV-254 nm after 30 min. The electrical energy per order of removal (EE/O) figure-of-merit value for the treatment of 10 mg L⁻¹ ofloxacin by the UV-365 nm/H₂O₂ process was 22.5 kWh m⁻³ per order. However, that of the UV-254 nm/H₂O₂ process was significantly lower, at 2.2 kWh m⁻³ per order.

Lin and Wu [38] studied the effectiveness of the UV/S₂O₈²⁻ process in the degradation of ciprofloxacin antibiotics in aqueous solutions without adjusting their pH using a large photoreactor. The EE/O values for 10 mg L⁻¹ ciprofloxacin treatment by the UV/S₂O₈²⁻ process at various Na₂S₂O₈ concentrations were calculated. The lowest EE/O value in the UV/S₂O₈²⁻ process was calculated as 0.653 kWh m⁻³ per order at Na₂S₂O₈ concentration of 3.84 g L⁻¹.

Only a small fraction of the scientific papers related to advanced oxidative technologies makes use of the electrical energy consumption figure-of-merit. In our understanding, one of the best response variables that could be used in the study of wastewater degradation (pharmaceuticals or not) would be EE/O. With EE/O as variable response in a design of experiments, not only the main factors associated to the advanced oxidative processes (light source, catalyst, H₂O₂, O₃, Fe²⁺, etc.), but also the kinetics of the reaction and the energy cost would be used in an experimental study to reach the objective of the process. There is a gap in the scientific community regarding the use of the EE/O tool that could be explored by researchers in conjunction with the traditional statistical tool design of experiments.

Acknowledgements

This work was funded in part by Federal Institute of Sao Paulo (PRP-IFSP #226/2016).

Author details

André Luís de Castro Peixoto^{1*}, Ademir Geraldo Cavallari Costalonga¹,
Mateus Nordi Esperança¹ and Rodrigo Fernando dos Santos Salazar²

*Address all correspondence to: alcpeixoto@ifsp.edu.br

1 Grupo de Química Tecnológica (GQT), Federal Institute of Sao Paulo (IFSP), Campus Capivari, Capivari, Brazil

2 Centro de Ciências da Saúde e Agrárias, University of Cruz Alta (UNICRUZ), Campus Dr. Ulysses Guimarães, Cruz Alta, Brazil

References

- [1] Glaze WH, Kang JW, Chapin DH. The chemistry of water treatment processes involving ozone, hydrogen peroxide and ultraviolet radiation. *Ozone: Science & Engineering*. 1987;**9**(4):335-352. DOI: 10.1080/01919518708552148
- [2] Parsons S, editor. *Advanced Oxidation Processes for Water and Wastewater Treatment*. IWA publishing; London, 2004
- [3] Araújo KS, Antonelli R, Gaydeczka B, Granato AC, Malpass GRP. Advanced oxidation processes: A review regarding the fundamentals and applications in wastewater treatment and industrial wastewater. *Ambiente e Agua-An Interdisciplinary Journal of Applied Science*. 2016;**11**(2):387-401. DOI: 10.4136/ambi-agua.1862
- [4] Nogueira RFP, Trovó AG, da Silva MRA, Villa RD, de Oliveira MC. Fundamentos e aplicações ambientais dos processos Fenton e foto-Fenton. *Química Nova*. 2007;**30**(2):400-408. DOI: 10.1590/S0100-40422007000200030
- [5] Qu X, Alvarez PJ, Li Q. Applications of nanotechnology in water and wastewater treatment. *Water Research*. 2013;**47**(12):3931-3946. DOI: 10.1016/j.watres.2012.09.058
- [6] Sa RM, Premalatha M. Applications of nanotechnology in wastewater treatment: A review. *Imperial Journal of Interdisciplinary Research*. 2016;**2**(11):1500-1511
- [7] Brown SD. The chemometrics revolution re-examined. *Journal of Chemometrics*. 2017;**31**(1):1-23. DOI: 10.1002/cem.2856
- [8] Myers RH, Montgomery DC, Anderson-Cook CM. *Response Surface Methodology: Process and Product Optimization using Designed Experiments*. 3rd ed. New Jersey: John Wiley & Sons; 2016. p. 704
- [9] Ay F, Kargi F. Advanced oxidation of amoxicillin by Fenton's reagent treatment. *Journal of Hazardous Materials*. 2010;**179**:622-627. DOI: 10.1016/j.jhazmat.2010.03.048
- [10] Ay F, Kargi F. Effects of reagent concentrations on advanced oxidation of amoxicillin by Photo-Fenton treatment. *Journal of Chemical Engineering*. 2011;**137**(6):472-480. DOI: 10.1061/(ASCE)EE.1943-7870.0000344
- [11] Irani M, Rad RR, Pourahmad H, Haririan I. Optimization of the combined adsorption/photo-Fenton method for the simultaneous removal of phenol and paracetamol in a binary system. *Microporous and Mesoporous Materials*. 2015;**206**:1-7. DOI: 10.1016/j.micromeso.2014.12.009
- [12] Diniz LM. *Avaliação do reagente de fenton e foto-fenton na remoção de matéria orgânica e toxicidade em um efluente hospitalar [thesis]*. Belo Horizonte: Federal University of Minas Gerais; 2015
- [13] Marcelino RBP. *Aplicação de processos oxidativos avançados para o tratamento de efluente da produção de antibióticos [thesis]*. Belo Horizonte: Federal University of Minas Gerais; 2014

- [14] Dwivedi K, Morone A, Chakrabarti T, Pandey RA. Evaluation and optimization of Fenton pretreatment integrated with granulated activated carbon (GAC) filtration for carbamazepine removal from complex wastewater of pharmaceutical industry. *Journal of Environmental Chemical Engineering*. 2016, DOI: 10.1016/j.jece.2016.12.054
- [15] Silva VV. Degradação de amoxicilina por Fenton e foto-Fenton [thesis]. Porto Alegre: Federal University of Rio Grande do Sul; 2015
- [16] Pérez-Moya M, Graells M, Castells G, Amigó J, Ortega E, Buhigas G, Pérez LM, Mansilla HD. Characterization of the degradation performance of the sulfamethazine antibiotic by photo-Fenton process. *Water Research*. 2010;**44**:2533-2540. DOI: 10.1016/j.watres.2010.01.032
- [17] Silva SS, Chiavone-Filho O, Barros-Neto EL, Foletto EL, Mota ALN. Effect of inorganic salt mixtures on phenol mineralization by Photo-Fenton-Analysis via an experimental design. *Water Air and Soil Pollution*. 2014;**225**:1784. DOI: 10.1007/s11270-013-1784-x
- [18] Affam AC, Chaudhuri M, Kutty SRM. Optimization of modified Fenton (FeGAC/H₂O₂) pretreatment of antibiotics. *Pertanika Journal of Science & Technology*. 2014;**22**(1):239-254
- [19] Almeida LC. Otimização de processo de mineralização de compostos orgânicos utilizando sistemas eletro-fenton e fotoeletro-fenton por irradiação UV artificial e solar [thesis]. São Carlos: Federal University of São Carlos; 2011
- [20] Frade VMF. Oxidação química de enrofloxacin pelo processo Fenton [thesis]. São Paulo: University of São Paulo; 2013
- [21] Homem V, Alves A, Santos L. Amoxicillin degradation at ppb levels by Fenton's oxidation using design of experiments. *Science of the Total Environment*. 2010;**408**:6272-6280. DOI: 10.1016/j.scitotenv.2010.08.058
- [22] Rozas O, Contreras D, Mondaca MA, Pérez-Moya M, Mansilla HD. Experimental design of Fenton and photo-Fenton reactions for the treatment of ampicillin solutions. *Journal of Hazardous Materials*. 2010;**177**:1025-1030. DOI: 10.1016/j.jhazmat.2010.01.023
- [23] Sarrai AE, Hanini S, Merzouk K, Tassalit D, Szabó T, Hernádi K, Nagy L. Using central composite experimental design to optimize the degradation of Tylosin from aqueous solution by Photo-Fenton reaction. *Materials*. 2016;**428**(9):428. DOI: 10.3390/ma9060428
- [24] Zaidan LEMC, Silva AMRB, Sales RVL, Salgado JBA, Moraes SCG, Souza DP, Galvão CC, Rodríguez-Díaz JM, Napoleão DC, Benachour M, Silva VL. Optimization of phenol degradation and its derivatives using photo-Fenton and application industrial. *Chemical and Process Engineering Research*. 2016;**42**:44-52
- [25] Arslan-Alaton I, Ayten N, Olmez-Hanci T. Photo-Fenton-like treatment of the commercially important H-acid: Process optimization by factorial design and effects of photocatalytic treatment on activated sludge inhibition. *Applied Catalysis B: Environmental*. 2010;**96**:208-217. DOI: 10.1016/j.apcatb.2010.02.023

- [26] Domínguez JR, González T, Palo P, Cuerda-Correa EM. Fenton + Fenton-like integrated process for carbamazepine degradation: Optimizing the system. *Industrial & Engineering Chemistry Research*. 2012;**51**:2531-2538. DOI: 10.1021/ie201980p
- [27] Montgomery DC. *Design and Analysis of Experiments*. 6th ed. John Wiley & Sons Inc; New Jersey, 2005
- [28] Fenton HJH. LXXIII—Oxidation of tartaric acid in presence of iron. *Journal of the Chemical Society, Transactions*. 1894;**65**:899-910. DOI: 10.1039/CT8946500899
- [29] Gligorovski S, Strekowski R, Barbati S, Vione D. Environmental implications of hydroxyl radicals ($\bullet\text{OH}$). *Chemical Reviews*. 2015;**115**(24):13051-13092. DOI: 10.1021/cr500310b
- [30] Collins J, Bolton J. *Advanced Oxidation Handbook*. 1st ed. Denver: American Water Works Association; 2016;1-194
- [31] Subramanian G, Madras G. Introducing saccharic acid as an efficient iron chelate to enhance photo-Fenton degradation of organic contaminants. *Water Research*. 2016;**104**:168-177. DOI: 10.1016/j.watres.2016.07.070
- [32] Marin ML, Santos-juanés L, Arques A, Amat AM, Miranda MA. Organic photocatalysts for the oxidation of pollutants and model compounds. *Chemical Reviews*. 2012;**112**:1710-1750. DOI: 10.1021/cr2000543
- [33] Vogelpohl A. Applications of AOPs in waste water treatment. *Water Science and Technology*. 2007;**55**(12):207-211
- [34] Oppenländer T. *Photochemical Purification of Water and Air*. 1st ed. Weinheim: Wiley-VCH; 2003. p. 368
- [35] Bolton JR, Bircher KG, Tumas W, Tolman CA. Figures of merit for the technical development and application of advanced oxidation technologies for both electric and solar driven systems. 2001;**73**(4):627-637 <http://dx.doi.org/10.1351/pac200173040627>
- [36] Asaithambi P, Sajjadi B, Raman A, Aziz A. Integrated ozone-photo-Fenton process for the removal of pollutant from industrial wastewater. *Chinese Journal of Chemical Engineering*. 2016, DOI: 10.1016/j.cjche.2016.10.005
- [37] Lin CC, Lin HY, Hsu LJ. Degradation of ofloxacin using UV/H₂O₂ process in a large photoreactor. *Separation and Purification Technology*. 2016;**168**:57-61. DOI: 10.1016/j.seppur.2016.04.052
- [38] Lin CC, Wu MS. Degradation of ciprofloxacin by UV/S₂O₈²⁻ process in a large photoreactor. *Journal of Photochemistry and Photobiology A: Chemistry*. 2014;**285**:1-6. DOI: 10.1016/j.jphotochem.2014.04.002