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Degradation of pharmaceuticals in hospital wastewater by solar photo-Fenton processes

Thesis presented as a partial requirement for the obtaining a Doctor of Chemistry degree

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THESIS FRAMEWORK

The present PhD Thesis, titled “Degradation of pharmaceuticals in hospital wastewater by solar photo-Fenton processes”, was been developed in the *Universidade Federal do Rio Grande do Sul* (Porto Alegre, Brazil) between August 2016 and October, 2020.

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The PhD candidate held a doctoral internship at the Laboratory of Separation and Reaction Engineering - Laboratory of Catalysis and Materials (LSRE-LCM) at Faculty of Engineering of the University of Port (Portugal) between May-July 2019 under supervision of Prof. Dr. Vitor J.P. Vilar. She was granted a scholarship by ELAP in the University of Manitoba (Canada) in which she engaged in research activities in the Environmental Engineering Department headed by Dr. Qiuyan Yuan (January 2nd to June 12th, 2020).

This thesis is the product of the teamwork of all members of the GMAPs, a research group headed by Dr. Carla Sirtori, in addition to GDMIT group collaboration led by Dr. Elaine R. L. Tiburtius and Dr. Sérgio Toshio Fujiwara (R. I. P) along with assistance from different national and international collaborations.

ABSTRACT

The presence of pharmaceuticals in wastewater represents a serious environmental issue that can contribute toward sanitary and health problems. One of the main points behind this matter, is the low efficiency of degradation in conventional wastewater treatment plants (WWTP), or the direct discharge of untreated effluents into water bodies. To overcome this concern, Advanced Oxidation Processes (AOPs) have been widely used due to their generation of highly reactive hydroxyl radicals ($HO^{\bullet}$), which oxidize the abundant organic contents present in wastewaters. Within AOPs, the Fenton process is widely recognized for its versatility, as there are different ways to produce $HO^{\bullet}$, facilitating compliance with the specific treatment requirements. The Fenton process is based on the use of iron and hydrogen peroxide for the production of $HO^{\bullet}$ and other radical oxygen species. This process is of particular interest, as sunlight can be used to improve its efficiency in removing emerging pollutants. Despite this, more research is still needed for its application in large scale wastewater treatment. This study was subsequently developed to evaluate different operational strategies of solar photo-Fenton to remove pharmaceuticals in hospital wastewater.

To achieve this goal, the solar photo-Fenton processes were studied using Fe^0, $Fe^{2+/3+}$-alginate and Fe^{3+}:EDDS under optimized experimental conditions. In addition, analytical monitoring of treatment processes, identification of transformation products (TPs) using LC-QTOF MS, coupled with the use of a purpose-designed database and toxicological/biodegradable predictions using (Q)SAR tools were performed in this research.

A batch reactor (1L) and a *raceway pond* reactor (10 L) made with low-cost materials were operated at pH close to neutrality. Additionally, three types of wastewater were worked on: distilled water (DW), simulated wastewater (SWW) and raw hospital wastewater (RHWW) fortified with a mixture of pharmaceuticals (Dipyrone-DIP, Diazepam-DZP, Fluoxetine-FXT, Furosemide-FRS, Gemfibrozil-GFZ, Nimesulide-NMD and Progesterone-PRG) as a model of micropollutants with different initial concentrations (500 μg L^{-1} and 50 μg L^{-1}), then treated by the solar processes mentioned above. The experiments being carried out on sunny days at noon, the measured solar UV radiation was used to calculate t_{30W}, which allows the comparison of solar experiments carried out on different days, months and seasons throughout the year.

Different operational strategies of solar photo-Fenton were evaluated for the removal of the tested pharmaceuticals from the hospital wastewater: in the first strategy, waste from the metallurgical industry as a source of zero valence iron was used to evaluate the efficiency of this type of material at acid pH **(Paper I- Degradation of a mixture of pharmaceuticals in hospital wastewater by a zero-valent scrap iron (ZVSI) combined reduction-oxidation process)**, this first research was supported by the publication of a review article on the different treatments with zero valent iron **(Paper II- Current trends in the use of zero-valent iron (Fe^0) for degradation of pharmaceuticals present in different water matrices)**. To overcome certain disadvantages of waste material in relation to the use of acidic pH in the paper I, we proceeded to carried out experiments at a pH closer to neutrality. For this purpose, dosage of iron immobilized in alginate spheres was evaluated for pharmaceutical degradation at pH 5.0 **(Paper III- Degradation of pharmaceuticals in different water matrices by a solar homo/heterogeneous photo-Fenton process over modified alginate spheres)** and Fe^{3+}:EDDS complex was performed at a pH 7.0 **(Paper IV- Solar photo-Fenton-like process at neutral pH: Fe(III)-EDDS complex formation and optimization of experimental conditions for degradation of pharmaceuticals)**. Both processes present high percentages of degradation of pharmaceutical, however, Fe^{3+}:EDDS presented higher percentage of degradation in lower reaction times, the main reason for choosing this process for the scale-up stage via homemade *raceway pond* reactor **(Paper V- manuscript submitted to journal)**. As a complement to the solar photo-Fenton processes, the use of an application (PhotoMetrix PRO®) for the quantification of H_2O_2 and Fe species, *in loco*, was developed and validated **(Paper VI- Total dissolved iron and hydrogen peroxide determination using the PhotoMetrixPRO application: A portable colorimetric analysis tool for controlling important conditions in the solar photo-Fenton process)**.

Some relevant aspects could be observed throughout the execution of the different studies that make up the present thesis.

Firstly, it can be considered that, solar photo-Fenton processes for the degradation of pharmaceutical products under circumneutral pH conditions is possible with a previous optimization of variables.

The study with steel scrap as source of iron (ZVI) reported level of catalyst leaching less than the maximum concentration for Brazilian legislation. However, some negative effects, such as increased salinity due to acidic pH required to perform the treatment was observed.

The homogeneous/heterogeneous alginate system has great advantages for catalyst dosage, allowing more than 3 times the use of Fe^{3+}-alginate beads. The disadvantages of this process are the possible adsorption/desorption that take place in the different reuse cycles and the partial depolymerization of alginate with H_2O_2, which leads to an increase in the organic load of the matrix.

On the other hand, Fe^{3+} complexed with EDDS is a suitable alternative for the degradation of pharmaceuticals in homogeneous systems, achieving high degradation rates in short periods of time and being efficient in matrices with a higher organic load such as SW and RHWW. Furthermore, EDDS is biodegradable and has high stability. Therefore, based on pharmaceutical and TPs mitigation efficiency, the Fe^{3+}-EDDS was the best reported treatment and the scale-up of this was carried out in the homemade *raceway ponds* reactor.

The scale up of the process presented percentage of degradation similar to those reported in the batch reactor. Additionally, it was confirmed that Fe^{3+}-EDDS (1:2) ratio favors the degradation of the TPs and principal component analysis (PCA) was performed to compare the toxicity of the TPs, it allows a consideration of two principal components which characterized 88% of the predicted dates. Most of the TPs did not show mutagenicity or bioaccumulation characteristics.

In relation to all solar processes, the importance of the PhotoMetrix PRO® application is highlighted, as experiments of this category are carried out in open areas where there is no possibility of accessing the UV-vis spectrophotometer. This application provides the option of monitoring Fe and H_2O_2 *in situ*. It also offers the opportunity to optimize the app for other colorimetric methods such as COD, among others.

In general, the most persistent pharmaceuticals were diazepam, fluoxetine, and progesterone. These pharmaceuticals do not have spontaneous reactions through an electron transfer mechanism with ROS due to the presence of strong electron-withdrawing groups in the structures.

The TPs identified in this thesis were assigned, as aforementioned, using a purpose built-database for the first time. On the basis of the TPs identified, it was observed that generally the breakdown of pharmaceuticals involved hydroxylation of the aromatic ring by an electrophilic attack from ROS, cleavage of C-O, C-N bonds, H-abstraction and free radical reactions of pharmaceuticals.

Mechanisms in the degradation of pharmaceuticals can be elucidated as follows: (i) free radical addition to the neutral pharmaceutical molecule- (ii) free radical abstract one H atom from the neutral molecule (iii) hydroxylation through interaction of $HO^{\bullet}$ with HO^{-}, O_2 or H_2O (iv) ring-opening reactions that generate less aromatic TPs.

With respect to TPs and (Q)SAR tools, in addition to having low biodegradability, most of the structures generated in all processes represent high to medium toxicity for different trophic levels in ecosystems and for human health. The data obtained are only predictions since the effect of each TP on the environment depends on various factors, such as concentration, reactivity, matrix characteristics, etc. (Q)SAR predictions are indicators of the possible impact of each TP and, as such more research is needed in this area to expand the domain and applicability of these tools.

The results of the solar process described in this thesis encourage further research in the area of AOPs as more sustainable processes. Operating conditions need to be optimized, low concentrations of reagents explored, charge recombination suppressed, and the quantum yield increased with more efficient catalytic systems. Similarly, major attention in the futures works could be dedicated to the identification of reaction mechanisms of TPs and criteria for cost effectiveness.

A further question to consider is whether the application of the chelate-assisted solar photo-Fenton process really addresses the problem of the cost of acidification and the basification of hospital effluents, considering the cost of some of these chelates compared to the cost of acids and bases used in neutralization. Cheaper and more accessible chelates could be investigated, for example, humic-like substances.

The coupling of AOPs to biological treatments at a pre-treatment or post-treatment stage should be considered as potential ways to improve biodegradability and reduce the toxicity of treated wastewater.

Studies are currently underway to investigate the potential use of enzymes (manganese peroxidase - EC 1.11.1.13) in pharmaceutical degradation with a focus on anti-cancer drugs (imatinib mesylate), these studies were started in January 2020 in collaboration with the University of Manitoba (Canada), through a six-month scholarship from the Canadian Government, and will be completed in Brazil at the UFRGS facilities, in the near future. This research aims to elucidate the mechanisms of enzyme-pharmaceutical degradation, transformation products, immobilization of enzymes, and toxicity studies. Additionally, this study hopes to assess whether there is a possibility of coupling AOPs and enzymatic degradation, in addition to investigating the best coupling strategy between both these systems.

Observance of current international and Brazilian legislation has shown that there is a lack of legislation for emerging pollutants. Be that as it may, Brazil may set maximum levels for hospital wastewater for some important pharmaceuticals (e.g. antibiotics) in the future. Therefore, the relationship between validated, sensitive, and rapid analytical methods together with analyses of toxicity, bacterial resistance, and transformation products are essential for providing solid evidence in order for this legislation to be established.

It is of crucial importance to promote activities or programs in which members of different sectors of society interact with professionals in scientific research and their efforts to reduce contamination of emerging pollutants. We cannot try to control a problem without intervening in its true cause, and it is here that science education and, scientific communication directed toward the population can make a difference in mitigating climate change and water pollution.

Forthcoming initiatives should include the promotion of youth participation and education in environmental science and decision-making as a means to help young people contribute to solving environmental problems in the future. This doctoral thesis has focused on treating an environmental problem based on scientific knowledge, but future research should include social and economic components, in order to improve scientific literacy in society.

Keywords: hospital wastewater, pharmaceuticals, solar photo-Fenton, transformation products, and (Q)SAR tools.