Research Article

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From waste to reuse: Fenton degradation of anticancer drugs in hospital wastewater using iron mining residue

Nayara de M Costa-Serge,[a†] Elissandro S Emídio,[a] Karla VL Lima,[a] Adriano L Tonetti[b] and Raquel F Pupo Nogueira[a*]

Abstract

BACKGROUND: The heterogeneous photo-Fenton process demands stable and efficient materials as catalysts to decompose hydrogen peroxide and generate reactive oxygen species to promote the degradation of organic contaminants in wastewater. In this study, the catalytic activity of an iron mining residue (IMR) was investigated for the heterogeneous photo-Fenton degradation of the anticancer drugs 5-fluorouracil (5-FU) and cyclophosphamide (CP) present in hospital wastewater (HW).

RESULTS: High degradation efficiency was observed for 5-FU (>99%) and CP (>95%) after 45 min at pH 2.5 using 1 mmol L^{-1} H_2O_2, and 0.3 g L^{-1} IMR in water. The generation of hydroxyl radical, especially under solar irradiation, indicated the role of the catalyst in generating this oxidizing species, which was confirmed by the drastic decrease of degradation in the presence of tert-butyl alcohol, and by the transformation products of 5-FU and CP identified during the photo-Fenton process. IMR showed stability and maintained >95% removal efficiencies over three reuse cycles with negligible iron leaching (< 1 μmol L^{-1}). For HW, the application of a vermifiltration pre-treatment reduced TOC levels from 129 mg L^{-1} to 21.9 mg L^{-1} and turbidity from 64 NTU to 12 NTU, enabling the degradation of >80% of 5-FU in 90 min under optimized conditions (0.3 g L^{-1} IMR, 3 mmol L^{-1} H_2O_2, solar irradiation).

CONCLUSION: It can be concluded that the IMR presents high stability and efficiency for the degradation of anticancer drugs in real wastewater highlighting its potential as a cost-effective and sustainable catalyst for the photo-Fenton treatment process.

Supporting information may be found in the online version of this article.

Keywords: 5-fluorouracil; cyclophosphamide; iron oxides; Fenton reaction; photodegradation

INTRODUCTION

Pharmaceutical residue has emerged as a critical environmental issue due to the growing production and consumption of drugs worldwide. Among these, cytotoxic drugs used in cancer chemotherapy, which can affect human health and the environment even at low concentrations, are of particular concern.[1] Cyclophosphamide (CP) and 5-fluorouracil (5-FU), two commonly used cytotoxic drugs, have been frequently detected in aquatic environments and are considered priority pollutants due to their adverse effects on ecosystems and human health.[2,3] For instance, CP and 5-FU have been reported in hospital wastewater (HW) at concentrations ranging from 0.2 to 22 100 ng L^{-1} and 0.6 to 124 000 ng L^{-1}, respectively, highlighting the need for effective removal strategies.[4-7]

The release of these pharmaceuticals into aquatic systems primarily results from the discharge of untreated or inadequately treated hospital and municipal wastewater. Once present in the environment, these pharmaceutical residues pose significant risks, exhibiting genotoxic, mutagenic, and teratogenic effects on aquatic organisms and potentially bioaccumulating through the food chain.[4-6] Given their low biodegradability and the inefficacy of conventional wastewater treatment methods such as coagulation, flocculation, biological degradation, or filtration to completely remove them,[8-10] there is a pressing need to develop

* *Correspondence to: RF Pupo Nogueira, São Paulo State University (UNESP), Institute of Chemistry, 14800-060 Araraquara, SP, Brazil E-mail: raquel.pupo@unesp.br (Pupo Nogueira)*

† *Present address: Department of Chemistry, Luminescent Materials Laboratory, Faculty of Philosophy, Science and Letters at Ribeirão Preto, University of São Paulo, 14040-901, Ribeirão Preto-SP, Brazil.*

a *São Paulo State University (UNESP), Institute of Chemistry, Araraquara, SP, Brazil*

b *School of Civil Engineering, Architecture and Urban Design-FEC, UNICAMP, University of Campinas, Campinas, Brazil*

advanced and cost-effective technologies to complement existing conventional treatment processes.

Advanced oxidation processes (AOPs), particularly Fenton-based reactions, have gathered attention for their efficiency in degrading recalcitrant organic pollutants through the generation of hydroxyl radicals (HO•).[11,12] Some degradation processes that have been proposed for CP and 5-FU include the use of simulated sunlight photolysis, photocatalysis, electrochemical oxidation, UV/H_2O_2, and homogeneous Fenton.[13-17] However, some limitations have been reported with the application of these technologies, such as the formation of iron sludge, slow regeneration of Fe(II), high operational costs as well as the energy consumption, leaching of metals, and impossibility of catalyst reuse.[11,12]

Nevertheless, the heterogeneous Fenton process has gained prominence as an effective alternative due to its high efficiency, lower environmental impact, and potential for catalyst reuse.[18-20] Given these advantages, various catalysts have been applied in the heterogeneous Fenton process to degrade a wide range of contaminants.[21] Although previous studies have introduced several innovative catalysts for contaminant removal, research on the application of heterogeneous Fenton systems, specifically for the degradation of 5-FU and CP, remains limited.[18,19,22-24]

To the best of our knowledge, the application of the heterogeneous Fenton process for wastewater treatment has been underexplored. This highlights the need for further investigation into innovative catalytic systems capable of efficiently removing pharmaceuticals from complex matrices such as HW.

The use of waste-derived materials as catalysts for AOPs has emerged as a sustainable solution, combining waste valorization with effective pollutant removal. The iron mining residue (IMR) is generated in large amounts, and generally disposed of in tailing dams, which can lead to contamination of groundwater and surface water. On the other hand, this residue is rich in magnetite (Fe_3O_4), hematite (γ-Fe_2O_3), goethite (α-FeOOH), lepidocrocite (γ-FeOOH), and pyrite (FeS_2), representing a practical and environmentally beneficial catalyst for the Fenton process.[25,26] Furthermore, the use of these industrial wastes can mitigate the environmental impact of mining by-products while offering an effective and economical solution for advanced wastewater treatment applications.

In view of the reuse of solid waste in the iron industry, this study aimed to investigate the effect of IMR for the removal of CP and 5-FU present in a pre-treated hospital wastewater (PTHW). The removal of anticancer drugs in the dark and under solar and artificial radiation is correlated with HO• generation, and the transformation products (TPs) formed are discussed.

MATERIALS AND METHODS

Reagents and materials

5-FU (>99%), CP (>98%), catalase from bovine liver (>10 000 units/mg protein), coumarin, 7-hydroxycoumarin, ammonium metavanadate, *tert*-butyl alcohol (TBA) and *para*-benzoquinone (p-BQ) were acquired from Sigma-Aldrich (Germany). Hydrogen peroxide (30% w/w) was obtained from Synth (Brazil). Methanol and acetonitrile (HPLC grade, 99,99%) were purchased from J.T. Baker (Mexico). 1,10-phenanthroline was obtained from Vetec (Brazil). Ultrapure water (UW) was obtained from a Milli-Q water purification system (Millipore, Bedford, MA, USA). The IMR was acquired from a Brazilian mining company without any previous treatment steps.

Degradation experiments

The degradation of 5-FU and CP mediated by IMR was conducted in a homemade photoreactor equipped with either two 15 W UV blacklight tubes (365 nm) or 7 W blue LEDs (460 nm), positioned 3.8 cm above a 100 mL solution under magnetic stirring. The optical path length was 4.3 cm. Solutions of 5-FU and CP (7.7 μmol L^{-1} each) were prepared in ultrapure water, HW, or PTHW, and the amount of IMR added ranged from 0.15 to 0.45 g L^{-1}. Degradation began with the simultaneous addition of H_2O_2 and activation of the light source.

Aliquots were collected at predetermined intervals, filtered through 0.45 μm polyvinylidene fluoride syringe filters, and analyzed. For experiments involving H_2O_2, the pH of the aliquots was adjusted to 6–8 with NaOH (0.1 mol L^{-1}), and 80 μL of bovine catalase (0.4 g L^{-1}) was added to decompose residual H_2O_2 and stop the Fenton reaction before analysis. All experiments were performed in duplicate, and the average result is shown in the graphs.

Solar photo-Fenton tests were carried out in Araraquara, Brazil (22° S, 48° W) during spring, on sunny days between 11 a.m. and 2 p.m. Solar irradiance and accumulated energy dose were measured using a radiometer (PMA 2100, Solar Light Co.), with the sensor positioned beside the reactor.

Catalyst reusability was evaluated over five cycles. After each cycle, the solid was washed with ultrapure water, centrifuged, and dried under vacuum at room temperature. The recovered material was reused in each cycle in the presence of 5-FU, CP, and H_2O_2 at pH 2.5 under UV irradiation for 60 min.

Chemical analysis

The concentrations of 5-FU and CP during the Fenton experiments were monitored using a High-Performance Liquid Chromatography (HPLC) system (Prominence LC 20AT instrument, Shimadzu, Kyoto, Japan) equipped with a diode array detector (DAD). The chromatographic conditions, including mobile phase composition, flow rates, and detection parameters, are detailed in Supporting Information (SI).

The TPs of CP and 5-FU were identified using Liquid Chromatography coupled to tandem mass spectrometry (LC–MS/MS). The analysis was performed on a Shimadzu Nexera X2 LC system (Kyoto, Japan) coupled to a 3200 QTRAP Mass Spectrometer (AB SCIEX Instruments, Framingham, MA, USA) with electrospray ionization. Instrumental settings and chromatographic conditions for TP analysis are provided in the Supporting Information.

Total soluble iron and residual H_2O_2 concentrations at the end of the heterogeneous Fenton processes were quantified spectrophotometrically using a UVmini-1240 spectrophotometer (Shimadzu, Kyoto, Japan). Residual H_2O_2 was determined using the metavanadate method, measuring absorbance at 450 nm.[27] Total iron was quantified with the 1,10-phenanthroline method, with maximum absorption at 510 nm.[28]

The accumulation of HO• during the reaction was estimated using the coumarin probing technique, where coumarin reacts with HO• to form the fluorescent compound 7-hydroxycoumarin. Excess coumarin (1 mmol L^{-1}) was added to the suspension, without the addition of 5-FU or CP, to ensure the complete trapping of HO• radicals. Detailed analytical parameters are provided in SI.

Experiments in the presence of the HO• scavenger TBA (rate constant: 0.4×10^9 L mol^{-1} s^{-1}) and the superoxide radical ($^{\bullet}O_2^-$) scavenger p-BQ (rate constant: 9.6×10^8 L mol^{-1} s^{-1}) were conducted under blacklight irradiation to evaluate the potential involvement of HO• and $^{\bullet}O_2^-$ in the degradation process.[29] To

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ensure complete scavenging of $HO^{\bullet}$ and $^{\bullet}O_2^-$ generated in the medium, an excess of the inhibitors was added (100 mmol L^{-1} TBA and 2 mmol L^{-1} *p*-BQ).

Sampling of hospital wastewater

The HW and PTHW samples were collected at the University Hospital at the State University of Campinas (UNICAMP) after passing through a sewage treatment system based on vermifiltration, used as a low-cost aerobic wastewater pre-treatment option. This system works as a biological filter that combines bacterial degradation with vermicomposting, resulting in a high efficiency for removing pollutants from sewage[30] (Supporting Information, Fig. S1).

The vermifilter was operated with intermittent flow and a Surface Application Rate (SAR) of 500 L m^{-2} day^{-1}. The reactors were built in a cylindrical PVC structure with a diameter of 300 mm, using a mixture of dried, unchopped Brachiaria grass (genus Brachiaria) and soil in a 3:1 volume ratio as the substrate for earthworms. To the substrate layer, 700 Eisenia Andrei earthworms were added, equivalent to an initial density of 25 000 earthworms m^{-3}.

The physical–chemical parameters determined in the samples are presented in Supporting Information, Table S1.

RESULTS AND DISCUSSION

Characterization of the catalyst

The detailed characterization of the IMR catalyst was previously reported.[26] Briefly, the material exhibits structural complexity with multiple phases, as confirmed by X-ray diffraction (XRD) patterns. Energy dispersive spectroscopy (EDS) analysis revealed O, Fe, Mg, Al, Si, P, and Ce as the most abundant elements. The catalyst particles were predominantly micrometric (75% smaller than 180 µm) with a specific surface area of 26 m^2g^{-1}. Optical characterization indicated strong absorption in the UV range (200–400 nm). X-ray photoelectron spectroscopy (XPS) identified Fe(III) oxides and hydroxides (hematite, magnetite, and goethite), alongside Ce(III) and Ce(IV) in similar proportions. Additional phases such as SiO_2, TiO_2, La_2O_3, and $Al(OH)_3$ were also detected. The zeta potential of the catalyst was determined using a Malvern Zetasizer Nano ZS equipment.

Degradation of 5-FU and CP

To evaluate the effect of the catalytic activity of IMR in heterogeneous Fenton processes on the removal of CP and 5-FU from HW and PTHW, experiments were initially performed in UW to establish the best experimental conditions for further application in HW. For this purpose, the effect of pH, irradiation source, catalyst concentration, and H_2O_2 were investigated, as discussed below. Subsequently, using the best operating conditions, the system was applied to HW.

Effect of the amount of catalyst for 5-FU and CP degradation

The evaluation of the amount of catalyst is essential in heterogeneous Fenton processes. As seen in the Fig. 1, under black light irradiation (365 nm) a higher degradation rate was observed as the catalyst concentration increased from 0.15 to 0.30 g L^{-1} and with 5-FU and CP at undetectable levels after 60 min of reaction with 0.3 g L^{-1}.

As shown in the Eqns (1)–(4), the efficiency of electron transfer between H_2O_2 and iron or cerium species in the IMR contributes to the degradation of the pharmaceuticals due to the generation of reactive oxygen species (ROS). Both Fe(II) and Ce(III) reacts with H_2O_2 to convert into Fe(III) and Ce(IV) with the generation of $HO^{\bullet}$.[26,31]

$$\equiv Fe(III) + H_2O_2 \rightarrow Fe(II) + HO_2^{\bullet} + H^+ \quad (1)$$

$$\equiv Fe(II) + H_2O_2 \rightarrow Fe(III) + HO^- + HO^{\bullet} \; k = 40-80\,M^{-1}\,s^{-1} \quad (2)$$

$$\equiv Ce(IV) + H_2O_2 \rightarrow Ce(III) + HO_2^{\bullet} + H^+ \quad (3)$$

$$\equiv Ce(III) + H_2O_2 \rightarrow Ce(IV) + HO^{\bullet} + OH^- \quad (4)$$

However, when the dosage was increased to 0.45 g L^{-1}, a slight inhibitory effect was observed, particularly for CP degradation, resulting in lower degradation rates compared to 0.3 g L^{-1} due to the increase of turbidity of the suspension. The increase of the turbidity can hinder the penetration of light, which leads to lower activation of the catalyst, reducing the generation of $HO^{\bullet}$.[32]

Considering that the increase in the IMR dosage above 0.30 g L^{-1} did not improve degradation efficiency, 0.30 g L^{-1} was selected as the optimal catalyst concentration for subsequent experiments. These results align with the work of Ayala-Durán *et al.*,[26] which also used a dosage of 0.3 g L^{-1} of IMR, since above this value there was a decrease in transmittance and lower process efficiency.

Effect of H_2O_2 concentration on 5-FU and CP degradation

The effect of H_2O_2 concentration on the degradation of CP and 5-FU was assessed within the range of 0 to 4 mmol L^{-1} (Fig. 2). The results indicate a significant increase in degradation efficiency as the H_2O_2 concentration increased from 0 to 0.5 mmol L^{-1}, confirming that the photocatalytic effect of IMR alone was minimal.

The presence of H_2O_2 was critical for promoting the degradation of the pharmaceuticals, as only 3% of 5-FU and CP were removed in its absence. Notably, at higher H_2O_2 concentrations (2 and 4 mmol L^{-1}), similar degradation levels were observed for both CP and 5-FU, with their concentrations dropping to undetectable levels within 60 min. This effect is likely due to the scavenging of $HO^{\bullet}$ by excess H_2O_2, leading to the formation of less reactive radicals ($HOO^{\bullet}$) (Eq. 5).[33]

$$H_2O_2 + HO^{\bullet} \rightarrow H_2O + HOO^{\bullet} \quad (5)$$

Effect of the pH on 5-FU and CP degradation in deionized water

The pH revealed to play an important role in the efficiency of the Fenton process for CP and 5-FU removal. As seen in Fig. 3, degradation rate of 5-FU and CP increased with decreasing pH from 4 or 6 to 2.5. At pH 2.5, > 99% of 5-FU (Fig. 3(a)) and > 95% of CP (Fig. 3(b)) were removed in 60 min. At pH 6, a maximum of 7% degradation was obtained for both pharmaceuticals. The increase of pH promotes a greater consumption of H_2O_2 but with less degradation of the pharmaceuticals (Fig. 3(c)).

The results obtained are similar to those reported by Dias *et al.*,[34] with 100% efficiency in the degradation of a textile dye (Reactive Black 5) after 60 min of photo-Fenton reaction at pH 3 using an iron rich aluminum industry residue (α-Fe_2O_3). Surface Fe(II) and Fe(III) species in the catalyst are favored under acidic conditions, playing an important role in the formation of $HO^{\bullet}$, which contributed to the efficiency of degradation.

The surface charge analysis of IMR at pH 2.5, 4.0, and 6.0 showed a zeta potential of −7.05, − 16.6, and − 22.0 mV, respectively. This

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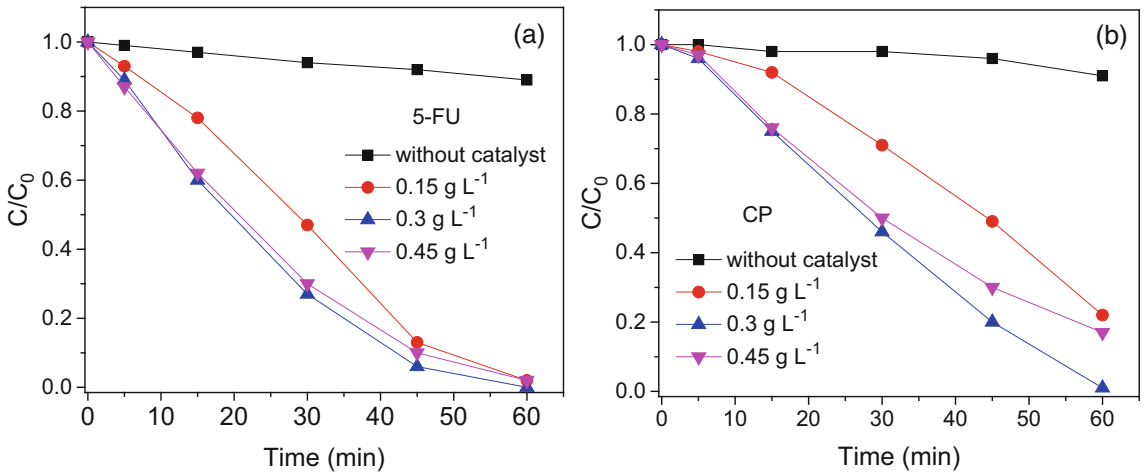

Figure 1. Effect of IMR amount on 5-FU (a) and CP (b) degradation. Conditions: black light irradiation; H_2O_2 1.0 mmol L^{-1}; 5-FU = CP = 7.7 μmol L^{-1}; initial pH = 2.5.

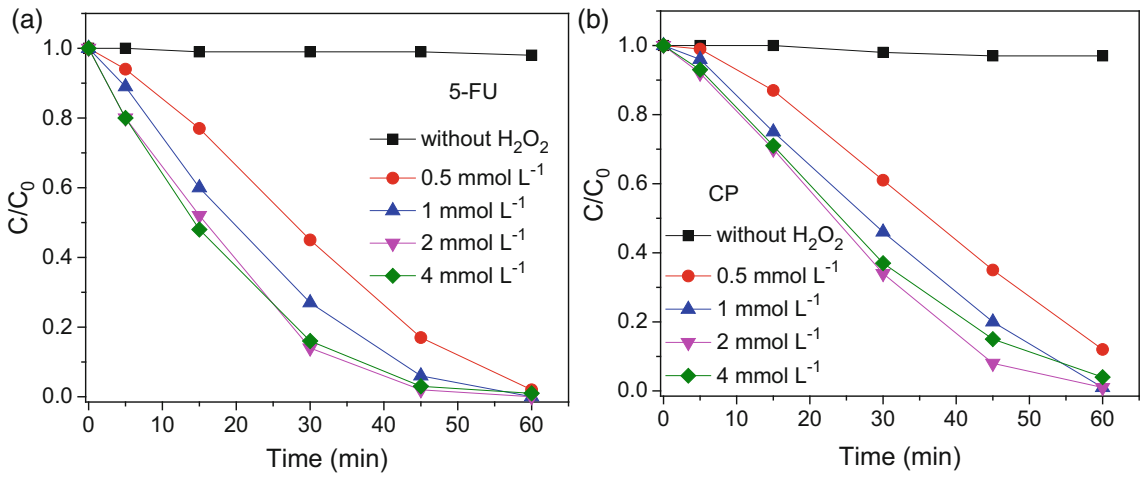

Figure 2. Effect of H_2O_2 concentration on 5-FU (a) and CP (b) degradation. Conditions: black light irradiation; 5-FU = CP = 7.7 μmol L^{-1}; Initial pH: 2.5; IMR = 0.3 g L^{-1}.

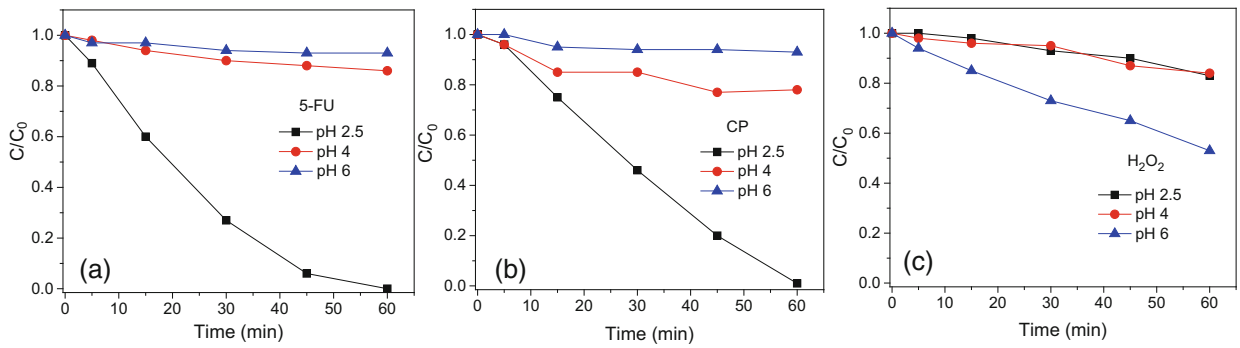

Figure 3. Effect of the pH on the degradation of 5-FU (a) and CP (b) in the heterogeneous Fenton process mediated by IMR and H_2O_2 consumption (c). Conditions: black light irradiation; H_2O_2 1.0 mmol L^{-1}; 5-FU = CP = 7.7 μmol L^{-1}; IMR: 0.3 g L^{-1}.

highly negative surface requires a high concentration of H^+ for surface neutralization. For pH 4.0 and 6.0, the lower degradation efficiency cannot be explained by the interaction between the charges on the catalyst surface and the species of the drugs at these pH values since both 5-FU and CP are mostly found in the non-ionized form (> 93% for 5-FU and > 99% for CP) (Supporting Information, Fig. S2), resulting in a smaller interaction with the catalyst surface.

The CeO_2/H_2O_2 heterogeneous redox system can be activated by surface modification to generate $HO^{\bullet}$ under acidic

conditions,[35] while in neutral medium no formation of HO• radicals is expected since the species Ce(III) − OOH^- formed between the reaction of Ce(III) and H_2O_2 is stable,[36] limiting the degradation process.

Effect of the irradiation source on 5-FU and CP degradation

The degradation of 5-FU and CP using IMR is highly affected by the type of irradiation applied with efficiencies following the order solar > black light > visible LED > dark under the same experimental conditions (Fig. 4).

Notably, IMR is more active in the photo-Fenton process compared to dark Fenton processes, which resulted in 79% degradation of 5-FU and 52% of CP after 60 min of reaction. When the reaction occurred under sunlight, degradation above 90% and 80% for 5-FU and CP after only 30 min was obtained. As for visible LED, the degradation efficiency was also improved in relation to the dark with 91% (5-FU) and 74% (CP) after 60 min.

According to absorbance data,[26] IMR shows maximum absorption in the UV region between 200 nm and 400 nm, with lower absorption between 400 and 550 nm, enabling the use of different sources of irradiation UV, visible or solar, for the heterogeneous photo-Fenton process. Due to extended IMR absorption up to the visible range, it tends to promote efficient photoreduction of the Fe(III) species contained in the material and consequently efficient production of HO• (Eqn 6).[37]

$$\equiv Fe(III) + H_2O + h\nu \rightarrow \equiv Fe(II) + HO^{\bullet} + H^+ \quad (6)$$

The use of ultraviolet lamps for treating industrial effluent consumes a large amount of expensive electrical energy. Therefore, it is desirable to find catalysts for the heterogeneous photo-Fenton process that show high efficiency under sunlight, particularly in Brazil, where high solar irradiation is available throughout the year. As observed in Fig. 4, the sunlight increases the rate of 5-FU and CP degradation compared to the dark process and other irradiation sources, increasing the chances of applicability of this system.

To better understand the interaction between pharmaceutical degradation efficiency and the amount of HO• generated in the Fenton process, the coumarin method was used to estimate HO• produced in the IMR reaction with H_2O_2.

The HO• concentration estimated by the concentration of 7-hydroxycoumarin generated was highest for the solar photo-Fenton process than any irradiation source evaluated and dark Fenton, with similar results under black light and visible LED irradiation (Fig. 5(a)). Moreover, the amount of HO• radicals produced under solar irradiation in the photo-Fenton process was about three times higher than the other irradiation sources and four times higher than the dark process (Fig. 5(a)). These results are consistent with the degradation efficiency, in which the photo-Fenton process under sunlight irradiation assists in the degradation process of contaminants.

The addition of TBA to the reaction medium used to scavenge generated HO•, and *p*-BQ, used to scavenge $^{\bullet}O_2^-$, highlighted the importance of HO• in the degradation process. The addition of TBA reduced drastically the 5-FU degradation from 100% to 10% after 60 min, a 90% inhibition. In contrast, a lower effect of *p*-BQ was observed in the medium, which inhibited 5-FU degradation by 60% inhibition, from 100% to 40% (Fig. 5(b)). The stronger inhibitory effect of TBA confirms the predominant role of HO• in the degradation process mediated by the iron mining residue.

In heterogeneous Fenton processes, it is essential to confirm the stability of the catalyst and its capacity to maintain catalytic activity during several degradation cycles. To verify the stability of the catalyst, the occurrence of iron leaching from the catalyst to the solution at different pH values (2.5, 4 and 5) was evaluated. After 60 min, less than 1 μmol L^{-1} (Limit of Quantification) of total soluble iron was released at the three pH values. This indicates that the process occurs in the heterogeneous phase, even at acid medium. Furthermore, the catalyst can be reused for at least three cycles with degradation efficiencies above 94% for 5-FU and > 95% for CP after 60 min (Fig. 6).

While monitoring other potential leached metal ions would provide additional insights into the environmental impact of the process, the leaching of other metal ions at significant concentrations is highly improbable, considering that iron, the major component of the iron-based catalyst (25.5 at. %),[26] was not leached at significant concentrations.

Nevertheless, changes in the catalyst during the process, such as alterations in the oxidation state of the metals present on the surface, can occur during reuse cycles and lead to a decrease in its ability to catalyze the Fenton reaction. Additionally, the loss

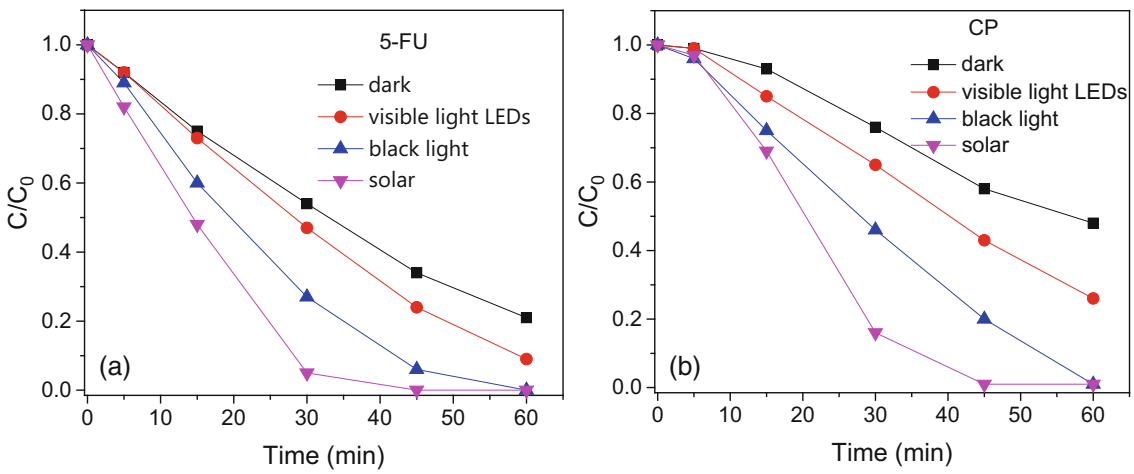

Figure 4. Effect of irradiation source on 5-FU (a) and CP (b) degradation mediated by IMR. Conditions: H_2O_2 1.0 mmol L^{-1}; 5-FU = CP = 7.7 μmol L^{-1}; Initial pH: 2.5; IMR: 0.3 g L^{-1}.

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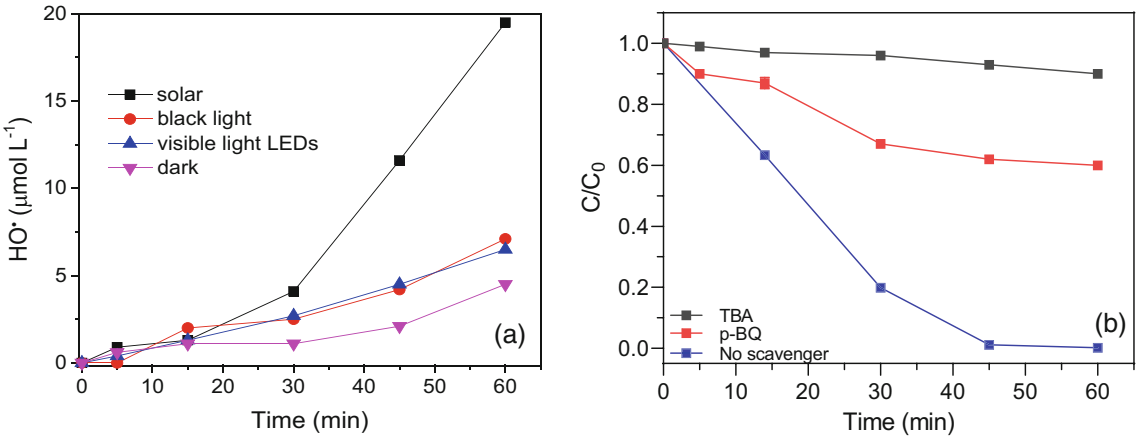

Figure 5. Production of HO• estimated in the presence of coumarin during the heterogeneous photo-Fenton reaction (a); Effect of the HO• scavenger TBA and $^{\bullet}O_2^-$ scavenger p-BQ, on the degradation of 5-FU (b). Conditions: H_2O_2 1.0 mmol L^{-1}; Initial pH: 2.5; IMR: 0.3 g L^{-1}.

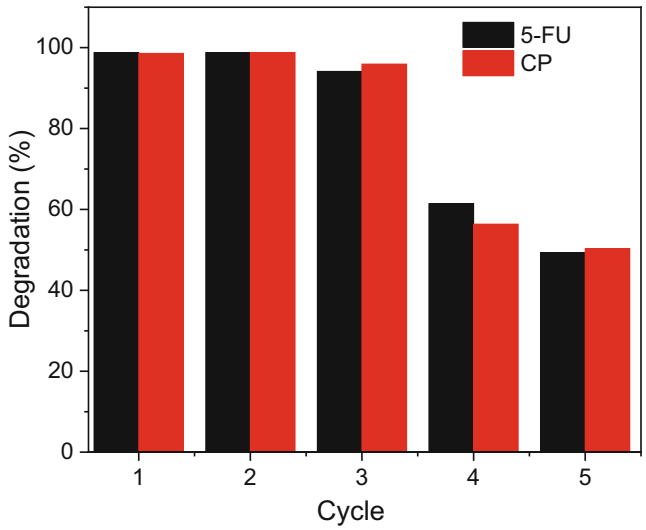

Figure 6. Degradation of 7.7 µmol L^{-1} of 5-FU and CP after 60 min and IMR catalyst reuse cycles. Conditions: black light irradiation; H_2O_2 1.0 mmol L^{-1}; 5-FU = CP = 7.7 µmol L^{-1}; Initial pH: 2.5; IMR: 0.3 g L^{-1}.

of catalytic activity may be exacerbated by the occupation of active sites by the TPs generated during degradation.[26] These combined effects contribute to the reduction in catalytic performance, resulting in approximately 60% degradation efficiency after the third reuse cycle.

Transformation products

The CP and 5-FU transformation pathways were elucidated based on the identification of TPs by heterogeneous photo-Fenton processes using LC–MS/MS (Fig. 7). A suspect screening approach in LC–MS/MS was adopted based on a database composed of a list of possible TPs already identified in the literature in different oxidative treatment processes. Supporting Information, Table S2 presents detailed information on the identification of 5-FU and CP TPs generated in the heterogeneous photo-Fenton process.

A single TP with mass/charge ratio (*m/z*) of $[M\text{-}H]^-$ = 143 (TP-5FU1) was identified in the case of 5-FU, which corresponds to $C_4H_3N_2O_4$, a dihydroxylated product generated from hydroxylation on the pyrimidine ring and electrophilic replacement of the fluorine atom by a hydroxyl group. TP-5FU1 was identified by Kosjek *et al.*,[38] during degradation under UVC + H_2O_2 and Ochoa-Chavez *et al.*,[39] using electrochemical oxidation. Although the monohydroxylated product was not detected in the reaction system, its rapid oxidation to TP-5FU1 is feasible considering the high reaction rate under the conditions employed. This finding agrees with the work of Ochoa-Chavez *et al.*,[39] who also did not detect the presence of the monohydroxylated product during the degradation of 5-FU.

The TPs of the CP were formed in two steps and the products identified showed *m/z* = 199 (TP-CP1), 259 (TP-CP2) and 275 (TP-CP3). The first step refers to the cleavage of the chloroethane - N bonding leading to the formation of TP-CP1 (m/z = 199). The second step is the dehydrogenation of the CP ring, leading to the formation of iminophosphamide (TP-CP2; m/z = 259), with subsequent hydroxylation and formation of 4-ketocyclophosphamide (TP-CP3; m/z = 275).[17,40]

In summary, hydroxylation plays a central role in the transformation of CP and 5-FU during the heterogeneous photo-Fenton process, highlighting the significant contribution of HO• radicals to the degradation of these pharmaceuticals.

Application of the heterogeneous photo-Fenton process for the treatment of hospital wastewater after vermifiltration

The average organic matter content, measured in terms of Chemical Oxygen Demand (COD), for the HW was 974 ± 241 mg L^{-1}, while the PTHW treated by the vermifilter showed an average of only 190 ± 33 mg L^{-1}, resulting in a removal efficiency of 80 ± 13%. The effluent quality was also assessed in terms of Biochemical Oxygen Demand (BOD), which reached an average of 85 ± 31 mg L^{-1}, meeting the requirements of Brazilian legislation for discharge into receiving bodies.[41] Additionally, a homogeneous accumulation of vermicompost was observed throughout the depth of the substrate in the vermifilter, which provides greater water retention and enhanced adsorption of both organic and inorganic particulate matter.

In the HW, 5-FU degradation reached only 23% after 90 min with 18% H_2O_2 consumption, much lower than in UW, in which, 45 min were sufficient for a complete degradation (> 99%) of 5-FU (Fig. 8(a)). Under the conditions of the heterogeneous photo-Fenton process adopted, the degradation of 5-FU followed pseudo-first order reaction kinetics, and the kinetic parameters

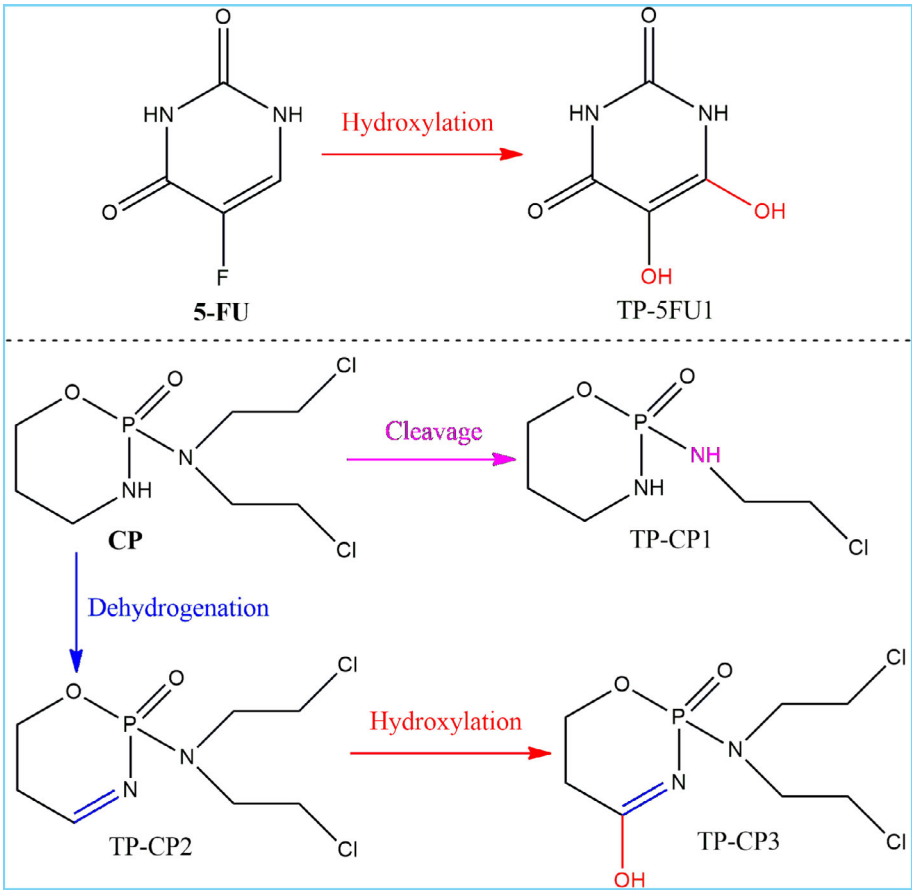

Figure 7. Proposed TPs of 5-FU and CP by photo-Fenton process using IMR. Conditions: black light irradiation; H_2O_2 1.0 mmol L^{-1}; 5-FU = CP = 7.7 μmol L^{-1}; IMR: 0.3 g L^{-1}.

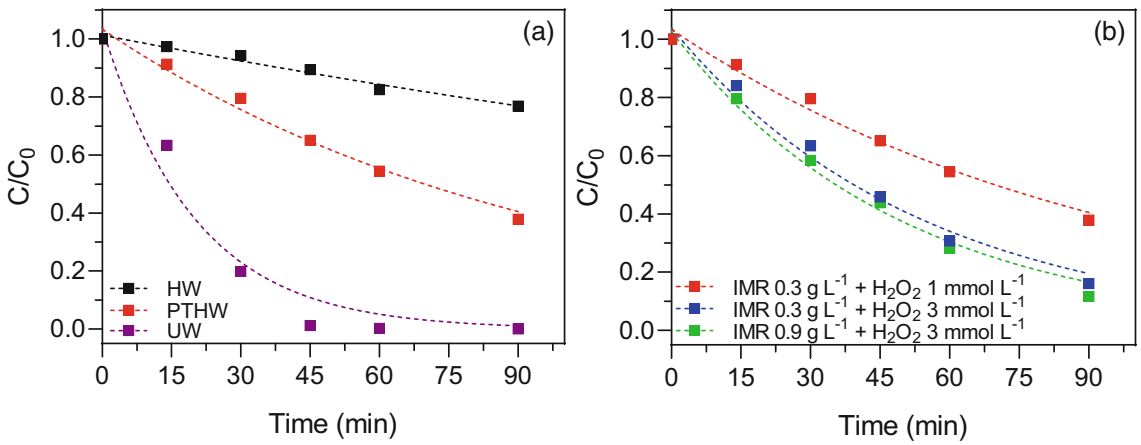

Figure 8. Degradation of 5-FU by heterogeneous photo-Fenton under sunlight in HW, PTHW and UW with IMR 0.3 g L^{-1} + H_2O_2 1 mmol L^{-1} (a) and in PTHW varying the H_2O_2 concentrations and IMR amount (b). Fittings to pseudo first-order model (dashed line) are represented together with the corresponding experimental results. Experimental conditions: 5-FU = 1 mg L^{-1}, pH = 2.5.

determined for the 5-FU degradation in HW, PTHW and UW are shown in Supporting Information, Table S3. In HW, very low kinetics (k = 0.003 min^{-1}) was observed in relation to that obtained in UW (k = 0.1094 min^{-1}). The strong inhibition observed in this case is due to matrix composition, mainly the high Total Organic Carbon concentration (TOC, 129.2 mg L^{-1}), inorganic carbon (56.2 mg L^{-1}) and high turbidity (64 NTU) (Supporting Information, Table S1). Natural organic matter and carbonate are common scavengers of ROS, which reduce degradation efficiency.[42,43]

The negative influence of these components is further supported by the higher degradation percentage observed in PTHW. In PTHW, following treatment with a vermifilter, TOC and turbidity levels were significantly lower, 21.9 mg L^{-1} and 12 NTU,

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respectively. This reduction likely contributed to the enhanced degradation of 5-FU in this matrix, achieving over 50%. In addition, the PTHW samples presented higher nitrate values, which photolysis may favor the formation of HO radical and consequently the degradation of the contaminant.[42]

The application of different conditions in the heterogeneous photo-Fenton system using IMR was evaluated for the degradation of pharmaceuticals in the PTHW (Fig. 8(b)). Increasing H_2O_2 concentration from 1 mmol L^{-1} to 3 mmol L^{-1}, resulted in a significant increase of the 5-FU degradation in PTHW from 62% to 88% after 90 min using 0.3 g L^{-1}. However, an increase in IMR concentration to 0.9 g L^{-1} did not result in further improvement in degradation efficiency achieving 84% after 90 min, indicating that H_2O_2 concentration is a more important parameter for 5-FU removal than catalyst concentration due to high concentration of organic matter demanding oxidizing agent.

According to our investigations, in 90 min of reaction it is possible to achieve more than 80% 5-FU removal at high concentrations (7.7 µmol L^{-1} or 1 mg L^{-1}) in a complex matrix, with 3 mmol L^{-1} of H_2O_2 and 0.3 g L^{-1} of IMR. For comparison, the study of Evgenidou *et al.*,[44] reported that the achieved degradation percentages ranged from 50% to 94% of 5-FU using TiO_2 films immobilized on polymers. However, their experiments were conducted exclusively in ultrapure water and with a significantly higher material dosage (1 g L^{-1}) than that used in this study. Another study by Emídio *et al.*,[19] reported 99% degradation of 5-FU with the same 5-FU concentration as in this study (7.7 µmol L^{-1}). However, this result was only achieved using an H_2O_2 concentration five times higher (15 mmol L^{-1}) than used in this study and in ultrapure water, a much less complex matrix compared to PTHW.

When comparing the degradation obtained by applying the IMR with previous studies on 5-FU degradation (Table 1), most catalysts require longer reaction times, higher dosages, or complex synthesis procedures. Emídio *et al.*,[19] reported 99% degradation of 1 mg L^{-1} 5-FU in deionized water using 0.125 g L^{-1} of $Fe_{2{\cdot}75}Cu_{0{\cdot}25}O_4$ under UV irradiation, requiring 150 min. Similarly, Perez-Poyatos *et al.*[23] achieved complete degradation within 60 min, but in ultrapure water, while Dinesh *et al.*[45] reported rapid 5-FU degradation (90.65% in 5 min) *via* sono-photocatalysis, demanding UV-C and ultrasound irradiation, which involve high energy costs.

Photocatalysts such as ZnO@CU/BEN,[47] TiO_2,[47] and Bi—B co-doped TiO_2[48] exhibited high degradation rates (≥ 90%) in purified water, in the absence of radical scavengers, such as natural organic matter, ions and other contaminants. On the other hand, TiO_2/NF system[49] and copper-based catalytic system[50] achieved much lower efficiency, 80% degradation after 360 min, and 24 h for complete degradation, respectively.

In contrast, the IMR-based solar photo-Fenton system achieved >80% degradation of 1 mg L^{-1} 5-FU within 90 min in a pre-treated hospital wastewater, a high efficiency in a complex matrix containing 21.9 mg L^{-1} of organic carbon and 47.6 mg L^{-1} inorganic carbon, which can scavenge hydroxyl radicals.

Additionally, IMR is a zero-cost material abundantly available, with approximately 0.4 tons being generated for each ton of iron ore processed. In this context, the use of IMR as a catalyst presents a promising approach to reduce the costs associated with the photo-Fenton process, as there are no expenses related to catalyst

Table 1. Comparison of catalysts performance for 5-FU degradation

Catalyst	Advanced oxidation process	Matrix	5-FU (mg L^{-1})	Degradation (%)	Mineralization (%)	Reference
$Fe_{2.75}Cu_{0.25}O_4$	Heterogeneous photo-Fenton	Deionized water	1	99 (150 min)	Not reported	Emídio *et al.*,[19]
g-C_3N_4	Sono-photocatalysis	Ultrapure Water	30	90.65 (5 min)	Complete	Dinesh *et al.*,[45]
Fe_3O_4	Solar photo-Fenton	Ultrapure Water	10	~100 (60 min)	Not reported	Perez-Poyatos *et al.*,[23]
ZnO Supported Curcumin Intercalated Bentonite (ZnO@CU/BEN)	Photo-Fenton	Ultrapure water	25	99 (80 min)	Complete	Othman *et al.*,[46]
CuMgFe-B(OH)$_4$ (LDH)	Solar photo-Fenton	Deionized water	0.2	99 (20 min)	Not reported	Costa-Serge *et al.*,[18]
CuMgFe-NO_3 (LDH)	Fenton	Deionized water	0.2	99 (120 min)	Not reported	Costa-Serge *et al.*,[18]
CuMgFe-SO_4 (LDH)	Fenton	Deionized water	0.2	70 (120 min)	Not reported	Costa-Serge *et al.*,[18]
TiO_2	Photocatalysis	Ultrapure water	26	92 (120 min)	Not reported	Kulaksız *et al.*,[47]
Bi–B co-doped TiO_2	Photocatalysis under simulated sunlight	Distilled water	1	99.9 (90 min)	5–7	Fiszka Borzyszkowska *et al.*,[48]
TiO_2/NF	Photocatalysis	Distilled water	20	80 (360 min)	23.2	Ren *et al.*,[49]
Copper-Based Nanoparticles	Fenton	Distilled water	244.8	99 (24 h)	Not reported	Javitt *et al.*,[50]
IMR	Solar photo-Fenton	Pre-treated Hospital wastewater	1	80 (90 min)	Not reported	This study

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production. These features and results indicate the IMR as an attractive option for large-scale wastewater treatment applications, cost effective and environmentally friendly catalyst.

CONCLUSIONS

The findings revealed the significant activity of IMR, a low-cost catalyst, for the removal of anticancer drugs from HW in heterogeneous photo-Fenton process. More than 80% removal of 1 mg L^{-1} 5-FU from PTHW was obtained after 90 min of reaction using 0.3 g L^{-1} IMR and 3 mmol L^{-1} H_2O_2. The $HO^{\bullet}$ was responsible for the initial transformation of 5-FU and CP, generating hydroxylated and defluorinated product of 5-FU and hydroxylated product of CP. In the case of CP, two other products were generated by the cleavage of the chloroethane-N bonding and dehydration. The good stability and catalytic efficiency of IMR, even after five cycles of use, make this material a potential candidate for use in heterogeneous photo-Fenton processes employed for anticancer drug degradation in HW.

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DATA AVAILABILITY STATEMENT

Data available upon reasonable request from corresponding author.

SUPPORTING INFORMATION

Supporting information may be found in the online version of this article.

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