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ADVANCED OXIDATION/REDUCTION TECHNOLOGIES: AN PERSPECTIVE FROM IBEROAMERICAN COUNTRIES

Is ionizing radiation effective in removing pharmaceuticals from wastewater?

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Abstract

Wastewater and effluent discharges are the main causes of receiving water body pollution and important challenges in water quality management. Among the emerging contaminants, pharmaceuticals have increasingly drawn attention due to their incomplete removal during conventional biological treatment, inducing potential and actual risks to living organisms following residue discharges in river effluent. Electron beam irradiation (EBI) is a clean process technology for organic compound degradation and mineralization, as well as persistent pollutant detoxification. This study aimed to evaluate EBI effects on the degradation and toxicity removal of anti-inflammatory aspirin (ASA) in a single solution and in a fluoxetine (FLX) mixture. Results indicate that 98% of the single aspirin was degraded at 5.0 kGy. Aspirin toxicity to *Daphnia similis*, however, increased with increasing absorbed dose (1.0 to 5.0 kGy), possibly as a result of the presence of H_2O_2 and other byproducts formed during the oxidation process. Regarding the irradiated mixture, complete degradation was achieved for both pharmaceuticals. Toxicity removals for the mixture were of 56.2 ± 0.9% and 58.8 ± 5.4% for 1.0 and 2.5 kGy, respectively. These findings demonstrate that EBI can be an interesting alternative process to be applied as a pre-treatment followed by biological treatment.

Keywords Antidepressant · Anti-inflammatory · Clean process technology · Electron beam irradiation · Mixture · Toxicity

Introduction

Water quality management has emerged as a global challenge, since many researchers and policymakers have targeted different issues related to water use in agriculture concerning the impact of future droughts on food security and on receiving water quality (Larsen et al. 2016). Concerns regarding the disposal of domestic wastewater without sufficient treatment are increasing, especially in developing countries, where the sewage system development has not caught up with urbanization. Situations in wastewater treatment plants (WWTPs) vary significantly in developing countries worldwide. For example, estimates indicated that 80% of household wastewater in most sub-Saharan African, Latin America, and Caribbean countries received at least secondary treatment in 2017, while less that 50% of wastewater was treated (WHO and UNICEF, 2019).

Several alternative sustainable technologies have been developed for reducing pollutant loads in the aquatic environment, such as membrane technology (Figoli and Criscuoli 2017), bioremediation (Shah and Shah 2020), light-driven processes (Foteinis et al. 2018), and radiation technology (Hossain et al. 2018), among others. Advanced oxidative processes (AOPs) have been applied as an interesting alternative for the degradation, mineralization, and toxicity removal of several pollutants. AOPs involve the *in situ* generation of highly selective reactive oxygen species (ROS), such as hydroxyl radicals (•OH), H_2O_2, O_3, and superoxide anion radicals ($O_2^{\bullet-}$), presenting low selectivity and providing pathways to complete compound mineralization to CO_2, H_2O, and inorganic acids (Kanakaraju et al. 2018). Several studies have reported the use of ozonation

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(Ashraf et al. 2016), photo Fenton (Bansal et al. 2018), photocatalysis (Mukherjee et al. 2016; Jallouli et al. 2018), ionizing radiation (Silva et al. 2016), and electrochemical oxidation (Ensano et al. 2016) for pollutant removal.

Electron beam irradiation (EBI) is considered a clean process that offers an environmentally friendly alternative for degrading pollutants in the aquatic environment. It is a non-chemical process that uses the fast formation of short-lived reactive radicals which can interact with a wide range of pollutants, leading to purification (Chmielewski and Han 2016). The degradation mechanism is based on chemical transformations induced by ionizing radiation through reactions with highly reactive species, such as the hydrated electron, •OH radicals, and H•, formed by water radiolysis (Buxton, 2008).

In recent decades, pharmaceuticals and personal care products and their bioactive metabolites have been recognized as contaminants of emerging concern, as they play an important role in impacting the aquatic environment. Unlike many pollutants, pharmaceuticals are molecules designed to interact with specific physiological pathways, in the living organisms, which makes them biologically active in non-target species (Godoy and Kummrow 2017). Several studies describe the presence of pharmaceuticals in aquatic environments and wastewater effluent at low concentrations (ng L^{-1} to μg L^{-1}) (Yang et al. 2017; Couto et al. 2019), although concentrations up to the mg L^{-1} range have been reported for formulation facilities and drug manufacturers (Larsson et al. 2007). Among them, fluoxetine (Prozac®) is commonly detected in water and wastewater (Brooks et al. 2003; Metcalfe et al. 2010; Paíga and Delerue-Matos 2016). This compound is a selective serotonin reuptake inhibitor (SSRI), a class of drugs commonly prescribed for treating clinical depression, obsessive-compulsive disorder, panic, social phobia, and attention-deficit disorder (Schultz and Furlong 2008; Silva et al. 2012), which displays high toxicity and the ability to bioaccumulate and alter both organism behavior and reproduction at environmentally relevant concentrations (Brooks et al. 2003; Ford and Fong 2016; Shaliutina-Kolešová et al. 2020). Another class of pharmaceuticals, acetylsalicylic acid and its metabolites, has been detected in several matrices, i.e., surface water (Wang et al. 2010; Tewari et al. 2013; Na et al. 2019), groundwater (Paíga and Delerue-Matos 2016), and in wastewater treatment plant effluents (Ternes 1998; Papageorgiou et al. 2016; de Jesus Gaffney et al. 2017). Aspirin is widely used in human medicine as an analgesic and anti-pyretic and in actively preventing platelet aggregation (Nunes et al. 2015) and is also frequently detected in influent samples at high concentrations. For instance, Papageorgiou et al. (2016) detected salicylic acid in 70.8% of influent samples of a municipal treatment plant in Central Greece at mean concentrations of 7852 ng L^{-1}. Higher salicylic acid and acetylsalicylic concentrations were detected in industrial wastewater, reaching concentrations up to 3295 μg L^{-1} and 650 μg L^{-1}, respectively (Camacho-Muñoz et al. 2014; Napoleao et al. 2018).

Several studies have reported EBI as an important and efficient technology for the degradation and detoxification of the anti-depressant fluoxetine (Silva et al. 2016; Shao et al. 2018) and anti-inflammatory compounds (He et al. 2014; Tominaga et al. 2018). For instance, Silva et al. (2016) obtained 80.0% and 22.2% decreases in acute toxicity towards *D. similis* and *Vibrio fischeri*, respectively, after irradiating an aqueous fluoxetine solution diluted 50% v/v in raw domestic sewage with 5.0 kGy. Most studies, however, focus on the effect of radiation on a single pharmaceutical. Therefore, there is a need to understand the mechanisms involved in the irradiation of pharmaceutical mixtures, the competition for the reactive species generated from water radiolysis, and the determination of suitable doses for target pharmaceutical and mixtures. Previous studies have a demonstrated negative influence on the degradation of pharmaceutical mixtures. For example, Zhuan and Wang (2020) verified a negative influence on the degradation efficiency of the anti-inflammatory diclofenac, from 80.8 to 62.9% in the presence of 30 mg L^{-1} of humic acid after gamma irradiation at 1 kGy, mainly due to the competition between humic acid and diclofenac for (•OH) radicals. Tominaga et al. (2018) observed the removal of approximately 30% and 3% of diclofenac in the absence and presence of fluoxetine irradiated by EBI at 1.0 kGy, respectively. Reinholds et al. (2017) evaluated the degradation of multi-class pharmaceuticals in municipal wastewater samples, where almost complete degradation was achieved (84 to 100%) for the studied pharmaceuticals at absorbed doses ranging from 3 to 7 kGy by electron beam and gamma irradiation. However, a lower decomposition rate was observed for macrolide antibiotics when compared to other contaminants, requiring higher doses (> 5 kGy) for removal. In this present study, we focused on the degradation and toxicity removal of acetylsalicylic acid as a single solution and in a binary mixture alongside fluoxetine (ASA + FXT).

Experimental

Reagents

Acetylsalicylic acid [$C_9H_8O_4$, 2-acetoxybenzoic acid, MM = 180.16 g mol^{-1}; CAS 50-78-2] and hydrogen peroxide (H_2O_2, 30%) were purchased from Labsynth (99.5%). Fluoxetine hydrochloride [$C_{17}H_{18}F_3NO{\cdot}HCl$; MM = 309.33 g mol^{-1}; methyl[(3S)-3-phenyl-3-[4-(trifluoromethyl) phenoxy] propyl] amine]; CAS 54910-89-3] was obtained from Divis Pharmaceuticals Pvt. Ltd. (98.8%). Sulfuric acid (H_2SO_4, 95–98%) was obtained from Neon; ammonium metavanadate (99.5%) was purchased from Carlo Erba. Hydroxide sodium (NaOH) and acid hydrochloric (HCl) were purchased from Alphatec. Acetonitrile and trifluoroacetic acid were both HPLC grade and purchased fromSigma-Aldrich). All aqueous

solution prepared for irradiations experiments were diluted using ultra-pure water (Millipore Milli-Q).

Degradation experiments

All experiments were performed in batch scale (220–250 mL), using a Dynamitron® electron beam accelerator at 37.5 kW and 1.4 MeV. Applieddoses were set at 1.0, 2.5, and 5.0 kGy,confirmed through a Perspex Harwell Red dosimeter (Batch KZ-4034) and variations lower than 5%. The aqueous solutions were placed in rectangular glass recipients (Pyrex®) and irradiated ensuring adequate and uniform electron beam penetration.A sample volume of 246 mL was used, totaling a maximum exposed liquid thickness of 4 mm, as described previously (Silva et al. 2016; Tominaga et al. 2018). The recipients passedunder the electron beam twice on an automated conveyor at 6.72 m min^{-1}. All experiments were performed in duplicate.

An initial ASA and FXT concentration of 10.0 mg L^{-1} for the individual degradation studies was used, which corresponded to 0.06 μmol L^{-1} ASA and 0.03 μmol L^{-1} FXT. Higher aspirin concentrations were used to assess degradation kinetics and toxicity. For the mixture experiments, the initial solution was prepared at 5.0 mg L^{-1} of each pharmaceutical (0.03 μmol L^{-1} ASA and 0.02 μmol L^{-1} FXT), based on the closest concentrations of salicylates detected in industrial wastewater (Camacho-Muñoz et al. 2014). All experiments were performed at room temperature and at an initial pH of 7, adjusted with 0.1 M NaOH or 0.1 M HCl. pH values were not corrected during the reaction time.

Analytical methods

Ultra-fast liquid chromatography (UFLC) analyses

An UFLC was employed to determine the aspirin (ASA) and fluoxetine (FLX) concentrations in aqueous solutions using a Shimadzu equipment (LC 20AD) with UV/vis (SPD 20A) and fluorescence (RF-10Axl) detectors. A C18 ACE 5 column (250 mm × 2.0 mm × 2.5 μm) was used and the oven temperature was set at 40 °C. Isocratic analyses were performed using (A) trifluoroacetic acid 0.2% and (B) acetonitrile at 65:35 at a flow rate of 1.0 mL min^{-1}. The fluorescence detector was used for FLX identification at 230 nm (excitation) and 290 nm (emission). ASA was detected by UV/vis absorption at 230 nm. The ASA and FLX retention times were 5.5 min and 26.5 min, respectively. The injection volumes were 50 μL. Calibration was performed using external standards prepared with known ASA and FXT concentrations. For ASA and FXT, curve 1 (R^2 = 0.9999, LD = 70.4 μg L^{-1}; LQ = 211 μg L^{-1}) and curve 2 (R^2 = 0.9994, LD = 202 μg L^{-1}; LQ = 607 μg L^{-1}) were determined, respectively, where LD and LQ refer to the limits of detection and quantification, respectively.

The total organic carbon

Pharmaceutical mineralizations were assessed by total organic carbon concentration (TOC) decays during degradation, determined for all applied doses on a Shimadzu TOC 5000A equipment.

Hydrogen peroxide formation

Hydrogen peroxide formationwas determined using a spectrophotometric method employing ammonium metavanadate in an acid medium (Nogueira et al. 2005). This method is based onH_2O_2 reaction with $(NH_4)_3VO_4$ in an acidic medium, resulting in the formation of a red-orange color peroxovanadium cation with maximum absorbance at 450 nm.

Toxicity assays using *Daphnia similis*

Stock solutions of single ASA, FXT, and their mixturewere used in the assays. Acute toxicity assays were performed with *D. similis* according to ABNT Brazilian Standard NBR-12713 (ABNT, 2016). Twenty neonates (6–24 h) were placed in four replicates for each concentration (five organisms/replicate). All tests were performed in a darkened room at 20 ± 1 °C. After 48 h, organismwas recorded. The EC50% (Effective Concentration 50) was calculated from the estimated endpoint by the Trimmed Spearman-Karber method (Hamilton et al. 1977). The significance of any differences between average values for the control and the experimental treatments were evaluated by analysis of variance (ANOVA) at a 5% significance threshold level. When the ANOVA revealed significant differences among treatments, a post hoc Tukey test was carried out (at $p = 0.05$) to prove the existence of significant differences.

Results and discussion

Single acetylsalicilyc acid and fluoxetine degradation in aqueous solutions treated by Electron Beam Irradiation

The results of the single anti-inflammatory and anti-depressant compound degradations are displayed in Fig. 1. EBI was effective for the removal of both single pharmaceutical solutions (0.06 μmol L^{-1} ASA and 0.03 μmol L^{-1} FXT) at a low dose of 1.0 kGy, resulting in concentrations below the limit of detection, 0.39 μmol L^{-1} for aspirin, and 0.65 μmol L^{-1} for fluoxetine. Apparently, fluoxetine is effectively degraded by EBI at relatively low doses, presenting over 90% FXT degradation at 0.5 kGy from an initial solution at 0.06 μmol L^{-1} and 98.0% degradation from 0.16 μmol L^{-1} at 1.0 kGy (Silva et al.

2016; Shao et al. 2018). Based on the effective removal of both pharmaceuticals at low concentrations and the lack of information on ASA degradation by EBI, higher concentrations were evaluated for the anti-inflammatory compound.

Electron beam irradiation excites and ionizes water molecules to produce highly reactive radicals, such as hydrated electron (e^-_{aq}), hydroxyl radicals (•OH), and the hydrogen atom (H•), which react and result in the rapid degradation of organic pollutants (Buxton 2008). Figure 2 displays the results of the degradation of the single anti-inflammatory solution at higher concentrations. The degradation kinetics presented a linear ln([ASA]/[ASA]$_0$) vs dose curve (Fig. 2a), indicating that aspirin degradation up to 5.0 kGy followed a pseudo-first-order behavior, with $k_0 = 0.7411$ kGy ($R^2 = 0.9911$). Furthermore, over 50% of aspirin degradation was achieved at 1.0 kGy. An increase in aspirin degradation was obtained by increasing the absorbed dose, reaching 97.41% ASA degradation at 5.0 kGy (Fig. 2b).

The transformation of organic molecules is a multistep process that occurs during the irradiation process, which can be detected as carbon content (TOC). The TOC results indicated that the EBI process did not reach complete pharmaceutical mineralization, inducing the formation of recalcitrant byproducts. Negligible TOC removal of about 3% was achieved after EBI dose application of up to 5 kGy (Fig. 2b). These results corroborate previous studies. For example, Szabó et al. (2014) evaluated the oxidation of 1–2 mmol L^{-1} aerated salicylate solutions (acetylsalicylic acid and salicylic acid) treated by gamma radiation, reporting that TOC measurements decreased linearly with absorbed doses in the 1 mmol L^{-1} ASA solution, achieving low ASA mineralization at doses up to 5 kGy.

Figure 3 indicates a decrease in the pH of the aqueous aspirin solution withincreasing absorbed dose. The solution pH ranged from 6.8 ± 0.1 to 5.1 ± 0.0 at 5.0 kGy. In contrast, solution conductivity increased from 77.8 μS cm^{-1} to 98.8 μS cm^{-1}. These trends are associated tothe formation of acid transformation products and increase indissolved ion concentrations (Dai et al. 2014; Mukherjee et al. 2016) due to the break of aromatic rings, first into longer carboxylic acids (maleic, fumaric acids) and then, into smaller acids (glyoxylic, oxalic, acetic, formic acids) in the presence of dissolved O_2 (Szabó et al. 2014). Szabó et al. (2014) reported the formation of the salicylate ion and acetylsalicylic acid dihydroxy derivatives after gamma irradiation. Moreover, the formation of several byproducts, such as salicylic, acetic, fumaric or maleic, and malic and malonic acid, has also been identified for aspirin degradation under solar light in the presence of a TiO_2-polymeric film (Mukherjee et al. 2016). Dai et al. (2014) reported the formation of intermediate compounds (salicylic acid, phenol, p-dihydroxybenzene, o-dihydroxy benzene, and maleic, fumaric, succinic, acetic acid) after ASA degradation by catalytic ozonation using CeO_2 nanoparticles.

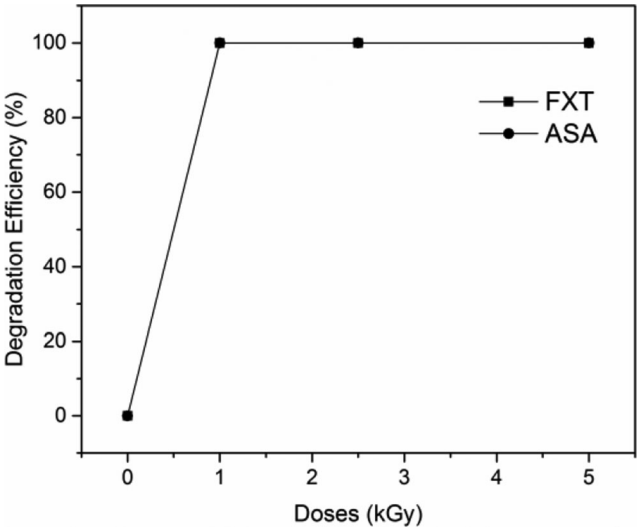

Fig. 1 Degradation efficiency of single ASA (*circle*) and FXT concentrations (*square*) vs. dose using EBI. Initial conditions: $[ASA]_0 = (0.053 \pm 0.006)$ μmol L^{-1} and $[FXT]_0 = (0.039 \pm 0.061)$μmol L^{-1}

Toxicity

The average effective concentrations that immobilized 50% of exposed daphnids, the EC50, for ASA and FXT were determined as 86.05 ± 4.63 mg L^{-1} and 1.45 ± 0.36 mg L^{-1}, respectively, indicating that *D. similis* is far more sensitive to FLX compared to ASA. This corroborates previous studies, since Silva et al. (2016) reported an EC50 of 1.32 mg L^{-1} for *D. similis* exposed to FXT, and an LC50 of 88.1 and 88.33 mg L^{-1} has been reported for *D. magna* after 48-h exposure to ASA (Cleuvers 2004; Gómez-Oliván et al. 2014). Although low acute toxicity has been reported in the literature, Gómez-Oliván et al. (2014) noted oxidative stress and DNA damage in *D. magna* after 48-h exposure at lower ASA concentrations (8.83 mg L^{-1}). Moreover, a lowest observed effect concentration (LOEC) of 1.8 mg L^{-1} during chronic exposure to ASA has been reported, associated to *D. magna* reproduction effects, causing abortions and abnormal neonates (Marques et al. 2004).

Toxicity measurements are useful tools to evaluate the potential danger of byproducts generated by AOPs since, after the degradation process, the formation of more toxic byproducts than the parental compound may occur. For FXT, high toxicity removal was achieved, from 7.23 ± 2.04 to 2.68 ± 0.12 and 2.88 ± 0.32 TU at 1.0 and 5.0 kGy (Fig. 4a), respectively, representing approximately 60% toxicity removal, indicating residual toxicity of the formed byproducts. The Tukey test indicated that irradiation was effective for toxicity removal of the irradiated samples, although no significant differences in the acute toxicity of FXT solutions between 1.0 and 5.0 kGy was observed, indicating that low doses can be applied for FXT toxicity removal. Nine transformation products have been elucidated for EBI-driven fluoxetine degradation through the electrophilic addition of hydroxyl

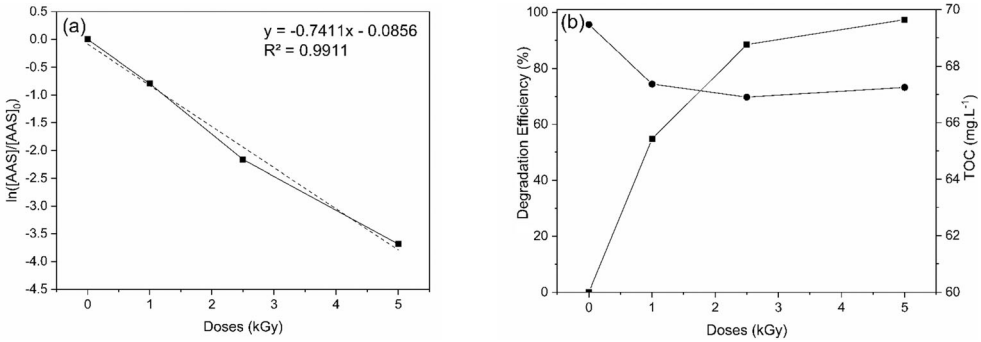

Fig. 2 **a** Logarithm of relative aspirin concentration vs.dose and **b** degradation efficiency (square) and TOC concentrations (circle)of ASA vs. dose using EBI. Initial conditions: $[ASA]_0 = (0.464 \pm 0.009)$ μmol L^{-1}; pH = 6.78 ± 0.98

radicals generated from water radiolysis to the aromatic groups, further hydroxylation of ring systems, and also release of fluoride anions (Silva et al. 2016). Nonetheless, for single ASA, the byproducts appeared to be more toxic than the parent compound due to the increased toxicity observed after irradiation to 2.93 ± 0.05 and 2.17 ± 0.22 at 1.0 and 5.0 kGy, respectively, despite no mortality at 10.0 mg L^{-1} for this compound (Fig. 4a). Tukey's test indicated significant differences between the control and the irradiated samples.

Additional assays were also performed at higher ASA concentrations for further investigation. The results also indicated an increase in acute toxicity from 1.2 ± 0.1 to 7.4 ± 0.1 TU at 5.0 kGy (Fig. 4b), demonstrating higher toxicity for the formed byproducts due to aspirin degradation. This toxicity increase has also been verified in the luminescent *Vibrio fischeri* bacteria test at up to 10 kGy of gamma-irradiated samples containing 0.5 mmol L^{-1} ASA (Szabó et al. 2014). This may occur during irradiation due to the formation of H_2O_2, especially in the presence of dissolved O_2, which may contribute to increased toxicity. In fact, after the irradiation process, an increase in H_2O_2 concentrations with increasing absorbed doses was noted up to 27.40 nmol L^{-1} at 5.0 kGy (Fig. 4b). Under aerated conditions, the hydrated electron (e^-_{aq}) and hydrogen atom (H•) of the water radiolysis are converted almost entirely into the $O_2^{\bullet-}/HO_2^{\bullet}$ pair. Hydrogen peroxide is formed in the aerated solution mainly through the reaction involving the hydrated electron, also contributing to hydroxyl radical production (Bielski et al. 1985):

$HO_2^{\bullet} \rightarrow H_2O_2 + O_2$ (1) $HO_2^{\bullet} + O_2^{\bullet-} + H_2O \rightarrow H_2O_2 + O_2 + OH^-$ (2) evaluated hydrogen peroxide formation during the water radiolysis of aerated aqueous solutions containing several aromatic organic molecules and reported that some amount of H_2O_2 does not degrade during radiolysis, remaining at concentrations of up to the 10^{-4} mol L^{-1} range. Hydrogen peroxide is detrimental for biological assays, since organisms are usually high sensitive to this compound. Additional ecotoxicological assays were performed with 0.06 μmol L^{-1} aspirin solutions irradiated at 1.0 and 2.5 kGy. It is important to note that in order to destroy H_2O_2 formed due to the irradiation process, catalase was added to the solutions before toxicity assays, as described by Szabó et al. (2014). This resulted in high toxicity reduction for *D. similis* after 48 h of exposure. About 50% and 40% mortality rates were observed for undiluted samples (100% exposure), indicating remaining toxicity of the hydroxylated aromatic byproducts formed after the treatment process. Szabó et al. (2014) also reported significant toxicity reduction in treated solutions after H_2O_2removal using catalase, also reporting low remaining toxicity for *V. fischeri*.

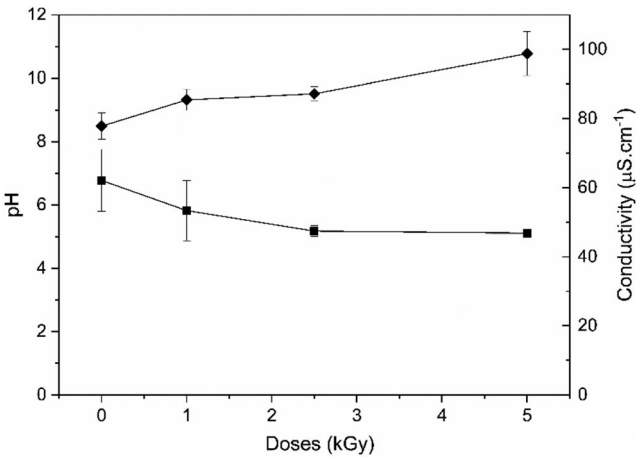

Fig. 3 Solution pH (*square*) and conductivity (*diamond*) vs. dose. Initial conditions: $[ASA]_0 = (0.464 \pm 0.009)$ μmol L^{-1}; pH = 6.78 ± 0.98

Degradation and toxicity in the (ASA + FXT) mixture treated by EBI

The risk of pharmaceutical mixtures in the environment can overcome the risk of each individual compound, with evidence that mixtures can be more toxic that each individual pharmaceutical, therefore significantly impacting the biota (Backhaus 2016). The results obtained herein demonstrate that EBI was effective in degrading both compounds at low doses to concentrations below their respective limits of detection of 0.39 μmol L^{-1} for aspirin and 0.65 μmol L^{-1} for fluoxetine at 1.0 kGy. Figure 5 presents the ASA and FXT mixture detoxification results for 1.0 and 2.5 kGy, although increased toxicity of the irradiated single aspirin solutions was demonstrated. The mixture toxicities decreased from 6.1 ± 0.7

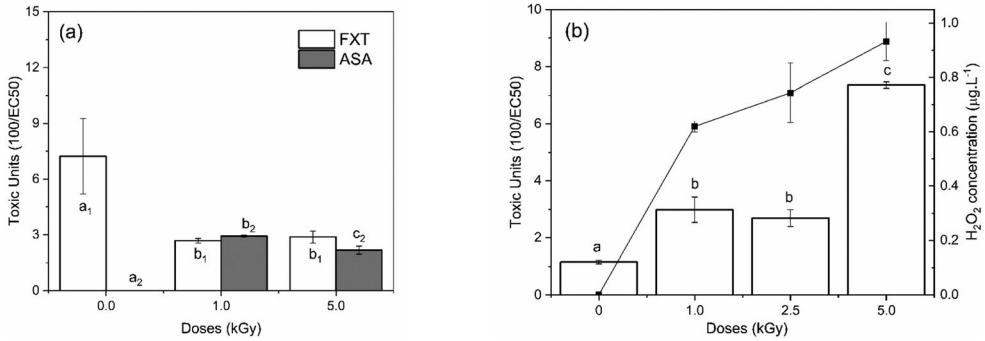

Fig. 4 **a** Acute toxicity (in toxic units, TU = 100/EC50%) assessed using *D. similis* for electron beam irradiated FXT and ASA at different doses. Initial conditions: $[ASA]_0 = (0.053 \pm 0.006)$ µmol L^{-1}; pH = 6.24 ± 0.31, $[FXT]_0 = (0.039 \pm 0.061)$ µmol L^{-1}; pH = 7.63 ± 0.39. **b** Acute toxicity and hydrogen peroxide formation (*square*) for electron beam irradiated samples at different doses. Initial conditions: $[ASA]_0 = (0.464 \pm 0.09)$ µmol L^{-1}; pH = 6.78 ± 0.98. Different letters (a–c) indicate significant differences (Tukey's test, $p < 0.05$)

to 2.8 ± 0.1 and 2.6 ± 0.8 at 1.0 and 2.5 kGy, respectively, corresponding to toxicity removal efficiencies of 54.4 ± 4.2% and 57.4 ± 0.8%, indicating residual byproduct toxicity. Tukey's test indicated significant differences between the control and the irradiated samples, although no significant difference in acute toxicity between the mixture solutions at 1.0 kGy and 2.5 kGy was verified. Therefore, the results obtained reinforce that low doses can be suitable for the detoxification of pharmaceutical samples, also demonstrating the importance of mixture assessments.

According to the literature, EBI is a feasible technology for the toxicity removal of binary and complex pharmaceutical mixtures at low doses. Boiani et al. (2019) reported approximately 80% of toxicity removal for *D. similis* and 20% for *V. fischeri* exposed to a binary mixture containing FXT and propranolol irradiated at 5.0 kGy. Tominaga et al. (2018) also studied the effects of radiation in a pharmaceutical mixture and obtained 50% toxicity reduction for a binary mixture containing FXT and diclofenac irradiated at 5.0 kGy. Silva et al. (2016) demonstrated 80% toxicity reduction for *D. similis* and 20% for *V. fischeri* using samples containing FXT diluted in raw domestic sewage irradiated at 5.0 kGy. Therefore, these results reinforce the importance of treated wastewater effluent toxicity assessments, in order to reduce environmental impacts, and of combining treatment technologies for wastewater treatment. Further investigations are required to optimize aquatic environment effluent impact reduction.

Conclusions

The results reported herein demonstrate the potential of electron accelerators to be effectively used for the removal of anti-

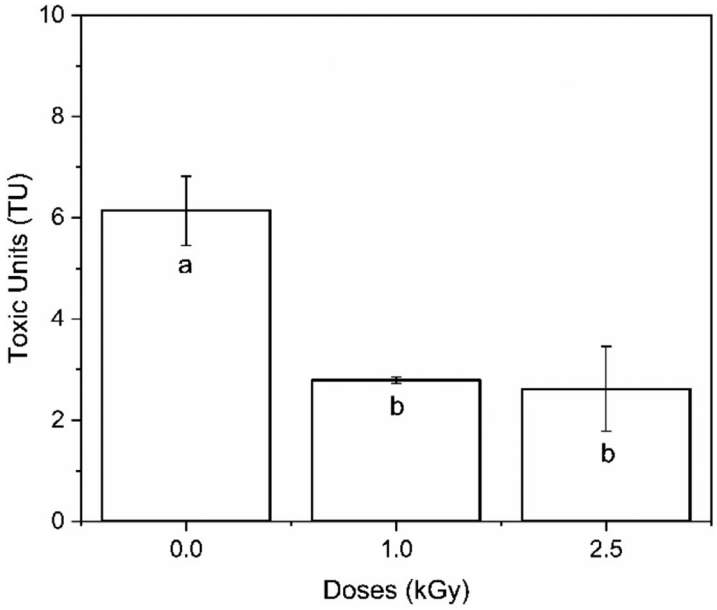

Fig. 5 Acute toxicity assessed using *D. similis* for electron beam irradiated samples at 1.0 and 2.5 kGy. Initial conditions: $[ASA]_0 = (0.026 \pm 0.003)$ µmol L^{-1}; $[FXT]_0 = (0.017 \pm 0.000)$ µmol L^{-1}; pH = 6.75 ± 0.05. Different letters (a–b) indicate significant differences (Tukey's test, $p < 0.05$).

inflammatory aspirin as a single solution and also in the presence of another pharmaceutical (fluoxetine). For the individual aspirin solution, 97.41% removal was achieved at 5.0 kGy. Negligible mineralization was obtained, indicating the formation of byproducts under experimental conditions. Increased toxicity and hydrogen peroxide formation was observed with increasing doses, due to H_2O_2 formation after the irradiation process. Concerning the mixture, anti-inflammatory and anti-depressant concentrations were reduced to below their respective limits of detection (0.39 μmol L^{-1} for aspirin and 0.65 μmol L^{-1} for fluoxetine). A toxicity removal of 56.2% was achieved at 1.0 kGy. Both these data and the literature indicate the need for further studies on mixtures, and that EBI can be an interesting alternative process applied as a pre-treatment technology able to degrade and detoxify many pharmaceuticals.

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