Catalytic Degradation of Fluorouracil and Its Derivatives by Copper-Based Nanoparticles

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Abstract

Fluorinated organic compounds (FOCs) are considered contaminants of emerging concern, and novel methods are required to achieve their degradation. 5-FU is a commonly used anticancer drug that is a representative example of a FOC. Use of copper-polyethylenimine nanoparticles (nCu-PEI) as a catalyst, with H_2O_2 as a radical source, is demonstrated for the degradation of 5-fluorouracil (5-FU). Optimal reaction conditions were found, and 5-FU was degraded completely within 24 h, following first-order kinetics with a reaction rate of 0.003 min^{-1} . Stoichiometric formation of F^- was shown with the degradation of 5-FU. Substitution of uracil with other halogen groups led to a decrease in the reaction rate. By comparison, the rate of 5-Chlorouracil degradation was 0.002 min^{-1} and that of 5-Bromouracil degradation was 0.001 min^{-1} . Stoichiometric formation of halogens was observed. A similar trend of decreasing reaction rate was found for the degradation of uracil in the presence of halogen salts. Results presented here suggest that this catalytic method can be an effective way to degrade FOCs.

Keywords: advanced oxidation process; Cu-PEI nanoparticles; emerging contaminants; fluorinated organic compounds

Introduction

IN RECENT YEARS, fluorinated organic compounds (FOCs) have been recognized as contaminants of emerging concern (Lai *et al.*, 2016). The C–F bond of the FOCs is considered strong and very difficult to activate, thus leading to persistence of these compounds in the natural environment. As FOCs are becoming very common in new and next-generation pharmaceuticals, agrochemicals, and polymers, their environmental footprint is also growing (Campagnolo *et al.*, 2002; Robinson *et al.*, 2005). These emerging contaminants have been found in the wastewater, and even the groundwaters, in China, Japan, Thailand, Spain, and Germany (Lin *et al.*, 2010; Shivakoti *et al.*, 2010; Yang *et al.*, 2011; Gómez-Canela *et al.*, 2012).

One example of a FOC that is often detected in water resources is 5-Fluorouracil (5-FU), which is among the most prescribed anticancer cytostatic drugs. In particular, 5-FU and capecitabine, a 5-FU prodrug, are used to treat breast and colorectal cancer. While cytostatic drugs are taken up by the body, they are not fully metabolized and can be excreted in their original form, resulting in their introduction to the sewage system. These drugs reach waterways from hospitals,

out-patient treatment centers, research centers, and even homes of patients (Zhang *et al.*, 2013). Because these drugs, and others like them, do not biodegrade readily, it is imperative to develop effective and affordable wastewater treatment options. In addition, partially decomposing the drug is insufficient as there are not enough data to indicate that the degradation products are not harmful. In terms of presence in water resources, several reports confirm notable concentrations of 5-FU. In Slovenia, for example, 5-FU concentrations ranging from 35 to 92 ng/L have been measured in hospital wastewater, while concentrations of 4.7–14 ng/L were found in municipal wastewater treatment plants (Kosjek *et al.*, 2013). Wastewater concentration of 5-FU in the Medical University of Vienna was estimated to range between 5 and 500 $\mu\text{g/L}$ based on actual consumption and excretion, as well as wastewater volumes (Mahnik *et al.*, 2004). Other estimates and measurements have yielded different values for the concentration of 5-FU in wastewater. The variation in the values can be attributed to the variation in 5-FU prescriptions in different countries, as well as differences in the factors used for the approximation, such as excretion rates and metabolism (Straub, 2007).

A study of the toxicity and mutagenicity of 5-FU on zebrafish found that at concentrations as low as 10 ng/L, there were changes to the hematopoietic kidney tissue (Kovács *et al.*, 2015). Other changes that were reported in the same study include chromosomal differences and changes in gene expression such as the downregulation of the major tumor

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suppressor gene p53. Effects on zebrafish were shown at levels that are an order of magnitude lower than the measured levels seen in hospital effluents (Kovács *et al.*, 2015). Other investigations of the toxicity of 5-FU show chronic toxicity in other animals such as crustaceans and rotifers (Parrella *et al.*, 2014). Using bacterial and algal assays, the lowest observed concentration for 5-FU was 10 $\mu\text{g/L}$, which is nearly the same level that can be expected to be found in wastewater (Zouneková *et al.*, 2007). Although these values do not relate to toxicity in humans, there is sufficient evidence to suggest ecological impacts of 5-FU.

5-FU is stable under natural sunlight conditions, but can degrade under UV light (Kosjek *et al.*, 2013; Lutterbeck *et al.*, 2016). Other studies found that 5-FU does not degrade in the presence of UV light without the addition of a photocatalyst (Lin and Lin, 2014). An analysis of the treatment products resulting from photodegradation showed that the majority of the degradation products retained the C–F bond (Gómez-Canela *et al.*, 2017). Even when H_2O_2 was introduced to the system, to increase the efficiency of photodegradation, the C–F bond was not broken (Zhang *et al.*, 2017). Conflicting results have been reported with regard to 5-FU biodegradation; Lutterbeck *et al.* (2015, 2016) reported that it does not biodegrade readily, while Kiffmeyer *et al.* (1998) reported complete degradation in a few days.

Another degradation method sometimes used in wastewater treatment is ozonation (Rice, 1996). 5-FU degrades rapidly when exposed to ozone (Lin *et al.*, 2015). However, Lin *et al.* (2015) showed that other commonly used pharmaceuticals exhibited increased toxicity when degraded using ozone, and, significantly, the efficacy of degradation is strongly dependent on pH, with a high pH being preferable (Lin *et al.*, 2015).

Advanced oxidation processes have been shown to effectively break down numerous pollutants, including 5-FU. Using TiO_2 as a photocatalyst and H_2O_2 , 5-FU was successfully degraded, breaking the C–F bond (Lutterbeck *et al.*, 2015; Koltsakidou *et al.*, 2017). TiO_2 and ZnO have been shown to be effective photocatalysts when used in conjunction with 254 nm light (Lin and Lin, 2014). The addition of H_2O_2 has been shown to improve the effectiveness of advanced oxidation methods (Lutterbeck *et al.*, 2015). Another method involving the electro-Fenton degradation of 5-FU also showed the formation of F^- when in an acidic environment (Ganzenko *et al.*, 2018). Fenton reaction was reported to effectively degrade 5-FU. However, when there is no exposure to light, the degradation products are more toxic than 5-FU (Governo *et al.*, 2017). UV light can be used to improve the efficacy of the Fenton reaction, allowing for lower concentrations of iron ions and oxidant to be used (Lutterbeck *et al.*, 2015; Governo *et al.*, 2017). Iron as a Fenton reagent has the distinct disadvantage of being usable only in acidic environments, while copper can be used in a broad range of pH. In addition, organic complexes with Cu^{2+} are readily degraded by OH^- , while similar complexes with Fe^{3+} are not (Bokare and Choi, 2014).

The main objective of this work was to study the degradation of 5-FU as a model fluorinated pharmaceutical compound, because of its environmental relevance. In addition, the availability of a homologous series of 5-FU (5-Chlorouracil [5-CIU], 5-Bromouracil [5-BrU], and Uracil) allows broader understanding of the described degradation

reaction mechanism. Our goal was to study degradation of 5-FU and its analogous chlorinated and brominated complexes, breaking of the C–F bond, by copper oxide nanoparticles as catalysts and without the need for UV light or ozone. We further aimed to account for the possible formation of by-products containing a fluorine (or another halogen atom)—carbon bond. Therefore, both the degradation of the initial complex and the formation of free halogen ions were monitored throughout the reaction.

The degradation reaction was accomplished using a combination of a nanosized copper-based catalyst and H_2O_2 . The optimal form of the catalyst, as well as the preferred concentrations of the catalyst and H_2O_2 , was selected by varying these parameters and measuring the degradation of the reaction after 24 h.

Experimental

Materials

The following materials were used in the study: nanosized copper oxide (nCuO, ≤ 50 nm; CAS #1317-38-0; Aldrich), 5-FU (99%; CAS #51-21-8; Sigma), H_2O_2 (30% v/v; CAS #7722-84-1; Frutarom), polyethylenimine (PEI; branched; MW $\sim 25,000$ Da; CAS #9002-98-6; Sigma-Aldrich), $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ (98%; CAS #10031-43-3; Fluka), NaBH_4 (96%; CAS #16940-66-2; Aldrich), 5-CIU (99%; CAS #1820-81-1; Sigma), 5-BrU (99%; CAS #51-20-7; Sigma), Uracil (CAS #66-22-8; Sigma), methanol (HPLC Grade; CAS #67-56-1; J.T. Baker), and formic acid (98%; CAS #64-18-6; J.T. Baker).

Synthesis of Cu-PEI nanoparticles

The synthesis and characterization of the Cu-PEI nanoparticles (nCu-PEI) catalysts used here were reported by Kalidhasan *et al.* (2017). Briefly, PEI (0.555 g) was first dissolved in 14 mL double distilled water (DDW). Then, 1.355 g $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ was dissolved in 20 mL DDW. The Cu solution was added slowly to the PEI solution during stirring; an additional 46 mL DDW was then added. NaBH_4 (0.378 g) was dissolved in 20 mL DDW; this solution was then added to the Cu-PEI solution, and the solution was subsequently mixed for 1 h. The solution was then divided into four portions, and each fraction underwent dialysis for 24 h in 800 mL DDW. The resulting suspension contained a copper concentration of ~ 50 mM. Full characterization of the nCu-PEI, including X-ray diffraction, zeta-potential measurements, light absorption spectra of the suspension, and transmission electron microscopy imaging, appears in (Kalidhasan *et al.*, 2017). A summary of the major observations is provided in Cu-PEI Nanoparticle Properties section of the Supplementary Data.

Pre-experiment preparations

Stock solutions of 5-FU, 5-CIU, 5-BrU, Uracil, each in concentration of 1.9 mM, and nCu-PEI were prepared at the outset of the experiment. The initial concentration was selected to allow in-depth study of the reaction in a way that would enable tracking of the degradation, even when most of the 5-FU was degraded. Concentrations of the halogenated uracils were determined using a calibration curve; calibration curve solutions were also prepared at the outset of the

experiment. Stock concentrations were stored at 4°C and checked periodically to ensure that the analyte remained stable in solution and did not degrade. Before the experiment, limit of detection and limit of quantification for each analyte were determined to be 0.02 and 0.05 ppm, respectively. The nCu-PEI were analyzed using differential light scattering to ensure a roughly narrow size distribution, as well as particle dimensions on the nanoscale (see Supplementary Fig. S8 for a representative size distribution diagram).

Reaction with nCuO and nCu-PEI catalysts

In a 100 mL glass bottle, 0.05 g nCuO (≤ 50 nm; Aldrich) was combined with 95 mL of 1.88 mM 5-FU solution and sonicated for 0.5 h; 5 mL H₂O₂ solution was then added. In parallel, 1 mL nCu-PEI was combined with 46.5 mL 1.88 mM 5-FU solution, and 2.5 mL H₂O₂ (30%) solution was then added. This procedure led to an initial concentration of 5-FU of 1.88 mM, with H₂O₂ concentration of 5%. The nCuO was added at a concentration of 0.4 g/L, which corresponds to a concentration of 5 mM Cu. The nCu-PEI was added as 0–10% of the reaction solution, which corresponds to concentrations of Cu ranging from ~ 0 –5 mM. The lids were placed loosely on the reaction bottles to allow gases to escape; fluoride ion concentrations, which indicate breaking of the C–F bond, and 5-FU concentrations were measured after 24 and 48 h. The concentration was determined using calibration curves in the appropriate range. Samples were passed through 0.2 μ m syringe filters (Sartorius Stedim Biotech; Minisart). The same method was used with Uracil, 5-CIU, or 5-BrU instead of 5-FU. It is further noted that all experiments were done at room temperature; in a previous analysis of similar catalytic systems (unpublished results), no substantial temperature effect was observed.

HPLC conditions

For 5-FU measurement: Waters 1525 binary HPLC pump was used with a Symmetry C18 5 μ m 4.6 $\times$ 250 mm column with dimethyloctadecylsilyl bonded amorphous silica and Waters 2487 dual λ absorbance detector. The mobile phase was water:methanol 70:30 (v:v) with 0.1% formic acid of both phases; a flow rate of 0.4 mL/min was used. The absorbance was measured at 266 nm.

For F[−] measurement: Waters 1525 binary HPLC pump was used with a Hamilton PRP-X100 10 μ m 2.1 $\times$ 150 mm column and an Alltech conductivity detector Model 650. The mobile phase was 0.85 mM NaHCO₃ in HPLC grade H₂O. The flow rate was 1.5 mL/min, although this was varied to maintain a pressure of 2000 psi.

For Br[−] and Cl[−] measurement: Waters 1525 binary HPLC pump was used with a Hamilton PRP-X100 10 μ m 2.1 $\times$ 150 mm column; an Alltech conductivity detector Model 650 was used. The mobile phase was 2.0 mM sodium benzoate in HPLC grade H₂O. The flow rate was 1.5 mL/min, although this was varied to maintain a pressure of 2000 psi.

Results and Discussion

Effect of catalyst type and concentration

Figure 1 shows the effects of the type (nCuO vs. nCu-PEI) and concentration of copper-based nanosized catalysts, on the degradation of 5-FU and the breaking of the C–F bond.

FIG. 1. Degradation of 5-FU and release of fluoride as reaction product comparing two copper-based nanocatalysts and varying concentrations of nCu-PEI. Reaction conditions: 5-FU concentration 1.88 mM, 5% H₂O₂, and reaction time 24 h. *Black columns:* 5-FU degradation compared to initial concentration, related to the left axis; *Gray columns:* fluoride formation compared to available fluorine in the 5-FU initial concentration, related to the right axis. Note that error bars indicate one standard deviation. 5-FU, 5-fluorouracil; nCu-PEI, Cu-PEI nanoparticles.

The y-axis shows both the molar fraction of degraded 5-FU normalized by the initial 5-FU concentration and the molar fraction of F[−] ions formed normalized by the initial concentration of fluorine in solution. The effectiveness of nCuO, where copper is in the form of Cu(II), was compared to nCu-PEI synthesized with Cu(I) as reported in Kalidhasan *et al.* (2017). Both copper-based catalysts were selected because they have been shown to be effective for degradation of organic and halogenated organic compounds (Ben-Moshe *et al.*, 2009; Fink *et al.*, 2012; Yecheval *et al.*, 2013; Kalidhasan *et al.*, 2017).

5-FU is stable and does not undergo any degradation without the addition of catalyst, as can be seen from Fig. 1. When 2–10% of nCu-PEI was used as catalyst, all 5-FU degraded and the formation of fluoride was almost stoichiometric, that is, in most cases, measurements lay within the small standard deviation range of the matching 5-FU and F[−] (Fig. 1). The ratio indicates that the C–F bond was broken during the reaction and that this bond is the main (essentially sole) target of the reaction. When only 1% nCu-PEI was used, 5-FU was degraded but the reaction was not complete and $\sim 60\%$ of the initial concentration was removed from the solution after 24 h. For this case, too, the ratio of fluoride formation to 5-FU degradation was found to be stoichiometric, indicating that the degradation of 5-FU and formation of fluorides occur simultaneously. In comparison, the use of nCuO in molar concentration comparable to the highest nCu-PEI concentration yielded only $\sim 80\%$ removal of 5-FU, but a stoichiometric formation of fluorides was found for this catalyst too.

Based on the results shown in Fig. 1, nCu-PEI was found to be a more efficient catalyst because lower concentrations could be used compared to nCuO. In addition, solutions of nCu-PEI are stable, making it easier to work with, and allowing for more control between experiments. The nCu-PEI

FIG. 2. Degradation of 5-FU and release of fluoride as reaction product as a function of varying concentrations of H₂O₂ reaction conditions: 5-FU concentration 1.88 mM, 5% H₂O₂, and reaction time 24 h. *Black columns:* 5-FU degradation compared to initial concentration, related to the left axis; *Gray columns:* fluoride formation compared to available fluorine in the 5-FU initial concentration, related to the right axis. Note that error bars indicate one standard deviation.

used in all replicates of the reactions was from a stock suspension synthesized at the outset of the study. Because the lowest concentration at which all the 5-FU was degraded was when a 2% solution of nCu-PEI was used, this concentration was selected for the rest of the experiments.

The effect of H₂O₂ concentration

Once it was determined that the presence of the catalysts is critical to the degradation reaction, and the optimal concentration was determined for the experimental setup, the optimized H₂O₂ concentration was examined. Figure 2 shows the effect of varying the concentration of H₂O₂ between 0% and 5% on the degradation of 5-FU and formation of fluorides.

FIG. 3. 5-FU degradation (black squares) and F⁻ formation (gray circles) versus time. Reaction conditions 5-FU concentration 1.88 mM, 2% nCu-PEI solution, and 5% H₂O₂. Concentration of 5-FU is presented in molar % relative to initial concentration (left axis), and F⁻ concentrations are given in molar % relative to initial fluorine concentration in the dissolved 5-FU (right axis). Note that error bars indicate one standard deviation.

The only concentration that results in degradation of all 5-FU after 24 h is 5% H₂O₂. In addition, the reaction with 0% H₂O₂, 4% nCu-PEI, and 1.88 mM 5-FU showed no degradation. The addition of 0.5%, 1%, 2.5%, and 5% resulted in degradation of ~84%, 89%, 96%, and 100% of 5-FU, respectively. The effect of H₂O₂ concentration is observed although H₂O₂ is in excess amount even at the lowest concentration. The higher concentration might have a small effect on the kinetics, and therefore, higher concentrations might be expected to result in faster degradation. In all cases, the degradation of 5-FU resulted in breaking the C–F bond and stoichiometric formation of fluorides.

Figures 1 and 2 show no reaction for the controls of (1) no nCu-PEI and (2) no H₂O₂. Because there is no change in the concentration of 5-FU with the addition of nCu-PEI alone, it can be concluded that 5-FU does not adsorb onto the surface of the nanoparticles. It is worth noting that if reaction time is not a critical factor, lower concentrations of both reagents can be used, or if even shorter degradation times are required, higher concentrations can be used.

It is known that copper can react with H₂O₂ in a Fenton-like reaction (Pham *et al.*, 2013). Cu(I) is oxidized by H₂O₂ resulting in the formation of the hydroxyl radical, while Cu(II) oxidizes H₂O₂ to form the superoxide; the reaction of Cu(I) with H₂O₂ can also result in the formation of Cu(III), another powerful oxidant (Nguyen *et al.*, 2013; Pham *et al.*, 2013). The generated radicals are then expected to be the oxidative reagents involved in the degradation of 5-FU.

Degradation kinetics and reaction comparison to other uracil derivatives

To better understand the reaction kinetics, the degradation of 5-FU and the formation of F⁻ were measured in 30 min increments over the course of 8 h, with a final measurement after being left overnight. Figure 3 shows a comparison of 5-FU degradation and F⁻ formation as a function of time. Triplicate samples of 1.88 mM 5-FU solution containing 2% nCu-PEI solution and 5% H₂O₂ were used. It is seen that the points representing 5-FU degradation (black squares) are

matched closely with the points representing F^- formation (gray circles). This indicates that 5-FU was degraded and that defluorination occurred. Moreover, this result indicates that defluorination occurred as part of the degradation reaction, because there is no lag between the onset of 5-FU degradation and the formation of F^- . After 8 h, $\sim 80\%$ of the 5-FU was degraded; after 24 h the amount of 5-FU remaining was below the detection limit.

Analogous reactions were performed using 5-CIU and 5-BrU. The goal of performing this reaction with different halogenated organics was twofold: first, to show the versatility of this degradation process and, second, to help elucidate the mechanism of the reaction. As shown in Fig. 4a, $\sim 70\%$ of the 5-CIU degraded after 8 h, and $\sim 95\%$ of the 5-CIU degraded after 24 h. Similar to the degradation of 5-FU, the formation of Cl^- closely matches the degradation of 5-CIU. The degradation reaction was also performed with 5-BrU,

shown in Fig. 4b. After 8 h, a little over 60% of the 5-BrU degraded, and after 24 h, $\sim 80\%$ of the 5-BrU had degraded. In this study, too, the formation of Br^- is seen to closely match the degradation of 5-BrU.

The reaction conditions were identical for the 5-FU, 5-CIU, and 5-BrU degradation experiments. There was no formation of the uracil peak on the chromatogram, indicating that the C–X bond is not the only one that is broken; rather, as expected, the entire molecule degrades. This is further evidenced by the degradation of uracil under the same reaction conditions. Representative chromatograms for all four derivatives, at the beginning, middle, and end of the reaction, which demonstrate the disappearance of the main peak and no formation of a new or any other peak, are provided in the Supplementary Data (Supplementary Figs. S4–S7).

The degradation reaction was also performed on unsubstituted uracil. This was done to determine if the halogens

FIG. 4. (a) 5-CIU degradation (black squares related to the left axis) and Cl^- formation (gray circles related to the right axis) versus time. (b) 5-BrU degradation (black squares) and Br^- formation (gray circles) versus time. Reaction conditions 5-Br/CIU concentration 1.88 mM, 2% nCu-PEI solution, and 5% H_2O_2 . The concentration of 5-Br/CIU is presented in molar fraction relative to initial concentration, and Br^-/Cl^- concentration is given in molar fraction relative to initial bromine/chlorine concentration in the dissolved 5-FU. Note that error bars indicate one standard deviation. 5-BrU, 5-Bromouracil; 5-CIU, 5-Chlorouracil.

FIG. 5. Degradation of Uracil, 5-FU, 5-CIU, and 5-BrU versus time. Note that error bars indicate one standard deviation.

were necessary for the degradation to occur, as well as to act as a control against which to compare the degradation reactions of the halogenated uracils. Figure 5 shows a comparison in reaction kinetics of uracil substituted with different halides. Interestingly, the reaction is the fastest for unsubstituted uracil, which was almost totally removed from solution after 5 h. The degradation rate of uracil is followed by 5-FU, followed by 5-CIU and then 5-BrU. After 1 week, all three of the initial compounds were fully degraded and showed a stoichiometric halide formation. The reaction follows first-order kinetics for most of the reaction. Based on analysis of the curves in Fig. 5, the reaction rate for uracil was found to be 0.006 min^{-1} , followed by 5-FU with a reaction rate of 0.003 min^{-1} , 5-CIU with a reaction rate of 0.002 min^{-1} , and 5-BrU with a reaction rate of 0.001 min^{-1} . The reaction rate of the substituted uracil was found to decrease linearly with the decreasing electrophilicity index, ω .

One possible explanation for the order of the degradation rates is that the halide forms a stable complex with Cu(I), preventing it from continuing its catalytic cycle by oxidizing to Cu(II). This is supported by the stability of the Cu(I)-halide complexes. The effect of halide presence on the oxidation rate of Cu(I) has been documented by Sharma and Millero (1988), showing a decrease in oxidation rate, and with the effect being more significant with I^- than Br^- , followed by Cl^- (Sharma and Millero, 1988; Millero *et al.*, 1992). This behavior is amplified by the scavenging effect of the halide on the hydroxyl radical. The larger the halide the less reactive is the formed reactive halogen species (Vleeschouwer *et al.*, 2008). Removing hydroxyl radicals by forming reactive halogen species, which react much more selectively than hydroxyl radicals, would significantly slow the reaction rate. The importance of hydroxyl radical formation for the reaction rate is also seen in the preliminary experiments, where decreasing the concentration of H_2O_2 led to a decrease in degradation after 24 h (Fig. 2). The linkage of hydroxyl radical formation [as reported in Kalidhasan *et al.* (2017) and

further discussed in the Supplementary Data] and the reaction rates is further supported by the much quicker reaction rate for the unsubstituted uracil. This suggested reaction mechanism implies that the critical step for the degradation of halo-organic molecules (specifically, the C-F bond) progresses through the formation of hydroxyl radicals and not through the formation of other copper-peroxide reactive intermediaries for the reported catalytic setup. The relatively similar reaction patterns of the substituted halogens at the onset of the degradation reaction (first 60 min), which diverge as the reaction progresses, in parallel to the increased release of halides to the solution, also fit the suggested explanation.

FIG. 6. Effect of different salts (0.1 M of NaF, NaCl, and NaBr) on uracil degradation after 5 h (black columns) and 24 h (gray columns) reaction. At 24 h, uracil concentrations were below detection limits for the no salt and 0.1 M NaF conditions. Note that error bars indicate one standard deviation.

Effect of ions in reaction solution

To measure the effects of additional halogen ions on the degradation reaction, 0.1 M NaF, NaCl, and NaBr were added to the degradation reaction of uracil with H₂O₂ and nCu-PEI. The fraction of remaining uracil was measured after 5 and 24 h. The results are shown in Fig. 6. The NaBr inhibited the degradation of uracil with 71% remaining after 5 h and 48% remaining after 24 h. With the addition of NaCl, 45% of the uracil remained after 5 h, but only 1% remained after 24 h. The addition of NaF inhibited the reaction the least, with only 11% remaining after 5 h, and there was no measurable uracil after 24 h. Without the addition of salts, ~5% uracil remained after 5 h, and no measurable uracil remained after 24 h.

These findings can be viewed in conjunction with Fig. 5, which displays the kinetics of the degradation reactions of uracil, fluorouracil, chlorouracil, and bromouracil. The trends of uracil degradation dynamics in the presence of halide salts support the posited reasoning that the degradation rates for the halogenated uracils are slower due to effects of having free halogens in solution, and not only because of the nature of the organo-halide bond.

Conclusions

FOCs are considered persistent contaminants of emerging concern. Their applications are diverse, and large volumes are being produced and used in the agrochemical, polymer, and pharmaceutical industry. These substances possess many appealing properties, but once their beneficial use is finished, they often remain or are released to the environment. Therefore, the need for methods that can break down the FOCs, especially the C–F bond, is crucial. In this study, we demonstrated the use of nCu-PEI as a catalyst for 5-FU degradation. The reaction conditions were optimized by varying the catalyst and H₂O₂ concentration. A study of the kinetics of the reaction was performed and was found to follow first-order kinetics. The effects of substitution of uracil with different halogens were also investigated; halogens, that are lower down in column VII of the periodic table, were found to slow the degradation rate. The same effect on the degradation rate of uracil was observed with the addition of an ionic salt. Overall, nCu-PEI was found to be an effective catalyst for the degradation of 5-FU.

The results indicate that the nCu-PEI catalyst is capable of degrading C–F bonds. It was further shown that fluorinated compounds degrade preferably by this method, compared to other halogenated compounds. Finally, we note that the catalytic method presented here is effective at ambient temperature and pressure. The fact that 5-FU is fully removed and no substantial by-product was detected suggest that oxidation with nCu-PEI catalysts could be an environmentally acceptable method to degrade FOCs.

Author Disclosure Statement

No competing financial interests exist.

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Supplementary Material

Supplementary Data

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