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A critical review over the removal of paracetamol (acetaminophen) from synthetic waters and real wastewaters by direct, hybrid catalytic, and sequential ozonation processes

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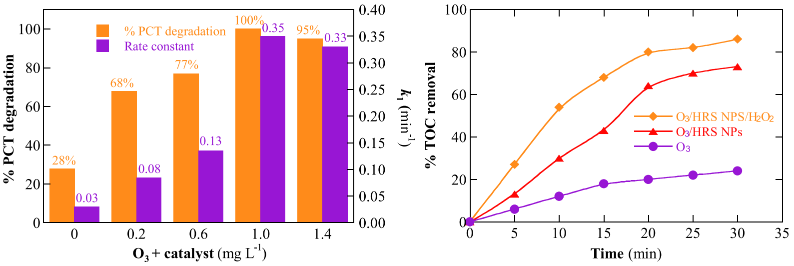
HIGHLIGHTS

- Rapid degradation of paracetamol by single ozonation in pure water, but with low mineralization.
- Larger enhancement of drug mineralization by ozonation with metal-based catalysts.
- More potent photolytic ozonation with Fe^{2+} and H_2O_2 than photocatalytic TiO_2 ozonation.
- Sequential treatments developed with wastewaters and in drinking water treatment plants.
- Generated hydroquinone and 2-hydroxy-4-(*N*-acetyl)-aminophenol give oxalic and oxamic acids.

GRAPHICAL ABSTRACT



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ABSTRACT

Paracetamol (PCT) or acetaminophen is a widely prescribed drug to treat fever and mild to moderate pain. The PCT uptake by animals and humans is not complete, being excreted through their urine to contaminate the aquatic/natural environments. Trace amounts of this drug have been found in sewage sludge, hospital wastewaters, wastewater plant treatments, surface waters, and even drinking water. PCT denatures proteins and oxidize lipids in cells with damage of their genetic code. Its toxicity over macrophytes, protozoan, algae, bacteria, and fishes has been reported. Ozonation methods have been proposed as efficient treatments to solve this pollution. This comprehensive and critical review is focused on the application of ozonation processes to remove PCT polluted water from different sources, like natural waters, synthetic waters, and real wastewaters. The fundamentals, operating variables, and best results by direct ozonation and hybrid catalytic ozonation are described, with attention to produced reactive oxygen species and their oxidative action. Single ozonation, catalytic modification of materials, and hybrid non-catalytic processes are detailed as direct ozonation methods. Ozonation with metal-based catalysts and photolytic and photocatalytic ozonation as hybrid catalytic methods are analyzed. Sequential non-biological and biological treatments with ozone and ozonation for wastewater remediation in treatment plants are described. Reaction sequences proposed for PCT mineralization are finally

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discussed, showing the initial formation of hydroquinone and 2-hydroxy-4-(*N*-acetyl)-aminophenol and their consecutive evolution to ultimate carboxylic acids like oxalic and oxamic. The ability of the methods to destroy these acids and their iron- and/or copper-complexes explains their mineralization performance.

1. Introduction

Over the last decades, animals and humans have consumed increasing quantities of drugs worldwide. It has been estimated that only in 2021, an expense of US$ 1170 billion has been made in the global pharmaceuticals market (Lee et al., 2020), making in evidence their large prescription by vets and doctors to palliate diseases. As a result, waters and wastewaters of all the world contain a mixture of many drugs as emerging pollutants, with potential toxic effects on the environment and living beings (Brillas, 2022). Paracetamol (PCT) or acetaminophen ($C_8H_9NO_2$, CAS number 130-90-2, $M = 151.165$ g mol^{-1}, solubility in water $= 14$ g L^{-1} at 20 °C, and p$K_a = 9.53$) is a well-known drug used to treat fever and mild to moderate pain. After consumption by animals and humans under medical treatment, it is excreted through the urine to contaminate aquatic/natural environments, including wastewater treatment plants (WWTPs) (Phong Vo et al., 2019; dos Santos et al., 2021). The industrial manufacturing process of PCT can also contribute to the release of this drug to the environment, as well as the waste of overdue or unused drug (Lee et al., 2020).

Due to its excessive usage, PCT has been found up to contents of 0.1–300 mg L^{-1} in effluents of many countries such as Spain, France, UK, China, and USA. In developing countries, wastewaters are often not collected and treated properly, giving rise to PCT prevalence in surface water. From 0.4 to 71 ng L^{-1} of this drug have been detected in rivers of Spain and France, whereas in several Asian countries, up to 33 ng L^{-1} have been reported (Phong Vo et al., 2019). While up to 71 ng L^{-1} of PCT have also been found in drinking water, the analysis of landfill and septic tanks has shown a more concentrated pollution between 0.1 and 1 g L^{-1}.

Conventional treatments including biodegradation, activated sludge with adsorption, sedimentation, filtration with membranes, and/or solar photolysis used in WWTPs are in many cases inefficient for the total removal of drugs, depending on its concentration. In many European countries, it has been reported that the treatment of many WWTP influents leads to a reduction from 65 to <10 μg L^{-1} of PCT (Lee et al., 2020). However, the lack of specific regulation in many countries limits the PCT discharge. Its long-term exposure in trace amounts over humans, animals, plants, and bacteria can yield chronic diseases and endocrine disruption (Phong Vo et al., 2019). It can denature the proteins and oxidize the lipids in cells with damage of their genetic code. Note that the PCT toxicity has been well-proven in several hosts like protozoan, macrophytes, algae, bacteria, and fishes. So, excellent studies have been published over several physiological and morphological alterations observed in Zebrafish embryo (Cedron et al., 2020) and Zebrafish larvae (Gorgulho et al., 2018), as well as toxicological liver affectations in Zebrafish (Driessen et al., 2015; Guo et al., 2015), upon exposition to PCT in waters.

The above considerations make evident the need of the removal of PCT and its metabolites/degradation products from wastewaters before discharging them to the environment, aiming to avoid their harmful health effects on living beings. In this sense, many research studies have proposed and tested different treatment technologies at lab and pilot scales to destroy this pollutant. The most potent methods developed are the so-called advanced oxidation processes (AOPs), which are environment-friendly techniques based on the attack of organics by generated oxidants like reactive oxygen species (ROS). They include sonochemical and Fenton processes (Salimi et al., 2017), TiO_2/UV photocatalysis and other UV photolytic processes (Leyva et al., 2018), and UV/H_2O_2 (Yang et al., 2014). AOPs like single and hybrid catalytic ozonation have also been recently investigated due to their high oxidation power to destroy organic pollutants (Phong Vo et al. al., 2019; Prada-Vásquez et al., 2021). Treatment with O_3 presents several advantages: (i) it does not require transportation or storage as dangerous material since it is generated on site, (ii) it has higher oxidation ability that active chlorine and other conventional methods, (iii) it does not produce chloroderivatives from organics in real wastewaters making dechlorination unnecessary, and (iv) it has a half-life of 20 min in water due to its easy conversion into O_2, thus avoiding its toxicity after treatment. Despite this, it uses expensive O_3 generators and its oxidative action is limited by its low solubility in water. Table SM-1 collects the main reactions involved in such ozonation treatments to produce different ROS (Skoumal et al., 2006; Quiñones et al., 2015b; Torun et al., 2015). O_3 is a selective and strong oxidant with a standard reduction potential (E°) of 2.07 V/SHE and can originate other oxidizing species such as ozonide ($O_3^{\bullet-}$), superoxide radical anion ($O_2^{\bullet-}$), hydroperoxyl radical ($HO_2^\bullet$, $E^\circ = 1.51$ V/SHE), H_2O_2 ($E^\circ = 1.78$ V/SHE), and hydroxyl radical ($^\bullet OH$, $E^\circ = 2.8$ V/SHE), The latter ROS is the strongest oxidant in the ozonation systems. To date, only partial and little information over the ability of ozonation technologies to destroy PCT and its by-products has been published.

This paper presents a critical and comprehensive review dealing with the application of ozonation to PCT removal for water and wastewater remediation. The fundamentals, characteristics, and main results of direct ozonation and hybrid catalytic ozonation processes are detailed and discussed, explaining the oxidation role of O_3 and the generated ROS. Single ozonation, catalytic modification of granular activated carbon (GAC) adsorption of PCT by activation with O_3 and the hybrid treatment with a membrane bioreactor (MBR) and O_3 are analyzed as direct ozonation. Two kinds of hybrid catalytic ozonation methods are considered, with metal-based catalysts or photolytic and photocatalytic processes upon the action of light irradiation. Sequential treatments involving ozonation are further described. They are related to sequential non-biological or biological processes as well as to complex systems used in water treatment plants. A last section corresponds to the analysis of reaction sequences proposed for PCT mineralization in pure water based on the by-products identified in different ozonation processes.

2. Search strategy and bibliometric analysis

Two literature searches, namely paracetamol AND ozonation and acetaminophen AND ozonation, were chosen in the Scopus database to retrieve the peer-reviewed literature regarding the oxidation treatments of PCT with O_3. Only reviews and scientific papers published in English were collected up to May 2022. The authors, title, and abstract of each retrieved publication were listed and individually analyzed to be excluded or included in the present review. Books, book chapters, and communications in congresses were not considered. The following criteria were used to decide the inclusion of the selected papers:

(i) Application of ozonation treatments to remove PCT from waters and wastewaters,
(ii) a deep study over the degradation and/or mineralization of PCT in aqueous matrices,
(iii) good exposition of the experimental setup and operating conditions used, with description of the analytical systems and the parameters needed to analyze the performance of the degradation and mineralization processes involved, and
(iv) appropriate description and discussion of the results obtained, including the abatement of PCT, its kinetic analysis, the efficiency of the removal of the chemical oxygen demand (COD) and/or total organic carbon (TOC) of the aqueous matrix, the effect of the

main operating variables, the estimation of the energy consumption, the change of the wastewater toxicity, and the detection of aromatic and aliphatic intermediates as well as final carboxylic acids with proposal of a plausible reaction sequence for its mineralization. This review presents 16 Figures and 3 Tables for understanding these issues in the different processes identified.

The above analysis allowed distinguishing 8 different applications involving single ozonation, catalytic modification with ozonation, hybrid non-catalytic ozonation, ozonation with metal-based catalysts, photolytic and photocatalytic ozonation, sequential non-biological ozonation, biological-ozonation processes, and ozonation in water treatment plants. The treatment of PCT was associated with each procedure, regardless of the aqueous matrix used. The present review is devoted on the description of the fundamentals, characteristics, and performance of the destruction of PCT for such processes. The oxidation capability of each treatment is related to the oxidizing agents produced, which depend on the operating variables tested. The by-products generated are finally remarked since they can be related to the variation of the solution toxicity and the power of the treatment to decontaminate waters and wastewaters.

The above criteria allowed the identification of 7 review articles. Some of these reviews described a general remediation of organics including PCT from waters by photo-Fenton and ozonation (Prada-Vásquez et al., 2021), AOPs and other methods (Oulton et al., 2010; Salimi et al., 2017), and using nanomaterials (Chauhan et al., 2019). Two specific reviews reported the occurrence, fate, and treatability of PCT and other pharmaceuticals by ozonation and other processes (Ziylan and Ince, 2011; Phong Vo et al., 2019), whereas another specific review was centered in the ozonation of municipal wastewater reclamation (Deng, 2020). No general reviews over the ozonation of PCT, as detailed in the present review, were found. The literature analysis was completed by selecting 56 scientific articles up to May 2022, starting from the pioneering work of Andreozzi et al. (2003) over the single ozonation of PCT in pure water.

Regarding the publication year, Fig. SM-1a shows that the higher number of reviews and scientific papers (37 in total) were published in the latter five years, making in evidence the interest of the ozonation techniques to destroy PCT. Thus, 8 articles were published in 2017, 7 in 2018, 8 in 2019, 3 in 2020, and 11 up to the beginning of 2022, whereas less than 5 articles per year were previously reported. Fig. SM-1b highlights that the 56 scientific articles corresponded to 21.4% of single ozonation (12 articles), 1.8% of catalytic modification with ozonation (1 article), 1.8% of hybrid non-catalytic ozonation (1 article), 16.2% ozonation with metal-based catalysts (9 articles), 16.2% of photolytic and photocatalytic ozonation (9 articles), 14.5% of sequential non-biological ozonation (8 articles), 8.9% of biological-ozonation processes (5 articles), and 19.6% of ozonation in water treatment plants (11 articles). Single ozonation and the use of ozonation in water treatment plants were then the major procedures investigated. It is also noticeable that about 50% of articles were devoted to real wastewater treatments and informed about the actual application of ozonation to water remediation, as will be detailed below.

3. Treatment of paracetamol waters and wastewaters by ozone

This section describes the fundamentals, characteristics, and main results reported for the remediation of PCT in different synthetic and real aqueous matrices. Direct ozonation is first detailed, including single ozonation, catalytic modification of materials with O_3, and hybrid non-catalytic processes. Hybrid catalytic ozonation was subsequently presented considering metal-based catalysts and photolytic and photocatalytic ozonation. Finally, several sequential treatments involving O_3 are discussed, which are based on the use of non-biological and biological systems and the application to water treatment plants. The role of the oxidizing agents acting in each process is also analyzed.

3.1. Direct ozonation

The treatment of PCT solutions by means of direct ozonation is highlighted in this subsection, The most common method consists in the simple O_3 bubbling through the aqueous matrix to oxidize organics in the well-known single ozonation process. Once described and analyzed this procedure, the catalytic modification of GAC adsorption of PCT by activation with O_3 and the hybrid treatment with a MBR and O_3 device will be detailed.

Fig. 1 schematizes some experimental systems used for direct ozonation. Fig. 1a shows a tubular column for the regeneration of granular zeolite loaded with the drug by single ozonation (Fu et al., 2021). The components of this device are quite like those of Fig. 1b, which is the most popular system for single and hybrid catalytic ozonation processes with O_3 inlet by the column top (Kohantorabi et al., 2022). Fig. 1c presents a sketch of a hybrid treatment involving a ceramic MBR coupled to direct ozonation and the possible mechanisms to improve the hydraulic performance of the ceramic MBR (Asif et al., 2021).

3.2. Single ozonation

O_3 is a toxic and instable gas that is rapidly transformed into O_2. For the single ozonation and other ozonation treatments of PCT removal in water and wastewater, O_3 must be continuously produced in situ by a generator or ozonator upon injection of air or pure O_2 by one side of the device. In the ozonator, the O_2 molecules are oxidized and converted into O_3 ones by passing through tubes.

Operating with the corona effect by applying frequencies between 600 Hz and 2 kHz and voltages between 4 and 20 kV. An O_3/air or O_3/O_2 stream is thus released by another side of the ozonator and directly injected to the cell containing the water or wastewater to be treated, usually through a diffuser. The amount of injected O_3 is measured as the flow rate of the gas mixture or the O_3 concentration in the aqueous matrix. In some cases, a given O_3 dose is added to the medium and the experiment is performed until its total consumption is reached. The non-reactive O_3 excess is released from the aqueous matrix contained in the reactor, and it is subsequently passed through a catalytic destructor or a destructor solution that reduces the toxic O_3 to innocuous O_2. A common destructor solution at lab scale is that of KI (see Fig. 1b), which acts by oxidizing I^- to I_2 while O_3 is reduced to O_2. Table 1 summarizes the system, experimental conditions used, and the best results obtained for selected papers dealing with the PCT remediation in different aqueous matrices by single ozonation.

The first article over the PCT destruction in pure water by single ozonation was published by Andreozzi et al. (2003), who treated 1.090 L of 4.9–5.3 mM drug at pH 2.0 and 7.0 by a system like of Fig. 1b upon an O_3 flow rate of 36 L h^{-1}. They found a quicker degradation at pH 2.0 where the drug completely disappeared in 15 min, whereas a longer time of 20 min was required at pH 7.0. The same trend was determined for COD reduction at 120 min, which attained a value of 63% for pH 2.0 in front of 51% for pH 7.0. The authors supposed that O_3 was the main oxidant of PCT and its by-products. This species can be reduced to $O_3^{\bullet-}$ that can be protonated to $HO_3^{\bullet}$ by reaction (3) to further evolve to the strong oxidant $^{\bullet}OH$ and the weaker species $HO_2^{\bullet}$ and H_2O_2 via reactions (5)–(9) (see Table SM-1), The quicker protonation of $O_3^{\bullet-}$ at pH 2.0 as compared to that of pH 7.0 could justify a faster generation of $^{\bullet}OH$ to favor the degradation and mineralization of PCT. A total of 19 by-products were detected by GC/MS in single ozonation, some of which were also identified during the H_2O_2/UV treatment of the same solution at pH 5.5. In this process, H_2O_2 is photolyzed to $^{\bullet}OH$ via reaction (16) (see Table SM-1) and thus, the authors justified the participation of the latter radical in the ozonation reaction sequence. The rate constant k ($^{\bullet}OH$) for the reaction (14) between PCT and OH was found of 2.2×10^9 M^{-1} s^{-1} from the H_2O_2/UV assays (see Table 1).

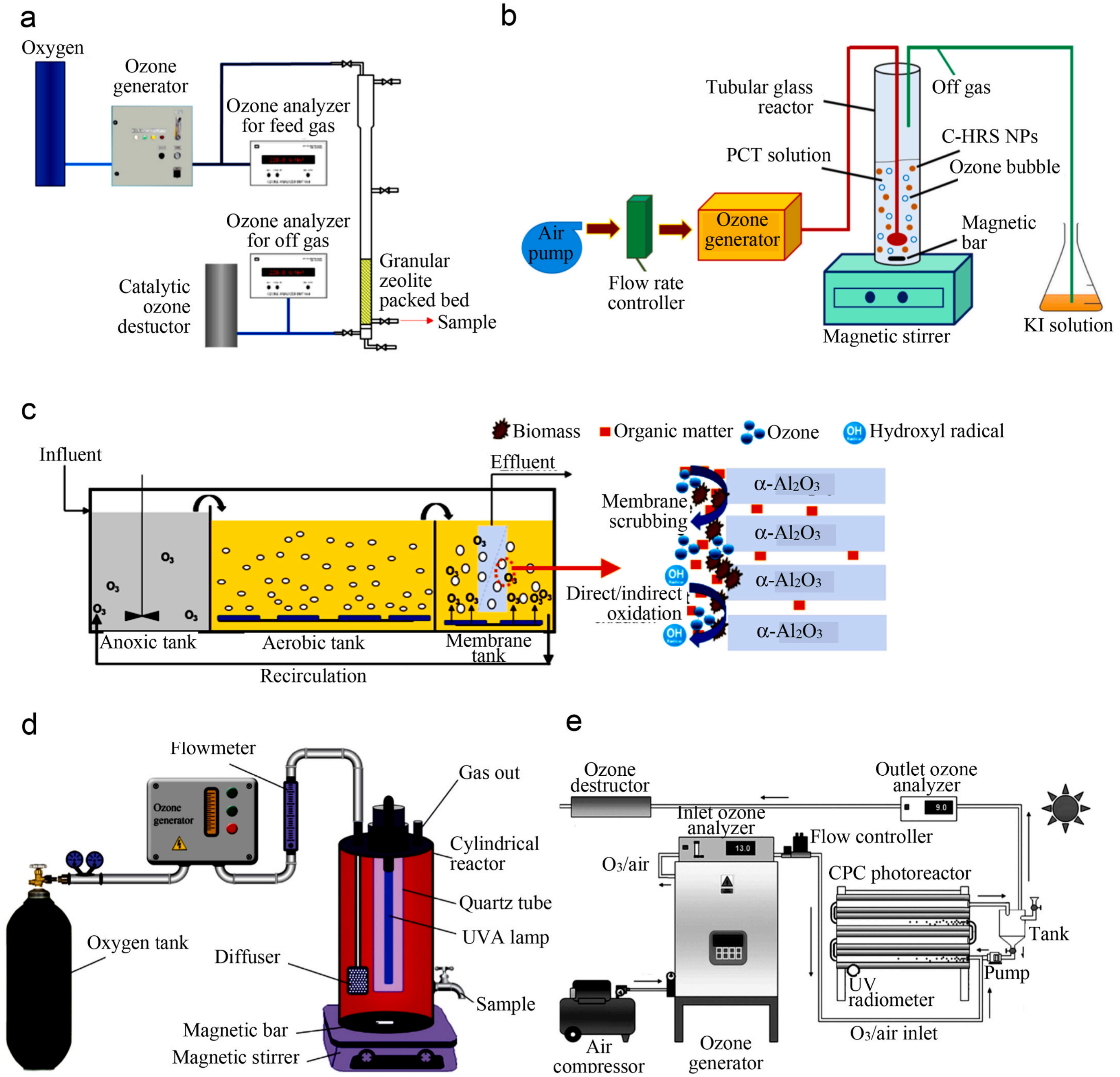

Fig. 1. Schemes of lab-scale systems for paracetamol (PCT) removal upon ozone oxidation. (a) Single ozonation process for the regeneration of granular zeolite loaded with the drug in a tubular column (adapted from Fu et al. (2021)), (b) catalytic ozonation process with calcined hematite red soil (HRS) nanoparticles (NPs) using a tubular column with O_3 inlet by its top (adapted from Kohantorabi et al. (2022)), (c) hybrid ozonation using a ceramic membrane bioreactor (MBR) coupled to direct ozonation (left), along with the possible mechanisms for improving the hydraulic performance of ceramic MBR (right) (adapted from Asif et al. (2021)), (d) photocatalytic ozonation with a cylindrical reactor with O_3 inlet by its top and an inner 8 W UVA light (adapted from Hassani et al. (2017)), and (e) solar photocatalytic ozonation using a compound parabolic collector (CPC) photoreactor with O_3 inlet and wastewater recirculation (adapted from Quiñones et al. (2015a)). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Other authors have studied more recently the PCT degradation in pure water by single ozonation as well. Hamdi El Najjar et al. (2014) prepared stock solutions with 21 mg L^{-1} O_3 using a system like of Fig. 1b and the degradation assays were made with batch reactors containing 100 mL of 1 μM drug at pH 7.2 upon addition of an O_3 dose up to 6.8 μM. The treatment was performed during 24 h ensuring the complete O_3 consumption. With this procedure, a rate constant of 2.57×10^6 M^{-1} s^{-1} for $k(O_3)$ related to the reaction (13) between PCT and O_3 was determined (see Table 1). They also found that $k(O_3)$ was much smaller than k ($^{\bullet}OH$), which was determined as 4.94×10^9 M^{-1} s^{-1} at pH 5.0 from parallel H_2O_2/UV tests. However, the PCT degradation via O_3 was much more largely produced due to its much higher concentration than generated $^{\bullet}OH$. This was corroborated by performing the process with a high concentration of 0.4 mg L^{-1} O_3 where PCT disappeared very rapidly with a half-time of 0.03 s. The solutions were analyzed by LCMS/MS and three by-products, namely hydroquinone, another aromatic, and 1 aliphatic derivative were identified. The study made by Trousil et al. (2018) was performed with a batch recirculation reactor. A

Table 1
Selected results obtained for single and hybrid ozonation processes of PCT in different aqueous matrices.

Pollutant	System	Experimental conditions	Best results	Ref.
Single ozonation				
PCT in pure water	Like of Fig. 1b reactor upon an O_3 flow rate of 36 L h^{-1}	1.090 L of 4.9–5.3 mM drug, pH 2.0 and 7.0, 120 min	Total degradation and TOC reduction: 15 min and 62% at pH 2.0 $<$ 20 min and 51% at pH 7.0. $k(^{\bullet}OH)$ for PCT from H_2O_2/UV: 2.2×10^9 M^{-1} s^{-1}. Identification of 19 by-products by GC/MS, Proposal of reaction sequence	Andreozzi et al. (2003)
PCT in pure water	21 mg L^{-1} O_3 stock solutions prepared with a system like of Fig. 1b. Then, assays with batch reactors with O_3 dose up to 6.8 μM	100 mL of 1 μM drug, pH 7.2, overall O_3 consumption in 24 h	$k(O_3)$ for PCT: 2.57×10^6 M^{-1} s^{-1}. Half-life of 0.03 s with 0.4 mg L^{-1} O_3. $k(^{\bullet}OH)$ for PCT from H_2O_2/UV: 4.94×10^9 M^{-1} s^{-1} at pH 5.0. Hydroquinone, 1 aromatic, and 1 aliphatic identified by LC-MS/MS	Hamdi El Najjar et al. (2014)
PCT in pure water	Batch recirculation reactor with liquid flow rate of 45 L min^{-1} and O_3 flow rate of 1 g h^{-1}	500 mL of 20 mg L-^{1} drug, pH 7.2, 20 °C, 60 min	Only 18% degradation, with about 10% COD and TOC reduction. Improvement up to 34% of BOD_5 [a] and enhancing the biodegradability. Small effect of 0.5 g L^{-1} H_2O_2 addition. Low toxicity to *Parachlorella kessleri*	Trousil et al. (2018)
PCT in pure water	Like of Fig. 1b upon an O_3 flow rate of 0.5 g h^{-1}	1.0 L of 20–50 mg L^{-1} drug, pH 2.0–10.0, 24 °C, 60 min	Degradation at 25 min for pH 10.0: 98% at 20 mg L^{-1} $>$ 95% at 30 mg L^{-1} $>$ 89% at 50 mg L^{-1}. For 50 mg L^{-1} at 60 min, degradation and COD removal: 69% and 35% at pH 2.0 $<$ 94% and 39% at natural pH $<$ 96% and 65% at pH 10.0. NMR analysis of by-products	De Sousa et al. (2018)
PCT in pure water	Like of Fig. 1b upon an O_3 flow rate of 4.2–25.0 mg min^{-1}	1.0 L of 50 mg L^{-1} drug, pH 3.0–12.0, 25 °C, 120 min	Faster drug removal with higher O_3 flow rate. For pH 12.0, total degradation in 50 and 120 min at 25.0 and 4.2 mg min^{-1} O_3 flow rate, respectively. Greater color formation in the latter conditions, decreasing with raising O_3 flow rate. Detection of 12 aromatic derivatives and 1 aliphatic by-product by LC-MS. Reaction sequence proposed.	Villota et al. (2019)
PCT in pure water	Fig. 1a with an O_3 flow rate of 0.2–0.8 L min^{-1} at concentration of 50–150 mg L^{-1}	5 g of granular zeolite was put in the column and 100 mL of 200 mg L^{-1} drug flowed at 0.74 m h^{-1}, for 120 h. Zeolite regeneration was carried out by O_3 flowing for 120 min	Higher zeolite regeneration with lower water content in its granules. For a consumed O_3 dose of 2160 mg, 95% and 74% PCT regeneration efficiency at 0.2 L min^{-1} and 50 mg L^{-1} O_3. Excellent PCT adsorption capacity after 4 consecutive cycles	Fu et al. (2021)
PCT in pure water	Stirred tank reactor upon an O_3 flow rate of 5 L min^{-1}. For *E*-peroxone[b], the reactor contained a Pt anode and a carbon-PTFE cathode by applying a *I* [c] = 20–300 mA	2 L of 100 mg L^{-1} drug, 0.50 M Na_2SO_4 for *E*-peroxone, pH 6.8, 25 °C, 60 min	Similar accumulation of $^{\bullet}OH$ and H_2O_2 in single ozonation and *E*-peroxone. Overall degradation in 45 min by *E*-peroxone at 300 mA $<$ 60 min by single ozonation. Detection of 3 aromatic derivatives and 2 final carboxylic acids in both treatments by HPLC	Östürk et al. (2021)
PCT in pure water or secondary WWTP effluent (COD: 26 mg L^{-1}, TOC: 12 mg L^{-1})	Like of Fig. 1b upon an O_3 flow rate of 12 L h^{-1} at concentration of 5–40 mg L^{-1}	1 L of 10 mg L^{-1} drug, pH 2.0, 7.8, or 11.0. 20 °C,	$k(O_3)$ for PCT in pure water (10^5 M^{-1} s^{-1}): 3.58, 2.70, and 15.7 at pH 2.0, 7.8, and 11.0, respectively. Total degradation in the secondary WWTP with 40 mg L^{-1} of O_3: 5 min at pH 2.0 and $>$ 8 min at pH 11.0.	Rivas et al. (2011)
6 EDCs [d]: 4 drugs (including PCT) and 2 hormones in waste activated sludge	Erlenmeyer flask with O_3 flow rate of 1.11 mg L^{-1} for 6 min up to 18.65 mg L^{-1} at 150 min for 4 consecutive d	500 mL of 2.3–4.2 g MLSS [e] L^{-1} with 200 ppb of each EDC, continuously aerated between 2 successive O_3 applications	95% MLSS reduction was achieved with only 1.05 g O_3/kg MLSS in the fourth day. More than 99% removal of all EDCs at the end of the process	Muz et al. (2013)
34 drugs (including PCT) detected in hospital wastewater	300 L of flow tank reactor operating in continuous upon O_3 submitted to 0.8 bar for 2.5 h d^{-1} during 63 d	1000 L of wastewater passing through the 300 L flow tank reactor with an HRT [f] of 18 and 9 min using a flow rate of 1 and 2 m^3 h^{-1}, respectively	PCT was the drug found with the higher content of 2.6 g L^{-1}, being removed a 39.1 and 2.9% operating at 1 and 2 m^3 h^{-1} flow rate, respectively. Under the former conditions, all drugs were significantly removed ($>$25%). A relatively low energy consumption of 19 MWh y^{-1} for the ozonation step was estimated	Svebrant et al. (2021)
Catalytic modification with ozonation				
PCT in pure water	Continuous flow column with as-received GAC [g] or activated with 8 mg min^{-1} O_3 for 3 h as adsorbent	40–120 mg L^{-1} drug, pH 6.8, 25 °C, liquid flow rate: 2–6 mL min^{-1} from the top to bottom of 25–45 cm of adsorbent in the column, 200 min	Longer time for adsorbing PCT from the O_3-treated GAC. More time needed for 40 mg L^{-1} drug, 2 mL min^{-1} flow rate, and 45 cm of O_3-treated adsorbent. Longer time needed to regenerate the exhausted O_3-treated GAC	Yanyan et al. (2018)

(*continued on next page*)

Table 1 (*continued*)

Pollutant	System	Experimental conditions	Best results	Ref.
Hybrid (no catalytic) ozonation				
Mixture of 8 drugs (including PCT) in a synthetic WWTP effluent (220, 50 and 10 mg L^{-1} of TOC, total nitrogen, and total phosphorous, respectively)	Fig. 1c with a MBR [h] composed of an anoxic (2 L), aerobic (3 L) and membrane tank (2 L) with an Al_2O_3 membrane. In situ ozonation at 5 mg L^{-1} for 20 min each 2 d	Recirculation at 0.5 L min^{-1} of 7 L of the WWTP effluent spiked with 500 ng L^{-1} of each drug for 65 d	At the end of the assay, higher drug degradation (10–26%) using the hybrid MBR/O_3 treatment. 100% PCT removal under such conditions. TOC reduction of 94%, whereas 70–80% of total nitrogen and phosphorous removal were achieved. 53% alleviation of membrane fouling upon the in-situ ozonation	Asif et al. (2021)

[a] BOD_5: 5-Day biological oxygen demand.
[b] *E*-peroxone: Electro-peroxone.
[c] *I*: current.
[d] EDCs: Endocrine disrupting chemicals.
[e] MLSS: Mixed liquor suspended solid.
[f] HRT: Hydraulic retention time.
[g] GAC: Granular activated carbon.
[h] MBR: Membrane bioreactor.

500 mL solution with 20 mg L^{-1} drug at pH 7.2 and 20 °C was recirculated through a cylindrical reactor at a liquid flow rate of 45 L min^{-1} under an O_3 flow rate of 1 g h^{-1}. Low degradation and mineralization were found under the above conditions since after 60 min of reaction, only a 18% of the drug was removed with about 10% of COD and TOC abatements (see Table 1). Nevertheless, a positive effect was observed over the 5-day biological oxygen demand (BOD_5) because it was improved a 34%, thus largely enhancing the solution biodegradability. It is noticeable that addition of 0.5 g L^{-1} H_2O_2 caused a little effect on the drug removal due to the low oxidation power of this compound and its low reaction rate with O_3. It was also found that the treated solution presented low toxicity to *Parachlorella kessleri* algae.

Deeper research has been reported by De Sousa et al. (2018) considering the influence of PCT concentration and pH on 1.0 L solution at 24 °C using a cylindrical column like of Fig. 1b with an O_3 flow rate of 0.5 g h^{-1}. Fig. 2a depicts the rapid decay of the normalized drug content with the ozonation time at pH 10.0, showing a smaller abatement with raising PCT concentration from 20 to 50 mg L^{-1}. At 25 min of treatment, the degradation was removed a 98% for 20 mg L^{-1}, 95% for 30 mg L^{-1}, and 89% for 50 mg L^{-1}. Considering that at this time a growing drug content was abated, from 19.6 to 44.5 mg L^{-1}, one can infer that the single ozonation becomes more efficient as the organic load increases because O_3 can attack a higher quantity of pollutants. The inhibition of the rate of its parasitic non-oxidizing reactions like (10) and (11) could also justify the quicker amount of drug destroyed at higher concentration due to the larger prevalence of •OH to react with more drug content. The effect of pH between 2.0 and 10.0 over the time course of the normalized concentration from 50 mg L^{-1} PCT is presented in Fig. 2b. A quicker drug disappearance at higher pH can be observed, attaining a 69%, 94%, and 96% reduction for pH 2.0, natural, and 10.0, respectively, after 60 min. The same tendency can be seen in Fig. 2c for the parallel COD evolution, with the corresponding drop of 35%, 39%, and 65% (see Table 1) These findings inform about the pre-eminent removal of the drug and its by-products in alkaline conditions. This can be related to a quicker oxidation of the more reactive phenolate form of PCT at pH 10.0 and a faster production of other oxidizing species following reactions (1)–(9) (see Table SM-1), especially the oxidant •OH that reacts more rapidly with PCT than O_3, as stated above..

The influence of O_3 flow rate over the degradation rate of the drug in pure water was studied by Villota et al. (2019). These authors used a system like of Fig. 1b for treating 1.0 L of 50 mg L^{-1} drug at pH 3.0–12.0 and 25 °C by O_3 flow rates of 4.2 and 25.0 mg min^{-1}. It was found a faster PCT removal operating at greater pH and O_3 flow rate. So, the best degradation rate was obtained at pH 12.0 and 25.0 mg O_3 min^{-1}, achieving total abatement in 50 min, in front of 120 min required for 4.2 mg O_3 min^{-1} (see Table 1). Higher O_3 concentration then favored the destruction of organics. This was confirmed by the fact that the treated solutions became more rapidly colorless with raising O_3 flow rate because of the quicker destruction of colored aromatic by-products. LC-MS analysis of ozonated solutions allowed detecting 12 aromatic derivatives and 11 aliphatic by-products.

An interesting application of single ozonation has been recently described by Fu et al. (2021) over the regeneration of granular zeolite previously contaminated with adsorbed PCT. The adsorption assays were carried with a recirculation tubular column containing 100 g zeolite and flowing 100 mL of drug solutions at a rate of 0.74 m h^{-1} during 120 h. Fig. SM-2a highlights the increasing drug adsorption capacity of the zeolite with raising its concentration in solution up to attain a quasi-steady saturation value of 91 mg g^{-1} for PCT contents $\geq$150 mg L^{-1}. An amount of 5 g zeolite contaminated until saturation with 200 mg L^{-1} drug were then introduced in the column of Fig. 2a to be regenerated upon an O_3 flow rate of 0.2–0.8 L min^{-1} with high concentrations of 50–150 mg O_3 L^{-1} for 120 min. The regeneration efficiency was more largely inhibited at higher percent of water content by zeolite weight, as can be seen in Fig. SM-2b. A maximum regeneration of 81% was obtained for $\leq$21% of water in its granules. Operating under these conditions, the effect of the O_3 flow rate and its concentration on the percent of regeneration efficiency was examined. Fig. SM-2c and d present the results obtained for such assays after the consumption of 2160 mg O_3, making in evidence that greater percentage of zeolite was regenerated at the lower O_3 flow rate (95% at 0.2 L min^{-1}) and O_3 concentration (74% at 50 mg L^{-1}), because the contaminated zeolite was longer time in contact with O_3. Fig. SM-2e makes evident that 86–93% of regeneration capacity was maintained during 4 consecutive cycles by consuming 2160 mg O_3 (see also Table 1), as expected if the by-products formed from the single ozonation of PCT are easily destroyed or desorbed of the zeolite surface and PCT can be again adsorbed until saturation. However, the effect of pH was not considered since only neutral pH was used. Note that a faster oxidation can be expected under alkaline conditions and hence, the process could be more cost-effective by using lesser dose of 2160 mg O_3 to obtain >90% of regeneration efficiency.

Öztürk et al. (2021) used a stirred tank reactor to compare the single ozonation of 2 L of 100 mg L^{-1} PCT at pH 6.8 and 25 °C with the electro-peroxone (*E*-peroxone) treatment. The latter method was made in the same reactor converted into an electrolytic cell with 0.50 M Na_2SO_4 as supporting electrolyte, a Pt anode, and a carbon-PTFE cathode that can electrogenerate H_2O_2 from the excess of O_2 added to the solution by applying a continuous current (*I*) of 300 mA. In both cases, an O_3 flow rate of 5 L min^{-1} was injected to the solution. •OH and H_2O_2 were produced as additional oxidants in the single ozonation from reactions (1)–(11) (see Table SM-1), as well as in *E*-peroxone since •OH radical is formed from water oxidation at the Pt anode while H_2O_2 is electrogenerated at the cathode (Brillas, 2022). Fig. 3a shows a similar evolution of both species in both treatments, with maximum •OH

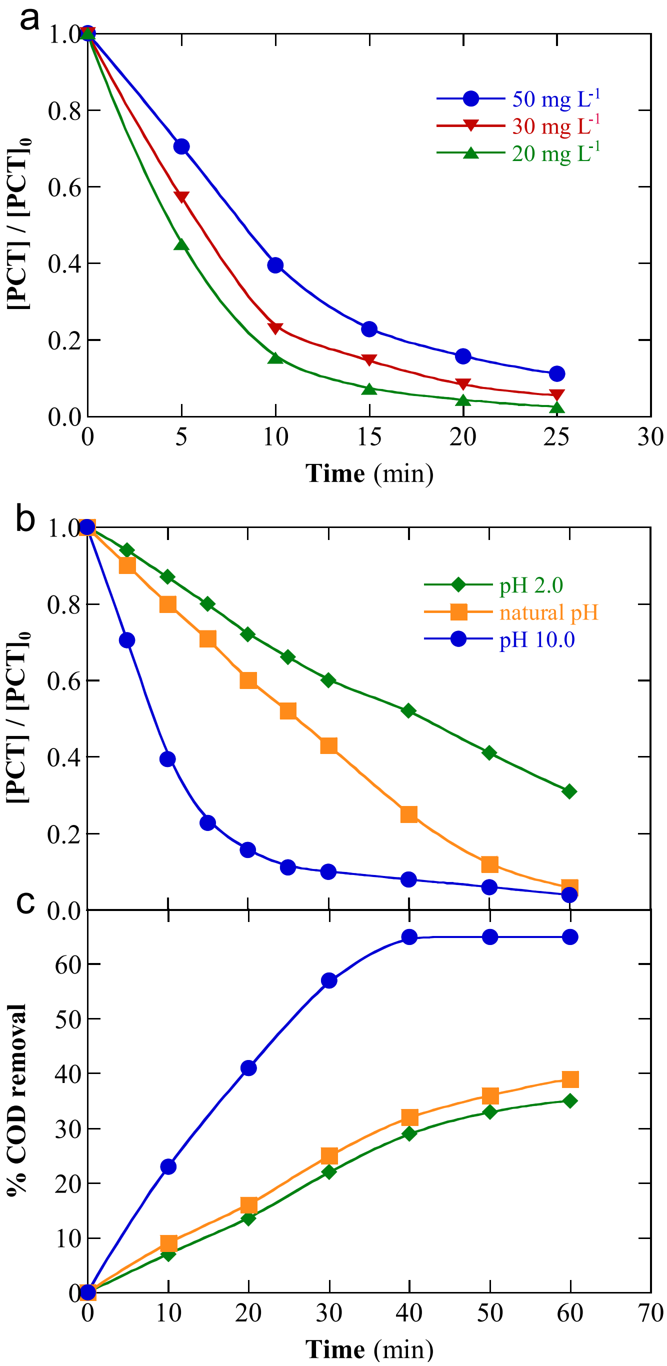

Fig. 2. (a) Effect of PCT content on the variation of its normalized concentration with ozonation time for the single ozonation process of 1.0 L of drug solutions at pH 10.0 and 24 °C using a bubbled cylindrical column like of Fig. 1b with an O_3 flow rate of 0.5 g h^{-1}. Influence of pH over the change of (b) the normalized PCT concentration and (c) the percentage of COD removal with ozonation time for the single ozonation treatment of 1.0 L of 50 mg L^{-1} drug solutions upon the above conditions. Adapted from De Sousa et al. (2018).

production between 19 and 25 μM at about 10 min and close to 2.5 g L^{-1} of accumulated H_2O_2 at 60 min. Considering that these oxidants are more largely generated by *E*-peroxone, one can conclude that they oxidize more largely PCT and its by-products in competence with injected O_3. This can be deduced from Fig. 3b, where the drug was completely removed in 60 min by single ozonation, whereas only 45 min were needed by *E*-peroxone (see Table 1). Moreover, three aromatic derivatives and two final carboxylic acids were detected in both treatments by HPLC, as can be seen in Fig. 3c and d. It is noticeable the low content of aromatics produced (hydroquinone, *p*-benzoquinone, and catechol), which evolve to a large accumulation of less oxidizable carboxylic acids.

that difficult the mineralization process. Oxalic acid attained a maximal of 40 mg L^{-1} in both cases at 50 min and was the more persistent by-product because of its hard oxidation with $^{\bullet}$OH (Brillas, 2022). Other papers focus on the remediation of natural waters either using a mobile water treatment system with individual modules including ozonation for rivers of Korea (Yu et al., 2018) or modeling the decomposition of O_3 and the exposure of O_3 and $^{\bullet}$OH to organics (Kim et al., 2020). Rivas et al. (2011) studied the single ozonation of 1 L of 10 mg L^{-1} PCT in pure water or a secondary WWTP effluent (see characteristics in Table 1). The runs were performed with a system like of Fig. 1b operating at pH 2.0–11.0 and 20 °C under an O_3 flow rate of 12 L h^{-1} with concentrations of 5–40 mg O_3 L^{-1}. In pure water, they determined an oscillating trend of $k(O_3)$ with values of 3.58×10^5, 2.70×10^5, and 15.7×10^5 M^{-1} s^{-1} at pH 2.0, 7.8, and 11.0, respectively. These $k(O_3)$-values agree with those reported by other authors, as stated above. The higher $k(O_3)$-value reached at pH 11.0 can be ascribed to the oxidation of the phenolate form of PCT ($pK_a = 9.53$), a more reactive molecule than the neutral one. Conversely, when the secondary WWTP effluent was considered using 40 mg O_3 L^{-1}, 10 mg L^{-1} of PCT were more quickly abated at pH 2.0 than at pH 11.0 (5 min vs. 8 min). This behavior can be associated with the parallel attack of O_3 over the organic components of the WWTP, which seems faster in alkaline medium, thus decreasing the degradation rate of the drug.

The destruction of some multi-components systems from waste activated sludge (Muz et al., 2013)) and hospital wastewater (Svebrant et al., 2021) has been reported to demonstrate the applicability of single ozonation for real wastewater remediation. Muz et al. (2013) treated 500 mL of a suspension of 2.3–4.2 g of mixed liquor suspended solid (MLSS) per liter in Erlenmeyer flasks with an O_3 flow rate from 1.11 mg L^{-1} at 6 min to 18.65 mg L^{-1} at 150 min during 4 consecutive days. Before each trial, 4 drugs, including PCT, and 2 hormones at concentrations of 200 ppb each were added to the activated sludge. The suspension was aerated between 2 consecutive O_3 applications and at the end of the trials, Table 1 shows that up to 95% MLSS reduction with 99% destruction of added pollutants was determined. The ozonation was so effective that only 1.05 g O_3 per kg of MLSS were needed, demonstrating the viability of the procedure. On the other hand, Svebrant et al. (2021) studied the removal of 34 drugs contained in hospital wastewaters with a flow tank reactor upon continuous O_3 injection maintained at a pressure of 0.8 bar for 2.5 h d^{-1} during 63 consecutive days. Each assay was carried out by recirculating 1000 L of the wastewater with a hydraulic retention time (HRT) of 18 or 9 min in the reactor, corresponding to a liquid flow rate of 1 or 2 m^3 h^{-1}. The drug with higher concentration was PCT (2.6 g L^{-1}) and at the end of the assays, it was reduced by 39.1% and 2.9% at 1 and 2 m^3 h^{-1} flow rate, respectively (see Table 1). This was explained by the longer contact time between the drug and O_3 at the lower liquid flow rate favoring its oxidation. Under these conditions, >25% of the other drugs were significantly removed and a low energy consumption of 19 MWh y^{-1} was estimated for the ozonation step. However, the authors did not investigate the change of toxicity and biodegradability of the ozonated solutions, still containing the remaining drugs and the by-products formed. This is an essential point to show if a further biological treatment was feasible to completely decontaminate the hospital wastewater.

3.1.2. Ozone induced adsorbent ozonation

The large oxidation power of O_3 has been used to activate the surface of carbon materials for improving their catalytic ability to adsorb PCT from contaminated waters. This phenomenon was investigated by Yanyan et al. (2018) for granular activated carbon (GAC). This material was activated with gaseous O_3 at a flow rate of 8 mg min^{-1} for 3 h, with production of –C=O and more –OH groups on its surface and the increase of the number of micropores and macropores of the carbon

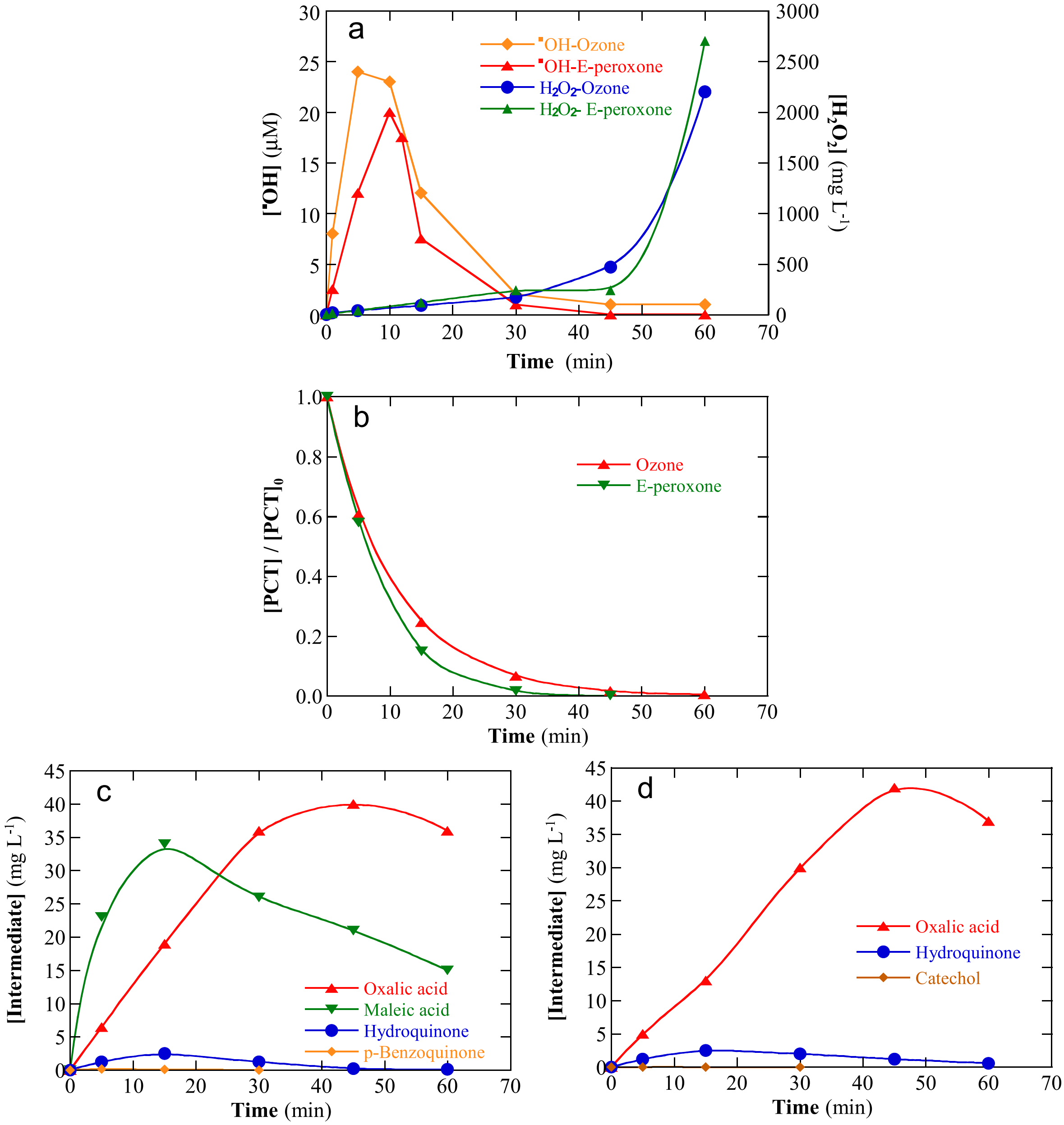

Fig. 3. Evolution of •OH and H_2O_2 concentrations generated during the single ozonation and electro-peroxone (*E*-peroxone) treatments of 2 L of pure water at pH 6.8 and 25 °C in a stirred tank reactor, An O_3 flow rate of 5 L min^{-1} was applied for the single ozonation, whereas the *E*-peroxone was performed in 0.50 M Na_2SO_4 with a Pt anode and a carbon-PTFE cathode by applying a continuous current (*I*) of 300 mA upon the same O_3 flow rate. (b) Normalized PCT concentration vs. time for 100 mg L^{-1} drug solutions for the above treatments. Time-course of aromatic and final carboxylic acids detected as intermediates during the (c) single ozonation and (d) *E*-peroxone processes. Adapted from Östürk et al. (2021).

particles that favors drug adsorption. This can be seen in Fig. 4a for assays made with 40 mg L^{-1} PCT in pure water at pH 6.8 and 25 °C flowing at 6 mL min^{-1} from the top to bottom of a tubular column of 35 cm bed depth. While the as-received GAC was completely saturated of adsorbed drug in 30 min, the ozone-activated GAC reached only a 92% saturation after a much longer time of 130 min, but adsorbing practically 4-fold greater quantity of PCT. For the activated GAC, the influence of PCT concentration (see Fig. 4b), liquid flow rate (see Fig. 4c), and bed depth (see Fig. 4d) on the evolution.

Of the ratio of PCT concentration between the effluent and influent was examined. These findings showed that the column reached a steady-state of adsorption (>83%) at longer time for 40 mg L^{-1}

drug, 2 mL min^{-1} flow rate, and 45 cm bed depth (see Table 1). The regeneration of exhausted columns was finally assessed by passing a NaOH solution at 6 mL min^{-1}. As expected, Fig. 4e corroborates that a time of 800 min was needed to regenerate the exhausted O_3-treated GAC, much longer than 250 min required for as-received GAC due to the greater quantity of drug adsorbed. However, it seems that this regeneration procedure should be improved because of the rapid loss of adsorbed PCT in consecutive runs, drastically lowering the adsorption ability of the O_3-activated GAC.

3.1.3. *Hybrid non-catalytic ozonation*

A limited number of articles has been published dealing with hybrid treatments with O_3 without considering a catalytic behavior. In this way, a recent study of Asif et al. (2021) reported a hybrid MBR/O_3 process for the decontamination of 8 drugs including PCT in a synthetic WWTP effluent with 220 mg L^{-1} TOC, 50 mg L^{-1} total nitrogen, and 10 mg L^{-1}

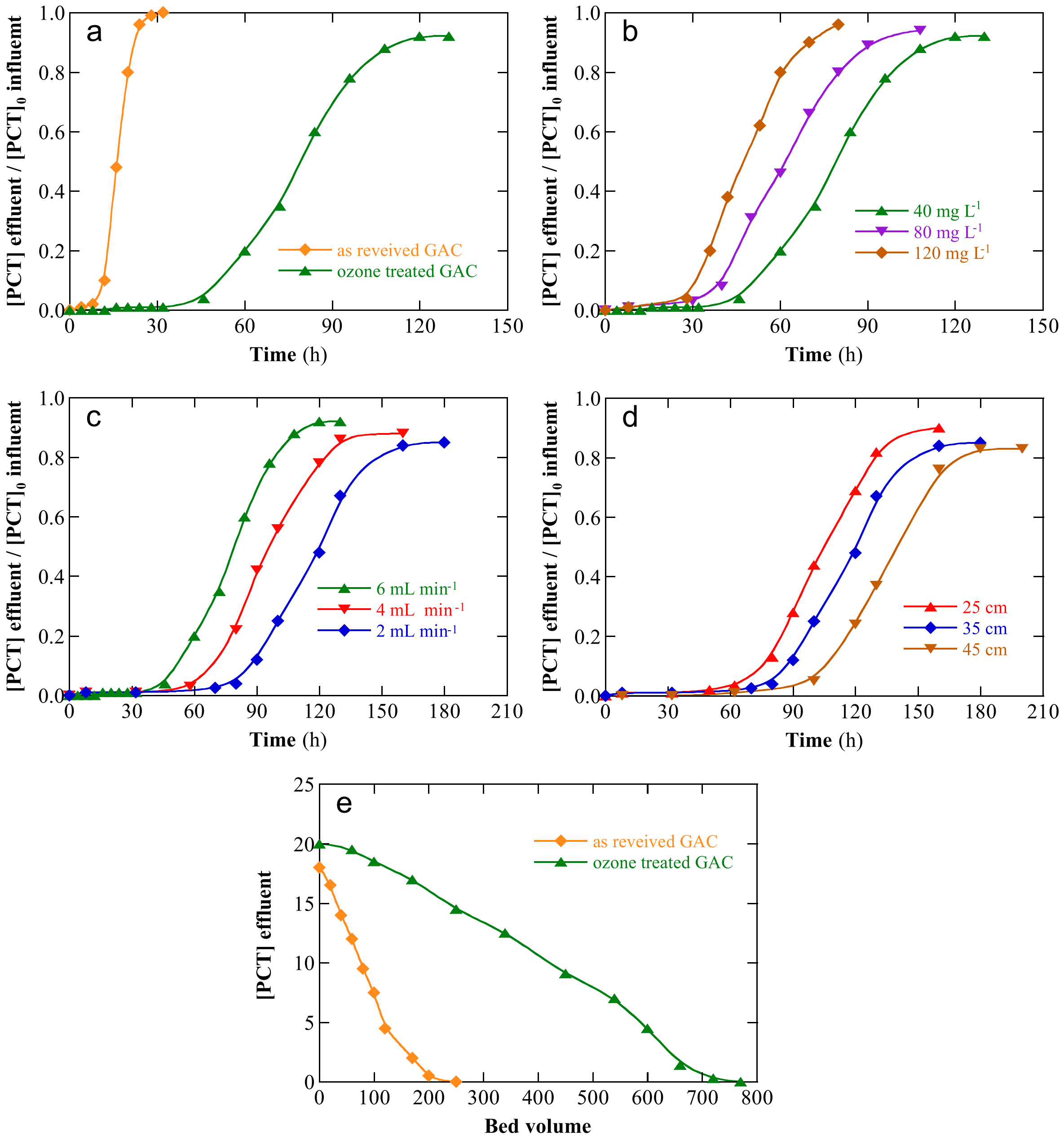

Fig. 4. (a) Ratio of PCT concentration between the effluent and influent (40 mg L^{-1} drug in pure water at pH 6.8 and 25 °C) with time by flowing the solution at 6 mL min^{-1} from the top to bottom of a column of 35 cm bed depth containing as received granular activated carbon (GAC) or activated with O_3, which was obtained by passing gaseous O_3 at a flow rate of 8 mg min^{-1} for 3 h. Effect of (b) PCT concentration influent (6 mL min^{-1} flow rate, 35 cm bed depth), (c) flow rate (40 mg L^{-1} PCT concentration influent, 35 cm bed depth), and (d) bed depth (40 mg L^{-1} PCT concentration influent, 2 mL min^{-1} flow rate) on the change of the ratio of PCT concentration between the effluent and influent with time. (e) PCT concentration vs. bed volume when passing a NaOH effluent at 6 mL min^{-1} for regeneration of exhausted columns. Adapted from Yanyan et al. (2018).

total phosphorous. The MBR system is schematized in Fig. 1c and was composed of three consecutive and separated anoxic (2 L), aerobic (3 L), and membrane (2 L) tanks. The latter tank was aerated at 0.5 L min^{-1} and contained an Al_2O_3 membrane where O_3 was directly injected at 5 mg L^{-1} for 20 min each 2 d. A volume of 7 L of the WWTP effluent was circulated through the MBR system at 0.5 L min^{-1} after addition of 500 ng L^{-1} of each drug. After 65 d of treatment, all PCT was destroyed, but only 10–26% of the other drugs were removed. Moreover, TOC was reduced by 94%, whereas 70–80% of total nitrogen and phosphorous removal were attained. Compared with the single MBR process, a 53% alleviation of membrane fouling upon the in-situ ozonation was found. They proposed two possible ways for improving the hydraulic performance of the ceramic MBR, namely membrane scrubbing and direct/indirect oxidation of precipitates (see Fig. 1c). This is an important result because the membrane collapse was avoided, allowing a longer duration of the hybrid process and a more-cost effective regeneration of MBR for consecutive treatments.

3.2. *Hybrid catalytic ozonation*

A high number of papers have investigated the PCT destruction from waters and wastewaters by means of hybrid catalytic ozonation aiming to enhance its degradation rate. Two approaches have been developed involving the ozonation with metal-based catalysts and the photolytic and photocatalytic ozonation, which will be analyzed and discussed in this subsection. Table 2 collects selected results obtained for such

Table 2
Selected results obtained for the catalytic ozonation of PCT in different aqueous matrices.

Pollutant	System	Experimental conditions	Best results	Ref.
Ozonation with metal-based catalysts				
PCT in pure water	Like of Fig. 1b with calcined HRS NPs [a] catalyst and O_3 flow rate of 1.2 mg min^{-1}	50 mL of 50 mg L^{-1} drug, 0–1.4 mg L^{-1} catalyst, 20 and 40 mM H_2O_2, pH 3–11, 30 min	Drug and TOC removal (30 min) at optimum 1.0 mg L^{-1} catalyst and pH 7: 28% (10 min) and 24% for O_3 < 100% (10 min) and 73% for O_3/HRS NPs <100% (4 min) and 86% for O_3/HRS NPs/H_2O_2. Higher PCT decay at higher pH for O_3/HRS NPs	Kohantorabi et al. (2022)
PCT in pure water	Stirred tank reactor using several synthetic MgO catalysts and O_3 flow rate of 1.8 mg min^{-1}	50 mL of 50 mg L^{-1} drug, 0.1 g MgO, natural pH (5.4), 30 min	For the best MgO catalyst, 100% degradation at 15 min and 94% for TOC decay at 30 min using O_3/MgO. Low reusability after 4 cycles of O_3/MgO. Detection of 6 aromatic derivatives and 6 carboxylic acids by LC-MS. and NO_3^- was also identified. Reaction sequence proposed.	Mashayekh-Salehi et al. (2017)
PCT in pure water	Like of Fig. 1b using the best previously synthesized MgO catalyst and O_3 flow rate of 0.3–3 mg min^{-1}	50 mL of 10–200 mg L^{-1} drug, 0.02–2.0 g MgO, pH 2.0–10.0, 30 min	Complete degradation and 94% mineralization of 50 mg L^{-1} drug at pH 5.4, with 2 g L^{-1} MgO and 1.8 mg O_3 min^{-1}. Cytotoxicity measurements showed large enhancement of the viability of human embryonic kidney cells after the O_3/MgO process	Yaghmaeian et al. (2017)
PCT in pure water	Like of Fig. 1b using Cu sheets as catalyst and O_3 flow rate of 10 mg min^{-1}	1.3 L of 50 mg L^{-1} drug, 10–80 g L^{-1} catalyst, pH 2.0–12.0, 120 min	TOC removal at pH 12.0: 27% by single ozonation <67% by O_3/Cu. Higher TOC decay at greater pH for O_3/Cu, only reduced by 36% at pH 2.0. Rise of TOC decay from 58% to 79% with 400 mg L^{-1} Cl^- at pH 6.0	Wang et al. (2018)
PCT in pure water	Like of Fig. 1b using zeolite 4A catalyst and O_3 flow rate of 0.9 mg min^{-1}	450 mL of 50 mg L^{-1} drug, 5.0 g catalyst, pH 3.0, 7.0, and 9.0, 25 °C, 60 min	Degradation for O_3 and O_3/zeolite 4A: 69% and 80% at pH 3.0, 73% and 90% at pH 7.0, and 95% and 87% at pH 9.0. Small formation of $^{\bullet}OH$ of $^{\bullet}O_2^-$ in the O_3/zeolite 4A process	Ikhlaq et al. (2018)
PCT in pure water	Stirred tank reactor using Al_2O_3 or Pt–Al_2O_3 catalyst and O_3 flow rate of 3–9 mg min^{-1}. US [b] at 572 kHz and 0.23 mW L^{-1} power density by a plate-type reactor	250 mL of 35 μM drug, pH 7.0–12.0, 5 mg L^{-1} of Al_2O_3 or Pt–Al_2O_3, 60 min	For single ozonation at pH 7.0, faster degradation at higher O_3 flow rate. Total removal in 3 min at 9 mg O_3 min^{-1}. Mineralization: 17% < 18% < 25% at 3, 6, and 9 mg O_3 min^{-1}. Quicker drug and greater TOC removals at alkaline pH. For catalytic ozonation, degradation rate raised as O_3/Al_2O_3 < O_3/Pt–Al_2O_3/US < O_3/Pt–Al_2O_3. TOC decay increased as 18% < 25% < 33%.	Ziylan-Yavaş and Ince (2018)
PCT in pure water	Like of Fig. 1b with SnO_2 NPs as catalyst and O_3 flow rate of 1.3 g h^{-1}	250 mL of 50 mg L^{-1} drug, 30 g L^{-1} catalyst, pH 7.0, 30 min	98% degradation and 84% mineralization at 20 and 30 min, respectively, for O_3/SnO_2 NPs and O_3, respectively. The corresponding mineralization was 83% and 34%, respectively, at 30 min. For the catalyst, $^{\bullet}OH$ as main oxidant. Catalytic activity preserved after 4 successive cycles. 2 aromatic derivatives and 14 short aliphatic by-products identified by LC-MS. Reaction sequence proposed.	Rashidashmagh et al. (2021)
PCT in pure water	Like of Fig. 1b with 1:1 Fe_3O_4@Ce-MOF (Ce-UiO-66) catalyst and O_3 flow rate of 0.8 mg min^{-1}	50 mL of 25 mg L^{-1} drug, 0.16 g L^{-1} of catalyst, pH 4.0–10.0, 25 °C, 10 min	Degradation and TOC decay at pH 5.6: 38% and 14% for O_3 < 51% and 20% for O_3/Fe_3O_4< 70% and 37% for O_3/Ce-MOF <87% and 55% for O_3/Fe_3O_4@Ce-MOF. OH as main oxidant. Catalyst reusable for 5 cycles. Detection of 11 aromatic and 16 small aliphatic by-products by LC-MS Reaction sequence proposed.	Mohebali et al. (2022)
Photolytic and photocatalytic ozonation				
PCT in pure water	Like of Fig. 1d upon O_3 concentration of 9.8 mg L^{-1} and an inner 15 W UVC light	1 L of 5 mM drug, pH 2.0, 7.0, and 9.0, 25 °C, 90 min	Degradation and TOC decay for O_3: 44% and 20% at pH 2.0 < 63% and 42% at pH 7.0 < 80% and 49% at pH 9.0. For the latter pH with O_3/UVC. 91% degradation and 53% mineralization	Neamtu et al. (2013)

(continued on next page)

Table 2 (*continued*)

Pollutant	System	Experimental conditions	Best results	Ref.
			Detection of 3 aromatic by-products, 6 carboxylic acids, acetamide, and NO_3^-. Reaction sequence proposed	
PCT in pure water	Stirred cylindrical reactor with Fe^{2+} and Cu^{2+} as catalyst, and O_3 flow rate of 1.0 mg h^{-1} upon an external 6 W UVA light	100 mL of 78–943 mg L^{-1} drug, 1.0 mM Fe^{2+} and/or 0.25 mM Cu^{2+}, pH 3.0, 240 min	Total degradation of 157 mg L^{-1} drug in 6 min regardless of the system used. TOC removal: 39% for O_3 < 91% for O_3/Fe^{2+}/UVA <94% for $O_3/Fe^{2+}+Cu^{2+}$/UVA <96% for O_3/UVA. Higher H_2O_2 accumulation for the latter system. More than 80% TOC decay for all drug contents by $O_3/Fe^{2+}+Cu^{2+}$/UVA. 3 aromatic by-products, 7 carboxylic acids, and acetamide detected by HPLC and GC/MS. Evolution of released NO_3^- and NH_4^+. Reaction sequence proposed.	Skoumal et al. (2006)
PCT in pure water	Like of Fig. 1b with 4% Ag-g-C_3N_4 catalyst, upon O_3 flow rate of 50 mg h^{-1} and an external 500 W Xe light	1 L of 10 mg L^{-1} drug, 0.25 g L^{-1} catalyst, pH 3.0–11.0, 25 °C, 120 min	Faster TOC removal at pH 7.0. At this pH, TOC decay: 84% for O_3/4% Ag-g-C_3N_4/sunlight >53% for O_3/g-C_3N_4/sunlight >28% for O_3/4% Ag-g-C_3N_4 > 26% for O_3/g-C_3N_4 > 22% for O_3. Relatively good reusability for 4 consecutive cycles. Detection of 3 aromatics derivatives and 1 aliphatic by-product by LC-MS. Proposal of reaction sequence	Ling et al. (2019)
Mixture of 9 drugs (including PCT) in pure water	Like of Fig. 1b stirred with air, with TiO_2 as photocatalyst upon O_3 flow rate of 30 L h^{-1} and an external UVB (313 nm) light from a 700 W high-pressure Hg lamp	1 L of 10 mg L^{-1} of each pollutant, 0.10–1.0 g L^{-1} TiO_2, pH 5.5, 20 °C, 120 min	Total degradation for PCT: 7 min by O_3 < 60 min by UVB <80 min by 0.25 g L^{-1} TiO_2/UVB. TOC decay of the mixture at 120 min: 21% by UVB <30% by O_3 < 60% by 0.25 g L^{-1} TiO_2/UVB <87% by O_3/UVB <96% by O_3/0.25 g L^{-1} TiO_2/UVB	Rivas et al. (2012)
Mixture of PCT, bisphenol A, and testosterone in pure water	Like of Fig. 1b with TiO_2, Fe^{3+}, and/or H_2O_2 as catalysts upon O_3 flow rate of 36 L h^{-1} and 2 external 15 W UVA lights	3 L of 1.5–3.0 mg L^{-1} of each drug, 0.1 g L^{-1} TiO_2, 2.8 mg L^{-1} Fe^{3+}, 17 mg L^{-1} H_2O_2, pH 3.0 or 6.5, 120 min	For PCT at pH 6.5. degradation: 50% at 120 min of TiO_2/UVA <100% at 15 min of O_3/UVA and O_3/TiO_2/UVA. For the mixture at pH 3.0, TOC removal at 120 min: 2% by Fe^{3+}/UVA <13% by O_3/UVA <46% by O_3/H_2O_2/UVA <80% by O_3/Fe^{3+}/UVA. At pH 6.5, 11% by TiO_2/UVA <15% by O_3/UVA <70% by O_3/TiO_2/UVA	Rodríguez et al. (2012)
Mixture of 6 drugs (including PCT) in secondary WWTP effluent (COD: 59 mg L^{-1}, TOC: 20 mg L^{-1})	Fig. 1e with a solar CPC [c] photoreactor (1.8 L) using TiO_2, Fe^{3+}, and/or H_2O_2 as catalysts upon O_3 concentration of 13 mg L^{-1} and sunlight irradiation	5 L of 0.2 mg L^{-1} of each pollutant, 200 mg L^{-1} TiO_2, 2.8 mg L^{-1} Fe^{3+}, 17 mg L^{-1} H_2O_2, pH 3.0 for iron-based systems and 7.0 for TiO_2-based systems, liquid flow rate 8.7 L min^{-1}, 300 min	Total removal of all pollutants: ≈35 min by O_3/sunlight, O_3/Fe^{3+}/sunlight, and $O_3/H_2O_2/Fe^{3+}$/sunlight at pH 3.0 < 42 min by O_3 at pH 3.0 < 60 min by O_3/TiO_2/sunlight at pH 7.0 < 67 min by O_3 at pH 7.0. Greater $^{\bullet}OH$ production for $O_3/H_2O_2/Fe^{3+}$/sunlight at pH 3.0. This method also yielded a 35% TOC reduction at 300 min (38,7 kJ L^{-1} radiation dose), removing the toxicity, and presenting the lower relative energy consumption	Quiñones et al. (2015a)
Mixture of 6 drugs (including PCT) in pure water	Fig. 1e with a solar CPC photoreactor (1.8 L) using TiO_2, Fe^{3+}, and/or H_2O_2 as catalysts upon O_3 concentration of 13 mg L^{-1} and sunlight irradiation of 41.2 W m^{-2}	5 L of 0.01 mM of each pollutant, 200 mg L^{-1} TiO_2, 2.8 mg L^{-1} Fe^{3+}, 17 mg L^{-1} H_2O_2, pH 3.0 for iron-based systems and 7.0 for TiO_2-based systems, liquid flow rate 8.7 L min^{-1}, 50 min	Total PCT removal in the mixture: 11 min for H_2O_2/Fe^{3+}/sunlight and $O_3/H_2O_2/Fe^{3+}$/sunlight at pH 3.0 < 15 min for O_3 at pH 3.0 and O_3/TiO_2/sunlight at pH 7.0 < 18 min for O_3/sunlight and O_3/Fe^{3+}/sunlight at pH 3.0 < 25 min for O_3 and O_3/sunlight at pH 7.0 < 40 min for TiO_2/sunlight at pH 7.0	Quiñones et al. (2015b)
Mixture of PCT, ciprofloxacin, and metronidazole in pure water	Fig. 1d with TiO_2 NPs immobilized onto montomormollite as photocatalyst, upon O_3 flow rate of 10 L h^{-1} and an 8 W UVA light	500 mL of 5–25 mg L^{-1} of each drug, 0.04 mg L^{-1} photocatalyst, 15 min	Maximum degradation of 50.1%, 80.6%, and 64.6% for 5 mg L^{-1} of PCT, 5 mg L^{-1} of ciprofloxacin, and 25 mg L^{-1} of metronidazole, determined by response surface methodology. Identification of 8 aromatic by-products and 1 aliphatic derivative from the mixture by GC/MS.	Hassani et al. (2017)
Mixture of 8 drugs (including PCT) in pure water or secondary WWTP	Like of Fig. 1b with GO [d]/TiO_2 photocatalyst, O_3 concentration of 10 mg L^{-1} and an external 176–313 W	500 mL of 10 mg L^{-1} of each pollutant, 0.10–0.40 g L^{-1} of GO/TiO_2, pH 5.6 and 8.3, 180 min	For O_3, O_3/GO/TiO_2, O_3/visible, and O_3/GO/TiO_2/visible in pure water at pH 5.6, overall degradation of all pollutants and TOC removal at 180	Checa et al. (2020)

(*continued on next page*)

Table 2 (*continued*)

Pollutant	System	Experimental conditions	Best results	Ref.
effluent (COD: 29 mg L^{-1}, TOC: 10 mg L^{-1})	m^{-2} irradiation from 44 LED lamps (λ_{max} = 425 nm)		min: 60 min and 31% < 30 min and 30% < 30 min and 60% < 15 min and 74%. For the same catalyzed processes with visible light at pH 8.3, TOC removal at 180 min: 53% < 81% in pure water, 32% < 92% in secondary WWTP	

[a] HRS NPs: Hematite red soil nanoparticles.
[b] US: Ultrasounds.
[c] CPC: Compound parabolic collector.
[d] GO: Graphene oxide.

treatments remarking the reaction medium checked and the system and operating variables tested.

3.2.1. Ozonation with metal-based catalysts

Similar systems to those of single ozonation were also used in the hybrid catalytic ozonation with metal-based catalysts. The main difference is that a heterogeneous solution was ozonated with the suspended insoluble catalyst, favoring the main reduction of the injected O_3 to the stronger oxidant OH on the catalyst surface (see Fig. 5a). Although this radical can remove rapidly organics on the catalyst surface, its short half-time prevents its direct reaction in the aqueous matrix.

Kohantorabi et al. (2022) studied the catalytic ozonation of PCT with calcined hematite red soil nanoparticles (HRS NPs) catalyst. The experiments were carried out with a system like of Fig. 1b and the tubular reactor was filled with 50 mL of 50 mg L^{-1} drug, up to 1.4 mg L^{-1} catalyst, and 20 and 40 mM H_2O_2 at pH 3–11 under a flow rate of 1.2 mg O_3 min^{-1}. Fig. 5b shows a very low adsorption of the drug onto the catalyst surface and its slow destruction with O_3 upon uncatalyzed conditions at pH 7, only yielding 28% degradation in 10 min. In contrast, total drug abatement was reached at this time with the catalyzed process with 1.0 mg L^{-1} HRS NPs, which was shorted to 4 min by adding 20 mM H_2O_2. The same tendency was found for the TOC removal at 30 min which increased in the sequence: O_3 (24%) < O_3/HRS NPs (73%) < O_3/HRS NPs/H_2O_2 (86%), as shown Fig. 5c (see also Table 2). This positive behavior of catalyzed systems can be explained by the conversion of O_3 and/or H_2O_2 into $^\bullet$OH that more rapidly destroy PCT, as schematized in the mechanism of Fig. 5a. At pH 11, O_3 can be activated by adsorbed HO_2^- (the basic form of H_2O_2) via reaction (12). Fig. 5d highlights.

a large influence of pH on the percentage of PCT removal after 6 min of the O_3/HRS NPs process. Total degradation was achieved at alkaline media (pH ≥ 9), probably because the more reactive phenolate form of the drug was more rapidly oxidized. The influence of the amount of catalyst added to the O_3/HRS NPs treatment at pH 7 on the percent of PCT degradation is given in Fig 5e and makes evident that the better performance was obtained with 1.0 mg L^{-1} catalyst related to an apparent rate constant k_1 of 0.35 min^{-1}. The HRS NPs material then seems a good candidate for the catalytic ozonation of PCT from waters and wastewaters.

Cheap simple or natural materials such as MgO (Mashayekh-Salehi et al., 2017; Yaghmaeian et al., 2017), Cu sheets (Wang et al., 2018), and zeolite 4A (Ikhlaq et al., 2018) have been tested as catalysts as well (see Table 2). Mashayekh-Salehi et al. (2017) studied the treatment of 50 mL of 50 mg L^{-1} drug and 0.1 g MgO at natural pH of 5.4 using a stirred tank reactor upon injection of 1.8 mg O_3 L^{-1}. Several MgO materials were synthesized by a sol-gel method with calcination at 500 °C. For the best synthesized catalyst, they found a rapid complete degradation at 15 min and 94% TOC abatement at 30 min, but with a low reusability after 4 successive cycles by the blocking of the catalytic sites of its surface by some by-products. LC-MS analysis of ozonated solutions revealed the formation of 6 aromatic derivatives and 6 carboxylic acids. The release of NO_3^- ion was confirmed. The same group presented a more complete study in Yaghmaeian et al. (2017) with 50 mL of 10–200 mg L^{-1} PCT in pure water, with 0.02–2.0 g of the best MgO synthesized previously, at pH 2.0–10.0. A system like of Fig. 1b was checked upon injection of an O_3 flow rate at 0.3–3 mg min^{-1}. The best performance with 100% drug removal and 94% mineralization was attained after 30 min of the O_3/MgO process of 50 mg L^{-1} PCT with 2 g L^{-1} MgO at pH 5.4 and 1.8 mg O_3 min^{-1}. At this pH, a larger affinity of the neutral drug molecules on the catalyst surface takes place, favoring its rapid oxidation with adsorbed O_3 and generated $^\bullet$OH. The authors measure the cytotoxicity of the resulting wastewater and found a large enhancement of the viability of human embryonic kidney cells, which is a very positive result for this treatment.

Further research of Wang et al. (2018) described the positive use of Cu sheets to remediate the contamination of 1.3 L of pure water with 50 mg L^{-1} PCT at pH 2.0–12.0. The trials were made with a system like of Fig. 1b by applying 10–80 mg L^{-1} catalyst and an O_3 flow rate of 10 mg min^{-1}. The performance increased with increasing pH and then, the best results were obtained at pH 12.0, where at 120 min, TOC was reduced by 27% by single ozonation and 67% by the O_3/Cu process. The superiority of the catalytic ozonation was due to the generation of $^\bullet$OH either at the Cu surface from O_3 reduction or by the Fenton-like reaction (30) involving dissolved Cu$^+$ and generated H_2O_2, as confirmed by the inhibition with the $^\bullet$OH-scavenger *tert*-butyl alcohol and the EPR analysis with DMPO. They observed a positive rise of TOC abatement from 58% to 79% in the O_3/Cu system with 400 mg L^{-1} Cl$^-$ at pH 6.0. This was explained by the attack of this ion corroding the metal surface, thus destroying the oxide surface layer, and generating active sites that accelerate organic reactions.

The applicability of natural zeolite 4A to catalytic ozonation was examined by Ikhlaq et al. (2018). These authors used a system like of Fig. 1b to abate PCT in 450 mL of pure water containing 50 mg L^{-1} drug with 5.0 g catalyst at pH 3.0, 5.0, and 9.0 at 25.0 °C. After flowing 0.9 mg O_3 min^{-1} for 60 min, its degradation at pH 3.0 rose from 69% to 80%–73% and 90% using single ozonation and the O_3/zeolite 4A process, respectively. In contrast, the latter treatment became less efficient (87% vs. 95%) at pH 9.0 (see Table 2), which was related to the low adsorption ability of the phenolate form of PCT on the zeolite surface (with zero-charge potential at pH 6.4) that inhibits its oxidation. The best results at pH 7.0 were then related to a maximum drug adsorption on zeolite 4A, enhancing its destruction. Since a low promotion of $^\bullet$OH of $O_2^{\bullet-}$ formation was found in the O_3/zeolite 4A process, the authors suggested that the PCT oxidation followed a non-radical mechanism, that is, by direct reaction with adsorbed O_3. This points to consider that zeolite 4A is not a good catalyst for O_3 activation because other stronger oxidants are not significantly generated.

Recent articles have reported the catalyzed ozonation with synthetic materials like alumina-based (Ziylan-Yavaş and Ince, 2018; Chassaing et al., 2021), SnO_2 NPs (Rashidashmagh et al., 2021), and Fe_3O_4@Ce-metal organic framework (MOF) (Ce-UiO-66) (Mohebali et al., 2022).

Ziylan-Yavaş and Ince (2018) described the use of Al_2O_3 or Pt–Al_2O_3 catalyst for treating 250 mL of 35 μM PCT in pure water at pH 7.0–12.0 using a stirred tank reactor. Comparative experiments for single and

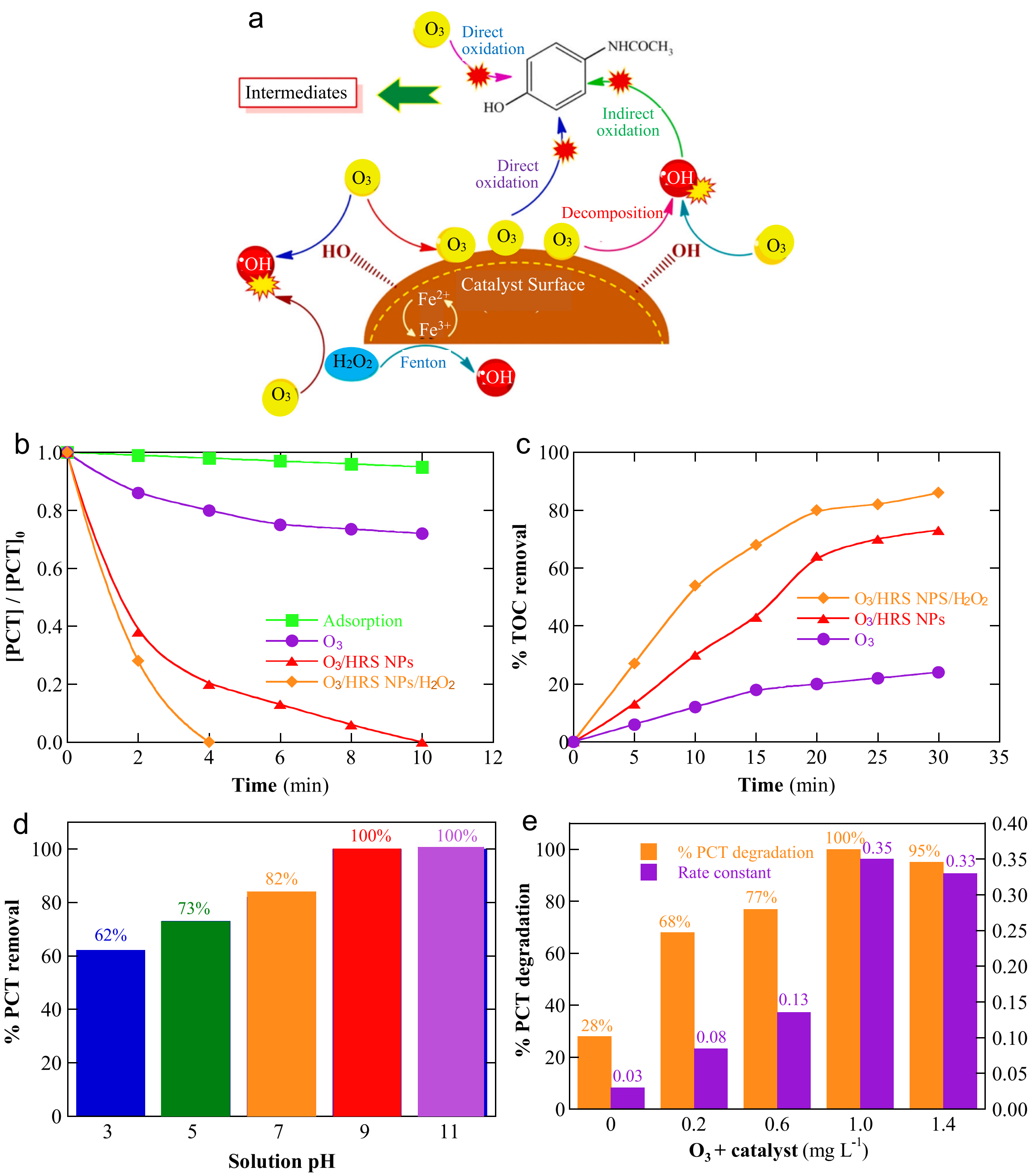

Fig. 5. (a) Proposed catalytic ozonation mechanism of PCT with calcined hematite red soil nanoparticles (HRS NPs) catalyst. Time-course of (b) normalized PCT concentration and (c) percent of TOC removal determined for 50 mL of 50 mg L^{-1} drug in pure water at pH 7 using the system of Fig. 1b for different processes. O_3 flow rate: 1.2 mg min^{-1}, [HRS-NPs]: 1.0 mg L^{-1}, [H_2O_2}: 20 mM for PCT degradation or 40 mM for TOC decay. (d) Effect of pH on the percentage of PCT degradation under the above conditions after 6 min of the O_3/HRS NPs process. (e) Influence of the amount of catalyst added to the O_3/HRS NPs treatment at pH 7 on the percent of PCT degradation and the corresponding k_1 value. Adapted from Kohantorabi et al. (2022). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

catalyzed ozonation were made with O_3 flow rates of 3, 6, and 9 mg min^{-1}. In the case of Pt–Al_2O_3, the study was complemented by applying a hybrid ultrasound (US) process with a plate-type reactor equipped with a 120 W generator and a piezo-electric transducer that emitted at 572 kHz frequency with 0.23 W mL^{-1} power density. Fig. SM-3a shows the effect of the O_3 flow rate on the normalized drug content vs. time for single ozonation at pH 7.0. As expected, more quantity of drug was abated with raising the O_3 flow rate because of the presence of more oxidizing agents. So, total degradation was achieved in 7 min for 3 mg O_3 min^{-1}, whereas only 3 min were required for 9 mg O_3 min^{-1}. This trend was also verified for the percentage of mineralization at 60 min, as shown in Fig. SM-3b, increasing in the order: 17% < 18% < 25% at 3, 6, and 9 mg O_3 min^{-1}, respectively. Moreover, quicker drug content and greater TOC were removed at alkaline pH due to the more rapid oxidation of the more reactive phenolate form of PCT. The following runs were performed with 5 mg L^{-1} of alumina catalyst at pH 7.0 and 6 mg O_3 min^{-1}. Fig. SM-3c highlights a dramatic decay of PCT removal by the O_3/Al_2O_3 system that needed 15 min for overall disappearance, a time much longer than that of single ozonation (see Fig. SM-3a). This was related to the low adsorption of the drug onto the catalyst surface that difficulties its reaction with O_3. In contrast, the O_3/Pt–Al_2O_3 system led to a much quicker degradation needing about 5 min for total removal. This was explained by the generation of large amounts of the stronger oxidant •OH on the catalyst surface, as confirmed from scavenging agents, which oxidize more rapidly the drug and its by-products. This behavior was reflected in the enhancement of the mineralization from 18% for O_3/Al_2O_3 to 33% for $O_3/Pt–Al_2O_3$ (see Fig. SM-3d). However, the coupling of US to the $O_3/Pt–Al_2O_3$ process was detrimental for PCT degradation and mineralization (see Fig. SM-3c and d). The failure in degradation was ascribed to two facts: (i) the reduction of O_3 direct reaction by its diffusion into the gaseous cavity bubbles formed by US and (ii) the damage of the catalyst surface by the cavitation collapse of the cavity bubbles. The rise of mineralization to 25% as compared to 18% for single ozonation was related to the shift of oxidation reactions to the solid surface and the gaseous cavity bubbles with large hydrophobicity.

The hybrid catalytic ozonation with SnO_2 NPs has been studied by Rashidashmagh et al. (2021) with a system like of Fig. 1b. The runs were carried out with 250 mL of 50 mg L^{-1} drug and 30 g L^{-1} catalyst in pure water at pH 7.0 upon diffusion of 1.3 g O_3 h^{-1}. A large enhancement of PCT degradation and mineralization was observed using the high content of SnO_2 NPs catalyst. While 84% degradation after 30 min of single ozonation was found, it grew up to 98% after 20 min of O_3/SnO_2 NPs. Similarly, the mineralization at 30 min increased largely from 34% for single ozonation to 83% for O_3/SnO_2 NPs (see Table 2), demonstrating the high catalytic power of this material. The fast inhibition of degradation in the O_3/SnO_2 NPs process in the presence of salicylic acid as scavenger indicated that •OH was the main oxidizing agent. This species was assumed to be produced from the interaction of the basic (-OH) functional groups of the catalyst surface with O_3 molecules favoring their reduction to •OH. The authors found an excellent preservation of the catalytic activity of SnO_2 NPs after 4 consecutive runs. The generation of 2 aromatic derivatives and 14 short aliphatic by-products was detected by LC-MS. Mohebali et al. (2022) synthesized a complex Fe_3O_4@Ce-MOF (Ce-UiO-66) catalyst to be combined with ozonation. A volume of 50 mL of pure water with 25 mg L^{-1} drug and 0.16 g L^{-1} of catalyst at pH 4.0–10.0 and 25 °C was treated in a system like of Fig. 1b with an O_3 flow rate of 0.8 mg min^{-1}. The best results were obtained at pH 5.6, where the PCT abatement at 10 min increased in the sequence: 38% for O_3 < 51% for O_3/Fe_3O_4< 70% for O_3/Ce-MOF <87% for O_3/Fe_3O_4@Ce-MOF. The large superiority of the O_3/Fe_3O_4@Ce-MOF treatment was reflected in the removal of 55% TOC in front of only 14% using single ozonation (see Table 2). For the catalytic process, the pre-eminent oxidative action of high amounts of •OH formed at the catalyst surface from O_3 decomposition was considered to explain its large performance. The authors confirmed the good reusability of the Fe_3O_4@Ce-MOF catalyst for 5 cycles and detected 11 aromatic derivatives and 16 small aliphatic by-products by means of LC-MS analysis.

3.2.2. *Photolytic and photocatalytic ozonation*

The coupling of light irradiation with O_3 treatments has allowed the development of several hybrid photolytic and photocatalytic processes for PCT destruction from waters and wastewaters. The efficiency of the photo-assisted process is related to the wavelength (λ) and the light intensity (Brillas, 2022). Lamps of UVC (190–280 nm, $\lambda_{max} = 254$ nm), high-pressure Hg vapor (simulating UVB with $\lambda_{max} = 313$ nm), UVA (315–400 nm, $\lambda_{max} = 360$ nm), and light emitting diode (LED) for visible light have been used. It is remarkable the alternative application of direct sunlight to obtain more cost-effective treatments, which can be simulated at lab scale with Xe lamps. The main reactions involved in these processes are listed in Table SM-1. The experimental setups contained the ozonated system illuminated with inner or external light. Some examples are depicted in Fig. 2. Fig. 1d presents the sketch of a cylindrical reactor with O_3 inlet by its top and an inner 8 W UVA light for photocatalytic ozonation (Hassani et al., 2017). Fig. 1e schematizes a system for solar photocatalytic ozonation containing a compound parabolic collector (CPC) photoreactor to absorb the sunlight rays with O_3 inlet and wastewater recirculation (Quiñones et al., 2015a).

The photolytic treatment of PCT in pure water through the O_3/UVC process has been reported by Neamtu et al. (2013). The effectiveness of this treatment was well-proved with a system like of Fig. 2d with an inner 15 W UVC light by providing an O_3 concentration of 9.8 mg L^{-1}. The degradation of 1 L of 5 mM PCT was tested at pH 2.0–9.0 and 25 °C. For single ozonation, the drug and TOC decays at 90 min rose in the sequence: 44% and 20% at pH 2.0 < 63% and 42% at pH 7.0 < 80% and 49% at pH 9.0. The study of the O_3/UVC process was centered at pH 9.0 and revealed a clear improvement of the above performance, yielding 91% degradation and 53% mineralization. This can be explained by the photolysis of O_3 to H_2O_2 from reaction (15), followed by the homolytic photolysis of this species to •OH from reaction (16), which more rapidly destroys the drug and its by-products. Additional photolysis of photoactive organics is feasible, accelerating their destruction. Several generated by-products like 3 aromatics, 6 carboxylic acids, acetamide, and NO_3^- were detected.

Skoumal et al. (2006) examined the photolytic behavior of Fe^{2+} and Cu^{2+} for the PCT destruction of 100 mL of 157 mg L^{-1} drug in pure water at pH 3.0 and 25 °C using a stirred cylindrical reactor with an O_3 flow rate of 1.0 mg h^{-1} and an external 6 W UVA light. Fig. SM-4a makes evident that the application of only O_3 gave the less potent process that required 6 min for total degradation, with an apparent rate constant k_1 of 0.775 min^{-1}. The drug decays by the O_3/UVA, O_3/1.0 mM Fe^{2+}/UVA, and O_3/1.0 mM Fe^{2+} + 0.25 mM Cu^{2+}/UVA methods were slightly quicker leading to overall disappearance in 4–5 min with k_1-values varying between 0.932 and 1.185 min^{-1}. A clear differentiation of the oxidation power of these processes was found from the mineralization abatement shown in Fig. SM-4b and the concentration of accumulated H_2O_2 presented in Fig. SM-4c. For O_3, a poor mineralization up to a 39% at 240 min can be observed. It achieved a steady H_2O_2 content as low as 0.16 mM, suggesting the main attack of organics by O_3 with low H_2O_2 participation. In contrast, the photolytic O_3/UVA process was much more potent, slowly leading to 96% mineralization with a rapid production of 1 mM H_2O_2 in 5 min that disappeared in 30 min. This is indicative of a rapid photolysis of O_3 to H_2O_2 by reaction (15) and the fast attack of this oxidant to activated photoactive intermediates because it cannot be photolyzed to •OH by reaction (16) upon UVA irradiation. The situation was very different in the presence of Fe^{2+} and/or Cu^{2+} as catalyst since TOC was rapidly reduced by 91% and 94%, respectively, while H_2O_2 was rapidly formed from reaction (15) and destroyed in 10 min. This can be associated with a fast attack of O_3 and •OH, which can be produced from various ways (see Table SM-1): (i) the hydrolysis of FeO^{2+}originated from the reaction of O_3 with Fe^{2+} following reactions (21)–(23), (ii) the Fenton's reaction (24) followed by reactions (25) and (26), (iii) the photoreduction of $Fe(OH)^{2+}$ formed from reaction (27) to Fe^{2+} from reaction (28), and (iv) the Fenton-like reaction (30) of Cu^{+} formed from Cu^{2+} reduction via reaction (29). Fig. SM-4d shows the excellent oxidation power of the O_3/1.0 mM Fe^{2+} + 0.25 mM Cu^{2+}/UVA process by mineralizing more than 80% of the organic matter of concentrated PCT solutions with 78–943 mg L^{-1}. The authors detected 3 aromatic by-products, 7 carboxylic acids, and acetamide by HPLC and GC/MS, following the release of NO_3^- and NH_4^+ ions. Oxamic and oxalic acids were ultimate by-products that can be directly mineralized by H_2O_2 upon UVA activation, the photolysis of their Fe(III) complexes, and the •OH attack of their Cu(II) complexes, as highlighted in their concentration profiles shown in Fig. SM-4e and f, respectively.

Ekowati et al. (2019) reported the interesting application of a hybrid process involving O_3/UVC and chlorination (with 15% NaClO) for the decontamination and disinfection of swimming pool water. The plant treated 170 m^3 of pool water at pH 8.3 and 10–12 °C circulating at 53 m^3 h^{-1} through a 22 L cylindrical reactor illuminated with four 180 W amalgam low-pressure UVC lamps positioned vertically upon an O_3 concentration of 0.01–0.46 mg L^{-1}, The initial PCT concentration of 5 μg L^{-1} was removed after 3 h of O_3/UVC/chlorination, but other drugs such as caffeine and ibuprofen needed 24 h of the hybrid treatment. A large inactivation of common bacteria and spores was also observed at this time. Since bromide was present in the pool water, trihalomethanes and haloacetic acids were formed in lesser extent in the hybrid process than using chlorination alone, because of the preferential generation of brominated derivatives by O_3/UVC. Although the hybrid procedure was well-effective for pool-water treatment, deeper study is needed in the future to clarify the toxicity of the transformation by-products formed that are even more hazardous than the parent drugs. This should be accompanied by a techno-economic analysis of the hybrid ozonation/chlorination process to show if it can be viable in front of simple chlorination.

Other articles considered the hybrid photocatalytic ozonation with solid semiconductors like Ag-g-C_3N_4 (Ling et al., 2019), and TiO_2 alone (Rivas et al., 2012; Rodríguez et al., 2012; Quiñones et al., 2015a, 2015b) or immobilized onto montomormollite (Hassani et al., 2017) or graphene oxide (GO) (Checa et al., 2020). In these processes, the light irradiation promotes the pass of electrons of the valence to the conduction band of the semiconductor, originating pairs with separated charges composed of a hole in the valence band (h^+_{VB}) and an electron in the conduction band (e^-_{CB}) from reaction (17). •OH can then be formed from the attack of h^+_{VB} on water from reaction (18) and the evolution of $O_2^{\bullet -}$ and O_3^- generated from the reaction of e^-_{CB} with O_2 and O_3 via reactions (19) and (20), respectively. Fig. SM-5a schematizes these reactions for the Ag-g-C_3N_4 photocatalyst (Ling et al. (2019)). These authors checked the TOC removal for 1 L of 10 mg L^{-1} PCT in pure water with 0.25 g L^{-1} catalyst at pH 3.0–11.0 and 25 °C using a tubular reactor like of Fig. 1b upon an external 500 W Xe light (mimicking sunlight) and an O_3 flow of 50 mg h^{-1}. Fig. SM-5b shows a rise of the mineralization at pH 7.0 for the processes: O_3 < O_3/g-C_3N_4 < O_3/4% Ag-g-C_3N_4 ≪ O_3/g-C_3N_4/sunlight ≪ O_3/4% Ag-g-C_3N_4/sunlight, i.e., following an increasing generation of OH. The higher mineralization of 84% at 120 min was achieved for the hybrid photocatalytic process O_3/4% Ag-g-C_3N_4/sunlight, showing the clear beneficial of coating Ag on the semiconductor g-C_3N_4. This photo-assisted process was optimal at pH 7.0, as shows Fig. SM-5c, because the increase of pH from 3.0 to 7.0 favored the conversion of O_3 into more OH, but at alkaline pH there was an electrostatic repulsion between the negative catalyst surface and the phenolate form of PCT that difficulted its oxidation. Fig. SM-5d reveals a relatively good reusability of the catalyst for 4 consecutive cycles upon optimum conditions. By LC-MS analysis, 3 aromatics derivatives and 1 aliphatic by-product were detected.

A mixture of 9 drugs including PCT at concentration of 10 mg L^{-1} of each pollutant in pure water was treated with a system like of Fig. 1b stirred with air using TiO_2 as photocatalyst upon O_3 flow rate of 30 L h^{-1} and an external 700 W high-pressure Hg lamp providing UVB light at $\lambda = 313$ nm (Rivas et al., 2012). The experiments were performed with 1 L of the above solution after adding 0.10–1.0 g L^{-1} TiO_2 at pH 5.5 and 20 °C. Total PCT degradation was achieved in the order: 7 min by O_3 < 60 min by UVB <80 min by 0.25 g L^{-1} TiO_2/UVB, meaning a low production of OH in the latter photocatalytic process. When TOC decay was determined at 120 min, surprisingly, this treatment yielded 60% mineralization, much higher than 30% and 21% found for O_3 and UVB, respectively, indicating a large reactivity of by-products with OH at the catalyst surface. In contrast, 87% and 96% TOC abatements were attained with the photolytic O_3/UVB and photocatalytic O_3/0.25 g L^{-1} TiO_2/UVB processes, respectively (see Table 2). Hybrid catalytic ozonation then produced the higher quantity of oxidant OH from reactions (15)–(20), showing an acceptable oxidizing power for the destruction of the mixture of drugs. The same behavior can be inferred from the further work of Rodríguez et al. (2012), who degraded a mixture of PCT, bisphenol A, and testosterone in pure water. The system tested was like of Fig. 1b upon an O_3 flow rate of 36 L h^{-1} and two external 15 W UVA lights. 3 L with 1.5–3.0 mg L^{-1} of each drug were treated after addition of 0.1 g L^{-1} TiO_2, 2.8 mg L^{-1} Fe^{3+}, or 17 mg L^{-1} H_2O_2 as catalyst at pH 3.0 or 6.5. The analysis of PCT concentration revealed that at pH 6.5, it was removed by 50% at 120 min of TiO_2/UVA, and 100% at 15 min of O_3/UVA and O_3/TiO_2/UVA, demonstrating the superior oxidation ability of both photolytic and photocatalytic ozonation processes. However, higher TOC decay at 120 min was again found for the photocatalytic ozonation (70% vs. 15%, see Table 2) due to the faster destruction of by-products at the catalyst surface. The photolytic runs at pH 3.0 were made under homogeneous conditions with Fe^{3+} and H_2O_2 that can form oxidant OH from reactions (21)–(28). TOC was removed in the order: 2% by Fe^{3+}/UVA <13% by O_3/UVA <46% by O_3/H_2O_2/UVA <80% by O_3/Fe^{3+}/UVA. The best photolytic combination was the photo-assisted ozonation-Fenton-like option with higher OH generation.

The same Spanish group extended the research to the solar pilot plant schematized in Fig. 1e with a solar CPC photoreactor with 1.8 L of irradiated volume upon an O_3 concentration of 13 mg L^{-1} and a liquid flow rate of 8.7 L min^{-1}. They treated 5 L of a mixture of 6 drugs including PCT with 0.2 mg L^{-1} of each pollutant in a secondary WWTP effluent (Quiñones et al., 2015a) or with 0.1 mg L^{-1} of each drug in pure water (Quiñones et al., 2015b). The assays were performed with 200 mg L^{-1} TiO_2, 2.8 mg L^{-1} Fe^{3+}, and/or 17 mg L^{-1} H_2O_2 at pH 3.0 for iron-based systems and pH 7.0 for TiO_2-based ones. For the WWTP effluent, all drugs were completely removed in approximately 35 min by the photolytic processes of O_3/sunlight, O_3/Fe^{3+}/sunlight, and O_3/H_2O_2/Fe^{3+}/sunlight, requiring a longer time of 42 min for O_3. Slower processes were obtained at pH 7.0, yielding total degradation in 60 min for the photocatalytic O_3/TiO_2/sunlight and 67 min for O_3 at pH 7.0. The greater OH production from the photo-assisted ozonation-Fenton-like O_3/H_2O_2/Fe^{3+}/sunlight process was confirmed at pH 3.0, with a 35% TOC reduction at 300 min under the absorption of a 38.7 kJ L^{-1} radiation dose (see Table 2). This treatment removed the toxicity and presented the lower relative energy consumption. All the above treatments were quicker in the trials made in pure water because of the presence of lower organic load. In this case, the results of Table 2 highlight that PCT disappeared in only 11 min for the photolytic treatments of H_2O_2/Fe^{3+}/sunlight and O_3/H_2O_2/Fe^{3+}/sunlight at pH 3.0, more rapidly than using O_3 and O_3/sunlight at pH 3.0 and 7.0, and O_3/Fe^{3+}/sunlight at pH 3.0. The photocatalytic TiO_2-based treatments such as TiO_2/sunlight and O_3/TiO_2/sunlight at pH 7.0 were much slower. These findings demonstrate again the superiority of hybrid photolytic processes with Fe^{3+} and H_2O_2 over hybrid photocatalytic treatments with TiO_2.

The work of Hassani et al. (2017) was centered on the photocatalytic study of the degradation of 500 mL of 5–25 mg L^{-1} of PCT, ciprofloxacin, and metronidazole mixed in pure water with the system of Fig. 1d with an O_3 flow rate of 10 L h^{-1} and an 8 W UVA light. The photocatalyst was a composite of TiO_2 NPs immobilized onto montomormollite at concentration of 0.04 mg L^{-1}. By means of response surface methodology, a maximum degradation of 50.1%, 80.6%, and 64.6% for 5 mg L^{-1} of PCT, 5 mg L^{-1} of ciprofloxacin, and 25 mg L^{-1} of metronidazole, respectively, was determined after 15 min of treatment. However, an essential parameter as TOC reduction to better assess the oxidation power of the system was not investigated. Eight aromatic by-products and one aliphatic derivative were identified in the treated mixture by GC/MS.

Checa et al. (2020) focus their research on the treatment of a mixture of 8 drugs including PCT either in pure water or in a secondary WWTP effluent with GO/TiO_2 composite as photocatalyst to operate with visible light. The runs were made with 500 mL of 10 mg L^{-1} of each pollutant and 0.10–0.40 g L^{-1} of GO/TiO_2 at pH 5.6 and 8.3 in a system like of Fig. 1b with an O_3 concentration of 10 mg L^{-1} and 44 external LED lamps ($\lambda_{max} = 425$ nm) providing 176–313 W m^{-2} of irradiation. In pure water, the degradation and mineralization at pH 5.6 of all pollutants was enhanced in the sequence: O_3 < O_3/GO/TiO_2 < O_3/visible < O_3/GO/TiO_2/visible (see Table 2), related to the production of more OH from O_3 reduction. At pH 8.3 and 180 min of treatment, TOC was more difficulty removed by the photolytic O_3/visible process in the secondary WWTP effluent than in pure water (32% vs. 53%) because of the parallel oxidation of the other pollutants present in the former matrix. In contrast, the photocatalytic O_3/GO/TiO_2/visible process showed the opposite tendency with higher mineralization of the secondary WWTP effluent (92% vs. 81%), indicating the existence of a large adsorption of the other components of this matrix onto the photocatalyst surface allowing their fast removal with photogenerated OH. These findings demonstrate the beneficial of the application of composites of TiO_2 with high adsorbent materials to the remediation of wastewaters contaminated with PCT and other drugs, also favored with visible light.

3.3. Sequential treatments

First, this subsection describes the main results obtained for the sequential coupling of ozonation with non-biological processes for PCT remediation mainly from real waters and wastewaters. The sequential processes involving biological treatments of PCT wastewaters followed by ozonation are further detailed. Finally, the use of ozonation in water treatment plants is discussed to show its benefits for the remediation of real wastewaters with PCT.

3.3.1. Sequential non-biological ozonation

The Beltrán group studied the oxidation of a mixture of 5 mg L^{-1} sulfamethoxale +25 mg L^{-1} PCT in pure water at pH 1.5 and 20 °C by single ozonation and the H_2O_2 produced was further used for sequential treatment with photo-Fenton (Aguinaco et al., 2014). Single ozonation was carried out with 1 L of solution in a stirred tank reactor under injection of 23.5 mg O_3 L^{-1} for 15 min. As expected, both drugs were completely removed after ozonation due to their fast reaction with O_3, but the by-products formed were poorly destroyed remaining a 90% of the initial TOC with 1.3×10^{-4} M of accumulated H_2O_2. The ozonated solution was then adjusted to pH 3.0 and 1.3×10^{-5} M Fe^{2+} was added to it to investigate the subsequent photo-Fenton process by irradiating the reactor with four 15 W UVA lights. However, only a 50% of the initial TOC was reduced after 120 min of irradiation as result of the low OH production via Fenton's reaction (24) and photolytic reaction (27) due to the small concentration of Fenton reagent (H_2O_2 and Fe^{2+}). These results indicate that the proposed sequential photo-Fenton process is not appropriate for a good remediation of PCT waters.

Torun et al. (2015) investigated the ozonation of 200 mL of 50 mg L^{-1} PCT in pure water at pH 6.4 using a cylindrical reactor upon an O_3 flow rate of 10 g h^{-1} during 30 s. Subsequent treatment was made by irradiating 0.03 kGy h^{-1} of ^{60}Co gamma-rays at 23 °C. Total PCT degradation was achieved after the consumption of 5 kGy, for which a too long irradiation time of about 165 h was required. This procedure was then not adequate for PCT remediation. The work revealed the formation of final carboxylic acids like acetic, formic, and oxalic, as well as the release of NO_2^- and NO_3^- ions.

Better results were obtained with sequential ozonation-adsorption processes. Mojiri et al. (2019) used the system of Fig. SM-6 for the removal of PCT in pure water. For ozonation, 2.1 L of 0.2–2.2 mg L^{-1} drug at pH 7 and 15 °C were oxidized with an O_3 concentration of 3–15 mg L^{-1} lasting 30 min. The process was optimized with an artificial neural network and the best performance was obtained for 0.2 mg L^{-1} drug and 15 mg O_3 L^{-1} yielding 84.8% of degradation. The authors also determined a $k(O_3) = 2.36 \times 10^6$ M^{-1} s^{-1} for the reaction between PCT and O_3, i.e., quite like reported by other authors, as pointed out above. After these best ozonation conditions, the solution was passed through a cross-linked fixed column of 4 g chitosan/4 g bentonite at 4 mL min^{-1} (HRT = 25 min) and all the remaining drug was adsorbed following a Langmuir and Freundlich isotherm. Knopp et al. (2016) used a pilot plat with sequential ozonation-GAC adsorption running 618 d to remediate a secondary WWTP effluent with 30 pollutants including PCT with a content of 15.5 μg L^{-1}. The ozonation treatment was made with two bubbled columns of 113 L each upon a specific ozone consumption of 0.87 ± 0.29 g O_3 g TOC^{-1} at an HRT = 17 ± 3 min. This process was so efficient that PCT and other 18 pollutants disappeared completely. The subsequent adsorption over 2.08 m^2 of GAC filters removed practically all the rest of remaining pollutants. These findings point to consider that sequential ozonation-adsorption treatments can be viable for the removal of PCT and other drugs from waters and wastewaters.

Sequential nanofiltration (NF)-ozonation (Azaïs et al., 2016) and sequential ozonation-NF (Azaïs et al., 2017; Yacouba et al., 2021) treatments have been described to be applied to secondary WWTP effluents. The former process reported by Azaïs et al. (2016) was checked for 50 L of wastewater with 750 μg L^{-1} PCT at pH 7.7 and 20 °C, which was passed through a commercial NF-9 membrane at 0.5 m s^{-1} and pressure of 800 kPa that reduced 10 times their volume. 3 L of the resulting NF retentate at pH 2.2 and 20 °C was further treated by single ozonation in a glass stirred reactor with 5 mg O_3 min^{-1} for 300 min. About 87% of initial PCT was retained in the membrane in the NF pre-treatment and the remaining drug was completely removed in less than 10 min for the subsequent ozonation process. Although this paper showed the high power of the combined treatment for PCT removal, a large proportion of the drug was only separated from the wastewater and remained adsorbed in the membrane without being destroyed. An additional treatment is then required for recovering the membrane, with the consequent increase in the process cost.

For the sequential ozonation-NF process, it is remarkable the recent work of Yacouba et al. (2021). Fig. 12a schematizes the ozonation system containing a glass stirred tank reactor with 3 L of a secondary WWTP effluent at 20 °C upon an O_3 concentration of 5 mg L^{-1} during 30 min. The solution contained 1 mg L^{-1} of PCT and other four drugs, which were destroyed along with almost all the dissolved organic matter in the ozonation process, only requiring 5 min for PCT (see Fig. SM-7b), A time of 60 min was needed to abate about 50% COD and 30% TOC of the ozonated water, without greater oxidation at longer time. The ozonated water was then post-treated with NF using a commercial NF-90 membrane by applying a pressure of 10 bar up to obtain an 80% of water, leading to almost removal of COD and TOC. Under the same conditions, Fig. SM-7c shows an increasing PCT removal from 87% to 93% when the transmembrane pressure rose from 6 to 10 bar to obtain 80% water from the NF process of 16 L of the initial wastewater operating with a liquid flow rate of 0.5 m s^{-1} for 15–25 h. The best pressure for NF was then identified as 10 bar. As important result, it was found that the fouling of the membrane was significantly reduced by 40% using the pre-ozonated water, making this process more efficient. Fouling investigation makes evident that size exclusion was the pre-eminent mechanism of drug rejection. However, the sequential ozonation-NF treatment results too expensive if the membrane must be cleaned for reuse.

3.3.2. Biological-ozonation processes

Several works have shown the overall removal of PCT contained in real WWTP effluents by means of biological systems. Sequential ozonation treatments were then used for the destruction of other organic pollutants alongside disinfection. Rosal et al. (2010) analyzed the concentration of pollutants in the influent and effluent (secondary) of a WWTP at pH 7.6 with anaerobic, anoxic, and oxic biological processes by LC-QTRAP-MS and GC/MS. They found that drugs such as PCT, caffeine, and paraxanthine with initial concentrations near 20 μg L^{-1} were completely removed after the biological process, but many other drugs even with lower concentration were only destroyed in less than 20%. Further ozonation of the resulting secondary effluent was carried out at pH 8.5 with a system like of Fig. 1b with a 5 L reactor upon injection of 9.7 mg O_3 L^{-1}, and most drugs disappeared in less of 15 min after application of O_3 doses between 50 and 220 μM. This very positive action of O_3 was attributed to the generation of oxidant OH, partially inhibited by its reaction with other components of the secondary WWTP effluent. The same behavior has been described by Lee et al. (2019) for an anaerobic, anoxic, and aerobic biologic process used in a WWTP, since it removed all PCT from 19 to 68 μg L^{-1} from the influent during 1-year period. Subsequent ozonation rapidly destroyed the remaining drugs detected like carbamazepine, diclofenac, sulfamethoxazole, and trimethoprim.

Similar results have been reported by Espejo et al. (2014) and Gimeno et al. (2016) for the treatment of a primary WWTP effluent by aerobic biological process followed by different ozonation systems such as single ozonation or photolytic ozonation with $Fe^{3+}$and UVA light. In Espejo et al. (2014), for example, the aerobic biological experiments were performed with a 30 L stirred cuboid tank containing 1.3 mg L^{-1} of mixed liquid volatile suspended solids by injecting 3.0 mg L^{-1} O_2 with an HRT = 24 h. The primary WWTP at pH 7.5 was spiked with 0.2 mg L^{-1} PCT along with the same content of other 8 drugs. PCT and caffeine were completely removed in 7 h, but less than 25% abatement was found for the other pollutants. At the end of the biological trial, the initial TOC of 57 mg L^{-1} was reduced by 59%. After solid removal by filtration, the ozonation was carried out with 1 L cylindrical reactor with an O_3 concentration of 13 mg L^{-1} and under irradiation of two external 15 W UVA lights. In the trials with Fe^{3+}, 2.8 mg L^{-1} of this ion were added, and the solution pH was adjusted to 3.0. All remaining drugs disappeared in 15 min, more rapidly by photolytic ozonation with Fe^{3+} than single ozonation, but only 35% and 13% of TOC were removed after 30 min, respectively. Both treatments increased a 100% the solution biodegradability, and the ecotoxicity with respect to *Daphnia magna* was enhanced for the photolytic ozonation with Fe^{3+} due to the presence of this toxic ion. They explained again the rapid oxidation of the ozonation processes by the generation of OH.

Shahbeig et al. (2017) prepared a synthetic wastewater with 3500 mg L^{-1} of COD, and 7.5, 1, and 1 mg L^{-1} of PCT, metformin, and fluoxetine, respectively, at pH 7.3 for sequential treatment by MBR-ozonation. Fig. SM-8 illustrates a scheme of the lab-scaled combined system used. The assay started by entering the synthetic wastewater at 2.5 mL min^{-1} to the aerated 5.2 L of the MBR, which contained polyethylene filters with 0.0117 m^2 area, and was fed with activated sludge during 30 d at HRT = 29–31.5 h. The filtered wastewater was then introduced in the ozonation tank where 139 mg O_3 min^{-1} L^{-1} were injected during 4 min and 15 s at 19–24 °C before disposal. During the 30 d of operation, 98.5% PCT, 57.8% fluoxetine, and 99.9% COD in average were removed by the sequential MBR-ozonation process. This very positive result for this system suggests its viability in practice. Unfortunately, it was observed that the high content of the drug pollutants destroyed gradually the cell wall of microorganisms and reduced the mixed liquid suspended solids. This caused a loss of biological activity with biopolymer generation and membrane fouling, reflected in a progressive grew of COD of the filtered wastewater and of the transmembrane pressure of MBR from 45 to 180 mbar in 30 d.

3.3.3. *Ozonation in water treatment plants*

Ozonation is used as a key sequential process in many water treatment plants. Yang et al. (2011) studied the evolution of 19 drugs for 12 months in a WWTP placed in Gwinnett County, GA, U.S.A. The sequential plant was composed of an activated sludge treatment, membrane filtration, GAC adsorption, and ozonation, and the pollutants were quantified by GC/MS and LC-MS/MS. PCT was found with the highest average concentration of 80 μg L^{-1} in the primary effluent and was already undetected after membrane filtration. Most drugs were detected after the last ozonation step. For example, a more recalcitrant drug like sulfamethoxazole with a lower initial average content of 2.6 μg L^{-1} remained at the highest content of 80 ng L^{-1} at the end of ozonation. The arrangement used then allowed an excellent removal of organic pollutants commonly up to concentrations of 10–80 ng L^{-1}. Igos et al. (2012, 2013) analyzed a Life Cycle Assessment including electricity, chemicals, transport, and sludge treatment for removing 10 drugs in a conventional WWTP or a decentralized plant for hospital wastewaters. In the former case, 98% of PCT was abated, attaining 100% if a last ozonation step was applied. A high 99% removal for PCT was also found for the decentralized plant, and the remaining drug in the effluent was degraded by 48%, 64%, and 83% with subsequent UV light, activated carbon, and ozonation, respectively. Similar tendencies were found for the other drugs. So, the authors conclude that the decentralized treatment of hospital wastewater as point source of drugs did not significantly improve their environmental impact as compared to the centralized WWTP and that ozonation as final step gave better performance for both systems. Zhang et al. (2016) constructed the pilot plant shown in Fig. SM-9a to remove 15 indicator compounds (drug, pesticides, steroids, and X-ray contrast agent) with 12 treatment trains including dissolved air flotation, pre- and intermediate ozonation with or without H_2O_2 addition, intermediate chlorination, dual media filtration, and GAC adsorption. A final UVC/H_2O_2 process was also proved, being quite effective with too high energy requirements that largely exceed the needs for disinfection. The influent was introduced at 13.63 m^3 h^{-1} with spiked pollutants between 215 ng L^{-1} and 9.6 μg L^{-1}, including a PCT concentration of 1.51 μg L^{-1}. For this drug, the higher 98% removal was achieved with 2.0 mg O_3 L^{-1} in pre-ozonation followed by direct air flotation, dual media filter, and virgin GAC. The other pollutants were removed >90%, demonstrating the large performance of the arrangement chosen.

Kovalova et al. (2013) investigated the behavior of a pilot scale treatment plant for hospital wastewaters containing 56 drugs. The sequential treatment was performed with a primary clarifier, MBR, O_3, O_3/H_2O_2, activated carbon, UVC, and H_2O_2/UVC. As expected, all PCT was removed after the MBR process. More than 90% of the content of the other drugs were reduced by the following ozonation step, more largely than alternatively using activated carbon or UVC. Ozonation can then be envisaged as a good oxidation process to remove drugs in waters, as shown by other authors as well. Azuma et al. (2016, 2019) analyzed the environmental fate of about 60 drugs grouped into 11 therapeutic classes in three consecutive waters taken from a hospital effluent, then supplied to a conventional WWTP, and the resulting effluent released to a river located in Takatsuki City, Japan. The contributions of drugs in the hospital effluent to the WWTP influent varied widely from <0.1% to 14.8%. The WWTP contained two chains, one formed by conventional activated sludge followed by chlorination for disinfection to treat 132, 000 m^3 d^{-1} and the other one by ozonation with 9.6 mg O_3 L^{-1} for 100 min following activated sludge for treating 2000 m^3 d^{-1}. The HRT of each process varied between 6 and 9 d. Almost all drugs could be removed below 1.0 ng L^{-1} at the WWTP effluent after O_3 treatment. Apart from PCT at 15 μg L^{-1} in the WWTP influent, they detected the presence of analogous concentration of two metabolites, PCT sulfate and PCT glucuronide. Once released the resulting effluent to the river water, concentrations of PCT at < 30 ng L^{-1} and PCT glucuronide at about 2 ng L^{-1} were found. In this way, the WWTP was able to significantly remove the drugs provided by the hospital wastewater before disposal to the aquatic environment.

Other papers considered the PCT removal in drinking water treatment plants (DWTPs) using large volumes of river waters. Fig. SM-9b presents a scheme of the consecutive steps of a DWTP plant with pre-ozonation, flocculation, sedimentation, ozonation, filtration, chlorination, and clear well steps (Padhye et al., 2014). Five surface waters (SW) for sampling are indicated as well. These authors followed the concentration of 30 drugs, personal care products, and EDCs during 1 y from a river of the southeastern of USA. The average total concentration of all detected pollutants in the source water was of 360 ng L^{-1}, which was notably reduced to 98 ng L^{-1} in the finished drinking water. The initial average PCT content of 19.2 ng L^{-1} was completely abated in the DWT. As a positive result, the ozonation process showed the higher removal efficiency, also confirmed by further researchers. Boleda et al. (2011) treated the water of the Ebro River, Spain, with a DWTP consisting of a common arrangement with chlorination, coagulation/flocculation, and sand filtration steps. The resulting water was then treated in two parallel lines: conventional (ozonation and carbon filtration) and advanced (ultrafiltration and reverse osmosis) to be blended, chlorinated, and distributed. Pollutants had contents between 2.0 and 16 ng L^{-1} in the influent and were abated about 94%, with a higher efficiency for conventional than advanced processes. The same behavior was found for PCT with a concentration of 15.2 ng L^{-1}, which unfortunately was not completely removed by ozonation. Similar two arrangements were used by Hu et al. (2017) to decontaminate the water of Taihu Lake, China, during 1 y by assessing the evolution of 25 drugs. Better performance was obtained again using the common sequential treatment of chlorination, coagulation/flocculation, and filtration steps, followed by conventional ozonation and GAC filtration. PCT was gradually reduced from 470 ng L^{-1} in the influent to about 75 ng L^{-1} after the common treatment, subsequently being reduced to about 62 ng L^{-1} after ozonation and 28 ng L^{-1} after GAC filtration. Unfortunately, relatively high contents of all the drugs were finally obtained, showing a low efficiency of the DWTP checked. Recently, Borrull et al. (2021) assessed the ability of a DWTP with pre-ozonation, flocculation-coagulation-decantation, sand filtration, post-ozonation, and GAC filtration to remove 60 contaminants (drugs, personal care products, pesticides, and per- and polyfluoroalkyl substances) from the Ebro River, Spain. Ozonation and GAC adsorption were found as the best efficient technologies So, 25.6 ng L^{-1} of PCT in the influent completely disappeared after the ozonation step at 0.5 mg O_3 L^{-1} for 5 min. The other pollutants presented overall removal efficiencies between 51% and 100%, being the polyalkylfluoro substances the most persistent. This plant then showed an excellent behavior to produce potable water.

4. Reaction sequences for paracetamol mineralization

Some works have analyzed the PCT solutions during their treatments in pure water by HPLC, LC-MS, and/or GC/MS to identify the by-products produced in its initial degradation and subsequent mineralization. Based on the detected intermediates, several reaction sequences for PCT mineralization have been proposed by Andreozzi et al. (2003) and Villota et al. (2019) using O_3, Mashayekh-Salehi et al. (2017) with O_3/MgO, Rashidashmagh et al. (2021) with O_3/SnO_2 NPs, Mohebali et al. (2022) with O_3/Fe_3O_4@Ce-MOF, Neamtu et al. (2013) with O_3/UVC, Skoumal et al. (2006) with O_3 and Fe^{2+}, Cu^{2+}, and/or UVA as catalysts, and Ling et al. (2019) with O_3/4% Ag-g-C_3N_4/sunlight. It is noticeable that similar by-products were detected in all cases, regardless of the ozonation process tested because the same kind of oxidizing agents (O_3 and OH) attacked and destroyed the organic pollutants. The common feature of the proposed sequences is either the initial loss of the acetamide group of PCT with formation of several aromatics from the oxidation of its phenolic moiety or the direct hydroxylation of PCT. The further cleavage of the benzene ring originates aliphatic by-products that evolve to short-linear carboxylic acids, which are finally transformed into CO_2 and H_2O. The acetamide group is oxidized to CO_2 as well, with release of NO_3^- and NH_4^+ ions.

The more complete reaction sequence for the single ozonation of PCT (**1**) was proposed by Andreozzi et al. (2003) and is presented in Fig. SM-10. OH and/or O_3 are the main oxidants in this sequence. The initial hydroxylation of **1** either on its C(4) atom with loss of acetamide yields hydroquinone (**2**) or its C(2) position leads to 2-hydroxy-4-(*N*-acetyl)-aminophenol (**3**). Further hydroxylation or ozonation of **2** and **3** gives 1,2,4-trihydroxybenzene (**4**). The subsequent cleavage of the benzene ring of **2** follows two pathways: (i) the carboxylation of its C (2) and C(3) atoms to produce succinic acid (**18**) via the intermediates **5** and **6**, and (ii) the carboxylation of its C(3) and C(4) positions to form the compound **7** that evolves to a mixture of dicarboxylic acids like maleic (**13**), glyoxylic (**14**), malonic (**15**), oxalacetic (**17**), and oxalic (**19**). Subsequent oxidation of **15** gives ketomalonic acid (**16**) that generates **19** and CO_2. On the other hand, the cleavage of **3** leads to the diacid **15** via the amino derivatives **11** and **12**. The compound **5** evolves to the long carboxylics **8**, **9**, and **20** that produce a mixture of short-linear acids including 2-hydroxy-butanodioic acid (**10**), **13**, **15**, **17**, and **19**. In this path, oxalic acid (**19**) is the ultimate product formed, but it is hardly oxidized to CO_2 by OH and O_3. This explains the small mineralization of PCT by single ozonation.

The use of hybrid catalytic ozonation enhances the PCT mineralization process by increasing the oxidation rate of final carboxylic acids. In this way, it is interesting to note the reaction sequence of Fig. SM-11 proposed by Skoumal et al. (2006) with O_3 activated with Fe^{2+}, Cu^{2+}, and UVA light. It can be observed that the drug **1** is initially transformed into hydroquinone (**2**) and 2-hydroxy-4-(*N*-acetyl)-aminophenol (**3**), i.e., the same primary by-products reported by Andreozzi et al. (2003) (see Fig. SM-10). Acetamide (**4**) is released from the formation of **2**. This aromatic is subsequently oxidized to *p*-benzoquinone (**5**), which along with **3** are degraded in consecutive steps to a mixture of carboxylic acids like glycolic (**7**), tartronic (**8**), maleic acid, (**9**), glyoxylic (**10**), and ketomalonic (**11**). These acids are finally converted into oxalic acid (**12**). On the other hand, the oxidation of **3** and **4** leads to oxamic acid (**6**). While **6** and **11** remain stable in the O_3 system, as stated above, they can be slowly mineralized by the action of generated H_2O_2 and UVA light in the O_3/UVA system. For the O_3/Fe^{2+}/UVA system, Fe^{3+}-oxalate and Fe^{3+}-oxamate complexes are formed and can be destroyed from different oxidative paths: the former ones are photodecarboxylated losing Fe^{2+} upon UVA irradiation, whereas the latter ones are mineralized with OH. When the $O_3/Fe^{2+} + Cu^{2+}$/UVA system is applied, Cu^{2+}-oxalate and Cu^{2+}-oxamate are competitively formed as well, then being rapidly oxidized by OH, enhancing its oxidation power as compared to that of the O_3/Fe^{2+}/UVA system. NO_3^- and NH_4^+ ions are formed when either oxamic acid or its Fe^{3+} and/or Cu^{2+}complexes are oxidized to CO_2.

5. Conclusions and prospects

O_3 is an instable compound that it is easily converted into O_2. As a powerful oxidant, it needs to be continuously produced by an ozonator from air or pure O_2 oxidation to be injected to the treated aqueous matrix. Since the pioneering work of Andreozzi et al. (2003), many authors have studied the fast PCT removal in pure water by single ozonation and in some cases, the $k(O_3)$-value related to the reaction (13) has been determined and compared with the much higher k(OH)-value determined for the reaction (14) by H_2O_2/UV process. Techno-economic studies should be made in the next future to show the treatment with better viability. The single ozonation involves the prevalent oxidation of PCT and its by-products by O_3 due to its higher concentration in the medium, with participation of generated OH. Single ozonation became more efficient as the organic load increased because O_3 can attack a higher quantity of pollutants but reaching a low mineralization. The drug disappeared and was mineralized more rapidly at higher pH due to the faster oxidation of the more reactive phenolate form of PCT under alkaline conditions and a larger production of the oxidant OH. Higher O_3 flow rate accelerated PCT abatement. The attack of oxidants over the organic components of a WWTP effluent inhibits the destruction of PCT and its by-products. The applicability of single ozonation to remove the drug from waste activated sludge and hospital wastewater with a pilot plant with a low energy consumption of 19 MWh y^{-1} has been well-proven. Good percentages of zeolite regeneration with adsorbed PCT using O_3 has been described, but the effect of pH should be studied to confirm if zeolite regeneration can be improved under alkaline conditions giving a more cost-effective process. The *E*-peroxone process is more effective than single ozonation, although techno-economic studied must be made to confirm the best treatment for PCT destruction.

O_3 can oxidize the surface of GAC to largely enhance their catalytic ability to adsorb PCT from contaminated waters. Promising results have been obtained for a MBR under direct ozonation, which allowed total PCT disappearance with 94% TOC reduction during 65%, with 53% alleviation of membrane fouling. It could be checked in WWTPs to enlarge the life of membrane steps.

Hybrid catalytic ozonation has been developed to accelerate the ozonation process of PCT. For metal-based catalysts, the injected O_3 was reduced to the stronger oxidant OH at the catalyst surface where destroys the adsorbed organics. The use of HRS NPs catalyst at pH 7 largely enhanced the degradation and mineralization of PCT as compared to single ozonation. This catalyst seems a good candidate for PCT treatment in waters and wastewaters. Good catalytic performance was also found for cheap and simple materials such as MgO and Cu sheets, but natural zeolite 4A catalyst is not recommended because it favors the oxidation with only O_3. Synthetic materials like Pt–Al_2O_3, SnO_2 NPs, and Fe_3O_4@Ce-MOF were very effective as catalysts due to their ability to produce large quantities of OH from adsorbed O_3. More natural catalysts should be tested for further use in WWTPs to accelerate the ozonation not only of PCT, but also of other drugs.

Photolytic ozonation upon UVC or UVA light generates OH from O_3 activation that strongly enhances the PCT destruction. Systems like O_3/UVA, O_3/1.0 mM Fe^{2+}/UVA, and O_3/1.0 mM Fe^{2+} + 0.25 mM Cu^{2+}/UVA can almost completely mineralize high PCT contents. Photocatalytic ozonation has been checked with Ag-g-C_3N_4, and TiO_2 alone or immobilized onto montomormollite or GO. These solid semiconductors photogenerate e_{CB}^-/h_{VB}^+ pairs upon UVA, UVB, visible light, or sunlight exposition that attack H_2O, O_2, and O_3 to produce surface OH. The PCT degradation and mineralization using TiO_2 was slower in secondary WWTP effluents than in pure water because of the parallel oxidation of their organic pollutants. In contrast, the composites of TiO_2 were high adsorbent materials that can remediate more rapidly secondary WWTP effluents, also favored with visible light. Further research over hybrid photolytic and photocatalytic ozonation should consider more extensively the sunlight irradiation to obtain more cost-effective processes avoiding the high cost of artificial lamps.

Sequential ozonation-adsorption processes with chitosan/bentonite or GAC as adsorbent can be viable for the removal of PCT and other drugs from waters and real wastewaters. Sequential ozonation-NF processes showed better performance than NF-ozonation ones for treating secondary WWTP effluents contaminated with PCT, presenting lower membrane fouling because of the destruction of their organic components by ozonation. On the other hand, several works have shown the overall removal of PCT contained in real WWTP effluents by prebiological treatments. Subsequent ozonation processes were then used for the destruction of other organic pollutants alongside disinfection. Many sequential processes at industrial scale have been reported using WWTPs, ozonation plants, and DWTPs to treat large volumes of real wastewaters, hospital wastewaters, and drinking waters from rivers or lakes, respectively. In these systems, the coupling of pre-ozonation and/or intermediate ozonation has shown an excellent oxidation power to destroy partially or totally PCT and other organic pollutants like personal care products and EDCs.

The by-products formed during PCT destruction in pure water by single and hybrid catalytic ozonation have been identified by HPLC, LC-MS, and/or GC/MS, and several reaction sequences for its mineralization have been proposed. Initial formation of aromatics such as hydroquinone and 2-hydroxy-4-(*N*-acetyl)-aminophenol and their consecutive evolution to ultimate carboxylic acids like oxalic and oxamic have been proposed. These acids are very persistent in single ozonation giving poor mineralization, whereas the large mineralization achieved by photolytic treatments can be justified by their fast destruction by H_2O_2/UVA, the photolysis or OH attack of their Fe^{3+} complexes, and/or the oxidation of their Cu^{2+} complexes by OH.

Author credit statement

Juan M. Peralta-Hernández: Conceptualization, Investigation, Methodology, Formal analysis, Funding acquisition. Roles/Writing - original draft, Writing - review & editing, **Enric Brillas:** Conceptualization, Investigation, Methodology, Formal analysis, Supervision, Roles/Writing - original draft; Writing - review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

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