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REMOVAL OF SELECTED PHARMACEUTICALS FROM SPIKED TAP WATER BY OZONATION

Pharmaceutical residues have been increasingly detected in water sources worldwide, raising concerns about their potential ecological and health impacts. This study investigated the removal of three commonly detected pharmaceuticals (carbamazepine (CBZ), paracetamol (PRC), and caffeine (CAF)) from tap water using a lab-scale ozonation process. Unlike previous studies conducted in synthetic matrices, experiments were performed in real tap water to better represent practical drinking water treatment conditions. The measured initial pharmaceutical concentrations were 123 μg/dm^3 for CBZ, 302 μg/dm^3 for CAF, and 80 μg/dm^3 for PRC, prepared from commercial tablet formulations. Ozone doses ranged from 0.093 to 3.6 mg/dm^3 with contact times of 30 min for removal studies and 14 min for kinetic investigations. The results showed that PRC was rapidly degraded with 67% removal achieved at the lowest ozone dose (0.093 mg/dm^3), while CBZ exhibited greater resistance to oxidation. Complete removal of all three pharmaceuticals was achieved at ozone doses ≥ 1.8 mg/dm^3. Kinetic analysis revealed that CAF degradation followed first-order kinetics, whereas CBZ and PRC degradation followed second-order kinetics, providing mechanistic insights into their differential reactivity with ozone. The findings demonstrate that ozonation is an effective method for removing pharmaceutical micropollutants from drinking water under realistic treatment conditions.

1. INTRODUCTION

Water scarcity and water quality have become issues of major concern in the last few decades of prevailing modern lifestyle. Developments in chemical analysis technology, such as instrumentation and new methods, have shown that water contains many new contaminants such as pharmaceuticals and personal care products (PPCPs) that were previously undetectable or unknown. The modern human lifestyle, especially in developed

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countries, includes the daily use of synthetic compounds such as PPCPs, hormones, pesticides, and other environmentally persistent chemicals. Consequently, the residues of these compounds themselves become micro and emerging pollutants in water and wastewater [1]. Many of these micropollutants cannot be entirely removed by conventional drinking water treatment processes, and consequently, they can be found in finished water [2]. Pharmaceuticals are widely used chemical compounds designed to prevent, diagnosis, or treat various diseases. Due to their extensive and continuous use, residues of pharmaceutical active ingredients have been increasingly detected in water bodies, including surface water, groundwater, and even drinking water sources. Their occurrence, even at trace levels, has raised concerns regarding potential long-term effects on aquatic ecosystems and human health. Even if some compounds (e.g., ibuprofen, paracetamol, estradiol, acetyl salicylicacid) are known to be biodegradable, others such as diclofenac, parabens, carbamazepine, cromiton, diazepam are not removed biologically and their concentration is maintained after treatment [3]. Although they are existing at very low concentration levels such as ng/dm^3 or $\mu g/dm^3$, many of them elevated substantial eco-toxicological concerns, either as single compounds or also when present as complex by-products and parent compounds [4]. International Water Association (IWA) and World Health Organization (WHO) suggest that to supply safe drinking water to whole populations preventive risk management must be carried out [5]. So, the removal performance of such chemicals that can be a risk for drinking and wastewater treatment plants should be improved in order to prevent contamination of surface and ground waters which are direct sources of drinking water, as well as to obtain safe drinking water directly.

It is well known that PPCPs and other trace organics are generally removed by the advanced chemical oxidation in which hydroxyl radicals ($OH^{\bullet}$) are generated as the main oxidant species [6]. Advanced oxidation processes (AOPs) are a set of chemical treatment procedures that are able to remove recalcitrant organic materials in wastewater by oxidation reactions with a powerful, non-selective $OH^{\bullet}$ radical which oxidize recalcitrant organic pollutants resistant to conventional approaches and can also enhance the biodegradability of wastewater [7]. AOP represents relatively new methods, and their mechanism is based on the generation of free hydroxyl radicals. The generation of these active free radicals occurs in the presence of ozone (O_3), hydrogen peroxide (H_2O_2), UV radiation (photolysis or photocatalysis), and ultrasonic exposure [8]. Previous studies have shown that ozonation is the most suitable method for effectively degrading and oxidizing pharmaceutical compounds in wastewater [9] and increasingly used to remove micropollutants from wastewater [10]. However, there are studies in the literature examining the removal of pharmaceutical residues by different processes.

Ozone processes attract attention as they imply the direct reaction of ozone and also the action of the produced $OH^{\bullet}$. In this way, a lot of studies in the literature notice that pharmaceutical substances can be immediately removed through the direct reaction of ozone and, when not feasible, through the action of $OH^{\bullet}$ [11]. In ozonation, both ozone

and the formed $OH^{\bullet}$ radicals contribute to the removal of micropollutants [12]. The formation of $OH^{\bullet}$ and ozone radicals in water and thus their availability for reactions is dependent on the pH value [13].

Ozone is a commonly used compound in treatment processes because of its ability to oxidize and disinfect. Furthermore, it is able to remove and/or decrease taste and odor, and can lead to hydroxyl radicals that are less specific and react quickly with a wide range of molecules and/or compounds throughout water treatment operations. Due to the electrophilic character of the molecule, it particularly reacts with high electronic density sites of the molecules, such as aromatics and unsaturated bonds. However, $OH^{\bullet}$ radicals are insufficient to oxidize specific organic functional groups. Moreover, $OH^{\bullet}$ radicals can be consumed due to the compounds that may be available in the water, such as natural organic matter and HCO_3^-, CO_3^{2-}, NO_3^-, NO_2^-, Cl^-, and Br^- [14].

Ozone could interact with microorganic pollutants through two main mechanisms:

- In the selective mechanism referred to as ozonolysis, ozone reacts directly with specific functional groups, mostly double bonds and aromatic rings of the organic compounds, which can also be found in the structure of pharmaceuticals.
- Ozone oxidizes indirectly, non-selectively, and rapidly micropollutants and intermediate products through $OH^{\bullet}$ radicals generated from the decomposition of ozone in water [15]. Water treatment plants need to utilize optimum ozone doses that accomplish adequate pharmaceutical removal while maintaining low operating costs because ozone production is an energy-intensive and so expensive process. Organic materials such as humic matter and microorganisms in the matrix in the tap water are also competing for ozone depletion with pharmaceuticals [1]. Because the content and amount of organic substances in water vary according to the treatment works applied to water and the source of water, it is quite difficult and variable to know the required ozone dose and its efficiency, and therefore, the cost. Ozone is a highly effective agent in the removal of structurally diverse pharmaceuticals encountered in increasing amounts in the aqueous environment [16]. The removal of such micro and specific pollutants by ozonation is more reasonable in treated waters. Therefore, the objective of this study was to determine the removal potential of selected pharmaceuticals, commonly found in tap water and representative compounds of different therapeutic classes, in real tap water by using a lab-scale ozonation process.

Three pharmaceutical compounds: caffeine (CAF), a xanthine alkaloid ascertained in chocolate, cocoa, energy drinks, tea, and other foods, carbamazepine (CBZ), an anticonvulsant and specific analgesic for trigeminal neuralgia, and paracetamol (PRC), also named as acetaminophen, a well-known and commonly used antipyretic and analgesic pharmaceutical and reduces headache, minor aches, and fever, have been selected as model compounds of diverse therapeutic classes. CBZ, PRC, and CAF are among the most frequently detected pharmaceutical residues in aquatic environments. Previous monitoring studies have reported the occurrence of the selected pharmaceuticals in drinking water sources. CBZ has been frequently detected in the range of 10–500 ng/dm^3, CAF in

the range of 50–250 ng/dm^3, and PRC usually below 100 ng/dm^3 due to its rapid degradation [2, 17, 18]. These findings confirm the environmental relevance of the selected compounds in tap water supplies. Several treatment technologies have been investigated for the removal of pharmaceuticals from water, including adsorption, membrane filtration, and advanced oxidation processes (AOPs). Among these, ozonation has attracted considerable attention due to its strong oxidizing power, ability to react with a wide range of organic compounds, and simultaneous disinfection capability. However, the efficiency of ozonation can vary depending on the compound structure, operational conditions, and water quality. Therefore, the objective of this study was to evaluate the removal efficiency and kinetics of CBZ, PRC, and CAF from spiked tap water using a lab-scale ozonation process. In addition, the practical implications of ozonation for drinking water treatment are discussed, with considerations regarding feasibility, operational challenges, and cost.

2. MATERIALS AND METHODS

Chemicals and medium. Carbamazepine (CBZ, Dr. Ehrenstorfer, purity ≥ 99.5%), Caffeine (CAF, Dr. Ehrenstorfer, purity ≥ 99%, paracetamol (PRC, Dr. Ehrenstorfer, purity ≥ 99.5%), and 1,7-dimethylxanthine (LGC GmbH, purity ≥ 99%) used in calibration have a high degree of purity, and other chemicals were analytical grades and HPLC grades. Ultrapure water (Merck Millipore Elix Advantage 5) was used for the preparation of the solutions in the analysis. Typical characteristics of the studied chemicals are displayed in Table 1.

Table 1

Some physicochemical properties of studied compounds

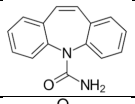
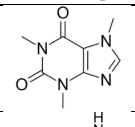
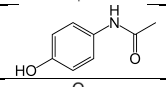
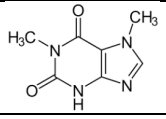
Name	Formula		Molecular weight [g/mol]	Water solubility a 20 °C [mg/dm^3]	Partition coefficient log $K_{o/w}$	pK_a
	Structural	Molecular				
Carbamazepine		$C_{15}H_{12}N_2O$	236.27	18	2.45	13.9
Caffeine		$C_8H_{10}N_4O_2$	194.19	21 600	–0.07	10.4
Paracetamol		$CH_3CONHC_6H_4OH$	151.16	14 000	0.46	9.38
1,7- -dimethylxanthine		$C_7H_8N_4O_2$	180.16	1000	–0.39	10.76

Table 2

Preparation of stock solutions of active pharmaceutical ingredients

Active ingredient	Tablet content [mg]	Weight [g]	Stock concentration [mg/dm^3]	Amount of drug in 1 dm^3 of tap water [g]
Carbamazepine	200	0.2799	100	0.1400
Paracetamol	500	0.5904	100	0.1181
Caffeine	60	0.4536	100	0.7560

The selected and investigated pharmaceuticals, whose active ingredients are carbamazepine, paracetamol, and caffeine, are available and often sold in the market. Trade names are Ergafine, Parol, and Tegretol, respectively, for CAF, PRC, and CBZ. 1.7-dimethylxanthine, one of the by-products of caffeine, was also monitored. The average weight of each tablet was determined. The tablets were finely pulverized, and stock solutions were prepared according to the active ingredient amounts declared in the product leaflet. Stock solutions were obtained by dissolving them in 0.5/0.5 (v/v) methanol/ultra-purified water by calculation based on tablet weight and active substance concentrations in each tablet. In the studies, drug active ingredients at desired concentrations were added to the tap water by diluting the prepared stock solutions. The weights and active ingredient contents of the tablets are given in Table 2. Since the solubility of the active pharmaceutical ingredients is different, input samples were also taken in each evaluation, and the removal efficiency evaluations were made based on these data.

Table 3

Characteristics of tap water used in the study

Parameters	Average±standard deviation
pH	7.62±0.08
EC, µS/cm	735.20±26.16
Hardness, mg/dm^3 $CaCO_3$	259.00±8.49
Alkalinity, mg/dm^3 $CaCO_3$	211.40±7.40
Turbidity, NTU	0.8±1.3
TOC	5.29 ±3.46
TN	0.95±0.41
NH_4^+-N	≤ 0.05
SO_4^{2-}	36.46±3.45
UV absorbance (254 nm)	0.024±0.001

Tap water in Aksaray, Turkey, was used in the studies. Commercially purchased drug active ingredients were added to the water tapped in the laboratory and dissolved. The prepared stock solutions were diluted with tap water to achieve the desired concentrations,

and the resulting samples were analyzed to confirm their theoretical values. The analyses were carried out at different times to determine other important components of tap water used in the studies, and the results are given in Table 3. The experiments were repeated five times with an initial pharmaceutical concentration of approximately 100 μg/dm^3 in spiked tap water, applying a reaction time of 30 min for removal studies and 14 min for kinetic investigations.

Analytical methods. Pharmaceuticals and intermediate analyses were performed using a Thermo Electron Corporation Accela UPLC coupled with a TSQ Quantum Access Max triple quadrupole mass spectrometer with electrospray ionization (ESI). The mobile phase consisted of 0.1% of formic acid (A) and methanol (B) with a gradient elution program (0–1 min, 90% A–10% B; 14–18 min, 1% A–9% B; 19–22 min, 90% A–10% B). Column temperature was maintained at 30 °C throughout the analysis. The injection volume was 20 μL. Mobile phases were filtered and degassed to prevent air bubbles before being analyzed by the liquid chromatography-tandem mass spectrometry (LC-MS/MS). All fragments were monitored in a positive mode of electrospray ionization (ESI) mass spectrometer. The sample flow rate was 0.4 μL/min in BDS HYPERSIL C18 (100 × 4.6 mm × 5 μm) column. After that, optimization studies of LC-MS/MS that aimed to determine the optimal working values and to introduce the pharmaceuticals to the instrument were carried out for the selected pharmaceuticals.

Calibration curves ranged from 1 to 100 μg/dm^3 for at least five points for the selected pharmaceutical. The limits of detection (LOD) and quantification (LOQ) for target compounds were obtained as 3 and 10, respectively, from signal/noise ratios (S/N). The validation values of the methods are given in Table 4.

Table 4

Validation values

Pharmaceutical	R^2	LOD [μg/dm^3]	LOQ [μg/dm^3]	*RT* [min]
Carbamazepine	0.998	0.003	0.009	13.35
Caffeine	0.994	0.714	2.379	9.52
Paracetamol	0.995	0.461	1.536	7.20
1,7-dimethylxanthine	0.999	0.074	0.246	8.29

For each pharmaceutical, initial and final concentrations (μg/dm^3) were determined by LC–MS/MS at $t = 0$ and after ozonation under the specified conditions. Paraxanthine (1,7-dimethylxanthine) was included in the LC-MS/MS MRM method and analyzed only in post-ozonation caffeine samples. Stock solutions were prepared from commercially available tablets based on the active ingredient amounts declared in the product leaflet. Although the target initial concentration was 100 μg/dm^3, the measured initial concentra-

tions were 123 µg/dm^3 for CBZ, 302 µg/dm^3 for CAF, and 80 µg/dm^3 for PRC; accordingly, removals were calculated relative to these measured values. Therefore, all removals were calculated with respect to the analytically measured initial concentrations. Each experimental condition was performed with n = 3 independent replicates, and results are reported as mean ± SD.

The electrical conductivity (EC) (WTW LF330/SET), pH value (WTW pH330i/SET), turbidity (WTW-TURB 355 IR), sulfate analyses (DIONEX ICS-1000), total organic carbon (TOC), total nitrogen (TN) (Shimadzu TOC-VCPN/TNM-1), and $UV2_{54}$ absorbance (SPECTRO UV-Vis RS) were performed by equipment and their available methods. The alkalinity and total hardness analyses were carried out by standard methods [19].

Ozonation process. It is aimed at determining the best ozone concentration for the removal of pharmaceutical residues by ozonation. The average pH value of tap water, which is about 7–7.5, was used in all ozonation studies without performing any adjustment [18, 20]. The ozone generator allows adjustment of the ozone output as a percentage, and these percentage settings were used to obtain different ozone concentrations. The ozonation process was performed separately for each pharmaceutical. The liquid phase containing the pharmaceuticals was maintained under batch conditions, whereas the ozone gas stream was continuously introduced into the reactor through a bottom diffuser (Fig. 1).

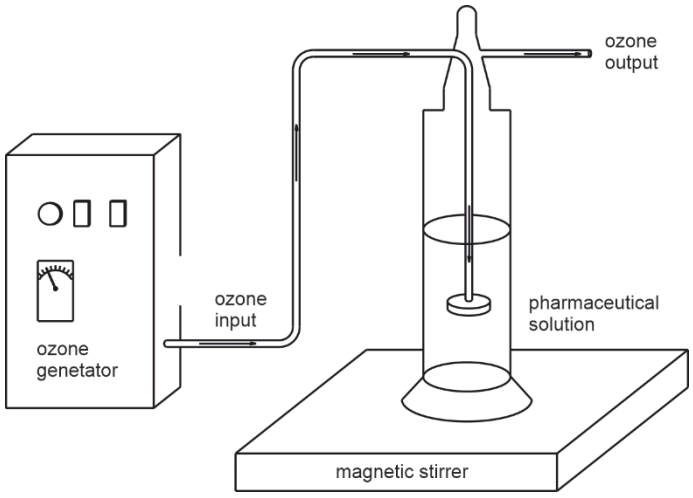


Fig. 1. Schematic representation of the ozonation process

The ozone generator was operated at air flow rates of 50 dm^3/h for all pharmaceuticals. Different ozone concentrations were obtained by adjusting the production capacity of the ozone generator (OZ-15G model 200W-220V-50Hz), ranging from 20 to 100%. Stable ozone concentrations given into the liquid for each production capacity were then

calculated by the iodometric method [21]. As a result, the initial ozone concentrations produced by the ozone generator with 5 different setting levels were found to be between 0.093 and 4.30 mg/dm^3 by the iodometric method in the water.

Kinetic studies. To determine the removal kinetics and reaction rate constants of the selected pharmaceuticals, batch experiments were performed with constant initial pharmaceutical concentrations in spiked tap water samples over a 14-minute test period. Each pharmaceutical was tested at its respective optimum ozone dose determined from the removal efficiency experiments (in mg/dm^3): 0.463 for CBZ, 3.2 for CAF, and 0.463 for PRC. Samples (10 cm^3) were collected at regular time intervals (0, 1, 2, 3, 4, 5, 6, 8, and 14 min) and immediately quenched with ascorbic acid (5 g/dm^3) to stop the oxidation reaction, as this method has been reported to be suitable for suppressing oxidant residuals [22, 23]. Data obtained from the batch tests were plotted with the *y*-axis representing *C*, ln*C*, and 1/*C* versus the *x*-axis representing time (*t*) to determine the kinetic model and reaction rate constants for zero-order, first-order, and second-order kinetics, respectively.

3. RESULTS AND DISCUSSIONS

3.1. REMOVAL OF PHARMACEUTICALS WITH OZONATION PROCESS

For each pharmaceutical, removal was evaluated from LC–MS/MS measurements at the beginning and at the end of ozonation, and was reported with respect to the measured initial concentrations.

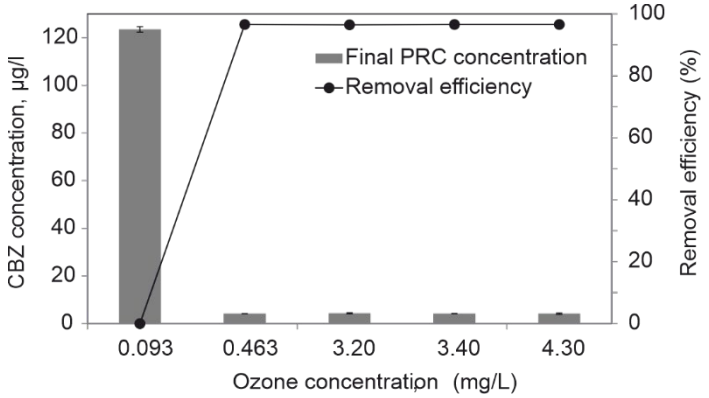


Fig. 2. Effect of ozone concentration (0.093–4.30 mg/dm^3) on CBZ removal in spiked tap water (initial concentration 123 µg/dm^3, pH 7–7.5, reaction time 30 min)

Figure 2 shows the removal of CBZ in the sample as a function of ozone concentration up to 4.30 mg/dm^3. The removal efficiency of CBZ increased with increasing ozone doses

applied. For example, the removal efficiency of CBZ was about zero % at the dose of 0.093 mg/dm^3, increased to about 100 % at the dose of 0.463 mg/dm^3. As a result, ozone levels must be higher than 0.463 mg/dm^3 for effective removal under these experimental conditions.

The second part of the work on the removal of ozone was done with caffeine. Caffeine is a highly used stimulant found in many pharmaceutical products as well as stimulant and pleasing beverages (coffee, tea, caffeinated beverages). It is a native alkaloid cultured by many plant species [17]. Caffeine is significantly metabolized; approximately 5% is excreted unchanged in urine after consumption. Paraxanthine (1,7-dimethylxanthine), is the main metabolite of caffeine, accounting for 80% of the total caffeine excretion in humans [24]. According to the results shown in Fig. 3, caffeine was eliminated at ozone concentrations of 3.2 mg/dm^3 and above. Partial caffeine removal was also achieved at lower ozone concentrations of 0.093 and 0.463 mg/dm^3.

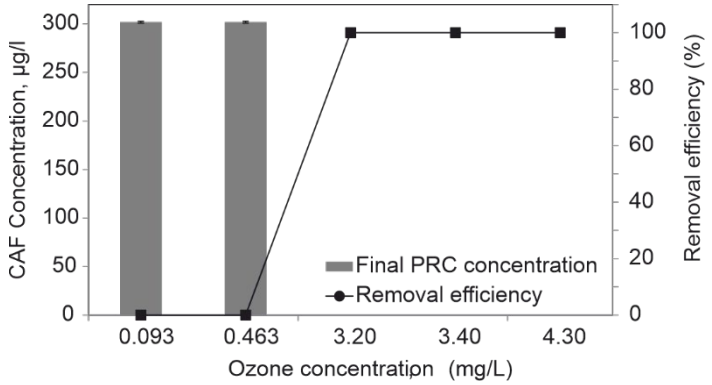


Fig. 3. Effect of ozone concentration (0.093–4.30 mg/dm^3) on CAF removal in spiked tap water (initial concentration 302 µg/dm^3, pH 7–7.5, reaction time 30 min)

In the caffeine experiments, paraxanthine (1,7-dimethylxanthine) was monitored after ozonation as a potential transformation product; however, it was not detected in any post-treatment sample (below the method LOD/LOQ), in contrast to Rodríguez et al. [11], who reported paraxanthine alongside caffeine in environmental waters. Rosal et al. [25] detected high concentrations of paraxanthine and caffeine in samples taken from wastewater treatment plants in Madrid. Although these compounds were refractory to biological degradation and could not be completely removed by conventional biological treatment, their removal was successfully achieved by ozonation using doses up to 3.6 mg O_3/dm^3. In particular, the pollution of natural water sources due to discharges from municipal wastewater treatment plants (MWTPs) is a critical concern because these waters serve as sources for drinking water supply systems. Researchers have detected numerous pharmaceuticals, such as CBZ and CAF, in tap water obtained from city water networks. These

drinking water treatment plants are supplied by surface waters that receive effluent from municipal wastewater treatment plants (MWTPs) [2, 14].

Finally, the elimination of the PRC by the ozonation process has been studied, and it has been observed that the removal efficiency increases with increasing concentrations, as in the others. However, unlike the others, 67% removal was obtained even at the lowest ozone concentration (Fig. 4). In other ozone concentrations, removal efficiencies of about 100% were obtained.

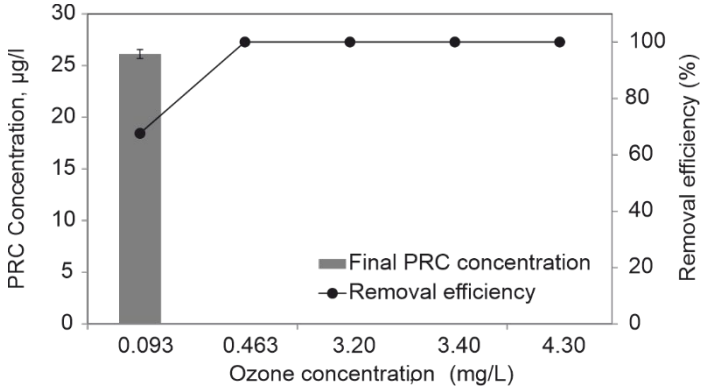


Fig. 4. Effect of ozone concentration (0.093–4.30 mg/dm^3) on PRC removal in spiked tap water (initial concentration 81 µg/dm^3, pH 7–7.5, reaction time 30 min)

The varying removal efficiencies of CBZ, CAF, and PRC are attributed to differences in their molecular structures and reactivity toward ozone. PRC contains electron-rich functional groups (phenolic –OH and amide groups) that are highly susceptible to ozone attack, resulting in rapid degradation even at low ozone doses (67% removal at 0.093 mg/dm^3). CAF, with its purine structure containing multiple nitrogen atoms, also shows good reactivity with ozone. In contrast, CBZ, with its tricyclic aromatic structure and lower electron density, exhibits higher resistance to ozonation, requiring higher ozone doses for effective removal. These findings are consistent with previous studies [11, 14, 22] showing that compounds with electron-donating groups are more readily oxidized by ozone.

In the treatment of drinking water, pathogenic bacteria and all viruses could be killed by providing an ozone concentration of 0.4 mg/dm^3 at 4 min of contact time [26]. In drinking water treatment, typical ozone doses for disinfection range from 0.4 to 2.0 mg/dm^3 with contact times of 4–10 min [12, 26]. These conventional doses are sufficient for microbial inactivation but insufficient for complete removal of recalcitrant pharmaceutical micropollutants, which require higher ozone doses (up to 3.6 mg/dm^3) and longer contact times (30 min), as demonstrated in this study. However, the ozone concentrations typically applied for disinfection can contribute to partial pharmaceutical removal, particularly for more reactive compounds such as PRC.

3.2. REMOVAL KINETICS OF PHARMACEUTICALS WITH OZONATION PROCESS

The kinetics of pharmaceutical removal by ozonation were investigated to understand the reaction mechanisms and to determine the reaction rate constants for each compound. As described in Section 2, kinetic experiments were conducted at the optimum ozone doses determined from the removal efficiency studies: 0.463 mg/dm^3 for CBZ, 3.2 mg/dm^3 for CAF, and 0.463 mg/dm^3 for PRC. Samples were collected at regular time intervals and analysed to evaluate the fit of zero-order, first-order, and second-order kinetic models.

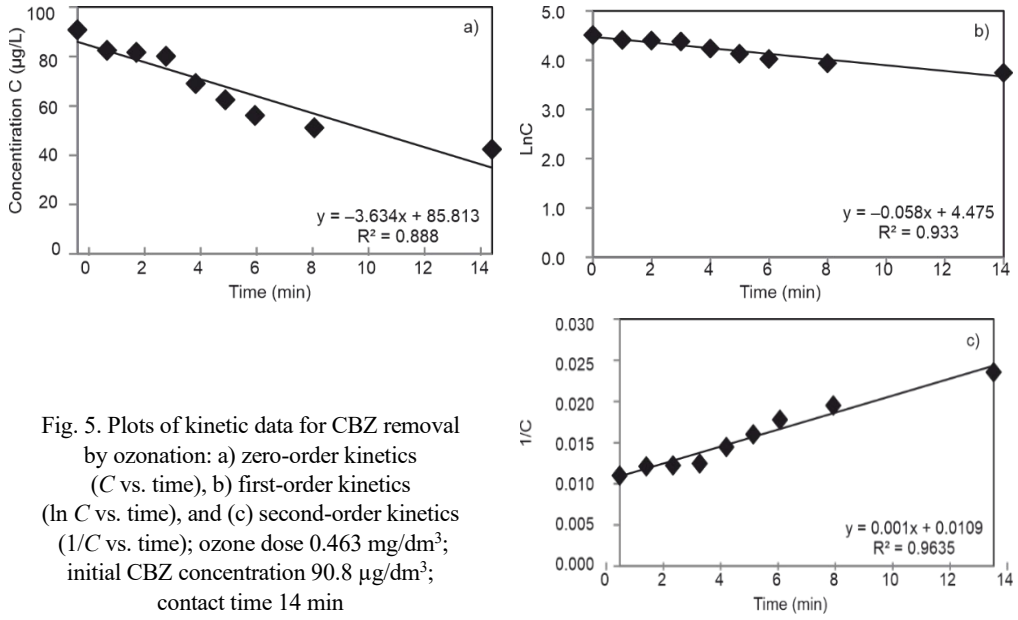


Fig. 5. Plots of kinetic data for CBZ removal by ozonation: a) zero-order kinetics (*C* vs. time), b) first-order kinetics (ln *C* vs. time), and (c) second-order kinetics (1/*C* vs. time); ozone dose 0.463 mg/dm^3; initial CBZ concentration 90.8 µg/dm^3; contact time 14 min

The kinetic plots for all three pharmaceuticals exhibited similar patterns, with varying degrees of linearity depending on the kinetic model applied. As a representative example, the kinetic plots for CBZ are presented in Fig. 5. The kinetic parameters (reaction rate constants and correlation coefficients) for all three pharmaceuticals are summarized in Table 5.

As a result of data, the most suitable kinetic model and kinetic constants were obtained from the model having the highest regression coefficients in the models of applied reaction kinetic. The strong linear correlations observed in the kinetic plots (Fig. 5) confirmed that pharmaceutical removal followed the respective kinetic models under the experimental conditions. In the literature, ozone oxidation of micropollutants typically follows second-order kinetics, as the reaction rate depends on both ozone and target pollutant concentrations [22]. In this study, CBZ and PRC removal followed second-order kinetics, whereas CAF removal followed first-order kinetics (Table 5).

Table 5

Removal rate constants for selected pharmaceuticals during ozonation tests

Pharmaceuticals	Order	Constants	
		Symbol	Value
CBZ	0	k_0, μg/(dm^3·min)	3.63
		R^2	0.888
	1	k_1, 1/min	0.058
		R^2	0.933
	2	k^2, (dm^3·min)/μg	0.001
		R^2	0.964
CAF	0	k_0, μg/(dm^3·min)	34.2
		R^2	0.799
	1	k_1, 1/min	1.12
		R^2	0.955
	2	k^2, (dm^3·min)/μg	1.10
		R^2	0.404
PRC	0	k_0, μg/(dm^3·min)	2.13
		R^2	0.40
	1	k_1, 1/min	0.124
		R^2	0.567
	2	k^2, (dm^3·min)/μg	0.009
		R^2	0.723

The first-order behavior of CAF may be attributed to its high reactivity with ozone, resulting in pseudo-first-order kinetics under conditions of excess ozone. For the same kinetic model, it may be said that PRC with a greater kinetic constant (0.086 dm^3·min/μg) is removed faster than CBZ with markedly lower kinetic constant (0.001 dm^3 min/μg) under these conditions. In the case of PRC, the correlation coefficients obtained for zero-, first-, and second-order kinetic models were relatively low compared with CBZ and CAF. This is mainly due to the very rapid and almost complete removal of PRC even at low ozone doses, which causes steep concentration decreases in the early stages and weakens the linear fit of the data to conventional kinetic models. Similar observations have been reported in the literature [18, 20], where paracetamol was found to degrade rapidly under ozonation, leading to deviations from ideal kinetic behavior. The results obtained in this study are consistent with previous findings reported in the literature. CBZ has been described as relatively persistent but removable by ozonation at sufficient doses [1, 22]. CAF showed rapid degradation under ozonation, in agreement with the results of Buerge et. al. [17] and Rosal et. al. [25]. PRC exhibited almost complete removal even at low ozone concentrations, which was consistent with reports by Benitez et. al. [20] and Nakada et. al. [18].

The results obtained in this study are consistent with previous findings reported in the literature, confirming the general reactivity trends of these pharmaceuticals toward ozone. CBZ has been described as relatively persistent but removable by ozonation at sufficient

doses [1, 22]. CAF showed rapid degradation [17, 25], and PRC exhibited high susceptibility to ozone oxidation [18, 20]. However, the present study provides several novel contributions that distinguish it from previous research. First, unlike most studies that used synthetic matrices or wastewater effluents, this research was conducted in real tap water, representing actual drinking water conditions with background organic matter (TOC = 5.29±3.46 mg/dm^3) and competing ions that more realistically reflect practical treatment scenarios. Second, the simultaneous evaluation of three pharmaceuticals with different structural characteristics (CBZ, CAF, and PRC) under identical experimental conditions allowed for direct comparison of their ozonation behavior and kinetics, which has rarely been reported in tap water matrices. Third, the kinetic analysis revealed distinct reaction orders for each compound (second-order for CBZ and PRC, first-order for CAF), providing mechanistic insights into their differential reactivity with ozone. Finally, this study evaluated ozone doses that are practically applicable in drinking water treatment plants (0.093–3.6 mg/dm^3), bridging the gap between laboratory research and real-world implementation. These contributed to the optimization of ozonation processes for pharmaceutical removal in drinking water treatment systems.

From a practical perspective, the findings of this study indicate that ozonation could be integrated into existing drinking water treatment plants as an advanced oxidation step. Since ozone is already applied in many utilities for disinfection and odor control, upgrading its use to also target pharmaceutical micropollutants would not necessarily require major structural modifications. However, challenges remain in terms of process optimization, operational costs, and by-product control. Ozone production is energy-intensive, and the required doses for pharmaceutical removal may increase operational expenditures [1]. Additionally, the formation of oxidation by-products must be carefully managed through appropriate downstream treatment steps [22]. Despite these challenges, the results of the present study support the feasibility of applying ozonation as a cost-effective and multifunctional process for both disinfection and micropollutant control in real water treatment scenarios.

4. CONCLUSIONS

In this study, the removal and kinetics of carbamazepine (CBZ), caffeine (CAF), and paracetamol (PRC) by ozonation were investigated in spiked tap water. Overall, ozonation removed overall CAF and PRC within 30 min at 3.20 mg/dm^3 and 0.46 mg/dm^3 of ozone concentration, respectively, but CBZ at 96% at 0.46 mg/dm^3 ozone concentration. All data achieved from this study display that ozone treatment allowed an effective removal of pharmaceuticals in tap water, obtaining greater removal with the higher dose of ozone. In order to evaluate the potential for removing selected pharmaceuticals by ozonation, a kinetic study is performed to estimate to what extent pharmaceuticals will be degraded after

a specified duration of treatment. The kinetic analysis revealed that CBZ and PRC removal followed second-order kinetics, while CAF removal was best described by first-order kinetics. In conclusion, this study demonstrated that ozonation is effective for the removal of selected pharmaceuticals from tap water. PRC was degraded rapidly, achieving nearly complete removal at low ozone doses, while CBZ showed higher resistance but was still significantly reduced. These findings are consistent with previous literature, confirming the suitability of ozonation for the treatment of pharmaceutical micropollutants.

Typical ozone concentrations and contact time in drinking water disinfection seem to be insufficient for the complete removal of micropollutants such as these pharmaceuticals. Therefore, the ozonation process should be optimized by arranging contact time and ozone concentration for all problematic micropollutants. In addition, ozone activity can be increased by the peroxeno process (O_3/H_2O_2), the combination of ozone with UV irradiation process (O_3/UV), and catalytic ozonation, which is the addition of catalysts to the ozonation process, mainly TiO_2, which allows rapid generation of OH radicals via ozonation (such as TiO_2/O_3). In the future, different advanced oxidation methods that can remove most of the micropollutants can be tried, and studies can be carried out to determine the most suitable press as economical and applicable.

From a practical perspective, ozonation can be integrated into existing drinking water treatment systems as an advanced oxidation step. Since ozone is already used in many facilities for disinfection and odor control, extending its application to pharmaceutical removal may be feasible. Nevertheless, challenges remain regarding optimization, energy consumption, operational costs, and the control of oxidation by-products. Despite these challenges, ozonation shows strong potential as a cost-effective and multifunctional process for ensuring safe drinking water.

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