Sonochemical advanced oxidation process for the degradation of furosemide in water: Effects of sonication's conditions and scavengers

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A R T I C L E   I N F O

A B S T R A C T

The intensive consumption of pharmaceuticals and drugs in the last decades has led to their increased concentrations in wastewaters from industrial sources. The present paper deals, for the first time, with the sonochemical degradation and mineralization of furosemide (FSM) in water. FSM is a potent loop diuretic used to treat fluid build-up due to heart failure, liver scarring, or kidney disease. The influence of several operating parameters such as acoustic intensity, ultrasonic frequency, initial FSM concentration, solution's pH, nature of the dissolved gas (Ar, air and N_2) and radical scavengers (2-propanol and *tert*-butanol) on the oxidation of FSM was assessed. The obtained results showed that the degradation rate of the drug increased significantly with the increase of the acoustic intensity in the range of 0.83 to 4.3 W cm^{-2} and decreased with the augmentation of the frequency in the range of 585–1140 kHz. It was also found that the initial rate of the sonolytic degradation of FSM increased with the increase of its initial concentration (2, 5, 10, 15 and 20 mg/L). The most significant degradation was achieved in acidic conditions at pH 2, while in terms of saturating gas, the rate of FSM degradation decreased in the order of Ar > air > N_2. The FSM degradation experiments with radical scavengers showed that the diuretic molecule degraded mainly at the interfacial region of the bubble by hydroxyl radical attack. Additionally, in terms of acoustic conditions, the sono-degradation of 30.24 µmol L^{-1} of FSM solution demonstrate an optimal performance at 585 kHz and 4.3 W/cm^2, the results indicated that even if the ultrasonic action eliminated the total concentration of FSM within 60 min, a low degree of mineralization was obtained due to the by-products formed during the sono-oxidation process. The ultrasonic process transforms FSM into biodegradable and environmentally friendly organic by-products that could be treated in a subsequent biological treatment. Besides, the efficiency of the sonolytic degradation of FSM in real environmental matrices such as natural mineral water and seawater was demonstrated. Consequently, the sonochemical advanced oxidation process represent a very interesting technique for the treatment of water contaminated with FSM.

1. Introduction

The contamination of the global water cycle by persistent organic contaminants remains one of the major challenges of the 21st century. These anthropogenic compounds, which have only recently been identified as significant persistent water pollutants [1], are commonly found in the effluents of sewage treatment plants, rivers, ground water sources as well as in municipal drinking water distribution mediums [2,3], which were found to be containing a large array of compounds [4,5]. These chemicals, also known as emergent micropollutants, can cause serious human health imbalances that can affect the endocrine system of humans [6] with the possibility of inducing cancerous tumors in living organisms [7]. In addition, due to their inherent and harmful malignant propensities, these toxins can sometimes cause irreversible damage to aquatic life as well as to the environment at all levels of the natural flora and fauna chain [8,9]. The majority of these organic substances are only partially removed by conventional wastewater treatment plants and are known to resist to primary and secondary wastewater treatments [10].

Furosemide (FSM) is a sulfamoylanthranilic acid derivative also known as a frusemide, a drug which has widely been used as a diuretic [11] employed to adjust the volume and/or composition of body fluids in a variety of situations, including hypertension, heart failure, renal failure, nephritic syndrome, and cirrhosis [12]. FSM is one of the forty compounds having the highest risk when containing a predicted

environmental concentration greater than 100 ng·L^{-1} [13]. It is often found as a persistent toxic waste and one of the most widely available poorly eliminated drugs, either unmodified or as glucuronide conjugate [14,15].

Thus, to remedy this major problem, several attempts have been made to clean up wastewater by removing all traces of FSM residues. The generally adopted methods consist of physical, chemical and biological techniques. However, these conventional processes used in wastewater treatment plants are not fully adapted to the degradation of recalcitrant pollutants [16,17]. These methods usually shift and displace the pollutants rather than remove them. Furthermore, these methods often involve a combination of costly equipment and chemicals that are likely to create secondary problems such as disposals [18]. In order to overcome the aforementioned ecological threats, some remarkable research efforts have been made to boost the efficiency of remediation techniques and developed more efficient technologies [19].

In this context, much attention has recently been focused on the so-called advanced oxidation processes (AOPs), which are generally proven to be environmentally friendly. The AOPs are of particular interest as they were shown to have a high removal efficiency and a capability to reach complete mineralization of the treated effluents [20]. AOPs are based on the generation of hydroxyl radicals HO$^{\bullet}$, the ultimate oxidant for the remediation of organic contaminants in wastewater. Due to its very high oxidation power (E° = 2.73 V/SHE) [21], hydroxyl radicals can efficiently destroy toxic, recalcitrant and low biodegradable compounds. Among the different AOPs, the sonolytic pathway has received considerable attention [22]. It is based on the mechanical effect of cavitational collapse in conjunction with the chemical effect of sonication known as sonochemistry [23]. Under the influence of an acoustic field, bubbles are generated from existing gas nuclei in liquids [24]. These bubbles oscillate in a nonlinear manner, and under specific experimental conditions, they violently collapse to generate high temperatures and pressures [25]. The extremely high temperatures and pressures formed in collapsing cavitation bubbles in aqueous solutions lead to the thermal dissociation of water vapor into reactive hydroxyl radicals and others oxidants [26].
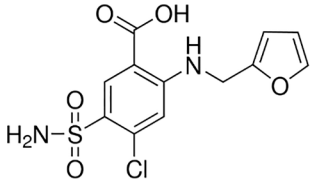
To the best of our knowledge, no work has been reported in the literature on the ultrasonic removal of FSM from polluted water. Consequently, the present study is dedicated to the sonochemical degradation of furosemide in water and aims to evaluate the effects of several operating parameters on the sono-degradation process. The effects of the initial FSM concentration, acoustic intensity, ultrasonic frequency, nature of the dissolved gas and solution's pH on the degradation of the drug molecules were carried out using multifrequency transducer operating at various electrical powers. Specific scavengers were also employed to identify some mechanistic aspects in the process of the sono-degradation of furosemide. Additionally, the degradation of FSM by sonochemical treatment in real water matrices such as natural mineral water and seawater was investigated.

2. Material and methods

2.1. Reagents

All the chemicals used in this investigation were of the highest available purity. Furosemide was supplied by Sigma-Aldrich (containing more than 98% of pure compound). It was used for the preparation of the treated solutions. The structural formula and main physiochemical properties of FSM are shown in Table 1. Acetonitrile was supplied by Acros Organics (HPLC-UV quality). Ultrapure water was used throughout the study and as a component of the mobile phase in the analysis by high performance liquid chromatography (HPLC). Potassium iodide and *tert*-butanol (Riedel-de Haën) and sulfuric acid, sodium hydroxide, ammonium heptamolybdate tetrahydrate and propanol-2 (Sigma-Aldrich), all of analytical grade, were used in the present work.

**Table 1**

Main physicochemical properties of FSM.

Molecule	Furosemide
CAS Number	54-31-9
Chemical structure	

Molecular formula	$C_{12}H_{11}ClN_2O_5S$
Synonyms	4-Chloro-N-furfuryl-5-sulfamoylanthranilic acid, 5-(Aminosulfonyl)-4-chloro-2-([2-furanylmethyl]amino) benzoic acid
Solubility (μg/mL)	>49.6 / 73.1 (mg/L) at 30 °C
Vapor pressure (mmHg)	3.1×10^{-11} at 25 °C
Octanol-water partition coefficient, log K_{ow}	2.03
pKa	3.8
Maximum absorption wavelength (λ_{max})	230, 277, 330 nm

2.2. Sonication procedures

Sonolysis experiments were realized in cylindrical water-jacketed glass reactor of a total volume of 500 mL. The ultrasonic waves of 585, 860 and 1140 kHz were introduced from the bottom through a Meinhardt multifrequency transducer (model E/805/T/M, diameter of the active area 5.3 cm). Fig. 1 shows a schematic of the experimental setup. The generator that feeds the multifrequency transducer operates at various electrical powers. The temperature of the solution was controlled through the cooling jacket and monitored using a thermocouple immersed in the reacting medium. Ultrasonic energy dissipated in the reactor was estimated by calorimetric method [27]. Sonochemical experiments have been carried out under different conditions using a volume of 300 mL containing 10 mg/L of furosemide.

2.3. Analytical procedures

Quantitative analysis of the contaminant (FSM) was accomplished by HPLC (YL9100 HPLC System) using a Supelcosil LC-18 column (4 μm dp and 250 × 4.6 mm) and a UV–vis detector (YL9120) set at 230 nm. The mobile phase, 30/70 (v/v) acetonitrile/water and 0.1 % of formic acid, was run in the isocratic mode (0.6 mL/min).
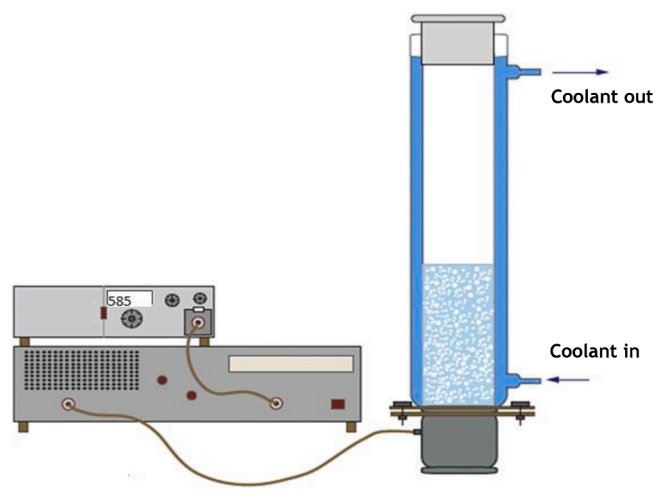
Fig. 1. Schematic of the experimental setup used for the sonochemical degradation of FSM in water (Meinhardt Ultrascheltechnik model E/805/T/M).

UV–Vis spectrophotometer (WPA Lightwave II) was used to measure hydrogen peroxide concentration using the iodometric method [28]. Samples aliquots of 200 μL were taken regularly from the reactor every 5 min during sonication and put in quartz cells containing 20 μL of ammonium heptamolybdate at 0.01 M and 1 mL of KI at 0.1 M prepared by dissolution of a KI mass equal to 16.6 g into 1 L of ultrapure water. The mixed solutions were allowed to stand for 5min before absorbance was measured at 353 nm, which corresponds to the maximum absorption of I_3^- (ε = 26,300 L/mol·cm) [29].

A MembraPure uniTOC·lab analyzer was used for the total organic carbon (TOC) measurements. The instrument is equipped with an automatic sample injector, it uses UV/persulfate oxidation followed by CO_2 selective highly sensitive non-dispersive infrared detection.

Chemical oxygen demand (COD) was determined using a dichromate solution as the oxidizer in a strong acid medium. Test solution (2 mL) was transferred into the dichromate reagent and digested at 150 °C for 2 h. The optical density for the color change of dichromate solution was determined with a spectrophotometer. Biochemical oxygen demand (BOD_5) analysis was carried out by a respirometric measuring device according to the OxiTop instruments procedure.

All trials were carried out in triplicate and the mean values were reported.

3. Results and discussion

3.1. Effect of acoustic intensity

The effect of acoustic intensity in the range of 0.83 to 4.3 W/cm^2 on the sonochemical degradation of the FSM was examined at an ultrasonic frequency of 585 kHz. The obtained results are presented in Fig. 2. The results clearly show that the increase in acoustic intensity from 0.83 to 4.3 W/cm^2 leads to a significant improvement in the sonochemical degradation of FSM. Similar trends are reported by Torres et al. [30] for the degradation of bisphenol A, Méndez-Arriaga et al. [31] for the oxidation of ibuprofen and Dalhatou et al. [32] for the destruction of naphthol blue black. At the microscopic scale, this effect is explained by the fact that the increase in the acoustic intensity induces a more violent collapse of cavitation bubbles and hence a higher concentration of sonochemical oxidants [29,33].

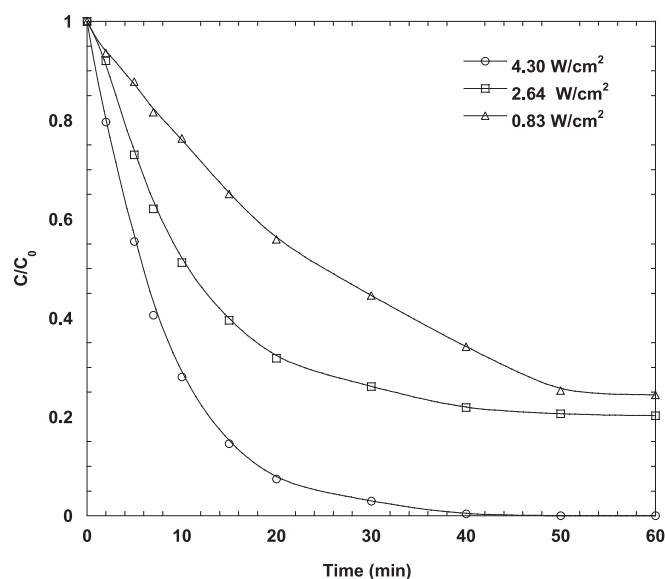Ferkous et al. [34] report that as the acoustic amplitude increases,

the bubble expansion ratio (R_{max}/R_0) increases (where R_{max} is the maximum bubble radius and R_0 is the initial bubble radius) leading to a greater amount of water vapor trapped in the cavitation bubble during collapse. Also, the compression ratio of the bubble (R_{max}/R_{min}) is proportional to the acoustic amplitude, which generates high temperatures in the bubble (R_{min} is the minimum radius of the bubble at the time of collapse). Therefore, the increase in both the amount of water vapor trapped and the temperature of the bubble favors the formation of free radicals since they are essentially produced by the dissociation of water vapor molecules inside the bubble [26]. Besides, as the acoustic intensity increases, the number of collapsing cavities also increases leading to enhanced FSM degradation.

3.2. Effect of the acoustic frequency

The effect of the acoustic frequency on the sonochemical degradation of FSM was examined using three ultrasonic frequencies, namely 585, 860 and 1140 kHz, whereas the acoustic intensity, the initial pH and the volume were maintained constant at 4.3 W/cm^2, 5.2 and 300 mL, respectively. Fig. 3 shows the effect of frequency on the degradation of 10 mg/L of FSM. It was observed that at very high frequencies, the degradation process becomes less efficient. Besides, the rate of H_2O_2 production in water was examined at the three tested frequencies and the obtained results are presented in Fig. 4.

Fig. 3 shows that the sonochemical degradation of FSM at 585 kHz is better than that obtained at 860 and 1140 kHz. It is well known that there is an optimum frequency beyond which there are detrimental effects of frequency on degradation rates [35,36]. There are two main factors that are affected by this variation in the acoustic frequency: (i) the efficiency of the single bubble and (ii) the number of active bubbles. A frequency of 585 kHz gives the cavitation bubble more time to develop, as compared to higher frequencies, which leads to higher expansion and compression ratios [37]. As a result, the implosion will be stronger and generate higher temperatures, which accelerates the dissociation of water vapor and oxygen molecules into free radicals and atoms. Subsequently, the decrease in the temperature inside the bubble and the time of collapse with the increase in frequency leads to a lower dissociation of the molecules of water vapor and oxygen, which decreases the rate of production of hydroxyl radicals in the bubble. On the other hand, the number of active bubbles increases significantly with the frequency increase in the range 585 to 1140 kHz [38]. However, the increase in the number of bubbles cannot compensate for the low yield of oxidizing species in a single bubble at higher frequencies, resulting in lower hydrogen peroxide formation rates at higher frequencies as shown in Fig. 4 [39]. The obtained results of the effect of frequency on the degradation of FSM are also consistent with the literature [37,38].

3.3. Effect of the initial concentration of FSM

FSM degradation was carried out in aerated solutions using various initial concentrations of pollutant, *i.e.,* 0.5, 1, 2, 5, 10.15 and 20 mg/L, while the frequency, acoustic intensity and initial pH of the solution were kept constant at 585 kHz, 4.3 W/cm^2 and 5.2, respectively. Fig. 5 represents the variation of the dimensionless concentration of FSM as a function of time obtained at different concentrations. The curves show that the higher the substrate concentration was, the higher the initial degradation rate. To illustrate, after 20 min of sonication, FSM was completely eliminated for a concentration of 0.5 and 1 mg/L, however, percentages of 98%, 95%, 92%, 80% and 70% were obtained for C_0 = 2, 5, 10, 15 and 20 mg/L, respectively.

Torres et al. [41] showed, through the measured yield of H_2O_2 for initial concentrations, that any increase in solute concentration would increase the probability of hydroxyl radical attack on pollutant molecules. Indeed, at the interface of the bubbles, the hydroxyl radical concentration is very high and the recombination of HO$^\bullet$ would be the dominant process, and the OH–OH recombination would be the

Fig. 2. Effect of acoustic intensity on sonochemical degradation of FSM (conditions: volume: 300 mL, initial FSM concentration: 10 mg/L, frequency: 585 kHz, temperature: 25 °C, pH: 5.2 (natural)).
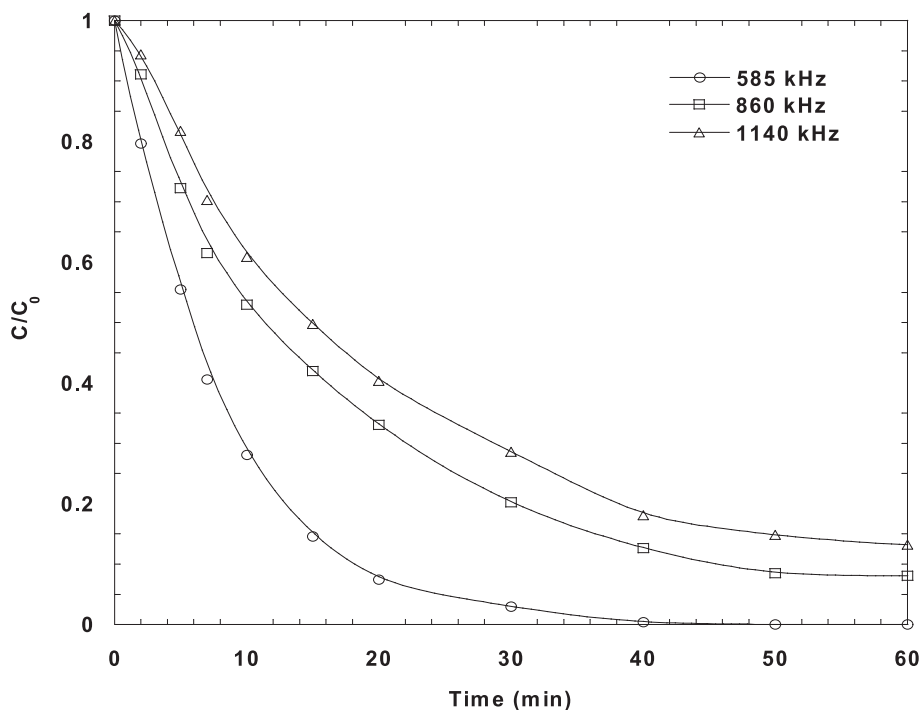
Fig. 3. Frequency effect on sonochemical degradation of FSM (conditions: volume: 300 mL, initial FSM concentration: 10 mg/L, temperature: 25 °C, pH: 5.2 (natural), acoustic intensity: 4.3 W/cm^2).
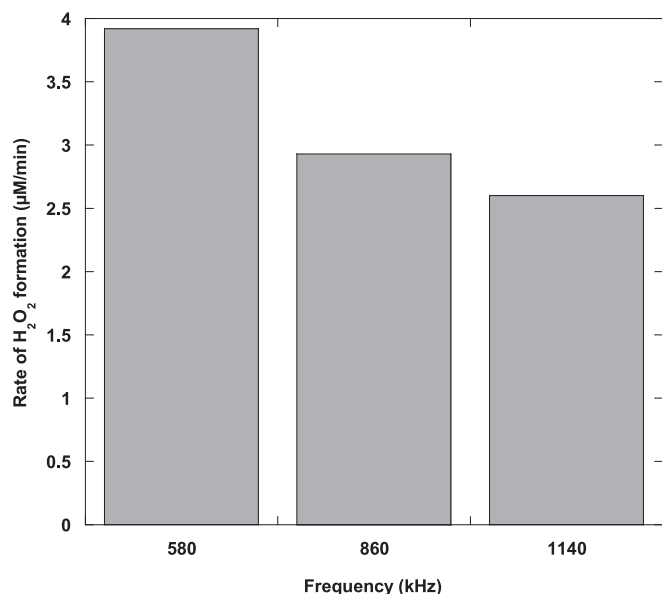

Fig. 4. Rates of H_2O_2 formation in pure water during ultrasonic treatment at various frequencies (conditions: volume: 300 mL, temperature: 25 °C, acoustic intensity: 4.3 W/cm^2).

dominant process [42], an increase in the substrate concentration would increase the fraction of HO$^\bullet$ that reacts with the substrate, and as a result, the degradation rate would be increased. Besides, these findings were also reported in the literature by Merouani et al. [29] and Pétrier et al. [43].

The pollutant employed in this study is a hydrophobic and non-volatile molecule [14]. Additionally, FSM is unable to enter the bulk volume of the bubble due to its low solubility in water (>49.6 g/mL), relatively high octanol/water partition coefficient (2.03), and vapor pressure of 400 Pa (3.1 × 10^{-11} mmHg). It may be degraded by the HO$^\bullet$

radicals present in the solution and at the interface bubble/solution. These results show that the sonochemical degradation of FSM is related to the local concentrations of both HO$^\bullet$ radicals and substrate. Additionally, several authors recently claim that the degradation of organic compounds does not follow a fist-order kinetics such as the sonolytic degradation of 2-phenoxyethanol [44] and BPA [30].

3.4. Effect of initial pH

In wastewater treatment, the solution's pH is a crucial parameter as it changes the degree of ionization of the organic molecule, which takes different forms depending on its ionizable functions. The pKa value of FSM is 3.8 [45], above this value, ionic FSM is the predominant species. On the other hand, at lower values, FSM is principally found in its molecular form. In fact, FSM is a non-volatile compound, so the site of degradation would be outside the cavitation bubble [46].

In order to study the influence of the initial pH on the sonochemical degradation of FSM, different experiments were carried out at various pH values adjusted by the addition of sodium hydroxide (NaOH) or sulfuric acid (H_2SO_4). In Fig. 6, the effect of the initial solution's pH on the sono-degradation of FSM is depicted as a function of time. An increase in the degradation rate of FSM was observed at pH 2 and demonstrated a gradual decrease with the increase in the initial pH value. Under acidic conditions, FSM is principally found in its molecular form and is accumulated at the interface of the cavitation bubbles where the production of hydroxyl radicals is maximum, which results in high degradation rates. Furthermore, above this value (pH greater than pKa), the degradation is slower because the hydrophilicity and solubility of the FSM molecule are enhanced within this range, the molecule tends to move away from the bubble/solution interface. Consequently, at the range 4–10, the degradation is achieved mainly within the solution where the concentration of hydroxyl radicals is low, it is believed that only 10% of the HO$^\bullet$ radicals generated in the bubble can be ejected into the solution [47]. To sum up, the degradation rate decreases in the range of pH 4–10 owing to the recombination of HO$^\bullet$ to H_2O_2, which prevents the direct interaction of the hydroxyl radicals with FSM. In contrast, in acidic conditions, the recombination of HO$^\bullet$ radicals is less effective due
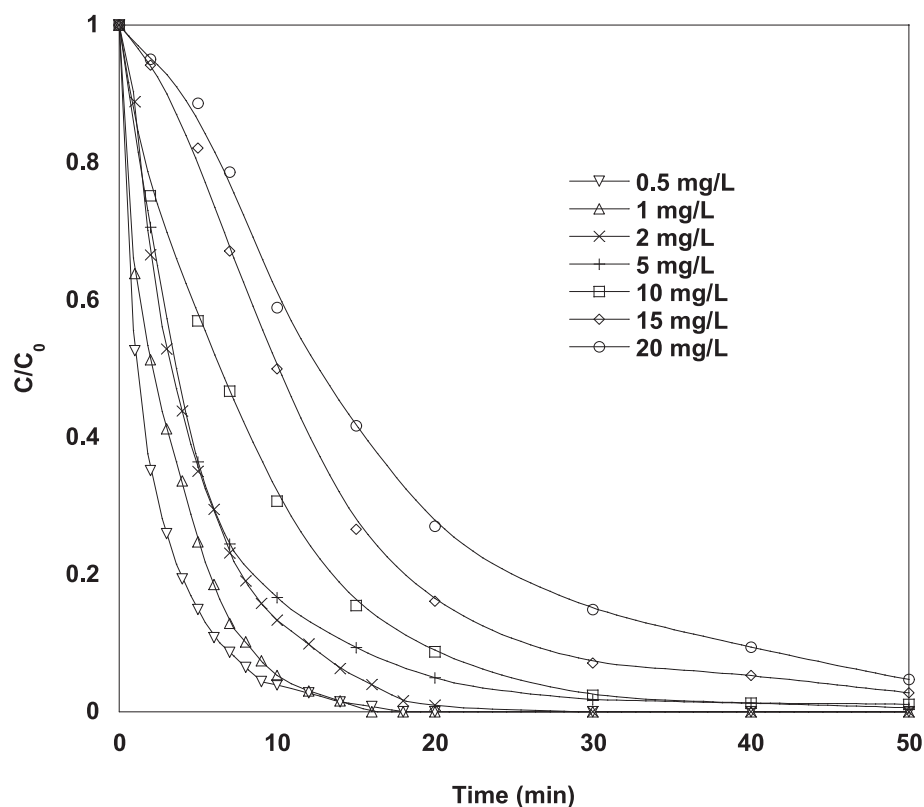
Fig. 5. Degradation kinetics of FSM at various initial substrate concentrations (Conditions: volume: 300 mL, initial FSM concentrations 0.5–20 mg/L, frequency: 585 kHz, acoustic intensity: 4.3 W/cm^2, temperature: 25 °C, pH: 5.2 (natural)).
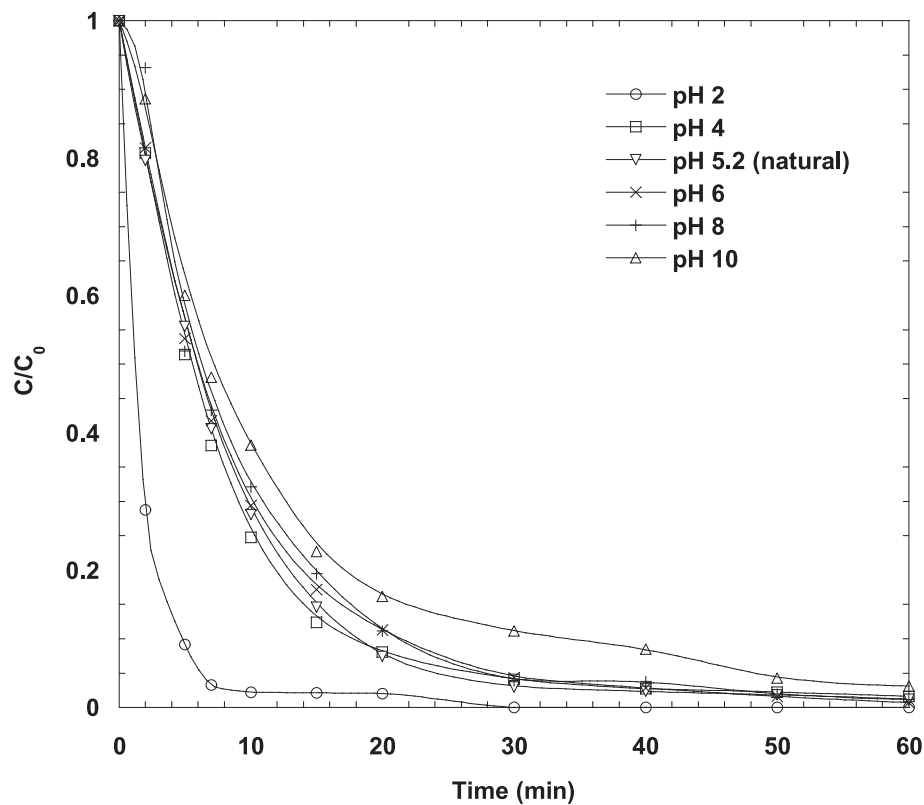

Fig. 6. Effect of initial pH on sonochemical degradation of FSM (Conditions: volume: 300 mL, initial concentration: 10 mg/L, temperature: 25 °C, pH: 2–10, frequency: 585 kHz, acoustic intensity: 4.3 W/cm^2).

to the reaction with FSM present at high concentration at the interface. The same behavior was demonstrated by Torres et al. [41] for the degradation of ibuprofene and Chiha et al. [48] for the degradation of 4-cumylphenol, who demonstrated that in the case of non-volatile compound, the degradation is faster under acidic media.

3.5. Effect of the saturating gas

The effects of different dissolved gases on the formation of H_2O_2 in the absence and presence of FSM and the degradation of FSM at 585 kHz
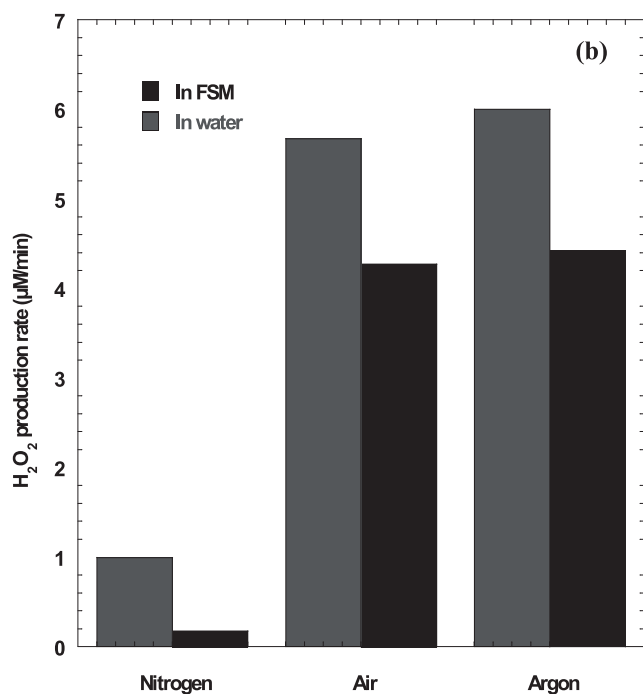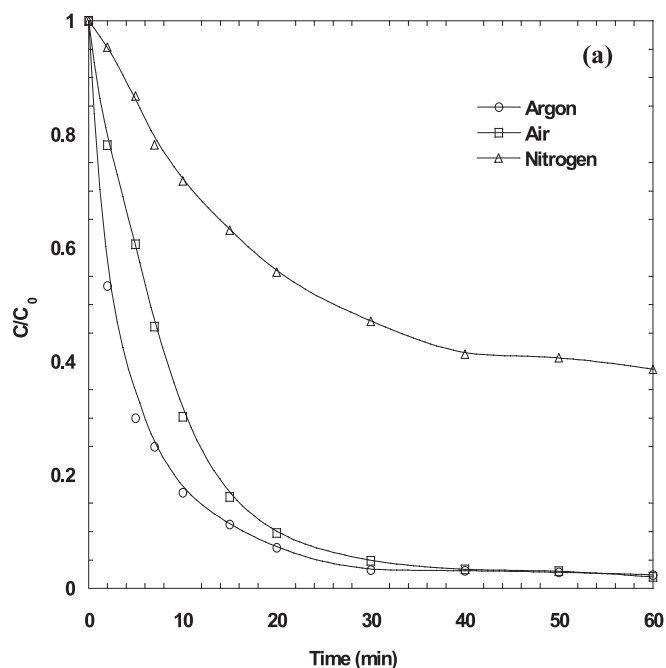

and 4.3 W/cm^2 are shown in Fig. 7(a) and (b). As observed from the figure, the highest degradation rate was reached under argon followed by air then nitrogen. FSM is characterized by a non-volatile character and should not transfer into the bubble. As a consequence, due to its hydrophobic character, FSM elimination should result from reaction with HO$^\bullet$ at the surface of the bubble. In a recent work, Kerboua et al. [49] examined numerically the ways in which the nature of dissolved gases, *i.e.*, argon, air and nitrogen, can influence the sonolytic hydrogen formation kinetics. They reported that the temperature of the bubble depends, on the one hand, on the specific calorific capacity of the saturating gas and on the other hand, its thermal conductivity λ. The higher the polytropic ratio $\gamma = C_P/C_V$, the higher the expected temperature; and the higher the thermal conductivity λ of the gas, the greater the conduction heat loss and the lower the achievable temperature.

According to experiments and theory, argon has the largest ratio of specific heats γ ($\gamma_{Ar} = 1.67$, $\gamma_{air} = 1.40$, $\gamma_{N2} = 1.40$) and the lowest thermal conductivity ($\lambda_{Ar} = 177 \times 10^{-4}$, $\lambda_{air} = 262 \times 10^{-4}$, $\lambda_{N2} = 240 \times 10^{-4}$ W/m K). Thus, it may enhance the phenomenon of compression of the cavity at higher pressure and temperature as compared to other gases [50–52]. That is why under pure argon, it is seen that the yield of H_2O_2 is drastically increased compared with air, which is equivalent to an association between O_2 and N_2 (21% and 79%, respectively). This explains the drop in H_2O_2 production over time in the presence of a percentage of nitrogen. Contrariwise, the presence of pure nitrogen has a negative effect on the formation of hydrogen peroxide both in the presence and absence of FSM. This is mainly due to the fact that nitrogen has a low polytropic ratio γ and higher thermal conductivity leading to a mechanism of complex reactions that occur inside the bubble and involve dissociation of the gas at high temperature [49]. Besides, the nitrogen atom tends to trap the O atom and leads to the formation of nitric acid and inhibition of H_2O_2 formation [50]. Mead et al. [53] reported that during the sonolysis of water saturated with nitrogen, the formation of nitric acid is preferential. Several authors also showed similar effects of the saturating gas on the sonochemical treatment of non-volatile organic pollutants [30].

3.6. Effect of 2-propanol addition

2-propanol is a volatile substrate (log K_{ow} = 4.86) that easily diffuses into the bulk of the cavitation bubble during its growth [54], it also acts as a scavenger of HO$^\bullet$ radicals. For this reason, 2-propanol is used as a HO$^\bullet$ trapping agent in the gas phase and in the interfacial region of the cavitation bubble.

In order to study the effect of 2-propanol addition on the sono-chemical degradation of FSM, different concentrations (0.1, 1 and 10 mM) of alcohol were selected. Fig. 8. reports the time variation of the dimensionless concentration of FSM for an initial concentration of 10 mg/L. It is noted that the inhibition of degradation kinetics increases with increasing the scavenger's concentration. In the first few minutes, in cases of low scavenger dose (0.1 and 1 mM), the degradation kinetics begin rapidly (first 5 min) then decelerate gradually. This is due to the competitive reactions of FSM and 2-propanol with HO$^\bullet$ radicals at the surface of the bubble. Nevertheless, after a period of sonolysis, despite the formation of volatile products, which results from the degradation of the alcohol and the accumulation of the resulting species inside the bubble, the degradation of the FSM is carried out at slower rate than that observed in the absence of scavenger. This is also applicable at higher concentrations of alcohol (10 mM), because high temperatures are reached inside the cavitation bubble even at high concentrations of alcohol [44]. Ashokkumar et al. [55–57] showed that the temperature in the bubble, at various concentrations of alcohol (methanol, ethanol, n-propanol, n-butanol, n-pentanol and t-butanol) up to 500 mM, is always above 2000 K.

The previous results clearly demonstrate that FSM does not undergo direct pyrolysis in the bubbles but oxidizes at the interface by reacting with HO$^\bullet$ radicals. These findings are consistent with those reported by

Fig. 7. Effect of different dissolved gases on the sonochemical degradation of FSM (a) and formation rate of H_2O_2 in the presence and absence of FSM (b) (Conditions: volume: 300 mL, initial FSM concentration: 10 mg/L, temperature: 25 °C, pH: 5.2 (natural), frequency: 585 kHz, acoustic intensity:4.3 W/cm^2).
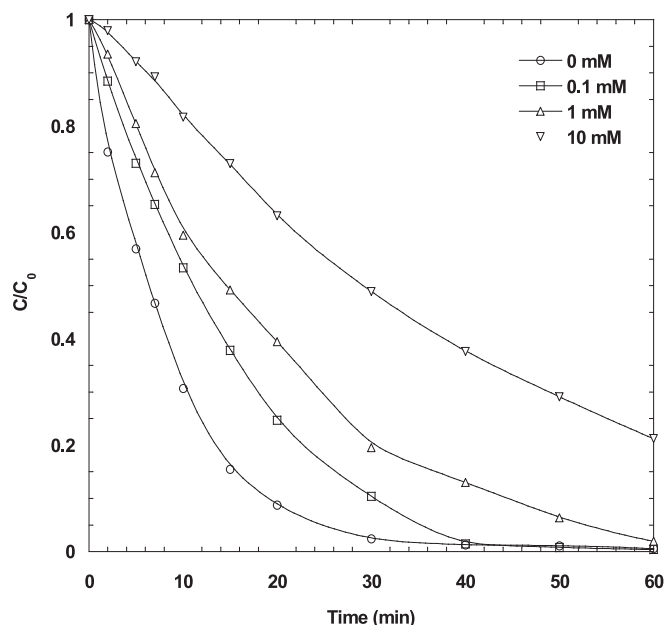
Fig. 8. Effect of 2-propanol on sonochemical degradation of FSM (Conditions: volume: 300 mL, initial FSM concentration: 10 mg/L, temperature: 25 °C, pH: 5.2 (natural), frequency: 585 kHz, acoustic intensity: 4.3 W/cm^2).

Peller et al. [58] for the sono-degradation of 2,4-dichlorophenoxyacetic acid.

3.7. Effect of tert-butanol addition

To confirm the reaction pathway of the sonochemical degradation of FSM, the scavenging effect of *tert*-butyl alcohol, in the presence of 10 mg/L of FSM, was studied for three concentrations of the alcohol of 0.1, 1, and 10 mM. Fig. 9 illustrates the obtained results. Examination of the figure shows that at low concentrations (0.1 and 1 mM) of alcohol, the degradation of FSM was marginally inhibited. However, at high concentration of *tert*-butanol (10 mM), the degradation is inhibited at 43%.

Tert-butyl alcohol is a highly volatile compound that penetrates easily into the bubble during its expansion phase. Wide work on the sonochemistry of *tert*-butyl alcohol has been reported by Tauber et al. [59] where they demonstrated that *tert*-butyl alcohol is able to scavenge HO$^\bullet$ radicals in the bubble and prevent the accumulation of HO$^\bullet$ radicals at the interface of the bubble. Besides, as reported by Buxton et al. [21], the degradation of *tert*-butanol alcohol leads to the formation of volatile products and enter the bulk volume of the bubble resulting in a decrease of the temperature inside it, which, in turn, affects the degradation rate of the pollutant. This result confirms that FSM does not undergo direct pyrolysis in the sonolytic bubbles but rather becomes oxidized at the interface of cavitation bubble by reacting with HO$^\bullet$ radicals.

3.8. Mineralization of the treated solutions

The evolution of the removal of the initial pollutant's concentration and the total organic carbon (TOC) of 30.24 μmol/L FSM solution were performed to investigate the capability of the ultrasound process to remove FSM and assess the degree of mineralization of the organic matter. The experiments were carried out under the same operating conditions (585 kHz, 4.3 W/cm^2 and natural pH of 5.12) and the obtained results are shown in Fig. 10. This figure demonstrates that FSM is completely removed after 60 min of irradiation, while the reduction of less than 25% of the TOC was noticed within 4 h of treatment, almost 75% of TOC remained in the solution. The reason could be related to the formation of byproducts of FSM that are poorly degraded by the ultrasonic action. These findings are in good agreement with several studies
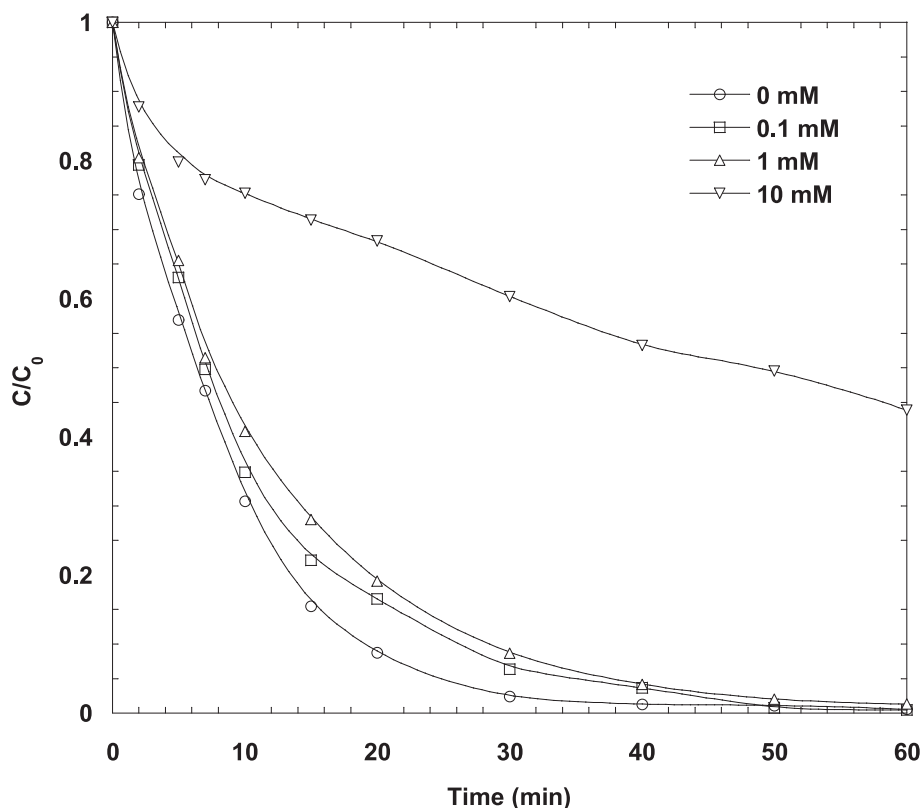

Fig. 9. Effect of *tert*-butanol on sonochemical degradation of FSM (Conditions: volume: 300 mL, initial FSM concentration: 10 mg/L, temperature: 25 °C, pH: 5.2 (natural), frequency: 585 kHz, acoustic intensity: 4.3 W/cm^2).
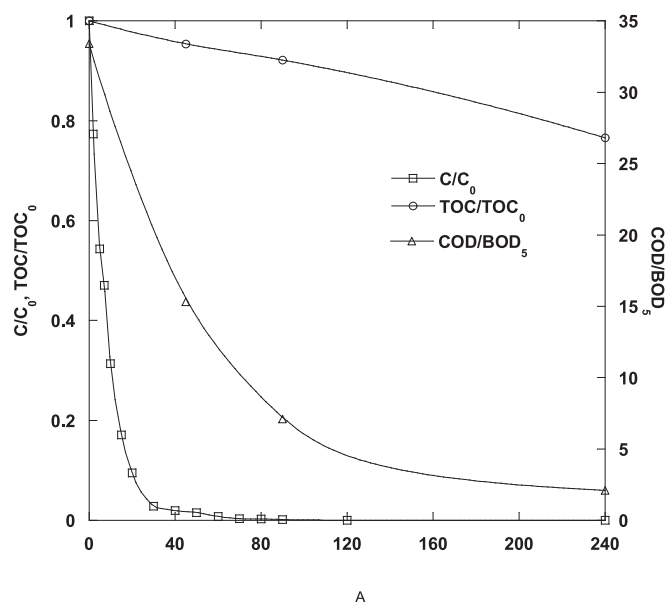
3.9. Biodegradability evaluation of the treated solutions

Since the FSM (30.24 μmol/L) was eliminated after 60 min, but mineralization was not accomplished even after 240 min (75% of TOC persisted in the solution), it is essential to evaluate the biodegradability (COD/BOD$_5$ ratio) during the ultrasonic treatment. A wastewater effluent is considered biodegradable and tolerable for discharge when the COD/BOD$_5$ ratio is ~ 2. Fig. 10 shows that the sonochemical process significantly improves the biodegradability of the treated solution. It was observed from this figure that the COD/BOD$_5$ decreases from 33.4 to 2.1 after 240 min of ultrasonic treatment. This indicates that the sonochemical process is able to transform the FSM solution into readily biodegradable and environmentally friendly compounds that could be easily eliminated in a subsequent economical biological treatment.

3.10. Degradation of FSM in real water matrices

Numerous studies have been carried out on the sonochemical degradation of pollutants but a limited number of them involve water matrices effects. The sonolytic degradation of FSM was examined by dissolving the substrate in natural mineral water and in seawater. The principal characteristics of the mineral water were: Ca^{2+}=92 mg/L, Mg^{2+}=18 mg/L, Na$^+$=129.5 mg/L, K$^+$=44.5 mg/L, Cl$^-$=164.5 mg/L, SO$_4^{2-}$=123.6 mg/L, HCO$_3^-$ = 172 mg/L and pH = 7.5. The seawater (pH ~ 8.4), collected in the region of Annaba, Algeria, has a high salinity (~35 g/L) mostly formed of Na$^+$ ≈ 11 g/L, Mg^{2+} = 1.3 g/L, Ca^{2+} ≈ 0.4 g/L, Cl$^-$ ≈ 20 g/L, SO$_4^{2-}$ = 3 g/L. The achieved results in comparison with those obtained in ultrapure water are shown in Fig. 11. As can be seen from this figure, a negative effect on the degradation kinetics of FSM was observed in the natural mineral water. After 15 min of treatment, the degradation percentage was reduced by ~ 12% in the natural mineral water. The reason of this decrease is the quenching effect of mineral anions toward •OH radicals, especially HCO$_3^-$ [61]. The inhibiting effect

Fig. 10. FSM and total organic carbon removal and biodegradability ratio (COD/BOD$_5$) evolution during ultrasonic treatment (conditions: volume: 300 mL, initial FSM concentration: 10 mg/L, temperature: 25 °C, pH: 5.2 (natural), frequency: 585 kHz, acoustic intensity: 4.3 W/cm^2).

where mineralization was found to be low compared to the degradation/removal of a specific pharmaceutical, such as in the degradation of acetaminophen [60] and ibuprofene [41], and leads to the formation of more oxidized organic compounds, which are only slightly degraded (TOC) even with a long treatment period.
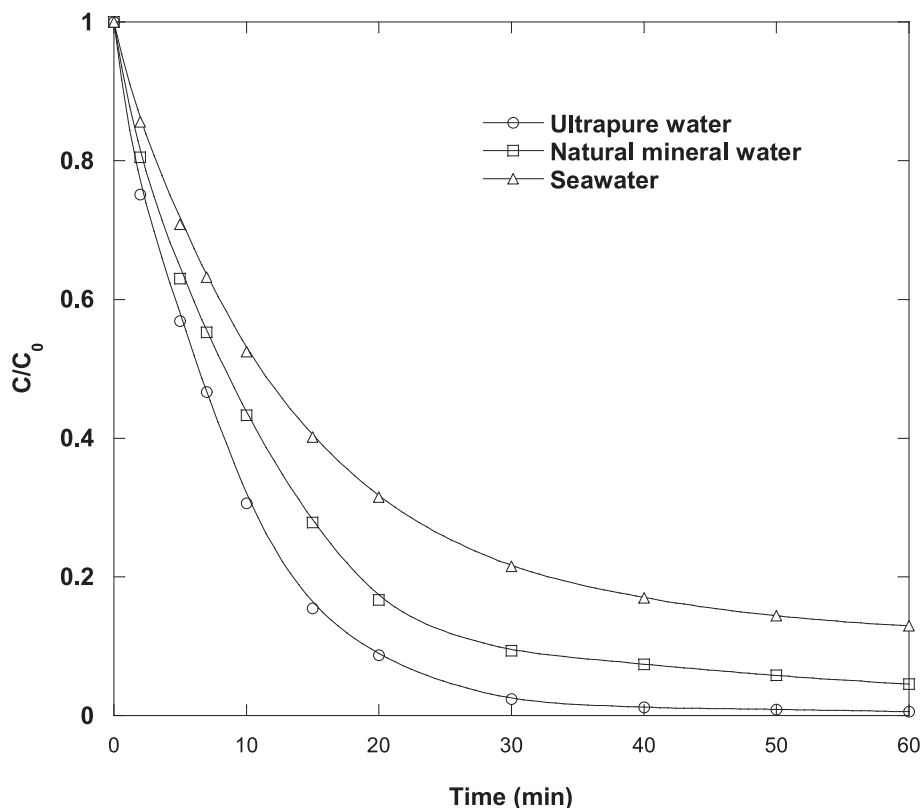

Fig. 11. Sonolytic degradation of FSM in ultrapure water, natural mineral water and seawater (conditions: volume: 300 mL, initial FSM concentration: 10 mg/L, temperature: 25 °C, frequency: 585 kHz, acoustic intensity: 4.3 W/cm^2).

in seawater was more pronounced, ~24% diminution compared to ultrapure water after 15 min of sonication, and is due to the high salinity of seawater.

4. Conclusion

The destruction of furosemide can be effectively achieved with high-frequency ultrasonic waves by promoting its oxidation in relatively dilute synthetic solutions. The extent of this degradation is highly dependent on the operating conditions, *i.e.*, acoustic intensity, initial concentration, and initial pH of the solution. The increase in acoustic intensity from 0.83 to 4.3 W/cm^2 leads to an important enhancement in the sonolytic degradation of FSM. The removal of FSM at 585 kHz is better than that obtained at 860 and 1140 kHz. The initial rate of the ultrasonic degradation of FSM augmented with the increase in its initial concentration from 2 to 20 mg/L. An increase in the degradation rate of substrate was observed at pH 2 and demonstrated a gradual diminution with the increase of the initial pH value in the interval 4–10. Under various saturating gases, the highest degradation rate was achieved under argon followed by air then nitrogen. Considering the effects of scavengers and saturation gases in the presence of FSM, it is deduced that hydroxyl radical-mediated reactions occurring at the gas-liquid interface appear to be the main degradation mechanism for this pollutant. Biodegradability evaluation of the treated solutions demonstrate that the ultrasonic technique is able to transform the FSM solution into readily biodegradable and environmentally friendly compounds that could be easily eliminated in a subsequent economical biological treatment. The sonochemical advanced oxidation process represents an efficient technique for the removal of FSM from dilute aqueous solutions even in real environmental matrices.

CRediT authorship contribution statement

Intissar Gasmi: Investigation, Visualization, Writing – original draft, Writing – review & editing. **Oualid Hamdaoui:** Investigation, Conceptualization, Methodology, Formal analysis, Project administration, Supervision, Visualization, Writing – review & editing. **Hamza Ferkous:** Investigation, Visualization, Writing – review & editing. **Abdulaziz Alghyamah:** Validation, Visualization, 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

No data was used for the research described in the article.

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