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Sonolytic degradation kinetics and mechanisms of antibiotics in water and cow milk☆

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ABSTRACT

Antibiotics (ABX) residues frequently occurred in water and cow milk. This work aims to understand the kinetics and mechanisms of sonolytic degradation of four ABX, *i.e.* ceftiofur hydrochloride (CEF), sulfamonomethoxine sodium (SMM), marbofloxacin (MAR), and oxytetracycline (OTC) in water and milk. In both water and milk, the sonolytic degradation of ABX follows pseudo-first order (PFO) kinetics well (R^2: 0.951–0.999), with significantly faster ABX degradation in water (PFO kinetics constants (k_1): 1.5×10^{-3}-1.2×10^{-1} min^{-1}) than in milk (k_1: 3.5×10^{-4}-5.6×10^{-2} min^{-1}). The k_1 values for SMM degradation in water increased by 118% with ultrasonic frequency (40–120 kHz), 174% with ultrasonic frequency (80–500 kHz), 649% with ultrasonic power (73–259 W), 22% with bulk temperature (12–40℃), and by 68% with reaction volume (50–250 mL), respectively, in other things being equal. The relevant k_1 values in milk increased by 326%, 231%, 122%, 10% as well as 82% with the above same effective factors, respectively. The oxidation by free radicals generated *in situ* dominates ABX degradation, and the hydrophobic CEF (54.0–971.7 nM min^{-1}) and SMM (39.2–798.4 nM min^{-1}) underwent faster degradation than the hydrophilic MAR (33.9–751.9 nM min^{-1}) and OTC (33.8–545.3 nM min^{-1}) in both water and milk. Adding an extra 0.5 mM H_2O_2 accelerated SMM degradation by 19% in water and 33% in milk. After 130–150 min sonication of 100 mL of 2.0 mg L^{-1} (6.62 μM) SMM in various milk with 500 kHz and 259 W, the residue concentrations (52.9–96.3 $\mu g\ L^{-1}$) can meet the relevant maximum residue limit (100 $\mu g\ L^{-1}$).

1. Introduction

The occurrence of antibiotic (ABX) residues in water environments and dairy products has been frequently reported [1]. In food animal products, ABX residues refer to the metabolites discovered in trace concentrations in any edible part of the products following the administration of the ABX [2]. In aquatic environments, ABX residues occur in wastewater, drinking water, river, *etc.* via different routes [3]. ABX production and use, especially misuse in both livestock and aquaculture, are major sources of ABX residues that cause serious water pollution and health risks, including allergic reactions, ABX-resistant bacteria, disruption of the body's reproductive, immune, endocrine, and nervous systems, *etc.* [4,5]. Approximately 63,151 tons of ABX are used in livestock production worldwide each year [6]. In the European Union, approx. 5,460 tons of ABX are consumed by humans and animals annually [7]. ABX-contained medicated milk, mainly caused by intramammary administration of mastitis, has led to enormous milk wastage and severe economic losses in the farming industry [8]. Both the U.S. Food and Drug Administration and the European Medicines Agency have thus established the residue tolerance levels (or the maximum

Abbreviations: ABX, antibiotics; *MRLs*, maximum residue limits; *DEs*, degradation efficiencies; CEF, ceftiofur hydrochloride; SMM, sulfamonomethoxine sodium; MAR, marbofloxacin; OTC, oxytetracycline; PFO, pseudo-first-order kinetics model; t_{MRL}, the time required to meet MRLs; US, ultrasound; f_{US}, US frequency; p_{US}, US power; T, bulk temperature; C_0, initial ABX concentration; V_0, reaction volume; RT, retention time.

☆ The authors would like to dedicate the manuscript to the memory of the late Prof. Vladimir O. Abramov, who was an invaluable scientist, mentor, colleague, and friend.

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residue limits, *MRLs*) for a large number of ABX in milk [9,10]. Moreover, quantitative and stringent standards for commonly used ABX are urgently needed to prevent the misuse and spread of ABX in aquatic environments [11]. Therefore, it is important to develop methods to remove ABX from wastewater and waste milk. So far, several methods have been developed to remove ABX from wastewater or medicated milk, *e.g.* adsorption, ozonation, photocatalysis, bioremediation, *etc.* [12–15]. Adsorption is a simple, economical, and environmentally friendly process with low energy consumption, high efficiency, and reliability. Adsorbents developed include activated carbons (ACs), carbon nanotubes, biochars, resins, clays, zeolites, *etc.* [16–18]. However, adsorption is a process of transferring ABX from the liquid phase to the adsorbent. Moreover, the adsorption performance strongly depends on the type of ABX and adsorbents. Therefore, the exhausted adsorbents must be further purified or regenerated for reuse. Otherwise, secondary pollution will occur [12]. Advanced oxidation processes (AOPs), *e.g.* ozonation, photocatalysis, hydrodynamic cavitation, *etc.*, are highly efficient for the degradation of ABX in water matrix thanks to the strong oxidation of non-selective oxidants, *i.e.* hydroxyl radicals ($^{\bullet}OH$), formed *in-situ* [15,19,20]. However, the degradation efficiencies of AOPs depend on many factors, such as dissolution, distribution, use of ozone, wavelength and intensity of light, type of catalysts, *etc.* [14,15,19,21,22]. In addition, the high cost and formation of potentially toxic intermediates limited the use of AOPs. The bioremediation process is readily accepted due to its low investment and operating costs and ease of use, while ABXs are recalcitrant to microorganisms above a certain concentration in wastewater, which affects the degradation and mineralization of ABXs, as well as the potential risk of resistance gene formation. Therefore, bioremediation has usually been combined with other physical or chemical treatment processes [12,14,23].

Sonolysis, one of the AOPs, is driven or enhanced by ultrasonic cavitation. The propagation of ultrasound (US) through compression-rarefaction cycles in water matrices leads to the formation, contraction and expansion, and implosion of numerous cavitation bubbles [24–26]. The accompanying physical effects induced by the collapse of cavitation bubbles include extremely high temperature (~5,000 K), high pressure (~500 atm), high velocity of micro-jets (>100 m s^{-1}), and shockwaves [27–31,91]. Meanwhile, reactive oxygen species, such as $^{\bullet}OH$ and $^{\bullet}O$ radicals and H_2O_2, could be *in situ* produced by pyrolysis of H_2O and O_2, as well as a series of radical reactions (Reactions 1–13) driven during the bubbles collapse [14,23,32,33].

$$H_2O \xleftrightarrow{US} {}^{\cdot}OH + {}^{\cdot}H \quad (1)$$

$$O_2 \xleftrightarrow{US} 2\ {}^{\cdot}O \quad (2)$$

$$H_2O \xleftrightarrow{US} H_2 + O \quad (3)$$

$$H_2O + O \leftrightarrow 2\ {}^{\cdot}OH \quad (4)$$

$$O_2 + {}^{\cdot}H \leftrightarrow HO_2^{\cdot} \quad (5)$$

$${}^{\cdot}OH + {}^{\cdot}H \leftrightarrow H_2 + O \quad (6)$$

$$H_2O + {}^{\cdot}H \leftrightarrow H_2 + {}^{\cdot}OH \quad (7)$$

$$HO_2^{\cdot} + O \leftrightarrow {}^{\cdot}OH + O_2 \quad (8)$$

$$HO_2^{\cdot} + {}^{\cdot}H \leftrightarrow {}^{\cdot}OH + {}^{\cdot}OH \quad (9)$$

$$HO_2^{\cdot} + {}^{\cdot}H \leftrightarrow H_2 + O_2 \quad (10)$$

$$HO_2^{\cdot} + {}^{\cdot}OH \leftrightarrow H_2O_2 + O \quad (11)$$

$${}^{\cdot}OH + {}^{\cdot}OH \leftrightarrow H_2O_2 \quad (12)$$

$$HO_2^{\cdot} + HO_2^{\cdot} \leftrightarrow H_2O_2 + O_2 \quad (13)$$

As a simple, safe, non-selective, and environmentally friendly method, sonolysis could be an alternative to the above methods and has already been used for the removal of several ABX in water matrices [23]. Serna-Galvis *et al.* reported that the antimicrobial activity of oxacillin in 250 mL of 47.0 μM (20.0 mg L^{-1}) solution was eliminated in 120 min by using sonication (275 kHz and 20.7 W) at 20℃, whereas the mineralization was low even after 180 min sonication [32]. De Bel *et al.* found that the degradation efficiency (*DE*) of ciprofloxacin in 150 mL of 45.3 μM (15.0 mg L^{-1}) aqueous solution reached 57.0% in 120 min by using sonication (500 kHz and 92 W L^{-1}) at 25℃ [34]. Gao *et al.* reported that sulfamethazine in 200 mL of a 180.0 μM (50.1 mg L^{-1}) solution was completely removed by sonication (800 kHz and 100 W) at 20℃ in 120 min, but only 8.3% mineralization was achieved [35]. The influence of crucial factors such as US frequency, US power, initial concentration, pH of matrices, and additives or scavengers on the degradation of the above ABX has been studied. However, little is known about the removal of ABX from milk by sonochemical processes. With the knowledge of the role of complex components in milk, *e.g.*, fats, proteins, carbohydrates, *etc.*, on the behavior of cavitation bubbles and the formation of reactive species and competitive oxidation, the difference of degradation of ABX in aqueous solutions and milk was investigated to clarify the degradation kinetics, mechanisms as well as the influence of effective factors [14].

In this study, the sonochemical degradation kinetics of four ABX, *i.e.*, ceftiofur hydrochloride (CEF), sulfamonomethoxine sodium (SMM), marbofloxacin (MAR), and oxytetracycline (OTC) in water and milk were investigated. This work aims to (1) clarify the differences in the degradation behaviors, kinetics, and mechanisms of ABX by sonication in water and milk; (2) demonstrate the feasibility of the sonolytic degradation of model ABX in water and milk; (3) evaluate the effect of sonication on milk nutrients. Specifically, the effect of critical factors, including US frequency (f_{US}), US power (p_{US}), bulk temperature (T), initial concentration (C_0), and reaction volume (V_0) on the degradation in water and milk were investigated. Sonolysis of the model ABX in the presence of radical scavengers (*n-*/*t*-butanol) and oxidative additives (H_2O_2 and $Na_2S_2O_8$) were performed. Moreover, nutrient change in milk before and after degradation, as well as antibacterial activity measurement was also discussed to evaluate the feasibility of ABX removal via sonolysis.

2. Materials and methods

2.1. Materials and chemicals

Ultra-high-temperature processed milk was purchased from the local branch of two major supermarkets in the city of Turin (Italy) and stored at room temperature. Milk composition is shown in Table S1. No model ABX residues were observed in any of the purchased milk.

CEF (50.0 mg mL^{-1}, Ceva Santé Animale), SMM (400.0 mg mL^{-1}, Daimeton 40, IZO Srl), MAR (100.0 mg mL^{-1}, Vetoquinol), and OTC (92.7 mg mL^{-1}, Oxtra MV 10, Huvepharma) have been used as stock solutions, which were stored at 4°C in a refrigerator. The structures of the model ABX are shown in Scheme S1. ABX standard solutions and medicated milk were prepared daily by diluting the appropriate ABX stock solutions with water and pasteurized milk, respectively.

Ethanol (EtOH, ≥ 99.8%), acetonitrile (MeCN, ≥ 99.9%), and trifluoroacetic acid (TFA, ≥ 99%) were purchased from Sigma-Aldrich (St. Louis, MO, USA). Ammonia solution (NH_4OH (aq), 30%) was provided by Carlo Erba. Hydrogen peroxide (H_2O_2 (aq), 35%), sodium persulfate ($Na_2S_2O_8$, ≥ 98%), *n*-butanol (> 98%), *t*-butanol (99%), and ethylenediaminetetraacetic acid disodium salt hydrate (> 99%) were purchased from Alfa Aesar (Thermo Fisher Scientific, Germany). Deionized water (conductivity ≤ 2 $\mu S\ cm^{-1}$) was used to prepare standard solutions

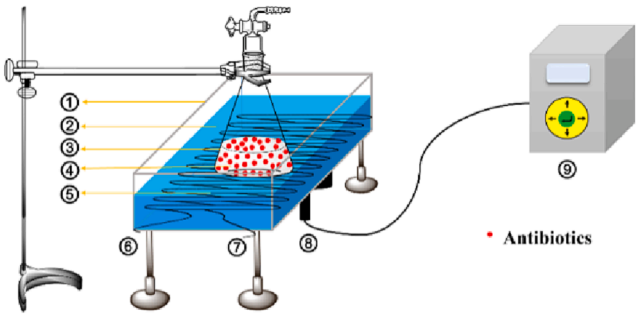

Fig. 1. Schematic diagram of the reaction system for sonication of ABX-medicated water or milk.

of ABX. Milli-Q water obtained using a Milli-Q Reference A + System (Merck Millipore, Darmstadt, DE, USA) was used for HPLC mobile phase preparation.

2.2. Devices and typical run

2.2.1. Setup

The device for sonochemical degradation is depicted in Fig. 1.

A high-frequency (500 kHz) device consists of an ultrasonic generator (maximum electrical output power of 318 W, UMC-Premium, Weber Ultrasonics, Germany), equipped with a stainless steel reservoir [20 cm (W) × 28 cm (L) × 10 cm (H)] with a 6 L capacity, a serpentine condenser (at 1 cm from the bottom), and a 1 L Erlenmeyer flask (bottom area: 113 cm^2, thickness: 2 mm). An adaptor was connected at the top of the flask to minimize solvent evaporation, which was always switched on to ensure atmosphere pressure. The reaction temperature in the 3-L water bath was controlled by the periodic measurement of the bulk temperature in the reservoir and fine-tuning of the cooling-water flow rates in the serpentine condenser. The ABX-spiked solution or milk surface inside the flask is always below the water surface outside. A multi-frequency device (MG 200, Weber Ultrasonics, Germany) consists of a sonic digital generator (operating at variable frequencies of 40, 80, and 120 kHz, with a maximum electrical output power of 150 W) equipped with the same structure and size as above sonication reactor. The actual power dissipated in the system was identified by calorimetric measurements using water as heating media, and all US powers mentioned below refer to powers calorimetrically [36]. The measured US powers and associated electric powers are listed in Table S2.

A centrifuge (Allegra 64R Benchtop Centrifuge, Beckman Coulter, Italy) with a maximum rotation speed of 26,000 rpm and a centrifuge (L530, Xiangyi, China) with a maximum rotation speed of 4,200 rpm were used to separate the supernatants from milk samples. An HPLC system (Waters Corp., Milford, MA, USA) was used for ABX determination as described in previous work [37]. A UPLC-MS/MS system (Acquity TQD LC-MS/MS System, Waters Corporation, Milford, MA, USA) equipped with a Kinetex C18 column (150 × 4.6 mm, 5 μm) coupled with a C18 cartridge (H1) was used to determine the intermediates of ABX degradation. A microprocessor pH meter (Hanna instruments, pH 211) was used to measure the pH values of water and milk samples before and after sonication. A digital thermometer with a pointed probe (Hanna instruments, HI 98501) was used to monitor the bulk temperature during the sonication.

2.2.2. Typical runs

A 1-L Erlenmeyer flask containing 50–250 mL of ABX solution or medicated milk was set over the serpentine condenser (at approx. 1 cm from the bottom) in the sonication reactor and sonicated at 500 kHz and 259 W under an ambient atmosphere at room temperature, respectively. The bulk temperature was continuously controlled by cooling water and monitored by a digital thermometer during the sonication. Water or milk samples were withdrawn periodically and analyzed by AC-based solid phase extraction coupled with HPLC (AC-SPE-HPLC).

2.3. Analysis and evaluation of ABX removal

2.3.1. Determination of ABX in water and milk

The collected water and milk samples were pretreated by enrichment and cleanup with AC-SPE-HPLC as described in previous work [37]. For the analysis of ABX in milk with high concentration (initial concentration: 192.8 μM), 1 mL ABX-contained milk samples were collected periodically and deproteinized by mixing with MeCN (1:1, *v:v*) and centrifuged at 4,200 rpm for 10 min. Subsequently, the supernatant was used for HPLC-UV analysis.

2.3.2. Evaluation of ABX removal in water and milk

The integrated rate equation for pseudo-first-order (PFO) kinetics, pseudo-second-order (PSO) kinetics, and the *DE* for ABX degradation are described in Eq. (1)–(3) [14,38]:

$$\frac{C_t}{C_0} = e^{-k_1 t} \tag{1}$$

$$\frac{1}{C_t} - \frac{1}{C_0} = k_2 t \tag{2}$$

$$DE\ (\%) = \frac{C_0 - C_t}{C_0} \times 100\% \tag{3}$$

where C_0 (μM or mg L^{-1}) is the initial concentration of ABX, C_t (μM or mg L^{-1}) is the ABX concentration at the given time t (min), k_1 (min^{-1}) is the PFO rate constant, which is equal to the slope of the plot of $\ln(C_0/C_t)$ versus t. k_2 (L mg^{-1} min^{-1}) is the PSO rate constant, which is equal to the slope of the plot of $[(1/C_t)- (1/C_0)]$ versus t.

All experiments were performed in duplicate. Error bars represent the standard error of duplicate experiments. Data without error bars mean that the standard errors of the replicates are zero or the size of the error bar is smaller than the labeling.

2.3.3. Analysis of intermediates of ABX degradation in water

The intermediates of ABX degradation were identified using the UPLC-MS/MS system. During the UPLC-MS/MS analysis, the C18 column was employed and the electrospray ion source was operated in positive ionization mode. Linear gradient elution was performed with 0.1%TFA in H_2O (Phase A) and 0.1%TFA in MeCN (Phase B) as described in Table S3. The flow rate was 1.0 mL min^{-1}. The injection volume was 40 μL.

2.3.4. Evaluation of the feasibility of sonication for ABX removal in milk

The nutrient testing was performed by the laboratory of the Piedmont Regional Breeders Association (ARAP Lab, Appendix A) in Italy. Before antimicrobial susceptibility testing, the collected medicated milk samples before and after sonication were kept in a freezer at approx. −18°C. The antimicrobial susceptibility testing of the samples was performed using the modified Kirby-Bauer disk diffusion method as described in a previous work [14].

3. Results and discussion

The sonolytic kinetics of ABX in water is essentially controlled by their physicochemical properties [23]. Besides, US frequency and power, bulk temperature, initial ABX concentration, reaction volume, etc., also influence the sonolytic behavior of ABX [23,39–41]. Adding radical scavengers or extra oxidants usually hinders or enhances the sonolysis of ABX, which favors understanding the sonolytic mechanisms [23]. The intermediates formed during ABX sonolysis may provide

useful information to clarify the degradation pathways. In addition, the feasibility of sonolysis of ABX could be further evaluated by analyzing the change in milk nutrients and antibacterial activity.

3.1. Comparison of sonolytic kinetics of various ABX in water and milk

In general, during sonication, three reaction zones for organics degradation occur around the cavitation bubbles, *i.e.*, the cavity, the gas–liquid interface, and bulk liquid [23]. Hydrophobic substrates are mainly oxidized or thermally decomposed under harsh conditions in or around collapsing cavities, while hydrophilic substrates are mainly oxidized in bulk liquid by reactive oxygen species [23,42]. Different sonolytic rates of hydrophilic fumaric acid ($LogK_{OW}$ (the *n*-octanol–water partition coefficient): 0.46), less hydrophobic phenol ($LogK_{OW}$: 1.46) and chloroform ($LogK_{OW}$: 1.97) in aqueous solutions have been identified [38]. However, little is known about the difference in the sonolytic kinetics of various ABX and the reasons for the difference [42]. In the preliminary study, ABX with a high concentration (192.8 μM) was sonolyzed to facilitate the analysis of ABX and degradation intermediates. The sonolytic degradation kinetics of model ABX, *i.e.*, CEF, SMM, MAR, and OTC, in 100 mL of water were investigated and compared under 500 kHz sonication. Meanwhile, the dependence of k_1 of ABX degradation on their $LogK_{OW}$ and k_{OH} (the second-order reaction rate constants of ABX with •OH in aqueous solutions) was discussed. For comparison with ABX degradation in water, significantly slower degradation of ABX was observed with the same initial concentration of ABX in milk. The results are shown in Fig. 2a and 2b. An enlarged view of ABX sonolytic degradation in milk is shown in Fig. S1.

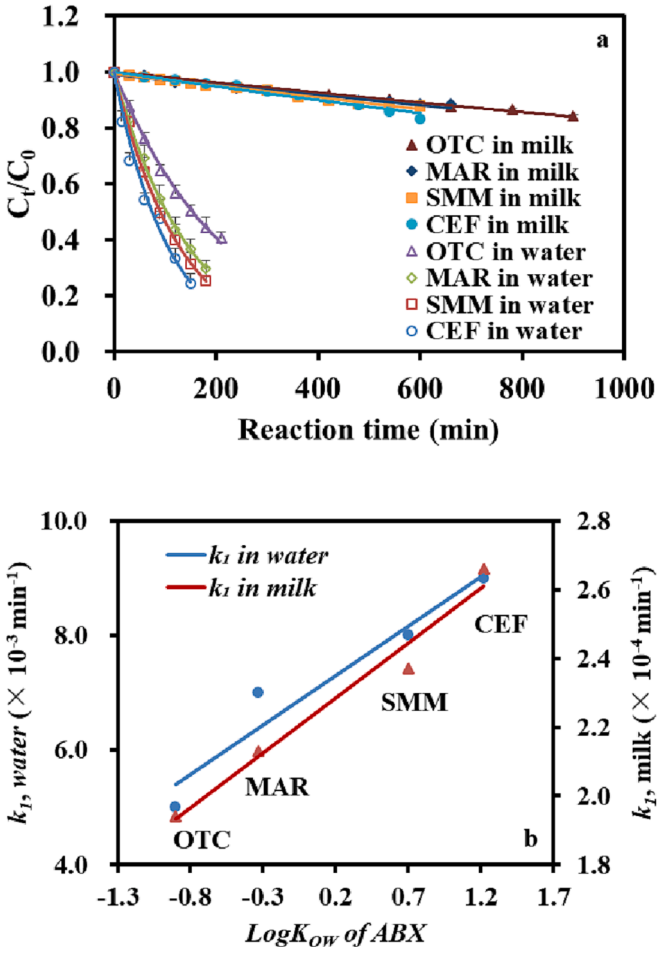

Fig. 2. Sonolytic degradation of various ABX in water and milk (a) and the dependence of k_1 on the $LogK_{OW}$ of the model ABX (b) (Sonication conditions: initial ABX concentration, 192.8 μM; reaction volume, 100 mL; US frequency, 500 kHz; US power, 259 W; initial pH in water and milk, 5.37–7.25 and 6.48–6.80; room temperature).

Based on Fig. 2a, the sonolytic rates of CEF, SMM, MAR, and OTC in water were calculated to be 971.7, 798.4, 751.9, and 545.3 (nM min^{-1}), respectively, thus, the sonolytic rates of ABX are ordered as follows: CEF > SMM > MAR > OTC. The degradation of CEF, SMM, MAR, and OTC in water follows the PFO kinetics and their k_1 values were 9.28 × 10^{-3}, 7.64 × 10^{-3}, 6.72 × 10^{-3}, 4.50 × 10^{-3} min^{-1} (R^2: 0.9827–0.9988), respectively, and their *DE*s were 75.6%, 68.7%, 63.4%, and 49.8% after 150 min sonication, respectively. In milk, however, the sonolytic rates of CEF, SMM, MAR, and OTC were calculated to be 54.0, 39.2, 33.9, and 33.8 (nM min^{-1}), respectively. Their k_1 values were 2.67 × 10^{-4}, 2.37 × 10^{-4}, 2.13 × 10^{-4}, 1.94 × 10^{-4} min^{-1} (R^2: 0.9523–0.9896), respectively, and their *DE*s were 16.9%, 12.2%, 11.4%, and 10.9% after 600 min sonication, respectively. The relevant k_2 values of the model ABX degradation in water and milk were summarized in Table S4, all the R^2 values of the PSO kinetics model (0.9307–0.9662) were lower than those of the PFO kinetics model. It is obvious that the PFO kinetics is more suitable to illustrate the sonolytic degradation of the model ABX in water and milk. Therefore, only PFO kinetics was used to fit the relevant results hereafter.

As shown in Fig. 2b, the k_1 values of ABX degradation in both water ($k_{1,\ water}$) and milk ($k_{1,\ milk}$) are proportional to their $LogK_{OW}$ values (Table S5). The relationship between k_1 values and $LogK_{OW}$ values of ABX can be fitted by the linear Eq. S1 (R^2: 0.8955) and S2 (R^2: 0.9804) in Table S6. The value of $k_{1,\ milk}$ is an order of magnitude less than that of $k_{1,\ water}$, illustrating the sonolytic degradation of the model ABX in milk is hugely slower than that in water. Based on the linear correlations, it can be speculated that the degradation of ABX in both water and milk is hydrophobicity-dependent. Moreover, the slope in Eq. S1 is much higher than that in Eq. S2, revealing that the role of hydrophobicity in water is more evident than in milk. The sonolytic degradation of various ABX suffers similar inhibition by components in milk (96.1%-97.0%), but it appears that the inhibition of ABX degradation by milk components is slightly influenced by the hydrophobicity of ABX. Xiao *et al.* also proved a positive correlation between the degradation rates of 10 μM pharmaceutics in water matrices and their $LogK_{OW}$, indicating that hydrophobic compounds were more readily sonolyzed compared with hydrophilic compounds [42]. However, the sonolytic degradation of hydrophobic ibuprofen, clonidine, estriol, and nifedipine suffered relatively smaller inhibition (20%-60%) by wastewater than hydrophilic fluorouracil and lovastatin (70%-90%).

Furthermore, the orders of k_1 values of ABX degradation in water and milk are consistence with the order of k_{OH}: CEF (9.6 × 10^{10} M^{-1} s^{-1} [43]) > SMM (9.3 × 10^9 M^{-1} s^{-1} [44]) > MAR (9.0 × 10^9 M^{-1} s^{-1} [45]) > OTC (7.0 × 10^9 M^{-1} s^{-1} [45]). Torii *et al.* found that •OH radicals could be fast produced (<10^{-7} s) regardless of the species of solute during sonication [46]. The •OH radicals possess minimal half-life (several μs), thus it is believed that more intense oxidative degradation of ABX occurred at the gas/liquid interface [47]. Although the k_{OH} value of CEF is orders of magnitude higher than the other model ABX, the k_1 value of CEF is only 1.1–1.8 folds faster than OTC, MAR, and SMM in water and milk, implying that the k_{OH} plays a minor role in ABX degradation compared with the role of $LogK_{OW}$, once again, demonstrating that the hydrophobicity of ABX dominates their sonolytic kinetics. Henglein *et al.* found higher-hydrophobicity substrates have stronger capacity to catch •OH radicals in solutions during sonication [24].

As a result, the sonolytic degradation of model ABX is much slower in milk than in water. This is attributed to the competitive oxidation of milk components with the reactive oxygen species generated *in situ*. Furthermore, the milk became sticky after prolonged sonication [48], *e.g.* 4 h, resulting in the difficulty of the deproteinization of milk by centrifugation. To obtain clear supernatants, up to 26,000 rpm of centrifuging rate was compulsory for 5 min centrifugation. Before (after)

Table 1
Effect of US frequency on the sonolytic degradation of SMM in water and milk.

Liquid	f_{US} (kHz)	p_{US} (W)	t (min)	k_1 ($\times 10^{-3}$ min^{-1})	R^2	*DEs* (%)	C_t* (μg L^{-1})	t_{MRL} (min)
Water	40	82	60	1.48	0.9521	7.8	1844.2	2996
	80	71	60	2.46	0.9899	13.4	1731.0	1498
	120	87	60	3.23	0.9661	17.1	1657.5	999
	500	73	60	6.74	0.9609	31.6	1367.3	428
Milk	40	82	180	0.35	0.9865	6.3	1874.5	9986
	80	71	180	0.75	0.9555	13.8	1724.8	4280
	120	87	180	1.49	0.9695	25.1	1497.0	2996
	500	73	60	2.48	0.9817	14.6	1707.4	1498

Sonication conditions: initial SMM concentration, 6.62 μM (2.0 mg L^{-1}); reaction volume, 50 mL; initial pH in water and milk, 6.83 and 6.67; room temperature. Note: *C_t, the ABX concentration in the given time t; t_{MRL}, the time required to meet the maximum residue limit.

sonication, the pH values of CEF-, SMM-, MAR-, and OTC-spiked aqueous solutions were 5.37 (5.01), 6.96 (6.46), 6.01 (6.51), and 7.25 (6.64), respectively. For milk, their pH values were 6.48 (6.50), 6.55 (6.73), 6.50 (6.78), and 6.80 (6.96) before (after) sonication, respectively.

Considering the residue concentrations of the model ABX in milk, the degradation was further conducted at a lower initial concentration of 4.92 μM, *i.e.*, 2.75 mg L^{-1} CEF, 1.49 mg L^{-1} SMM, 1.78 mg L^{-1} MAR, and 2.26 mg L^{-1} OTC by sonication at 500 kHz and 259 W. To save the consumption of milk and shorten the reaction time, 50 mL ABX-spiked milk was used in this study. The sonolytic degradation of the various model ABX in milk follows PFO kinetics well (R^2: 0.9513–0.9636). The k_1 values of CEF, SMM, MAR, and OTC were calculated to be 3.8×10^{-2}, 3.6×10^{-2}, 3.3×10^{-2}, and 3.1×10^{-2} min^{-1}, respectively, leading to 92.1%, 89.9%, 87.6%, and 84.5% of *DEs* after 60 min sonication at 500 kHz and 259 W. The corresponding residue concentration and time met the MRLs are 217.6, 150.1, 220.9, 350.9 μg L^{-1} and 87, 75, 96, and 104 min for CEF, SMM, MAR, and OTC, respectively. The relationship between $lnk_{1,\ milk}$ values, and $LogK_{OW}$ values of the model ABX can be well-fitted by the linear Eq. S3 (R^2: 0.9975), indicating again that the sonolysis of the model ABX degradation is $LogK_{OW}$-dependent.

3.2. Critical factors affecting the sonolytic kinetics of SMM in water and milk

Sonolysis kinetics usually depends on various factors, such as US frequency and power, bulk temperature, initial ABX concentration, reaction volume, *etc.* [23]. The influence of the above factors on the sonolytic degradation kinetics of SMM in water and milk was investigated as follows.

3.2.1. Effect of ultrasonic frequency

Generally, the sonolytic kinetics of organics is US frequency-dependent [35,41,49]. Higher US frequencies (300–860 kHz) enhance the occurrence of cavitation events, the generation rate and amount of smaller cavities, and the collapse intensity, causing higher concentrations of reactive oxygen species during sonication. Thus, higher US frequencies favor the sonolytic degradation of contaminants [23,41,49]. Herein, the effect of US frequency on sonolytic degradation of SMM in water and milk was compared at 40, 80, 120, and 500 kHz at the power of 71–87 W. To save the use of milk and simulate the actual ABX concentration in milk during the experiment, 50 mL of 2.0 mg L^{-1} (6.62 μM) SMM solutions were sonicated. The results are shown in Table 1.

As shown in Table 1, the degradation of SMM in both water and milk follows the PFO kinetics well and SMM is much faster to be sonolytically degraded in water than in milk. A positive correlation between the k_1 values of SMM degradation in water or milk and the US frequencies was observed, verifying that high US frequencies favor ABX degradation. With reference to the Arrhenius equation in Section 3.2.3, the relationship between lnk_1 values of SMM degradation in water ($lnk_{1,\ water}$) or milk ($lnk_{1,\ milk}$) and the $1/f_{US}$ values can be fitted by the linear Eq. S4 (R^2: 0.9883) and S5 (R^2: 0.9384) in Table S6. The slope value (*i.e.* enhancement efficiency of the k_1 values of SMM degradation) in Eq. S5 is 1.8 folds higher than that in Eq. S4, indicating that the enhancement efficiency of increasing US frequency on the k_1 of SMM degradation in milk is more significant than that in water. The k_1 values of SMM degradation in water and milk at 120 kHz increase by 118% and 326% in comparison with that at 40 kHz in comparable US powers, respectively. The k_1 values of SMM degradation in water and milk at 500 kHz increase by 174% and 231% in comparison with that at 80 kHz in comparable US power, respectively. Moreover, the increasing US frequency also increases *DEs*, decreases residue concentrations, and shortens the sonication time required to meet the *MRL*.

The smaller microbubbles induced by higher US frequencies trigger Rayleigh contraction, causing more intense cavitation effects [50]. In general, an optimal range of US frequencies exists for the organic degradation by sonication, and 400–860 kHz US was usually regarded to bring about the strongest chemical effects [40,41,51]. Likewise, the

Table 2
Effect of US power on the sonolytic degradation of SMM in water and milk.

Liquid	p_{US} (W)	k_1 ($\times 10^{-2}$ min^{-1})	R^2	*DEs* (%)	C_t * (μg L^{-1})	t_{MRL} (min)
Water	73	0.67	0.9609	31.6	1367.3	428
	113	1.13	0.9575	50.8	983.5	272
	129	1.50	0.9667	60.4	791.0	200
	163	1.82	0.9557	69.5	609.1	166
	207	2.65	0.9768	79.8	404.8	115
	259**	5.02	0.9846	91.7	165.1	60
Milk	73	0.25	0.9817	14.6	1707.4	1498
	113	0.60	0.9637	28.1	1438.6	499
	129	0.75	0.9905	35.3	1293.1	374
	163	0.96	0.9932	43.2	1135.0	300
	207	1.65	0.9505	59.5	810.8	176
	259	3.30	0.9817	83.8	324.1	91

Sonication conditions: initial SMM concentration, 6.62 μM (2.0 mg L^{-1}); reaction volume, 50 mL; US frequency, 500 kHz; reaction time, 60 min; initial pH in water and milk, 6.81 and 6.66; room temperature. Note: *C_t, the ABX concentration in the given time t; t_{MRL}, the time required to meet the maximum residue limit; ** The reaction time is 50 min.

sonolytic efficiency at 500–860 kHz was scanned to be ~ 10 folds higher than that at 20 kHz [40,51]. Much lower *DEs* (66% and 67%) of 25 mg L^{-1} levodopa and paracetamol in 300 mL of aqueous solutions were obtained at 1,134 kHz (27 W) than those (91% and 90%) at 574 kHz (32 W) and those (95% and 92%) at 860 kHz (32 W) for 240 min sonication at 20°C [40].

3.2.2. Effect of ultrasonic power

In general, higher US powers also increase the occurrence of cavitation events, the generation rates, and the number of larger microbubbles, as well as the collapse intensity of microbubbles [23,41,49]. Under optimal US powers, the appropriate size and amount of microbubbles generated promote the formation of •OH radicals followed by an intensified sonolytic degradation [41]. To investigate the effect of US power, 50 mL of 2.0 mg L^{-1} (6.62 μM) SMM-spiked water/milk was sonicated at 73–259 W at room temperature. 500 kHz US was used as it exhibits stronger degradation of SMM above. The results are listed in Table 2.

As shown in Table 2, higher US power favors the sonolytic degradation of SMM both in water and milk. Moreover, much faster degradation of SMM was observed in water than in milk. The increasing US power also increases *DEs* and shortens the sonication time met the MRL. With reference to the Arrhenius equation in Section 3.2.3, the relationship between $lnk_{1,\ water}$ or $lnk_{1,\ milk}$ of SMM degradation in water or milk and the $1/p_{US}$ values can be fitted by the linear Eq. S6 (R^2: 0.8851) and S7 (R^2: 0.9196) in Table S6. The slope value in Eq. S7 is 1.29 folds higher than that in Eq. S6, indicating that the enhancement efficiency of increasing US power on the k_1 of SMM degradation in milk is more significant than that in water. The k_1 values of SMM degradation increased by 649.3% in water and 122.0% in milk with the increasing US power from 73 to 259 W. Lastre-Acosta *et al.* reported that the initial removal rates of 25 mg L^{-1} sulfadiazine in solutions increased from 2% to 79% at 1,142 kHz; 5.6% to 90% at 580 kHz; and 0.1% to 71% at 862 kHz with increasing power (1.5–31.0 W) for 120 min sonication at 30°C and pH 5.5 [41]. Isariebel *et al.* also found that the removal rates of levodopa and paracetamol in solution increase linearly with the US power [40]. The accelerated degradation of ABX can be attributed to the enhanced generation of reactive oxygen species at higher US powers.

3.2.3. Effect of bulk temperature

The bulk liquid temperature is of great importance for chemical reactions, as it determines the amount, size, implosion intensity, and local temperature of cavitation bubbles, as well as the effectiveness of sonolytic degradation. In general, the higher the bulk liquid temperature leads to more and larger cavitation bubbles [39,52]. To evaluate the influence of bulk temperature on the sonolysis of SMM, 50 mL of 2.0 mg L^{-1} (6.62 μM) SMM-spiked solution was sonicated at the above optimized US frequency of 500 kHz and US power of 259 W at 12, 25, and 40°C. The results are shown in Fig. 3. In addition, the effect of bulk temperature on the sonolysis of SMM in milk was studied under the same conditions as in water, and the results are discussed below in this section.

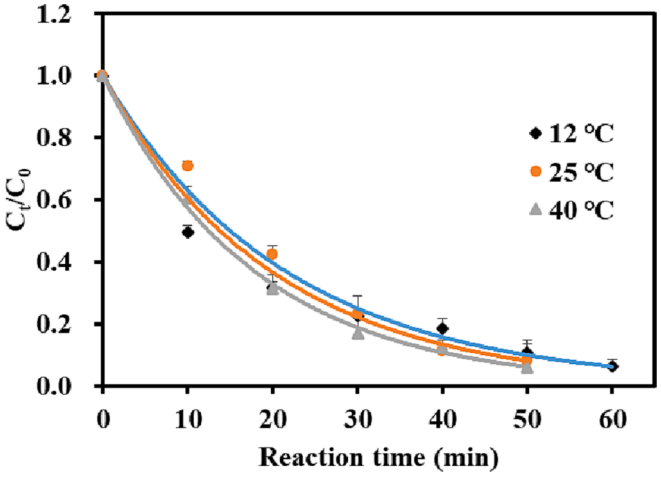

Fig. 3. Effect of bulk temperature on the sonolytic degradation of SMM in aqueous solutions (Sonication conditions: initial SMM concentration, 6.62 μM (2.0 mg L^{-1}); US frequency, 500 kHz; US power, 259 W; initial pH, 6.66).

As shown in Fig. 3, accelerated degradation of SMM was observed at high temperatures, but the difference in k_1 values (R^2: 0.9706–0.9996) is very slight. The k_1 values for SMM degradation are 4.6 × 10^{-2}, 5.0 × 10^{-2}, and 5.6 × 10^{-2} min^{-1} at 12, 25, and 40°C, respectively, leading to the relevant *DEs* are 89.2%, 91.7%, and 94.0% after 50 min sonication, respectively. The relevant residue concentrations of SMM are 123.7, 165.1, and 120.0 μg L^{-1} after 60, 50, and 50 min sonication, respectively. It is similar to the observation by De Bel *et al.*, *i.e.*, the k_1 values increased from 5.5 × 10^{-3} to 10.5 × 10^{-3} min^{-1} as the bulk temperature increased from 15 to 45°C during the sonolysis of 15.0 mg L^{-1} ciprofloxacin at 544 kHz and 200 W in aqueous solutions for 120 min at pH 7 [39].

In milk, the difference in k_1 values (R^2: 0.9738–0.9817) obtained among different temperatures is also tiny. The k_1 values are 3.1 × 10^{-2}, 3.3 × 10^{-2}, and 3.4 × 10^{-2} min^{-1} at 12, 25, and 40°C, respectively, leading to the relevant *DEs* are 82.0%, 83.8%, and 84.8% after 60 min sonication. The relevant residue concentrations of SMM in milk are 359.3, 324.1, and 304.6 μg L^{-1} after 60 min sonication, and the time values reached the *MRL* were calculated to be 97, 91, and 88 min at 12, 25, and 40°C, respectively.

Similarly, the enhancement efficiency of the k_1 values of SMM degradation in water and milk by increasing bulk temperature can be evaluated using the Arrhenius equation, where the larger the slope, the higher the enhancement efficiency, *i.e.*, the reaction is more sensitive to bulk temperature. The relationship between $lnk_{1,\ water}$ or $lnk_{1,\ milk}$ of SMM degradation in water or milk and the bulk temperature is thus fitted by the linear Eq. S8 (R^2: 0.9946) and S9 (R^2: 0.9542) in Table S6. The slope value in Eq. S8 is 2.14 folds larger than that in Eq. S9, indicating that the enhancement efficiency of bulk temperature on the k_1 of SMM degradation in water is more significant than that in milk [39,52]. It has been reported that bulk temperature shows complex effects on the sonolytic degradation of organics as it is closely associated with the key factors *e.g.*, the viscosity of matrix vapor pressure, the surface tension of bubbles, gas solubility, *etc.* [53]. Herein, the accelerated degradation of SMM may be contributed to the enhanced generation of cavitation of microbubbles, the occurrence of cavitation events, and the production of reactive oxygen species caused by the declined surface tension, viscosity, and the threshold of cavitation [54]. Another possible reason is the promoted mass transfer of SMM and the active species, as well as the reactivity at higher bulk temperatures [39].

The apparent activation energy for the sonolytic degradation of SMM was calculated using the Arrhenius equation, as shown in Eq. (4) [14,39]:

$$\ln k_1 = -E_a/RT + \ln A \quad (4)$$

where E_a is apparent activation energy (J mol^{-1}), R is gas constant (8.314 J mol^{-1} K^{-1}), A is a pre-exponential factor (min^{-1}), k_1 is the PFO constant (min^{-1}), and T is bulk temperature (K).

The E_a value of the sonolytic degradation of SMM in water is calculated to be 5.2 kJ mol^{-1}, but that in milk cannot be calculated due to the complex component of milk. De Bel *et al.* reported that the relevant apparent activation energy for the sonolysis of 15 mg L^{-1} ciprofloxacin in water was 17.5 kJ mol^{-1} [39]. These results suggest that the sonolytic degradation in water is diffusion controlled, and the apparent degradation rate may represent the transmission rate of SMM in bulk matrices to the active species-rich zones of the gas/liquid interface [55].

Table 3
Effect of initial SMM concentration on the sonolytic degradation of SMM in water and milk.

Liquid	C_0 (mg L^{-1})	t (min)	k_1 ($\times 10^{-2}$ min^{-1})	R^2	*DEs* (%)	*RRs** (μg min^{-1})	C_t** (μg L^{-1})	t_{MRL} (min)
Water	0.5	20	11.9	0.9574	96.1	1.20	32.6	14
	1.0	40	7.9	0.9687	96.9	1.21	31.2	29
	2.0	50	5.0	0.9846	91.7	1.83	165.1	60
Milk	0.5	20	5.6	0.9598	71.3	0.89	143.3	29
	1.0	40	4.5	0.9804	85.4	1.07	146.3	51
	2.0	60	3.3	0.9817	83.8	1.40	324.1	91

Sonication conditions: reaction volume, 50 mL; US frequency, 500 kHz; US power, 259 W; initial pH in water and milk, 6.81 and 6.66; room temperature. Note: **RRs*: removal rates; **C_t, ABX concentration in the given time *t*; t_{MRL}, time met the maximum residue limit.

Table 4
Effect of reaction volume on the sonolytic degradation of SMM in water and milk.

Liquid	V_0 (mL)	t (min)	k_1 ($\times 10^{-2}$ min^{-1})	R^2	*DEs* (%)	*RRs** (μg min^{-1})	C_t** (μg L^{-1})	t_{MRL} (min)
Water	50	50	5.0	0.9846	91.7	1.83	165.1	60
	100	60	4.1	0.9785	89.2	2.97	216.4	73
	150	60	3.3	0.9789	83.4	4.17	331.4	91
	200	60	2.0	0.9513	64.1	4.27	717.5	150
	250	90	1.6	0.9907	76.5	4.25	470.4	187
Milk	50	60	3.3	0.9817	83.8	1.40	324.1	91
	100	120	2.2	0.9620	94.9	1.58	102.6	136
	150	150	1.6	0.9700	92.6	1.85	147.2	187
	200	180	1.1	0.9818	88.8	1.97	224.6	272
	250	180	0.6	0.9751	68.1	1.89	637.9	499

Sonication conditions: initial SMM concentration, 6.62 μM (2.0 mg L^{-1}); US frequency, 500 kHz; US power, 259 W; initial pH in water and milk, 6.81 and 6.67; room temperature. Note: **RRs*, Removal rates; **C_t, ABX concentration in the given time *t* (min); t_{MRL}, time met the maximum residue limit.

3.2.4. *Effect of initial SMM concentration and reaction volume*

Initial concentration is also a critical factor affecting ABX degradation by sonication [35,39]. In this study, 50 mL of 1.66 μM (0.5 mg L^{-1}), 3.31 μM (1.0 mg L^{-1}), and 6.62 μM (2.0 mg L^{-1}) SMM was sonicated in water or milk at 500 kHz and 259 W at room temperature. The results are shown in Table 3.

As shown in Table 3, the sonolytic degradation of SMM at various initial SMM concentrations in water and milk follows PFO kinetics well (R^2: 0.9574–0.9818). The degradation of SMM was faster in water than in milk. With the increasing initial SMM concentration from 0.5 to 2.0 mg L^{-1} in water and milk, the k_1 values decreased by 58.0% and 41.1%, respectively. De Bel *et al.* reported that the k_1 values decreased from 2.04×10^{-2} to 9.00×10^{-4} min^{-1} as the initial ciprofloxacin concentration increased from 0.15 to 150.00 mg L^{-1} by sonication at 544 kHz, 200 W, and pH 7 for 120 min [39]. With reference to the Arrhenius equation in this section, the relationship between k_1 values of SMM degradation and the initial SMM concentration in water or milk can be fitted by the linear Eq. S10 (R^2: 0.9751) and S11 (R^2: 0.9918) in Table S6. The slope value in Eq. S10 is 1.62 folds higher than that in Eq. S11, indicating that the influence of initial SMM concentration on the k_1 of SMM degradation in water is more significant than that in milk. Significantly, the residue concentrations raised and the sonication time reached the MRL of SMM prolonged as the increasing initial SMM concentration. In addition, the removal rates (μg min^{-1}) of SMM in water and milk were almost stable at lower initial concentrations (0.5–1.0 mg L^{-1}), but increased at a higher initial concentration (2.0 mg L^{-1}), indicating that more amounts of SMM were degraded at higher initial concentration.

SMM possesses high hydrophobicity and it can be relatively accumulated in the gas/liquid interface of cavitational bubbles during bubble oscillation and is subsequently oxidized by active species formed *in situ*. The formation rate of $^{\bullet}$OH radicals during sonochemical reactions is found to be irrelevant to the initial concentration of nonvolatile substrates, and the concentration of $^{\bullet}$OH radicals (or active sites) in solutions could almost instantly reach a stable value [39,46]. It can be also inferred that the concentration of active species in milk is lower than that in aqueous solutions. Therefore, the sonolytic degradation of SMM was alleviated in milk with a higher initial SMM concentration. Moreover, the increasing concentration of SMM can improve the reaction opportunity of SMM with reactive oxygen species, thereby more amount of SMM could be oxidized [56].

The reaction volume can also affect the power density of the reaction system followed by a significant effect on the degradation rates of ABX. The degradation rates generally mitigate with increasing reaction volume [23]. To investigate the effect of reaction volume (V_0), 50–250 mL of 2.0 mg L^{-1} (6.62 μM) SMM in water or milk were sonicated at 500 kHz and 259 W at room temperature. The results are presented in Table 4.

As summarized in Table 4, the degradation of SMM in water and milk follows the PFO kinetics well (R^2: 0.9513–0.9906), and the smaller the water/milk volume, the faster the degradation of SMM. In comparison with milk, the degradation of SMM could be relatively faster in water by sonication. The k_1 values decreased by 68.0% (water) and 81.8% (milk) with increasing reaction volume from 50 to 250 mL, respectively. At the same time, the increased reaction volume increased the residue concentrations and the sonication time to reach the *MRL* of SMM. The relationship between k_1 values of SMM degradation and reaction volume can be fitted by the linear Eq. S12 (R^2: 0.9714) and S13 (R^2: 0.9853) in Table S6. The slope value in Eq. S13 is 1.37 folds higher than that in Eq. S12, indicating that the influence of reaction volume on the k_1 of SMM degradation in milk is more significant than that in water. These results could be attributed to the more energy consumed by milk components and more intense competitive reactions with large reaction volumes.

Matouq *et al.* also reported a decreased degradation on 50 or 100 ppm amoxicillin with increasing reaction volumes from 40 to 60 mL in the presence of 2 mL of 50% H_2O_2 at 2.4 MHz and 9.5 W (electric power) for 90 min [57]. It was reported that the increased operating volume creates more dead zones, in which the cavitational activity is the weakest among the system followed by impair effects [58]. In addition,

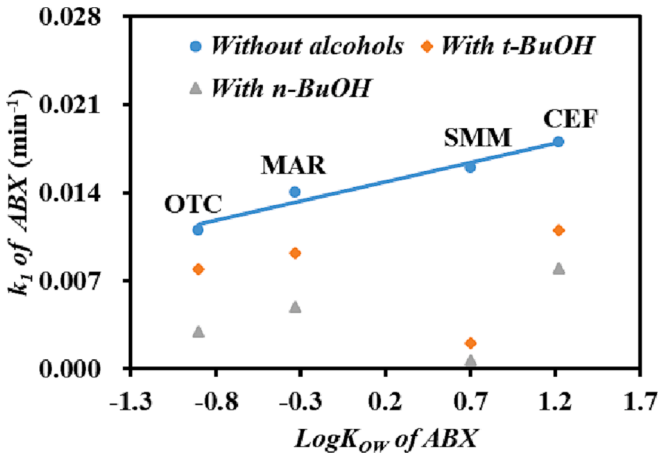

Fig. 4. The dependence of k_1 on the $LogK_{OW}$ of the model ABX in aqueous solutions (Sonication conditions: initial ABX concentration, 6.62 μM (2.0 mg L^{-1}); reaction volume, 250 mL; concentration of *n*-butanol, 1,144 μL (50 mM); concentration of *t*-butanol, 1,179 μL (50 mM); US frequency, 500 kHz; US power, 259 W; reaction time, 90 min; initial pH, 5.35–7.21; room temperature). Note: *t*-BuOH, *t*-butanol; *n*-BuOH, *n*-butanol.

the increasing reaction volume results in a decrease in US power density [38], but the removal rates (μg min^{-1}) increased with the increasing reaction volume and reach stable values. In this study, the optimal reaction volume is 150 mL in both water and milk. It can be speculated that the generated reactive oxygen species in 150–250 mL were almost constant as the increasing reaction volume will form the so-called dead zones [58].

3.3. Influence of radical scavengers on ABX degradation in water

The investigation of ABX degradation in the presence of radical scavengers, such as *n*-butanol and *t*-butanol, is beneficial to elaborate the sonolytic degradation mechanism [38,39,41]. 250 mL of 6.62 μM ABX-spiked solutions (equal to 3.7 mg L^{-1} CEF, 2.0 mg L^{-1} SMM, 2.4 mg L^{-1} MAR, and 3.0 mg L^{-1} OTC, respectively) were sonicated at 500 kHz, and 259 W for 90 min in the absence or presence of 1,144 μL *n*-butanol (50 mM) or 1,179 μL *t*-butanol (50 mM) at room temperature. To facilitate the addition of *n*-butanol or *t*-butanol and the analysis of ABX, large reaction volumes were used in this study. The results are shown in Fig. 4.

As shown in Fig. 4, k_1 values of ABX sonolysis obviously depend on their $LogK_{OW}$ values, *i.e.* the higher the $LogK_{OW}$ values of ABX result in faster degradation in water. The relationship between k_1 values and $LogK_{OW}$ values of ABX can be well fitted by the linear Eq. S14 (R^2: 0.9425). Furthermore, the addition of *n*-/*t*-butanol obviously inhibited the sonolytic degradation of ABX in solutions, indicating that the degradation of model ABX was mainly induced by reactive oxygen species formed *in situ*.

In Fig. 4, the presence of *n*-butanol exhibits more serious inhibition than *t*-butanol on the sonolytic degradation of ABX. The $LogK_{OW}$ value of *n*-butanol ($LogK_{OW}$: 0.88) is much higher than that of *t*-butanol ($LogK_{OW}$: 0.35), which means that the former is a hydrophobic compound and closer to the formed cavitational bubbles than the hydrophilic latter during sonication. Thus, more generated reactive oxygen species could be eliminated by *n*-butanol rather than by *t*-butanol. Moreover, it has been reported that *n*-butanol and *t*-butanol can enhance the generation of cavitation bubbles and shrink the size of bubbles in ultrasonic systems to hinder the cavitation bubbles aggregation, which favors the generation of free radicals [14,59–61].

The inhibition efficiencies by *t*-butanol and *n*-butanol on the sonolysis of SMM reached the maximal of 87.5% and 95.6%, relatively. The $LogK_{OW}$ value of SMM (0.70) is closest to those of both *t*-butanol and *n*-butanol among the four model ABX, where more serious competitive free radicals reactions in the sonolysis system may occur between alcohols and SMM than other model ABX. Meanwhile, *n*-butanol exhibits more significant inhibition on SMM degradation than *t*-butanol, which can be attributed to the closer $LogK_{OW}$ values of *n*-butanol than *t*-butanol to SMM.

Besides SMM, the inhibition efficiencies by *t*-butanol are ordered as follows: CEF (38.9%) > MAR (34.3%) > OTC (28.2%), however, the inhibition efficiencies by *n*-butanol are ordered as follows: OTC (73.6%) > MAR (65.0%) > CEF (55.6%). Specifically, apart from SMM, the inhibition efficiencies by *t*-butanol are proportional to $LogK_{OW}$ values, while an opposite trend was observed with the addition of *n*-butanol. This result demonstrates that the degradation of model ABX occurs in different zones around the bubbles.

Since the model ABX are non-volatile substances (the boil points of the model ABX are in the range of 548.5–817.1°C, Table S5 [14,37]), thus they are mainly oxidized in bulk solution or at the interface of bubbles [38]. The hydrophobic CEF were mainly oxidized near the bubbles, where the concentration of free radicals is highest among the three reaction zones. For example, the k_{OH} values of the model ABX and *n*-butanol in aqueous solutions are ordered as follows: CEF (9.6×10^{10} M^{-1} s^{-1}) > MAR (9.0×10^{9} M^{-1} s^{-1}) > OTC (7.0×10^{9} M^{-1} s^{-1}) > *n*-butanol (5.5×10^{8} M^{-1} s^{-1}) [43–45,62], while their $LogK_{OW}$ values are ordered as follows: CEF (1.2) > *n*-butanol > MAR (-0.3) > OTC (-0.9). Despite the generated free radicals being partly consumed by *n*-butanol, CEF still can be rapidly removed since it possesses larger reaction rates and is closer to bubbles than *n*-butanol. In terms of the relevant hydrophilic MAR and OTC, they have mainly degraded in the bulk solution by free radicals transferred from the gas/liquid interface of the bubbles since their lower $LogK_{OW}$ values among the model ABX. However, the presence of *n*-butanol reduced the transferred amount of free radicals and lowered the concentration of free radicals in bulk solutions. OTC shares a smaller $LogK_{OW}$ value than MAR, leading to a poorer mass transfer of OTC to the free radicals-rich zone than MAR followed by a slower degradation rate of OTC than MAR. It is speculated that the larger inhibition efficiency of CEF by *t*-butanol may be caused by the increased dispersion of CEF in *t*-butanol (as a dispersant) in the bulk solution, meaning that it is more difficult for CEF transfer from the bulk solution to the gas/liquid interface [63]. In bulk solutions, however, the available free radicals for the oxidation of CEF are much less than in gas/liquid interface. Thus, it is reasonable that *t*-butanol imposed smaller inhibition to MAR and OTC than CEF. The higher inhibition efficiency by *t*-butanol for degrading MAR than OTC may arise from the same reason.

To be mentioned, it is predictable that the degradation of ABX in milk is relatively slower than in water since there are multiple radicals scavengers in milk, such as caseins, ascorbate, urate, *etc.*, which increases the difficulty in clarifying the role of *n*-/*t*-butanol on ABX sonolytic degradation in milk [64]. Therefore, the effect of scavengers on ABX degradation in milk was not evaluated in this study.

3.4. Role of adding extra H_2O_2 and $Na_2S_2O_8$ on SMM degradation in water and milk

The degradation of ABX by sonication alone has several disadvantages such as relatively high energy consumption, long reaction time, and low mineralization [23]. Adding extra common oxidants, such as H_2O_2 and $Na_2S_2O_8$, can overcome the above limitation and promote AOPs by producing extra $^{\bullet}OH$ ($E(^{\bullet}OH/H_2O) = 1.9–2.7$ V) or $SO_4^{\bullet-}$ ($E(SO_4^{\bullet-}/SO_4^{2-}) = 2.5–3.1$ V), and other reactive species (Reactions 14–16) [14,23,44,65]. It has been reported that H_2O_2 can act as a radical

promoter or scavenger, depending on the product and the conditions used (Reaction 17) [38,40,57]. Similarly, high doses of persulfate can lead to a scavenging reaction by $SO_4^{\bullet-}$ itself or with the remaining persulfate ions (Reactions 18 and 19) [23,33,66].

$$HO_2^{\cdot} + H_2O_2 \rightarrow {}^{\cdot}OH + H_2O + O_2 \quad (14)$$

$$S_2O_8^{2-} \xrightarrow{OH^-/thermal/US} 2\,SO_4^{\cdot-}\ (or\ S_2O_8^{2-} + {}^{\cdot}OH \rightarrow SO_4^{\cdot-} + 0.5\,O_2) \quad (15)$$

$$SO_4^{\cdot-} + H_2O \rightarrow SO_4^{2-} + {}^{\cdot}OH + H^+ \quad (16)$$

$$H_2O_2 + {}^{\cdot}OH \leftrightarrow H_2O + HO_2^{\cdot} \quad (17)$$

$$2\,SO_4^{\cdot-} \rightarrow S_2O_8^{2-}\ k = 4.0 \times 10^8\ M^{-1}s^{-1} \quad (18)$$

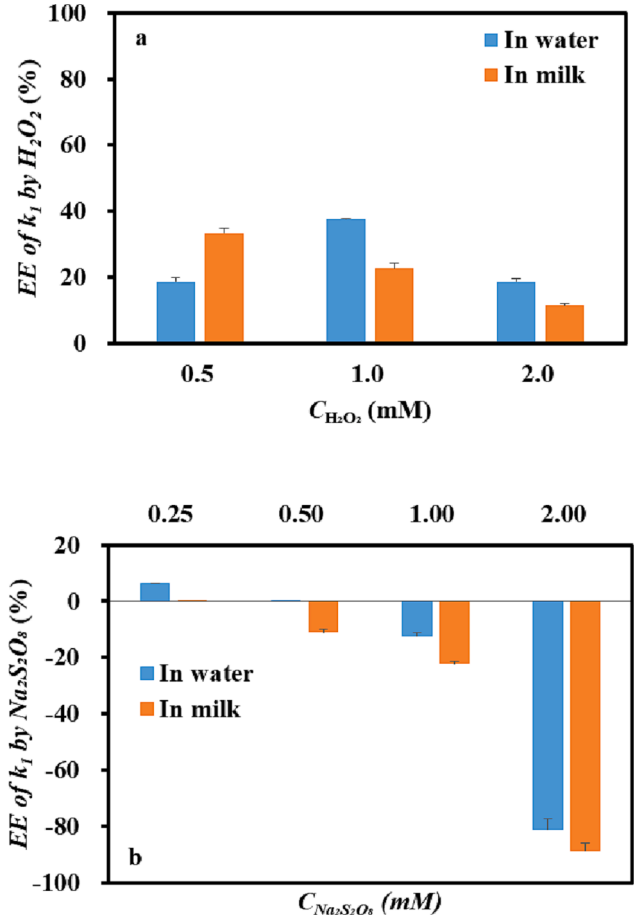

Fig. 5. Effect of adding extra H_2O_2 (a) and $Na_2S_2O_8$ (b) on the sonolytic degradation of SMM in water and milk (Sonication conditions: initial SMM concentration, 6.62 μM (2.0 mg L^{-1}); reaction volume, 250 mL (aqueous solution) or 125 mL (milk); US frequency, 500 kHz; US power, 259 W; initial pH in water and milk, 7.40–7.61 and 6.53–6.56; room temperature). Note: *EE*, enhancement efficiency.

$$S_2O_8^{2-} + SO_4^{\cdot-} \rightarrow SO_4^{2-} + S_2O_8^{\cdot 2-}\ k = 6.1 \times 10^5\ M^{-1}s^{-1} \quad (19)$$

To optimize and further understand the mechanism of ABX degradation, 2.0 mg L^{-1} (6.62 μM) SMM-spiked solution or medicated milk was sonicated at 500 kHz and 259 W in the presence of 0.50, 1.00, and 2.00 mM H_2O_2 (or 0.25, 0.50, 1.00, and 2.00 mM $Na_2S_2O_8$) at room temperature. Considering the effect of sampling on the total volume and the feasibility of adding H_2O_2 or $Na_2S_2O_8$, a large volume (250 mL) of SMM solutions was used in this study. To reduce reaction time and milk consumption, however, 125 mL of milk was used for the investigation of SMM degradation under the same conditions. The results are shown in Fig. 5.

As shown in Fig. 5a, adding extra H_2O_2 in the reaction system remarkably improved SMM removal. With the addition of 0.5, 1.0, and 2.0 mM H_2O_2 in water, the k_1 values reached 1.9×10^{-2}, 2.2×10^{-2}, and 1.9×10^{-2} min^{-1}, respectively, which increased by 18.8%, 37.5%, and 18.8% as compared without extra H_2O_2. In milk, the k_1 values reached 1.2×10^{-2}, 1.1×10^{-2}, and 1.0×10^{-2} min^{-1} in the presence of 0.5, 1.0, and 2.0 mM H_2O_2, respectively, which increased by 33.3%, 22.6%, and 11.5%. Moreover, the pH values of the SMM-spiked aqueous solutions and milk before and after degradation are in the range of 7.40–7.61 and 6.53–6.56, respectively. Overall, the appropriate dosages of H_2O_2 for promoting SMM degradation in water and milk are 1.0 and 0.5 mM, respectively. H_2O_2 facilitates SMM degradation by increasing concentration of reactive species (Reaction 14), but excess H_2O_2, as a radical scavenger, could decrease the *DEs* in the reaction system (Reaction 17).

As shown in Fig. 5b, adding small amounts of $Na_2S_2O_8$ (0.25 or 0.50 mM) in the reaction system slightly promoted the degradation of SMM, but excess $Na_2S_2O_8$ (0.25–1.00 mM) significantly inhibited the degradation of SMM in both water and milk. With the addition of 1.0 and 2.0 mM $Na_2S_2O_8$ in water, the k_1 values dropped to 1.4×10^{-2} and 0.3×10^{-2} min^{-1}, respectively, which decreased by 12.5%, and 81.3%. However, adding the lower dosage of $Na_2S_2O_8$ (0.25 and 0.5 mM) in water slightly increased the k_1 values of SMM degradation by 6.25% and 0.12%, respectively. Similarly, adding 0.5, 1.0, and 2.0 mM $Na_2S_2O_8$ in milk, the k_1 values dropped to 8.0×10^{-3}, 7.0×10^{-3}, and 1.0×10^{-3} min^{-1}, respectively, which decreased by 11.1%, 22.2%, and 88.9%. Nevertheless, the k_1 value of SMM degradation increased by 0.1% by adding the lower dosage of $Na_2S_2O_8$ (0.25 mM) in milk. Moreover, the pH values of 2.0 mg L^{-1} (6.62 μM) SMM-spiked solution and milk in the presence of $Na_2S_2O_8$ are in the range of 7.26–7.45 and 6.50–6.56 before and after sonication, respectively.

The added $Na_2S_2O_8$ may not be effectively activated under sonication [23]. Thus, the inhibition of the sonolytic degradation of SMM in water and milk may also be contributed by the consumption of free radicals by $S_2O_8^{2-}$ (Reaction 20) [65], for example:

$$S_2O_8^{2-} + {}^{\cdot}OH \rightarrow OH^- + S_2O_8^{\cdot-}\ k = 1.2 \times 10^7\ M^{-1}s^{-1} \quad (20)$$

It has also been reported that the sulfate ion can scavenge free radicals, leading to the generation of fewer reactive species [67]. Moreover, $SO_4^{\bullet-}$ is the predominant radical at a pH < 7; both $SO_4^{\bullet-}$ and $^{\bullet}OH$ are present at pH 9; $^{\bullet}OH$ is the predominant radical at a more basic pH (*i.e.* pH 12) [65,67]. At pH > 7, the reaction of $SO_4^{\bullet-}$ with OH^- resulted in the formation of SO_4^{2-} and $^{\bullet}OH$ (Reaction 16). However, the removal efficiency decreased due to the elimination of $SO_4^{\bullet-}$ and $^{\bullet}OH$ via their

Table 5
Sonolytic degradation of SMM in various kinds of milk.

Milk	*t* (min)	k_1 ($\times 10^{-2}$ min^{-1})	R^2	*DEs* (%)	*RRs** (μg min^{-1})	C_t** (μg L^{-1})	t_{MRL} (min)
M1	130	2.2	0.9620	95.2	1.46	96.3	136
M2	150	2.1	0.9599	97.4	1.30	52.9	143
M3	150	2.0	0.9917	95.8	1.28	83.7	150

Sonication conditions: initial SMM concentration, 6.62 μM (2.0 mg L^{-1}); milk volume, 100 mL; US frequency, 500 kHz; US power, 259 W; initial pH, 6.56–6.65; room temperature. Note: **RRs*, Removal rates; ***C*$_t$, the ABX concentration in the given time *t* (min); t_{MRL}, the time required to meet the maximum residue limit.

interaction (Reaction 21) [23].

$$SO_4^{\cdot-} + {}^{\cdot}OH \rightarrow HSO_4^- + 0.5\ O_2 \quad (21)$$

3.5. Sonolytic degradation of SMM in various kinds of milk

Milk components may interact with ABX degradation processes [14,68]. In our previous work, fat and fatty acids in milk diminished the ozonolytic degradation of SMM and OTC [14]. To understand the effect of various kinds of milk on SMM degradation, 2.0 mg L^{-1} (6.62 μM) SMM-spiked milk was sonicated for 130–150 min at 500 kHz and 259 W in various kinds of milk (labeled as M1, M2, and M3) at room temperature. To reduce milk consumption and shorten the reaction time, 100 mL of milk was sonicated for each batch. The component of milk is shown in Table S1. The results are shown in Table 5.

As shown in Table 5, all the SMM residues in any milk can meet the MRL (100 μg L^{-1}) after 130–150 min sonication. There is a tiny difference in the k_1 values (<9.1%) of SMM degradation among the various kinds of milk, and the k_1 values are ordered as follows: M1 > M2 > M3, which is consistent with the order of their thickness and creaminess in milk. Compared with M1, the time met the *MRL* value for SMM degradation in M2 and M3 increased by 5.1% and 10.3%, respectively. Moreover, the pH values of the SMM-spiked milk before (after) sonication were 6.56 (6.70), 6.64 (6.70), and 6.65 (6.74) for M1, M2, and M3, respectively. The relationship between k_1 values of SMM degradation and saturated fat or fatty acid in milk (*SF* or *FA*) can be fitted by the linear Eq. S15 (R^2: 0.9770) and S16 (R^2: 0.9631) in Table S6. The slope value in Eq. S16 is 1.39 folds larger than that in Eq. S15, indicating that the fat acid shows more significant inhibition efficiency than saturated fat on the k_1 of SMM degradation in milk. In addition, the removal rates (μg min^{-1}) of SMM slightly decreased (<12.3%) with the increasing thickness and creaminess of milk, indicating that fewer SMM were degraded in more viscous milk. Briefly, the sonolytic degradation rates of SMM are slightly affected by the milk components. Antti *et al.* stated that the increase in viscosity of the solution leads to a decrease in degradation. It is known that cavitation can be hampered by viscous liquids. On the other hand, bubbles collapse in viscous liquids is stronger than the collapse in low-viscosity media [69]. Xiao *et al.* summarized that the concentration and diffusivity of matrix organics in complex water matrices dominate the degradation of substrates by sonication at 20 or 620 kHz and 400 W L^{-1}, and low concentrations and large sizes of substrates show a small influence on their sonochemical degradation [70]. Kitazono *et al.* found that the degradation rates of 100 mg L^{-1} OTC in raw milk were lower than those in whole milk. >99% of OTC in the fat-free milk was removed during the 6-h electrochemical oxidation, whereas that was 83% in raw milk. The calculated k_1 value for OTC was 0.65 min^{-1} in the fat-free milk [68].

3.6. Intermediates and pathways of ABX degradation via sonication in water

The determination of intermediates formed during the ABX degradation contributes to the understanding of sonolytic mechanisms and the identification of degradation pathways. To determine major by-products of the model ABX in aqueous solutions, the four treated samples (192.8 μM CEF sonicated for 150 min, 192.8 μM SMM sonicated for 120 min, 192.8 μM MAR sonicated for 120 min, and 192.8 μM OTC sonicated for 180 min) via the experiments described in Section 3.1 in solutions were selected and analyzed by LC/MS. The ion chromatograms obtained in positive ion electrospray for the model ABX and their intermediates are shown in Appendix B.

As shown in Appendix B, the main fragment of protonated molecular ion ($[M + H]^+$) of CEF included *m/z* (*m/z* mass-to-charge ratio) 379.025 (retention time (*RT*): 16.96 min), *m/z* 354.554 (*RT*: 16.32 min), *m/z* 307.515 (*RT*: 9.79 min), *m/z* 290.794 (*RT*: 12.90 min), *m/z* 277.039 (*RT*: 12.05 min), and *m/z* 178.476 (*RT*: 1.45 min). CEF underwent the cleavage of amide bonds (connecting with β-lactam ring) to generate *m/z* 201, it was further produced *m/z* 178 via a dehydration reaction, deamination reaction, and hydroxylation. Another possible pathway is the indirect generation of *m/z* 379 from desfuroylceftiofur (DFC), the main intermediate during the degradation of CEF (not identified in this study), via oxidation of thiols, hydroxylation, deamination reaction, demethoxylation reaction. Furthermore, *m/z* 290, *m/z* 354, and *m/z* 277 can directly derive from CEF via the carboxylation of carbonyl groups, cleavage of thioester bonds; the demethoxylation reaction, deathiazol-2-amine reaction, hydrazonation of amino and cyano groups, cleavage of the β-lactam ring, decarboxylation reaction; as well as demethylation, cleavage of the β-lactam ring, and hydroxylation, respectively [71–75].

For SMM, the peak of the parent compound, with an *RT* value of 5.50 min, was confirmed by molecular ions of $[M + H]^+$ at *m/z* 281.981. The main fragment ions of SMM included *m/z* 308.009 (*RT*: 9.77 min), *m/z* 291.371 (*RT*: 12.80 min), *m/z* 277.039 (*RT*: 12.039 min), and *m/z* 178.147 (*RT*: 1.47 min). SMM was undergone the hydroxylation, demethylation, and opening of the pyrimidine ring to generation *m/z* 291. Afterward, *m/z* 308, *m/z* 277, and *m/z* 178 directly stemmed from *m/z* 291 via hydroxylation and deamidation; hydroxylation, deamidation, and dehydroxylation; as well as deamidation and dihydroxylation, SO_2 abstraction, and dehydrogenation, respectively. Moreover, *m/z* 277 can also be generated via demethylation, the opening of the pyrimidine ring, deamidation, and hydroxylation of SMM [76–78].

For MAR, the peak of the parent compound, with an *RT* value of 4.78 min, was confirmed by molecular ions of $[M + H]^+$ at *m/z* 363.123. The main fragment ions of MAR included *m/z* 379.766 (*RT*: 3.54 min), *m/z* 307.186 (*RT*: 9.77 min), *m/z* 292.03 (*RT*: 12.88 min), *m/z* 277.698 (*RT*: 12.04 min), and *m/z* 275.804 (*RT*: 1.45 min). The intermediates *m/z* 292 with isomeric structures could be derived from *m/z* 336, the main intermediate of MAR (not identified in this study), via decarboxylation reaction. Another possible pathway is the demethylation, hydroxylation, and decarboxylation reaction of MAR to generate *m/z* 307. Afterward, *m/z* 277 and *m/z* 275 stemmed from *m/z* 307 via dehydroxylation, demethylation; and defluoridation, demethylation, respectively. Additionally, the oxygenation reaction of MAR can generate *m/z* 379 (a) and (b) with isomeric structures [79–81].

For OTC, the peak of the parent compound, with an *RT* value of 4.90 min, was confirmed by molecular ions of $[M + H]^+$ at *m/z* 461.267. The main fragment ions of OTC included *m/z* 308.092 (*RT*: 9.76 min), *m/z* 292.03 (*RT*: 12.82 min), *m/z* 277.039 (*RT*: 12.05 min), and *m/z* 178.559 (*RT*: 1.46 min). OTC underwent electrophilic addition, hydrogen abstraction, opening ring reaction, and hydroxylation to generate *m/z* 308. Then, *m/z* 292 (a) and (b) were derived from *m/z* 308 via dehydration; and hydroxylation, hydrogen abstraction, and demethanol, respectively. The *m/z* 178 can be generated via further oxygenation reaction, opening ring, forming ring, and hydrogen abstraction of *m/z* 292 (a). Another possible pathway is dehydration, electrophilic addition, hydrogen abstraction, opening ring reaction, and hydroxylation of OTC to generate *m/z* 292 (a), and electrophilic addition, hydrogen abstraction, opening ring reaction, and hydroxylation of OTC to generate *m/z* 292 (b). The further dihydroxylation of *m/z* 292 (b) could generate *m/z* 277 (a) and (b) [82–87]. From the above-described results, the sonolytic degradation pathways of the model ABX was presented in Fig. 6.

The aforementioned intermediates could be gradually transferred to smaller molecules and finally decomposed into H_2O and CO_2.

3.7. Changes in the main nutrients of milk and antibacterial activity after sonication

The evaluation of nutrient changes in milk after sonication is crucial information for the economic feasibility of the sonochemical process for ABX removal from milk. The nutrient components in milk before and after sonication for 30 and 60 min are shown in Table S7 (The original version is shown in Appendix A in Italian). As shown in Table S7, there is

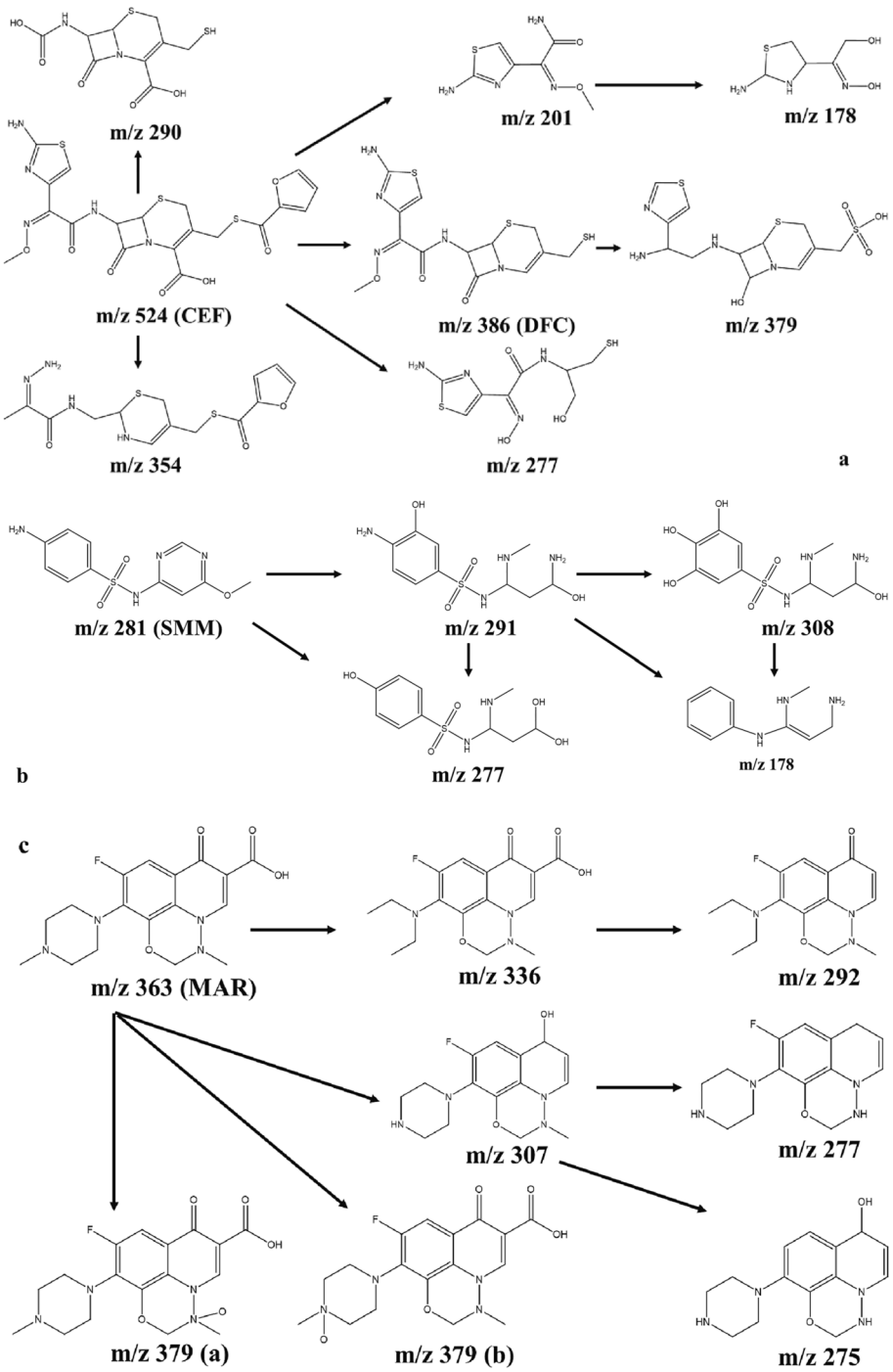

Fig. 6. The proposed scheme of CEF (a), SMM (b), MAR (c), and OTC (d) sonolytic degradation pathways in water.

a slight increase in fat (2.0%), protein (3.0%), caseins (2.9%) contents, and lean dry residue (0.8%) in milk, while a slight decrease in lactose (0.9%) and urea (8.2%) contents were observed by 60 min sonication. The casein index (Casein/protein, %) and the cryoscopy temperature are slightly increased after sonication. In addition, the amounts of somatic cells (Cell × 1000/mL) increased by 70.8% and 133.3% after 30 and 60 min sonication, respectively. Nevertheless, sonication did not lessen the total bacterial load (ufc × 1000/mL, where ufc stands for *unité formant colonie*, meaning the colony forming unit) within 60 min sonication. It has been reported that milk exerts a sono-protective effect on bacteria, such as *Escherichia coli* and *Listeria monocytogenes*, *etc.* [88]. In addition, no foams above milk were observed during sonication as compared with ozonation [14]. Overall, there is no obvious change in the contents of nutrients in milk caused by sonication. A similar result has also been reported by Deshwal *et al.*, merging treatment including sonication showed minimal changes in milk nutrients were stated there [89]. Overall, from a qualitative point of view, the main components in milk will react with reactive species produced by sonication, leading to slight changes in the nutrients of milk. From a quantitative point of view, however, the nutrient content in milk does not change significantly during the <3-hour sonication since the concentration of reactive oxygen species (about μM level) produced by sonication is minor compared to the nutrient content (1%–10%) [89]. On the other hand, it should be noted that the decontaminant waste milk after sonication will not be

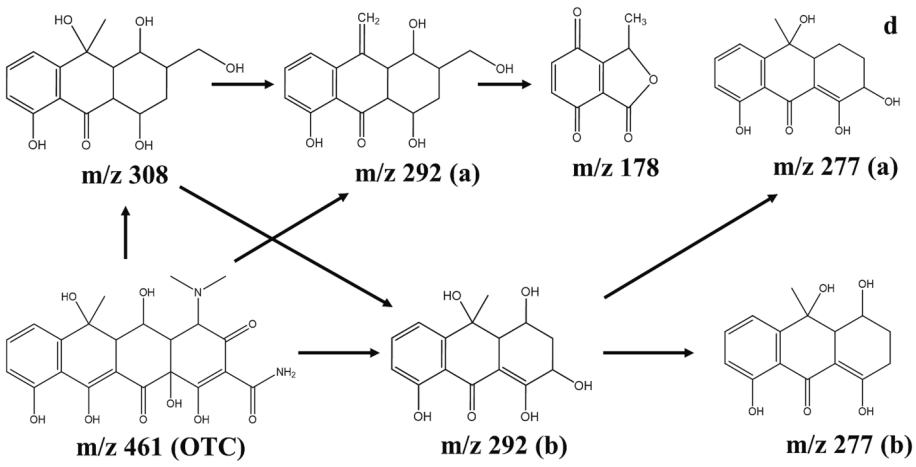

Fig. 6. (*continued*).

Table 6
Comparison of the model ABX degradation by using ultrasonic sonication, hydrodynamic cavitation and ozonation.

Matrix	C_0 (μM)	V_0 (mL)	t (min)	Other conditions	Process	ABX	k_1 (min^{-1})	*DE* (%)	C_t (μg L^{-1})	*MRL* (μg L^{-1})	t_{MRL} (min)	*Ref.*
Milk	4.92	50	60	500 kHz	US	CEF	3.8×10^{-2}	92.1	217.6	100	87	This study
				259 W	US	SMM	3.6×10^{-2}	89.9	150.1	100	75	This study
					US	MAR	3.3×10^{-2}	87.6	220.9	75	96	This study
					US	OTC	3.1×10^{-2}	84.5	350.9	100	104	This study
	6.62	400		No orifice plate	HC-1	SMM	2.1×10^{-4}	1.2	1,977.0	100	14,268	[14]
	6.62			3 mm single orifice plate	HC-2	SMM	1.9×10^{-3}	5.6	1,889.0	100	1,577	[14]
	6.62			5 mm single orifice plate	HC-3	SMM	2.3×10^{-3}	7.0	1,861.0	100	1,308	[14]
	5.52		20	5 mm single orifice plate	HC/O_3	CEF	1.7×10^{-1}	98.1	58.7	100	20	[14]
	5.52		20	O_3: 4 L h^{-1}, 1.134 mg L^{-1}	HC/O_3	SMM	1.5×10^{-1}	95.0	83.4	100	19	[14]
	5.52		30		HC/O_3	MAR	1.4×10^{-1}	96.8	64.0	75	29	[14]
	5.52		30		HC/O_3	OTC	5.4×10^{-2}	84.9	383.8	100	60	[14]
Water	192.8	100	150	500 kHz, 259 W	US	OTC	4.5×10^{-3}	49.8	44,563.9	–	–	This study
	21.7	5,000	90	10-hole, 2.0-mm orifice plate	HC	OTC	3.8×10^{-1}	34.0	58,598.8	–	–	[90]

Note: US, ultrasonic sonication; HC, hydrodynamic cavitation alone; HC/O_3, hydrodynamic cavitation combined with ozonation.

used as food. Most of them, as a nutrient waste liquid, will be mixed with ordinary wastewater for further biological treatment, and the safe and harmless decontaminant milk with qualified nutritional content will be used as animal feed partially.

The *E. coli* bacteria inhibition zone diameter via antimicrobial-susceptibility testing with 2–8,000 mg L^{-1} ABX spiked milk and saline samples are listed in Table S8. As shown in Table S8, the limited concentrations that inhibited the growth of *E. coli* are 60.0 mg L^{-1} CEF, 16.0 mg L^{-1} SMM, 2.0 mg L^{-1} MAR, and 29.7 mg L^{-1} OTC. There was no antibacterial activity in the treated milk samples after sonication. Briefly, sonication preserves nutrients integrity in treated milk and the ABX removal enables the use as calf food, animal feed, organic fertilizer, *etc.*

3.8. Comparison of the model ABX degradation by sonication, hydrodynamic cavitation, and ozonation

To compare the degradation efficiency of the model ABX by using various technologies including ultrasonic sonication (US), hydrodynamic cavitation (HC), and ozonation, the degradation results and the reaction conditions were summarized in Table 6.

As shown in Table 6, higher k_1 values and *DEs* of the model ABX by using US alone were observed compared with HC alone. This result may be attributed to the higher initial reaction volume in the HC process. In comparison, the degradation of the model ABX was accelerated by using ozonation in the HC process. Thus, the degradation efficiencies of the model ABX in milk by using US alone and HC alone are relatively low, while the energy and economic efficiencies by ozonation in the cavitation system are higher. In water, there are limited reports about the degradation of the model ABX by using HC [90]. It was almost impossible to compare the degradation efficiency due to the huge difference in reaction conditions.

4. Conclusions

The sonolytic degradation of CEF, SMM, MAR, and OTC in water and milk fits PFO kinetics well. ABX with high hydrophobicity (CEF and SMM) can be degraded faster than hydrophilic ABX (MAR and OTC) in both water and milk and their $LogK_{OW}$ values play an important role. Both the inhibition by adding *n-*/*t*-butanol and the enhancement of adding extra H_2O_2 and $Na_2S_2O_8$ further demonstrated the role of free radicals generated at the cavitation bubble/liquid interface. Both ultrasonic frequency and power showed the most significant effect, while the bulk temperature on SMM degradation is a minor factor in both water and milk. Increasing ultrasonic frequency and power, as well as bulk temperature accelerated the degradation and shortened the time met for the relevant *MRLs*. Furthermore, the reaction volume affects SMM degradation more significantly in milk than in water, and the higher initial concentrations and a large reaction volume resulted in slower degradation and longer times to meet the *MRLs*. After sonication, no evident changes in milk nutrients were observed and no antimicrobial activity was detected. The limitation of this work is that the sonication alone is relatively inefficient for removing ABX in milk, thus the degradation efficiency of the model ABX could be improved by adding

extra oxidants or catalysts. Moreover, the efficient degradation of the model ABX in wastewater and various milk in the pilot scale should be further implemented in the future.

CRediT authorship contribution statement

Pengyun Liu: Data curation, Writing – original draft, Validation, Investigation. **Zhilin Wu:** Conceptualization, Methodology, Supervision, Writing – review & editing. **Zhen Fang:** Data curation, Investigation. **Giancarlo Cravotto:** Conceptualization, Supervision, 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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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ultsonch.2023.106518.

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