Sonochemical Degradation of Pharmaceuticals and Personal Care Products

Dissertation

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Abstract

The widespread use of pharmaceuticals and personal care products (PPCPs) has raised environmental concerns due to their presence in aquatic environments, unknown chronic low-dose exposure to humans, and recalcitrance to conventional water treatment technologies. In this dissertation, ultrasound, especially in pulsed wave (PW) mode has been explored to remove PPCPs. The focus was to fundamentally and mechanistically understand how ultrasound degrades PPCPs and what controls degradation kinetics.

First, ultrasound was employed to degrade the pharmaceuticals, ciprofloxacin (CIPRO) and ibuprofen (IBU), in the presence of Suwannee River fulvic acid (SRFA) and terephthalic acid (TA) to gain an understanding of the effect of environmentally relevant matrix organics on degradation kinetics. The matrix organics inhibited the sonolysis of CIPRO and IBU to different extents. Based on the results, SRFA stays in bulk solution, either quenching •OH and/or associating with the target compounds. Similar to SRFA, TA, a commonly used •OH scavenger, reacts with •OH in the bulk region but we also suspect it accumulates on or interacts with cavitation bubbles. The indication has caused us to reexamine the validity that TA can be used as a bulk •OH scavenger, because a flawed bulk •OH scavenger not only misestimates the contribution of •OH in bulk solution to the overall contaminant degradation, but also misrepresents the nature of the reaction in the aqueous cavitational systems.
By using PW ultrasound we evaluated the performance of different •OH scavengers (i.e., formic acid (FA), carbonic acid (CA), terephthalic acid (TA)/terephthalate (TPA), potassium iodide (KI), methanesulfonate (MS), benzenesulfonate (BS), and acetic acid (AA)/acetate) to determine which •OH scavengers react only in bulk solution and which •OH scavengers interact with cavitation bubbles. The degradation of carbamazepine (CBZ), a probe compound serving as the reference compound occurred primarily at bubble-water interface in the study. Based on the pulsed enhancement (PE) of CBZ, acetic acid/acetate appears to scavenge •OH in bulk solution, and not interact with cavitation bubbles. Methanesulfonate acts as reaction promoter, increasing rather than inhibiting the degradation of CBZ. For formic acid, carbonic acid, terephthalic acid/terephthalate, benzenesulfonate, and iodide, the PE was significantly decreased compared to in the absence of the scavenger. These scavengers not only quench •OH in bulk solution but also affect the cavity interface.

To apply the knowledge of AA as a bulk •OH scavenger, seven PPCPs, namely CBZ, IBU, CIPRO, acetaminophen (ATP), sulfamethoxazole (SFT), propyl gallate (PG), and diethyl phthalate (DP) were degraded by ultrasound. Degradation rates by PW ultrasound were compound dependent with degradation either faster for smaller compounds or slower for larger compounds than that under CW ultrasound. To investigate the discrepancy of degradation rate of the PPCPs between CW and PW ultrasound, AA was added and irradiated with each compound to differentiate the contribution of bulk •OH oxidation in its overall degradation. The results showed that the fraction of degradation occurring in bulk solution is positively correlated with the molar volume of the compound. Smaller PPCP compounds are able to more readily diffuse to bubble
interfaces and are impacted most by pulsing ultrasound. Our results suggest PW ultrasound improves the energy efficiency of ultrasound as a treatment technology for small size PPCPs.

In order to test the application of ultrasound to wastewater effluent and gain a mechanistic understanding of the importance of the octanol-water partition coefficient ($K_{ow}$) and diffusivity ($D_{iw}$) on cavitational systems, we investigated the sonochemical degradation of a series of pharmaceuticals in DI water and municipal wastewater effluent under CW and PW ultrasound, respectively. The selection of six target pharmaceuticals was based on $K_{ow}$ and $D_{iw}$. In deionized water, pharmaceuticals with the highest $D_{iw}$ (i.e., fluorouracil (5-FU)) and $K_{ow}$ (i.e., lovastatin (LOVS)) exhibited the greatest enhancement in degradation rates in PW mode as compared to CW mode. This result suggests that a pharmaceutical with either high diffusivity or hydrophobicity more readily populates the bubble-water interface during the silent cycle of PW ultrasound. However, in municipal wastewater effluent, the PE for 5-FU and LOVS disappeared. Our results showed that the presence of matrix inorganics (i.e., bicarbonate and sulfate anions) did not affect the PE, indicating that the wastewater effluent organic matter (EfOM) is the cause of the disappearance of PE. Irradiating 5-FU and LOVS in hydrophobic (HPO), transphilic (TPI), and hydrophilic (HPI) fractions of EfOM showed that the TPI fraction reduced the pulse enhancement the most, followed by HPI and HPO fractions. The smaller molecular weight and high aromaticity of TPI suggests that the TPI fraction is able to diffuse to cavitation bubble surfaces and interact with pharmaceuticals, resulting in less benefit of pulsing in the presence of EfOM.
Dedication

Dedicated to my doctoral advisor Dr. Linda K. Weavers
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I could not have come this far without the help and support of many and I would like to acknowledge them now.

Dr. Linda Weavers, my advisor, offered me admission to her renowned group, provided freedom for me to do the research I am interested in, encouraged me to always scrutinize my work critically, and urged me to never lose sight of the magnitude and scope of the scientific world.

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1.1 Pharmaceuticals and personal care products contamination in water bodies

Pharmaceuticals and personal care products (PPCPs) are defined as “any products used by individuals for personal health or cosmetic reasons or used by agribusiness to enhance growth or health of livestock” (EPA, 2010). These compounds have greatly improved our quality of living. In spite of this, PPCPs have received a significant amount of attention as potential environmental contaminants. Although the information of exact amounts of PPCPs produced and consumed is hard to obtain, the sale of pharmaceuticals was as high as $290.1 billion in 2007 (Khetan and Collins, 2007). Depending on the medication, up to 90% of these products pass through a human body unchanged (Daughton and Ternes, 1999), resulting in a substantial amount of anthropogenic compounds being directly or indirectly released into the aquatic environment.

Numerous studies investigated the occurrence of PPCPs in aquatic environments around the world (Barcelo and Petrovic, 2007; Boyd et al., 2004; Nakada et al., 2007; Snyder et al., 2003; Xu et al., 2009). The U.S. Geological Survey (USGS) provided the first overview of the occurrence of PPCPs in water resources across the United States during 1999-2000 and concluded that these compounds were prevalent at 139 sampling sites, found in 80% of the streams sampled (Kolpin et al., 2002). In Ohio, eight sampling sites have been monitored, a median of seven anthropogenic organic contaminants were
found at these sites (Kolpin et al., 2002). Miege et al., (2009) reported that acidic drugs, such as bezabrate, ibuprofen, indomethacin, and naproxen, were ubiquitous in German rivers and streams with concentration in the ng/L range. Both the Lake Erie Millennium Plan and U.S. Environmental Protection Agency (EPA) and Environment Canada have reported that PPCPs have been detected in Lake Erie and the other Great Lakes (LAMP, 2006; U.S.EPA, 2007). Peck et al., (2006) reported galaxolide, a synthetic musk, in Lake Erie sediment cores from a site near Cleveland, OH. They found a strong correlation between the concentration of galaxolide and the consumption of fragrances in the United States.

Toxicological studies have explicitly shown that exposure of fish and other aquatic organisms to PPCPs cause adverse reproductive effects, such as reduced viability of eggs, endocrine disruption, and changes in sperm density (Crane et al., 2006; Daughton and Ternes, 1999; Gu et al., 2002; Porte et al., 2009). A full understanding of the hazards of PPCPs, especially at environmental concentrations over long exposure times, and exposure to mixtures of PPCPs, to human health is limited, causing relatively incomplete environmental regulations and laws. However, as knowledge of risk of exposure to PPCPs via water, regulations are likely to change. Therefore, technologies to treat these contaminants need to be developed.

1.2 Conventional treatment technologies

Avoiding consumption of PPCPs is unlikely, because they are medically necessary and improve our quality of life. Thus, considerable effort has been spent on understanding removal efficiencies (i.e., fast degradation kinetics) of PPCPs in drinking
Researchers evaluated the removal efficiency of various PPCPs by different conventional water treatment and advanced oxidation processes (AOPs) (Westerhoff et al., 2005). Technologies were tested using bench-scale models and included coagulation, lime softening, powder-activated carbon (PAC), chlorination, and ozonation. The removal efficiency of PPCPs was technology dependent, ranging from approximately 20% removal using coagulation to 90% using PAC. In addition, they reported that the removal efficiency of a PPCP depended on its physicochemical properties, including molecular weight, octanol-water partition coefficient (K_{ow}), aromatic carbon content, and functional group composition.

It is noted that each technology has both advantages and disadvantages. In the study above (Westerhoff et al., 2005), after a 4 hour contact time with PAC, about 90% removal of the initial concentration of PPCPs was achieved. However, a 4 hour contact time of PAC with PPCPs is too long to be applied to large water treatment facilities which process millions of gallons of water a day. Another example is chlorination. The removal efficiency of PPCPs by chlorination was also 90% (Westerhoff et al., 2005), but chlorine reacts with natural organic matter (NOM), generating toxic disinfection byproducts (DBPs). Therefore, researchers are searching for other high efficiency and green water treatment technologies.

1.3 Sonochemistry as an AOP technology

Ultrasound is one example of an advanced oxidation process (AOP) that transforms organic contaminants. Ultrasound contains unique advantages compared to other
technologies, including no addition of chemicals, ease of use, and short contact time (Adewuyi, 2005a; b; Hoffmann et al., 1996). Ultrasonic irradiation in water induces collapsing bubbles, known as cavitation bubbles. When water is exposed to ultrasound, acoustic pressure waves are produced. The acoustic pressure waves consist of compression and rarefaction cycles. In the rarefaction cycle of the acoustic pressure wave, it leads to the formation of bubbles from the gas nuclei, dissolved gas that preexists in water. In the compression cycle of the acoustic wave, the bubble volume decreases due to increasing pressure in the surrounding water. Thus, bubbles grow and shrink in response to acoustic pressure. The motion for the gas bubble in a sonicated solution can be defined by the Rayleigh-Plesset (RP) equation (Leighton, 1994):

\[
\ddot{R} + \frac{3}{2} \dot{R}^2 = \frac{1}{\rho} \left\{ \left[ p_v - p_{\infty}(t) \right] + p_{g0}(R_0/R)^\eta \right\} - \frac{2\sigma}{R} - 4\mu \dot{R}/R \quad (1.1)
\]

where \( \dot{R} \) and \( \ddot{R} \) are the first and second order derivatives of the bubble radius in terms of time; \( \rho \) is the density of liquid; \( p_v \) is the vapor pressure; \( p_{\infty} \) is the ambient pressure; \( p_{g0} \) is gas pressure inside the bubble; \( R \) and \( R_0 \) are the instantaneous and equilibrium radii of the bubble, respectively; \( \eta \) is polytropic coefficient (under isothermal conditions, \( \eta \) is 1; under adiabatic conditions, \( \eta \) is the heat capacities, \( \gamma \), of the gas in liquid); \( \sigma \) is the surface tension coefficient in N/m or J/m\(^2\); and \( \mu \) is the viscosity of the liquid. The first term in the curly bracket on the right side of reaction indicates the discrepancy of the applied pressure in the liquid and the vapor pressure in gas pocket. It is the driving force that accounts for the growth of the bubble. This term is associated with the entire life of the
bubble, including shrinking, growing, collapsing, and oscillating. The second, third, and fourth terms in the curly bracket are the contribution of non condensable gas, the contribution of surface tension, and the contribution of dynamic viscosity, respectively (Leighton, 1994).

When the sound intensity is greater than the cavitation threshold, within several cycles of growing and shrinking, bubbles exponentially and eventually collapse. However, the RP equation fails to accurately describe the collapse, in which interesting chemistry happens (Suslick and Flannigan, 2008). The collapse of bubbles causes extremely high temperatures and pressures (Suslick et al., 1986) within a microenvironment in the liquid, known as hot spots. The average temperatures within the bubble is estimated as high as 5000 K (Flint and Suslick, 1991), leading to the breakdown of gaseous water molecules in the bubbles to hydroxyl radicals (•OH).

\[ \text{H}_2\text{O} \rightarrow \text{•OH} + \text{•H} \]  \hspace{1cm} (1.2)

The hot spot theory (Suslick et al., 1986) is frequently used to interpret how a contaminant is degraded by ultrasound. The schematic diagram of hot spot is illustrated in Figure 1.1. In the center of collapsing bubble (i.e., gas region), the temperature and pressure are about 5000 K and 500 atm (Flint and Suslick, 1991), respectively, so that water molecules are thermolyzed to •OH and •H. The temperature in the interfacial region surrounding the hot core is estimated to be 1900 K, and the •OH concentration is estimated to be up to 4 mM (Gutierrez et al., 1991). The thickness of the interfacial region is estimated to be 200 nm (Mason et al., 1990). The temperature of bulk region of
the cavitation bubble is ambient. •OH forms in the gaseous bubble core and diffuses to bulk solution to this region (Adewuyi, 2005a). In terms of distribution of concentration of reactants and products, the concentrations of solutes decrease from bulk solution to interfacial region of cavitation bubbles; the maximum concentration of products is at the interfacial region.

In a sonicated solution, organic contaminants undergo degradation by two different pathways: decomposition by heat in the gas and interfacial regions of the cavitation bubbles and •OH oxidation in the gas, interfacial, and bulk region of the cavitation bubbles (Adewuyi, 2001; Hoffmann et al., 1996; Mendez-Arriaga et al., 2008; Riesz et al., 1985; Weavers et al., 2005). The proportion of each pathway is dependent on the physicochemical properties of organic contaminants (Adewuyi, 2001; Hoffmann et al., 1996). For example, the major degradation location for volatile contaminants is in the gas region; hydrophobic pollutants in the interfacial region; and hydrophilic contaminants in the bulk region.

1.4 Sonochemical degradation of organic contaminants in water

In the past two decades intensive efforts have been exerted to understand what determines the treatability of ultrasound in removing organic contaminants from water. However, more and more studies revealed that the sonication system is so complex that any change in ultrasonic operating conditions (Adewuyi, 2005a; b; Franconi and Petrier, 1996; Mendez-Arriaga et al., 2008; Petrier et al., 1996), physicochemical properties of organic compounds (Colussi et al., 1999; Mizukoshi et al., 1999; Nanzai et al., 2008), and solution chemistry (Bolong et al., 2009; Brotchie et al., 2009; Jiang et al., 2002) has an
influence on the cavitational effects, thus affecting the effectiveness of ultrasound in wastewater and drinking water treatment. This section of the dissertation will discuss the effect of ultrasonic operating conditions, physicochemical properties of organic compounds, and solution chemistry, respectively.

1.4.1 Ultrasonic operating conditions

The ultrasonic operating conditions typically include ultrasonic intensity, ultrasonic frequency, and ultrasonic mode (i.e. continuous wave and pulsed wave mode).

1.4.1.1 Ultrasonic intensity

The impact of ultrasonic intensity on chemical reactivity in different sonochemical systems has undergone considerable examination (Hua and Hoffmann, 1997; Kuijpers et al., 2002; Mendez-Arriaga et al., 2008; Sunartio et al., 2005; Suri et al., 2007). The ultrasonic intensity imported to the system (I) is positively correlated to the square of the acoustic amplitude of the ultrasonic wave, $P_A$ (eqn. 1.3) (Leighton, 1994):

$$ I = \frac{P_A^2}{2c\rho} \quad (1.3) $$

where $c$ is the speed of sound in water (1482 m/s in water at 20 °C) and $\rho$ is the density of water (998 g/L at 20 °C). In addition, the ultrasonic intensity also affects the bubble collapse time, $\tau$, as indicated by eqn. 1.4.
\[ \tau = 0.915R_{\text{max}} \left( \frac{\rho}{\rho_A} \right)^{1/2} \left( 1 + \frac{P_{\text{vapor}}}{P_A} \right) \]  

(1.4)

where \( R_{\text{max}} \) is the maximum radius reached by a bubble during expansion; \( \rho \) is the density of the liquid; and \( P_{\text{vapor}} \) is the vapor pressure in the bubble. Therefore, with higher amplitude ultrasonic wave, the cavitation bubbles collapse within a shorter time.

The acoustic intensity has been measured using different chemical dosimeters, including 5, 5-dimethylpyrroline-N-oxide (DMPO) (Riesz et al., 1985; Sostaric and Riesz, 2001), terephthalic acid (Fang et al., 1996; Villeneuve et al., 2009), potassium iodide (Entezari and Kruus, 1994; Weissler et al., 1950), and luminol (Price et al., 2010; Tuziuti et al., 2004). Every chemical used in the dosimetry has advantages and disadvantages. For example, DMPO has been frequently used in dosimetry. Although Electron spin resonance (ESR) spectroscopy sensitively traps the spin-adduct signal in cavitational systems, the ESR spectroscopy is not commonly used due to its high cost and difficulty in quantification. The terephthalate dosimeter measures •OH by detecting the fluorescence signal of the •OH-trap adduct. Although a fluorescence spectrophotometer is not expensive, terephthalic acid has low solubility in an acidic solution (15 mg/L at 25°C (Yalkowsky and Banerjee, 1992)). In addition, all these methods depend on •OH reacting with chemical dosimeters. These dosimeters may not sufficiently differentiate the locations of •OH reaction, because the •OH-trap adduct forms proportionally based on the concentration of •OH and the •OH trap in the cavitation bubble, at bubble-water interface and in bulk solution.
The correlation between sonochemical reactivity and ultrasonic intensity has been studied by previous researchers (Hua and Hoffmann, 1997; Kanthale et al., 2008; Merouani et al., 2010; Price and Lenz, 1993; Weissler et al., 1950). Merouani et al. (2010) monitored the formation rate of triiodide in 0.1 M KI aqueous solution at the frequency of 300 kHz and observed that the rate increased as a function of power input, ranging from 45.6 to 85.3 W/L. Weissler et al., (1950) also observed the linear formation of triiodide under sonication at the frequency of 1 MHz as the power input increased from 0 to 600 W, which is a wider range than that in Merouani et al. study. They both attributed the strong correlation between sonochemical reactivity (i.e., triiodide formation in this case) and power input to a greater number of cavitation bubbles and a more complete bubble implosion.

However, increasing power input does not necessarily cause a faster degradation rate for all contaminants. Hua et al. examined the dependence of the first-order degradation rate constant of para-nitrophenol (p-NP) on the power input (Hua and Hoffmann, 1997). The input power was varied from 0.3 to 1.5 W/cm² and an optimum rate was observed. They found the rate constant first increased with an increase of intensity, but it started to decrease when the power intensity reached at 1.2 W/cm². A similar trend has been observed by other studies. Henglein and Gutierrez (1988) degraded polyacrylamide with 1 MHz continuous wave ultrasound in aqueous solution. They observed that the first-order degradation rate constant reached its maximum at 100 W and gradually decreased as the power input increased. The decrease in the degradation rate of the target compounds was attributed to incomplete bubble collapse, a greater extent of coalescence.
of multi-bubbles, and formation of a bubble shroud at the surface of the transducer, resulting in less penetration of the acoustic wave (Hua and Hoffmann, 1997).

1.4.1.2 Ultrasonic frequency

Many studies have shown that ultrasonic frequency determines the size of cavitation bubbles (Beckett and Hua, 2001; Brotchie et al., 2009; Hung and Hoffmann, 1999; Leighton, 1994; Price et al., 2010). As shown in eqn. 1.5 (Leighton, 1994), the maximum radius reached by a bubble during expansion, \( R_{\text{max}} \), is dependent on ultrasonic frequency, \( f \), the hydrostatic pressure, \( P_0 \), and acoustic pressure, \( P_A \), and the density of the solution, \( \rho \). \( f \) is inversely proportional to the \( R_{\text{max}} \), indicating that at higher frequency the size of the collapsing bubble is smaller than at low frequency.

\[
R_{\text{max}} = \frac{4}{6\pi f} (P_A - P_0) \left( \frac{2}{\rho P_A} \right)^{1/2} \left( 1 + \frac{2}{3P_0} (P_A - P_0) \right)^{1/3}
\]  

(1.5)

In addition, Petrier et al., (1996) investigated the sonochemical degradation of 2,2,6,6-tetramethyl-4-piperidinon with and without argon at 20 kHz and 514 kHz, respectively. By measuring the formation of triiodide in KI solution under different conditions, they concluded that, as frequency decreases, large sized cavitation bubble forms and it collapses more violently, resulting in less \( \cdot \text{OH} \) to be rejected out of bubbles. Brotchie et al., (2010) reported that the frequency also affects the lifetime of cavitation bubbles, which is defined as the time of the cavitation bubbles between their nucleation and collapse. Cavitation bubbles at a high frequency have more acoustic cycles per unit
time with a shorter lifetime than those at low frequencies. For example, at 20 kHz, the bubble lifetime is 0.26 ms as compared to 0.22 ms at 355 kHz (Brotchie et al., 2010). The acoustic cycle at 20 kHz is $\frac{0.26 \times 10^{-3}}{20 \times 10^3} \approx 5$ as compared to $\frac{0.22 \times 10^{-3}}{355 \times 10^3} \approx 75$ at 355 kHz. However, the dependence of radius, acoustic cycles, and lifetime of the cavitation bubble on frequency does not demonstrate the influence of frequency on chemical reactivity.

Therefore, a number of techniques were employed to elucidate the dependence of chemical reactivity on frequency (Beckett and Hua, 2001; Brotchie et al., 2009; Kang et al., 1999; Petrier et al., 1994; Yang et al., 2008). Yang et al., (2008) applied a terephthalate dosimeter to measure $\cdot$OH by detecting the fluorescence of the $\cdot$OH-trap adduct (i.e., hydroxyterephthalate) at different frequencies. They found that the order of $\cdot$OH yield was 354 kHz > 620 kHz > 803 kHz > 206 kHz > 1062 kHz. Beckett and Hua (2001) monitored the production of H$_2$O$_2$ at four frequencies (205, 358, 618, and 1071 kHz). H$_2$O$_2$ is a product that is generated from the recombination of $\cdot$OH, as illustrated in eqn. 1.6

$$\cdot$OH + $\cdot$OH $\rightarrow$ H$_2$O$_2$$ \quad (1.6)$$

The order of production of H$_2$O$_2$ was 358 kHz > 205 kHz > 618 kHz > 1071 kHz. Kang et al., (1999) also investigated the formation of H$_2$O$_2$ at 205 kHz, 358 kHz, 618 kHz, and 1078 kHz and the order of production of H$_2$O$_2$ was 358 kHz > 618 kHz 205 kHz > 1078 kHz. The studies above observed an optimum at 200-600 kHz. The increased $\cdot$OH yield
at high ultrasonic frequency is explained by the fact that cavitation at a high frequency rejects more •OH, resulting in high •OH yield. But when the ultrasound frequency increases into megahertz range, high frequency does not produce more •OH, because rarefaction and compression cycles decrease, resulting in a shorter time for nucleation process of cavitation bubbles to expand to bubbles. In addition, the collapsing temperature at higher ultrasound frequencies reduce the •OH yield due to a less adiabatic collapse (Yang et al., 2008).

In terms of the effects of frequency on contaminant removal, many studies have investigated the influence of ultrasonic frequency on contaminant degradation (Beckett and Hua, 2001; Hung and Hoffmann, 1999; Kang et al., 1999; Petrier et al., 1994; Yang et al., 2008). These studies revealed a similar trend to that of the •OH yield discussed above. For instance, Hung and Hoffmann (1999) compared the rates of sonolysis of CCl₄, a precursor to refrigerants and a cleaning agent, at different frequencies. The results showed that the degradation rate increased from 20 to 618 kHz and then decreased gradually as frequency increased to 1078 kHz. They attributed the high degradation rate observed at 618 kHz to the long lifetimes and the high surface area to volume ratios of the cavitation bubbles. Yang et al., (2008) also observed that the initial degradation rates of octylbenzene sulfonic acid (OBS), a surface active contaminant, as a function of frequency, were in the order: 620 kHz > 803 kHz = 354 kHz > 1062 kHz > 206 kHz. They also attributed the higher initial degradation of OBS at 354 and 803 kHz to the higher extent of adsorption of the surfactant to bubble interfaces due to prolonged bubble lifetimes and bubble-water interface of cavitation bubbles.
In summary, as we discussed above, the extent that frequency affects the removal of contaminants depends on •OH yield, mass transfer of •OH out of cavitation bubbles, and accumulation of contaminants on cavitation bubbles. The dependence suggests that, when ultrasound is applied to water treatment, •OH production rate and physicochemical properties of target contaminants should be taken into consideration.

1.4.1.3 Ultrasonic mode

The ultrasound is transmitted to the solution in continuous wave (CW) and pulsed wave (PW) modes. PW ultrasound is widely used as a tool in medical diagnosis due to less potential biohazard as compared to CW ultrasound. In the PW ultrasound, the continuous ultrasonic signal train is separated by gaps of no signal (Leighton, 1994). Figure 1.2 describes the similarity and difference between CW and PW ultrasound in our study. Both CW and PW ultrasonic signal trains have same amplitude. In order to expose the solution to the same amount of acoustic energy, a longer total sonication time is applied under pulsed conditions. The total sonication time is obtained from eqn. 1.7.

\[
\text{t}_\text{sonication} = \frac{\text{t}_\text{total}}{1 + \frac{1}{R}} \quad \text{(1.7)}
\]

where \(\text{t}_\text{sonication}\) is the actual sonication time; \(\text{t}_\text{total}\) is the total time for an experimental run; and \(R\) is the signal on/off ratio (\(T_{\text{on}}:T_{\text{off}}\)). In our study, \(T_{\text{on}}=T_{\text{off}}=100\) ms was used for all the experiments.
Many studies have shown that at proper settings the degradation kinetics of a contaminant under pulsed wave (PW) ultrasound is more effective than that under CW ultrasound (Flynn and Church, 1984; Henglein, 1995; Henglein et al., 1989; Neppolian et al., 2009; Yang et al., 2007). For instance, with ultrasound 100 ms on and 100 ms off, the degradation rate of 0.1 mM surface-active contaminant, OBS, was approximately 30% faster than that of CW (Yang et al., 2005). Xiao et al., observed that the removal efficiency of 10 μM carbamazepine (CBZ) under PW ultrasound was greater than CW by about 6%. Flynn and Church (1984) investigated the iodine release at T_on= 60 s but various T_off time intervals, with the acoustic intensity of 30 W/cm², the maxima in iodine release was at T_off=6 ms. However, with the acoustic intensity of 20 W/cm², the maxima in iodine release was at T_off=60 ms. Surprisingly, with the acoustic intensity of 10 W/cm², there is no maxima in iodine release. Neppolian et al., (2009) found a remarkable enhancement (1.3 fold) of oxidation of arsenic (III) to arsenic (V) under PW ultrasound at ca. 35 W/L and duty cycle 1:1, as compared to CW ultrasound.

However, the mechanisms for the enhanced sonochemical reactivity under PW ultrasound remain unclear. The enhanced degradation kinetics in Yang et al. (2005) was attributed to the accumulation of the surfactant on cavitation bubble surfaces, resulting in reduced surface tension and lowering the cavitation threshold. In addition, surfactants inhibit bubble dissolution during the off cycle, resulting in a larger active cavitation bubble population and increased absorption sites. Deojay et al. (2011) attributed the enhanced degradation kinetics to the accumulation of OBS. During the time interval between two successive pulses, surface active OBS molecules accumulate on the surface of the bubble. In the subsequent pulse more OBS molecules react compared to CW
ultrasound. Flynn and Church (1984) attributed the increased formation of iodine in PW mode to the survival of unstabilized nuclei during the off-time, which survived as stable cavities from one pulse and caused more violent collapse in subsequent pulse. Neppolian et al., (2009) attributed the increased sonochemical degradation of arsenic (III) by PW ultrasound to the “silent” oxidation reactions and the increased number of active cavitation bubbles. The controversy on the enhancement by PW ultrasound reveals that there are many uncertainties and fundamental mechanisms need to be answered.

1.4.2 Physicochemical properties of organic solute

The physicochemical properties of an organic contaminant itself impact contaminant removal efficiency. In a sonicated solution, thermodynamic parameters, such as surface excess (Γ), octanol-water partition coefficient (K_{ow}), and Henry’s law constant (K_{H}), have been related to the ability of contaminants to populate cavitation bubbles; kinetic parameters, such as diffusivity (D_{iw}), control how fast contaminants are able to populate cavitation bubbles.

1.4.2.1 Surface excess

Surface excess is defined as “the difference between the amount of a component actually present in the system, and that which would be present (in a reference system) if the bulk concentration in the adjoining phases were maintained up to a chosen geometrical dividing surface” (McNaught et al., 2000). The surface excess is calculated from surface tension (γ) (eqn. 1.8)
\[ \Gamma = -\frac{1}{RT} \frac{d\gamma}{d\ln[S]} \]  

(1.8)

where \([S]\) is the solute concentration, \(R\) is the universal gas constant and \(T\) is temperature.

The equilibrium surface excess is positively correlated to the degree of accumulation of organics on the bubble-water interface, where thermolysis occurs. A compound with higher surface excess accumulates to a larger degree on bubble surfaces, quenching sonoluminescence (SL), a phenomenon arising from vibrationally excited states of molecules produced as a result of the high temperatures and pressures at bubble collapse (Didenko et al., 2000). The quenching effect results from organics partitioning into the cavitation bubbles and reacting with excited-state molecules, ultimately lowering the collapse temperature (Ashokkumar and Grieser, 2000). Therefore, the decrease of SL is considered a sign for enrichment of a substance at the bubble-water interface. A high degree of quenching indicates a high extent of accumulation of organics on the interfacial region. Several studies examined the quenching effects of surface active agents, such as aliphatic alcohols and surfactants, on SL (Ashokkumar et al., 2000; Ashokkumar et al., 1997). Ashokkumar et al., (1997) measured the SL and surface tension of \(C_1-C_5\) aliphatic alcohols and the surfactants sodium dodecyl sulfate, dodecyltrimethylammonium chloride, and N-dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate at a frequency of 515 kHz. They found that the SL signal decreased as surface tension increased, suggesting a substance with high surface activity tends to accumulate at the interfacial region. However, using ESR spectroscopy and the spin-trap, 3,5-dibromo-4-nitrosobenzenesulfonate to trap primary and secondary radicals, Sostaric and Riesz (2001)
did not observe a correlation between equilibrium surface excess and the extent of ultrasonic decomposition of the surfactants, n-alkanesulfonates, n-alkyl sulfates, n-alkylammoniopropanesulfonates, and poly(oxyethylenes) at 47 kHz. Their results showed that the surface excess did not sufficiently describe the behavior of the surfactants at the bubble-water interface. Sonolysis of the surfactants depended on their chemical structure and their ability to diffuse from the bulk solution to the interfacial region of cavitation bubbles.

1.4.2.2 Octanol water partition coefficient

$K_{ow}$ is “a measure of the way in which a compound will partition itself between the octanol and water phases in the two-phase octanol-water system” (Lide, 2005). Octanol is a typical organic solvent to describe the partitioning behavior of an organic compound between natural organic phases and water due to its amphiphilic character (favorably interacting with both bipolar and monopolar solutes). $K_{ow}$ is a physicochemical property that is a measure of the hydrophobicity of a compound.

Many studies have evaluated the effect of $K_{ow}$ on the sonolytic degradation of organic contaminants (Emery et al., 2005; Fu et al., 2007; Nanzai et al., 2008; Park et al., 2011; Wu and Ondruschka, 2006). Nanzai et al., (2008) sonolyzed a variety of monocyclic aromatic organic compounds, including nitrobenzene, aniline, phenol, benzoic acid, salicylic acid, 2-chlorophenol, 4-chlorophenol, styrene, chlorobenzene, toluene, ethylbenzene and n-propylbenzene at the frequency of 200 kHz and power density of 3333.3 W/L. They found the degradation rate was positively correlated to log $K_{ow}$ for these compounds and concluded that $K_{ow}$ is the most important factor for
sonolysis of aromatic compounds. Park et al., (2011) examined the sonolysis of phenol, 4-chlorophenol, 2,6-dichlorophenol, 2,4,6-trichlorophenol, 2,3,4,6-tetrachlorophenol, and pentachlorophenol under three different frequencies, 28 kHz, 580 kHz, and 1000 kHz, respectively. They reported a strong positive relationship between log K_{ow} and first-order degradation rate, indicating that a hydrophobic compound undergoes faster sonochemical degradation. The reported correlations in previous studies may be attributed to the fact that the investigated compounds belong to monocyclic aromatics with similar structure but with varied properties, thereby simplifying the comparison.

However, the dependence of degradation kinetics on log K_{ow} failed when the target compounds covered a wide range of physicochemical properties and structures. Wu and Ondruschka (2006) compared the sonochemical degradation kinetics of diethyl sulfide, diallyl sulfide, dipropyl sulfide, dibutyl sulfide, diethyl disulfide, and dipropyl disulfide at 850 kHz. In their study, the hydrophobicity failed to predict the observed rate; diethyl disulfide did not fit the trend. Although authors did not provide a reason for lack of correlation, it may be due to the two double bonds at the α position, resulting in the H on the secondary carbon being easily abstracted. In addition, Fu et al., (2007) investigated the sonolysis of nine different estrogenic compounds and evaluated the relationship between estrogen degradation rate and K_{ow} value. However, no correlation whose R^{2} was greater than 0.8 was observed between the two variables. They explained the lack of dependence to the inaccuracy of the documented K_{ow} values.

Although their explanations may be valid in their cases, the sonochemical process involves thermolysis and •OH oxidation of contaminants and formation of byproducts in gas, interfacial, and bulk regions of cavitation bubbles. Therefore, in this heterogeneous
cavitational system, a single physiochemical property of the parent PPCP may have limited capability to accurately govern the complex kinetics, especially when the investigated compounds cover a wide range of physicochemical properties and diversity of structures. In addition, bubbles in the ultrasound field are subjected to high velocity oscillations and translations (Leighton, 1994). These phenomena significantly affect the fluid dynamics in the reactor, resulting in a more complex factor to take into consideration when it comes to prediction the degradation kinetic using a single physiochemical property of a PPCP.

1.4.2.3 Henry’s law constant

\( K_H \) is a measure of the distribution of a compound between the gas and water phase defined by eqn. 1.9

\[
K_H = \frac{p_i}{C_i} \tag{1.9}
\]

where \( p_i \) is the partial pressure of compound and \( C_i \) is the concentration of compound in aqueous solution. \( K_H \) is in unit of Pa-m\(^3\)/mol in this equation. Similar to any thermodynamic properties, \( K_H \) is dependent on temperature, as indicated by eqn. 1.10.

\[
k_H = k_{H}^{0}\exp\left(-\frac{\Delta_{\text{soln}}H}{R} \left(\frac{1}{T} - \frac{1}{T_0}\right)\right) \tag{1.10}
\]
where $\Delta H_{\text{soln}}$ is the enthalpy of solution; $k_H^{*}$ and $T^*$ are the Henry’s law constant at the reference temperature and the reference temperature, respectively.

The Henry’s law is applicable to an ideal dilute solution and is relevant in cavitational systems, since the gas region of cavitation bubbles is the source of chemical reactivity (i.e., high temperature and high concentration of $[\bullet \text{OH}]$).

Previous studies show that $K_H$ influences sonochemical degradation kinetics (Ayyildiz et al., 2007; Colussi et al., 1999; De Visscher, 2003; Nanzai et al., 2008; Petrier et al., 1998; Petrier et al., 2010). Colussi et al., (1999) reported a dependence of first-order rate constant on Henry’s law constants of various chlorinated hydrocarbons such as $\text{CCl}_4$, $\text{CHCl}_3$, $\text{C}_2\text{Cl}_6$, or $\text{CH}_2\text{Cl}_2$ at the frequencies of 205, 358, 618, and 1078 kHz. A compound exhibiting a greater tendency to enter the gas region (i.e., a high $K_H$) degrades faster than a compound with a low $K_H$ in a sonicated solution.

However, degradation does not always correlate with Henry’s law constant. Nanzai et al., (2008) investigated the relationship between the $K_H$ of twelve aromatic organics and the first-order rate constant of degradation at 200 kHz CW ultrasound. The first-order rate constant remained unchanged as $K_H$ increased from $10^{-9}$ to $10^{-4}$ atm m$^3$ mol$^{-1}$, and then became positively correlated to $K_H$ when it increased from $10^{-4}$ to $10^{-1}$ atm m$^3$ mol$^{-1}$, suggesting there is a threshold effect of $K_H$ on the sonolysis of organics. De Visscher et al., (2003) evaluated the relationship between the degradation rate of ethylbenzene, benzene, o-chlorotoluene, and styrene and their Henry’s law constants. No apparent relationship between degradation rate and Henry’s law constant was observed. They attributed the independence to the fact that diffusion limitations governed the partitioning of the aromatic compounds in water to the cavitation bubbles.
Similar to $K_{ow}$, degradation rates are correlated to $K_H$ in some cases but not others. The effect of $K_H$ on sonolysis may be more pronounced when the investigated compounds have similar structures or physicochemical properties, thereby simplifying the comparison.

1.4.2.4 Diffusivity

The degradation of organic contaminants in a sonicated solution may be controlled not only by thermodynamics as discussed above, but also kinetics. In aqueous solution, Fick’s first law, defined in eqn.1.11, dictates that the ability of a substance to travel through a mixture by Brownian motion (Fick, 1995).

$$J_i = -D_{iw} \frac{dC_i}{dz} \quad (1.11)$$

where $J_i$ is the mass flux of chemical i in direction of concentration gradient with the unit of mg/m$^2$·s; $D_{iw}$ is the diffusion coefficient of chemical i in water with the unit of m$^2$/s; $C_i$ is the concentration of i with the unit of mg/L; and z is distance in direction of concentration gradient with the unit of m (i.e., thickness of boundary layer).

It is clear that the mass flux depends on the concentration gradient and diffusivity coefficient. A greater concentration gradient before and after the boundary layer induces a faster mass flux. Furthermore, the diffusivity coefficient is a function of molar volume of an organic compound in water (Hayduk and Laudie, 1974) (eqn. 1.12).
\[
D_{iw} = \frac{13.26 \times 10^{-5}}{\mu_w^{1.14} \cdot V_i^{0.589}} \quad (1.12)
\]

where \(V_i\) is the molar volume in the unit of mL/mol; and \(\mu_w\) is the viscosity of water. In some cases, \(V_i\) is approximated by molecular weight, since the database for \(V_i\) is not large resulting in \(V_i\) being difficult to obtain. The viscosity of water is constant at a certain temperature; eqn. 1.12 indicates that a smaller molecule has a higher degree of mobility.

There are several studies focusing on the impact of diffusivity of an organic contaminant on sonolysis (Ayyildiz et al., 2007; De Visscher, 2003; DeVisscher et al., 1996; Dewulf et al., 2001; Fu et al., 2007; Yang et al., 2005). Fu et al., (2007) reported the rate of sonolysis of the estrogen family of compounds (e.g. 17β-estradiol, 17α-estradiol, ethinyl-estradiol, estrone, equilin, gestodene, levonorgestrel, and norgestrel) at the frequency of 20 kHz. Their results showed a dependence of first-order degradation rate on molecular weight. The estrogenic compound with smaller molecular weight degraded faster than those with larger molecular weight. Fu et al., (2007) attributed this to the small size of the molecule allowing them to diffuse to the gas or interfacial region of cavitation bubbles, where the reaction occurs. Yang et al., (2005) applied PW ultrasound to degrade surfactants OBS and sodium dodecylbenzenesulfonate (DBS) at the frequency of 354 kHz with a pulsed time on and off ratio of 1:1. The pulsed enhancement (PE), which is a measure of the effect of pulsing on the rate of sonochemical degradation as indicated by eqn. 1.13, for OBS (31%) was observed to be higher than that of DBS (7%). They attributed the difference in PE to the different diffusion coefficients:
where \( \left( \frac{d[C]}{dt} \right)_{cw} \) and \( \left( \frac{d[C]}{dt} \right)_{pw} \) are initial degradation rate of the target compounds under CW and PW ultrasound, respectively. The diffusion coefficient ratio between OBS and DBS, \( D_{\text{OBS}}/D_{\text{DBS}} \), was calculated to be 1.17. Thus, OBS diffuses to the bubble surface faster than that of DBS, resulting in more accumulation of surfactant at the bubble-water interface.

Diffusivity plays an important role in cavitation systems. First, previous studies showed that the lifetime of bubble is not long enough for a solute to reach equilibrium partitioning (Price et al., 2004; Sostaric and Riesz, 2002; 2001; Yang et al., 2006). Thus, the diffusivity, rather than the equilibrium properties, of a solute controls its ability to accumulate on the bubble-water interface, which is the source of reactivity. Second, the concept of PE is based on a comparative method (eqn. 1.13). The observed degradation rate of the target compounds (i.e., PPCPs in this study) by sonolysis involves both high temperature decomposition and •OH oxidation in the vicinity of cavitation bubbles and the bulk solution, as indicated by eqn. 1.14.

\[
\frac{dC}{dt}_{\text{obs}} = \frac{dC}{dt}_{\text{bulk}} + \frac{dC}{dt}_{\text{interface}} + \frac{dC}{dt}_{\text{bubble}}
\]  

(1.14)

where \( \frac{dC}{dt} \) represents the degradation rate of a target compound, occurring in bulk solution (bulk), occurring at the interface (interface), and occurring in the gas region of
cavitation bubble (bubble), respectively. The contribution from $\frac{dC}{dt_{\text{bulk}}}$ to $\frac{dC}{dt_{\text{obs}}}$ under CW ultrasound is similar to that under PW ultrasound (Deojay et al., 2011; Yang et al., 2005), thus there is no contribution of bulk reaction to PE. In addition, the PPCPs investigated are not likely to degrade inside the cavitation bubble due to their low Henry’s law constants, suggesting that a negligible contribution of bubble reaction to PE. Thus, the remaining component, $\frac{dC}{dt_{\text{interface}}}$, the reaction at bubble-water interfaces, results in the controlling mechanism, diffusion, becoming more pronounced in our system.

1.4.2.5 Relative importance of each physicochemical property

The target contaminants in this study are PPCPs. Most PPCPs in aquatic systems are non-volatile, non-surface active, and present at trace levels (nM to µM) (Daughton and Ternes, 1999; Ellis, 2006; Kolpin et al., 2002). Thus, the effects of Henry’s law constant and surface excess on sonochemical degradation kinetics are less influential as compared to the effect of hydrophobicity and diffusivity.

1.4.3 Solution chemistry

The studies of the influence of solution chemistry on sonolysis of contaminants often focus on the pH and organic and inorganic matrices in solution (Chakinala et al., 2007; Ince et al., 2009; Jiang et al., 2002; Tauber et al., 2000; Uddin and Hayashi, 2009). These studies are of importance for understanding the application of ultrasound in wastewater and drinking water treatment, since drinking water source waters and wastewaters usually exhibit different pH values and concentrations of organic and inorganic matrices,
depending on geological conditions or/and the sources of waters to be treated (i.e. industrial or domestic source).

1.4.3.1 pH

Previous studies have shown that pH is an important parameter in ultrasound treatment technology (Chakinala et al., 2007; Ince et al., 2009; Tauber et al., 2000; Uddin and Hayashi, 2009). It is generally accepted that the effect of solution pH determines the protonation of organic acids/bases, thus altering the degradation kinetics. Mendez-Arriaga et al., (2008) stated that ultrasound may be used to eliminate ibuprofen (IBU) in aqueous solutions and the initial degradation rate of IBU at pH 3 was significantly faster than those at pH 5 and 11. At pH values lower than its pK_a, 4.9, the protonation of the carboxylic group on IBU increases its hydrophobicity, resulting in a higher portion of IBU being degraded at the interface of the cavitation bubbles, leading to a faster degradation rate. Jiang et al., (2002) studied the sonolysis of 4-nitrophenol (pK_a =7.08) and aniline (pK_a= 4.6) with pH values ranging from 2 to 9. They observed that the degradation rate of 4-nitrophenol decreased with an increase of pH, but the degradation rate of aniline increased with an increase of pH. They attributed the faster degradation rates of neutral 4-nitrophenol and aniline over their ionic forms to the protonation of hydroxyl and deprotonation of amino groups, resulting in hydrophobic neutral species that more easily diffuse to and accumulate at bubble-water interfaces.

Several studies explain the change of solution pH to the alteration in electrical change on bubble surfaces (Cheng et al., 2008; De Bel et al., 2009; Watmough et al., 1992), ultimately resulting in increased degradation kinetics. De Bel et al. examined the
application of ultrasound for the degradation of ciproflaxin (CIPRO) in water and showed that pH affected its degradation rate as well (2009). The degradation rate at pH 3 was almost four times faster than that at pH 7 and 10. They suggested that the electrostatic attractive force between the CIPRO molecule and the negatively charged liquid-bubble interface, which increased with decreasing pH, enhanced the CIPRO degradation rate. As pH decreased, the bubble surfaces became more and more negatively charged. In addition, Watmough et al., (1992) used a 1 kV potential electrode to record the dye (i.e., methylene blue and sky blue dye) deposition on paper in a sonicated solution. They claimed that the ultrasound induced gas bubbles carry a negative electric charge with a field charge of about $7 \times 10^5$ V/m.

Other researchers have come up with different explanations (Beattie et al., 2009; Cheng et al., 2008; Winter et al., 2009). Cheng et al., (2008) monitored degradation of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) at different pH values and attributed the fast kinetics at low pH to interactions of protons with the bubble-water interface. They suggested that the bubble-water interface becomes increasingly positively charged as pH decreases below 4. Winter et al., (2009) summarized the surface-selective spectroscopy (photoelectron spectroscopy) results and molecular dynamics simulations and concluded that the air-water interface is more positively charged than the bulk due to the presence of hydronium ion in acidic solution. The conflicting studies all confirmed that the surface charge on bubbles changes as pH decreases, but it is controversial whether the charge becomes more positive or negative.

1.4.3.2 Organic and inorganic matrices
When AOPs are investigated in water treatment, the water matrix containing organic and inorganic components significantly alters the degradation of the target contaminants (Cheng et al., 2010; 2008; Lu et al., 2002; Sanchez-Prado et al., 2008; Seymour and Gupta, 1997; Taylor et al., 1999; Westerhoff et al., 1999). The mechanisms by which the matrices of organic and inorganic components affect the sonochemical degradation of contaminants are complex and not yet completely understood.

Several studies investigated the presence of natural organic matter (NOM), such as Suwannee River fulvic and humic acid (SRFA/SRHA) on sonochemical degradation of target contaminants (Cheng et al., 2008; Laughrey et al., 2001; Lu and Weavers, 2002; Taylor et al., 1999). Some studies reported that NOM reduces the sonochemical degradation of target contaminants, such as 4-chlorobiphenyl (4-CB) (Lu and Weavers, 2002), and polycyclic aromatic hydrocarbons (PAHs) (Taylor et al., 1999). The reduction in degradation was attributed to two factors: (1) NOM competes for •OH, potentially hindering target contaminant degradation, and (2) SRFA alters cavitation bubbles via surface tension changes, reducing the bubble-water interfacial temperatures during transient cavitation, ultimately decreasing observed sonochemical degradation rates of PAHs.

However, other studies claimed that the presence of NOM did not affect the sonochemical degradation of target contaminants, such as methyl tert-butyl ether (MTBE) (Kang et al., 1999), PFOS, and PFOA (Cheng et al., 2008). Kang et al., (1999) investigated the effect of NOM (i.e., made from Fluka AG) on MTBE at 358 kHz and did not observed any change in degradation rate until the NOM concentration increased to 4 mg/L. The minimal interference for MTBE may be due to first, the high volatility of
MTBE, resulting in MTBE reacting in the cavitation bubbles; second, the low mobility of NOM in sonicated solution, thus less interference by NOM. Cheng et al., evaluated the effect of the presence of NOM (e.g., humic acid and fulvic acid) on sonolysis of PFOS and PFOA at 612 kHz. With the 15 mg/L NOM, the degradation kinetics of both PFOS and PFOA were not altered by the presence of NOM. They attributed the unchanged kinetics to the nonvolatilility of humic and fulvic acids and a greater surface activity of PFOS/PFOA than NOM.

For the inorganic matrix, studies have been mainly focused on the impact of ions, especially anions, on sonolysis (Cheng et al., 2010; Minero et al., 2008; Petrier et al., 2010; Seymour and Gupta, 1997; Suri et al., 2010). However, there is no consensus of opinions on how anions affect the extent of sonochemical degradation, since a wide range of results have been reported. It is generally accepted that anions alter the sonochemical degradation of contaminants through several mechanisms: competition for •OH, alterations in water structure and accumulation of organic compounds at the bubble-water interface through salting-out effects. Suri et al., (2010) observed a wide range of anionic effects when investigating the degradation of seven different kinds of estrogenic compounds using a 20 kHz sonication unit operating at 2 kW. With the increase of HCO$_3^-$ from 0 to 10 mM, lack of effect was observed on the degradation of 17α-estradiol, 17β-estradiol, and 17α-ethinyl estradiol. However, equilin and 17α-dihydroequilin exhibited a decrease in degradation rates. Surprisingly, the presence of HCO$_3^-$ enhanced, rather reduced, the degradation of estradiol and estrone. In addition, Petrier et al., (2010) investigated the sonochemical degradation of 22 nM bisphenol-A in the presence of bicarbonate anion at 300 kHz and observed degradation rate was increased by a factor 3.2.
They attributed the enhanced degradation kinetics to oxidation of bisphenol-A by carbonate radical, a product from the reaction between •OH and bicarbonate.

\[ \text{HCO}_3^- + \cdot \text{OH} \rightarrow \cdot \text{HCO}_3 + \text{OH}^- \quad (1.15) \]

\[ \cdot \text{HCO}_3 \rightarrow \cdot \text{CO}_3^{2-} + \text{H}^+ \quad (1.16) \]

The carbonate radical, •CO_3^{2-}, with a standard electron potential 1.78 V at pH 7, may diffuse to bulk solution, resulting in oxidation of bisphenol-A. Cheng et al., (2010) investigated the effect of the specific anion on sonolysis of PFOS and PFOA at the frequency of 612 kHz. They observed that the role anions played on the degradation kinetics of PFOS and PFOA followed the Hofmeister series: ClO_4^- > NO_3^- > Cl^- > SO_4^{2-}.

They speculated that the changing water structure at the bubble-water interface due to the ions may alter water vapor transported into the bubble, resulting in a decreased collapse temperature. Seymour and Gupta (1997) observed a 6-fold increase in degradation rate for chlorobenzene, 7-fold for p-ethylphenol, and 3-fold for phenol in the presence of 1.38 M NaCl at 20 kHz. They explained that since the major portion of degradation of chlorobenzene, p-ethylphenol, and phenol occurs in the bubble-water interface, the addition of salt drove the organic compounds to the bubble surface, which is source of ultrasonic reactivity, hence resulting in a faster degradation rate.

The application of ultrasound in removal of contaminants in water is a complex process. Any change in a single parameter results in an alteration in removal efficiency. In the studies discussed above, although an explanation has been successfully applied to
each individual case, it often fails to explain other similar experimental observations. The difficulty in understanding the characteristics of ultrasonic systems is due to limited knowledge in fluid and bubble dynamics, and combined effects of the thermodynamics and kinetics of target contaminants.

1.5 Importance of scavenger study in sonochemistry

According to hot spot theory, the gas and interfacial regions of cavitation bubbles are the source of reactivity (i.e., thermolysis and •OH oxidation) and the reactions in bulk solution are due to •OH diffusing out from collapsing bubbles. In terms of •OH distribution, it is generally believed that •OH is concentrated at the bubble-water interface and the amount of •OH escaping from the hot spot to the bulk region is small. However, how much •OH escapes to the bulk solution and contributes to the overall degradation of a contaminant remains unclear, since there is no direct measurement of free •OH in the bulk region. ESR measures •OH by detecting the spin signal of an •OH-trap adduct (Riesz et al., 1985), and the terephthalate dosimeter measures •OH by detecting the fluorescence of the •OH-trap adduct (Rivas et al., 2010; Song et al., 2005). These methods do not sufficiently differentiate the locations of the •OH reaction, because the •OH-trap adduct is not selective for •OH at either the interfacial region or in bulk solution. However, the question is rather important, because it not only helps one to estimate the contribution of •OH in bulk solution to the contaminant degradation as a whole, but also to conceptualize the hot spot model and understand the spatial distribution of reaction sites.
Therefore, researchers have used •OH scavenger studies in attempts to answer this question (Beckett and Hua, 2001; Czechowska-Biskup et al., 2005; Drijvers et al., 1998; Henglein and Kormann, 1985; Nam et al., 2003; Rivas et al., 2010; Song et al., 2005; Tiehm and Neis, 2005; Wayment and Casadonte, 2002). Frequently used scavengers include terephthalic acid/terephthalate (Rivas et al., 2010; Song et al., 2005), iodide (Wayment and Casadonte, 2002), and t-butanol (Czechowska-Biskup et al., 2005; Song et al., 2005). Less commonly used scavengers include bicarbonate (Beckett and Hua, 2001), acetic acid/acetate (Tiehm and Neis, 2005), and benzoic acid/benzoate (Drijvers et al., 1998). These studies implicitly assume that the scavenger only quenches •OH.

1.6 Motivations of this study

Environmentally relevant matrix organics have been shown to have different effects on sonochemical degradation of target compounds. How the matrix of organic components affects the sonochemical degradation of contaminants is complex and not yet completely elucidated. On one hand, the presence of an organic matrix reduces the sonochemical degradation of target contaminants (Taylor et al., 1999). NOM is reported to react rapidly with •OH with a second-order rate constant $k_{OH-SRFA} = 2.7 \times 10^4$ (mgC/L)$^{-1}$ s$^{-1}$ (Goldstone et al., 2002), potentially hindering target contaminant degradation. On the other hand, the presence of organic matter did not affect the sonochemical degradation of methyl tert-butyl ether (MTBE) (Kang et al., 1999), perfluorooctane sulfonate (PFOS), and perfluorooctanoate (PFOA) (Cheng et al., 2008). In order to understand the role of matrix organics on pharmaceutical compound degradation, we degraded a hydrophilic compound, CIPRO, and a hydrophobic compound, IBU, in the presence of terephthalic
acid (TA) and SRFA. For TA, we hypothesized that, similar to matrix organics in wastewater effluent and raw drinking water, it resides and traps •OH in bulk solution. Therefore, it is used to assess the contribution of bulk •OH in overall degradation of the target contaminant.

Many studies have shown that at proper settings, the degradation of contaminants under pulsed wave (PW) ultrasound is more effective than under continuous wave (CW) ultrasound (Ciaravino et al., 1981; Deojay et al., 2011; Flynn and Church, 1984; Neppolian et al., 2009; Yang et al., 2006). PW ultrasound allows time for the surface active compound to diffuse to bubble-water interfaces, the sources of reactivity. Considering many PPCPs are hydrophobic and surface active in water with a wide range of diffusivity, PW ultrasound is expected to exhibit the potential to be a better method to remove PPCPs, as compared to CW ultrasound. Therefore, we linked the importance of physicochemical properties of the compound to degradation under PW ultrasound.

The impacts of physiochemical properties, such as surface excess (Γ) (Ashokkumar et al., 2000; Tronson et al., 2003), octanol-water partition coefficient (K_{ow}) (Nanzai et al., 2008; Park et al., 2011), vapor pressure (p) (Mizukoshi et al., 1999; Nanzai et al., 2008), Henry’s law constant (K_{H}) (Ayyildiz et al., 2007; Colussi et al., 1999), second-order rate constant (k) (Henglein and Kormann, 1985; Tauber et al., 2000), and diffusivity (D_{iw}) (De Visscher, 2003; Drijvers et al., 2000), on sonolysis of pharmaceuticals in aqueous solution have been examined. These investigated physiochemical properties can be classified into thermodynamic (e.g., Γ, K_{ow}, p, and K_{H}) and kinetic (e.g., k and D_{iw}) parameters. The thermodynamic parameters predict the ability of compounds accumulate in specific regions of the cavitation bubbles. The kinetic parameters predict the rates that
the compounds accumulate on bubbles and react with ultrasound-induced reactivity (i.e., heat and •OH). Although the dependence of degradation rate on both thermodynamic and kinetic parameters have been reported, the question regarding which aspect has a more profound influence on the cavitation systems remain unclear. We used PW ultrasound to systematically study the roles that thermodynamic (i.e., $K_{ow}$) and kinetic parameters (i.e., $D_{iw}$) play in determining pharmaceutical degradation. Previous studies found that PW ultrasound, under certain optimal conditions, enhances the degradation of a compound, because it allows time (i.e., silent cycle) for the surface active compound to diffuse to bubble-water interfaces, the sources of reactivity. Thus, with the silent cycle in PW mode, we can compare the relative influence of each parameter in determining degradation kinetics.

In addition, we investigated the degradation kinetics of these six pharmaceuticals in DI and in a wastewater effluent to evaluate the effect of environmentally relevant matrices. Since previous studies reported that under certain optimal conditions enhanced degradation was observed with PW ultrasound in pure aqueous solutions, PW ultrasound exhibits practical potential to effectively remove pharmaceuticals in a wastewater effluent. Moreover, the selected six pharmaceuticals have been detected in wastewater effluent (Batt et al., 2008; Langford and Thomas, 2009; Martin et al., 2011; Matamoros et al., 2009; Nakada et al., 2004; Yu et al., 2006). Thus our study investigated the treatability of a frequently-detected pharmaceutical by ultrasound.

1.7 Organization of the dissertation
The dissertation is composed of five chapters. Chapter 1 introduces the background and motivations of the study. Chapter 2 investigates sonochemical degradation of IBU and CIPRO in the presence of matrix organics, SRFA and TA. Chapter 3 evaluates the commonly used •OH scavengers by using PW ultrasound. Chapter 4 studies the impact of PW vs. CW ultrasound on degradation kinetics of the PPCPs, including CBP, IBU, CIPRO, ATP, SFT, PG, and DP. Chapter 5 demonstrates the treatability of ultrasound to remove the PPCPs, including 5-FU, IBU, clonidine (CLND), estriol (ESTO), nifedipine (NIFE), and LOVS in municipal wastewater. Finally, Chapter 6 summarizes all the conclusions we drew in this study and describes the future work to be conducted to complement this study. During my PhD study, my interest in computational chemistry has developed. Under the supervision of Dr. Richard Spinney in the Chemistry department, I studied the thermodynamics and kinetics of ibuprofen with hydroxyl radical in aqueous solution. Considering this work is independent of my own PPCPs project, it is in the Appendix.
Figure 1.1: Spatial distribution of temperature and different species in the three reaction zones in cavitation bubble.
Figure 1.2: Schematic diagram of continuous wave (CW) and pulsed wave (PW) ultrasound.


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Chapter 2: Sonochemical Degradation of Ciprofloxacin and Ibuprofen in the Presence of Matrix Organic Compounds

21. Abstract

Ultrasonic irradiation was employed to degrade ciprofloxacin (CIPRO) and ibuprofen (IBU), a hydrophilic and a hydrophobic compound, respectively, at the frequencies of 20 and 620 kHz. Results show that the initial degradation rate depends on solute concentration, ultrasound frequency, and the presence of matrix organic matter. The initial degradation rate of IBU was approximately 1 to 4 fold faster than that of CIPRO under equivalent conditions, indicating that the hydrophobicity of the compound plays an important role in sonochemical degradation. In the presence of terephthalic acid (TA), a commonly used •OH scavenger, CIPRO degradation was inhibited by a factor of 40 to 1500 depending on the frequency and initial concentration. However, the degradation rates of IBU were only reduced between 30% and 80%. Similar to TA, the presence of Suwannee River Fulvic Acid (SRFA) inhibited CIPRO to a greater extent than that of IBU but overall inhibition by SRFA was dramatically less than by TA. Although both TA and SRFA inhibited the degradation of CIPRO and IBU, the controlling mechanisms are different. TA reacts with •OH in bulk solution but we also suspect it accumulates on or interacts with cavitation bubbles. On the other hand, SRFA stays in bulk solution, quenching •OH and/or associating with the target compounds. Our
results suggest that CIPRO primarily degrades by •OH oxidation in bulk solution. However, both interfacial and bulk solution degradation play important roles in the sonolysis of IBU, and the relative importance of the two pathways depends on the initial concentration, the presence of matrix organics, and the ultrasonic frequency.

2.2 Introduction

Numerous studies have reported measuring pharmaceuticals at parts-per-trillion to parts-per-billion concentrations in aquatic systems (Boyd et al., 2003; Ellis, 2006; Kolpin et al., 2002; Hartmann et al. 1999; (Miege et al., 2009). Since these microconstituents are present in much lower concentrations than conventional contaminants, it is difficult to remove them in the presence of organic and inorganic matrices that are a thousand to a million fold more abundant. Although the toxicity of continual low level exposure to these compounds by humans is uncertain and these emerging pollutants are unregulated, studies have shown adverse effects on aquatic microorganisms (Christensen et al., 2006) and fish (Carlsson et al., 2009). To date, an effective strategy to mitigate these unforeseen microconstituents from the aquatic environment does not exist.

Advanced oxidation processes (AOPs) have the potential to substantially reduce contaminants from water and wastewater (Shannon et al., 2008; Snyder et al., 2003; Westerhoff et al., 2005). Ultrasonic irradiation is an emerging AOP with advantages over other AOPs due to its ease of use, lack of chemical addition, and unique degradation mechanisms. Sonochemical techniques involve the use of ultrasonic waves to produce cavitation bubbles in solution. During the collapse of cavitation bubbles localized hot
spots are formed (Gutierrez et al., 1986), reaching average bubble temperatures of roughly 5000 K and pressures of approximately 500 atm (Suslick, 1990).

Considering these cavitation bubbles as microreactors, three different reaction zones have been postulated: (i) the gaseous interiors of collapsing cavities resulting in dissociation of volatile compounds including water through thermolysis; (ii) the interfacial liquid surrounding cavitation bubbles where high temperature (ca. 1000-2000 K) and high concentrations of •OH (4 mM) exist (Gutierrez et al., 1991); and (iii) bulk solution (at ambient temperature) where small amounts of •OH diffusing from bubble interfaces may contribute to contaminant destruction reactions (Suslick, 1990; Suslick et al., 1986). The degradation pathway of a particular organic compound depends on its physicochemical properties, surface activity, and hydroxyl radical reactivity. Thus, sonochemistry is a complex phenomenon with two primary mechanisms: thermolysis and radical species reactions.

Recently, sonication of aqueous solutions has been shown to be effective for the destruction of IBU and CIPRO. Mendez-Arriaga et al. (2008) concluded that ultrasound may be used to eliminate IBU in aqueous solution and demonstrated that applied sonication power, dissolved gas, pH and initial concentration played roles during the process. Madhavan et al., (2010) studied the degradation of IBU in the sonolytic, photocatalytic, and sonophotocatalytic systems, and observed synergistic degradation during sonophotocatalysis. De Bel et al., observed that pH affected the ultrasonic degradation rate, biodegradability, and ecotoxicity of aqueous CIPRO solution (De Bel et al., 2009; De Bel et al., 2011). Our study verifies and builds upon the previous work.
Matrix organics have been shown to have different effects on sonochemical degradation of the target compounds. Matrix organics may inhibit the degradation of compounds through competing for hydroxyl radicals and/or altering the availability of compounds to sonolytic activity (Laughrey et al., 2001; Lu and Weavers, 2002). Terephthalic acid (TA), a typical \( \cdot \)OH scavenger and dissolved Suwannee River FA (SRFA), a model natural organic matter (NOM) were used as a bulk \( \cdot \)OH scavenger and as a model matrix organic compound, respectively. The very low concentrations of CIPRO and IBU observed in water and wastewater compared to matrix organics indicates the need to understand the role of matrix organics on pharmaceutical compound degradation. IBU and CIPRO were chosen because they are, respectively, relatively hydrophobic (true log \( K_{\text{ow}} \) =3.97) and hydrophilic (log \( K_{\text{ow}} \) =0.28) examples within these classes of compounds.

2.3 Materials and Methods

IBU (99%, Acros) and CIPRO (BioChemika, \( \geq \)98%) were purchased from Aldrich and used as target compounds without further purification. Table 2.1 lists relevant data for both pharmaceuticals. Water used to prepare solutions was from a Millipore system (\( R = 18.2 \ \text{M} \Omega\cdot\text{cm} \)). Terephthalic acid (99 %) was purchased from Fluka. SRFA reference material was obtained from the International Humic Substances Society and used without further purification.

Two ultrasonic units, a 20 kHz ultrasonic probe system (Sonic Dismembrator 550, Fisher Scientific) with an irradiating area of 1.27 cm\(^2\) and a 620 kHz transducer system
(ELAC Nautik, Inc., Kiel, Germany) with a 23 cm² transducer were applied to irradiate CIPRO and IBU in water. In both systems, sonochemical power density input into the reactor was adjusted and measured by calorimetry to be approximately 400 W/L. Water jacketed glass reactors containing 50 mL (for 20 kHz) and 125 mL (for 620 kHz) reaction solutions were controlled at 20 °C by a cooling bath (Fisher Scientific, 1006S). Although the power densities are the same, the cavitation fields between the two sonication systems are different due to different geometries and irradiating surface areas.

Solution pH was continuously monitored and kept constant at pH 8.5 by adding 0.01 M NaOH or HNO₃ solution during sonication. Initial individual compound concentrations of 1, 10, and 100 μM were used to probe the concentration effect under different conditions. In select experiments, 2 mM of TA was added to CIPRO and IBU solution. The effect of SRFA on the degradation of CIPRO and IBU was examined at three different initial concentrations (0.66, 3.1 and 16.5 mgC/L of SRFA). All the experiments were carried out in, at least, duplicate.

At specific times during sonolysis, 0.5 mL of sample was taken from the batch reactors for analysis. The total volume withdrawn during a single run was less than 5% of the total sonicating volume. Analysis of CIPRO and IBU was performed using a high performance liquid chromatograph (HPLC) (Hewlett Packard 1100), with an Allure C₁₈ column (5 μm, 150 × 3.2 mm, Restek). CIPRO and IBU were detected at wavelengths of 274 nm and 223 nm, respectively. A pH 3.0 phosphate buffer: 7 % acetonitrile mobile phase was ramped to 78% acetonitrile at a flow rate 0.5 mL/min. An eluent (0.8 mL/min) of 50 % of acetonitrile: 50 % pH 3.0 phosphate buffer was used for IBU. The initial SRFA concentration in solution was quantified by a Shimadzu TOC-5000A analyzer.
2.4 Results and Discussion

2.4.1 Degradation of Ciprofloxacin and Ibuprofen

The sonochemical degradation of CIPRO and IBU is shown in Figure 2.1. Consistent with previous studies (De Bel et al., 2009; De Bel et al., 2011; Madhavan et al., 2010; Mendez-Arriaga et al., 2008), both compounds were degraded by ultrasound. However, due to different initial concentrations, frequencies and power input, comparing the degradation rates in their studies and those in ours is not appropriate. In comparing the sonolysis of CIPRO to IBU, we observed that, with one exception, the degradation rate of IBU was faster than that of CIPRO (Table 2.2). At 620 kHz the half-life for IBU was a factor of 3 to 4 times shorter than CIPRO at the same initial concentration. The difference in half-life between IBU and CIPRO was less pronounced at 20 kHz with IBU degrading approximately twice as fast as CIPRO at 100 μM and similarly at 1 μM.

The discrepancy in degradation rates between CIPRO and IBU is attributed to different physiochemical properties of the compounds. First, as shown in Table 2.1, IBU is more hydrophobic than CIPRO based on their true and apparent Kow values, indicating that IBU is more likely to accumulate to a large extent in the cavitation bubble interfacial region where it is subjected to thermolysis and higher [•OH].

Also, the diffusion coefficient of IBU (D_{IBU}) in dilute solution is greater than that of CIPRO (D_{CIPRO}) (D_{IBU}/D_{CIPRO}=1.3), suggesting that IBU has a greater chance to encounter ultrasound-induced reactivity and be degraded. Drijvers, et al., (2000) observed that sonochemical degradation rates of halobenzenes were determined by their diffusion
coefficient (i.e., the compound with a greater diffusion coefficient exhibited a faster degradation rate). Our results are consistent with previous studies and corroborates that the degradation rate is dependent on the hydrophobicity (Nanzai et al., 2008; Okuno et al., 2000) and diffusivity (Ayyildiz et al., 2007; Drijvers et al., 2000) of the compounds.

As shown in Table 2.2 and Figure 2.2, sonolysis at 620 kHz resulted in faster degradation than 20 kHz for both IBU and CIPRO with rates being approximately 1 to 100 fold faster, depending on the initial concentrations. It is well-known that ultrasonic frequency significantly affects sonolysis due to both the critical size and the lifetime of cavitation bubbles, which consequently affect the number of cavitation bubbles, the violence of bubble collapse, and the amount of hydroxyl radical production (Petrier et al., 1996; Petrier et al., 1992). Many studies have reported faster degradation of organic compounds at frequencies ranging from about 200 to 600 kHz, as compared to 20 kHz (Chen et al., 2004; Francony and Petrier, 1996; Petrier et al., 1996; Weavers et al., 2000). Our results are consistent with these previous studies.

The concentration effect on sonochemical degradation rates is also depicted in Figure 2.2. The degradation rate increases as the initial concentration increases. However, since the degradation follows apparent pseudo first-order kinetics at each concentration, faster degradation occurs with lower initial concentration of CIPRO and IBU. The $k_{obs}$ values for CIPRO and IBU at 1 $\mu$M were approximately 2 to 20 times higher than those at 10 $\mu$M and 100 $\mu$M under equivalent conditions (Table 2.2). Similar results have been obtained by others (Drijvers et al., 1999; Drijvers et al., 1998; Weavers et al., 2000). A degradation study of estrogen hormones at levels as low as 1 $\mu$g/L (~3 nM) at a frequency
of 20 kHz demonstrated that this trend is valid at even lower concentrations (Fu et al., 2007).

As shown in Figure 2.2 and Table 2.2, the effect of concentration on degradation rates is more pronounced for IBU than that of CIPRO especially at 620 kHz. For example, at 20 kHz for IBU, \( \left( \frac{dC}{dt} \right)_{100\mu M} : \left( \frac{dC}{dt} \right)_{1\mu M} \) is 6.1, but for CIPRO \( \left( \frac{dC}{dt} \right)_{100\mu M} : \left( \frac{dC}{dt} \right)_{1\mu M} \) is 2.8; at 620 kHz for IBU \( \left( \frac{dC}{dt} \right)_{100\mu M} : \left( \frac{dC}{dt} \right)_{1\mu M} \) is 38, but for CIPRO \( \left( \frac{dC}{dt} \right)_{100\mu M} : \left( \frac{dC}{dt} \right)_{1\mu M} \) is 33.8.

The small difference in rates at 20 kHz and large difference at 620 kHz with increasing concentration are attributed to bubbles undergoing more oscillations during their lifetime at 620 kHz compared to 20 kHz. At high frequency (620 kHz), stable cavitation bubbles, experiencing more oscillations and a longer lifetime before collapsing, dominate the whole bubble population, leading to greater adsorption of CIPRO/IBU to bubble surfaces (Price et al., 2010; Sunartio et al., 2007). Thus, the high adsorption capacities of stable cavitation bubbles make the concentration effect more pronounced.

At low frequency (20 kHz), transient cavitation bubbles, undergoing fewer oscillations, are in the majority; hence, low adsorption capacity results in a smaller concentration effect. A smaller increase in rate with increase in concentration is observed with Langmuir type adsorption when reactive surfaces are not saturated. Our results are consistent with Tronson et al., (2002) who reported that surface active aliphatic alcohols significantly inhibited sonoluminescence (SL) intensity at a frequency of 515 kHz but not
at 20 kHz, suggesting that organics are more able to accumulate on bubble surfaces at 515 kHz compared to 20 kHz.

In addition, the effect of concentration is greater for IBU than CIPRO at both frequencies, which is attributed to the greater hydrophobicity and diffusivity of IBU. A compound like IBU will have both a thermodynamic and kinetic advantage increasing its ability to accumulate on the bubble interface, resulting in thermolysis and •OH reactions. Thus, with the increase of concentration of the target compound, the advantage becomes more obvious. Although the potential of CIPRO and IBU to volatilize into the gas phase of the bubble is low due to low Henry’s law constants, the higher hydrophobicity of IBU compared to CIPRO suggests that, given a long enough bubble lifetime, IBU will accumulate at the bubble interface. The smaller difference in rate as a function of concentration at 620 kHz for CIPRO over IBU suggests that with CIPRO reactive bubble surfaces are farther from saturation. Therefore, the higher hydrophobicity and diffusivity of IBU compared to CIPRO leads to more IBU accumulation at the bubble interface; this effect is more pronounced at 620 kHz.

The feature of faster $k_{\text{obs}}$ (Table 2.2) with the decrease in solute concentrations is promising for the application of sonochemistry to eliminate PPCPs in aqueous systems, especially for low levels of microconstituents. For instance, the $t_{1/2}$ is significantly reduced from 103 min to 6.3 min for IBU at 20 kHz as its initial concentration decreases from 100 μM to 1 μM. Many PPCPs such as antibiotics, fragrances and estrogens are more hydrophobic than IBU and CIPRO and the reported levels in water supplies are as
low as nM. Therefore, the sonochemical degradation of PPCPs is expected to succeed under short treatment times.

2.4.2 Effects of Matrix Organics on Degradation

When AOPs are investigated in water treatment, the water matrix containing inorganic and organic components significantly slows the degradation of the target contaminants (Cheng et al., 2010; 2008; Westerhoff et al., 1999). How the matrix of organic components affect the sonochemical degradation of contaminants is complex and not yet completely elucidated. On one hand, the presence of an organic matrix reduces the sonochemical degradation of target contaminants (Lu and Weavers, 2002; Taylor et al., 1999). NOM is reported to react rapidly with •OH with a second-order rate constant $k_{\text{•OH-SRFA}} = 2.7 \times 10^4 \text{(mgC/L)}^{-1} \text{s}^{-1}$ (Goldstone et al., 2002), potentially hindering target contaminant degradation. Lu and Weavers (2002) observed that humic acid (HA) decreased the sonochemical degradation rate of 4-chlorobiphenyl (4-CB) and the effect was more pronounced with an increase in HA concentration. Additionally, the sonication of polycyclic aromatic hydrocarbons (PAHs) with fulvic acid (FA) dramatically reduced the degradation rate of PAHs (Taylor et al., 1999). On the other hand, the presence of organic matter did not affect the sonochemical degradation of methyl tert-butyl ether (MTBE) (Kang et al., 1999), perfluorooctane sulfonate (PFOS), and perfluorooctanoate (PFOA) (Cheng et al., 2008). In order to remove PPCPs from wastewater effluent or raw drinking water, ultrasound will need to be selective for PPCPs over matrix organics.

2.4.2.1 Terephthalic Acid
To gain a sense of the interference of non-target organic compounds, we first employed TA as a bulk •OH scavenger. TA has been widely used to monitor the yields of •OH in different oxidation systems (Matthews, 1980; Page et al., 2010; Price and Lenz, 1993). Sonochemical researchers have employed it as a bulk •OH scavenger (Price et al., 1997; Song et al., 2005; Villeneuve et al., 2009) due to its high second-order •OH rate constant \(3.3 \times 10^9 \text{ M}^{-1} \text{s}^{-1}\) (Buxton et al., 1988) and its deprotonated form in neutral and alkaline solution (pK\(_a\) values, 3.52 and 4.46), suggesting that it will stay in bulk solution during sonication (Mason et al., 1994; Song et al., 2005). Consistent with others, we assume that, similar to matrix organics in wastewater effluent and raw drinking water, TA resides and traps •OH in bulk solution. Therefore, it is used to assess the contribution of bulk •OH in overall degradation of the target contaminant.

As shown in Table 2.2 and Figure 2.2, in the presence of 2 mM TA, the degradation rates at different initial CIPRO and IBU concentrations are significantly reduced compared to no TA present \((p<0.01)\). The degradation rate of CIPRO was reduced by a factor of between 40 and 70 at 620 kHz, and between 70 and 1500 at 20 kHz in the presence of TA as compared to degradation in its absence. The degradation rate of IBU was decreased by a factor of 2 and 10 at 20 kHz and 2 at 620 kHz in the presence of TA as compared to that in its absence.

To predict the impact of TA on degradation rates, the bulk •OH quenching ratio \((Q)\) of TA was calculated (MWH, 2005):

\[
Q_{TA} = \frac{k_c[C]}{k_{TA}[C] + k_c[C]} \tag{2.1}
\]
where $k_C$ and $k_{TA}$ are the reported second order rate constants of $\cdot$OH reacting with the target compound (i.e., CIPRO or IBU) and TA, respectively. $[C]$ and $[TA]$ are the concentrations of the target compound and TA, respectively. Assuming bulk reactions of TA and the target compounds, the predicted impact of TA was determined by multiplying $Q_{TA}$ by the observed degradation rate of IBU or CIPRO in the absence of TA:

$$
\frac{dC}{dt}_{\text{0,predicted}} = Q_{TA} \times \frac{dC}{dt}_{\text{0,obs w/o TA}}
$$

As shown in Figure 2.3, the observed values for IBU are significantly higher than the predicted values at all concentrations and frequencies, indicating that IBU degradation is reduced less by TA than predicted if both compounds are equally distributed in the system. The preferential degradation of IBU is consistent with it preferentially accumulating on cavitation bubble surfaces. However, for CIPRO the observed values are lower than the predicted values at 100 $\mu$M under both 20 and 620 kHz frequencies. The higher predicted rates than the observed rates at 100 $\mu$M initial concentration indicates that TA is preferentially degraded over CIPRO.

In addition to $\cdot$OH reaction in bulk solution, sonochemical degradation of compounds occurs by high temperature and $\cdot$OH reaction in and on cavitation bubbles (Gutierrez et al., 1986). Thus, sonochemical degradation is described by eqn. 2.3:

$$
\frac{dC}{dt}_{\text{obs}} = \frac{dC}{dt}_{\text{bulk}} + \frac{dC}{dt}_{\text{interface}} + \frac{dC}{dt}_{\text{bubble}}
$$

where $\frac{dC}{dt}$ represents the degradation rate of either CIPRO or IBU observed (obs), occurring in bulk solution (bulk), occurring at the interface (interface), and occurring in the gas region of cavitation bubble (bubble), respectively. Assuming that TA remains in
bulk solution and quenches bulk •OH, its presence only impacts \( \frac{dC}{dt_{\text{bulk}}} \). A predicted degradation rate with TA similar to or greater than the observed degradation rate suggests that reaction of CIPRO occurs dominantly in bulk solution (i.e., \( \frac{dC}{dt_{\text{bulk}}} \gg \frac{dC}{dt_{\text{interface}}} + \frac{dC}{dt_{\text{bubble}}} \)). Therefore, at 100 μM either CIPRO does not partition to the cavitation bubble interface and gas region, TA does partition to the bubble interface, or both.

De Bel et al., (2011) modeled CIPRO degradation in sonochemical systems and concluded that most of the CIPRO degradation takes place at the bubble-liquid interface. However, an apparent log \( K_{\text{ow}} \) value of -1.52 at the pH used in our experiments suggests that CIPRO will not accumulate at bubble surfaces. Our results are consistent with CIPRO mainly reacting in bulk solution, contrary to De Bel et al., (2011).

Table 2.2 and Figure 2.2 demonstrate that the presence of TA decreased IBU degradation to different extents. As shown in eqn. 2.3, with the assumption that TA quenches •OH in bulk solution, the difference between the observed degradation rate and the predicted degradation rate is attributed to the portion that degraded in non-bulk solution (i.e., \( \frac{dC}{dt_{\text{interface}}} + \frac{dC}{dt_{\text{bubble}}} \)). With low Henry’s law constants for IBU and TA, the portion reacting in the gas region of cavitation bubbles (i.e., \( \frac{dC}{dt_{\text{bubble}}} \)) is expected to be negligible; hence these results suggest that the majority of IBU degradation occurs at interface (i.e., \( \frac{dC}{dt_{\text{interface}}} \)) at 20 and 620 kHz, respectively. The smaller effect of TA at 620
kHz and with IBU over CIPRO is consistent with more IBU accumulation on the bubble surfaces, particularly at 620 kHz.

The difference in cavitation bubble features between the 20 kHz probe and the 620 kHz transducer systems may also result in a larger effect of TA on CIPRO and IBU degradation at 20 kHz. Hydroxyl radical is a direct product of the collapse of cavitation bubbles. Sonochemically-induced chemiluminescence has been applied to elucidate the spatial distribution of ultrasonic cavitation in solution (Chen et al., 2004; Petrier et al., 1994; Price et al., 2010). Using a 20 kHz probe system, Chen et al (2004) observed localized cavitation in the vicinity of the probe surface extending approximately 1 cm into solution. In a study by Petrier et al. (1994), a 487 kHz transducer sonication system resulted in a dispersive spatial distribution of cavitation bubbles. In our study, a similar localized bubble cloud is expected to be in the vicinity of the sonication probe tip at 20 kHz, while the cavitation bubbles at 620 kHz system are expected to affect the entire reactor. The dense bubble cloud at 20 kHz results in TA being more likely to enter the localized bubble cloud and quench ultrasound-induced reactivity. TA penetrating the bubble cloud, therefore, reduces CIPRO and IBU degradation more at 20 kHz than at 620 kHz. The more pronounced reduction in degradation for CIPRO over IBU with TA present does suggest that IBU does accumulate more than CIPRO even at 20 kHz but the ability or extent of CIPRO and IBU to accumulate on bubbles is reduced compared to 620 kHz.

Predicted CIPRO degradation rates in the presence of TA greater than the corresponding observed rates indicating preferential degradation of TA over CIPRO has caused us to reexamine the assumption that TA resides and traps •OH in bulk solution.
Although the apparent log $K_{ow}$ of TA (-2.15 at pH 8.5) indicates it will not be favorable to partition to bubble interfaces as compared to CIPRO (log $K_{ow} = -1.52$) and IBU (log $K_{ow} = 0.24$), previous studies have shown that mass transport of target compounds to the bubble surface is controlled by diffusion (De Visscher, 2003; DeVisscher et al., 1996; Drijvers et al., 2000; Yang et al., 2005). The calculated diffusion coefficient of TA ($D_{TA}$) in dilute solution is greater than that of CIPRO ($D_{CIPRO}$) and IBU ($D_{IBU}$) with diffusion coefficient ratios, $D_{TA}/D_{CIPRO} = 1.5$ and $D_{TA}/D_{IBU} = 1.1$, respectively, suggesting that TA will diffuse more rapidly in solution and to bubbles. Therefore, the discrepancy between these results indicating preferential degradation of TA over CIPRO at 100 $\mu$M (Figure 2.3) and previous studies indicating degradation of CIPRO occurs primarily at bubble interfaces combined with the higher diffusion coefficient of TA suggests that TA is not an optimal bulk phase $\cdot$OH scavenger. We suspect that TA may partition to or otherwise affect cavitation bubbles.

2.4.2.2 Suwannee River Fulvic Acid

It is well known that the presence of NOM, which is ubiquitous in natural waters, poses significant challenges in the implementation of AOPs due to the reaction of NOM with $\cdot$OH (Snyder et al., 2003; Westerhoff et al., 1999). Therefore, CIPRO and IBU were sonicated together with SRFA, a representative water soluble NOM, to elucidate the ability of NOM to reduce target contaminant degradation and to examine the impact of hydrophobicity of the pharmaceutical on degradation in the presence of SRFA.

As shown in Table 2.2 and Figure 2.4, similar to TA, the presence of SRFA reduced the initial degradation rate of CIPRO and IBU, but the reduction in the rate by TA was
greater than by SRFA. At 620 kHz the degradation rates of CIPRO at 1 and 10 μM are almost completely inhibited by TA but ca. 60-70% reduced by SRFA even at the highest SRFA concentration. SRFA inhibited the degradation rate of IBU at 20 kHz (Figure 2.4a), but little reduction in rates was observed at 620 kHz (Figure 2.4b). The presence of SRFA had a more pronounced effect on reducing the degradation rate of CIPRO at both 20 and 620 kHz, particularly as the SRFA concentration increased. This decrease is more pronounced at 20 kHz than 620 kHz.

In comparing SRFA to TA, a greater reduction of degradation of CIPRO and IBU by TA than SRFA was observed. SRFA is rich in carboxyl and hydroxyl functional groups, which makes SRFA very soluble and hydrophilic (Chiou, 2002). Thus, SRFA is expected to remain in bulk solution and not expected accumulate on bubble surfaces. The weight-average molecular weight of SRFA ranges from 1000 to 26000 Dalton (Wagoner et al., 1997). Molecular weight of a compound is correlated to size of a compound and the size of a compound is inversely related to diffusivity. Although the diffusivity of SRFA has not been reported, it is expected to be significant smaller than CIPRO, IBU, and TA because of the large molecular weight of SRFA (Wagoner et al., 1997) compared to CIPRO, IBU, and TA. In addition, Goldstone et al., (2002) measured its second order rate constant with •OH to be 2.7×10^4 (mgC/L)^1 s^-1. At the NOM and CIPRO and IBU concentrations in these experiments, SRFA will compete with CIPRO and IBU for •OH in bulk solution. Therefore, SRFA is expected to stay in bulk solution, diffuse comparatively slowly through solution, and quench •OH reactions with CIPRO and IBU in bulk solution at high [SRFA] and/or low [CIPRO] and [IBU]. TA, on the contrary, is an effective bulk •OH quencher under all conditions and diffuses quickly in solution.
Previous studies have observed varying effects of organic matter on the sonolysis of contaminants. Using a 20 kHz probe, Taylor et al., (1999) observed that SRFA inhibited sonochemical degradation of anthracene, phenanthrene, and pyrene. They attributed inhibition by SRFA to sequestering of the compounds away from the cavitation bubbles by SRFA, or changing cavitational conditions due to surface tension changes in the presence of SRFA. Lu and Weavers (2002) observed that Aldrich HA affected 4-CB degradation at 20 kHz and its presence increased with an increase of HA concentration. The reduction in rate was related to two factors: 4-CB and HA competing for •OH, and 4-CB associating with HA sequestering 4-CB from cavitation sites. Kang et al., (1999) reported no effect of Fluka HA on MTBE degradation at 358 kHz, and attributed the lack of effect to the high volatility of MTBE, resulting in MTBE reacting in the cavitation bubbles. Cheng et al., (2008) found that the effect of NOM (i.e., SRHA and SRFA) on sonochemical degradation rates of PFOS and PFOA was not significant due to little interference by the NOM on the interfacial region of cavitation bubbles. Based on our results and those of others described above, organic matter may compete for •OH, sequester target contaminant from cavitation bubbles, and alter cavitation bubbles. Contaminant degradation may be inhibited to varying degrees depending on the nature of the cavitation and the characteristics of the contaminant.

SRFA competes with CIPRO and IBU for •OH, resulting in a reduction in CIPRO and IBU degradation. Similar to quenching by TA, the quenching ratio (Q) of SRFA in bulk solution was calculated by eqn. 2.4 (MWH, 2005):

\[
Q_{SRFA} = \frac{k_c[C] \times (1-S)}{k_{SRFA}[SRFA] + k_c[C] \times (1-S)}
\]  

(2.4)
where $k_{SRFA}$ is the second order rate constant of $\cdot \text{OH}$ reacting with SRFA. $S$ is the fraction of C sequestered by SRFA calculated from Chin et al., (1997). The term $1-S$ represents the fraction of CIPRO or IBU that is not interacting with SRFA and thus available in solution. Similar to the quenching ratio with TA, assuming SRFA and C are equally distributed in solution, the degradation rate of CIPRO or IBU in the presence of SRFA is predicted by multiplying the quenching ratio by the initial degradation rate in the absence of SRFA.

$$
\frac{dC}{dt}\bigg|_{0,\text{predicted}} = Q_{SRFA} \times (1-S) \times \frac{dC}{dt}\bigg|_{0,\text{obs w/o SRFA}}
$$

(2.5)

where $k_{obs \ w/o \ SRFA}$ is the observed first-order degradation rate ($\text{min}^{-1}$) of IBU or CIPRO in the absence of SRFA; $C_0$ is the initial concentration of the target compound. As shown in Figure 2.5, all the reported values are greater than or equal to the predicted values. The trend suggests that, as compared to SRFA, both CIPRO and IBU have a relatively greater mobility towards the cavitation bubbles. The difference between observed rates and predicted rates is attributed to CIPRO and IBU reaction at cavitation bubble interfaces.

The fractions of CIPRO and IBU associating with SRFA at different concentrations of SRFA are approximately 1%, 5% and 25% at SRFA concentrations of 0.66, 3.1, 16.5 mgC/L, respectively (Table 2.3). The predicted fractions of the CIPRO and IBU sequestered by SRFA are smaller than the amount of reduction in degradation. For example, a 95% reduction in IBU degradation at a concentration of 1 µM at 20 kHz was observed but only 1% of IBU is predicted to be associated with SRFA. Thus, sequestration of CIPRO and IBU by SRFA binding alone is not sufficient to explain the reduction in degradation.
Although Taylor et al., (1999) attributed reduced PAHs degradation to SRFA sequestration of PAHs from cavitation bubbles, they also proposed that SRFA may alter cavitation bubbles via surface tension changes. Yates and von Wandruszka (1999) showed the surface tension of bulk solution remained unchanged (ca. 72 mN/m) at 500 mg/L SRFA and pH 8.0. In our work, the highest concentration of SRFA used was 16.5 mgC/L (25 mg/L). In addition, NOM is more aggregated in neutral and basic solution than in acidic solution, resulting in less ability to change surface tension at pH 8.5 (Yates and von Wandruszka, 1999). Therefore, we do not expect that SRFA directly impacts cavitation bubbles.

In comparing Figure 2.4a and b, more interference of SRFA is observed at 20 kHz than 620 kHz with both IBU and CIPRO. The minimal influence of SRFA on sonolysis of IBU at 620 kHz suggests that at 620 kHz IBU accumulates on the bubbles to a greater extent compared to 20 kHz. The limited impact of SRFA on IBU degradation at 620 kHz is attributed to the affinity of IBU to bubble surfaces and the characteristics of the cavitation bubbles produced at 620 kHz. The features of ultrasound at 620 kHz include more bubble oscillations within a bubble lifetime, more bubbles, and a more dispersive bubble population (Petrier et al., 1996; Petrier et al., 1992), all favoring accumulation of compounds. On the contrary, the bubbles generated at 20 kHz are not favorable for accumulation due to the localized bubble population (Petrier, et al. 1992).

Similar to the observation that TA impacted IBU degradation less than CIPRO, the presence of SRFA has a more pronounced effect on the degradation rate of CIPRO than IBU. IBU is a more hydrophobic compound with a higher diffusivity as compared to CIPRO ($D_{IBU}/D_{CIPRO}=1.3$); therefore, IBU is more likely to transport to and accumulate
on the bubble surface. On the contrary, SRFA has a sizeable volume (Zhou et al., 2000), which hinders its propensity and ability to move to cavitation bubbles, the sources of reactivity. The greater effect of SRFA on CIPRO degradation than IBU degradation also supports our suggestion that CIPRO undergoes bulk solution degradation to a larger extent than IBU due to the differences in their hydrophobicities and diffusivities.

2.5 Conclusions

Our results show that in the absence of matrix organics the degradation rates of CIPRO and IBU depend on their initial concentrations and ultrasonic frequencies: a short half-life is observed as the initial concentration decreases, and 620 kHz is more effective as compared to 20 kHz.

The sonochemical degradation of target compounds proceeds at different rates in the presence of matrix organics, which provides insight to the application of ultrasound in wastewater and drinking water treatment. Specifically, a more hydrophobic target compound with higher diffusivity is impacted little by presence of matrix organics. The diffusivity and concentration of matrix organics determine treatability by ultrasound. A larger size and lower concentration of matrix organics in water have a smaller impact on the treatability of target contaminants by ultrasound as compared to a smaller size and higher concentration of matrix organics. Obviously, it is optimal to remove of matrix organics (especially small sized organics) before ultrasound treatment to maximize its efficiency. However, when this is not feasible, ultrasound may be effective for removal of hydrophobic and surface active contaminants in the presence of matrix organics that reside in bulk solution, such as SRFA. Our results provide further insight on the minimal
influence of FA and HA on sonochemical degradation of MTBE, PFOS, and PFOA. Like MTBE, PFOS and PFOA, IBU migrates from bulk solution to cavitation bubbles, the sources of reactivity. Our results indicate that CIPRO does not migrate to cavitation bubbles resulting in greater competition with NOM for bulk •OH. The cavitation conditions in 20 kHz ultrasound limit the ability of IBU to accumulate on bubble surfaces resulting in more competition with NOM for bulk •OH.
Table 2.1: Physicochemical Properties of CIPRO and IBU

<table>
<thead>
<tr>
<th>compounds</th>
<th>ciprofloxacin (CIPRO)</th>
<th>ibuprofen (IBU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>structure</td>
<td><img src="image" alt="CIPRO structure" /></td>
<td><img src="image" alt="IBU structure" /></td>
</tr>
<tr>
<td>use class</td>
<td>antibiotic</td>
<td>painkiller</td>
</tr>
<tr>
<td>solubility (mg L(^{-1}))</td>
<td>700</td>
<td>21</td>
</tr>
<tr>
<td>log Henry’s law constant at 25 °C (atm-m(^3) mol(^{-1}))</td>
<td>-18.30</td>
<td>-6.82</td>
</tr>
<tr>
<td>true log (K_{ow})</td>
<td>0.28</td>
<td>3.97</td>
</tr>
<tr>
<td>(Takacsnovak et al., 1992)</td>
<td>(Avdeef et al., 1998)</td>
<td></td>
</tr>
<tr>
<td>apparent log (K_{ow})</td>
<td>-1.52 (pH=8.5)</td>
<td>0.24 (pH=8.5)</td>
</tr>
<tr>
<td>(ACD/Labs6.00, 2002)</td>
<td>(Avdeef et al., 1998)</td>
<td></td>
</tr>
<tr>
<td>(pK_a)</td>
<td>3.64, 5.05, 6.95, 8.95</td>
<td>4.90</td>
</tr>
<tr>
<td>(De Bel, et al. 2009)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>second-order •OH rate constant (M(^{-1}) s(^{-1}))</td>
<td>(4.1 \pm 0.3 \times 10^9) (pH=7.0)</td>
<td>(6.5 \pm 0.2 \times 10^9) (pH=7.0)</td>
</tr>
<tr>
<td>(Packer et al., 2003)</td>
<td>(Dodd, et al. 2006)</td>
<td></td>
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</table>
Table 2.2: Degradation Kinetics of CIPRO and IBU under Various Conditions.

<table>
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<tr>
<th>S</th>
<th>C&lt;sub&gt;s&lt;/sub&gt;</th>
<th>TC&lt;sub&gt;c&lt;/sub&gt;</th>
<th>ΔC&lt;sub&gt;d&lt;/sub&gt;</th>
<th>k&lt;sub&gt;b&lt;/sub&gt;&lt;sup&gt;0&lt;/sup&gt;</th>
<th>k&lt;sub&gt;obs&lt;/sub&gt;</th>
<th>t&lt;sub&gt;b/2, 25kHz&lt;/sub&gt;</th>
<th>k&lt;sub&gt;b&lt;/sub&gt;</th>
<th>t&lt;sub&gt;b/2, 62kHz&lt;/sub&gt;</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>µM</td>
<td>µM/min</td>
<td>µM/min</td>
<td>min&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>µM/min</td>
<td>min&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>µM/min</td>
<td>min&lt;sup&gt;-1&lt;/sup&gt;</td>
</tr>
<tr>
<td>None</td>
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<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>CIPRO</td>
<td>1</td>
<td>0.11 ± 0.01</td>
<td>0.11</td>
<td>6.30</td>
<td>0.13 ± 0.01</td>
<td>0.13</td>
<td>5.33</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>0.22 ± 0.01</td>
<td>0.02</td>
<td>31.5</td>
<td>1.1 ± 0.30</td>
<td>0.11</td>
<td>6.30</td>
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</tr>
<tr>
<td></td>
<td>100</td>
<td>0.31 ± 0.10</td>
<td>3.1 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
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<td>4.4 ± 0.50</td>
<td>0.04</td>
<td>15.8</td>
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<td>0.11</td>
<td>6.30</td>
<td>0.42 ± 0.01</td>
<td>0.42</td>
<td>1.65</td>
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<tr>
<td></td>
<td>10</td>
<td>0.42 ± 0.02</td>
<td>0.04</td>
<td>16.5</td>
<td>3.0 ± 0.06</td>
<td>0.30</td>
<td>2.31</td>
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<tr>
<td></td>
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<td>0.67 ± 0.01</td>
<td>6.7 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>103</td>
<td>16 ± 0.61</td>
<td>0.16</td>
<td>4.33</td>
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<td>TA 2 mM</td>
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<td>7.1 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>976</td>
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<td>3.1 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>2.23 × 10&lt;sup&gt;5&lt;/sup&gt;</td>
<td>6.0 × 10&lt;sup&gt;4&lt;/sup&gt;</td>
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<td>2.1 × 10&lt;sup&gt;4&lt;/sup&gt;</td>
<td>3.30 × 10&lt;sup&gt;2&lt;/sup&gt;</td>
<td>0.19 ± 0.05</td>
<td>1.0 × 10&lt;sup&gt;3&lt;/sup&gt;</td>
<td>693</td>
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<tr>
<td>IBU</td>
<td>1</td>
<td>1.8 × 10&lt;sup&gt;-4&lt;/sup&gt;</td>
<td>1.8 × 10&lt;sup&gt;-4&lt;/sup&gt;</td>
<td>38.5</td>
<td>0.20 ± 0.03</td>
<td>0.20</td>
<td>3.47</td>
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<td>1.2 × 10&lt;sup&gt;-4&lt;/sup&gt;</td>
<td>57.8</td>
<td>2.1 ± 0.31</td>
<td>0.21</td>
<td>3.30</td>
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<td>100</td>
<td>0.38 ± 0.04</td>
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<tr>
<td>SRFA 0.66 mgC/L</td>
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<td>5.9 × 10&lt;sup&gt;-2&lt;/sup&gt;</td>
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<td>1.3 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
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<td>0.92 ± 0.03</td>
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<td>7.53</td>
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<td>0.11 ± 3.5 × 10&lt;sup&gt;-4&lt;/sup&gt;</td>
<td>1.1 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>63.0</td>
<td>0.72 ± 0.05</td>
<td>7.2 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>9.63</td>
<td></td>
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<tr>
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<td>7.5 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
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<td>8.4 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
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<td>0.39 ± 0.03</td>
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</tr>
<tr>
<td></td>
<td>10</td>
<td>0.28 ± 0.04</td>
<td>2.8 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>24.7</td>
<td>2.7 ± 0.42</td>
<td>2.7 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>2.57</td>
<td></td>
</tr>
<tr>
<td>SRFA 16.5 mgC/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIPRO</td>
<td>1</td>
<td>7.8 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>7.8 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>88.9</td>
<td>0.34 ± 0.03</td>
<td>0.34</td>
<td>2.04</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>0.24 ± 0.02</td>
<td>2.4 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>28.9</td>
<td>2.8 ± 0.24</td>
<td>2.8 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>2.48</td>
<td></td>
</tr>
<tr>
<td>IBU</td>
<td>1</td>
<td>6.6 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>6.6 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>80.6</td>
<td>0.32 ± 0.02</td>
<td>0.32</td>
<td>2.17</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>0.20 ± 0.01</td>
<td>2.0 × 10&lt;sup&gt;-3&lt;/sup&gt;</td>
<td>34.7</td>
<td>3.0 ± 0.15</td>
<td>3.0</td>
<td>2.31</td>
<td></td>
</tr>
</tbody>
</table>

a substrate (S)
b concentration of substrate (C<sub>s</sub>)
c target compound (TC)
d concentration of target compound (C<sub>TC</sub>)
e errors were not listed because of limited space.
Table 2.3: CIPRO and IBU Association with Suwannee River Fulvic Acid

<table>
<thead>
<tr>
<th>compounds</th>
<th>$K_{oc}$ (L/kg)</th>
<th>organic carbon (mgC/L)</th>
<th>sequestering ratio, $S$ (%) $^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIPRO</td>
<td>$2.00 \times 10^4$ pH=7.3 (Cardoza et al., 2005)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.66</td>
<td>1.30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.10</td>
<td>5.83</td>
<td></td>
</tr>
<tr>
<td></td>
<td>16.50</td>
<td>24.77</td>
<td></td>
</tr>
<tr>
<td>IBU</td>
<td>$1.58 \times 10^4$ pH=7.0 (Yamamoto et al., 2005)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.66</td>
<td>1.04</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.10</td>
<td>4.68</td>
<td></td>
</tr>
<tr>
<td></td>
<td>16.50</td>
<td>20.73</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ sequestering ratio, $S$, (%) was calculated from Chin et al., (1997)
Figure 2.1: Sonolysis of CIPRO and IBU at 620 kHz (pH 8.5, 20 °C, and sonication power density at 400 W/L).
Figure 2.2: Sonochemical degradation rates at different concentrations of IBU (a) and CIPRO (b) with 2 mM terephthalic acid (TA) (pH 8.5, 20 °C and sonication power density at 400 W/L).
Figure 2.3: Predicted and observed initial degradation rates with 2 mM terephthalic acid (TA) at the frequency of 20 kHz (a) and 620 kHz (b) (pH 8.5, 20 °C and sonication power density at 400 W/L).
Figure 2.4: The sonochemical degradation rates of CIPRO and IBU with different concentrations of SRFA at 20 kHz (a) and 620 kHz (b) (pH 8.5, 20 °C, and sonication power density at 400 W/L).
Figure 2.5: Predicted and observed initial degradation rates of CIPRO and IBU with SRFA at 20 kHz (a. 1 μM and b. 10 μM) and 620 kHz (c. 1 μM and d. 10 μM) (pH 8.5, 20 °C, and sonication power density at 400 W/L).
References:

ACD/Labs6.00 (2002), Advanced Chemistry Development Inc., Toronto, Canada.


Chapter 3: Using Pulsed Wave Ultrasound to Evaluate the Suitability of Hydroxyl Radical Scavengers in Sonochemical Systems

3.1 Abstract

Hydroxyl radical (•OH) scavengers are commonly used in sonochemistry to probe the site and nature of reaction in aqueous cavitational systems. By using pulsed wave (PW) ultrasound we evaluated the performance of several different •OH scavengers (i.e., formic acid, carbonic acid, terephthalic acid/terephthalate, iodide, methanesulfonate, benzenesulfonate, and acetic acid/acetate) in a sonochemical system to determine which •OH scavengers react only in bulk solution and which •OH scavengers interact with cavitation bubbles. The ability of each scavenger to interact with cavitation bubbles was assessed by comparing the pulse enhancement (PE) of 10 μM of a probe compound, carbamazepine (CBZ), in the presence and absence of a scavenger. Based on PE results, acetic acid/acetate appears to scavenge •OH in bulk solution, and not interact with cavitation bubbles. Methanesulfonate acts as reaction promoter, increasing rather than inhibiting the degradation of CBZ. For formic acid, carbonic acid, terephthalic acid/terephthalate, benzenesulfonate, and iodide, the PE was significantly decreased compared to in the absence of the scavenger. These scavengers not only quench •OH in bulk solution but also affect the cavity interface. The robustness of acetic acid/acetate as
a bulk •OH scavenger was validated for pH values between 3.5 and 8.9 and acetic acid/acetate concentrations from 0.5 mM to 0.1 M.

3.2 Introduction

The transformation of organic pollutants in aqueous solution using ultrasound has been studied for decades [1-3]. In general, ultrasonic waves produce cavitation bubbles in water and the collapse of cavitation bubbles generates localized hot spots [4]. The hot spots initiate thermolytic and redox reactions with pollutants [4]. Hydroxyl radical (•OH) is the primary species attributed to redox reactions. •OH forms in the gaseous bubble core and diffuses to bulk solution to oxidize contaminants [5]. This process is considered an important degradation pathway for hydrophilic and non-polar pollutants [6-7].

It is generally believed that •OH concentrates at the bubble-water interface and the amount of •OH escaping from the hot spot and diffusing to bulk solution is small [8]. However, the question regarding how much •OH escapes to bulk solution and contributes to the overall degradation of a pollutant remains unclear, since there is no direct measurement of free •OH in bulk solution.

Two methods are commonly used to detect •OH in cavitation systems. Electron spin resonance (ESR) spectroscopy measures •OH by detecting the spin signal of the •OH-trap adduct [9]. The terephthalate dosimeter measures •OH by detecting the fluorescence signal of the •OH-trap adduct [10]. However, these methods do not sufficiently differentiate the locations of •OH reaction, because the •OH-trap adduct forms proportionally based on the concentration of •OH and the •OH trap in the cavitation bubble, at bubble-water interface and in bulk solution.
The question of location of reaction is important. It not only helps one to estimate the contribution of bulk solution •OH to contaminant degradation as a whole, but also to understand the spatial distribution of reaction sites. Therefore, researchers have used •OH scavenger studies to answer this question [11-20]. Frequently used scavengers include terephthalic acid/terephthalate [11, 13], iodide [14-15], and t-butanol [11, 16]. Less commonly used scavengers include bicarbonate [17], acetic acid/acetate [18], and benzoic acid/benzoate [19]. These studies implicitly assume that the scavenger only quenches •OH.

In reality, the •OH scavengers may interact with the bubble-water interface and enter cavitation bubbles. Volatile scavengers not only quench •OH in gas, interfacial, and bulk regions of cavitation bubbles, but also decrease the energy available for thermolysis of H₂O, reducing •OH formation [12, 20-21]. For example, Rae et al., demonstrated that even trace amounts of alcohols (such as n-butanol or t-butanol) evaporated into the bubble during the expansion phase of bubbles, decreasing the measured bubble temperature [21]. Therefore, because alcohol scavengers, such as t-butanol, methanol, and n-hexanol, are already known to interact with cavitation bubbles, they were not investigated in our study. •OH scavenging compounds with surface activity may interact with cavitation bubbles, affecting bubble collapse dynamics. As these surface active compounds preferentially partition to bubble surfaces, they affect assessments of bulk •OH reactivity as well. As a consequence, without assurance that scavengers do not interact with cavitation bubbles, attempts to infer mechanisms or sites of reaction, such as bulk •OH reaction to overall contaminant degradation using these scavengers is speculative.
In this study, pulsed wave (PW) ultrasound was used to systematically study whether and how \( \cdot \text{OH} \) scavengers affect cavitation bubbles. Previous studies [22-25] found that PW ultrasound, under certain optimal conditions, enhances the degradation of a compound, because it allows time for the compound to diffuse to bubble-water interfaces, the sources of reactivity. On the contrary, an ideal bulk \( \cdot \text{OH} \) scavenger stays in bulk solution and does not accumulate in the interfacial and gas region of cavitation bubbles between two successive pulses. We used a surface active probe compound, CBZ, as a reference compound that undergoes faster degradation under PW conditions compared to CW due to CBZ accumulation at bubble-water interfaces. Thus, in the presence of a bulk \( \cdot \text{OH} \) scavenger, faster degradation under PW over CW is expected. The PW enhancement is due to accumulation at the bubble-water interfaces. Any change in the enhancement is an indication of interaction of the scavengers with CBZ or the cavitation bubbles.

3.3 Experimental

CBZ (Sigma-Aldrich, 99%), KI (Acros, 99%), sodium formate (Fluka, 99%), sodium acetate (Fisher-Scientific, 99%), sodium bicarbonate (Fisher, 99%), sodium phosphate (monobasic and dibasic) (Fisher-Scientific, 99%), terephthalic acid (TA) (Sigma-Aldrich, 98%), benzenesulfonate (BS) (Sigma-Aldrich, 98%), methanesulfonate (MS) (Sigma-Aldrich, 98%), and phosphoric acid (Fisher-Scientific, 85%) were used as received. Stock solutions of these chemicals were prepared using Millipore purified water (Millipore, MA) with the resistivity \( R = 18.2 \, \text{M}\Omega \, \text{cm} \).
A 10 µM initial concentration of CBZ was used for all experiments. The •OH scavenger concentration was 1 mM, a 100-fold excess relative to CBZ, unless specified. A 1 mM phosphate buffer was used because of its low •OH reactivity \((10^4 \sim 10^5 \text{ M}^{-1} \text{s}^{-1})\) [26]. The pH of solution was adjusted by adding phosphoric acid or NaOH (Reagent ACS, Pellets 97%, Fisher Scientific).

Ultrasound at 205 kHz was emitted from a USW 51-52 ultrasonic flat plate transducer \((A = 23.4 \text{ cm}^2)\) (ELAC Nautik, Inc., Kiel, Germany) into a glass vessel with a volume of 300 mL. The reactor was equipped with a cooling water jacket to maintain solutions at 20 °C. A SM-1020 Function/Pulse generator (Signametrics Corp., Seattle, WA) generated sound waves continuously or by pulsing with an operation mode of 100 ms on and 100 ms off. A linear amplifier (T & C Power Conversion, Inc., Rochester, NY) magnified the generated electrical signal. The acoustic energy density to the reactor, determined by calorimetry, was measured to be 45 W/L. Calorimetry was monitored periodically during experiments to confirm system functionality. During sonication, 0.5 mL samples were taken from the reactor at designated times using a 1 mL glass syringe (Gastight 1001, Hamilton Corp.) for chemical analysis. The sample volume taken during the course of sonication did not exceed 1 % of the total volume in order to maintain the distribution of the acoustic field in the reactor. The experiments were carried out, at least, in duplicate. Statistical \(t\)-test analysis was conducted using SPSS 13.0 (LEAD Technologies Inc).

A Hewlett-Packard 1100 high performance liquid chromatograph (HPLC) equipped with a diode array detector (DAD) was used to analyze the concentration following sonolysis of CBZ. A 5 µm, 150 × 2.1 mm SB-C18 column (883700-922, Agilent
Technologies) was employed. An isocratic flow of acetonitrile/water (40/60, v/v) was the mobile phase for the quantification of CBZ. The injection volume was 50 µL and the UV wavelength was set at 220 nm.

Gibbs surface tension ($\gamma$) was measured by a McVan Analite Surface Tension meter (2141, McVan Instruments) with a glass Wilhelmy plate. All measurements were carried out in triplicate at room temperature. Gibbs surface excess ($\Gamma$) was obtained from the change of $\gamma$: surface tension,

$$\Gamma = -\frac{1}{RT} \frac{d\gamma}{d\ln[C]} \quad (3.1)$$

where R is gas constant, T is temperature, and C is concentration of solute. Surface tension was smoothed using a Fast Fourier Transform (FFT) tool to eliminate instrument noise (Origin 8.1, OriginLab Inc).

3.4. Results and Discussion
3.4.1. Degradation of CBZ

The sonochemical degradation rate of the probe compound, CBZ, in the absence and presence of $\cdot$OH scavengers at pH 3.5 is shown in Figure 3.1. In the absence of $\cdot$OH scavengers, CBZ degraded 5.8 % ($p < 0.01$) faster by PW ultrasound compared to CW ultrasound. Similar to previous work [22-25], the higher degradation rate under PW ultrasound indicates that a higher fraction of CBZ is degraded in the interfacial region of cavitation bubbles.

During the time interval between two successive pulses, CBZ molecules accumulate on the surface of the bubble. In the subsequent pulse more CBZ molecules react
compared to CW ultrasound. Faster degradation by PW ultrasound is consistent with Naddeo et al. [27]. They attributed the majority of decomposition of CBZ to reaction in the vicinity of the cavitation bubbles.

Figure 3.1 also shows the initial degradation rates of CBZ in the presence of 1 mM concentration of each individual •OH scavenging agent. With the exception of MS, the presence of the •OH scavenger reduced the initial degradation rate of CBZ in both CW and PW conditions. Using eqn. 3.2, the inhibitory effect of each individual scavenger on the sonolysis of CBZ was calculated.

\[
\text{inhibition \%} = \frac{\left(\frac{d[C]}{dt}\right)_{\text{without scavenger}} - \left(\frac{d[C]}{dt}\right)_{\text{with scavenger}}}{\left(\frac{d[C]}{dt}\right)_{\text{without scavenger}}} \times 100\% \quad (3.2)
\]

where \( \frac{d[C]}{dt}_{\text{with scavenger}} \) and \( \frac{d[C]}{dt}_{\text{without scavenger}} \) are the initial degradation rates of CBZ with or without an •OH scavenger, respectively. Figure 2 indicates that these seven scavengers have different effects on the sonolysis of CBZ.

The changing level of inhibition of all the scavenger candidates, as shown in Figure 3.2, implies that they exert different influences on the sonochemical system. In addition, the benefit of pulsing in the presence of the scavenger is only observed with MS and AA.

3.4.2 PE of CBZ in the presence of the •OH scavengers

In order to investigate the effects of scavengers on cavitation bubbles, a pulse enhancement (PE) was calculated. By comparing the degradation of CBZ between CW and PW ultrasound through PE, the effect of pulsing was determined:
where \( \left( \frac{d[C]}{dt} \right)_{CW/PW} \) is the degradation rate of CBZ under CW or PW ultrasound. In the presence of a bulk •OH scavenger, the PE of CBZ is expected to be equal to that in the absence of the scavenger, indicating that the presence of the scavenger does not have any pronounced effects on the degradation of CBZ (i.e., competing for adsorption sites at interface and diffusing to gas region).

In the absence of •OH scavengers, the PE of CBZ is 5.8%. The PE of CBZ in the presence of various scavengers is shown in Figure 3.3. In the presence of FA, CA, TA, and KI, the PE of CBZ is negative ranging from -20% to -5%. Again, a similar PE value with and without the scavenger indicates its influence on cavitation bubbles is negligible. The results suggest that FA, CA, TA, and KI not only scavenge •OH in the system but also significantly affect cavitation bubbles. In the presence of MS, BS, and AA, the PE ranges from 0.92% to 11.3%, suggesting little influence on cavitation bubbles. To understand the effects of these scavengers on cavitation bubbles, we will discuss each scavenger separately below.

3.4.2.1. Formic acid

FA has been characterized as an ideal •OH scavenger in radiolysis [28]. It has a fast reaction rate constant and known reaction pathways with •OH. However, when it comes to its application in sonochemistry, FA shows a negative pulse enhancement (PE=-6.2%).
Partitioning of FA and its ultrasound-induced reaction products to the gaseous bubble and bubble interface has been reported in the literature. Hart and Henglein observed CO production during sonication of FA at 300 kHz [29]. Substantial formation of CO in sonicated aqueous FA solution is attributed to thermal decomposition of FA (eqn. 3.4), indicating that FA enters the high temperature gas region of cavitation bubbles.

\[
\text{HCOOH} \rightarrow \text{CO} + \text{H}_2\text{O} \tag{3.4}
\]

In addition, Jolly et al., investigated products formed from \(\cdot\text{OH}\) reacting with FA during laser-irradiated photolysis [30]. They proposed that the oxidation of FA by \(\cdot\text{OH}\) releases CO\(_2\) according to eqns. 3.5 and 3.6:

\[
\text{HCOOH} + \cdot\text{OH} \rightarrow \cdot\text{COOH} + \text{H}_2\text{O} \tag{3.5}
\]

\[
\cdot\text{COOH} + \cdot\text{OH} \rightarrow \text{CO}_2 + \text{H}_2\text{O} \tag{3.6}
\]

Gaseous CO\(_2\) formed enters cavitation bubbles and decreases the polytropic index, \(\kappa\), \((\kappa_{\text{air}} = 1.405 \) and \(\kappa_{\text{CO}_2} = 1.312\)) of the gas phase, resulting in a decreased bubble collapse temperature as shown in eqn. 3.7:

\[
T_{\text{max}} = T_0 \left[ \frac{(p_0 + p_\lambda)(\kappa - 1)}{P} \right] \tag{3.7}
\]

where \(T_{\text{max}}\) is the maximum bubble collapse temperature; \(T_0\) is the ambient temperature of the liquid; \(p_0\) is the hydrostatic pressure; \(p_\lambda\) is the applied acoustical pressure; and \(P\) is the pressure in the bubble at its maximum size, which is set to the vapor pressure of the liquid. The lower collapse temperature of the bubble produces comparatively less \(\cdot\text{OH}\). Therefore, we do not recommend the use of FA as bulk \(\cdot\text{OH}\) scavenger in cavitation systems.
3.4.2.2 Carbonic acid

CA has not been reported as a •OH scavenger. Our interest in CA was primarily to explore the effect of CO₂ on the cavitation bubbles, rather than as an •OH scavenger. Based on FA results, we suspected that H₂CO₃ would significantly affect cavitation bubbles mostly due to its equilibrium with gaseous CO₂ at pH 3.5 in aqueous solution.

\[ H₂CO₃ \rightleftharpoons H₂O + CO₂ \]  \hspace{1cm} (3.8)

Figure 3.3 shows that CA significantly affects cavitation bubbles, resulting in the lowest pulse enhancement -20.9% among the scavengers tested. Gaseous CO₂ is expected to enter stable microbubbles during the interval between the pulses, reducing the bubble collapse temperature, resulting in less reaction of CBZ under PW ultrasound. In addition, Henglein observed that the main product of the sonolysis of CO₂ is CO [31], which is also capable of reducing the maximum bubble collapse temperature, T_{max}, (eqn. 3.7) due to a decrease in the polytropic index \( \kappa \) (\( \kappa_{\text{Air}} =1.405 \) and \( \kappa_{\text{CO}} =1.380 \)). Further, CO formation is attributed to thermal decomposition of CO₂ [31].

\[ CO₂ \rightarrow CO + \cdot O \]  \hspace{1cm} (3.9)

Thus, CO₂ reduces the temperature of collapsing cavitation bubbles, resulting in a negative impact on •OH formation and contaminant degradation.

3.4.2.3 Terephthalic acid/terephthalate

TA has been widely used as an •OH scavenger in sonochemistry, radiochemistry, and photochemistry due to its high sensitivity to trap •OH to form the fluorescent product, hydroxyterephthalate [32-35]. In addition, in neutral and basic solution, the anionic form of TA, terephthalate (TPA), dominates (pK_{a,1}=3.52 and pK_{a,2}=4.46). Thus, the polar
anionic TPA is assumed to reside in bulk solution and not partition to the interface or vapor region of cavitation bubbles [10-11]. At pH 3.5, the PE of 1 mM TA was -10.0%, suggesting that TA interacts with bubble-water interface. As TA is not in its anionic form at pH 3.5, we retested at pH 7.4. However, the PE remained negative (-5.9%). Unlike FA and CA which enter into microbubbles, we suspect that TA competes for adsorption sites during the silent cycle, and accumulates at the interface of oscillating and collapsing gas bubbles, causing reduced degradation of CBZ in PW as compared to CW. As a result, a negative PE was observed.

This result is in agreement with our previous work investigating the sonolysis of ibuprofen and ciprofloxacin in the presence of TPA [36]. To understand these results we calculated the hydrophobic enrichment factor, $C_{\text{interface}}/C_{\text{aq}}$, following the method from Tauber et al. [14]. Tauber et al., used this concept to study the enrichment of 4-nitrophenol at the interfacial region and concluded that 4-nitrophenol, with $C_{\text{interface}}/C_{\text{aq}} \approx 80$, primarily degraded in the gas-liquid boundary layer. $C_{\text{interface}}/C_{\text{aq}}$ for TA was calculated to be 7.7 at pH 3.5, indicating that TA readily partitions to the bubble-water interface. Thus, we do not recommend the use of TA or TPA as bulk $\cdot\text{OH}$ scavenger in cavitation systems.

3.4.2.4 Potassium iodide

KI is one of the most popular $\cdot\text{OH}$ scavengers [12, 14-15]. Figure 3.3 shows a PE of -11.5% for CBZ when KI is present. The reduced PE of CBZ with KI compared to in the absence of KI suggests that KI interacts with the bubble-water interface, resulting in a reduced degradation rate of CBZ in PW mode compared to CW mode.
Although iodide is a non-volatile solute, the sonication of a solution of KI liberates considerable iodine [37], and, in fact, is the reported pathway for quantifying the reaction of KI with •OH:

\[
\begin{align*}
\Gamma + \cdot \text{OH} & \rightarrow \Gamma \cdot + \text{OH}^- \\
\Gamma \cdot + \Gamma \cdot & \rightarrow \text{I}_2 \\
\text{I}_2 + \Gamma & \rightarrow \Gamma_3^-
\end{align*}
\] (3.10) (3.11) (3.12)

Kotronarou [37] observed that the rate of I\(_3^-\) formation in an aqueous solution decreased by 1/3 when the ports of the sonication reactor were left open compared to closed conditions, suggesting substantial iodine degassing. Although no studies directly report iodine entering into the gas phase of cavitation bubbles, I\(_2\) is volatile with a reported Henry’s law constant of 0.0245 atm-m\(^3\)/mol [38]. For comparison purposes, Drijvers et al., [19] investigated the sonolysis of chlorobenzene with a Henry’s law constant of 0.00311 atm-m\(^3\)/mol in aqueous solution. They concluded that chlorobenzene penetrated the gas/liquid boundary layer, lowering the specific heat ratio of the gas inside the cavitation bubbles, reducing the bubble collapse temperature, and ultimately reducing degradation of chlorobenzene by ultrasound. The Henry’s law constant of iodine is nearly one order of magnitude greater than that of chlorobenzene, suggesting that the ultrasound-induced byproduct, iodine, partitions to the gas phase of the cavitation bubble. In addition, Liu et al., [39] revealed that the hydrogen bonding network at the air/water interface is disturbed by the addition of iodide due to its large size and high polarizability, suggesting iodide itself perturbs the bubble-water interface. Therefore, \(\Gamma\) itself and its reaction product \(\text{I}_2\) interact with cavitation bubbles; we do not recommend the use of KI as bulk •OH scavenger in cavitational systems.
3.4.2.5 Benzenesulfonate

Although not a commonly reported •OH scavenger, BS was considered in our study since it is hydrophilic (apparent log $K_{ow}=-2.93$ at pH 3.5) [40] due to its sulfonate functional group, and can sensitively trap •OH ($4.7 \times 10^9 \text{ M}^{-1} \text{s}^{-1}$) [26]. Thus, we expected BS to effectively scavenge •OH in bulk solution. In Figure 3.3, the PE in the presence of 1 mM BS (0.93%) is statistically less than in its absence (5.8%) ($p<0.01$). This reduction in PE with BS suggests that BS affects cavitation bubble collapse. Measurements of the Gibbs surface tension of BS showed that the surface excess remained unaltered until the concentration of BS reached 0.1 M (Figure 3.4). The Gibbs surface excess of a substance, which has been directly correlated to the intensity of sonoluminescence, is a measure of enrichment of the substance at the bubble-water interface [41-42]. Although Gibbs surface excess changes were not detected at low concentration (<0.1 M), the hydrophobic enrichment factor, $C_{\text{interface}}/C_{\text{aq}}$, was calculated to be 40.7 for BS. Because of the lower PE of CBZ in the presence of BS and the high calculated enrichment factor, we do not recommend the use of BS as a bulk •OH scavenger in cavitation systems.

3.4.2.6. Methanesulfonate

MS shows a greater pulse enhancement (PE=11.3%), as compared to that in the absence of MS (5.8%) ($p<0.01$). In addition, the presence of MS promoted, rather than inhibited the degradation of CBZ. Enhanced degradation of CBZ with MS may be attributed to reactive secondary reaction species [43]. Therefore, because of the enhanced degradation of CBZ with MS, it is not appropriate for use as an •OH scavenger.
3.4.2.7 Acetic acid

The PE of CBZ in the presence of AA was 4.6 %, as compared to 5.8 % in the absence of the scavenger (Figure 3.3). Unlike the other scavengers tested, the lack of statistical difference in PE values (p<0.01) suggest that AA and its by-products neither perturb the adsorption sites of CBZ at the bubble-water interface, nor partition into gas microbubbles during the silent cycles in PW mode, but rather reside in bulk solution.

To confirm that AA does not partition to the bubble-water interface of cavitation bubbles, surface tension measurements and corresponding Gibbs surface excess calculations were performed for the AA-water binary system at room temperature. Results indicate that AA does not accumulate on gas-water interfaces until the AA concentration reaches 140 mM (Figure 3.4). This observation is similar to multi-bubble sonoluminescence of acetate [44]. The reported sonoluminescence intensity of acetate remained relatively constant until the concentration reached 100 mM, indicating that acetate does not accumulate on the bubble surface at concentrations lower than 100 mM; thus, no sonoluminescence quenching was observed. The similar point at which acetic acid (140 mM) and acetate (100 mM) appear to accumulate on interfaces suggests that AA and acetate behave similarly in the ultrasonic field.

In addition to surface accumulation, AA has the potential to enter the gas phase of cavitation bubbles. Henry’s law predicts the distribution of AA between aqueous solution and the gas at equilibrium. Nanzai et al., investigated the sonolysis of twelve organic compounds with Henry’s law constant (K_H) ranging from 7.34 × 10^{-9} to 1.05 × 10^{-2} atm-m^3/mol. Their results showed that the effect of the Henry’s law constants on the
degradation rates became pronounced at $K_H$ above $2.40 \times 10^{-5}$ atm-m$^3$/mol and the correlation between degradation and $K_H$ was observed only at high $K_H$ values [45]. Chiha et al., examined sonochemical degradation of phenol ($K_H = 3.33 \times 10^{-7}$ atm-m$^3$/mol), 4-isopropylphenol ($K_H = 1.09 \times 10^{-6}$ atm-m$^3$/mol), and Rhodamine B ($K_H = 2.20 \times 10^{-21}$ atm-m$^3$/mol) in aqueous solutions [46]. They claimed that these compounds are not degraded inside the cavitation bubbles because of their low Henry’s law constants. Based on these studies of the effects of Henry’s law constants on sonolysis of contaminants, AA, with a Henry’s law constant $1.00 \times 10^{-7}$ atm-m$^3$/mol [38], does not appear likely to diffuse to the gas phase of cavitation bubbles to a large degree.

Calculations were also conducted to validate our conclusion that AA will not migrate to bubble interfaces or interiors. Based on the method from Tauber et al., [14] the hydrophobic enrichment factors, $C_{\text{interface}}/C_{\text{aq}}$ and $C_{\text{aq}}/C_g$, for acetic acid were calculated to be 0.8 and $8.13 \times 10^4$, respectively. Both factors indicate that AA preferentially stays in bulk solution.

While our macroscopic observations and calculations do not provide molecular level information regarding AA on the bubble-water interface, Johnson et al., studied the AA [47] and acetate [48] molecular orientation and speciation at the air interface by vibrational sum frequency spectroscopy. They found that the structure of the interface is disrupted in the presence of 0.3 mole % (0.165 M) AA with AA covering 7% of the interface [47], whereas acetate was not observed to disrupt the interface [48]. Although they did not investigate lower AA concentration, their work is consistent with our surface tension measurement; thus we expect the observed perturbation of the interface will disappear at concentration below 0.1 M.
The kinetics and mechanism of the sonolysis of acetate solution was studied by Gutierrez et al. [8]. A large concentration (~0.1 M for acetate and ~0.01 M for acetic acid) was required to suppress the overall formation of 50% H₂O₂. However, based on product formation yields, half of •OH in bulk solution was scavenged at an acetate concentration of 1.2 µM, four to five orders of magnitude less than the bulk acetate concentration. Based on the low CO to H₂ product formation ratio at [acetate]₀ = 0.1 M, they stated that the sonolysis of acetate (≤ 0.1 M) occurs via decomposition of water, attack of acetate by •OH, and the reaction of the secondary radicals with the oxygen. The trace amount of CO formed at 0.1 M acetate may be due to sputtering of acetate in bulk solution into the gas bubbles during sonolysis [12, 49]. They concluded that the amount of •OH in bulk solution is small, and acetate is inert toward the interfacial and gas region.

Figure 3.2 depicts the effectiveness of AA scavenging for •OH on sonochemical degradation of CBZ. In the absence of AA, the degradation rates of CBZ were 0.519 and 0.549 µM min⁻¹ under CW and PW, respectively. In the presence of 1 mM AA the observed rate was 0.362 and 0.379 µM min⁻¹ under CW and PW, respectively, representing a ~30% inhibition in the presence of a bulk •OH scavenger in both modes of ultrasound. The result indicates that •OH in bulk solution is responsible for ~30% of CBZ degradation, being consistent with our assumption that the interfacial region of the cavitation bubbles are the dominant location responsible for CBZ degradation.

AA/acetate has been investigated in sonochemical system previously as a pollutant and a co-existing pollutant. [12, 18, 50-51]. Findik and Gunduz investigated the degradation of AA in the presence of NaCl to examine the salting-out effect on sonolysis [51]. The presence of NaCl exhibited a positive enhancement on AA degradation until its
concentrations reached 0.75 M, suggesting that AA favors bulk solution, thus, a high NaCl concentration is needed to push AA from bulk solution to the bubble interface. For comparison purposes, Seymour and Gupta examined the salting-out effect on the sonolysis of chlorobenzene, a surface active pollutant with major degradation occurring in the gas and interfacial region of cavitation bubbles [52]. In their study, the degradation efficiency is enhanced by 10% with 0.17 M NaCl as compared to in its absence. Tiehm and Neis [18] examined sonochemical degradation of chlorophenol in the presence of acetate and observed that the degradation rate was reduced slightly less than it was in the presence of glucose. They concluded that hydrophilic acetate or glucose did not interfere with chlorophenol, which was mainly degraded in the bubble-water interface. These studies confirm that AA preferentially stays in bulk solution and inertially diffuses to bubble surfaces.

3.4.3 Robustness of AA/acetate as bulk solution •OH scavenger

In order to determine the range of conditions in which AA/acetate acts as a bulk •OH scavenger, its effect on CBZ degradation was tested under different conditions. Our goals were to explore the concentration and pH conditions at which AA/acetate adequately scavenges bulk •OH but does not affect cavitation bubbles. First, the sonolysis of the probe compound, CBZ, was conducted at pH 3.5 with an AA concentration ranging from 0.5 mM to 100 mM.

Figure 3.5 illustrates that with different concentrations of AA, the reported initial degradation rates of CBZ remain relatively constant in both CW and PW mode ultrasound. At high concentration of AA/acetate, AA/acetate has been shown to interact
with cavitation bubbles, while at very low concentration AA/acetate may not adequately scavenges •OH in bulk solution. The degradation rate of CBZ in the presence of AA was predicted by multiplying the degradation rate of the target compound in the absence of AA by the quenching ratio, Q, the ratio of reaction occurring by •OH between competing solutes. Q of AA of the degradation of CBZ was predicted from eqn. 3.13:

\[ Q = \frac{k_{CBZ}C_{CBZ}}{k_{AA}C_{AA} + k_{CBZ}C_{CBZ}} \times 100\% \]  

(3.13)

where \( k_{CBZ} \) and \( k_{AA} \) are the second order rate constants of •OH reacting with CBZ and AA, respectively, and \( C_{CBZ} \) and \( C_{AA} \) are the concentrations of CBZ and AA, respectively.

The predicted initial degradation rates monotonously decrease from 0.35 to 0.0048 \( \mu \text{M min}^{-1} \) under either CW or PW ultrasound. The significantly higher and relatively stable observed initial rates of CBZ degradation compared to predicted initial rates suggests that CBZ diffuses to the interfacial region of cavitation bubbles, regions of high temperature and •OH concentration. The lack of effect of AA within a wide concentration range indicates that AA does not affect the interfacial and gas region of cavitation bubbles. Further, because adding more of the •OH scavenger does not alter the initial degradation rate of CBZ, the lowest concentration of AA appears to adequately scavenge the bulk •OH. Only a small amount of •OH diffuses to bulk solution during sonication; thus, the presence of small amount of AA sufficiently outcompetes CBZ, scavenging the •OH in bulk solution. An increase in the AA concentration has little impact on the observed initial degradation rates of CBZ for the concentration of CBZ used. Generalizing to other systems, the lowest concentration of AA may not be appropriate if a high compound concentration will be used and AA is used as a bulk •OH scavenger.
Next, we tested the robustness of AA/acetate within a range of pH values. Sonolysis of 10 μM CBZ was conducted in the presence of 1 mM AA/acetate from pH 3.5 to 8.9. Figure 3.6 shows that the PE of CBZ remains constant through the entire pH range tested. Henglein and Kormann [12], suggested that both AA and acetate have similar scavenging behaviors based on the concentration needed to inhibit formation of 50% H₂O₂. Our results are consistent with their work, suggesting that acetate behaves similarly to AA.

3.5 Conclusions

The effects of the •OH scavengers, FA, CA, TA/TPA, KI, MS, BS, and AA/acetate, on cavitation bubbles have been examined with the sonolysis of the probe compound, CBZ, under CW and PW ultrasound. PW ultrasound provides a technique to determine whether scavengers affect the interfacial and gas region of cavitation bubbles. All the scavengers, except for MS, exhibited inhibitory effects on CBZ sonolysis. Based on the reduction in PE of CBZ, all the scavengers except AA/acetate affect cavitation bubbles and are not recommended to use as bulk •OH scavengers in cavitationsal systems.

We recommend acetic acid/acetate as a bulk •OH scavenger. It efficiently quenches •OH in bulk solution, resulting in a reduced degradation rate of CBZ. The range of utility of AA/acetate as a bulk •OH scavenger was tested under different concentrations and pH values. The observed degradation rates of CBZ within the range of concentrations and pH values tested were unaltered. Evidence suggests that at concentrations below 0.1 M and all pH values tested, AA/acetate is an ideal bulk •OH scavenger in sonochemical systems.

Acknowledgments
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Figure 3.1: Initial degradation rates of 10 μM CBZ in the absence and presence of 1 mM •OH scavenger candidates under PW and CW ultrasound at pH 3.5
Figure 3.2: Inhibitory effects of each bulk •OH scavenger candidate on sonolysis of 10 μM CBZ under CW and PW ultrasound at pH 3.5.
Figure 3.3: PE of 10 μM CBZ in the absence and presence of the various bulk •OH scavenger candidates at pH 3.5 (TPA was tested at pH 7.4).
Figure 3.4: Gibbs surface tension ($\Gamma$) and surface excess ($\gamma$) for acetic acid (AA) and benzenesulfonate (BS) as a function of concentration at room temperature.
Figure 3.5: Observed and predicted initial degradation rates of 10 μM CBZ at pH 3.5 under CW and PW ultrasound as a function of acetic acid concentrations ranging from 0.5 mM to 100 mM.
Figure 3.6: Pulse enhancement of 10 µM CBZ in the presence of 1 mM bulk phase •OH scavenger AA/acetate as a function of pH.
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Chapter 4: Degradation of Pharmaceuticals and Personal Care Products (PPCPs) in Aqueous Solution Using Pulsed Wave Ultrasound

4.1 Abstract

In this study, continuous wave (CW) and pulsed wave (PW) ultrasound at 205 kHz was used to degrade five pharmaceuticals (carbamazepine, ibuprofen, acetaminophen, sulfamethoxazole and ciprofloxacin), and two personal care products (propyl gallate and diethyl phthalate). These seven compounds, covering a range of physicochemical properties and a diversity of structures, are degraded to different degrees by ultrasound. Acetaminophen is the most recalcitrant compound to ultrasound with degradation rates of 0.27 and 0.44 µM/min under CW and PW ultrasound, respectively, whereas, the degradation rates of propyl gallate are almost one order of magnitude faster. Degradation rates by PW ultrasound are compound dependent with degradation faster for smaller compounds or slower for larger compounds than that under CW ultrasound. The addition of a bulk solution •OH trapping agent, acetic acid, to PPCP solutions indicates that the fraction of degradation occurring in bulk solution is positively correlated with the molar volume of the compound. Overall, smaller PPCP compounds with molar volumes less than 130 mL/mol are able to more readily diffuse to bubble interfaces and are impacted most by pulsing ultrasound.
4.2 Introduction

Pharmaceuticals and personal care products (PPCPs) are a large and diverse class of compounds, consisting of prescription and over-the-counter therapeutic drugs, veterinary drugs, fragrances, and cosmetics. According to the National Center for Health Statistics, annual pharmaceutical sales in North America was $299.6 billion in the year 2008 (Sebelius et al., 2010). Unavoidably, a large fraction of these PPCPs are disposed of or discharged into the environment on a continual basis through various pathways, including domestic sewage, landfills, and wet weather runoff (Daughton and Ternes, 1999), resulting in both aquatic and terrestrial biota and human exposure to these compounds. The U.S. Geological Survey provided the first nationwide reconnaissance of the occurrence of PPCPs in water resources during 1999-2000 and found PPCPs in 80% of the streams sampled (Kolpin et al., 2002). Moreover, studies have shown that certain PPCPs, such as estrogenic compounds, persist in the environment and have a very high bioaccumulation potential (Ternes et al., 2004; Topp et al., 2008).

In addition to changing disposal practices of PPCPs, a variety of water treatment technologies have been investigated and developed to reduce the concentrations of PPCPs in water (Oulton et al., 2010). Among these treatment technologies, ultrasound is an emerging option with advantages that include ease of use, lack of chemical addition, and ability to degrade contaminants with a wide range of physicochemical properties (Adewuyi, 2005a; b; Weavers et al., 2000).

Ultrasound decomposes contaminants through thermal degradation and/or radical oxidation mechanisms. When continuous or pulsed ultrasound waves propagate through water, cavitation bubbles form. These bubbles oscillate with the rarefaction and
compression phases of the ultrasound wave. Once the bubbles reach a critical size, the bubbles implode resulting in an enormous concentration of energy at localized hot spots in the solution (Gutierrez et al., 1986; Suslick, 1990). These hot spots not only provide sufficient heat to dissociate chemical bonds in contaminants (i.e., thermolysis) (Currell et al., 1963; Song and O'Shea, 2007), they also dissociate water, forming hydroxyl radical (•OH) and initiating oxidation reactions in water (Kotronarou, 1992; Petrier et al., 1994).

Applying ultrasound to remove PPCPs from drinking water and wastewater has drawn increasing interest. However, predicting removal efficiencies for PPCPs, especially pharmaceuticals, is challenging. Nanzai et al., (2008) concluded that a more hydrophobic monocyclic aromatic compound undergoes a faster degradation due to a higher degree of accumulation on bubble-water interface. Fu et al., (2007) stated that smaller compounds diffuse faster in bulk solution to the interfacial/gas region of cavitation bubble, resulting in a faster degradation rate.

Many studies have shown that at proper settings, the degradation of contaminants under pulsed wave (PW) ultrasound is more effective than under continuous wave (CW) ultrasound (Ciaravino et al., 1981; Neppolian et al., 2009). For instance, pulsing ultrasound at 100 ms on and 100 ms off, the degradation rate of 0.1 mM sodium 4-octylbenzene sulfonate (OBS), was approximately 30 % faster than that under CW (Yang et al., 2005). Xiao et al., (2012) observed that the removal efficiency of 10 μM carbamazepine (CBZ) under PW ultrasound was greater than CW by about 6 %.

The mechanisms for the enhanced sonochemical reactivity under PW ultrasound remain unclear though. Yang et al., (2005) and Xiao et al., (2012) attributed the enhanced degradation by PW ultrasound to increased contaminant accumulation on the surface of
the bubbles during the intervals between pulses, causing more molecules to react with the cavitation bubbles. However, Ciaravino et al., (1981) attributed the increased formation of iodine in PW mode to the survival of unstabilized nuclei during the off-time, resulting in more violent collapse in the subsequent pulse. Neppolian et al., (2009) attributed the increased sonochemical oxidation of arsenic (III) by PW ultrasound to the “silent” oxidation reactions and an increased number of active cavitation bubbles.

In this study, we investigated the effect of pulsing on the degradation of PPCPs. Five pharmaceuticals (carbamazepine (CBZ), ibuprofen (IBU), acetaminophen (ATP), sulfamethoxazole (SFT) and ciprofloxacin (CIPRO)), and two personal care products (propyl gallate (PG) and diethyl phthalate (DP)), were selected on the basis of environmental relevance (Daughton and Ternes, 1999; Kolpin et al., 2002) and diversity in physicochemical properties and structures (Table 4.1). Many PPCPs are hydrophobic and surface active in water; thus, PW ultrasound exhibits potential to be a better method to remove PPCPs, as compared to CW ultrasound. Further, we linked the importance of physicochemical properties of a compound to degradation under pulsed ultrasound.

4.3 Experimental Methods

CBZ, IBU, ATP, and PG all 99% from Sigma-Aldrich, SFT (99%), DP (99%) and CIPRO (98%) from Fluka, and sodium phosphate and sodium acetate both 99% from Fisher-Scientific, were used as received. Table 4.1 lists physicochemical properties for these PPCPs. Stock solutions of these chemicals were prepared using Milli-Q purified water (Millipore, MA) with the resistivity $R = 18.2$ M$\Omega$ cm. A 10 $\mu$M initial concentration was chosen to be close to an environmentally relevant concentration yet
concentrated enough to be analyzed. Due to its low •OH reactivity, solutions were buffered by 1 mM NaH$_2$PO$_4$ at pH 3.5. A pH value of 3.5 was selected because the apparent and true $K_{ow}$ values for the PPCPs are equivalent at this pH value, recognizing that hydrophobicity changes dramatically as pH varies due to ion-pair partitioning (Avdeef et al., 1998). In select experiments, 1 mM acetic acid was added to 10 μM PPCP solutions to scavenge bulk •OH (Xiao et al., 2012).

Ultrasound at 205 kHz was emitted from a USW 51-52 ultrasonic flat plate transducer ($A = 23.4$ cm$^2$) (ELAC Nautik, Inc., Kiel, Germany) into a glass vessel with a volume of 300 ml. The reactor was equipped with a cooling water jacket (Isotemp 1006S, Fisher Scientific) to maintain the temperature of solutions at 20 °C. A SM-1020 Function/Pulse generator (Signametrics Corp., Seattle, WA) was used to deliver a pulse of 100 ms on and 100 ms off. The selection of PW ultrasound settings was based on previous studies which showed enhanced degradation of surfactants by PW compared to CW (Yang et al., 2006). A linear amplifier (T&C Power Conversion, Inc., Rochester, NY) magnified the generated electrical signal to drive the transducer in either CW or PW ultrasound. A digitizing oscilloscope (54501, Hewlett-Packard) was used to detect the pulse signal received by the transducer. The acoustic energy density to the reactor, determined by calorimetry, was measured to be 45 W/L. Throughout the experimental runs, calorimetry and the pulsed signal were monitored periodically to confirm system functionality.

0.5 mL samples were taken from the reactor at designated times using a 1 mL glass syringe (Gastight 1001, Hamilton Corp.). The sample volume taken during the course of sonication did not exceed 1 % of the total volume in order to keep the distribution of
acoustic field in the reactor consistent. All the experiments were carried out in, at least, duplicate.

A Hewlett-Packard 1100 high performance liquid chromatograph (HPLC) equipped with a diode array detector (DAD) and a 5 μm, 150 × 2.1 mm SB-C18 column (883700-922, Agilent Technologies) was used to analyze the concentration following sonolysis of PPCPs. 0.5 mL/min eluent consisted of 20 mM pH 3 phosphoric acid buffer and acetonitrile (HPLC grade, Fisher Scientific). Eluent ratios and the injection volumes varied depending on the compound analyzed. The UV wavelengths were set at 220, 223, 215, 214, 274, 225, and 230 nm for CBZ, IBU, ATP, SFT, CIPRO, PG, and DP, respectively.

Gibbs surface tension (γ) were measured for each PPCP solution by a McVan Analite Surface Tension meter (2141, McVan Instruments) with a glass Wilhelmy plate. The measurements were carried out in triplicate at room temperature.

A non empirical calculation at Hartree Fock (HF) level of theory with 6-31+G* basis set was applied to determine the molar volume of the molecules (mL/mol) in water, using the polarizable continuum model solvation method. HF/6-31+G* is a reliable level of theory to calculate the geometry of large organic molecules (Cummins and Gready, 1989; Schlegel, 1982). All molecules were drawn using GaussView 4.0.8, and calculations were performed using Gaussian 03 at the Ohio Supercomputer Center (OSC).

Statistical analysis, including the Bivariate Pearson two-tailed correlation test and the t-test, were performed using SPSS 13.0 (LEAD Technologies, Inc).

4.4 Results and Discussion
4.4.1 Sonochemical degradation kinetics

The sonochemical degradation of CBZ, SFT, IBU, ATP, CIPRO, PG, and DP is shown in Figure 4.1. The initial degradation rates of the seven PPCPs varied. For example, the initial degradation rates of PG under CW and PW ultrasound are 2.98 and 2.90 µM/min, respectively, approximate one order of magnitude faster than the other compounds. ATP degrades the slowest by CW ultrasound, 0.27 µM/min.

Strong correlations have been reported between sonochemical degradation rates of contaminants and their physicochemical properties (Colussi et al., 1999; Nanzai et al., 2008; Shemer and Narkis, 2005). For instance, Fu et al., (2007) observed a linear correlation between the rate of sonolysis of eight different estrogen compounds and their molecular weight. Shemer and Narkis (2005) observed, for a series of trihalomethanes (THMs), a linear correlation between the vapor pressure and the sonochemical degradation rate. Similarly, Colussi et al., (1999) found that at various frequencies the sonolytic degradation rate of chlorinated hydrocarbons, including CCl₄, CHCl₃, C₂Cl₆, and CH₂Cl₂, was faster for compounds with larger Henry’s law constants. Nanzai et al., (2008) reported that the initial degradation rate of twelve monocyclic aromatic compounds linearly correlated to their log Kₐw values.

The dependence of degradation rates of the PPCPs under both CW and PW ultrasound on physicochemical properties, including molecular weight, molar volume, vapor pressure, log Kₐw, and Henry’s law constant, was evaluated by non-parametric correlations (Spearman’s rho) to analyze for any possible relationships. We did not observe any correlation between degradation rate and any single property (p>0.05) under either CW or PW ultrasound (Figure 4.6 in the Supporting Information). The reported
correlations in previous studies may be attributed to the fact that the compounds investigated lie within classes of compounds with similar structure, thereby simplifying the correlations. Previous correlations have been made using equilibrium and kinetic parameters. Sonochemical degradation involves thermolysis and •OH oxidation of PPCPs and their byproducts in gas, interfacial, and bulk regions of cavitation bubbles. In this heterogeneous system, a single physicochemical property of the parent PPCP has limited capability to accurately govern the complex kinetics, especially when the investigated PPCPs cover a wide range of physicochemical properties and diversity of structures.

The results may have significant implications for the ultrasonic treatment of PPCPs in wastewaters and drinking waters. Contaminants, to be removed in municipal water and wastewater treatment plants, consist of a wide variety of classes of contaminants. Hence, the physicochemical properties of target contaminants may not be the principal consideration in determining the degradation of a contaminant by ultrasound. Unlike other treatment technologies, such as sedimentation or activated carbon adsorption, whose treatment depends on a specific physicochemical property (Halden and Heidler, 2008), our results suggest that one physicochemical property does not predict treatment by ultrasound. Moreover ultrasound can remove PPCPs covering a wide range of physicochemical properties.

4.4.2 Pulse enhancement

Pulse Enhancement (PE), defined as the difference in initial degradation rates between PW and CW over that of CW (eqn. 4.1), is a measure used to compare the difference in the rate of degradation between CW and PW ultrasound
\[
\text{PE} \%(\%) = \frac{\left( \frac{d[C]}{dt} \right)_{\text{PW}} - \left( \frac{d[C]}{dt} \right)_{\text{CW}}}{\left( \frac{d[C]}{dt} \right)_{\text{CW}}} \times 100\%
\]

where \( \left( \frac{d[C]}{dt} \right)_{\text{CW}} \) and \( \left( \frac{d[C]}{dt} \right)_{\text{PW}} \) are initial degradation rate of the PPCPs under CW and PW ultrasound, respectively. Accordingly, the PE is positive, negative or zero. If the PE is positive, PW ultrasound is more efficient than CW and vice versa.

Figure 4.2 shows the PE for the seven PPCPs. For ATP, IBU, and CBZ, pulsing caused a statistically significant increase (\( p<0.01 \)) as compared to CW ultrasound. For instance, ATP under PW is 1.6 times faster than that under CW. However, for PG, SFT, DP, and CIPRO, PW ultrasound is slower than that under CW mode by 2.45 \%, 5.89 \%, 5.87 \% and 15.34 \%, respectively.

Several studies investigated and compared the degradation of compounds under CW and PW ultrasound (Clarke and Hill, 1970; Deojay et al., 2011; Neppolian et al., 2009; Yang et al., 2005). Clarke and Hill (1970) observed a 1.5 fold increase in iodine production from KI solution under PW ultrasound as compared to CW ultrasound. Bubble size reduction below the bubble resonant size during the silent cycle was attributed to the enhancement by pulsing; in the subsequent ultrasonic pulse, this batch of bubbles and pre-existing nuclei in solution grow to resonant size. A 1.3 fold enhancement for the oxidation of arsenic (III) to arsenic (V) by PW ultrasound, compared to CW, was attributed to an increased number of active cavitation bubbles and “silent” oxidation reactions initiated by \( \cdot \text{OH} \) (Neppolian et al., 2009). Both studies imply that pulsing will
be beneficial for all PPCPs; however, we observed a negative PE for PG, SFT, DP, and CIPRO.

Yang et al. (2005) investigated the sonolysis of a surfactant, OBS, and non-surfactant, 4-ethylbenzene sulfonic acid (EBS). PW ultrasound was better than CW ultrasound with a PE of 94 %; however, the increase in degradation rate of PW over CW was not statistically significant for EBS. Enhancement was attributed to the accumulation of the surfactant on cavitation bubble surfaces, resulting in reduced surface tension and lowering the cavitation threshold (Yang et al., 2005). In addition, surfactants inhibit bubble dissolution during the off cycle, resulting in a larger active cavitation bubble population and increased absorption sites (Fyrillas and Szeri, 1995). Their mechanism is specific to surfactants; the PPCPs in our study did not exhibit any alteration in surface tension at 10 μM (data not shown).

While previous explanations of the enhancement of PW ultrasound are not applicable to our results, studies conducted by Yang et al., (2005; 2006) and others (De Visscher, 2003; DeVisscher et al., 1996; Drijvers et al., 2000; Fu et al., 2007), showed that mass transport of target compounds to the bubble surface is controlled by diffusion. For instance, Fu et al., (2007) correlated the degradation rate constants of seven estrogen compounds to MW and stated that small sized compounds diffuse faster to the vicinity of cavitation bubbles, resulting in a faster degradation rate. Drijvers et al., (2001) found that the monohalogenated benzene concentration ratios between the vicinity of cavitation bubbles and the bulk solution strongly correlated to their diffusion coefficients rather than their Henry’s law constants. Based on their studies, we hypothesized that, during the silent cycle, different size of PPCPs may diffuse to and accumulate on cavitation bubbles.
to different extents, resulting in different PE values. Thus, the molecular size would play a role in this diffusion-controlled process.

To test the hypothesis, a correlation analysis was conducted between PE and physicochemical properties listed in Table 4.1 (Figure 4.7 in the Supporting Information). Correlations were not observed. However, diffusion governs the transport of PPCPs based on the diffusivity equation of Hayduk and Laudie (1974) (eqn. 4.2), diffusion coefficients ($D_{iw}$, cm$^2$/s) in water are correlated to the molar volume ($V_i$, in the unit of mL/mol) in of a compound.

$$D_{iw} = \frac{13.26 \times 10^{-5}}{\mu_w^{1.14} V_i^{0.589}} \quad (4.2)$$

where $\mu_w$ is the viscosity of water at 25 °C. $V_i$ can be approximated by molecular weight when documented values and computational resource are not available.

Thus, PE was plotted against molar volume (Figure 4.3a) and molecular weight (Figure 4.3b) of the PPCPs, respectively. Figure 4.3 shows that small sized PPCPs exhibit a positive PE, while large sized PPCPs exhibit a negative PE. The results suggest that diffusion to the cavitation bubble surface is an important mechanism, resulting in enhanced degradation of the PPCPs by pulsing in our study.

Unlike Figure 4.3a and b, the degradation rate of the PPCPs under CW and PW ultrasound were not correlated to either their molar volumes or molecular weight (Figure 4.6a and b in the Supporting Information). The observed degradation rate of the PPCPs by sonolysis involves both high temperature decomposition and $\cdot$OH oxidation in the vicinity of cavitation bubbles and the bulk solution, as indicated by eqn. 4.3.
\[
\frac{dC}{dt}_{\text{obs}} = \frac{dC}{dt}_{\text{bulk}} + \frac{dC}{dt}_{\text{interface}} + \frac{dC}{dt}_{\text{bubble}}
\]  

(4.3)

where \( \frac{dC}{dt} \) represents the degradation rate of a PPCP, occurring in bulk solution (bulk), occurring at the interface (interface), and occurring in the gas region of cavitation bubble (bubble), respectively. Clearly, a single physicochemical property of a PPCP is unlikely to determine the degradation rate.

However, the concept of PE is based on a comparative method (eqn.4.1). The contribution from \( \frac{dC}{dt}_{\text{bulk}} \) to \( \frac{dC}{dt}_{\text{obs}} \) under CW ultrasound is similar to that under PW ultrasound (Deojay et al., 2011; Yang et al., 2005), thus there is no contribution of bulk reaction to PE. In addition, the PPCPs investigated are not likely to degrade inside the cavitation bubble due to their low Henry’s law constants (Table 4.1), suggesting that a negligible contribution of bubble reaction to PE. The remaining component, \( \frac{dC}{dt}_{\text{interface}} \), reaction at bubble-water interfaces, results in the controlling mechanism, diffusion, becoming more pronounced in our system.

During the on time, ultrasound induces the formation, growth through many wave cycles, and subsequent collapse of microbubbles. During the off time, microbubbles may: (1) coalesce and be removed by buoyancy, (2) dissolve and disappear or (3) shrink by dissolution to size whereby it will actively cavitate during the next on cycle (Leighton, 1994). Also, during the silent cycle (i.e., 100 ms) of a pulse sequence, PPCP molecules have more time to diffuse to and accumulate on the bubble surfaces. Although the time scale during the silence cycle is too short for equilibrium partitioning to be reached
(Eastoe and Dalton, 2000; Yang et al., 2005), when sonication resumes, the remaining bubbles and pre-existing nuclei surface populate with more PPCP molecules than before the silent cycle, grow to resonance size, and collapse. Hence, more PPCP molecules are in the vicinity of highest temperature and radical concentrations. In this diffusion-controlled process, small PPCP molecules more quickly diffuse to and accumulate on the cavitation bubbles during the off time, resulting in a positive PE. Large molecules take longer to diffuse to the surface, resulting in less accumulation. The competing process of bubble dissolution results in an overall negative PE for these larger compounds.

As observed in Figure 4.3a, the relationship between PE and molar volume is not perfect, especially when the compounds have similar molar volumes. For the five compounds (IBU, PG, DP, CBZ, and SFT) that assemble around 170 mL/mol (Figure 4.3), the hydrophobicity varies significantly. For example, the highest and lowest log $K_{ow}$ values among these five compounds are IBU (3.70) and SFT (0.89), respectively. Correspondingly, the highest and lowest PE values among these five compounds are also IBU (8.61) and SFT (-5.90), respectively, suggesting that the hydrophobicity affects the PE to some extent. Similar to Figure 4.3a, the relationship between PE and molecular weight in Figure 4.3b is not perfect, suggesting that the size of PPCPs may not be perfectly predict the PE value and hydrophobicity play a role in PE. However, although not studied explicitly, the impact of hydrophobicity on PE appears to be smaller than the size of PPCPs.

4.4.3 PPCPs degradation in bulk solution
Studies have shown a relationship between the aqueous diffusion coefficient of a compound and the fraction of a compound degraded in and on cavitation bubbles (DeVisscher et al., 1996; Drijvers et al., 2000). Specifically, small compound fast diffusing degrade in and on cavitation bubbles whereas large compounds slowly diffusing degrade primarily in bulk solution. Our interpretation of the trend of increasing PE with decreasing molar volume is similar. Small PPCP molecules more readily diffuse to and accumulate on the bubble surfaces during the silent cycle; upon the subsequent ultrasonic pulse, more PPCP molecules are in the vicinity of high temperature and high \( [\bullet \text{OH}] \), resulting in a positive PE.

To validate the role of PPCPs diffusion during the silent cycle, a bulk solution \( \bullet \text{OH} \) trapping agent, acetic acid (AA), was irradiated with each compound to differentiate the contribution of bulk \( \bullet \text{OH} \) oxidation in the overall degradation under CW ultrasound. Acetic acid (log \( K_{ow} = -0.17 \)) in bulk solution reacts with \( \bullet \text{OH} \), rather than migrating to the interface or gas region of cavitation bubbles (Xiao et al., 2012).

The portion of each PPCP degraded in bulk solution was determined from eqn. 4.4.

\[
\text{% degradation in bulk solution} = \frac{\left( \frac{d[C]}{dt} \right)_{\text{without AA}} - \left( \frac{d[C]}{dt} \right)_{\text{with AA}}}{\left( \frac{d[C]}{dt} \right)_{\text{without AA}}} \times 100 \%
\] (4.4)

where \( \left( \frac{d[C]}{dt} \right)_{\text{without AA}} \) and \( \left( \frac{d[C]}{dt} \right)_{\text{with AA}} \) represent the degradation rate for each PPCP without and with 1 mM of the bulk \( \bullet \text{OH} \) scavenger, acetic acid. As shown in Figure 4.4, the degradation rates were significantly reduced in the presence of AA for all the compounds. Based on eqn. 4.4, \( \bullet \text{OH} \) in bulk solution is responsible for 6.0 % of
degradation of PG, the compound least affected by AA. The relatively small reduction in the degradation rates with AA presence reveals that the majority of the degradation occurred in and around cavitation bubbles. CIPRO degradation decreased by 66.2 % in the presence of AA. Unlike the other PPCPs tested, the high decrease in degradation with AA indicates that the degradation of CIPRO primarily occurred in the bulk solution.

As shown in Figure 4.5a and b, the amount of degradation in bulk solution trends with increasing molar volume and molecular weight of a PPCP, respectively. The result indicates that the smaller and hence more mobile compound is more able to reach the bubble surfaces, the sources of reactivity, resulting in a greater proportion degraded in non-bulk solution. However, larger PPCP molecules (e.g., CIPRO) have greater steric hindrance slowing diffusion in solution. Slower diffusion results in a smaller portion of the compound reaching the bubble surface ending up with a higher fraction degraded in bulk solution. Therefore, there is an inherent link between the fraction that degraded in bulk solution and PE, corroborating that molecular size plays a role in the diffusion-controlled process in the cavitational system.

4.5 Conclusion

The independence of degradation rates of the PPCPs under both CW and PW ultrasound on their physicochemical properties indicated that there is no single property that controls the degradation kinetics. In addition, a comparison between CW and PW modes of ultrasound demonstrates that the enhancement of degradation of PPCPs under PW ultrasound was compound dependent. For the enhancement due to pulsing, there exists a relationship between PE and the molar volume and molecular weight, indicating
that small size PPCPs exhibit positive PE values, while large PPCPs yield negative PE values. This relationship implies that diffusion and transport of the PPCPs to the bubble surface during the silent cycle is key to pulsing. To explore this phenomena, a bulk solution •OH scavenger, acetic acid, was added in the sonicated system to differentiate the contribution of bulk •OH oxidation to the overall degradation. It is observed that the portion of degradation of the PPCPs in bulk solution is associated with their sizes. Small size molecules may quickly diffuse to the cavitation bubbles, resulting in a higher portion of the PPCP in and around cavitation bubbles. Large size molecules slowly diffuse to the surface due to their large size, resulting in a higher portion of these PPCPs molecules degraded in bulk solution. This trend in bulk degradation is consistent with the PE results. Our results suggest that PW ultrasound is a method to enhance degradation for the small PPCPs, while CW ultrasound is more effective to degrade large PPCPs in aqueous solution.

Acknowledgments

Financial support provided by Ohio Sea Grant College Program is gratefully acknowledged. R. X. gratefully acknowledges Dr. Chinmin Cheng and Matthew Noerpel for the valuable comments on this manuscript.
Table 4.1: Selected physicochemical properties of CBZ, IBU, ATP, SFT, CIPRO, PG, and DP at 25°C.

<table>
<thead>
<tr>
<th>compound</th>
<th>structure</th>
<th>molecular weight (g mol(^{-1}))</th>
<th>molar volume (mL mol(^{-1}))</th>
<th>vapor pressure (mm Hg)</th>
<th>log (K_{ow})</th>
<th>log Henry's law constant (atm·m(^3) mol(^{-1}))</th>
<th>•OH rate constant (M(^{-1}) s(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBZ</td>
<td><img src="image" alt="CBZ structure" /></td>
<td>236.27</td>
<td>186.39</td>
<td>6.32×10(^{-4})</td>
<td>2.45</td>
<td>-9.97 (\textsuperscript{2})</td>
<td>4.86×10(^{10})</td>
</tr>
<tr>
<td>IBU</td>
<td><img src="image" alt="IBU structure" /></td>
<td>206.28</td>
<td>176.40</td>
<td>7.56×10(^{-2})</td>
<td>3.70</td>
<td>-6.82 (\textsuperscript{2})</td>
<td>7.10×10(^{9})</td>
</tr>
<tr>
<td>ATP</td>
<td><img src="image" alt="ATP structure" /></td>
<td>151.17</td>
<td>128.43</td>
<td>1.18×10(^{-11})</td>
<td>0.46</td>
<td>-12.19 (\textsuperscript{2})</td>
<td>1.07×10(^{10})</td>
</tr>
<tr>
<td>SFT</td>
<td><img src="image" alt="SFT structure" /></td>
<td>253.28</td>
<td>165.01</td>
<td>1.77×10(^{-11})</td>
<td>0.89</td>
<td>-12.02 (\textsuperscript{2})</td>
<td>5.50×10(^{9})</td>
</tr>
<tr>
<td>CIPRO</td>
<td><img src="image" alt="CIPRO structure" /></td>
<td>331.34</td>
<td>234.21</td>
<td>2.00×10(^{-10})</td>
<td>0.28</td>
<td>-18.29 (\textsuperscript{2})</td>
<td>2.15×10(^{10})</td>
</tr>
<tr>
<td>PG</td>
<td><img src="image" alt="PG structure" /></td>
<td>212.20</td>
<td>158.80</td>
<td>3.13×10(^{-10})</td>
<td>1.80</td>
<td>-16.16 (\textsuperscript{2})</td>
<td>5.55×10(^{10})</td>
</tr>
<tr>
<td>DP</td>
<td><img src="image" alt="DP structure" /></td>
<td>222.24</td>
<td>162.59</td>
<td>9.22×10(^{-11})</td>
<td>2.42</td>
<td>-6.21</td>
<td>2.09×10(^{9})</td>
</tr>
</tbody>
</table>

1. Molar volume was calculated at Hartree Fock (HF) level of theory with 6-31+G* basis set and PCM solvation method.
2. Estimated from the group method using EPI Suite\textsuperscript{TM} v.4.0 (U.S. EPA).
Figure 4.1: Initial degradation rates of pharmaceuticals (CBZ, SFT, IBU, ATP, and CIPRO) and personal care products (PG and DP) at initial concentration of 10 µM and pH 3.5 sonicated under CW and PW ultrasound.
Figure 4.2: Pulsed enhancements of 10 µM individual PPCP degradation by PW ultrasound with a pulse length of 100 ms and pulse interval of 100 ms at pH 3.5.
Figure 4.3: PE was plotted against the molar volumes (a) and molecular weight (b) of the PPCPs.
Figure 4.4: Initial degradation rates of 10 µM CBZ, IBU, ATP, SFT, CIPRO, PG, and DP in the absence and presence of 1 mM •OH scavenger AA under CW ultrasound at pH 3.5.
Figure 4.5: The portion of degradation that occurred in the bulk solution under CW ultrasound is plotted against molar volume (a) and molecular weight (b) of each PPCP molecule.


Supporting Information
Figure 4.6: Degradation rates of the PPCPs under CW and PW ultrasound were plotted against molecular weight (a), molar volume (b), log vapor pressure (c), log $K_{ow}$ (d), log Henry’s law constant (e) and log *OH rate constant (f).
Figure 4.7: PE of the PPCPs were plotted against log vapor pressure (a), log $K_{ow}$ (b), log Henry’s law constant (c) and log $k_{OH}$ rate constant (d).
Chapter 5: Probing the Utility of Pulsed Wave Ultrasound for the Degradation of Pharmaceuticals in Municipal Wastewater

5.1 Abstract

Both the octanol-water partition coefficient ($K_{ow}$) and diffusivity ($D_{iw}$) have been correlated to the rate of contaminant degradation by ultrasound. However, the relative importance and a mechanistic understanding of the importance of both properties on cavitation systems are poorly understood. In this study, a series of six pharmaceuticals were selected based on their $K_{ow}$ and $D_{iw}$ values to probe the importance of both properties on pharmaceutical degradation during continuous wave (CW) and pulsed wave (PW) ultrasound. In deionized water, pharmaceuticals with the highest $D_{iw}$ (i.e., fluorouracil (5-FU)) and $K_{ow}$ (i.e., lovastatin (LOVS)) exhibited the greatest enhancement in degradation rates in PW mode as compared to CW mode. This result suggests that a pharmaceutical with either high diffusivity or hydrophobicity more readily populates the bubble-water interface during the silent cycle of PW ultrasound. However, in municipal wastewater effluent, the pulse enhancement (PE) for 5-FU and LOVS disappeared. The presence of matrix inorganics (i.e., bicarbonate and sulfate anions) did not affect the PE, indicating that the wastewater effluent organic matter (EfOM) is the cause of the disappearance of PE. Irradiating 5-FU and LOVS in hydrophobic (HPO), transphilic (TPI), and hydrophilic (HPI) fractions of EfOM showed that the TPI fraction reduced the
pulse enhancement the most, followed by HPI and HPO fractions. The smaller molecular weight of TPI suggests that the TPI fraction is able to diffuse to cavitation bubble surfaces, causing the reduction in pharmaceutical degradation in the presence of EfOM.

5.2 Introduction

Many studies have reported the occurrence of various pharmaceuticals in different waters around the world, including tap water, wastewater, and receiving streams, ranging from parts-per-trillion to parts-per-billion concentrations (1-6). Although the knowledge of adverse effects of chronic low-dose exposure to pharmaceutical mixtures on human health is limited, many toxicological studies have shown that exposures of fish and other aquatic organisms to these anthropogenic compounds causes reproductive and behavioral disorders (2, 7-9).

To minimize risk, efforts are underway to reduce human and aquatic organism exposure to pharmaceuticals in waters, especially from municipal wastewater effluent, the main route for pharmaceuticals to enter natural waters (10-13). Activated sludge treatment in wastewater treatment plants has been shown to improve the removal of some pharmaceuticals by using long sludge retention times (14-15). However, the majority of pharmaceuticals are not completely degraded, and most existing municipal wastewater treatment plants are not designed for operation using prolonged sludge retention times (16). Finding alternative technologies that effectively remove pharmaceuticals from wastewater effluents has, therefore, been of research interest (17-19).

Ultrasound, an advanced oxidation process (AOP), shows great potential to degrade pharmaceuticals in wastewater as a tertiary treatment technology (20-23). Ultrasound has
unique advantages as compared to other technologies, such as no addition of chemicals, ease of use, and short contact times (24-25). Ultrasonic irradiation induces chemical reactions in water from the collapse of cavitation bubbles (26). The collapse of cavitation bubbles generates localized hot spots (27-28), and these localized hot spots initiate thermolytic and oxidation reactions with pharmaceuticals.

Properties of compounds, including surface excess (Γ) (29-30), octanol-water partition coefficient (K_{ow}) (31-32), vapor pressure (p) (31, 33), Henry’s law constant (K_{H}) (34-35), second-order rate constant with •OH (k_{•OH}) (36-37), and diffusivity (D_{iw}) (38-39), have been shown to affect their degradation rates by ultrasound. These properties are either thermodynamic (e.g., Γ, K_{ow}, p, and K_{H}) or kinetic (e.g., k_{•OH} and D_{iw}) parameters. The thermodynamic parameters describe the tendency of pharmaceuticals to reach equilibrium with specific regions of the cavitation bubbles. The kinetic parameters determine the rates at which these compounds move to cavitation bubbles and react with ultrasound-induced reactivity (i.e., heat and •OH). Although the dependence of both thermodynamic and kinetic parameters on overall compound degradation has been reported (26-36), the question regarding which aspect has a more profound influence on the cavitation system remains unclear.

Pulsed wave (PW) ultrasound, whose ultrasonic signal train is separated by gaps of no signal (40), features the discontinuation of bubble growth during the silent cycle. Previous studies (41-44) found that PW ultrasound, under certain optimal conditions, enhances the degradation of a compound, because it allows time (i.e., silent cycle) for the surface active or small sized compound to diffuse to bubble-water interfaces, the sources of reactivity. For instance, Xiao et al., (44) observed that degradation rates of seven
different pharmaceuticals and personal care products (PPCPs) by PW ultrasound are compound dependent with degradation faster for smaller compounds or slower for larger compounds than that under CW ultrasound. They linked the pulsed enhancement (PE) of PPCPs to their $D_{iw}$, specifically, a smaller sized PPCP is more able to diffuse to bubble surfaces as compared to a larger sized PPCP. Yang et al. (45) investigated the sonolysis of the surfactant 4-octylbenzene sulfonate, and the non-surfactant 4-ethylbenzene sulfonate (EBS) in CW and PW mode. PW ultrasound was more effective than CW ultrasound for OBS with a PE of 94 %; however, the increase in degradation rate of PW over CW was not statistically significant for EBS. Enhancement was attributed to the accumulation of the surfactant on cavitation bubble surfaces, resulting in reduced surface tension and lowering the cavitation threshold (45). Our previous work evaluated PE for a group of PPCPs. We observed a link between $D_{iw}$ and PE over a limited range of $D_{iw}$ and $K_{ow}$ in deionized (DI) water.

In this study, pulsed wave (PW) ultrasound was used to systematically study the roles that kinetic (i.e., $D_{iw}$) and thermodynamic (i.e., $K_{ow}$) parameters play in determining pharmaceutical degradation. We selected six pharmaceuticals, namely fluorouracil (5-FU), ibuprofen (IBU), clonidine (CLND), estriol (ESTO), nifedipine (NIFE), and lovastatin (LOVS), on the basis of $K_{ow}$ and $D_{iw}$. The $K_{ow}$ of these six compounds is in the increasing order and $D_{iw}$ is in decreasing order (Figure 5.6 in the Supporting Information), allowing us to observe trends in PE with $D_{iw}$, $K_{ow}$ and PE. We investigated the degradation of these six pharmaceuticals in DI and in a wastewater effluent to evaluate the effect of environmentally relevant matrices on PE.
5.3 Experimental Methods

5.3.1 Materials

5-FU (99%), IBU (99%), CLND (99%), ESTO (97%), NIFE (98%), sodium bicarbonate (99%), and sodium sulfate bicarbonate (99%) from Sigma-Aldrich, LOVS (98%) from TCI, methanol (HPLC Grade), acetonitrile (HPLC Grade), HCl (Trace metal Grade) and NaOH (97%) from Fisher Scientific, were used as received. Table 5.1 in the Supporting Information lists physicochemical properties of the pharmaceuticals. Supelite™ XAD8 and Amberlite® XAD4 resins were purchased from Sigma Aldrich. A Chromaflex Chromatography column (1085 mL, 4.8 cm × 60 cm) with 0.20 mm bed supports was purchased from Kontes (Vineland, NJ). Water used was from a Millipore System (Millipore, MA) with a resistivity \( R = 18.2 \, \text{M}\Omega \, \text{cm} \).

5.3.2 Wastewater effluent collection

The wastewater effluent was collected in December 2011 from a wastewater treatment plant, located in the vicinity of Columbus, Ohio, U.S.A. The facility was established in 2001 and has a treatment capacity of 10 million gallons per day. The plant uses traditional activated sludge treatment and denitrification technologies, but no primary clarification. The wastewater is mainly composed of municipal wastewater. The wastewater sample was collected from a tertiary filtered effluent stream and poured into a 50 L polyethylene carboy with minimal headspace. Using a Masterflex pump (Cole Parmer), the wastewater was consecutively prefILTERed through 5 and 0.45 μm groundwater filtration capsules (Pall Gelman). Capsules were pre-rinsed with Milli-Q water before use. Filtered wastewater effluent was acidified to pH 2 with HCl, air
stripped for 2 hours to remove H₂S and NH₃, and stored in the dark at 4 °C until use. Before use the pH of a wastewater effluent aliquot was readjusted the field pH using NaOH. The presence of Na⁺ and Cl⁻ ions due to pH adjustment (from pH 2 to 7.7) is believed not to interfere with the cavitation system; the lowest reported concentration affecting cavitation is 0.1 M (46-49).

5.3.3 Wastewater effluent organic matter isolation

The XAD8 and XAD4 resins were cleaned and packed according to Standley and Kaplan (50). Organic matter from wastewater effluent was isolated using XAD 8 and XAD 4 resin columns following Quaranta et al. (51). The XAD8 and XAD4 resin columns were used to retain operationally defined hydrophobic (HPO) and transphilic (TPI) fractions of organic matter, respectively. The organic matter that passed through both columns consisted of the hydrophilic (HPI) fraction of organic matter and inorganic salts. The two columns were connected consecutively by Teflon tubing. Approximately 40 empty bed volumes of filtered wastewater effluent passed through the columns with a flow rate of 15 empty bed volumes per hour to ensure that a significant amount of organic matter was sufficiently retained. The organic matter was back-eluted from each column individually using 0.1 M NaOH and the wastewater effluent organic matter fractions were stored in the dark at 4 °C prior to use.

5.3.4 Wastewater effluent organic matter characterization

Characterization of the original wastewater effluent was conducted before pH adjustment and is summarized in Table 5.2 in the Supporting Information. The
concentration of dissolved organic carbon in the solution was quantified by a Shimadzu TOC-5000A analyzer. Specific ultraviolet absorbance was measured at 280 nm (SUVA$_{280}$) with a photospectrometer (model UV-2401, Shimadzu), since SUVA$_{280}$ is strongly correlated to the aromaticity of organic matter (52). Concentrations of common elements were measured by inductively coupled plasma Atomic Emission spectroscopy, ICP-AES (Vista AX, Varian). The dominant cations included calcium and sodium. Anion concentrations were determined by ion chromatography (DX-120, Dionex). The dominant anions included chloride and sulfate. The dominant ions are believed not to interfere with cavitational systems at the measured concentration. Molecular weight (MW) distributions of the original and fractionated wastewater effluent organic matter were determined with size exclusion chromatography (SEC) (Hewlett Packard 1050). A 1 mL/min mobile phase of pH 7.0 buffer solution of 0.1 M tris(hydroxymethyl)methylamine and HCl flowed through a Protein-Pak 125 size exclusion column (Waters Associates) and into a UV detector analyzing at 235 nm. Calibration was performed using sodium polystyrene sulfonates (Polysciences) with molecular weights of 18K, 8K, 4.6K, and 1.8K, and acetone, following the method of Chin et al. (53). A linear calibration curve ($R^2 = 0.99$) was obtained between log MW and elution volume.

5.3.5 Sonochemical experiments

Ultrasound at 205 kHz was emitted from a USW 51-52 ultrasonic flat plate transducer (A = 23.4 cm$^2$) (ELAC Nautik, Inc., Kiel, Germany) into a water jacketed glass vessel with a volume of 300 mL. The temperature of the reactor was maintained at
20 °C. A SM-1020 Function/Pulse generator (Signametrics Corp.) delivered sound waves with an operation mode of 100 ms on and 100 ms off. The acoustic energy density to the reactor, determined by calorimetry, was 45 W/L.

During experiments, 0.5 mL samples for chemical analysis were taken from the reactor at designated times using a 1 mL glass syringe (Gastight 1001, Hamilton Corp.). The total sample volume taken during the course of sonication did not exceed 1 % of the initial volume.

5.3.6 Chemical analysis

A Hewlett-Packard 1100 HPLC equipped with a diode array detector (DAD) and a 5 µm, 150 × 2.1 mm SB-C18 column (Agilent Technologies) was used to quantify the concentration of the pharmaceuticals. Eluents consisted of 20 mM pH 3 phosphoric buffer and acetonitrile with a flowrate of 0.5 mL/min. The eluent ratios were different for different compounds. The UV wavelengths were set at 265, 220, 220, 225, 238, and 238 nm for 5-FU, IBU, CLND, ESTO, NIFE, and LOVS, respectively.

5.3.7 Computational modeling

A non empirical calculation at the Hartree Fock (HF) level of theory with 6-31+G* basis set was applied to determine the molar volume of the molecules (mL/mol) in water, using the polarizable continuum model solvation method. HF/6-31+G* is considered to be a reliable level of theory to calculate the geometry of large organic molecules (54-55). All calculations were performed using Gaussian 09 (56) at the Ohio Supercomputer Center.
5.4 Results and discussion

5.4.1 Sonochemical degradation in DI water

Sonochemical degradation rates of 5-FU, IBU, CLND, ESTO, NIFE, and LOVS in DI water are shown in Figure 5.1a. The initial degradation rates of LOVS under CW and PW ultrasound are 0.55 and 0.67 µM/min, respectively, which is faster than the other compounds. 5-FU degraded slowest, with the degradation rates 0.11 and 0.13 µM/min under CW and PW ultrasound, respectively.

Linear correlations have been reported between sonochemical degradation rates of contaminants and their log Henry’s law constants (35), log K_{ow} values (31), and molecular weight (57) in aqueous solutions. For instance, Colussi et al., (35) found that at various frequencies the sonolytic degradation rate of chlorinated hydrocarbons, including CCl_{4}, CHCl_{3}, C_{2}Cl_{6}, and CH_{2}Cl_{2}, was faster with larger Henry’s law constants. Nanzai et al., (31) reported that the initial degradation rate of twelve monocyclic aromatic compounds linearly correlated to their log K_{ow} values. Fu et al., (2007) observed a negative correlation between the rate of sonolysis of eight different estrogen compounds and their molecular weight. The dependence of degradation rates of the pharmaceuticals under both CW and PW ultrasound on physicochemical properties, including log Henry’s law constants, log K_{ow}, molecular weight, and molar volume was evaluated by non-parametric correlations (Spearman’s rho) to analyze for any possible relationships. Surprisingly, there is a positive correlation between degradation rate and molar volume (Figure 5.7d in the Supporting Information), suggesting that a larger sized pharmaceutical is destroyed faster than the small sized one. The suggestion is inconsistent with Fu et al.
(57) and may result from the set of PPCPs chosen in our study. Although the degradation rate is not perfectly correlated ($R^2 > 0.8$) with $K_{ow}$, Figure 5.7b shows a hydrophobic compound degrades faster than hydrophilic one. The observation is consistent with Nanzai et al. (31).

In Figure 5.1a the initial degradation rates for 5-FU, NIFE, and LOVS are faster under PW mode as compared to CW mode. For IBU, CLND, and ESTO, exhibit the opposite trend. In order to evaluate the effect of pulsing ultrasound on degradation kinetics, PE, a measure used to compare the difference in initial degradation rates between CW and PW ultrasound, was determined by eqn. 5.1.

$$PE(\%) = \frac{\left(\frac{d[C]}{dt}\right)_{PW} - \left(\frac{d[C]}{dt}\right)_{CW}}{\left(\frac{d[C]}{dt}\right)_{CW}} \times 100$$

(5.1)

where $\left(\frac{d[C]}{dt}\right)_{CW}$ and $\left(\frac{d[C]}{dt}\right)_{PW}$ are the initial degradation rates of a pharmaceutical under CW and PW ultrasound, respectively.

The PE of the six pharmaceuticals in DI water is illustrated in Figure 5.2a. Pulsing ultrasound is beneficial for 5-FU, NIFE, and LOVS, while IBU, CLND, and ESTO have negative PE values. The U-shaped curve of PE vs. molecular weight in DI water shows that, a pharmaceutical with either the smallest MW (i.e., 5-FU, MW = 131 g/mol) or the greatest $K_{ow}$ (i.e., LOVS, $K_{ow} = 4.26$) was positively affected by pulsing. For the compounds with medium diffusivity and hydrophobicity, PW ultrasound did not increase the degradation kinetics.
In Chapter 4, we investigated the effect of pulsing on seven PPCPs which covered a range of physicochemical properties and a diversity of structures. The PE of PPCPs was linked to the diffusivity of the PPCP by observing an inverse relationship between the molar volume of a PPCP and its PE. We did not explore the impact of hydrophobicity on PE explicitly. Thus, this study verifies and builds on the previous work.

The benefit of PW ultrasound is the retardation of bubble growth during the silent cycle, providing time for a pharmaceutical to diffuse to bubble-water interfaces and react with the cavitation bubbles within the subsequent pulse. Thus, a strong hydrophobic or highly diffusive compound has the preference or momentum to migrate to bubble-water interfaces during the silent cycle, resulting in more molecules reacted by ultrasound-induced reactivity. Our results suggest that a pharmaceutical with either high diffusivity or hydrophobicity more readily populates the bubble-water interface during the silent cycle of PW ultrasound. However, for the compounds with medium hydrophobicity and diffusivity, their PE values are smaller suggesting that there is little to no benefit to using PW ultrasound.

This can be explained by Fick’s law, defined in eqn. 5.2.

\[
J_i = -D_{iw} \frac{dC_i}{dz} \tag{5.2}
\]

where \( J_i \) is the mass flux of chemical \( i \) in direction of concentration gradient with; \( C_i \) is the concentration of \( i \); and \( z \) is distance in the direction of concentration gradient (i.e., thickness of bubble interface). As shown in eqn. 5.2, the flux towards to bubble-water surface is a function of diffusivity and concentration gradient. The concentration gradient depends on the enrichment of a pharmaceutical on bubble surfaces, a hydrophobic
compound accumulates more on bubble surfaces than a hydrophilic one; thus, for the same initial concentration and diffusivity, a hydrophobic compound results in a greater concentration gradient, ultimately a greater flux into bubbles. Similarly, two compounds at the same concentration and hydrophobicity will accumulate on a bubble surface to the same degree at equilibrium but the compound with a high $D_w$ will result in a higher flux and consequently, higher PE value. Therefore, pharmaceuticals with a combination of diffusivity and concentration gradient result in the largest flux exhibit greater PE values.

Diffusivity is an inverse function of the molar volume of the diffusing compound (58). However, molar volume information is not readily available. Easily obtainable molecular weight generally correlates well with molar volume, resulting in its use (Figure 5.8 in the Supporting Information). Although molecular weight correlates well with molar volume, the smoother curve of Figure 5.2b demonstrates that molar volume is a better parameter than molecular weight for investigating relative effects of diffusivity.

5.4.2 Sonochemical degradation in wastewater effluent

The sonochemical degradation rates of 5-FU, IBU, CLND, ESTO, NIFE, and LOVS in wastewater effluent are shown in Figure 5.1b. Unlike the trend observed in DI water, NIFE degraded faster than the other compounds with the initial degradation rates 0.35 and 0.34 µM/min under CW and PW, respectively. 5-FU decomposed slowest, approximately one order of magnitude slower than that of NIFE. The slowest degradation kinetics of 5-FU in wastewater effluent is similar to that in DI water, suggesting that 5-FU is recalcitrant to ultrasound-induced reactivity.
As expected, the overall slower degradation of the pharmaceuticals in the wastewater effluent indicated that environmentally relevant matrices inhibit degradation. For example, the initial degradation rates of LOVS and CLND in wastewater were reduced by approximately 90% and 60%, respectively, as compared to in DI water. Previous work has observed a similar effect (59-62). Sanchez-Prado investigated the sonochemical degradation of triclosan in DI water and domestic wastewater (62). The degradation rate constant was reduced by 76.8% in the matrix as compared to in DI water. Cheng et al., investigated the effects of organic and inorganic matrices in groundwater on sonochemical degradation of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) (59-60). They concluded that both matrices negatively affect the sonochemical kinetics due to organic matter adsorption to the bubble-water interface and inorganic ions partitioning to and interaction with cavitation bubbles, hence decreasing the degradation rates.

In wastewater effluent, the enhancement of degradation rates of the pharmaceuticals in PW ultrasound disappeared. This effect was most prominent for 5-FU and LOVS (Figure 5.2a). Therefore, the benefit of pulsing ultrasound in DI water may not be applicable to municipal wastewater effluent. This lack of benefit of pulsing ultrasound in wastewater effluent may be due to salts or effluent organic matter interfering with degradation.

5.4.3 Effect of inorganic and organic matrix on PE of pharmaceuticals

When AOPs are investigated in water treatment, the water matrix containing inorganic and organic components significantly slows the degradation of the target
contaminants (59-60, 63) due to matrix competition for •OH and/or sequestration of contaminants from AOP reactivity. In ultrasound, the matrix may react with •OH, diffuse to cavitation bubbles, quenching bubble dynamics, and alter the availability of compounds to ultrasound-induced reactivity (64-65). However, there is little known about how environmentally relevant matrices influence the enhanced degradation kinetics under PW ultrasound. To this end, we evaluated the effect of inorganic and organic matrices, independently.

5.4.3.1 Effect of inorganics on PE of pharmaceuticals

Previous studies (49, 66) indicated that sulfate and bicarbonate significantly affect bubble dynamics as compared to other anions, such as chloride and nitrate (49). Therefore, sulfate and bicarbonate anions were selected as matrix inorganics to elucidate their effect on the PE of pharmaceuticals. Decreased degradation of PFOA and PFOS was attributed to sulfate and bicarbonate decreasing the negative charge at the bubble-water interface and altering the interfacial water structure and adsorption kinetics of target compounds to bubble surfaces. Sun et al., (66) investigated the degradation kinetics of acid black 1 (AB1) in the presence of 0.5 g/L sulfate and bicarbonate in the ultrasound/Fenton system and they attributed the inhibited degradation to anions reacting with •OH (eqn. 5.3 and 5.4).

\[
\begin{align*}
\text{HCO}_3^- + \cdot\text{OH} &\rightarrow \cdot\text{CO}_3^- + \text{H}_2\text{O} & (5.3) \\
\text{SO}_4^{2-} + \cdot\text{OH} &\rightarrow \cdot\text{SO}_4^- + \text{OH}^- & (5.4)
\end{align*}
\]
We expected that the presence of $\text{SO}_4^{2-}$ and $\text{HCO}_3^-$ would either react with $\bullet\text{OH}$ or partition to the bubble-water interface, reducing the temperature of collapsing cavitation bubbles, ultimately resulting in reduction of PE.

The PE of the six pharmaceuticals in the presence of 2 mM $\text{SO}_4^{2-}$ and $\text{HCO}_3^-$ is shown in Figure 5.3. Similar to the results of PE of the pharmaceuticals in DI water, the PE values for 5-FU and LOVS are highest among the six compounds. In the presence of sulfate anion, the PE for 5-FU and LOVS were 28.4 % and 20.4 %, respectively. With the presence of bicarbonate anion, the PE for 5-FU and LOVS were 39.6 % and 12.3 %, respectively. The presence of anions reduced the PE of NIFE, from 9.3% in the absence to -35.3% and -44.7% for $\text{SO}_4^{2-}$ and $\text{HCO}_3^-$, respectively. Cheng et al., reported $\text{SO}_4^{2-}$ and $\text{HCO}_3^-$ could accumulate on bubble-water interface and change bubble dynamic (49). The accumulation causes localized concentration of the anion within a certain distance from bubble interfaces higher than in bulk solution. The hydrophobic NIFE accumulates on the bubble surfaces to the same extent as $\text{SO}_4^{2-}$ and $\text{HCO}_3^-$, thus resulting in the most pronounced interference by the anions, ultimately reducing PE of NIFE. For the other compounds, the presence of anions seems to not decrease their PE values. The little influence of the anions may be due to more accumulation of target compounds (e.g. 5-FU and LOVS) or less accumulation of target compounds (e.g. IBU, CLND, and ESTO) on bubble surfaces as compared to anions. The U-shaped curve (Figure 5.3) in the presence of the anions resembles that of the DI water curve, indicating that inorganics do not significantly affect the accumulation behavior of the pharmaceuticals on bubble surfaces during the silent cycle, thus not altering the effect of pulsing on degradation kinetics.
5.4.3.2 Effect of organics on PE of pharmaceuticals

Matrix organics have been shown to have different effects on sonochemical degradation of the target compounds (61, 67-69). Matrix organics are substances with diverse size and polarity; the influence of various components on sonochemical degradation rates in CW or PW ultrasound is unknown. In order to gain a mechanistic understanding of the role of matrix organics in wastewater effluent on sonolysis of pharmaceuticals, we fractionated the effluent organic matter (EfOM) into operationally defined HPO, TPI, and HPI fractions to determine how size and hydrophobicity of EfOM affects sonolysis of target compounds. As illustrated in Table 5.3 in the Supporting Information, the weight-averaged molecular weights of EfOM were smaller than observed for natural DOM (53). In addition, the SUVA$_{280}$ value of the TPI fraction was larger than the corresponding HPO and HPI fractions, suggesting that the TPI fraction may have more aromatic character than the HPO and HPI fractions (51). Sonolysis of 5-FU and LOVS was conducted in these three fractions with a DOC of 3 mgC/L in each fraction.

Figure 5.4 shows the initial sonochemical degradation rates of 5-FU and LOVS in different fractions of EfOM. It is clear that the TPI fraction negatively affects the initial degradation rates of both pharmaceuticals more than the HPO and HPI fractions of EfOM. For 5-FU, compared to DI water, the presence of the TPI fraction reduced the rates by 53.1% and 66.9% in CW and PW ultrasound, respectively. HPO and HPI fractions of EfOM both had a similar effect on the degradation kinetics of 5-FU. For LOVS, the HPI fraction inhibited the degradation to a greater extent than the HPO fraction.
The pulsing effect on the degradation of 5-FU and LOVS in different fractions is illustrated in Figure 5.5. Both compounds exhibited a negative PE in all fractions of EfOM, while the TPI fraction reduced the PE the most.

The reduction in PE can be explained by both molecular size and the hydrophobicity of the TPI portion of EfOM. The molecular weight of TPI (146 g/mol) is considerably less than HPO (474 g/mol), suggesting that the size of transphilic fraction of EfOM is significantly smaller that the hydrophobic fraction. Consistent with our previous observations (70), small sized matrix organics perturb the accumulation of pharmaceuticals during the silent cycle, quenching the ultrasound induced reactivity under PW ultrasound. Xiao et al., (70) sonolyzed ciprofloxacin and ibuprofen in the matrix organics of terephthalic acid (TA) and Suwannee River Fulvic Acid (SRFA). Smaller-sized matrix organics (i.e., TA) had a greater impact on the degradation rates of target contaminants by ultrasound compared to larger-sized matrix organics (i.e., SRFA). Although with molecular weight of TPI (146 g/mol) slightly greater than HPI (128 g/mol), the PE of LOVS in presence of TPI is less than that in the presence of HPI, suggesting that the size of pharmaceutical may not be the exclusive reason for PE reduction.

As illustrated in eqn. 5.2, the diffusivity and concentration gradient co-determine the flux of organic matrix towards to bubble surfaces. The molecular weight of TPI is similar to HPI, indicating that the diffusivity of these two fractions is similar. In addition, the TPI fraction is operationally more hydrophobic than HPI based on our isolation method. Therefore, with the same DOC and similar diffusivity of TPI and HPI, the concentration gradient for TPI fraction is greater than HPI, resulting in a greater flux of TPI into
bubbles than that of HPI during the silent cycle. Thus, the TPI fraction reduces the PE to a greater extent than HPI.

Figure 5.5 shows that, in the presence of the HPI fraction, the PE of LOVS (-9.44%) is significantly less than that of the HPO fraction (-40.47%). Considering the molecular weight for HPI is less than HPO (MW\textsubscript{HPI}=128 g/mol and MW\textsubscript{HPO}=474 g/mol) but the HPO fraction is operationally more hydrophobic than HPI, the result of less PE in the presence of HPI than HPO suggested that the effect of molecular weight of EfOM is more influential than that of hydrophobicity in determining PE of target compounds.

Figure 5.5 also shows the PE for 5-FU is greater than that of LOVS in each fraction of EfOM. For instance, in the HPO fraction of EfOM, the PE values for 5-FU and LOVS are similar, but in TPI fraction, PE values for 5-FU and LOVS were -11.5 and -69.3%, respectively. The discrepancy indicates that the size and hydrophobicity of target pharmaceuticals influence PE in the presence of EfOM. We suspected the size may be more influential than hydrophobicity in determining the PE in different fractions of EfOM. For the HPO fraction, the PE of two compounds was similar. This is due to the larger molecular weight of HPO (MW\textsubscript{HPO}=474 g/mol) than LOVS (MW\textsubscript{LOVS}= 404 g/mol) and 5-FU (MW\textsubscript{5-FU}= 103 g/mol), resulting in the presence of HPO fraction does not change their PE values. For the TPI and HPI fractions, the molecular weight of TPI (MW\textsubscript{TPI}=146 g/mol) and HPI (MW\textsubscript{HPI}=128 g/mol) are significantly less than LOVS but greater than 5-FU, suggesting that a large sized pharmaceutical (i.e., LOVS) is less steadily to diffuse to bubble surfaces, consequently resulting in a less PE value than small size one (i.e., 5-FU). It is noted that, although 5-FU (log K\textsubscript{ow}=-1) is less hydrophobic than LOVS (log K\textsubscript{ow}= 4.26), the K\textsubscript{ow} value may not correctly reflect the partitioning
behavior of 5-FU and LOVS to different fractions of EfOM in water, especially for the compound with log \( K_{ow} \) greater than 4 (71).

In summary, the presence of EfOM, especially small sized EfOM, negatively affects the sonochemical degradation of pharmaceuticals under PW ultrasound. EfOM diffuses or partition to bubble surfaces during the silent cycle, thus either competing the adsorption sites for target compounds or interacting at the bubble-water interface, lowering the bubble dynamics. These interferences will unavoidably reduce the pulsing effect on pharmaceutical degradation, hence resulting in a negative PE value.

5.5 Environmental application

We evaluated the effect of inorganic and organic matrices to determine the components in wastewater effluent reduced the pulsing effect on the sonolysis of the pharmaceuticals. Our results showed that the organic matrix was the cause of the reduction in PE. By isolating the EfOM, we further concluded that the TPI fraction caused the most significant drop in PE during the sonolysis of pharmaceuticals. Small sized EfOM diffuses to and accumulates at the bubble-water interface during the silent cycle, thus impede the sonochemical degradation of the target pharmaceuticals under the PW ultrasound the most. The inhibition effect is more prominent for hydrophobic target pharmaceuticals. Overall, CW ultrasound is preferred over PW to enhance removal efficiency of target pharmaceuticals by ultrasound in the presence of EfOM. It is optimal to remove of matrix organics (especially small sized organics) before ultrasound treatment to maximize its efficiency.
Acknowledgements

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Supporting Information

Supporting information contains three tables and three figures. This material is available free of charge via the Internet at http://pubs.acs.org.
Figure 5.1: The initial sonochemical degradation rates of 5-FU, IBU, CLND, ESTO, NIFE, and LOVS in DI water (a) and wastewater effluent (b) (pH 7.7, 20 °C, [pharmaceutical]₀ = 10 μM, and sonication power density at 45 W/L).
Figure 5.2: The PE of the six pharmaceuticals in DI water and wastewater effluent (a). PE in DI water was plotted as a function of molar volume (b) (pH 7.7, 20 °C, [pharmaceutical]₀ = 10 μM, and sonication power density at 45 W/L).
Figure 5.3: The PE of the six pharmaceuticals in DI water (pH 7.7, 20 °C, [pharmaceutical]₀ = 10 μM, and sonication power density at 45 W/L). In DI water, the concentration of bicarbonate is 2.5 ×10⁻⁴ M, assuming water is equilibrated with the atmosphere.
Figure 5.4: The initial sonochemical degradation rates of 5-FU and LOVS in DI water and different fractions of effluent organic matter (pH 7.7, 20 °C, [pharmaceutical]₀ = 10 μM, [DOC]= 3 mgC/L, and sonication power density at 45 W/L).
Figure 5.5: The PE of 5-FU and LOVS in different fractions of effluent organic matter (pH 7.7, 20 °C, [pharmaceutical]₀ = 10 μM, [DOC]= 3 mgC/L, and sonication power density at 45 W/L).
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(60) Cheng, J.; Vecitis, C. D.; Park, H.; Mader, B. T.; Hoffmann, M. R., Sonochemical Degradation of Perfluorooctane Sulfonate (PFOS) and Perfluorooctanoate (PFOA) in


Supporting Information
Table 5.1: Selected physicochemical properties of 5-FU, IBU, CLND, ESTO, NIFE, and LOVS at 25°C.

<table>
<thead>
<tr>
<th>compound</th>
<th>•OH rate constant (M² s⁻¹)</th>
<th>Henry’s law constant (atm m³/mol)</th>
<th>heat stability¹ (kcal/mol)</th>
<th>apparent log K_{ow} at pH 7.7²</th>
<th>molecular weight (g/mol)</th>
<th>molar volume ³ (mL/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-FU</td>
<td>$5.2 \times 10^9$</td>
<td>$1.66 \times 10^{-10}$</td>
<td>73</td>
<td>-1</td>
<td>130.08</td>
<td>79.89</td>
</tr>
<tr>
<td>IBU</td>
<td>$6.5 \times 10^9$</td>
<td>$1.51 \times 10^{-7}$</td>
<td>83</td>
<td>0.56</td>
<td>206.29</td>
<td>193.25</td>
</tr>
<tr>
<td>CLND</td>
<td>N.A.</td>
<td>$1.51 \times 10^{-11}$</td>
<td>73</td>
<td>1.24</td>
<td>230.09</td>
<td>136.82</td>
</tr>
<tr>
<td>ESTO</td>
<td>$3.89 \times 10^9$</td>
<td>$3.8 \times 10^{-10}$</td>
<td>83</td>
<td>2.24</td>
<td>288.43</td>
<td>209.44</td>
</tr>
<tr>
<td>NIFE</td>
<td>N.A.</td>
<td>$7.31 \times 10^{-14}$</td>
<td>73</td>
<td>2.97</td>
<td>346.33</td>
<td>248.99</td>
</tr>
<tr>
<td>LOVS</td>
<td>$2.9 \times 10^9$</td>
<td>$2.12 \times 10^{-10}$</td>
<td>73</td>
<td>4.26</td>
<td>404.54</td>
<td>375.58</td>
</tr>
</tbody>
</table>

¹: The heat stability of the pharmaceutical was approximated by the lowest bond energy in that compound.
²: The apparent log K_{ow} values for the pharmaceutical at pH 7.7 were determined by ACD/LogD version 6.00.
³: Molar volume was calculated at Hartree Fock (HF) level of theory with 6-31+G* basis set and PCM solvation method.
Table 5.2: Summary of main wastewater effluent characteristics

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>PO₄³⁻ (mg/L)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.7</td>
<td></td>
<td>5.8</td>
</tr>
<tr>
<td>TOC (mgC/L)</td>
<td>8.88</td>
<td>Ca (mg/L)</td>
<td>75.85</td>
</tr>
<tr>
<td>alkalinity (mg/L as CaCO₃)</td>
<td>39.4</td>
<td>K (mg/L)</td>
<td>12.65</td>
</tr>
<tr>
<td>conductivity (μS/cm)</td>
<td>845</td>
<td>Mg (mg/L)</td>
<td>19.3</td>
</tr>
<tr>
<td>Cl⁻ (mg/L)</td>
<td>70.4</td>
<td>Na (mg/L)</td>
<td>57.8</td>
</tr>
<tr>
<td>SO₄²⁻ (mg/L)</td>
<td>94.5</td>
<td>S (mg/L)</td>
<td>35.4</td>
</tr>
</tbody>
</table>
Table 5.3: Summary of main characteristics for different fractions of EfOM

<table>
<thead>
<tr>
<th></th>
<th>HPO</th>
<th>TPI</th>
<th>HPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>weight-averaged MW (g/mol)</td>
<td>474</td>
<td>146</td>
<td>128</td>
</tr>
<tr>
<td>SUVA$_{280}$ (L mg$^{-1}$ m$^{-1}$)</td>
<td>1.09</td>
<td>2.17</td>
<td>0.74</td>
</tr>
<tr>
<td>% total DOC</td>
<td>47.9</td>
<td>5.4</td>
<td>46.6</td>
</tr>
</tbody>
</table>
Figure 5.6: The molar weight of 5-FU, IBU, CLND, ESTO, NIFE, and LOVS was plotted against their apparent log $K_{ow}$ at pH 7.7.
Figure 5.7: Degradation rates of the pharmaceuticals under CW and PW ultrasound in DI water were plotted against log Henry’s law constant (a), apparent log $K_{ow}$ (b), molecular weight (c), and molar volume (d).
Figure 5.8: The molar volume of 5-FU, IBU, CLND, ESTO, NIFE, and LOVS was plotted against their molecular weight. (Molar volume was calculated at Hartree Fock (HF) level of theory with 6-31+G* basis set and PCM solvation method)
6.1 Conclusions

Ultrasound, as a water treatment technology, has been studied in this dissertation to remove PPCPs under different conditions. The major conclusions we drew are the following.

First, as discussed in Chapter 2, matrix organics play roles in sonochemical degradation of CIPRO and IBU, an example for hydrophilic and hydrophobic pharmaceuticals, respectively. In the absence of matrix organics, the degradation rates of CIPRO and IBU depend on their initial concentrations and ultrasonic frequencies: a short half-life is observed as the initial concentration decreases, and 620 kHz is more effective as compared to 20 kHz. In the presence of matrix organics, the degradation of CIPRO and IBU was affected by matrix organics to a different extent. A more hydrophobic target compound with higher diffusivity is impacted little by the presence of matrix organics. The diffusivity and concentration of matrix organics determine treatability by ultrasound. A smaller size and higher concentration of matrix organics in water have a larger impact on the treatability of target contaminants by ultrasound as compared to a larger size and lower concentration of matrix organics.

Second, PW ultrasound was used to systematically study whether and how •OH scavengers affect cavitation bubbles in Chapter 3. Based on the reduction in PE of the
probe compound, CBZ, all the tested scavengers (e.g. FA, CA, TA/TPA, KI, MS, BS, and AA/acetate) except AA/acetate affect cavitation bubbles and are not recommended to use as bulk •OH scavengers in cavitational systems. The range of utility of AA/acetate as a bulk •OH scavenger was tested under different concentrations (0.5 mM to 0.1 M) and pH values (3.5 to 8.9).

Third, in Chapter 4, five pharmaceuticals (CBZ, IBU, ATP, SFT, and CIPRO), and two personal care products (PG and DP) have been degraded under CW and PW ultrasound, respectively in aqueous solutions. The independence of degradation rates of the PPCPs under both CW and PW ultrasound on their physicochemical properties indicates that there is no single property that controls the degradation kinetics. For the enhancement due to pulsing, there exists a relationship between PE and the molar volume, indicating that a small size PPCP exhibits a positive PE, while a large size PPCP yields a negative PE. This correlation implies that diffusion governs transport of the PPCPs to the bubble surface during the silent cycle. To explore this phenomenon, we applied the knowledge gained in Chapter 3. A bulk solution •OH scavenger, acetic acid, was added in the sonicated system to differentiate the contribution of bulk •OH oxidation to the overall degradation. The fraction of degradation occurring in bulk solution is positively correlated with the molar volume of the compound. Small size molecules may quickly diffuse to the cavitation bubbles, resulting in a higher portion of the PPCP in and around cavitation bubbles. Our results suggest that PW ultrasound is an efficient method to enhance degradation for the small size PPCPs, while CW ultrasound is more effective to degrade large size PPCPs in aqueous solution.
In Chapter 5, we investigated the sonolysis of six pharmaceuticals, namely 5-FU, IBU, CLND, ESTO, NIFE, and LOVS, in DI water and wastewater effluent. Unlike in Chapter 4, our results showed that in DI water pharmaceuticals with the highest $D_{iw}$ (i.e., 5-FU) and $K_{ow}$ (i.e., LOVS) exhibited the greatest enhancement in degradation rates in PW mode as compared to CW mode. However, in municipal wastewater effluent, the PE for 5-FU and LOVS disappeared. By evaluating the effect of inorganic and organic matrices, we concluded that the organic matrix was the cause of the reduction in PE in the wastewater effluent matrix. By isolating the EfOM, we confirmed that the TPI fraction caused the most significant drop in PE during the sonolysis of pharmaceuticals, because it had combined characteristics of both high diffusivity and aromaticity compared to HPO and HPI fractions of EfOM, further corroborating that small sized matrix organics inhibit the pulsing effect on degradation kinetics. This conclusion was consistent with the conclusion in Chapter 2. Our results provide insight into the application of ultrasound as a water treatment technology. Overall, CW ultrasound is preferred over PW to enhance removal efficiency of target pharmaceuticals by ultrasound in the presence of EfOM. If EfOM is removed before sonication of the pharmaceuticals, PW ultrasound exhibits a faster degradation of pharmaceuticals with either high diffusivity or great hydrophobicity.

6.2 Future work

Our study showed the ultrasound is able to degrade PPCPs under different conditions and the degradation kinetics depend on the ultrasonic mode and
physicochemical properties of PPCPs. However, there are several questions need to address to better understand the system.

(1) Extend the study of EfOM in determining PPCPs degradation kinetics under PW ultrasound. We observed that the PE values for 5-FU and LOVS disappeared in wastewater matrix as compared to that in DI water and attributed the disappearance of PE to the presence of EfOM. The TPI fraction of EfOM diffuses to cavitation bubble surfaces and interacts with pharmaceuticals during the silent cycle. Although the size distribution and aromaticity for different fraction have been measured, the aromaticity of EfOM is approximated to hydrophobicity but not necessarily equal to hydrophobicity. Measuring the hydrophobicity of different fractions of EfOM can help us to be more accurate to understand the intermolecular interaction between pharmaceuticals and each fraction of EfOM. To confirm the role of each fraction of EfOM played, it is beneficial to sonicate a pharmaceutical that does not affected by pulsing in DI water (e.g. IBU) in different fractions of EfOM. It is expected that such a compound should have little alteration of PE in the presence of EfOM. Based on our theory, a compound without a positive PE in DI water should not have preference or momentum to diffuse to the bubble-water interface during the silent cycle. Therefore, the presence of different fractions of EfOM should not change its PE value.

(2) Extend the study of the role of PPCPs diffusivity in determining PE. In Chapter 5, seven PPCPs were degraded under CW and PW ultrasound, respectively. We observed that the degradation rates by PW ultrasound are compound dependent with degradation either faster for smaller compounds or slower for larger compounds than that under CW ultrasound. The diffusivity was linked to the PE: small sized PPCPs have higher PE
values than the large sized PPCPs. Although we have verified our conclusion by using a bulk •OH scavenger, acetic acid, there may be an alternative way to elucidate the role of diffusivity of the PPCP in PE. We could investigate the sonolysis of mixtures of PPCPs. This study is interesting from both a fundamental and a practical point of view. The sonolysis of mixtures of PPCPs will help us to better understand the role of diffusivity. We expect that a small sized PPCP will degrade faster than a large sized PPCP in binary mixtures based on our conclusion in Chapter 4. Additionally, when it comes to application of ultrasound in wastewater, mixtures of PPCPs are expected. Thus, a better understand of how the presence of other PPCPs impacts degradation kinetics is practically necessary.

(3) Investigate the frequency effect on PPCPs removal under PW ultrasound. Our study have showed that both small size and hydrophobic PPCPs are able to more readily diffuse to bubble interface and are impacted more by pulsing ultrasound in aqueous solutions. The enhanced degradation rate is attributed to the accumulation of small size or hydrophobic PPCPs during the silent cycle. Therefore, increasing the accumulation of target compounds on bubble interface will result in a faster degradation rate under PW mode. We could test our theory at higher frequencies (up to a megahertz). Since the surface to volume ratio of bubble is larger and bubble population is denser at higher frequency as compared to low frequency. The increased bubble surface could increase the accumulation of PPCPs during the silent cycle, which ultimately resulting in fast degradation kinetics under PW ultrasound.

(4) Investigate the effect of solid particles on sonolysis of PPCPs. We examined the effects of inorganic and organic matrices on PPCPs degradation. However, it is
interesting to examine the degradation kinetics in presence of total suspended solids. Particles may serve as additional nuclei, thus increasing the numbers of cavitation events and accelerating the degradation of PPCPs. The presence of solid particles may exhibit different influences on degradation kinetics. On the other hand, the particles scatter the ultrasonic wave in water, weakening the energy dissipating into water, and perturbing the bubble distribution, eventually decreasing the removal efficiency of PPCPs. Understanding the effect of solid particles will help us better design the application of ultrasound in PPCPs removal in water treatment plants.
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Appendix: Thermodynamic and kinetic study of ibuprofen with hydroxyl radical: A density functional theory approach

A.1 Abstract

Ibuprofen, a common non-prescription non-steroidal anti-inflammatory drug (NSAID) and a frequently-detected pharmaceutical in natural waters, was studied using density functional theory (DFT) at the B3LYP/6-31+G**//B3LYP/6-31G* level of theory in its reaction with hydroxyl radicals. The reaction pathways that were studied included •OH addition to the aromatic ring, abstraction of a hydrogen atom, and nucleophilic attack on the carbonyl group. The energy barriers for most additions are moderate, while abstraction and nucleophilic attack reaction barriers are low or non-existent. The hydrogen-atom abstraction and nucleophilic attack pathways are more favorable than •OH addition, which is in agreement with previous experimental observations. The enthalpy change for H-atom abstraction reactions range from -35.31 to -17.32 kcal/mol, with a median of -32.04 kcal/mol; the enthalpy change for nucleophilic attack on the carbonyl group is -35.41; and the enthalpy change for •OH addition ranges from -18.17 to -11.71 kcal/mol, with a median of -13.07 kcal/mol. The calculated rate constant, $7.4 \times 10^9$ M$^{-1}$ s$^{-1}$, is in agreement with experimentally determined values. Our results suggest that advanced oxidation processes which generate reactive hydroxyl radicals, as tertiary
treatment technology in water and wastewater treatment plants, has a great potential to remove ibuprofen in water.

A.2 Introduction

Thousands of tons of pharmaceuticals are consumed or discarded by the public every year [1-3]. These compounds find their way into the water system as pollutants from the pharmaceutical industry, excretory products of medically treated humans, and incomplete removal in wastewater treatment plants [4]. The U.S. Geological Survey (USGS) provided the first overview of the occurrence of pharmaceuticals in water resources across the United States during 1999-2000 [5]. They found these anthropogenic compounds were prevalent at 139 sampling sites, 80% of the streams sampled. In their study, the frequency of detection of ibuprofen, a non-prescription non-steroidal anti-inflammatory (NSAID), was 9.5% among all of the 84 samples, and the median detectable concentration was 0.2 µg/L. More recent studies reported environmental concentrations of ibuprofen in the range of 10 ng/L to 169 µg/L in an analysis of effluent from waste treatment plants in Spain [6].

Although the concentrations are very low, they may represent a potential hazard for human health. In addition, the metabolites can be more harmful than the parent organic compounds [7-9]. Toxicological studies have shown that exposure of fish and other aquatic organisms to the pharmaceuticals can cause adverse reproductive effects such as reduced viability of eggs, sexual disruption, and changes in sperm density [10-11]. However, a full understanding of the comprehensive hazards of these pharmaceuticals at
environmental concentrations, which may cause modification of genetic expression and protein function, is limited.

Therefore, based on precautionary principles, pharmaceuticals in water sources, especially in drinking water resources, should be sufficiently treated to minimize their potential risk to the ecosystem and human health.

Efforts have been made to improve the pharmaceutical removal efficiency in water treatment plants. Studies have shown the conventional adsorptive treatment technologies, such as solids removal, activated carbon, and conventional activated sludge, are not always capable of eliminating pharmaceuticals in water with satisfactory efficiency [12-14]. Oulton et al. [12], investigated the removal efficiency of ibuprofen in the influent and effluent wastewater from 65 traditional treatment plants around the world and found that the efficiency was plant dependent, ranging from ca. 0 to 100%. On the other hand, advanced oxidation processes (AOPs), processes in which hydroxyl radicals (\(\bullet OH\)) are formed at ambient temperature and atmospheric pressure, have been found to be promising for degrading organic pollutants in waters. AOPs generate highly reactive \(\bullet OH\) with oxidation potentials of 2.74 V and 1.77 V in acidic and neutral/basic solution, respectively [15]. Consequently, \(\bullet OH\) could non-selectively and rapidly oxidize nearly all organic pollutants, thus exhibiting a high potential to remove pharmaceuticals.

There are considerable numbers of experimental AOPs studies which have investigated the degradation kinetics for pharmaceuticals, including ibuprofen [16-18]. Packer et al. [18] determined the degradation rate of ibuprofen in both direct photolysis and \(\bullet OH\) mediated indirect photolysis. The second order rate constant of ibuprofen reacting with \(\bullet OH\) was measured to be \(6.5 \pm 0.2 \times 10^9 \text{ M}^{-1} \text{s}^{-1}\). Xiao et al. [19] irradiated
ibuprofen in the presence of natural organic matter (NOM) using ultrasound and concluded that ibuprofen competes with NOM in water for ultrasound-induced •OH. Mendez-Arriaga et al. [20] identified several byproducts of ibuprofen in the photo-Fenton system and found that two major byproducts in their system were decarboxylated and hydroxylated metabolites of ibuprofen. Although the removal of ibuprofen in water by AOPs has been achieved, it is still unknown how ibuprofen reacts with •OH the on molecular level, what the possible degradation pathways are, and whether the detected metabolites are directly derived from the oxidation of ibuprofen or if they are secondary/tertiary byproducts.

Quantum mechanical calculations provide unique insights about chemical reactivity on the molecular level, thus it becomes very attractive to investigate the degradation of organic pollutants by AOPs technologies. Among all of the quantum mechanics methods, density functional theory (DFT) methods [21] have been reported to be a reliable and affordable approach in predicting reaction mechanisms, byproduct formation, and reaction kinetics [22-24]. For example, Minakata and Crittenden [25] modeled rate constants between •OH and eight simple pollutants (i.e., CH₃OH, CH₃CHO, CH₃OCH₃, CH₃COCH₃, CH₃COOH, CH₃F, CH₃Cl and CH₃Br). The estimated rate constants calculated by the DFT approach were within a factor of 5 of the experimental values. Morales-Roque et al. [26] studied •OH oxidation process of phenol in water with DFT method and demonstrated that the ortho position is more readily attacked by •OH compared to para and meta positions based on free energy change before and after the reaction. However, modeling pharmaceuticals, especially ibuprofen, with •OH through
the DFT method has not been explored sufficiently as indicated by the lack of data in the literature.

The first step of the oxidation reaction between ibuprofen and •OH in water was modeled using DFT. Ibuprofen was selected for study because it is a commonly detected pharmaceutical in aquatic environments [5, 27]; and experimental evidence exists which can be compared to calculated results; finally ibuprofen, containing 33 atoms, is a reasonable target compound for the DFT method. Both thermodynamic and kinetic behavior of the possible reaction pathways were modeled, providing insights into the thermodynamics of product formation, reaction energy profiles and the potential energy surface, branching ratio, and ibuprofen degradation rate constant on the molecular level.

A.3 Methodology

The structure of ibuprofen is illustrated in Figure A.1 and the physiochemical properties regarding its environmental behavior and fate are summarized in Table A.1.

Geometry optimizations and transition state searches were performed using Gaussian 09 (Revision A.01) [28]. The geometries of the reactants, transition state (TS) species, and products were optimized at the B3LYP/6-31G* level. Single-point energies were calculated for the optimized B3LYP/6-31G* geometries with the same functional and a more flexible basis set, i.e. B3LYP/6-31+G**. The solvent (water) effect on the reaction was modeled with the integral equation formalism (IEF) version of the polarizable continuum model (PCM) [29] as part of the B3LYP/6-31+G** single-point energy calculation. The \( <S^2> \) values for the various TS structures typically show minimal spin contamination, ranging from 0.75 to 0.80. The nature of all stationary points, either
minima or transition states, was determined by calculating the vibrational frequencies at the B3LYP/6-31G* level. Intrinsic reaction coordinates (IRC) calculations were performed for all TS species to confirm that they connect to the anticipated reactants and products on the potential energy surface. The thermal and entropic contributions to the free energies were also obtained from the B3LYP/6-31G* vibrational frequency calculations, using the unscaled frequencies.

The likely sites of reaction can be based on the free radical stability of the resulting carbon radical. In the case of hydrogen abstraction, the benzylic position (C11 and C24 in Figure A.1) form stable carbon radicals and would be expected to be highly reactive to •OH. Tertiary carbon radicals are also stable so H abstraction at C14 could be expected. C16, C20, and C24 are all primary carbons and do not form stable radicals so H abstraction is not as likely at these positions.

In the case of •OH addition, this is most likely to occur at the aromatic ring with its “high” electron density. Addition forms a resonance stabilized carbon radical in the ring and could be expected to be a favorable process. Since the two faces of the benzene ring are asymmetric the thermodynamics of addition to both faces needs to be determined. In Figure A.1, the “top” or upper face of the benzene ring is anti to the carboxylic acid hydroxyl group and represents an “anti” addition, while addition to the syn face (or bottom face in Figure A.1) represents “syn” additions.

Finally the carboxylic acid group is susceptible to two modes of attack. First the •OH could react with the acidic proton which would lead to a decarboxylation reaction ultimately leaving a carbon radical at C24. Second the •OH could react via a
“nucleophilic” attack on C30 resulting in the loss of carbonic acid and again leaving a carbon radical at C24. All of these processes will be modeled and compared.

The possible pathways for the reactions of ibuprofen with •OH based on these three mechanisms are illustrated in Figure A.2. These reactions represent the first step of the oxidative degradation of ibuprofen. Subsequent steps could involve the addition of •OH to the carbon radical or the loss of a second H atom and formation of a carbon-carbon double bond. Multiple steps would lead to the oxidative products seen by Mendez-Arriaga et al., [20] Zheng et al., [30] and Madhavan et al. [31].

The enthalpies (\( \Delta H_R^\circ \)) and free energies (\( \Delta G_R^\circ \)) of the reactions corrected by thermal effects at 298 K were calculated using eqns. A.1 and A.2.

\[
\Delta H_R^\circ (298K) = \sum_{\text{products}} (E_0 + H_{\text{corrected}})_{\text{products}} - \sum_{\text{reactants}} (E_0 + H_{\text{corrected}})_{\text{reactants}} \tag{A.1}
\]

\[
\Delta G_R^\circ (298K) = \sum_{\text{products}} (E_0 + G_{\text{corrected}})_{\text{products}} - \sum_{\text{reactants}} (E_0 + G_{\text{corrected}})_{\text{reactants}} \tag{A.2}
\]

where \( E_0 \) is the total electronic energy at \( T = 0 \) K, \( G_{\text{corrected}} \) and \( H_{\text{corrected}} \) are the thermal correction to Gibbs free energy and enthalpy, respectively.

For the transition state for each reaction pathway, the relative activation energy, \( \Delta G^\dagger \), was calculated as indicated in eqn. A.3

\[
\Delta G^\dagger = (E_0 + G_{\text{corrected}})_{\text{TS}} - \sum_{\text{reactants}} (E_0 + G_{\text{corrected}})_{\text{reactants}} \tag{A.3}
\]
The energy of activation is the minimum amount of energy needed for a reaction to proceed.

Conventional transition state theory (TST) was employed to predict the rate of reaction ($M^{-1} s^{-1}$) between ibuprofen and •OH at 298 K in water through eqn. A.4

$$k(T) = \Gamma(T) \frac{k_B T}{h} \exp\left(-\Delta G^\ddagger_0/RT\right)$$

(A.4)

where h is Planck’s constant, $k_B$ is Boltzmann’s constant, and $\Delta G^\ddagger_0$ is the kinetic energy barrier. $\Gamma(T)$, temperature-dependent factor, corresponds to quantum mechanical tunneling and is approximated by the Wigner method, eqn. A.5 [32].

$$\Gamma(T) = 1 + \left(\frac{1}{24}\right)[1.44 \frac{v_i}{T}]^2$$

(A.5)

where $v_i$ is the imaginary frequency, whose vibrational motion is the direction of the reaction.

A.4 Result and discussion

A.4.1 Thermodynamics

The free energy and enthalpy of the reactions were calculated at the B3LYP/6-31+G**//B3LYP/6-31G* level of theory using the IEFPCM water model. The enthalpies and free energies of the reactions for the three different mechanisms, •OH addition, H abstraction, and nucleophilic attack, are tabulated in Table A.2. All of the reactions are
thermodynamically favorable processes \( (\Delta G^\circ_R < 0) \). In addition, all the reactions are exothermic \( (\Delta H^\circ_R < 0) \). The activation energy \( \Delta G^\ddagger \), imaginary vibrational frequencies, rate constants and branching ratios are tabulated in Table A.3. Figure A.3 plots the relative TS and product energies for all reactions.

A.4.1.1 •OH Addition

For •OH addition, the enthalpy change ranges from -18.17 to -11.71 kcal/mol, with a median of -13.07 kcal/mol while the free energy change ranges from -4.99 to -1.76 kcal/mol. The difference can be attributed to a large negative change in entropy as the reaction proceeds from two reactants to a single product.

The activation barrier ranges from 7.58 to 11.56 kcal/mol (average: 9.67 kcal/mol) with the exception of C4 “syn” which has an activation barrier of only 2.08 kcal/mol. This very low activation barrier results from an intermolecular hydrogen bond which forms with the acid hydroxyl group as the •OH approaches the C4 carbon atom, see Figure A.4. The hydrogen bond forms before the TS is reached and lowers the barrier significantly, approximately 7.6 kcal/mol compared to other additions to either face of the aromatic ring. The product for the addition at C4 “syn” also maintains a hydrogen bond resulting in a significantly lower free energy, -7.23 kcal/mol compared to an average of -3.17 kcal/mol for the other addition products. Of the eight possible addition reactions, addition to C4 “syn” is clearly the most favorable either under kinetic or thermodynamic conditions. However all addition reactions are less favorable than the other reaction pathways due to the loss of aromaticity in the addition products.
A.4.1.2 H Abstraction

The hydrogen abstraction reactions can produce two different benzylic carbon radicals at C11 and C24 (H12, H13; and H25 respectively), one tertiary radical C14 (H15) and abstraction of the acidic hydrogen (H32). The benzylic radicals have an enthalpy change ranging from -35.31 to -32.08 kcal/mol (average -33.12 kcal/mol) and free energy change from -36.11 to -33.50 kcal/mol (average -34.40 kcal/mol). The tertiary radical has an enthalpy of -23.68 kcal/mol and free energy change of -26.14 kcal/mol. The acidic hydrogen abstraction has an enthalpy of -17.32 kcal/mol and free energy change of -18.46 kcal/mol. In contrast to the •OH addition reactions, there is a more favorable entropy change for H abstraction since the number of molecules/radicals does not change.

The activation barrier ranges from 6.15 to 8.07 kcal/mol (average 7.04 kcal/mol) for the benzylic radicals. After extensive searches TS geometries could not be located for either the tertiary radical or for the abstraction of the acidic proton at this level of theory. The implication is that while the formation of the benzylic radicals are under kinetic control, and would be faster than the OH addition reactions, the tertiary and acidic proton abstractions are barrierless in terms of enthalpy and the reaction will proceed as soon as the •OH encounters an ibuprofen molecule in solution.

All hydrogen abstraction products are more thermodynamically stable than the addition products; along with their lower activation barriers the abstraction reactions would dominate over addition reactions.

Subsequence secondary reaction of the C24 carbon radical would lead to decarboxylation and secondary oxidation leading to a ketone group. This product, and its
A further degradation products have been detected as oxidation products of ibuprofen using sonolysis [31], gamma irradiation [30], and the photo-Fenton process (AOPs) [20].

A.4.1.3 Reaction at the Carboxylic acid

The final mode of interaction studied was the “nucleophilic” attack of •OH on the carboxylic acid carbon, C30. This mode results in the formation of carbonic acid and leaves a carbon radical at C24, see Figure A.2 c. The enthalpy for this reaction is -35.41 kcal/mol with a free energy change of -29.48 kcal/mol. Again, after an extensive search it proved impossible to locate a stable TS complex at this level of theory. Again this would imply that this reaction is barrierless in terms of enthalpy and the reaction will occur as soon as a •OH encounters an ibuprofen molecule in solution.

Subsequence secondary reaction of the carbon radical would lead to hydroxylation followed by additional rounds of oxidation leading to a ketone, similar to the H abstraction of H32.

A.4.2 Comparison to experiment

The formation of hydroxylated ibuprofen has been detected in several different AOPs systems, such as sonochemical, photochemical, and photochemical-catalytical degradation of ibuprofen. Madhavan et al. [31], sonolyzed ibuprofen at the frequency of 213 kHz with a power output of 55 W/L and identified the structure of sonochemical byproducts with electrospray ionization mass spectrometric technique. They found sonochemical degradation of ibuprofen formed mono- and di-hydroxylated intermediates, thus corroborating our results that the major and first step of ibuprofen reacting with •OH.
is to undergo H-atom abstraction and then an additional •OH reacts with the ibuprofen radical. Although they did not report the abundance of the decarboxylation byproduct 4-isobutylacetophenone, its formation has been detected, suggesting that nucleophilic attack is also thermodynamically favorable. Mendez-Arriaga et al. studied the photochemical degradation of ibuprofen with TiO₂ and also found the formation of hydroxylated intermediates [33]. They indicated that the hydroxylation process can be the first step followed by demethylation or decarboxylation. However based on our calculations, both decarboxylation and hydroxylation processes via a carbon radical intermediate are equally thermodynamically favorable.

The •OH addition to ibuprofen is thermodynamically less favorable than H abstraction or nucleophilic attack as can clearly be seen in Table A.2. The ΔG_r^‡ and ΔH_r^‡ for •OH addition is substantially less negative or exothermic than either abstraction or nucleophilic attack. One would assume from these trends that the •OH addition should occur less frequently than either abstraction or nucleophilic attack. This is confirmed by experiment where only a two •OH addition products was detected [31], both corresponding to addition ortho to the propanoic acid group, likely via a C4 hydrogen bonded mechanism, see Figure A.4.

A.4.3 Kinetics

The transition state for each reaction pathway was located at the B3LYP/6-31G* level of theory and the energy of the TS species was calculated at the B3LYP/6-31+G** level of theory. Relative ΔG‡, rate constants and imaginary frequency for the TS species involved in the reactions of ibuprofen with •OH in aqueous solution are tabulated in
Table A.3. The $\Delta G^\ddagger$ for TS species the ranges from 0.00 to 11.56 kcal/mol, with a median 9.33 kcal/mol. Energy profiles for the potential energy surface of the $^\cdot$OH addition, H abstraction and nucleophilic attack reactions are plotted in Figure A.3. Figure A.3 shows that the energy barrier height for H abstraction and nucleophilic attack pathways are lower than that of $^\cdot$OH addition, indicating the rate constants for these two modes is generally faster than $^\cdot$OH addition. Calculated rate constants for H abstractions where the TS could be located range from $8.57 \times 10^6$ M$^{-1}$s$^{-1}$ to $1.95 \times 10^8$ M$^{-1}$s$^{-1}$ (average $9.14 \times 10^7$ M$^{-1}$s$^{-1}$) compared to $9.80 \times 10^4$ M$^{-1}$s$^{-1}$ to $1.75 \times 10^7$ M$^{-1}$s$^{-1}$ (average $3.00 \times 10^6$ M$^{-1}$s$^{-1}$) for the addition reactions. The C4 syn addition has an anomalously high TST rate constant of $1.87 \times 10^{11}$ M$^{-1}$s$^{-1}$. This is likely due to limitations both in TST theory which fails for reactions with low barrier highs [39] and limitations in the calculation. Explicit solvation of the acid group was not included which would have to be desolvated for the hydrogen bond to form. In this case collision or diffusion theory would give a better approximation, although likely an over estimation of the rate constant.

After an exhaustive search the TS species for H abstraction occurring at H15 and H32 and nucleophilic attack at C30 could not be located at B3LYP/6-31G* level of theory, implying that the energy barrier for $^\cdot$OH reacting with ibuprofen at these positions is zero and hence the reaction is controlled by the diffusion of reactants in aqueous solution.

Since the reaction is diffusion-controlled, TST is not applicable. Thus, the simplified version of the Roman Smoluchowski equation was used to predict the rate constant [34], calculated in eqn. A.6
\[ k_D = 4N_A \pi (r_{\text{OH}} + r_{\text{IBU}})(D_{\text{OH}} + D_{\text{IBU}}) \]  

(A.6)

where \( N_A \) is the Avogadro constant; \( r_{\text{OH}} \) and \( r_{\text{IBU}} \) are radii for \( \cdot \text{OH} \) and ibuprofen, respectively. \( D_{\text{OH}} \) and \( D_{\text{IBU}} \) are the diffusion coefficients for \( \cdot \text{OH} \) and ibuprofen, respectively. The second order rate constant for the reaction is calculated to be \( 7.4 \times 10^9 \) M\(^{-1}\) s\(^{-1}\) which is comparable to the experimental value \( 6.5 \pm 0.2 \times 10^9 \) M\(^{-1}\) s\(^{-1}\) [18].

The branching ratios, referring to the contribution of each reaction pathway to the overall degradation, for the products through different pathways are also tabulated in Table A.3. H abstraction at H15 and H32, syn addition at C4 and nucleophilic attack on C30 are equally dominant compared to other positions, corroborating that decarboxylated and hydroxylated products were experimentally detected in the reaction between ibuprofen and \( \cdot \text{OH} \) [20, 30-31]. The syn addition ortho to the carboxylic acid group is observed experimentally, but as noted the rate constant is likely an over estimation as explicit solvation was ignored in the calculation due to the complexity it added.

A.5 Conclusion

In this study, the first step of the oxidation reaction between ibuprofen and \( \cdot \text{OH} \) in water was calculated. We proposed three possible pathways for the reactions of ibuprofen with \( \cdot \text{OH} \), \( \cdot \text{OH} \) addition, H abstraction, and nucleophilic attack on carbonyl group. The reactions are generally controlled by thermodynamics, more specifically enthalpy. The hydroxylation at the benzylic and tertiary carbon atoms and decarboxylation processes are the dominant degradation pathway. Based on diffusion theory, the calculated second order rate constant of ibuprofen with \( \cdot \text{OH} \) is in agreement with the experimental value.
Our results theoretically support that AOPs, as tertiary treatment technology in water and wastewater treatment plants, has a great potential to remove ibuprofen in waters.
Table A.1: Physiochemical properties of ibuprofen

<table>
<thead>
<tr>
<th>use class</th>
<th>anti-inflammatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>solubility (mg L(^{-1}))</td>
<td>21 (^a)</td>
</tr>
<tr>
<td>log Henry’s law constant at 25 °C (atm-m(^3) mol(^{-1}))</td>
<td>-6.82 (^b)</td>
</tr>
<tr>
<td>true log (K_{ow})</td>
<td>3.97 (^c)</td>
</tr>
<tr>
<td>vapor pressure (mm Hg)</td>
<td>0.0756 (^d)</td>
</tr>
<tr>
<td>(pK_a)</td>
<td>4.90 (^e)</td>
</tr>
<tr>
<td>second-order •OH rate constant (M(^{-1}) s(^{-1}))</td>
<td>6.5 ± 0.2×10(^9).(^f)</td>
</tr>
</tbody>
</table>

\(^{a}\): [35]; \(^{b}\): estimated value [36]; \(^{c}\): [37]; \(^{d}\): [36]; \(^{e}\): [38]; and \(^{f}\): [18].
Table A.2: $\Delta G^\circ_R$ and $\Delta H^\circ_R$ (kcal/mol) for the products involved in the reactions of ibuprofen with •OH in aqueous solution

<table>
<thead>
<tr>
<th>reaction mechanism</th>
<th>Position/atom number</th>
<th>$\Delta G^\circ_R$ (kcal/mol)</th>
<th>$\Delta H^\circ_R$ (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>•OH addition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>C5 anti</td>
<td>-3.76</td>
<td>-13.81</td>
</tr>
<tr>
<td></td>
<td>C5 syn</td>
<td>-4.99</td>
<td>-14.80</td>
</tr>
<tr>
<td></td>
<td>C4 anti</td>
<td>-2.48</td>
<td>-12.33</td>
</tr>
<tr>
<td></td>
<td>C4 syn</td>
<td>-7.23</td>
<td>-18.17</td>
</tr>
<tr>
<td></td>
<td>C2 anti</td>
<td>-1.76</td>
<td>-11.83</td>
</tr>
<tr>
<td></td>
<td>C2 syn</td>
<td>-4.12</td>
<td>-14.70</td>
</tr>
<tr>
<td></td>
<td>C1 anti</td>
<td>-2.10</td>
<td>-11.71</td>
</tr>
<tr>
<td></td>
<td>C1 syn</td>
<td>-2.99</td>
<td>-12.12</td>
</tr>
<tr>
<td>H abstraction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>H12 (C11)</td>
<td>-33.50</td>
<td>-32.08</td>
</tr>
<tr>
<td></td>
<td>H13 (C11)</td>
<td>-33.58</td>
<td>-32.04</td>
</tr>
<tr>
<td></td>
<td>H15 (C14)</td>
<td>-26.14</td>
<td>-23.68</td>
</tr>
<tr>
<td></td>
<td>H25 (C24)</td>
<td>-36.11</td>
<td>-35.31</td>
</tr>
<tr>
<td></td>
<td>H32 (O31)</td>
<td>-18.46</td>
<td>-17.32</td>
</tr>
<tr>
<td>nucleophilic attack</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>C30</td>
<td>-29.48</td>
<td>-35.41</td>
</tr>
</tbody>
</table>
Table A.3: $\Delta G^\ddagger$ (kcal/mol) and imaginary frequency for the transition state species involved in the reactions of ibuprofen with $\cdot$OH in aqueous solution.

<table>
<thead>
<tr>
<th>reaction mechanism</th>
<th>Position/atom number</th>
<th>$\Delta G^\ddagger$ kcal/mol</th>
<th>imaginary frequency cm$^{-1}$</th>
<th>Rate constant k (M$^{-1}$ s$^{-1}$)</th>
<th>branching ratio %</th>
</tr>
</thead>
<tbody>
<tr>
<td>•OH addition</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C5 anti</td>
<td>9.38</td>
<td>287.56</td>
<td>$8.94 \times 10^5$</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>C5 syn</td>
<td>9.33</td>
<td>376.01</td>
<td>$1.02 \times 10^6$</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>C4 anti</td>
<td>10.71</td>
<td>348.18</td>
<td>$9.80 \times 10^4$</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>C4 syn</td>
<td>2.08</td>
<td>82.06</td>
<td>$7.40 \times 10^9$</td>
<td>24.75</td>
<td></td>
</tr>
<tr>
<td>C2 anti</td>
<td>11.56</td>
<td>353.58</td>
<td>$2.34 \times 10^4$</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>C2 syn</td>
<td>7.58</td>
<td>121.83</td>
<td>$1.75 \times 10^7$</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>C1 anti</td>
<td>9.77</td>
<td>297.17</td>
<td>$4.65 \times 10^5$</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>C1 syn</td>
<td>9.36</td>
<td>383.30</td>
<td>$9.78 \times 10^4$</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>H12 (C11)</td>
<td>6.15</td>
<td>99.67</td>
<td>$1.95 \times 10^8$</td>
<td>0.65</td>
<td></td>
</tr>
<tr>
<td>H13 (C11)</td>
<td>8.07</td>
<td>372.03</td>
<td>$8.57 \times 10^6$</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>H abstraction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H15 (C14)</td>
<td>0.00$^a$</td>
<td>N.A.</td>
<td>$7.40 \times 10^6$</td>
<td>24.75</td>
<td></td>
</tr>
<tr>
<td>H25 (C24)</td>
<td>6.90</td>
<td>552.78</td>
<td>$7.05 \times 10^7$</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>H32 (O31)</td>
<td>0.00$^a$</td>
<td>N.A.</td>
<td>$7.40 \times 10^9$</td>
<td>24.75</td>
<td></td>
</tr>
<tr>
<td>nucleophilic attack</td>
<td>C30</td>
<td>0.00$^a$</td>
<td>N.A.</td>
<td>$7.40 \times 10^9$</td>
<td></td>
</tr>
</tbody>
</table>

a: TS does not exist at B3LYP/6-31G* level of theory; N.A: not available.
b: see section 3.3 of the text.
c: these values calculated by diffusion theory.
Figure A.1: Optimized geometry of ibuprofen at B3LYP/6-31+G** level of theory with IEFPCM water model. The “syn” face is on the bottom of this diagram and the “anti” face the top.
Figure A.2: Possible pathways for the reactions of ibuprofen with •OH based on (a) H abstraction, (b) •OH addition, and (c) nucleophilic attack.
Figure A.3: Profile of the potential energy surface (a. •OH addition pathway; b. H abstraction and nucleophilic attack pathways) for the reaction between ibuprofen and •OH at the B3LYP/6-31+G** level of theory.
Figure A.4: Product of “syn” addition to C4 with hydrogen bonding.
References:


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