Hydroxyl Radical Production via Acoustic Cavitation in Ultrasonic Humidifier Systems

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ACADEMIC ABSTRACT

Ultrasonic humidifiers use sound vibrations at frequencies higher than can be heard by humans (> 20,000 Hz) to generate aerosolized water also have potential for inducing sonochemical reactions for chemicals present in water. This research focuses on examining oxidants formed within ultrasonic humidifiers, as well as the oxidants effects of contaminants in water used in the systems. Hydroxyl radicals were found using DMPO as a spin trap. Caffeine and 17β-estradiol, as pharmaceutical contaminants of drinking water, were both emitted from the humidifier when present in the water reservoir and would enter breathing air. Emitted 17β-estradiol was found at 60% of the initial concentration filled in the ultrasonic humidifier after 480 minutes. Caffeine exhibited less degradation than 17β-estradiol. Degradation of both pharmaceuticals was attributed to ultrasonic processes, most likely oxidation with hydroxyl radicals produced. Bromide as a contaminant of the fill water was found to remain constant over time.

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GENERAL AUDIENCE ABSTRACT

Ultrasonic humidifiers carry health benefits from humidified air, but also have potential for chemical reactions within the systems that can impact human health. This research focuses on examining oxidants formed in ultrasonic humidifiers, as well as the degradation of contaminants in water used in the ultrasonic humidifiers. Hydroxyl radicals were found to be generated within the humidifier system. Caffeine and 17β-estradiol, a common estrogen, are possible contaminants in drinking water, which may be used to fill a humidifier. Both were introduced and emitted from the ultrasonic humidifier. Emitted 17β-estradiol was found at 60% of the initial concentration filled in the ultrasonic humidifier at the start of 8 hours. Degradation of both pharmaceuticals was attributed to ultrasonic processes, most likely oxidation with hydroxyl radicals produced.

DEDICATION

I dedicate this thesis and the energy expended into this project to the concept of scientific progress. Let all of our curiosities, endeavors, failures, and successes in the name of science be not for selfish profit, but for that of the good of mankind and all sentient beings.

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Abbreviation	**Meaning**
USH	Ultrasonic Humidifier
LR	Lower Reservoir
UR	Upper Reservoir
C	Condensate
AOP	Advanced oxidation process

1 A Brief History of Ultrasonic Cavitation

Today, humidifier systems commonly utilize ultrasound in order to produce mist which is emitted into the surrounding area. The process by which mist is formed from ultrasound must be examined and defined. The term “mist” is defined here as water particles small and light enough to be carried on air. By definition, a mist is type of aerosol. For the purposes of this research, the two terms can be used synonymously, however the term “aerosol” is more commonly utilized. The process by which an aerosol is produced is commonly termed “aerosolization,” however, both, “nebulization” and “atomization” have been used synonymously in areas of research associated with aerosols of any type. Aerosolization using ultrasound does not have a unique term and is not entirely understood within the scientific community. A few principle ideas and observations have helped to guide to the best understanding that is acknowledged thus far.

Aerosol formation via ultrasound was first observed by Wood and Loomis in 1927 (Harvey, 1930). A decade later, Karl Söllner developed the cavitation theory (Söllner, 1936) in an attempt to explain the formation of aerosols by ultrasound. Söllner found similarities between emulsification and atomization, primarily in the existence of the formation of vapor cavities in the media by a process termed “cavitation.” The vapor cavities, commonly referred to as “voids” or “bubbles,” are created when ultrasonic forces act on the media to create stress. One of two pathways result, depending on the conditions of the media. If the media is free of impurities (e.g. particulates, organic molecules), the process will undergo homogenous nucleation. If inhomogeneities exist, heterogeneous nucleation takes place by advancing the growth of a previously existing gas pocket. The cavity will undergo diffusion of gas into and out of the bubble until the rate of gas going in exceeds the amount leaving, resulting in the bursting of the bubble. Prior to the collapse, cavitation bubbles typically contain pressures greater than 1000 atmospheres and temperatures greater than 5000 Kelvin (Ashokkumar, 2011). The collapse exerts a shockwave into the media. Söllner was able to visually observe the bubbles when aerosol formed at the surface of his media during ultrasonic irradiation. Another observation of cavitation was a distinct “hissing” noise during aerosol emission. Söllner concluded that cavitation did not occur when the media was under high external gas pressure or had a lack of any external pressure. Söllner unfortunately did not report the frequency used to propagate cavitation, however most research in cavitation accepts a frequency range of about 15 kilohertz to 2 megahertz as acceptable frequency conditions (Ashokkumar, 2011). The lower limit of 15 kilohertz falls into the range of human hearing, which is typically around 20 kilohertz.

Another idea which attempts to describe the phenomena of ultrasonic aerosolization is Lang's "capillary wave hypothesis" (Lang, 1962). According to Lang, capillary waves are generated from the ultrasonic transducer and travel along the surface boundary of the body of water subjected to the irradiation. The capillary waves can be thought of simply as ripples in water, which are controlled by surface tension effects. It is thought that aerosol droplets are formed when the crests of the capillary waves collapse at the air-water interface. Lang's primary conclusions are derived from principles stated by J. W. Rayleigh in his *The Theory of Sound*. The first principle is Kelvin's equation, which states that the vapor pressure at a convex surface is greater than that of a flat surface (Rayleigh, 1894).

$$ln\frac{p}{p_0} = \frac{2\gamma V_m}{rRT}$$

Equation 1: Kelvin's Equation: p = measured vapor pressure, p_0 =saturated vapor pressure, γ =surface tension, V_m = molar volume of liquid, R = gas constant, r = radius of droplet, T = temperature

Kelvin's equation provides a "will" for the aerosol, assuming that the surface of the capillary waves in the media are in fact convex. The second principle guiding Lang's conclusion is "Rayleigh's Instability," (Rayleigh, 1894-1895) which states that liquids tend to minimize surface area by utilizing the force of surface tension. Rayleigh's Instability suggests why the droplet formation becomes preferable as opposed to remaining in the body of water. Lang developed an equation using empirical evidence to approximate average droplet diameter of a produced aerosol by knowing the liquid density, interfacial tension and the frequency being used. The most problematic detail of Lang's equation lies in the fact that his constant multiplier only applied when frequencies used fell between 10 to 800 kilohertz (kHz).

$$D = 0.34(8\pi T\ /\ \rho F^2)^{\frac{1}{3}}$$

Equation 2: Lang's Equation, D = particle diameter in cm, T = surface tension, p = liquid density, F = frequency used

Though distinct, Söllner and Lang's hypotheses are not contradictory. The generally accepted modern theory has come from Boguslavskii and Eknadiosyants in 1969 with their "conjunction theory," which states that capillary waves and acoustic cavitation are interrelated in aerosol formation (Kirpalani and Suzuki, 2011). In brief, it is stated that the breaking of capillary waves at the liquid surface is enhanced by momentary shockwaves from collapsing cavitation voids.

With the collapsing of cavitation voids releasing high amounts of energy, different effects occur in different media. One of the most studied reactions resulting from cavitation collapse is the formation of hydroxyl radicals (Suslick et al., 1997). Radicals, being defined as atoms or molecules with an unpaired valence electron, are generally highly reactive, thus short lived (Lobo et al., 2010). Hydroxyl radicals were first documented by Haber and Weiss in 1934 through what is now referred to as Fentonian chemistry, which involves the use of iron and hydrogen peroxide (Gligorovski et al., 2015).

$$H_2O \underset{US}{\rightarrow} H \bullet + HO \bullet$$

Equation 3: Formation of hydroxyl radical in presence of ultrasound (US)

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + HO \bullet + OH^-$$

Equation 4: Fenton reaction

As hydroxyl radicals are great oxidants, they have become a focus in the field of advanced oxidation processes (AOPs), which utilizes the radicals to degrade and remove contaminants, particularly organics (Deng and Zhao, 2015). These processes typically involve the use of ozone or Fenton chemistry to generate radicals. However, ultrasound as a means for generation of radicals has been utilized (Rayaroth et al., 2017). Many processes rely on two methods, such as combining ultrasound with either ozone or Fentonian mechanisms. The primary reason for not utilizing solely ultrasonic cavitation generation seems to be economic feasibility, with some studies showing up an upwards of 174 times costlier when using ultrasound alone for the removal of certain contaminants (Mahamuni and Adewuyi, 2010). As technology advances, it is hoped that ultrasound can one day be a cost-efficient method of chemical free, water contaminant oxidation.

2 Introduction

2.1 Ultrasonic Humidifiers and Sonochemistry

Ultrasonic humidifiers are a commonly used household humidifier, often sold as "cool mist humidifiers". The systems operate by generating ultrasonic pressure waves into a body of water to form an aerosol, also called "mist" which is then distributed throughout the indoor environment. The aerosols can be inhaled and deposited in the lungs with sizes and numbers that vary with the mineral content of the water used to fill the humidifier. Waters containing lower amounts of minerals produce smaller and fewer aerosols (Sain et al., 2018). Previous studies have documented possible human health concerns associated with inhalation of contaminants in the aerosol emitted from the ultrasonic humidifier units filled with tap water (Highsmith et al., 1988; Davis et al., 2016; Sain and Dietrich, 2015). The possible inhalation risks led to EPA recommending only distilled water to fill humidifier systems, although few data are available that indicate consumers use distilled water. Little research has explored the possibility for sonochemical reactions inside of the ultrasonic humidifier systems.

The exact mechanism that produces the aerosol emitted from the ultrasonic humidifiers are unknown, but is best described by the conjunction theory of Lang's capillary wave hypothesis and Söllner's cavitation theory by Boguslavskii and Eknadiosyants (Kirpalani and Suzuki, 2011). It is well documented that this phenomenon is correlated with the process of acoustic cavitation. Acoustic cavitation is the production of small bubbles formed by pressure differentials, specifically caused by sound waves. The bubbles, or cavitation pockets, are known to reach up to 5000 Kelvin and 2000 atm of pressure (Ashokkumar, 2011). It is the disruption of cavitation pockets that catalyze sonochemical reactions within liquid media. A major reaction occurring from the disruption of cavitation pockets is the production of highly reactive hydroxyl radicals (Suslick et al., 1997).

2.2 Advanced oxidation for water treatment

Advanced oxidative processes (AOP) are methods of utilizing hydroxyl and sulfate radicals to oxidize primarily organic contaminants (Deng and Zhao, 2015). As radicals react with organic contaminants, the organic chemicals are potentially broken down to carbon dioxide and water. Some organic and inorganic chemicals can be transformed by AOPs to species that may be more toxic than the initial chemical (von Guten and Oliveras, 1998). The hydroxyl radical is typically the most employed radical, as it is highly reactive and generally non-specific in its targets (Solarchem, 1994). There are many methods by which hydroxyl radicals are produced for AOPs including: ozone, UV/H_2O_2, Fentonian chemistry, and ultrasonic irradiation (Deng and Zhao, 2015).

While ultrasonic irradiation can be combined with other hydroxyl radical-generating AOPs such as ozone and UV/peroxide, it has also shown promise as a singular method for removal of organic contaminants and disinfection (Goncharuk et al., 2008). Reviews of ultrasound as an AOP have spanned a wide variety of foci, including removal of emerging contaminants (Rayaroth et al., 2017; Salimi et al., 2017) and endocrine disrupting compounds (Torres et al., 2007) in surface waters, as well as more specialized uses such as leachate remediation (Deng, 2009). The primary inhibitor for a more widespread use of ultrasound as an AOP is its economic feasibility (Mahamuni and Adewuyi, 2010).

2.3 Oxidative transformation of inorganic and organic contaminants

Inorganic chemical reactions oxidized by AOPs include bromide conversion to the more toxic bromate (von Guten and Oliveras, 1998). Naturally occurring bromide concentrations in surface waters are usually low unless the local geology or industry causes a high concentration. von Gunten (2003) reported 0.05-0.1 mg/L as a typical range and Amy and Siddiqui (1998) reported a median concentration of 0.035 mg/L. While bromide is not typically regulated as a contaminant in drinking water or source water, bromide can be converted during ozonation to bromate which is regulated in drinking water at µg/L concentrations (von Guten, 2003; Amy and Siddiqui, 1998). In the presence of free chlorine, bromide can be converted to hypobromous acid which reacts rapidly with natural organic matter to form brominated disinfection by-products (DBP) (Luong et al, 1980). The fate of bromide in a USH system has yet to be evaluated.

Globally, the stimulant caffeine is frequently detected in source waters and may be present in drinking water, usually at low μg/L concentrations (Koplin et al. ES&T 2002 vol 36; Machado et al. 2016) In 2016, a study of emerging contaminants in drinking and source waters in Brazil detected caffeine in 93% of all tested samples, with drinking water concentrations in the range of 0.018 μg /L to 2.0 μg/L and source water concentrations ranging from 0.040 μg/L to 19 μg/L (Machado et al, 2016). Caffeine is documented to be removed using advanced oxidation processes (Dalmázio et al, 2005). Hydroxyl radicals, are capable of degrading caffeine to 1,3,7-trimethyluric acid (Dalmázio et al, 2005; Telo and Vieira, 1997). Lab scale processes which generate hydroxyl radicals, such as Fentonian chemistry reactions, have also been well documented to degrade caffeine (Trovó et al, 2013, Telo and Vieira, 1997). With caffeine consumption increasing in the parts of the world (Verster and Koenig, 2017), it is likely that tap water containing caffeine could be present in water that fills USH.

A primary concern in drinking water is the emergence of endocrine disrupting chemicals (EDC) and other pharmaceuticals. AOPs have been evaluated to show great reduction in many of these organics (Snyder, 2008). Among the strongest EDCs are estrogenic compounds, which are responsible for the regulation and development of the human reproductive system. 17β-estradiol (E2), a common estrogenic compound, has been detected in natural waterways and wastewater systems in previous studies (Westerhoff et al, 2005). Concerns have risen regarding the presence of 17β-estradiol in tap water, leading to the compound being added to the EPA's Contaminant Candidate List 3 (EPA, 2011). Studies have displayed the degradation of 17β-estradiol by use of AOPs such as ozonation (Westerhoff et al, 2005). The production of hydroxyl radicals via Fentonian reactions have also shown to degrade 17β-estradiol (Sun et al, 2016). The fate of 17β-estradiol in an ultrasonic humidifier system has yet to be explored.

2.4 Objectives

The research focuses on identifying the fate, transport, and human exposure to chemicals in water when subjected to sonochemical reactions within the ultrasonic humidifier systems. The specific objectives of this research were to: 1) determine oxidant species generated in the upper and lower reservoir of a commercial ultrasonic humidifier; 2) investigate the fate and transport of bromide ions, caffeine, and 17β-estradiol present in water used to fill the ultrasonic humidifier.

3 Materials and methods

3.1 Ultrasonic humidifier unit

The ultrasonic humidifier was purchased from a local retail store and is ranked in the top five portable humidifiers and rated a "Best Buy" by Consumer Report. (Consumer Reports, 2015) The USH is separated into two parts: a 3.0 L reservoir for the storage of water (upper reservoir) and a 0.5 L reservoir where ultrasound is emitted to produce the mist (lower reservoir). A ceramic transducer plate is present in the bottom of the lower reservoir. The system is designed as a continuous flow system: as water is emitted as mist, water is refilled from the upper reservoir to the lower reservoir. An adjustment knob allows the user to control the amount of mist emitted.

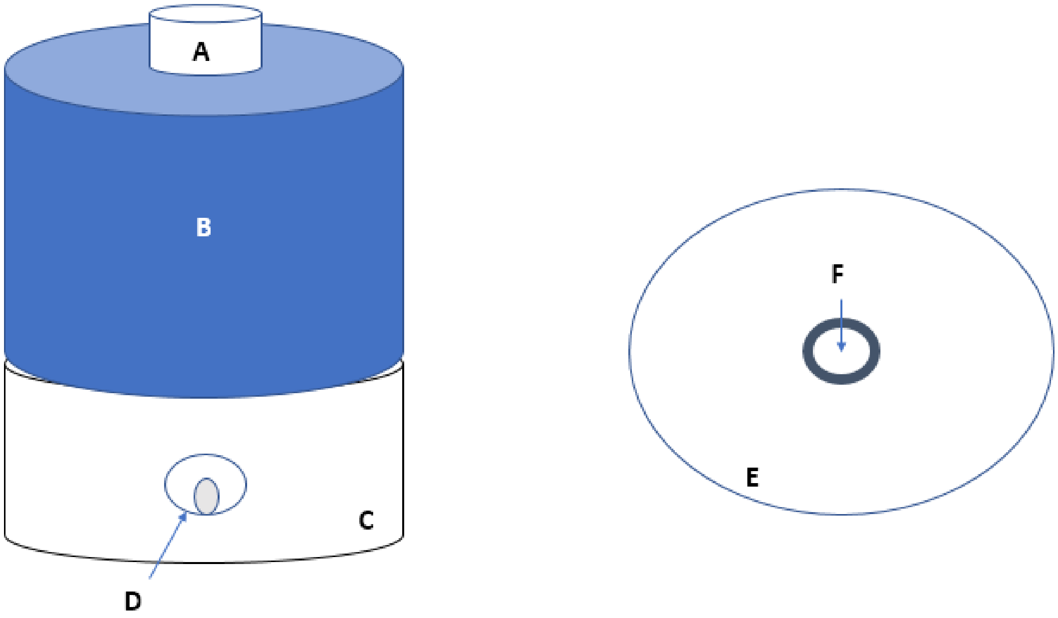

Figure 1: Ultrasonic Humidifier System: A) Upper Reservoir Cap; B) Upper reservoir; C) Lower reservoir; D) mist adjustment knob; E) Lower reservoir from top-down view with upper reservoir removed; F) Ceramic transducer plate

3.2 Reagents

Chemicals purchased from Fisher Scientific (Hampton, New Hampshire, USA) were: acetic acid, glacial (CAS 64-19-7); acetonitrile (CAS 75-05-8); NaOH (CAS 1310-73-2); NaBr (CAS 7647-15-6); NaH_2PO_4 (CAS 7558-80-7). Chemicals purchased from Sigma-Aldrich (St. Lois, Missouri, USA) were: bromate (CAS 15541-45-4, TraceCERT®) caffeine (CAS 58-08-2, ReagentPlus™ grade); 17β-estradiol (CAS 50-28-2); lissamine green (CAS 3087-16-9). Indigo trisulfonate potassium salt (CAS 67627-18-3) was obtained from Riedel-de Haen (Hanover, Germany) and potassium iodide (CAS 7681-11-0, ACS grade) from AMRESCO (Solon, Ohio, USA). DMPO (CAS 3317-61-1) was obtained from Cayman Chemical (Ann Arbor, Michigan, USA).

Reagent water was generated by a Barnstead NANOpure ultrapure water system (model D4744). Minimum resistivity of produced water was 16.0 MΩ-cm.

Compound	**CAS**	**Aqueous Solubility 20˚C (mg/L)**	**Melting Point (˚C)**	**Log K_{OW}**	**K_{OC}**	**pKa at 25˚C**	**pKa at 40˚C**
Caffeine[a]	58-08-2	21600	235	-0.07	741	14.0	10.4
17β-estradiol [b]	50-28-2	3.6	178.5	4.01	30,000	10.7	NA[c]

Table 1: Physiochemical properties of caffeine and 17β-estradiol; (a) PubChem, Open Chemistry Database, https://pubchem.ncbi.nlm.nih.gov/compound/caffeine (b) Pubchem, Open Chemistry Database, https://pubchem.ncbi.nlm.nih.gov/compound/17β-estradiol , accessed 4/10/18;(c) NA=not available

3.3 Analytical methods and instrumentation

A Polytec© PSV-500 scanning vibrometer was used to determine the frequency emitted from the ultrasonic humidifier transducer. A Milton Roy Company Spectronic 21 spectrophotometer was used to measure visible absorbance.

An Adani CMS8400 electron paramagnetic resonance (EPR) spectrometer was used for detection of radicals. Center field was set to 337 mT. Modulation amplitude was set to 150 uT. Power attenuation was set to 7 dB.

Bromide and bromate were analyzed using a Thermo-Scientific Dionex ICS-1600 ion chromatography system with a Dionex IonPac™ AS9-HC 4x250mm analytical column and 4x50mm guard column. The eluent consisted of 9mM sodium carbonate at a flow of 1.0 mL/min. The sample loop volume was 50 µL. Limits of detection for bromide and bromate were 0.05 mg/L.

Caffeine and 17β-estradiol were analyzed using a Shimadzu Prominence HPLC system with diode array detection. A 3.0 µm pore, Thermo-Scientific Hypersil GOLD, 150x3 mm analytical column was used for both compounds. A 10%·90% acetonitrile:water eluent was used for caffeine, while a 50:50 acetonitrile:water eluent was used for 17β-estradiol; both used a 1.0 mL/min flow rate. The sample loop volume was 50 µL. The lowest concentration for caffeine and 17β-estradiol were both 0.1 mg/L; this concentration was consistently and readily integrated by the HPLC system.

3.4 USH Frequency determination and operation

The lower reservoir was rinsed with reagent water, dried, and placed under the vibrometer laser beam adjusted to target the center of the transducer plate. With the mist adjustment knob set to maximum, the spectra generated from the scan of 3 different USH units were determined. The mist adjustment knob was lowered and a spectrum was generated.

To understand the basic interactions between the reservoirs, an informal mixing experiment was performed by adding lissamine green dye to reagent water in the LR while the UR received pure reagent water. Visual assessment of mixing was performed at 5 minute intervals.

3.5 Experimental design

3.5.1 USH Experiments

The following experimental designs were used throughout the course of the research. Solutions and specifications are included in individual descriptions.

3.5.1.1 Focused ultrasonic degradation

An experimental condition was designed to assess the sonochemical ability of the isolated ultrasonic frequency (Miyaji et al., 2017). The lower reservoir was filled with 500 mL of reagent water. A 60 mL VOA vial was used as a reactor and filled with 10 to 40 mL of the appropriate solution, capped, and held in the lower reservoir, in the water, directly over the ultrasonic transducer, using a support stand with a clamp (see Figure 2). 2 mL samples were collected with a pipette at 5 second to 5 minute intervals for up to 60 minutes and stored in glass vials or cuvettes for HPLC analysis or spectrophotometric analysis, respectively. Controls were solutions of individual organic and inorganic contaminants in reactor vials without sonication. Triplicate experiments were performed.

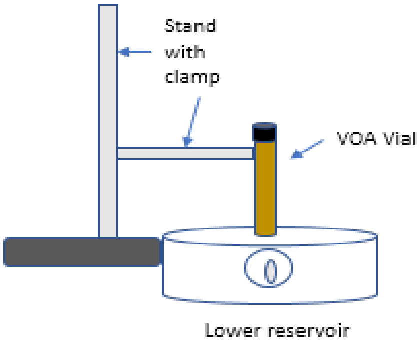

Figure 2: Focused sonication experimental design

3.5.1.2 Ultrasonic Degradation of Contaminants in Lower Reservoir

Ultrasonication of chemicals was performed in triplicates by adding the individual chemical in reagent water to the UHS lower reservoir. The upper reservoir was not filled but plugged with a glass stopper and sealed with Parafilm® to prevent the escape of aerosols and water. The USH was operated at maximum amplitude. Temperature of the water in the reservoir was measured every 15 minutes, at the same time as a 2 mL water sample was taken with a pipette. For control experiments, the same solution was placed in a 5 separate glass containers and warmed to 60°C in a water bath. One glass container was sampled and discarded every 30 minutes. Samples were stored in glass vials or cuvettes for HPLC analysis or spectrophotometric analysis, respectively.

3.5.1.3 Full Scale UHS Operation

A full-scale operation procedure was adopted from Sain and Dietrich (2015). UHS was filled with 1.3 to 2 L of a solution and operated for 120 to 480 minutes. 2 mL samples were collected hourly with a pipette from the upper and lower reservoirs, and first point of condensation in the condensation tube (see Figure 3). Samples were stored in glass vials or cuvettes for HPLC analysis or spectrophotometric analysis, respectively. Triplicate experiments were performed.

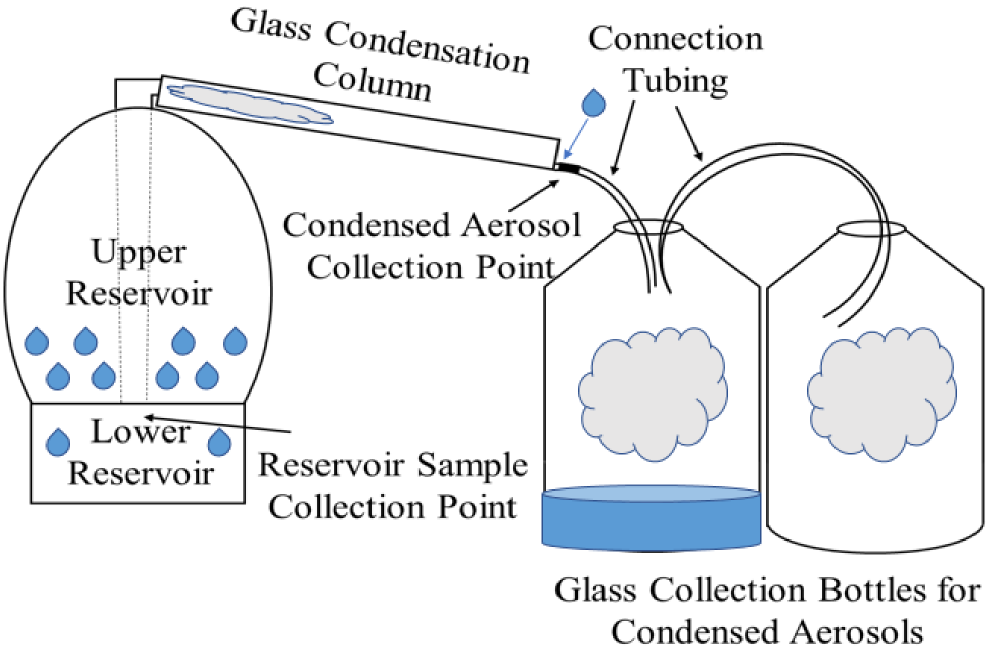

Figure 3: Full scale experimental design (Yao et al., 2018)

3.6 Oxidants in the USH system

3.6.1 Total Oxidants

Total oxidants were measured by conversion of colorless potassium iodide to yellow iodate (Deutsch, 1968). For focused sonication (see 3.5.1.1), degradation in the LR (see 3.5.1.2), and full scale operation (see 3.5.1.3), a solution consisting of 1.25 L reagent water, 50 mL acetic acid, 4 g NaOH and 15 g KI was used. The final pH was 3-4. Oxidized iodide in the form of iodate was measured spectrophotometrically at 360 nm.

3.6.2 Ozone

Triplicate measurements of ozone were made according to Standard Method 4500-O_3 B (APHA, 2005). 1 mL H_3PO_4 was added to a 513 mg/L indigo trisulfonate potassium stock solution in reagent water. 20 mL of the stock solution, 10 g NaH_2PO_4 and 7 mL H_3PO_4 were diluted to 1.0 L with reagent water. The lower reservoir was filled with 50 mL of the reagent and diluted to 500 mL. The upper reservoir was removed. The USH was operated at maximum. For a control experiment, an equal ratio of reagent was diluted in a flask maintained at constant temperature.

2.0 mL samples were collected in cuvettes at 30-minute intervals and analyzed spectrophotometrically at 600 nm.

3.6.3 Hydroxyl Radicals

Hydroxyl radicals were measured by using DMPO as a spin trap. 10 mL of a 100 mM DMPO solution in reagent water was used for a focused sonication experiment (see 3.5.1.1). The LR was operated at maximum for 1 minute. Adjustments to the physical location of the VOA vial were made until a visible mist was produced in the VOA vial. 0.5 mL samples were collected at 5 second intervals and stored in closed ended capillary tubes and placed in nuclear magnetic resonance (NMR) tubes for analysis with electron paramagnetic resonance (EPR).

3.7 Emission of Oxidants

An experiment was designed to assess the possible emission of oxidants from the USH. A solution of 10 g KI, 2.7 g NaOH, and 35 mL acetic acid was diluted to 250 mL with reagent water and placed in a glass collection bottle (Deutsch, 1968). The experimental apparatus modeled the full scale operation (see 3.5.1.3). The USH was filled with 2 L of reagent water and operated so that mist could enter the glass collection bottle. For a control, the KI solution was placed in a glass container in contact with the surrounding environment. 2 mL samples were taken from the USH collection bottle and control, stored in cuvettes and analyzed spectrophotometrically at 360 nm.

3.8 Ultrasonic Degradation of Contaminants

Ultrasonication of each contaminant was performed in triplicate under three separate experimental conditions: focused sonication (see 3.5.1.1), degradation in the LR (see 3.5.1.2), and full-scale operation (see 3.5.1.3). Specific conditions are listed for each contaminant.

3.8.1.1 Bromide

A 1.0 mg/L Br^- in reagent water was used for focused sonication and degradation in the LR. Full scale operation with bromide was omitted. 5 mL samples were collected at 20-minute intervals for degradation in the LR and 2 second intervals for focused sonication. Samples were stored in vials for IC analysis.

3.8.1.2 Caffeine

A 5 mg/L solution of caffeine in reagent water was used for all three experimental conditions.

3.8.1.3 17β-estradiol

A 1 mg/L solution of 17β-estradiol was prepared by dissolving 100 mg in 25 mL acetonitrile and then diluted in reagent water. The final solution contained 1 mg/L 17β-estradiol and 197 mg/L acetonitrile.

3.8.1.4 Competition between organics

To observe competition between caffeine and 17β-estradiol, a solution was used comprised of 5 mg/L caffeine and 1 mg/L 17β-estradiol in acetonitrile. An equal solution was used for focused sonication and full-scale operation experiments.

3.9 Statistical analysis

All statistics were performed using R statistical program. For tests comparing one rate of change to another, a linear model with an indicator variable was used. For comparing more than two rates of change, a pairwise t-test with Bonferroni correction was performed. For tests to determine if rates of change were significant from 0, a linear model was fit and p-value was assessed. All tests were performed with an alpha (α) of 0.05. Linear fits to all data were performed on raw data, save for data from focused sonication conditions, in which a linear fit was performed on natural log transformed data.

4 Results & Discussion

4.1 Ultrasonic humidifier frequency and operation

With the mist adjustment knob set to maximum, the vibrometer spectra resulted in prominent peaks around the 1.6 MHz to 1.8 MHz range (see SI). The most prominent peak was measured at 1.78 MHz (Figure S1). Minor peaks occurred at 40 kHz, 137 kHz and 847 kHz, which are in the range of known sonochemical effects. The same data trends were found for 2 USH units of the same make and model. Lowering of the mist density dial resulted in identical frequencies at lower amplitudes.

For operation, the UR is designed to refill the LR. As mist is emitted, solution from the UR flows through an approximately 0.5 cm diameter gasket that is opened when the UR and LR are connected. The solution then receives ultrasonic irradiation and a mist is formed. The mist travels through a hollowed portion of the UR that does not contain solution.

For the mixing experiment, lissamine green dye from the LR was found to transfer to the UR in less than 5 minutes. After 30 minutes, signs of complete mixing between the LR and UR had been observed.

During plugged conditions described in section 3.5.1.2, temperature inside the LR was found to reach approximately 65˚C after 90 minutes. During full scale operation conditions described in section 3.5.1.3, temperature in the LR was found to reach approximately 40˚C after 120 minutes and remained roughly constant, suggesting steady-state conditions arising after 120 minutes. Temperature stabilization was consistent with data from Sain and Dietrich (2015). The temperature in the UR was found reach approximately 30˚C after 180 minutes of operation.

4.2 Oxidants produced by USH

4.2.1 Total oxidants in USH

When KI solutions were exposed to ultrasound or used in the full-scale operation, the colorless iodide was oxidized to iodate and the solution turned a dark yellow to brown. All experiments were performed in triplicate. Heated control solutions exposed to only atmospheric oxygen and no ultrasound, did not visibly change color. The rate of change in absorbance in the control, however, was statistically greater than 0 (p-value: 0.006), as iodide oxidizes to iodate in the presence of atmospheric oxygen. Iodide can also be oxidized to iodate by a variety of oxidants including ozone (Parry and Hern, 1973) and hydrogen peroxide (Bray and Liebhafsky, 1931), both of which are precursors to hydroxyl radicals in advanced oxidation processes.

4.2.1.1 Total oxidants: Focused sonication of potassium iodide

Absolute absorbance readings for all samples were between 1.100 and 1.500. Linear regression analysis was performed on each trial and its associated control (Figure S3). Mean change in absorbance per minute was 0.0487 ± 0.002. Apparent reaction order was zero-order. A combined linear model with an indicator variable displayed absorbance rates of change for each sonicated trial were significantly greater than the associated control, indicating oxidation of iodide due to sonication. P-values for all tests were < 0.001.

4.2.1.2 Total oxidants: Lower reservoir

Absolute absorbance readings for all samples were between 1.100 and 1.300. Linear regression analysis was performed on each trial and associated control (Figure S4). Mean change in absorbance per minute was 1.8e-03 ± 6.0e-04. Apparent reaction order was zero-order. A combined linear model with an indicator variable displayed absorbance rates of change for each sonicated trial were significantly greater than the associated control, indicating oxidation of iodide due to sonication. P-values for all tests were < 0.001.

4.2.1.3 Total oxidants: full-scale operation

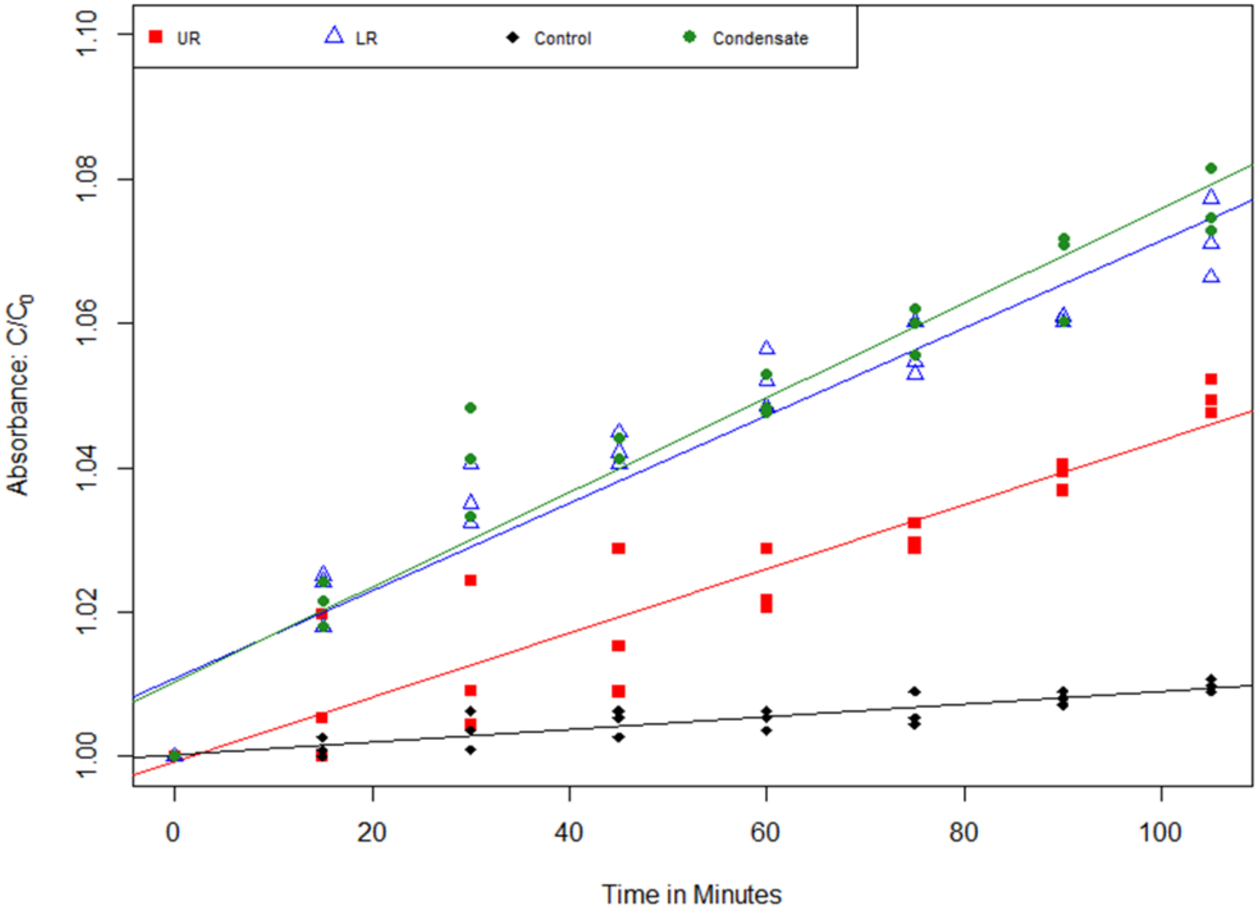

Figure 4: Determination of total oxidants during full scale operation of ultrasonic humidifier

Absolute absorbance readings for all samples were between 1.100 and 1.210 (Figure 4). A pairwise t-test with a Bonferroni correction was performed. UR, LR and condensate rates of change of absorbance were greater than control rates of change (p-values: UR: < 0.001; LR: < 0.001; condensate: < 0.001). Rates of change of absorbance between LR and condensate were not statistically different (p-value: 0.1164), suggesting that no oxidation occurred after the mist left the LR and condensed. LR rate of change of absorbance was greater than that of the UR (p-value: 0.0011). All apparent reaction orders were zero-order.

4.2.2 Hydroxyl radical trapping: DMPO

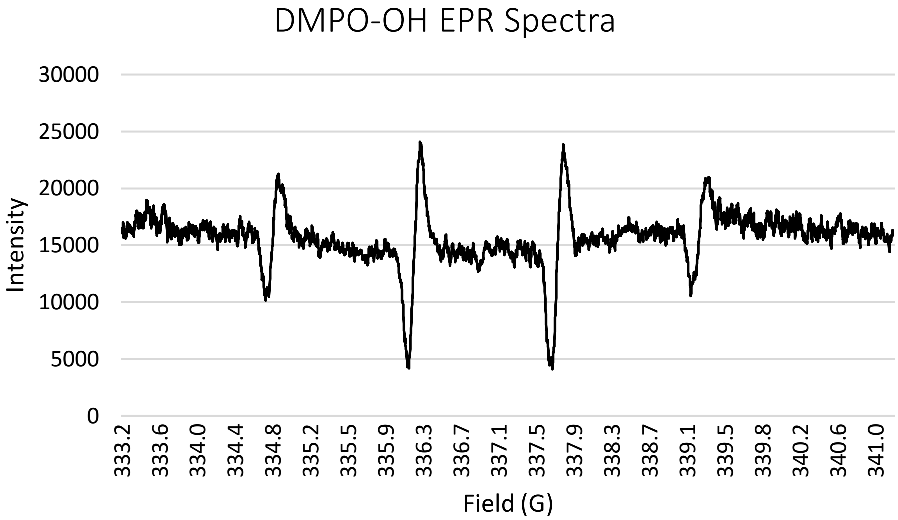

Fig. 5: Electron paramagnetic resonance spectrum of DMPO-OH radical formed during ultrasonic irradiation of DMPO

A 4-peaked spectrum was detected with EPR after 2 minutes of ultrasonic irradiation of reagent water with DMPO, as shown in Fig. 5. Intensity ratio of 1:2:2:1 was observed. The signal was attributed to the DMPO-OH radical, which possesses hyperfine splittings of 15.3 G (a_N) and 15.3 ($a_{\beta\text{-}H}$) G (Perkins, 1980). Peak was distinguishable from DMPO-H and DMPO-OOH radicals, which possess hyperfine splittings of 16.7 G (a_N) and 22.4 G ($a_{\beta\text{-}H}$) and 14.3 G (a_N) and 11.7 G ($a_{\beta\text{-}H}$), respectively. Hence, under experimental conditions, neither DMPO-H nor DMPO-OOH were formed.

The spectrum generated was nearly identical to that produced by Miyaji et al. (2017), in which ultrasound at 1.6 MHz was used to generate hydroxyl radicals in a pure water system. What differentiates between the system used in this research and the system used by Miyaji et al. (2017) is the frequency used, as well as how the ultrasound was generated. The Miyaji et al. (2017) system utilized a stainless-steel vessel with a transducer connected to an external power supply. Little detail is given regarding specifications of the system, however it is apparent that the system differed greatly than the ultrasonic humidifier system.

4.2.3 Ozone in the Lower Reservoir

Indigo trisulfonate was added to the LR and received ultrasonic irradiation to measure ozone production. A linear model with an indicator variable was created using absorbance for indigo trisulfonate between sonicated and control samples. No significant difference was observed (p-value = 0.622, n=3). This indicates that no ozone formed when the UHS system was operated.

4.2.4 Emission of oxidants

The mist emitted from the full-scale humidifier operation was condensed and total oxidants were measured. Absorbance measurements were between 1.106 and 1.109. A linear model fit to the control and mist exposed sample data showed no difference in the change in absorbance over time between the two groups (p-value: 0.554). Iodide did not oxidize to iodate at a faster rate in either group.

4.3 Contaminants

4.3.1 Bromide

No bromate was detected in any of the samples of the focused sonication or in the LR, nor was there a decrease in bromide concentrations over time. The slope of the linear regression line for bromide concentration over time was not statistically different from 0 (p-value: 0.6752, n=3).

Previous models and experiments have demonstrated the reaction of bromide to bromate requires the presence of both hydroxyl radicals and ozone together (Westerhoff et al, 1998; von Guten and Oliveras, 1998**).** The lack of bromate produced in the UHS is indicative of the lack of both hydroxyl radicals and ozone existing together, however, did not rule out the possibility of one of the two existing within the system.

4.3.2 Caffeine

A concern with organic contaminants is that they can sorb into plastic materials used to construct the humidifier. Control experiments indicate that caffeine from a 5 mg/L aqueous solution did not sorb into the hard plastic of the upper reservoir or lower reservoir over an 8 h contact time with no sonication (Figure S5). The slopes of the regression lines for the UR and LR controls were not significantly different than zero with p-values of 0.3318 and 0.3360 respectively. Controls of caffeine in glass containers warmed to 60˚C demonstrated that caffeine was stable in warm water for 480 minutes and the slope of the regression line was not different than 0 (p-value = 0.3507) (Figure S4).

4.3.2.1 Caffeine: Focused sonication

In triplicate focused sonication trials, caffeine degraded rapidly in the reactor vial. A visible mist was produced inside of the reactor vial. The mean rate of degradation was -0.0635 ± 0.0037 min^{-1} (n=3). The apparent reaction order was 1st order decay.

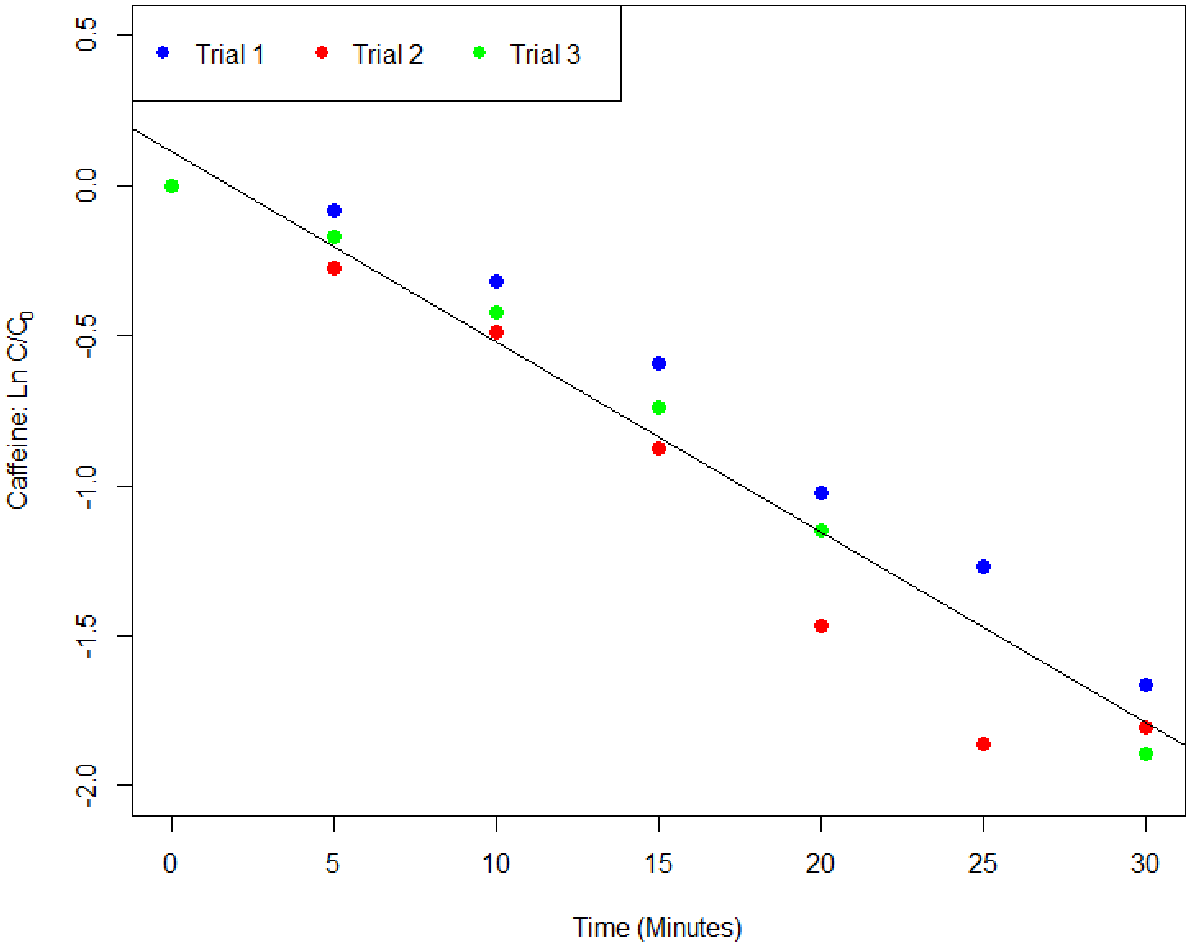

Figure 6: Natural log transformed data for focused sonication of caffeine

4.3.2.2 Caffeine: Degradation in the lower reservoir

For the degradation of caffeine in the lower reservoir, it was found that caffeine was readily degradable. Mean degradation rate for triplicate sonicated samples followed zero order kinetics and was -0.0039 ± 2.2e-04 mg/(L-min). Linear regressions were performed on each trial and control individually. A Welch 2-sample t-test was performed on the individual degradation rates between sonicated trials and controls. Sonicated trial degradation rates were significantly higher from than control degradation rates (p-value: < 0.001, n=3). Control degradation rates were not statistically different from 0 (p-value: 0.8675, n=3).

4.3.2.3 Caffeine: Full scale operation

For full-scale operation, caffeine concentrations in different compartments of the USH were determined and compared. To accommodate the time to steady state operation of the USH (Sain and Dietrich, 2015), a pairwise t-test with Bonferroni correction was performed on slopes of linear regressions for minutes 120-480 of the triplicate measurements of the UR, LR and condensate trials, as well as heated controls. No rates were significantly different from controls, which were not significantly different from 0 (All p-values > 0.2, n=3). The decrease in caffeine in the condensate observed after 360 minutes was not statistically significant.

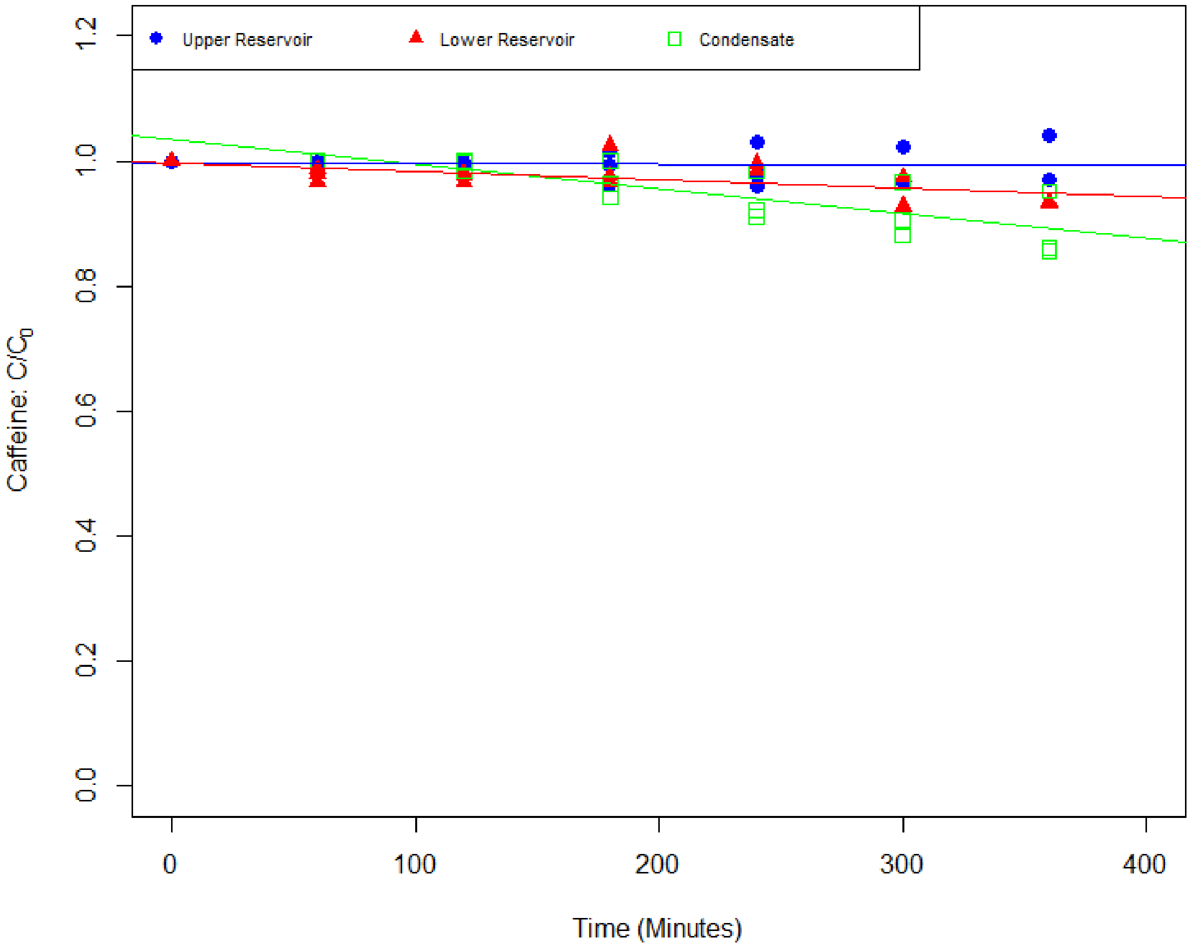

Figure 7: Change in concentrations for caffeine in full scale operation

4.3.3 17β-estradiol

17β-estradiol was demonstrated not to sorb into the hard plastic used to construct the upper and lower reservoirs of the humidifier during an 480-minute period without sonication. The slopes of the regression lines for the UR and LR were not significantly different than zero with p-values of 0.794 and 0.449 respectively (Figure S8). A control of 17β-estradiol in a glass container warmed to 60˚C also demonstrated that 17β-estradiol was stable in warm water. The slope of the regression line was not different than 0 (p-value = 0.124) (Figure S9).

The presence of acetonitrile in the 17β-estradiol solution was of concern, as acetonitrile is known to be a scavenger of hydroxyl radicals (Mitroka et al., 2010), however was deemed to be an insignificant variable throughout trials with 17β-estradiol.

4.3.3.1 17β-estradiol: Focused sonication

For triplicate trials of focused sonication, 17β-estradiol was observed to degrade 98.8%, on average, within 30 minutes. Mean degradation rate was -0.134 ± 0.03 min^{-1}. The apparent reaction order was 1st order decay (Figure 8).

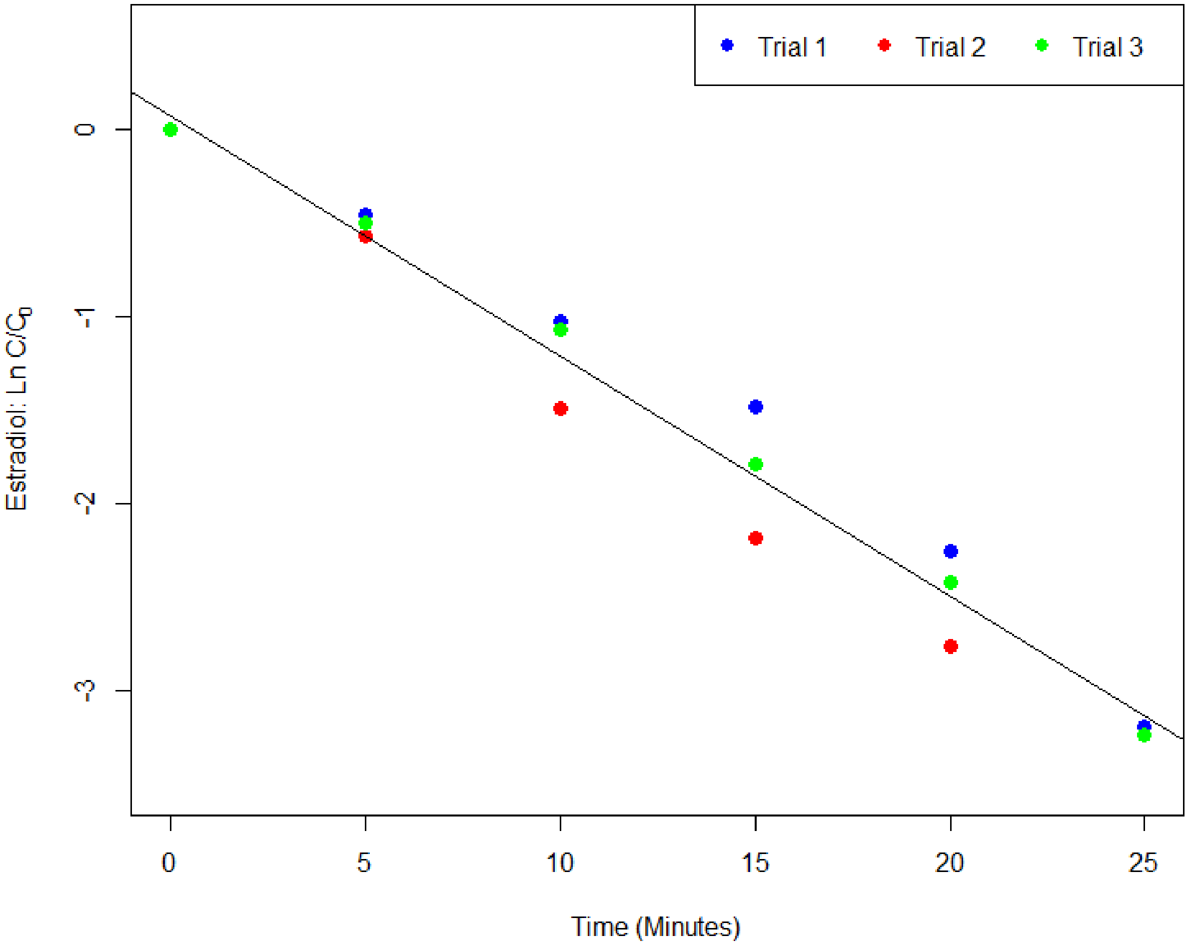

Figure 8: Natural log transformed data for focused sonication of 17β-estradiol

4.3.3.2 17β-estradiol: degradation in lower reservoir

For the degradation of 17β-estradiol in the plugged USH system, initial concentrations for each trial of 17β-estradiol was between 0.8 and 1.0 mg/L. Concentrations exposed to sonication in the USH system displayed a 14.6% decrease on average after 60 minutes (Figure 9). Using a Welch 2-sample t-test, it was found that sonicated degradation rates were significantly lower than control degradation rates (p-value: 0.01374, n=3). Mean degradation rate when sonicated was 0.0020 ± 0.00041 mg/(L-min). No degradation was observed in the control group. Control degradation rates were not statistically significant from 0 mg/L/min (p-value: 0.07283, n=3).

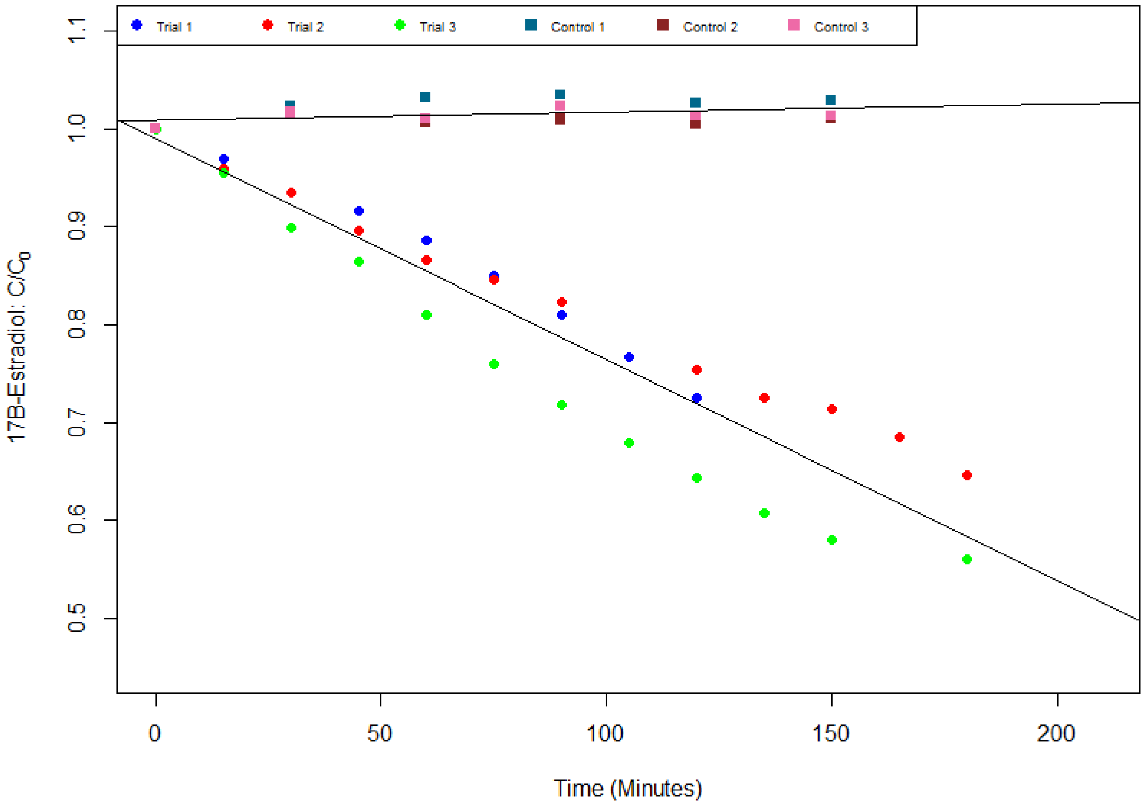

Figure 9: Change in 17β-estradiol over time during sonication in lower reservoir

4.3.4 Competition between caffeine and 17β-estradiol

Competition between organics was assessed by using a solution containing 5 mg/L caffeine and 1 mg/L 17β-estradiol in focused sonication and full-scale operation experiments.

4.3.4.1 Focused sonication

In triplicate focused sonication trials, caffeine degradation rates were dependent upon the precise placement of the VOA vial over the ultrasonic transducer. In trials where visible mist was observed, degradation rates of caffeine were greater, leading to 50% degradation after 25 minutes. Mean degradation rate was -0.024 ± 0.008 min^{-1}. Apparent reaction rates displayed 1st order decay (Figure 10).

17β-estradiol was observed to degrade 93.2%, on average, within 30 minutes. Mean degradation rate was -0.132 ± 0.009 min^{-1}. Apparent reaction order displayed 1st order decay (Figure 10). Degradation rates were greater when mist was observed forming inside of the reactor vial, similar to caffeine (Figure 10).

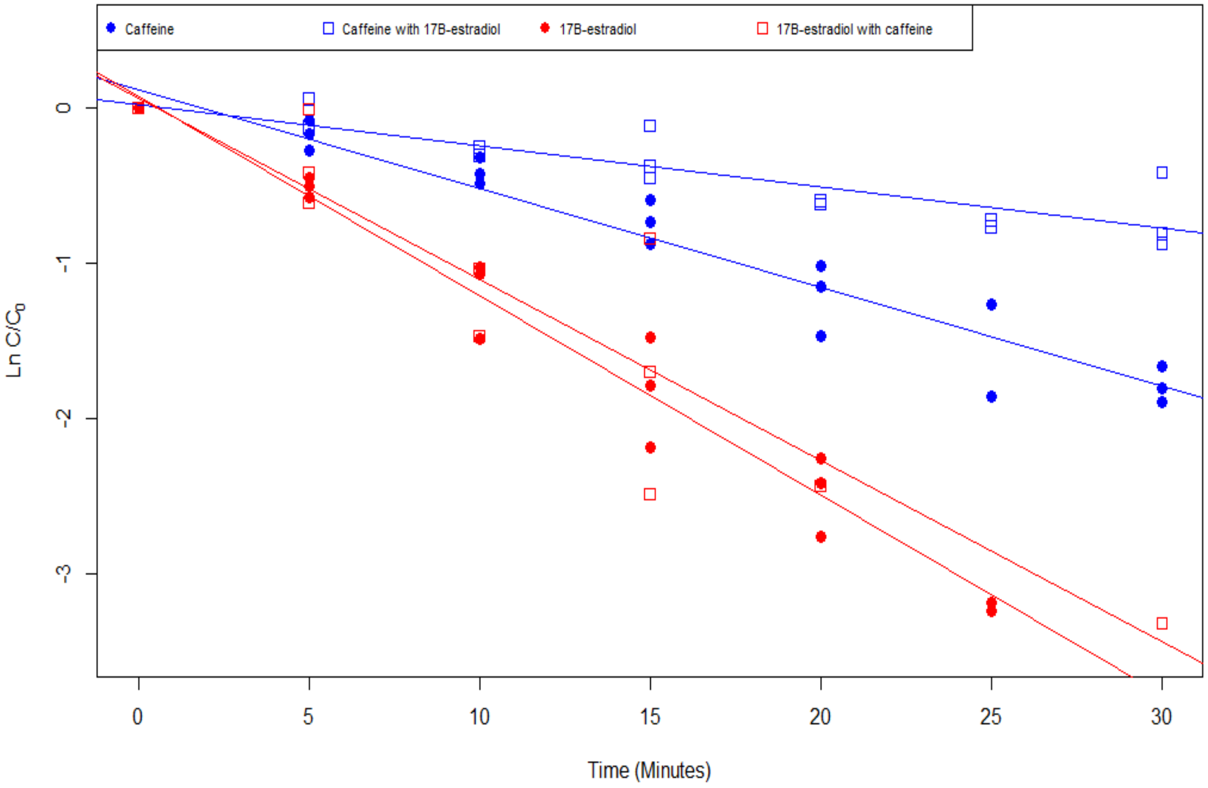

Figure 10: Natural log transformed change in concentration over time for caffeine and 17B-estradiol in same solution for focused sonication

4.3.4.2 Full scale operation

For full-scale operation, caffeine concentrations in different compartments of the USH were determined and compared. To accommodate the time to steady state operation of the USH (Sain and Dietrich, 2015), a pairwise t-test with Bonferroni correction was performed on slopes of linear regressions for minutes 120-480 of the triplicate measurements of the UR, LR and condensate trials, as well as heated controls. Condensate rates were significantly greater than UR, LR, and controls, with a mean rate of -1.93e-03 ± 3.30e-04 (p-values: UR-condensate: 0.0097, n=3; LR-condensate: 0.0074, n=3; control-condensate: 0.0013, n=3). UR and LR rates of change were not significantly different from controls, which were shown to not be significantly different from 0 (p-values: controls: 0.8675, n=3; UR-control: 0.7833, n=3; LR-control: 1.0, n=3).

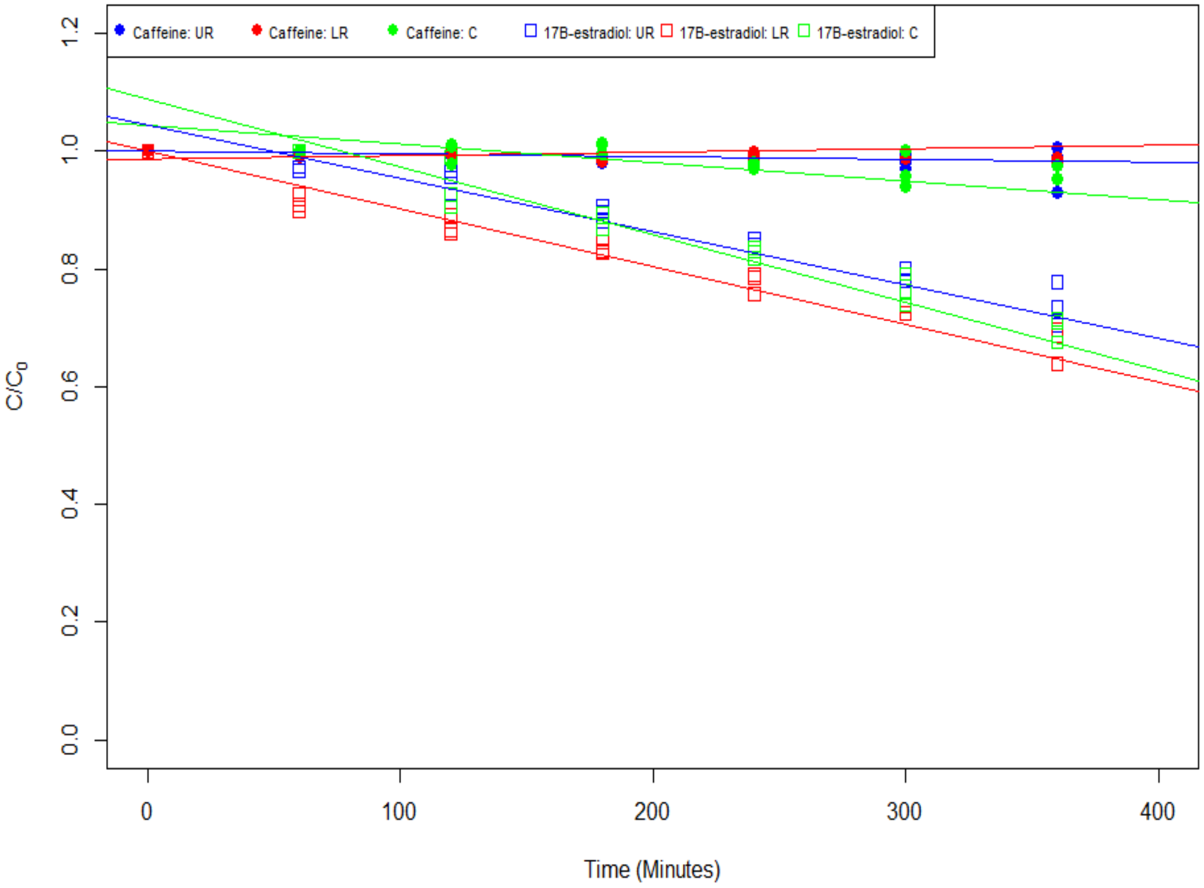

Figure 11: Figure of concentration change over time by relative initial concentrations for trials of full scale operation with caffeine and 17β-estradiol; n=3 for each condition

Zero order degradation of 17β-estradiol was observed in the UR and LR in full scale trials (Figure 11; Table S3). To accommodate the time to steady state, a pairwise t-test with a Bonferonni correction was performed on regression slopes generated from data at minutes 120-480 of the triplicate measurements of the UR, LR and condensate trials, as well as heated controls. Significant degradation took place in the UR. UR, LR and condensate rates of change were significantly greater than that of the controls (all p-values: < 0.001). A one-way ANOVA accounting for steady state showed no significant difference between UR, LR, and condensate rates of change (p-value: 0.154). Thus, no additional degradation occurred in aerosols leaving the LR or during condensation.

Chemical Reaction	Units	Mean Rates of Change due to Ultrasonification			
		Focused	**Lower Reservoir**	**Full Scale**	
				Upper Reservoir	**Lower Reservoir**
Iodate Formation	Δ Abs/min	0.0487 ±0.002	0.0018 ±6.0e-04	4.95e-04 ±4.9e-05	6.70e-04 ±3.2e-05
Bromide Degradation	Apparent Rate mg/(L-min)	0.0015 ±0.004 (NS)^{b}	2.45e-04 ±6.0e-04 (NS)^{b}	NA	NA
Caffeine Degradation	Apparent Rate mg/(L-min)	-0.064 ±0.004^{a}	-0.0039 ±2.2e-04	-4.00e-04 ±1.1e-03 (NS)^{b}	-5.33e-04 ±9.1e-04 (NS)^{b}
	Half-life min	10.8	641	6250	4688
17β-estradiol Degradation	Apparent Rate mg/(L-min)	-0.134 ±0.030^{a}	-0.0020 ±4.1e-04	NA	NA
	Half-life min	5.2	250	NA	NA
Caffeine Degradation with 17β-estradiol	Apparent Rate mg/(L-min)	-0.024 ±0.008^{a}	NA	-4.90e-04 ±4.4e-04 (NS)^{b}	-2.70e-04 ±8.9e-05 (NS)^{b}
	Half-life min	28.9	NA	5612	10185
17β-estradiol Degradation with caffeine	Apparent Rate mg/(L-min)	-0.132 ±0.009^{a}	NA	-9.84e-04 ± 3.0e-05	-1.00e-03 ± 2.7e-04
	Half-life min	5.3	NA	508	500

Table 2: Summary of reaction rates for organic and inorganic chemicals during ultrasonication under different conditions in the humidifier system; a) Apparent reaction rate is first order reaction with units of min^{-1}; b) Rate was not statistically different than 0 (p-values > 0.05); NS = not statistically significant from 0; NA = not available

5 Discussion

5.1 Operation of Ultrasonic Humidifier

Whereas mixing was found to occur from the LR to the UR, any change in the concentration of contaminants in the UR were reasoned to be the product of mixing between the two reservoirs. As degradation occurs in the LR, the concentration of the contaminant decreases, which is then mixed into UR, therefore diluting the UR solution.

The accelerated conversion of iodide to iodate in the all experimental conditions suggested the production of oxidants within the USH system. The greatest apparent reaction rates were observed in the focused sonication trials. The second greatest was in the plugged LR condition. This trend was also seen for both caffeine and 17β-estradiol, alone and together.

The capture of the hydroxyl radical confirms previous research linking mist formation to acoustic cavitation and thus hydroxyl radical production (Sollner, 1936). Variability between degradation rates of focused sonication experiments suggest that cavitation and, subsequently, hydroxyl radical production, are more effective when a mist is able to be formed. Mist formation was dependent on the precise angle and location of which the VOA vial was situated over the transducer. Mist formation in the VOA vials correlated to the fastest degradation rate of pharmaceuticals. This suggests that shape and size of the container plays a role in hydroxyl radical production.

5.2 Chemical Reactions

Bromide was not oxidized to bromate, nor degraded during sonication. This was indicative of the lack of ozone in the system, as ozone is required for the oxidation of bromide to bromate when involving hydroxyl radicals (von Guten and Oliveras, 1998). The indigo method for ozone also confirmed no ozone formed in the UHS.

Both 17β-estradiol and caffeine were most readily degraded in the focused sonication experiments. This indicates that degradation due to ultrasonication is dependent upon physical variables that affect the properties of the sound waves. The presence of mist also correlated to higher degradation rates in focused sonication for both pharmaceuticals, further supporting this idea.

Overall, reactions in the LR of the USH system when plugged were greater compared to the full-scale operation. This is due to the contaminants being unable to leave via mist, thus being further degraded in a shorter amount of time. Another observation that differentiated the plugged and full-scale systems was the act of refill.

17β-estradiol displayed a significantly higher degradation rate in the full-scale operation than caffeine when both contaminants were present together. The most prominent difference found between the two pharmaceuticals in the full-scale operation are the rates of change in the UHS reservoirs. Caffeine showed statistically no change in the UR and LR while 17β-estradiol degraded readily (see Table 2). Caffeine concentration rates of change during full scale operation with 17β-estradiol were found to exist only in the condensate, and then only after 200 minutes as a slight decrease. One possible explanation is that the interface of the surface of the water and where mist is produced is a “hot spot” for acoustic cavitation and thus hydroxyl radical production, leading to more oxidation just prior to leaving the LR.

In comparing caffeine trends with and without the presence of 17β-estradiol, apparent rates of degradation were much faster without the presence of 17β-estradiol in focused sonication trials. The rate of change in 17β-estradiol with and without caffeine remained constant in focused sonication trials. The results of comparing the two pharmaceuticals with and without the other suggest that 17β-estradiol is the more efficient scavenger of hydroxyl radicals. Apparent degradation rates of caffeine were faster without the presence of 17β-estradiol in full-scale operation in the LR. This further suggested that 17β-estradiol was the primary scavenger of hydroxyl radicals.

17β-estradiol and caffeine were good indicator pharmaceuticals, as they are not very volatile and represented two different levels of health impacts: caffeine, in low concentrations, displays low human health effects, while 17β-estradiol carries a high human health risk factor. Theses pharmaceuticals demonstrate two routes for human exposure to aqueous contaminants in water used to fill the USH. Some contaminants like caffeine will be poorly degraded in the oxidizing environment in the UHS and will be emitted from the UHS and inhaled in breathing air. Other contaminants like 17β-estradiol will be degraded over time in the UHS. Initially, exposure to contaminants like 17β-estradiol will be high, but will decrease over time. A lower exposure dose will be incurred the longer the humidifier is operated.

6 Conclusion

Performance of an ultrasonic humidifier was assessed to determine the production of oxidants within the unit and potential chemical reactions when contaminants were present in the fill water used. The research results indicate that:

- The ultrasonic humidifier system analyzed was found to have higher than atmospheric levels of total oxidants during time of operation.
- Hydroxyl radicals were observed using DMPO as a spin trap in an altered form of standard humidifier use. Results indicate the presence of hydroxyl radicals existing within the ultrasonic humidifier system.
- The oxidants produced by the UHS did not include ozone.
- Processes driven by ultrasonication were responsible for the degradation of pharmaceuticals that are known to degrade in reactions with hydroxyl radicals.
- Pharmaceuticals were degraded in the UHS at different rates. Significant differences occur in rates of degradation of caffeine and 17β-estradiol in the ultrasonic humidifier system. 17β-estradiol was readily degraded while caffeine resisted degradation.
- Bromide was not oxidized to bromate as ozone is required for this reaction and was not measured in the ultrasonic humidifier system.
- Measurable levels of reactive oxidants, as determined by oxidizing iodide, were not observed in the condensed mist from the lower reservoir.
- Organic contaminants, like caffeine and 17β-estradiol, will be emitted from the USH into breathing air if contaminants are present in water used to fill the UHS.

7 Highlights

- Household ultrasonic humidifiers investigated for contaminant transformation
- Ultrasonic humidifiers confirmed to produce hydroxyl radicals
- Caffeine and 17β-estradiol partially degraded during normal operation
- Aerosols emit contaminants present in water into breathing air

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10 Appendix A: Supplemental Information

Abbreviation	**Meaning**
USH	Ultrasonic Humidifier
LR	Lower Reservoir
UR	Upper Reservoir
AOP	Advanced oxidative process

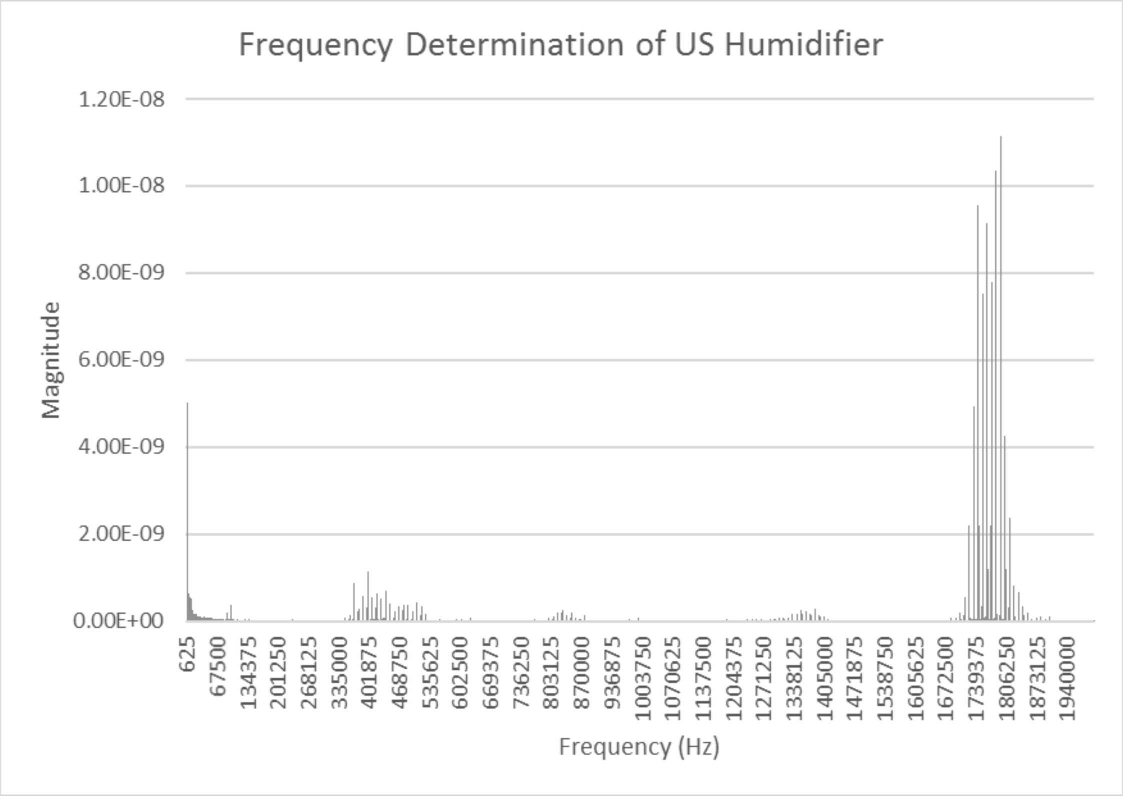

Figure S 1: Scanning vibrometer spectra of US transducer

Major peaks observed in the 1.6 to 1.7 MHz range. Small peaks prior indicate harmonic frequencies.

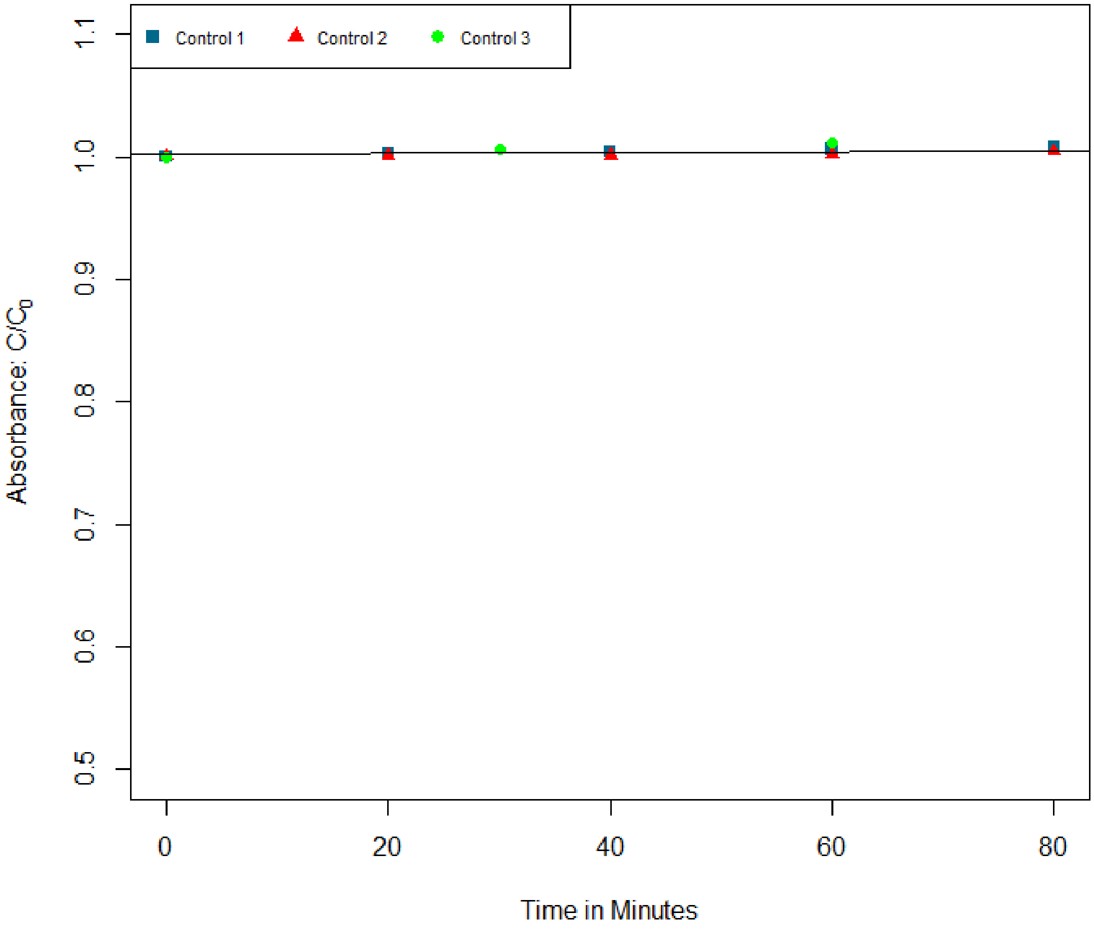

Figure S 2: Potassium iodide heated controls for determining total oxidants

Best fit line to all data is shown with an $R^2 = 0.3519$ and a p-value of 0.006. Slope was 4.4e-05 ± 1.4e-05. Slope was not equal to 0 as KI oxidizes to iodate with or without ultrasonic irradiation in acidic conditions.

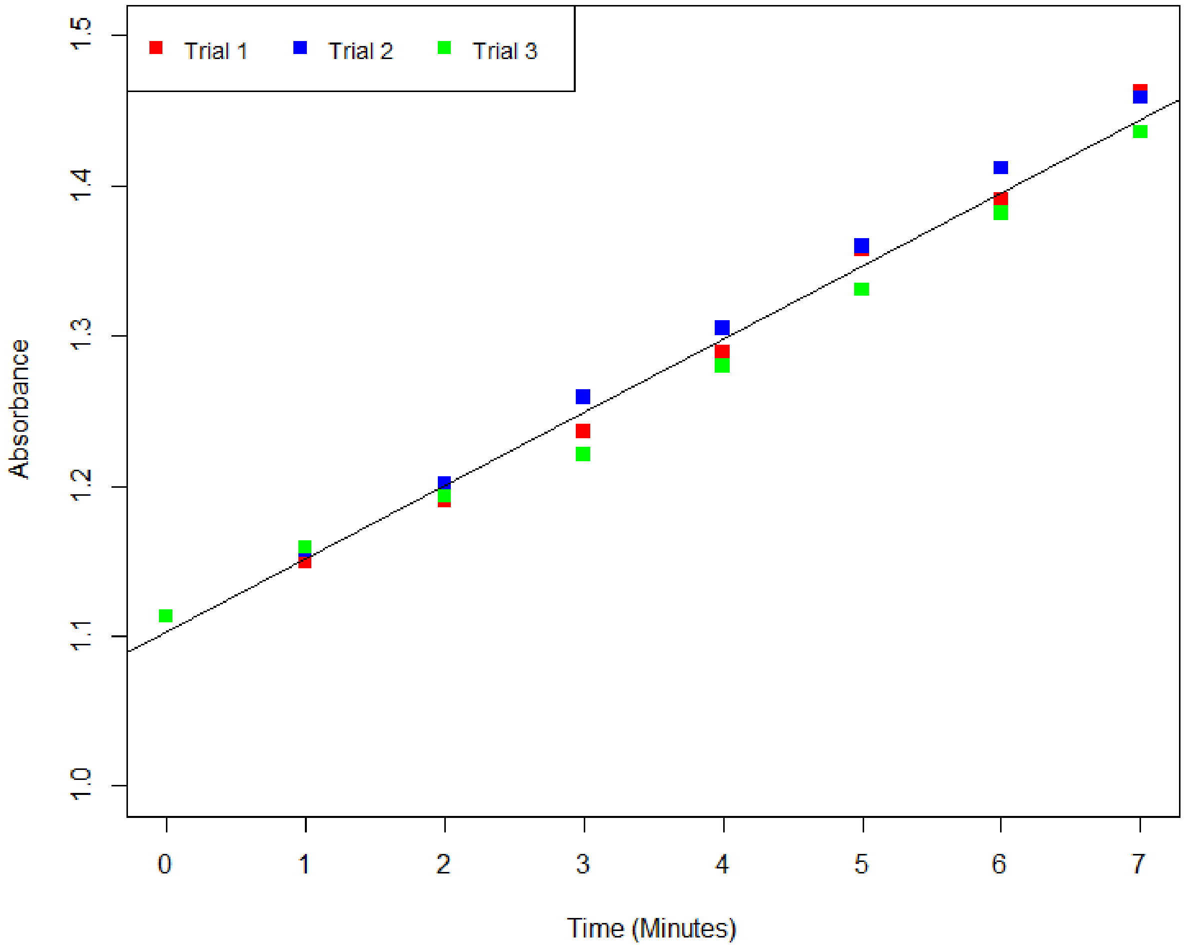

Figure S 3: Determining total oxidants by focused sonication of potassium iodide

Best fit line to all data is shown for sonicated trials with an $R^2 = 0.9871$ and a p-value < 0.001. Slope was 0.0487 ± 0.001.

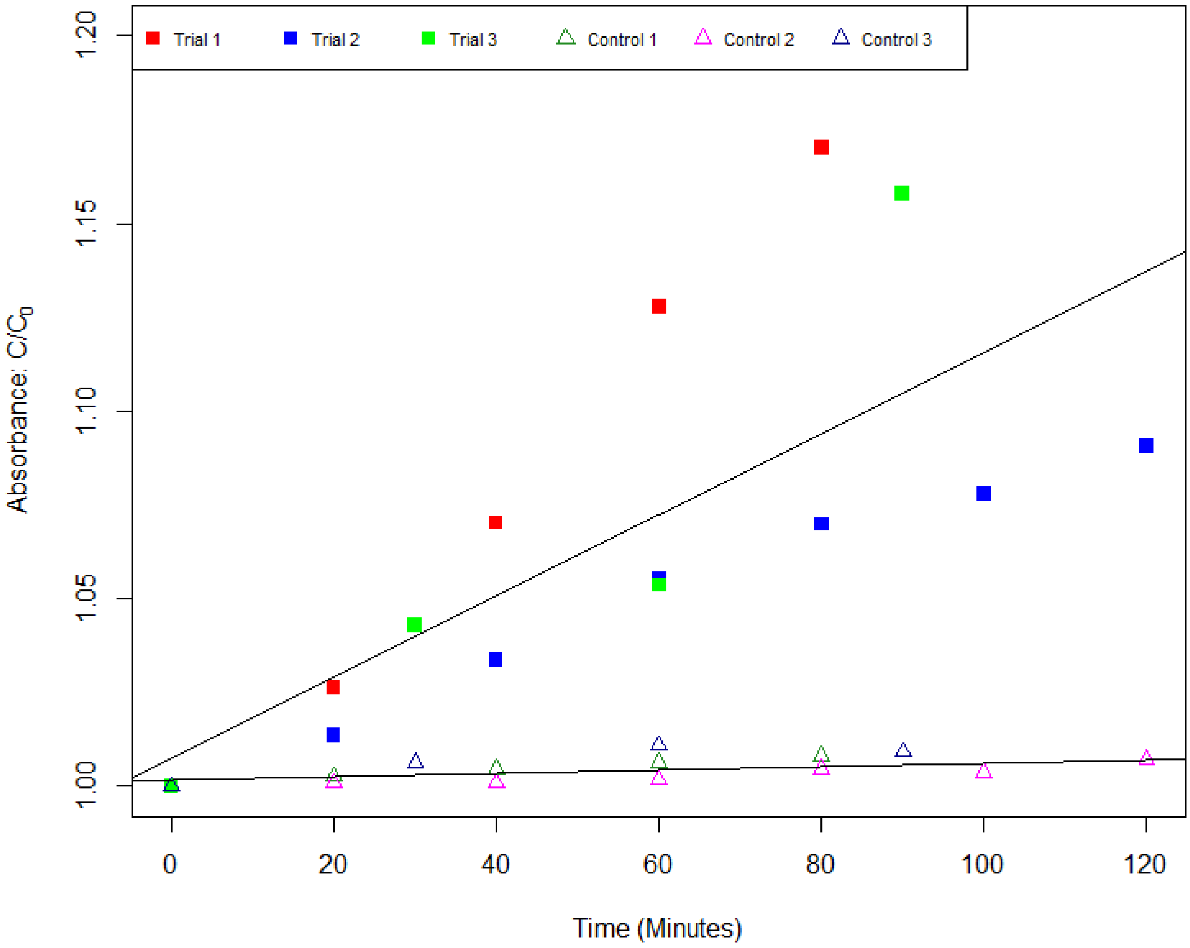

Figure S 4: Determining total oxidants by oxidation in LR of potassium iodide and associated controls

Best fit line to all data is shown for sonicated trials with an $R^2 = 0.7034$ and a p-value < 0.001. Slope was 0.0011 ± 0.0001. Best fit line to all data is shown for controls with an $R^2 = 0.8342$ and a p-value < 0.001. Slope was 9.8e-05 ± 9.2e-06. Slope of control was not equal to 0 as KI oxidizes to iodate with or without ultrasound in acidic conditions.

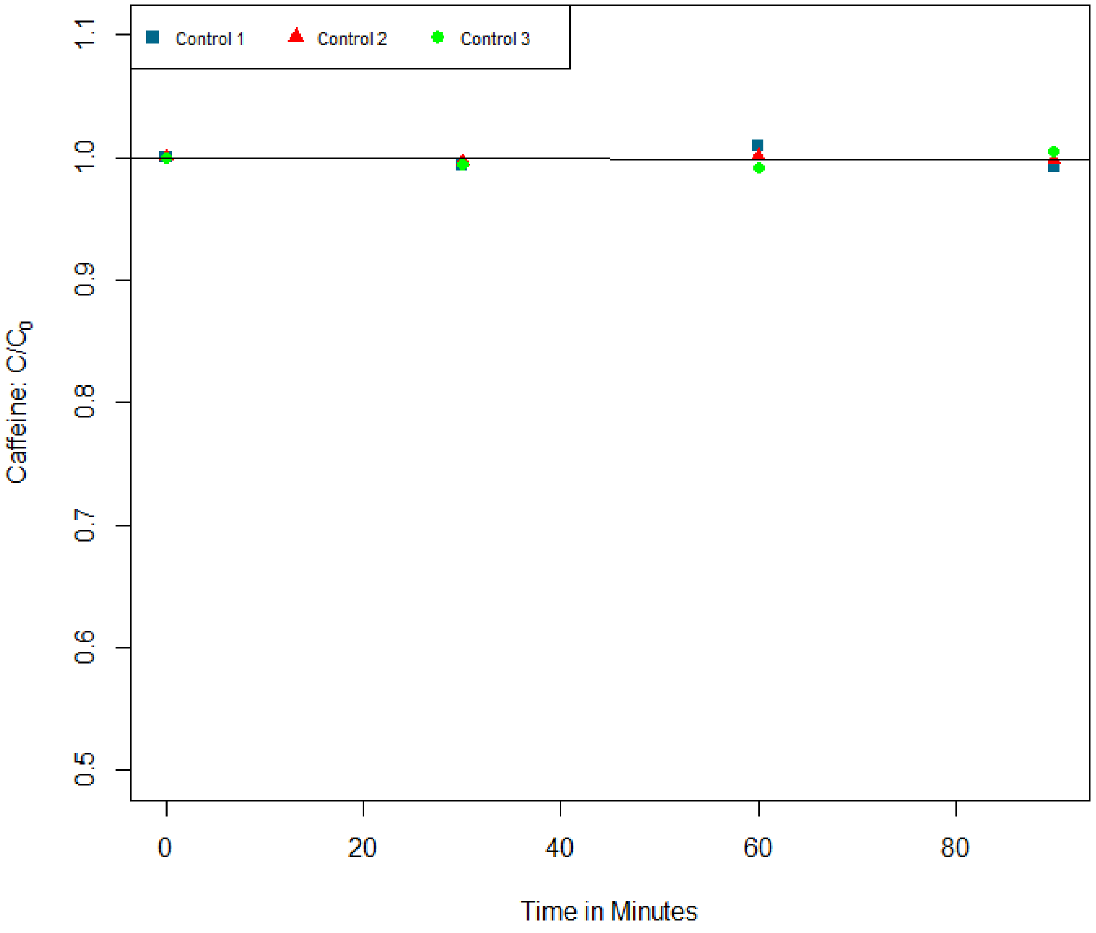

Figure S 1: Stability of caffeine in water heated to 65˚C

Best fit line to all data is shown for controls with an R^2 = -0.0585 and a p-value of 0.6423. Slope was -1.71e-05 ± 3.6e-05. Slope was not statistically different than 0.

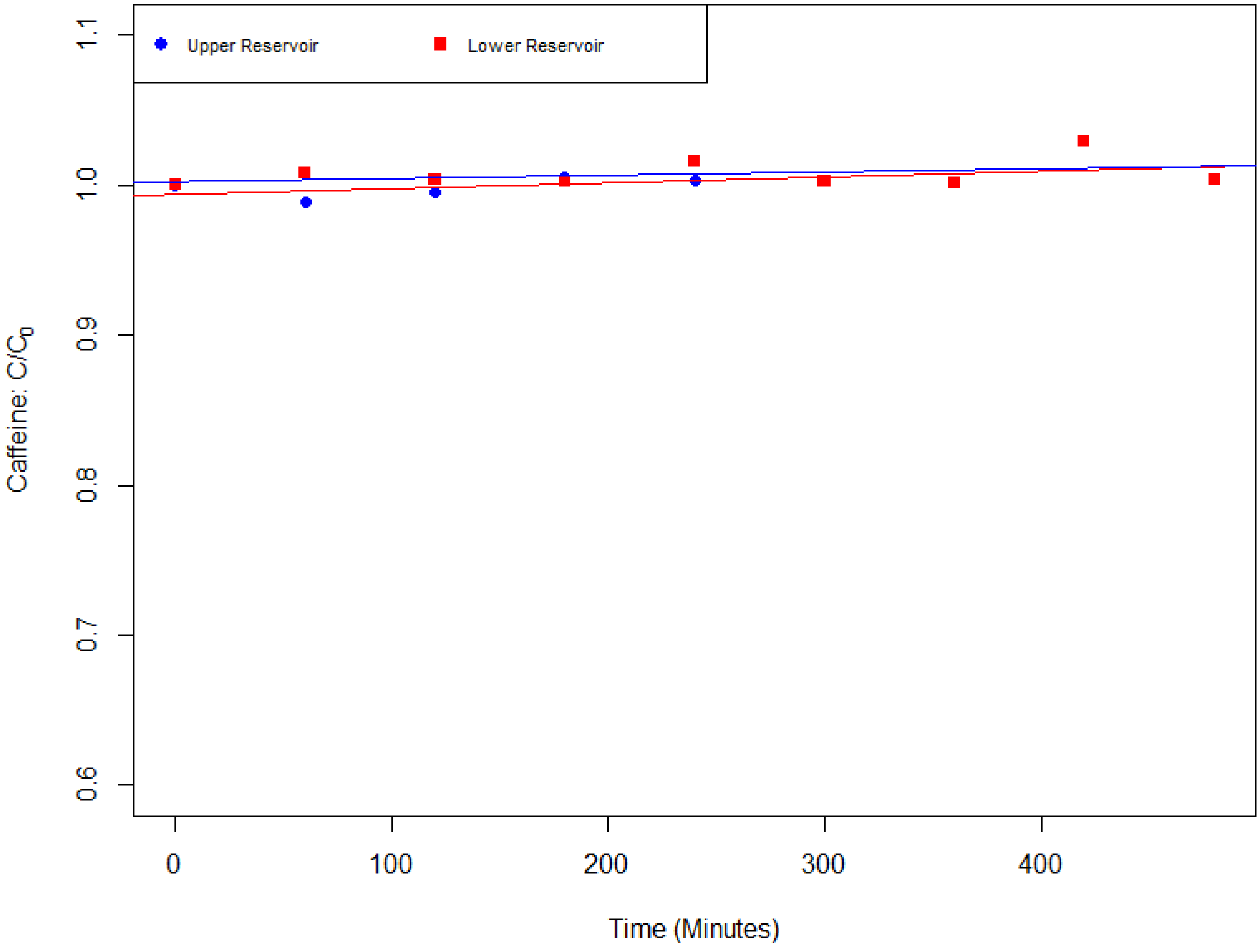

Figure S 2: Caffeine concentrations over time for caffeine in contact with plastic of upper and lower reservoirs to test for sorption

Best fit line to all data is shown for controls with an $R^2 = 0.1965$ and a p-value of 0.06348. Slope was 0.0019 ± 9.2e-04. Slope was not statistically different than 0.

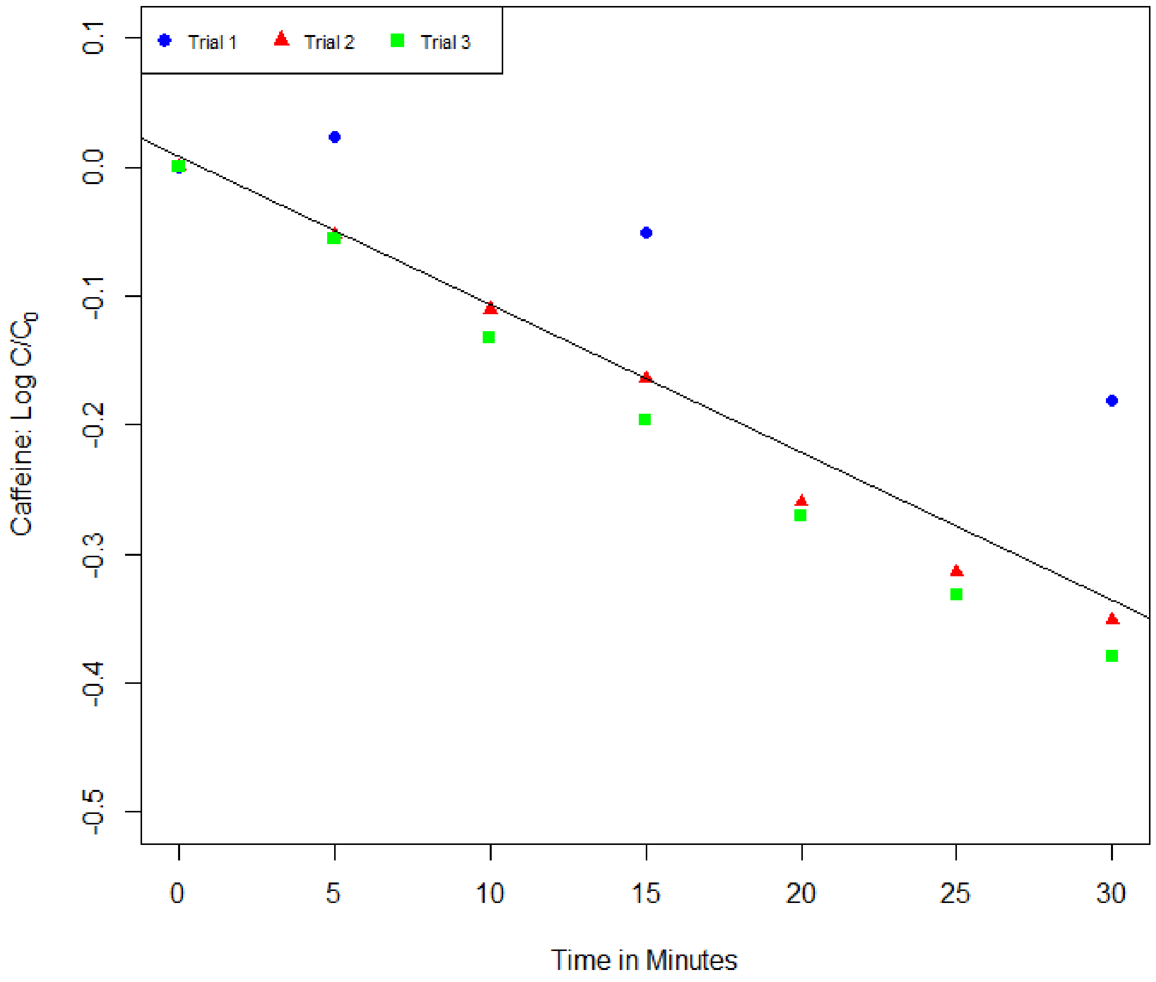

Figure S 3: Log transformed caffeine concentration over time for focused sonication experiments.

Best fit line to all data is shown for sonicated trials with an $R^2 = 0.8142$ and a $p\text{-value} < 0.001$. Slope was -0.0115 ± 0.001. Slope was statistically different than 0. For trial 1, no mist was apparent in the reactor.

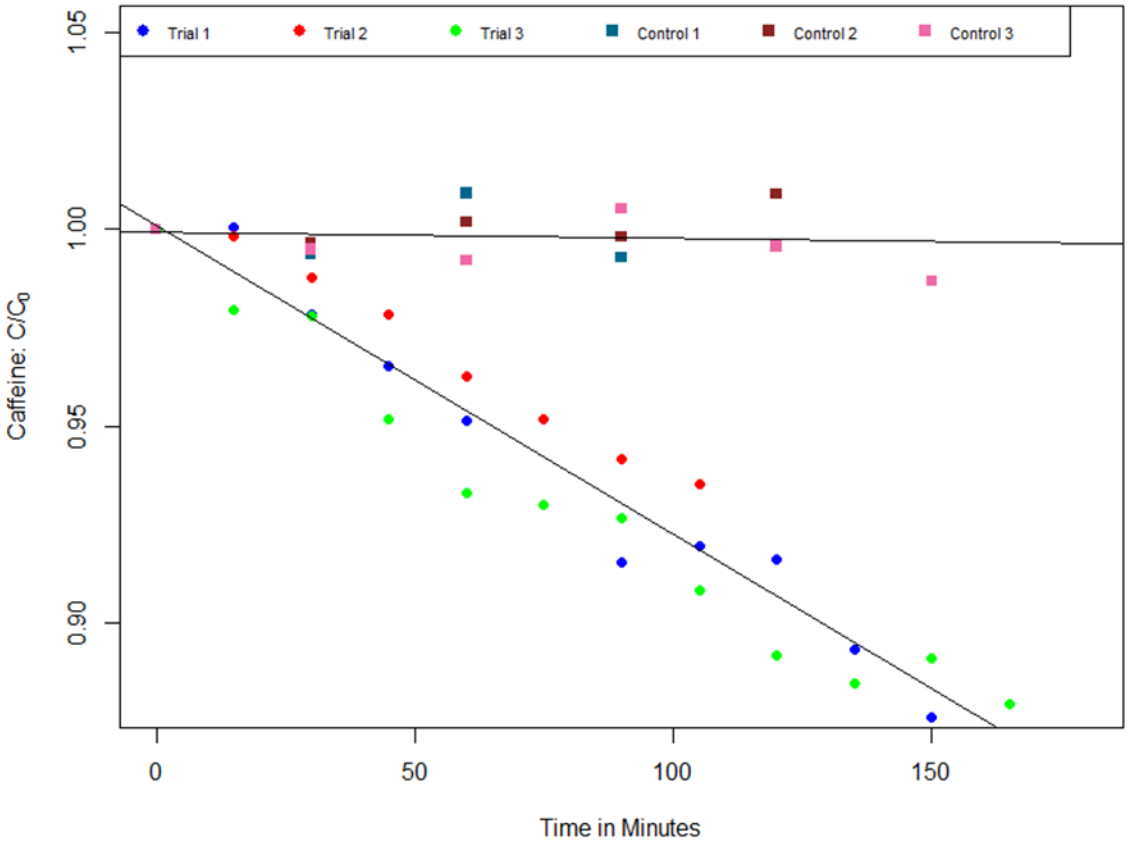

Figure S 4: Caffeine degradation in lower reservoir vs heated controls at 65˚C

Best fit line to all data is shown for sonicated trials with an $R^2 = 0.9425$ and a p-value < 0.001. Slope was -7.82e-04 ± 3.5e-05. Slope was statistically different than 0. Statistics for heated controls shown in Figure A 4.

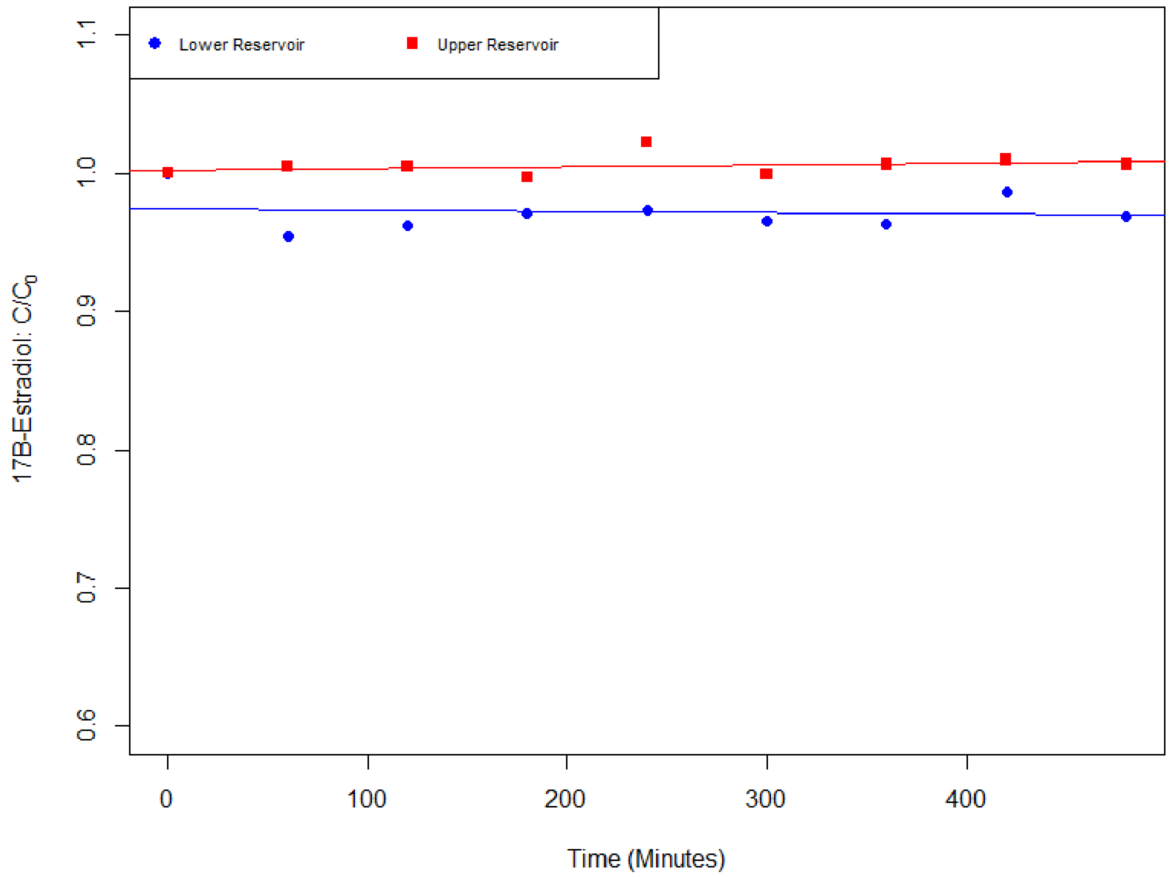

Figure S 5: 17β-estradiol sorption to plastic materials of upper reservoir and control reservoir

No loss of 17β-estradiol was observed. Slopes were not statistically different than 0 (p-values: UR=0.449; LR=0.7939)

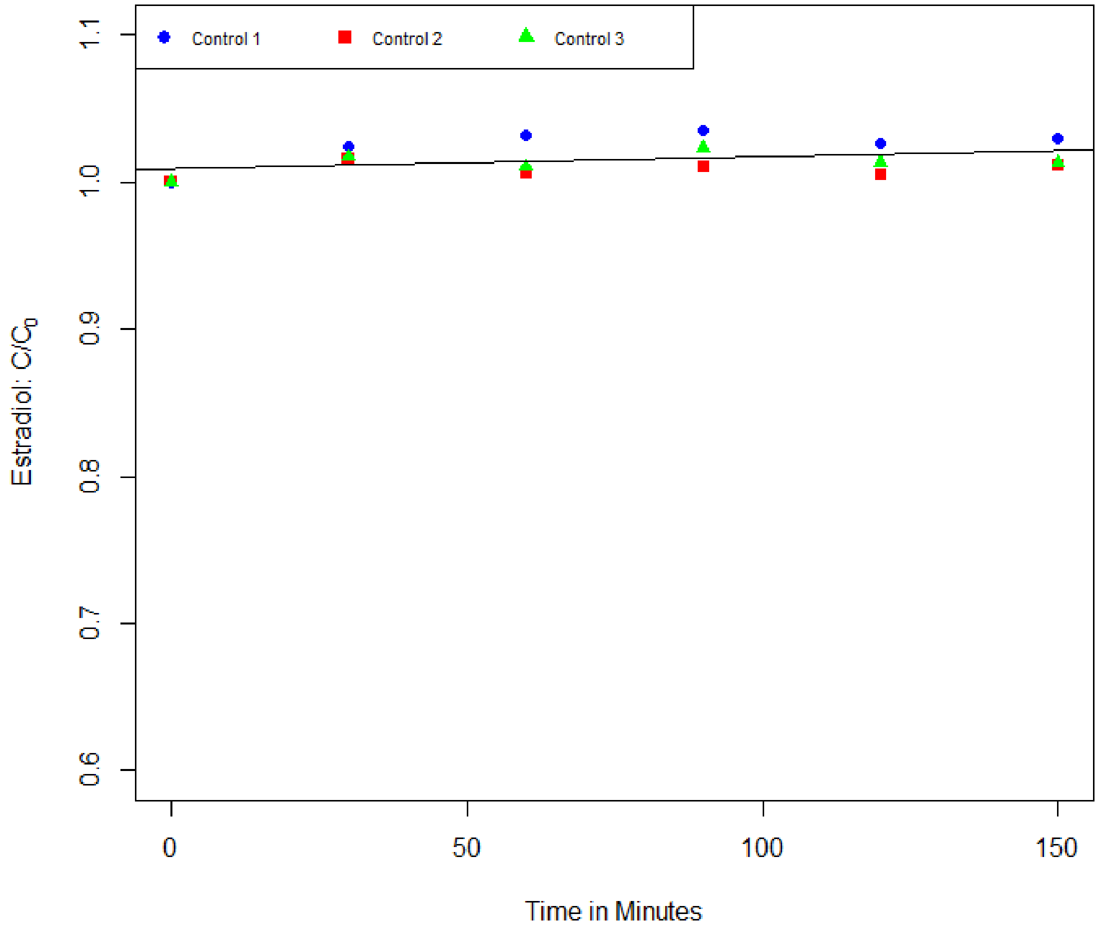

Figure S 6: Stability of 17β-estradiol at 65˚C

Best fit line to all data is shown for controls with an $R^2 = 0.08742$ and a p-value of 0.1245. Slope was 7.93e-05 ± 4.9e-05. Slope was not statistically different than 0.

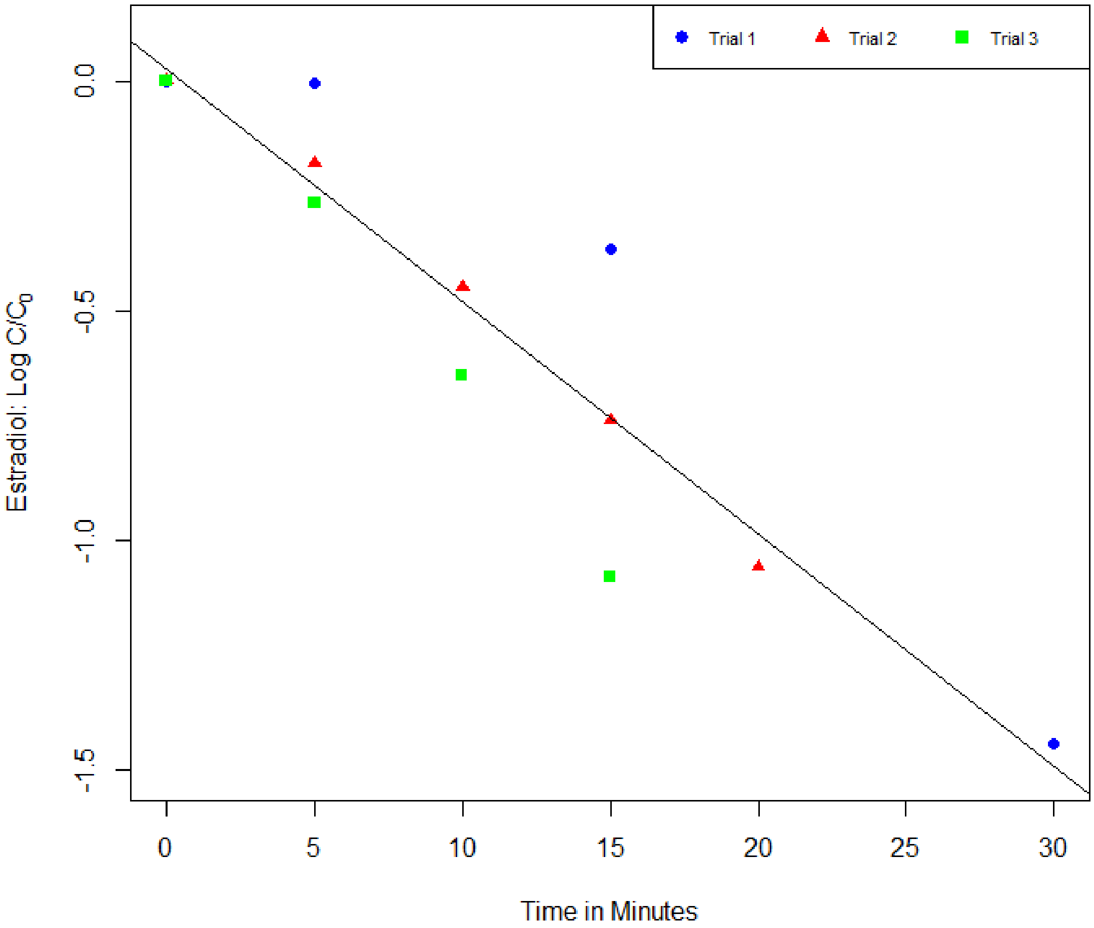

Figure S7: Log transformed data for focused sonication of 17β-estradiol

Best fit line to all data is shown for sonicated trials with an $R^2 = 0.8647$ and a p-value < 0.001. Slope was -0.0506 ± 0.006. Slope was statistically different than 0.

Trial	Slope of Regression Line min^{-1}	Mist Visually Observed in Reactor Vial
1	-0.015 ± 0.003	No
2	-0.028 ± 0.001	Yes
3	-0.030 ± 0.001	Yes

Table S 1: 17β-estradiol degradation with focused sonication

Trial	Initial Concentration mg/L	Percent decrease in 90 minutes	Degradation rate in mg/(L-min)
1	0.935	19.0%	0.0021 ± 8.1e-05
2	0.809	17.7%	0.0015 ± 3.0e-05
3	0.868	28.2%	0.0023 ± 1.1e-04

Table S 2: Kinetics of 17β-estradiol degradation in lower reservoir

Humidifier Sample Point	Change in concentration in mg/(L-min)[a]
Upper Reservoir	-4.90e-04 ± 4.4e-04
Lower Reservoir	-2.70e-04 ± 8.9e-05
Condensate	-1.93e-03 ± 3.30e-04

Table S 3: Results of full scale operation with caffeine with 17β-estradiol at approximately 5 mg/L (a) rates generated using mean of trials

Humidifier Sample Point	**Rate of change in mg/(L-min)[a]**	**Intercept**	**p-value[b]**
Upper Reservoir (n=3)	-9.84e-04 ± 3.0e-05	1.01	< 0.001
Lower Reservoir (n=3)	-1.00e-03 ± 2.7e-04	0.95	< 0.001
Condensate (n=3)	-1.27e-03 ± 3.0e-04	1.13	< 0.001

Table S 4: Results for 17β-estradiol with caffeine in full scale operation at approximately 1 mg/L; (a) rates are representative of means of slopes; (b) p-values test if the slope of the best fit line (n=3) is significantly different than zero