University of Nevada, Reno

Quantification of Trace Anthropogenic Compounds in Reclaimed Wastewater

A thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in Civil and Environmental Engineering

by

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THE GRADUATE SCHOOL

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Abstract

Reclaimed wastewater contains trace anthropogenic compounds that are poorly removed during conventional wastewater treatment. Notable reclaimed wastewater applications include supplementing drinking water supplies and crop irrigation. This thesis aims to quantify *N*-nitrosodimethylamine (NDMA), NDMA precursors, and pharmaceuticals and personal care products (PPCPs) from reclaimed wastewater applications as an indication of anthropogenic impact. The applications include aquifer storage and recovery (ASR) and crop irrigation using gas chromatography-tandem mass spectrometry (GC-MS/MS) analysis. NDMA and NDMA precursors were quantified in a treated wastewater effluent-fed recharge utility applying ASR in two sampling events from March 2017 and August 2018. Lagrangian sampling was applied for microfiltration effluent, reverse osmosis effluent, ultraviolet radiation (UV) feed, and UV product for both events in the recharge utility. Solid-phase extraction (SPE) was applied to concentrate NDMA and NDMA precursors. NDMA formation potential (FP) tests were performed to indirectly determine NDMA precursor concentration. NDMA and NDMA precursor concentration decreased after microfiltration across both events by greater than 93% and 89%, respectively. Permeate from older RO membranes contained 31% more NDMA and 14% more NDMA precursor concentration than newer membrane permeate.

Another reclaimed wastewater scheme studied was crop irrigation. This releases PPCPs to agricultural soils where they can be taken up by plants in the transpiration stream. Dry mass concentration of nine PPCPs were quantified in field-grown alfalfa irrigated with treated wastewater, groundwater-irrigated crops from private farms, and market-sourced produce. For the PPCPs quantified, field-grown alfalfa had a dry mass concentration range of 0.03-54 ng g^{-1}, groundwater-irrigated crops had a range of 0.03-62 ng g^{-1}, and market-sourced produce had a range of 0.04-162 ng g^{-1}. Neutral compounds more readily accumulated compared to compounds that were ionized at environmental pH, indicating that PPCP uptake was likely related to

physicochemical properties. Preliminary health impacts associated with consumption of affected market produce were estimated from acceptable daily intake. Negligible health impacts were typically found due to low PPCP concentration in market produce. PPCP transport from crop irrigation to different environmental compartments was estimated using EPI Suite. Compounds with low sorption potential and long half-lives could transport to groundwater whereas compounds with intermediate to high sorption potential were predicted to accumulate in plants or remain in the soil. The approach implemented to quantify NDMA and PPCPs in different environmental media indicates that trace anthropogenic compound transport depends on the reclaimed wastewater application and compound physicochemical properties.

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Chapter 1 Introduction

1.1 Sustainability and Water Reuse in Arid Climates

Sustainability and water reuse are important practices in arid areas of the world, to the extent that providing access to clean water is one of the 14 Grand Challenges for engineers (NAE, 2008). Global climate change coupled with population growth places strain on freshwater sources, forcing alternative options such as reclaimed wastewater use to be explored. Currently, reclaimed wastewater use focuses on aquifer storage and recovery (ASR), crop irrigation, and industrial supply. Reno and regions of Southern California reside in semi-arid areas that experience 7.4 in and 13 in of rainfall per year, respectively, which is markedly less than the nationwide average of 39 in (NWSFO, 2018). Additionally, Reno and Southern Californian regions have experienced population growth of 10.4% and 6%, respectively, since 2010 (USCB, 2018). Alternative options to ensure the longevity of freshwater supplies in these arid and semi-arid climates are crucial for the sustained survival of cities with less natural freshwater influx than other areas. Recently, emphasis has been placed on treated wastewater as a suitable reuse option.

1.2 Trace Anthropogenic Compounds in Treated Wastewater

One issue hindering reclaimed wastewater use is a psychological public perception driven by negative messaging that speciously contends reclaimed wastewater is unclean. These negative perceptions have steadily decreased as the impact of climate change and restricted water supply becomes clear, coupled with positive educational strategies (Ormerod, 2016; Tricas et al., 2018). Pharmaceuticals and personal care products (PPCPs) as well as disinfection by-products (DBPs) are potentially hazardous compounds that exist in treated wastewater. Some PPCPs exhibit a lack of removal through conventional wastewater treatment plants (WWTPs), whereas DBPs form from disinfection. There is currently not enough known about long-term exposure effects to chemical cocktails and their products at trace levels (WHO, 2012). This suggests that trace

anthropogenic compounds could represent a hindrance to reclaimed wastewater use, given the public health unknowns.

1.2.1 N-DBPs in Indirect Potable Reuse

The hazards surrounding DBPs have blossomed over the last 30 years (Crittenden, Trussell, Hand, Howe, & Tchobanoglous, 2012) with nitrosamines (N-DBPs) being heavily focused on. One such N-DBP, *N*-nitrosodimethylamine (NDMA) is a probable human carcinogen with a drinking water concentration of 0.7 ng L^{-1} corresponding to a 1 in 10^{-6} cancer risk level (IRIS, 1993). A Californian recharge utility applies ASR by injecting and percolating treated water via wells and spreading basins, respectively. The utility performs conventional wastewater treatment followed by microfiltration, reverse osmosis (RO), and ultraviolet radiation (UV) with hydrogen peroxide (H_2O_2) addition before ASR. The utility schematic is presented in Figure 1-1.

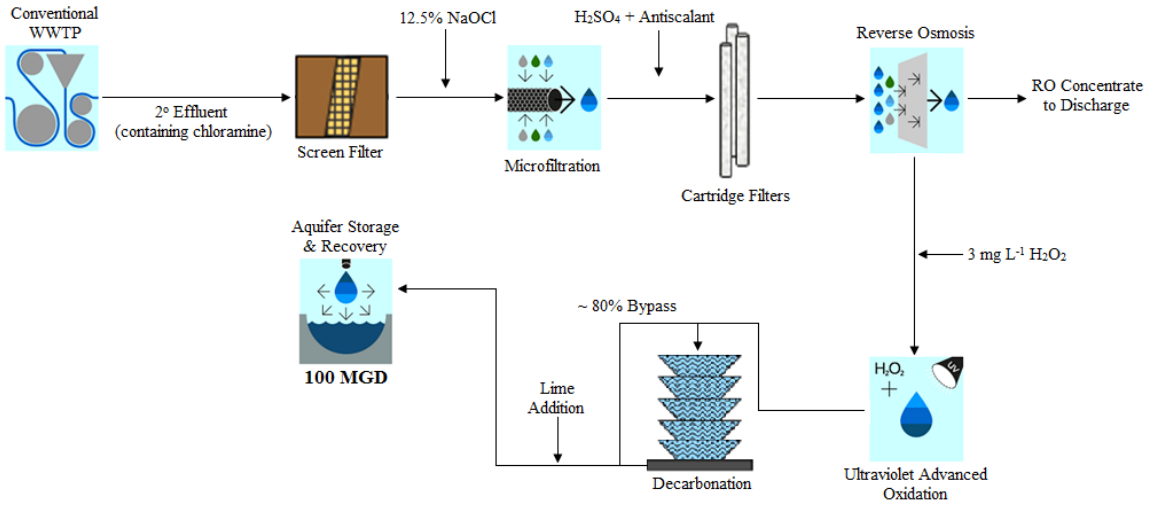


Figure 1-1 Schematic of the recharge utility including each treatment process and point of chemical addition (adapted from Roback et al. (2018))

The ASR system is an indirect potable reuse process that provides an environmental buffer prior to groundwater pumping that can then be used as drinking water. The utility monitors NDMA discharge to determine if this water sustainability application negatively affects groundwater quality from NDMA concentration above the cancer risk level. Additionally, monitoring NDMA discharge is useful for potential development of direct potable reuse applications.

1.2.2 PPCPs in Treated Wastewater

The practice of using treated wastewater to irrigate crops has the potential to reduce freshwater withdrawals (Bichai, Polo-López, & Fernández Ibañez, 2012). Treated wastewater irrigation has proliferated due to freshwater scarcity concerns in arid and semi-arid areas such as the western USA, Australia, and southern Europe (Sato, Qadir, Yamamoto, Endo, & Zahoor, 2013). 65% of irrigated cropland downstream of urban areas is likely to source water from either treated or untreated wastewater (Thebo, Drechsel, Lambin, & Nelson, 2017). The use of treated wastewater as an irrigation source has led to increased PPCP release to the environment and a concern over how these compounds behave and translocate in crops. Understanding PPCP translocation in agricultural crops upon irrigation is vital to understanding the risk of ingestion of the affected plants. The alfalfa crops at UNR Farms are irrigated with the effluent of a local wastewater utility. The utility treatment schematic is displayed in Figure 1-2.

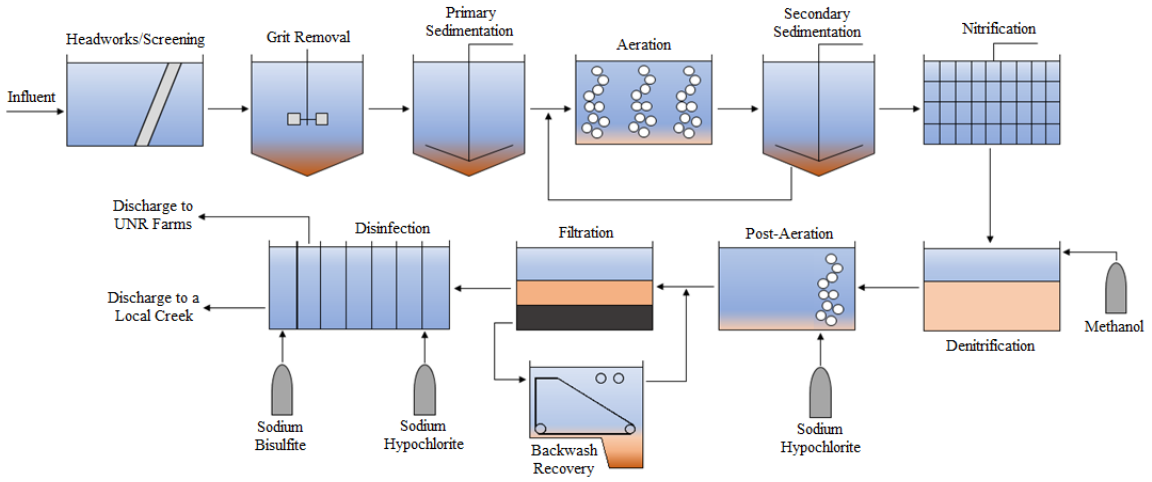


Figure 1-2 Excerpt of the schematic of the local wastewater utility. Discharge to UNR Farms occurs prior to dechlorination (adapted from Carollo (2018))

Following disinfection and prior to dechlorination, water is diverted to a pumping station and transported to UNR Farms. The UNR Farms site is a good source for determining plant uptake trends of PPCPs at the field scale, for which little data is available compared to hydroponic or greenhouse studies. It is essential for the assurance of public safety to illuminate the transport pathways of N-DBPs and PPCPs to elucidate if ASR and reclaimed wastewater irrigation constitute effective applications of water sustainability.

1.3 Thesis Objectives

The central hypothesis of the NDMA study was: NDMA forms from chloramination through advanced treatment utilities from the lack of removal of NDMA precursors. The specific objectives of the NDMA study were to: a) quantify NDMA formation and discharge in the recharge utility (Chapter 2); b) investigate the impact of RO membrane age on NDMA formation potential (Chapter 2); c) identify NDMA precursors in post-RO samples (Chapter 2); d) quantify NDMA formation from ozonation in a pilot plant (Chapter 2).

The central hypothesis of the PPCP study was: crops irrigated with treated wastewater accumulate PPCPs in different plant components. The specific objectives of the PPCP study were to: a) quantify the dry mass concentration of PPCPs in field-grown alfalfa irrigated with treated wastewater (Chapter 3); b) quantify PPCPs in market-sourced and groundwater irrigated crops (Chapter 3); c) investigate PPCP transport to different environmental compartments from treated wastewater irrigation (Chapter 4).

Chapter 2 NDMA in Reclaimed Wastewater

2.1 NDMA Literature Review

2.1.1 Historic NDMA Detection

Originally, nitrosamines were studied in food and consumer products such as alcoholic beverages, meats, dairy products, and vegetables. Table 2-1 shows an excerpt of the results of a five-year study for food and beverage products.

Table 2-1 Occurrence of NDMA in foodstuffs and beverages in France in 1987-1992. The corresponding daily intake was based on typical consumption of a 35 year old European male (Biaudet, Mavelle, & Debry, 1994)

Foodstuff or Beverage	NDMA (ng g^{-1})	Daily NDMA Intake (ng)
Beer	0.24	25
Wine	0.06	11.7
Other Alcoholic Beverages	1.74	26.2
Fresh Fish	0.12	1.6
Sausage Products	0.45	5.2
Ham	0.31	3.8
Pork	0.28	5.1
Bacon	0.31	0.6
Beef, Veal	0.10	4.6
Bread	0.1	11.2
Cheese	0.32	19
Milk	0.03	5.3
Dried Milk	0.06	0.5
Eggs	0.15	4.8
Coffee	0.11	1
Tinned Vegetables	0.23	10.8
Fresh Vegetables	0.18	30.1

The study found that from 1987-1992, the average daily intake of NDMA was 0.19 μg per person. This was dependent on typical dietary intake and varies between countries. Wine, milk, eggs, and bread were focused on in France because they are consumed in greater quantities.

Attention concerning NDMA in the environment has shifted from food and beverages to groundwater. This was primarily due to runoff from an industrial point source at a rocket engine testing facility in Sacramento, California (MacDonald, 2002). The first detection of the contaminated groundwater found NDMA at levels of 400 μg L^{-1} on site and 20 μg L^{-1} off site (Mitch et al., 2003). The facility used unsymmetrical dimethylhydrazine (UDMH) based rocket fuel that was oxidized to NDMA once released. The groundwater findings forced the closure of drinking water wells downgradient of the facility and sparked investigation of NDMA in California drinking waters to determine occurrence levels. Based on occurrence and toxicity, nitrosamines may pose higher health risks than trihalomethanes (THMs) and haloacetic acids (HAAs), despite the shift to chloramination aimed at reducing the health risks associated with halogenated DBPs.

2.1.2 NDMA Formation in Water from Chloramination

DBPs have been an issue since the inception of water disinfection. In the USA, chlorine disinfection has historically been used which resulted in formation of THMs and HAAs (Crittenden et al., 2012). Chloramination has been implemented to a greater extent since the inception of the Stage 2 DBP Rule for drinking water treatment plants to control regulated DBPs (Li, 2011). Chloramines form potent carcinogens called nitrosamines (Mitch & Sedlak, 2002). Of the nitrosamines, NDMA is the most studied due to its high occurrence in treated drinking water (Krasner, Mitch, McCurry, Hanigan, & Westerhoff, 2013). NDMA can form from reactions between dichloramine and organic nitrogen sources, with UDMH forming as an intermediate before being oxidized by dissolved oxygen to form NDMA. NDMA also has slow formation kinetics that can take greater than 72 hr (Mitch & Sedlak, 2002). Figure 2-1 shows the likely NDMA formation pathway.

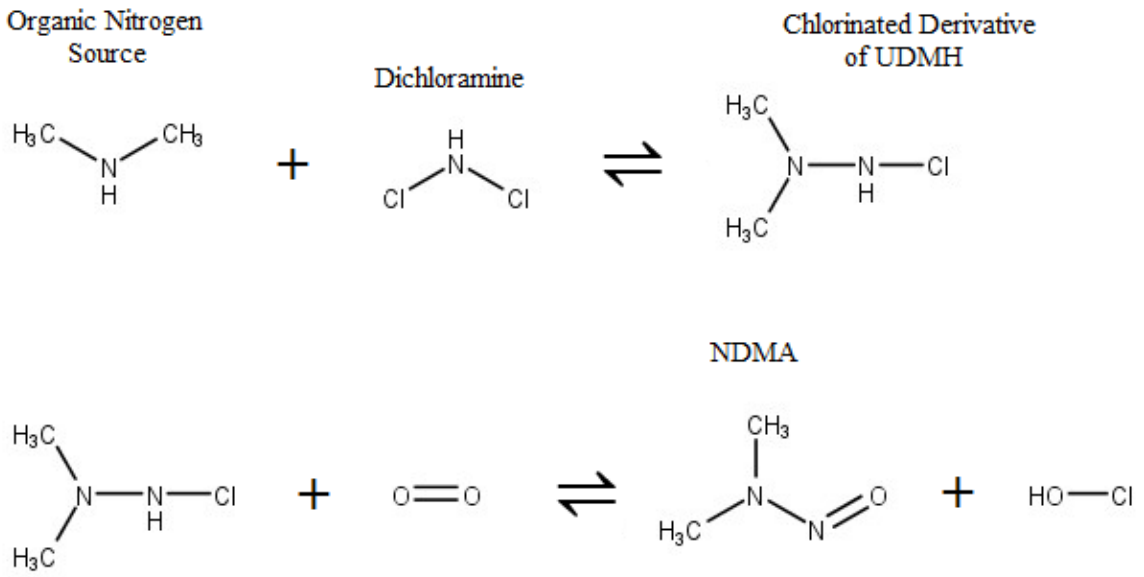


Figure 2-1 Likely NDMA formation pathway from chloramination of an organic nitrogen source (adapted from Schreiber & Mitch (2006))

NDMA formation is also dependent on pH and the corresponding dominant chloramine species. Schreiber and Mitch (2006) determined that dichloramine is the dominant chloramine species in NDMA formation. Figure 2-2 shows chloramine speciation relative to pH.

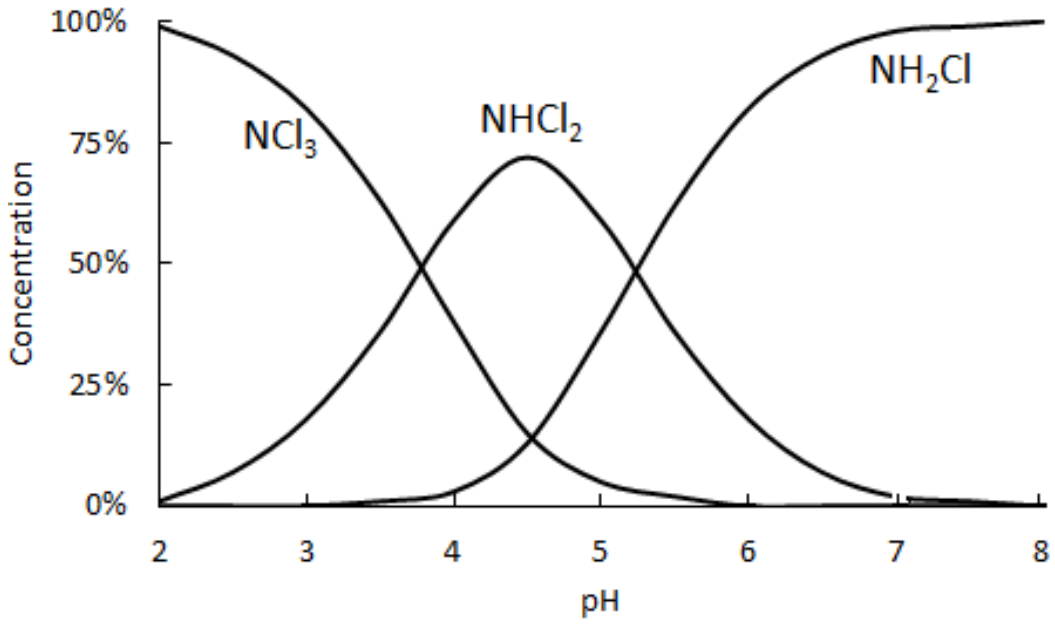


Figure 2-2 Chloramine speciation versus pH. NCl_3 (trichloramine), $NHCl_2$ (dichloramine), NH_2Cl (monochloramine) (Cimetière, De Laat, & Berne, 2009)

The maximum dichloramine concentration in water with respect to the other chloramine species is at approximately pH 4.5. Dichloramine and monochloramine can coexist in water when chloramines are formed at Cl:N molar ratios < 1.5 (Schreiber & Mitch, 2006). For advanced water treatment systems, the use of RO typically decreases the permeate water pH below neutral (Qin, Oo, & Coniglio, 2005), thus increasing dichloramine formation and promoting NDMA formation (McCurry, Ishida, Oelker, & Mitch, 2017).

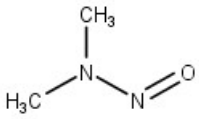
2.1.3 NDMA Formation in Water from Ozonation

NDMA formation can also occur as a product of ozonation and has a distinct set of precursors compared to the chloramination pathway. However, both formation pathways are not clearly defined and are a source of ongoing study. Compounds containing hydrazines or sulfamide functional groups are the primary source of concern due to NDMA yields over 50% for ozone (Kosaka, Asami, Konno, Oya, & Kunikane, 2009; Schmidt & Brauch, 2008; von Gunten, Salhi, Schmidt, & Arnold, 2010) and formation in less than 1 hr. Increased contact time leads to increased NDMA formation, especially at pH levels greater than 8 (Andrzejewski, Kasprzyk-Hordern, & Nawrocki, 2008). Marti et al. (2015) determined that an ozone dose of 4.8-24 mg L^{-1} resulted in NDMA yields of up to 70% for ultrapure water containing precursors. NDMA formation stabilized at the high dose point due to the complete reaction of precursors with ozone. Despite the high NDMA yield and fast reaction kinetics from ozonation of precursors, the risk of NDMA formation from ozonation in drinking water is thought to be low. Drinking water sources would need to originate from areas of high industrial or agricultural activity that discharge a high concentration of hydrazine or sulfamide-containing compounds for NDMA formation to be a concern (Krasner et al., 2013).

2.1.4 Conventional Treatment Ineffectiveness for NDMA and NDMA Precursor Removal

Conventional treatment consisting of coagulation, flocculation, sedimentation, filtration, and disinfection poorly removes NDMA. Table 2-2 shows the physicochemical properties of NDMA derived from its structure and how this relates to conventional water treatment.

Table 2-2 NDMA physicochemical properties and their relationship to NDMA removal in water treatment

	Structure	**log K_{ow}**	**Henry's Law Constant**
	$C_2H_6N_2O$		
CAS Number 62-75-9		-0.57 (ATSDR, 1989)	1×10^{-4} (Haruta, Jiao, Chen, Chang, & Gan, 2011)
Physicochemical Property Influence in Water Treatment	Low molar mass, uncharged. Poorly removed by reverse osmosis	Hydrophilic, poorly sorbs to soils, activated carbon, and other sorbents	Some volatilization from natural waters but air stripping is unlikely to efficiently remove

The relative ineffectiveness of conventional treatment for NDMA removal indicates that adequate NDMA removal must include treatment of any pre-formed NDMA, as well as removal of its precursors. As such, conventional treatment followed by advanced treatment involving ozonation is an effective option (Lee, Schmidt, Yoon, & von Gunten, 2007).

2.1.5 Specific Treatment Technologies for NDMA and NDMA Precursor Removal

Advanced treatment incorporating NDMA and NDMA precursor removal is an effective measure to limit NDMA discharge. For advanced treatment systems implementing RO processes, monochloramine is typically added to reduce membrane biofouling (Farhat et al., 2018). Precursors passing through conventional treatment prior to RO can react with monochloramine and form NDMA. Ultraviolet radiation/advanced oxidation processes (UV/AOP) can then be applied for NDMA photolysis. Figure 2-3 shows the interaction between UV radiation and NDMA.

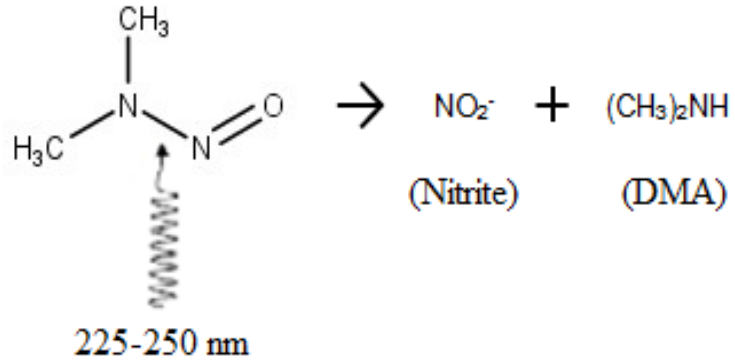


Figure 2-3 NDMA bond cleavage from UV radiation (Stefan & Bolton, 2002)

UV radiation is effective for NDMA destruction provided that NDMA has sufficiently formed. The hydraulic retention time and placement of chloramine addition points are of paramount importance to successfully apply UV radiation for NDMA destruction, given the slow NDMA formation kinetics.

NDMA precursor removal can be achieved through activated carbon (AC). Hanigan et al. (2012) found that 91% of NDMA precursors were removed from a treated wastewater secondary effluent when using 75 mg L^{-1} of powdered activated carbon (PAC) with a 4 hr contact time. Additionally, in a full-scale plant, greater than 60% of NDMA precursors were removed using granular activated carbon (GAC). Unfortunately, NDMA was always formed to some extent after chloramination, highlighting that complete precursor removal using PAC or GAC was not possible despite its wide range of selectivity. As such, employing other processes to complement AC is necessary if complete precursor removal is desired. Coupling AC with UV radiation constitutes an effective treatment option to remove NDMA precursors and NDMA, respectively.

2.1.6 NDMA in Direct and Indirect Potable Reuse Water

Using reclaimed wastewater for ASR could constitute a potential contamination issue due to NDMA release, the low concentration associated with health impacts, and transport to wellheads. Gunnison et al. (2000) concluded from laboratory studies that biodegradation processes can remove 100% of NDMA in groundwater aquifers at neutral pH and microaerobic conditions. Zhou et al. (2009) observed *in situ* biodegradation of NDMA over seven years in groundwater from incidental and active recharge of treated wastewater. A 90% mass reduction of NDMA in groundwater was observed over the period with 80% of the reduction estimated to result from biodegradation. Site-specific natural attenuation of NDMA expands the feasibility of applying reclaimed wastewater to ASR. However, the potential for low NDMA concentrations to transition to wellheads is real due to the lack of dilution if the affected water is injected in close proximity to the wellhead. Additionally, spring runoff combined with groundwater pumping during summer indicates that water injected to aquifers may not remain there long enough for NDMA biodegradation.

2.1.7 NDMA in Reclaimed Wastewater Research Objectives

The objectives of NDMA quantification in a recharge utility applying ASR were to quantify NDMA formation and discharge, investigate the impact of RO membrane age on NDMA formation potential, and to identify NDMA precursors in post-RO samples. The objectives of NDMA quantification in a pilot plant applying ozone contact and biological activated carbon (BAC) were to quantify NDMA formation and removal.

2.2 NDMA Materials and Methods

2.2.1 Recharge Utility Sampling Procedure

Water samples were collected on 15 March 2017 and 1 August 2018 from the recharge utility and shipped overnight to UNR in coolers before being refrigerated until extraction. Figure 2-4 shows the recharge utility configuration and sampling locations for both events.

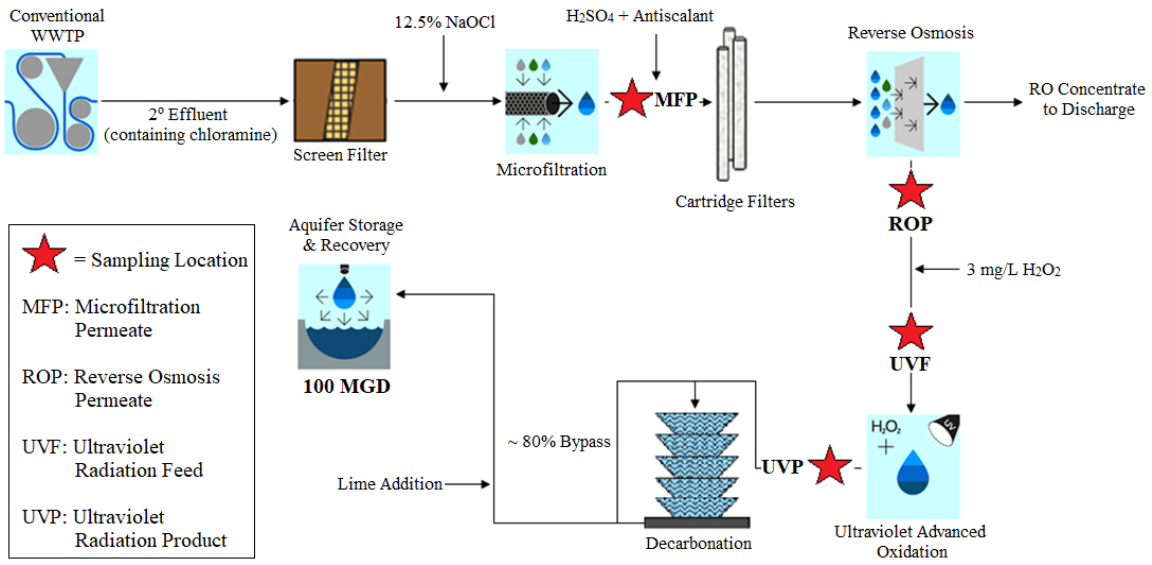


Figure 2-4 Sampling locations in the recharge utility. MFP, ROP, and UVP were sampled for the 2017 event whereas ROP, UVF, and UVP were sampled for the 2018 event (adapted from Roback et al. (2018))

The 2017 samples were collected from the microfiltration permeate (MFP), reverse osmosis membrane permeate (ROP), and ultraviolet radiation/advanced oxidation product (UVP). The 2018 samples were collected from the ROP, ultraviolet radiation/advanced oxidation feed (UVF) after H_2O_2 addition, and the UVP. 1 L amber bottles that had been rinsed, washed, and furnaced at 500°C were used as collection vessels to minimize contamination.

2.2.2 Local Pilot Plant Sampling Procedure

Water samples from a pilot plant located at a small, local WWTP were collected on 1 August 2018 and transported to UNR before being refrigerated. The WWTP plant configuration is shown in Figure 2-5.

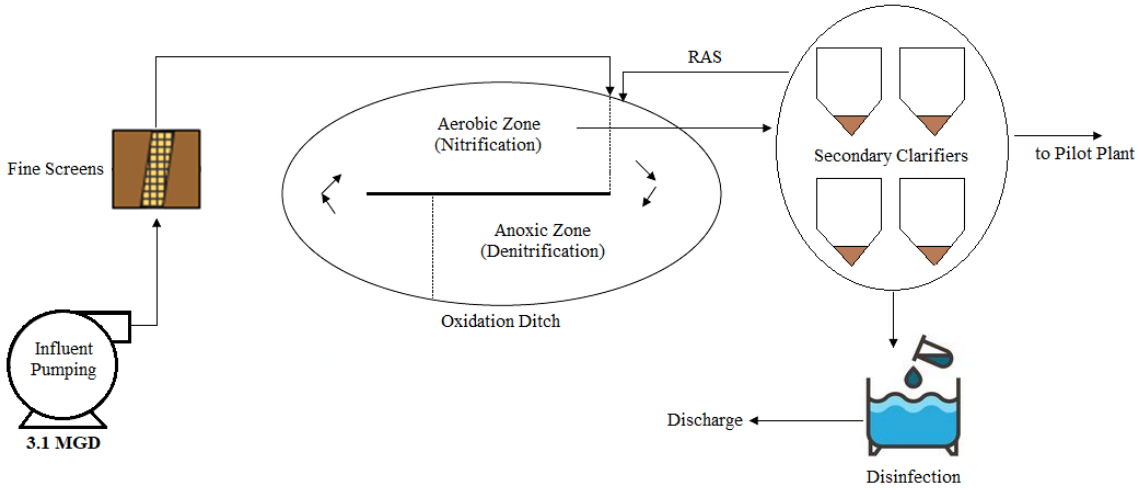


Figure 2-5 Schematic of the small, local WWTP. Pilot plant influent was sourced from the secondary clarification effluent

The WWTP process consists of fine screening, an oxidation ditch process with an aerobic and anoxic zone for nitrification and denitrification, respectively, secondary clarification for solids separation, and disinfection. A portion of the secondary clarifier effluent is also returned to the beginning of the anoxic zone as return activated sludge (RAS).

Disinfected water is discharged to a reservoir for storage. Treated wastewater is also used to irrigate parks, high schools, golf courses, as well as commercial and thoroughfare median landscapes. A portion of the secondary treated water is diverted to the pilot plant. The pilot plant configuration is shown in Figure 2-6 and involves an ozone contactor followed by two BAC filters operated in parallel. The ozone contactor receives a varying dose of 6-20 mg L^{-1} O_3

dependent on the total organic carbon (TOC) present in the system and is monitored daily. The BAC filters receive flow rates of 8 and 4 gpm with empty bed contact times (EBCTs) of 10 and 20 min, respectively. Samples were collected from the pilot plant influent, ozone contactor effluent, and the two BAC filter effluents. Samples were passed through pre-combusted GB-140 glass fiber 0.4 µm filters (Advantec, California, USA) using vacuum pumps.

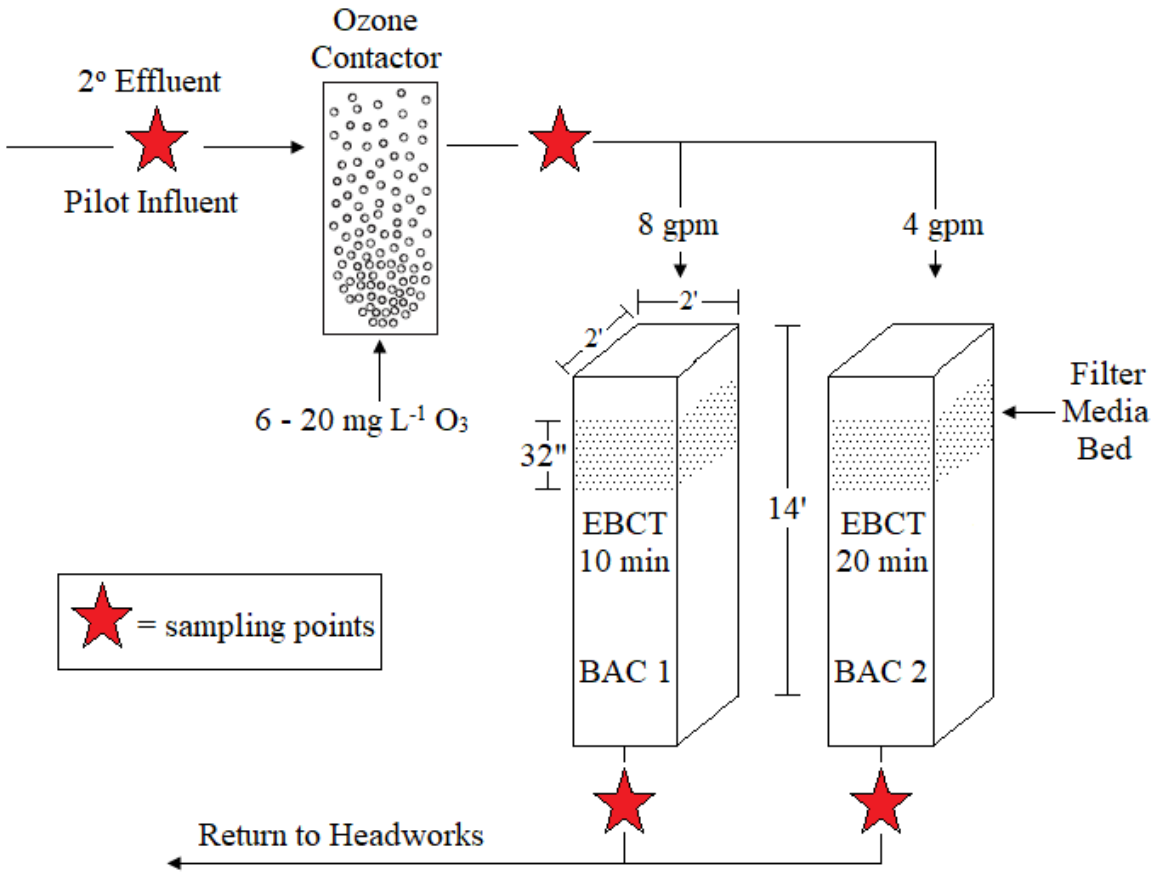


Figure 2-6 Pilot plant schematic with sampling locations, ozone dose, flow rates, and EBCT for each BAC unit

2.2.3 NDMA Precursor Extraction from the Recharge Utility

NDMA precursors were extracted and concentrated to determine their composition by non-target mass spectrometric analysis using liquid chromatography-quadrupole time-of-flight mass spectrometry (LC-QTOF/MS) performed at the University of Colorado, Boulder. Samples were poured into 2 L rapidly stirred flasks. 1 M and 0.1 M sulfuric acid (H_2SO_4) were added until the pH of the sample was 3. Samples were solid-phase extracted (SPE) using a Dionex AutoTrace 280 (Thermo Fisher Scientific, Massachusetts, USA) with Oasis MCX 6 cc/500 mg cartridges (Waters Corporation, Massachusetts, USA). The cartridges were first conditioned with 2 times 10 mL methanol (MeOH) and 3 times 10 mL Milli-Q water (18.2 MΩ·cm) (Thermo Fisher Scientific, Massachusetts, USA) before samples were loaded at 5 mL min^{-1}. The 2L samples were loaded concurrently with two input sample lines per volumetric flask meaning that a single sample was split between two cartridges. Cartridges were then dried with ultra-high purity (UHP) N_2 gas for 45 min before being eluted with 10 mL of 5% ammonium hydroxide (NH_4OH) in MeOH. Samples were transferred into 10 mL glass conical centrifuge tubes and evaporated in a TurboVap LV (Biotage, Uppsala, Sweden) under a gentle (5-10 psi) UHP N_2 gas stream. Like samples were then combined and evaporated to just less than 1 mL before being topped up to 1 mL with MeOH. Samples were then transferred with pasteur pipettes to 2 mL amber vials and placed in the freezer.

2.2.4 NDMA Modified Precursor Extraction

A modified precursor isolation and extraction method was used on two ROP samples of 1 L each from the 2018 sampling event. The conditioning step was altered from the original precursor isolation method to limit any potential contaminants already present in the cartridges from eluting into samples and influencing measurements. The cartridges were conditioned with 5 mL of 5% NH_4OH in MeOH to elute any contaminants followed by 4 times 10 mL acidified Milli-Q water at pH 2 to acidify the cartridges and mimic the conditions in the flasks.

2.2.5 NDMA Formation Potential

Formation potential is an indirect way to measure NDMA precursor concentration by reacting all precursors to form NDMA. A 1 M borate buffer solution was prepared by dissolving 8.5046 g sodium tetraborate (borax) and 56.3086 g boric acid into 1 L Milli-Q water. The borax and boric acid were slowly added to the Milli-Q water at approximately 30°C while being constantly stirred. Once the solution was completely dissolved, the pH was measured in a 1:1000 diluted solution and confirmed to be 8.

10 mL of a 5.65-6% sodium hypochlorite solution was added to 240 mL Milli-Q water to make a chlorine solution. The free chlorine concentration of the chlorine solution was measured using a DR 6000 UV-VIS spectrophotometer (Hach Company, Colorado, USA) and Program 80 (Chlorine F&T PP). The chlorine solution was diluted 2000 times using Milli-Q water before the contents of a DPD Free Chlorine Reagent powder pillow pack (Hach Company, Colorado, USA) was added to the diluted mixture. The mixture was lightly swirled for 3 min to dissolve the powder before being measured using Program 80. The Cl_2 concentration readout from the Hach instrument (X) was put into Equation 2-1 to find the required ammonium chloride (NH_4Cl) addition.

Equation 2-1 $$\text{g } NH_4Cl \text{ required} = \frac{1.2 \text{ mol N}}{\text{mol } Cl_2} * 2000 \text{ (dilution factor)} * \frac{1 \text{ mmol } Cl_2}{71 \text{ mg } Cl_2} * \frac{(X) \text{ mg } Cl_2}{\text{L}} * \frac{\text{mmol } NH_4Cl}{\text{mmol N}} * \frac{53.5 \text{ g } NH_4Cl}{\text{mmol } NH_4Cl} * \frac{1 \text{ g}}{1000 \text{ mg}} * 0.5 \text{ L} = \frac{(X) \frac{\text{mg}}{\text{L}} Cl_2}{2.212}$$

The required NH_4Cl mass was dissolved with 245 mL Milli-Q water and 5 mL of the 1 M borate buffer solution in a 500 mL amber bottle. The chlorine solution was slowly passed through a burette into the rapidly stirred buffered ammonia solution to promote monochloramine production and limit dichloramine and trichloramine production. This gave a final buffer concentration of the monochloramine solution of 10 mM. The solution was then left in the dark for 1 hr to equilibrate. 5 mL of the buffer solution was added to each 500 mL sample and measured to ensure the pH was 8. The monochloramine concentration in the solution was then measured using the Hach instrument and Program 66 (Monochloramine LR) by adding the contents of a Monochlor F Reagent powder pillow pack (Hach Company, Colorado, USA). The necessary added volume of monochloramine solution was then added to each sample using Equation 2-2 where (Y) is the concentration of monochloramine in the solution and 18 mg L^{-1} Cl_2 is the intended dose.

Equation 2-2 $$\text{Added volume} = \frac{18 \frac{\text{mg}}{\text{L}} Cl_2 * 500 \text{ mL sample}}{(Y) \frac{\text{mg}}{\text{L}} Cl_2}$$

Samples were then stored at room temperature in the dark for 72 hours to facilitate NDMA formation. A 0.5 M (88 g L^{-1}) ascorbic acid solution in Milli-Q water was prepared with 5 mL from the solution used to quench samples to achieve a final ascorbic acid concentration of 5 mM. An NDMA-d_6 (Cambridge Isotope Laboratories, Massachusetts, USA) isotope solution of 100 µg L^{-1} in Milli-Q water was prepared with 1 mL added to each sample to achieve a concentration of 0.2 µg L^{-1} prior to SPE. The SPE method conformed to EPA Method 521 and uses EPA Method 521 6 mL cartridges (Restek Corporation, Pennsylvania, USA). Cartridges were conditioned with 5 mL of dichloromethane (DCM), MeOH, and Milli-Q water before samples were loaded at 5 mL min^{-1}. Cartridges were then dried with UHP N_2 gas for 30 min before being eluted with 5 mL DCM. The DCM eluate was pushed through anhydrous sodium sulfate cartridges (Agilent Bond Elut JR-Sodium sulf. 1.4 gm) into 10 mL glass conical centrifuge tubes to remove any water. Samples were then evaporated under a gentle UHP N_2 gas stream to 1 mL using the TurboVap. The TurboVap water was kept to 23°C to mitigate the high volatility of DCM. Samples were then transferred into 2 mL amber vials using pasteur pipettes and placed in the freezer.

2.2.6 NDMA Precursor Reconstitution

Precursor reconstitution was performed in conjunction with an NDMA FP test to determine NDMA precursor recovery. 250 µL from each 1 mL sample from the NDMA precursor extraction procedure in Chapter 2.2.3 was reconstituted into separate amber bottles containing 500 mL Milli-Q water. NDMA FP tests were then performed following the procedure in Chapter 2.2.5.

2.2.7 NDMA GC-MS Positive Chemical Ionization Analysis

The samples were analyzed by gas chromatography-mass spectrometry (GC-MS/MS). The instrument was an Agilent 6890 gas chromatograph (Agilent Technologies, California, USA) with a Waters Micromass Quattro micro GC mass detector (Waters Corporation, Massachusetts, USA). The mass analyzer consists of two quadrupoles separated by a hexapole collision cell. The analysis method was a slightly modified version of the method described by (Charrois, Arend, Froese, & Hrudey, 2004). Separation was achieved on a DB-1701P (30 m x 0.25 mm x 0.25 µm) capillary column (Agilent Technologies, California, USA) with UHP helium as the carrier gas (1 mL min^{-1}). 4 µL samples were injected in splitless mode into a 0.75 mm I.D. SPME Injection Liner (Supelco, Pennsylvania, USA) at an injection temperature of 280°C. The temperature program of the GC oven was initially set at 50°C, held for 1 min and then ramped at 10°C min^{-1} to 80°C, at 15°C min^{-1} to 180°C, at 35°C min^{-1} to 260°C and held for 5 min. The MS was operated in CI+ ionization mode at 70 eV using anhydrous ammonia as the ionizing gas. Quantification was conducted in selected ion monitoring (SIM) mode using a single quadrupole and monitoring the following ions: m/z 92.1 (NDMA + NH_4^+) and m/z 98.1 (NDMA-d_6 + NH_4^+). NDMA was quantified from the ratio of the peak area of the analyte (m/z 92.1) to the internal standard (m/z 98.1).

2.3 NDMA in a Recharge Utility Results and Discussion

2.3.1 NDMA Concentration in the Recharge Utility

NDMA concentration was measured from multiple points in the recharge utility treatment process. The 2017 sampling event focused on the efficacy of microfiltration and RO membrane age on NDMA and NDMA precursor removal. The RO process used Hydranautics ESPA2-LD membranes. The old membranes had been installed for approximately nine years whereas the new membranes had been installed for approximately one year. The pooled RO permeate consisted of permeate from all operating RO membranes. The 2018 sampling event focused on the effects of H_2O_2 addition and contact after RO treatment but before UV/AOP treatment. RO permeate was subjected to H_2O_2 addition or kept at ambient conditions. Both the UV feed and product experienced H_2O_2 addition. Figure 2-7 shows the NDMA concentration determined from each sampling point from both events.

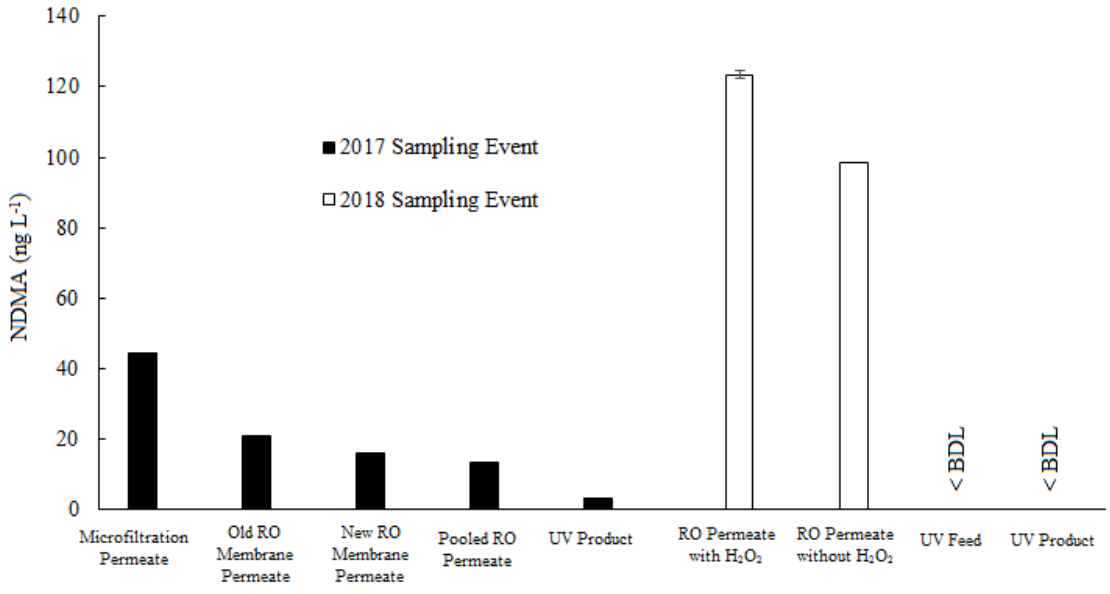


Figure 2-7 NDMA concentration for recharge utility processes from the 2017/18 events. <BDL indicates that NDMA concentration was below the detection limit. Error bars represent individual samples (duplicates) with columns displaying average concentration

NDMA decreased through the advanced treatment system for the 2017 event. There was a 93% decrease between the microfiltration effluent and the UV product, highlighting the effectiveness of advanced treatment on NDMA destruction. 3 ng L^{-1} of NDMA was measured in the UV product despite UV radiation being extremely effective at NDMA photolysis.

The RO membrane age had an effect on NDMA permeation. Older membranes had 31% higher NDMA permeate concentration than newer membranes. The 2017 event had a 59% difference between the pooled RO membrane permeate and the old membrane permeate NDMA concentration, highlighting the removal efficiency fluctuations between membranes of different age.

The 2018 sampling event had an average RO permeate NDMA concentration of 115.1 ng L^{-1}. Compared to the 2017 sampling event, the average RO permeate NDMA concentration was 88% higher. This indicates that there has either been an operational or source water change in the recharge utility or preceding WWTP. Additionally, further RO membrane degradation would likely result in less rejection of NDMA precursors, but unlikely to account for the determined 88% concentration difference. The difference may be due to possible exposure to oxidants during shipping and is discussed later.

Despite the increased NDMA concentration in the RO permeate, no NDMA was detected in the UV feed with H_2O_2 addition. This could be due to NDMA destruction by hydroxyl radicals produced by the H_2O_2 addition or improper addition of a quenching agent prior to shipping.

2.3.2 NDMA Formation Potential

NDMA formation potential (FP) is an indirect measure of the NDMA precursor load and was determined from stages in the recharge utility from the 2017 and 2018 sampling events. The efficacy of the new and old RO membranes in terms of NDMA precursor rejection was determined. Additionally, the NDMA FP after UV/AOP was determined to recognize if any NDMA precursors passed through the full treatment process. Figure 2-8 displays NDMA FP through multiple processes and highlights the NDMA precursor removal efficacy of advanced treatment systems.

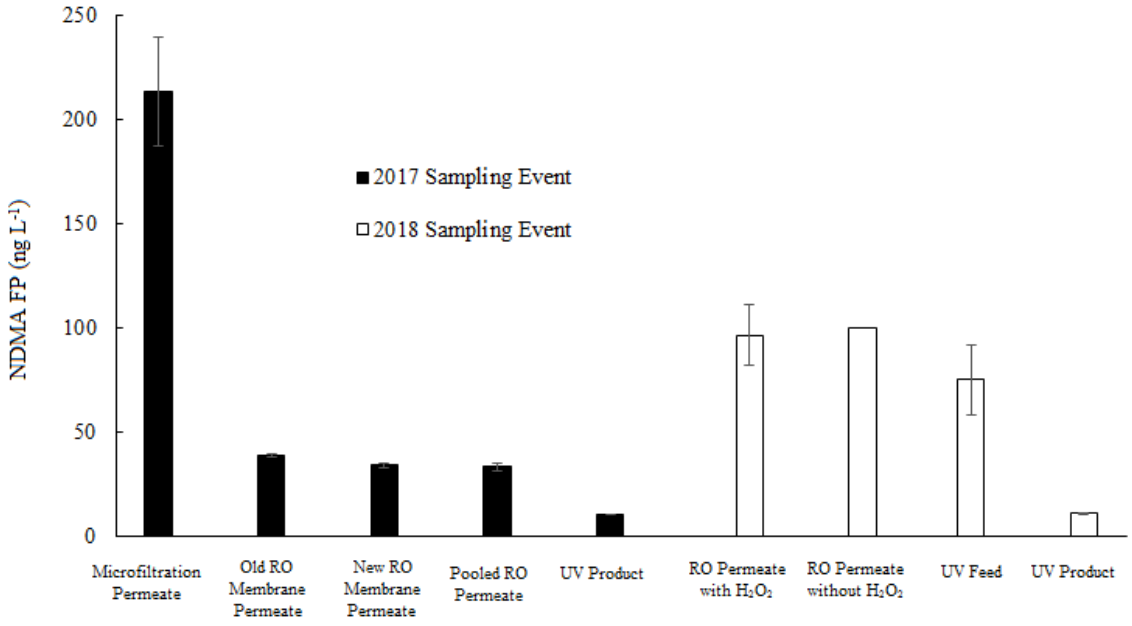


Figure 2-8 NDMA FP concentration for recharge utility processes from the 2017/18 events. Error bars represent individual samples (duplicates) with columns displaying average concentration

Microfiltration permeate contained a considerable amount of NDMA precursors due to the high NDMA formation determined. Microfiltration likely does not effectively remove precursors due to the lack of chemical or biological interaction. An 84% removal of NDMA FP was determined from the microfiltration effluent to the pooled RO membrane permeate. There was 2.3% increased removal of NDMA precursors for the newer membranes compared to the older membranes and a 4.85 ng L^{-1} average removal difference between them. A similar difference was noted for the 2018 sampling event, with the two RO units having on average a 3.55 ng L^{-1} difference. Both sampling events revealed that RO treatment is useful as an intermediate step to remove some precursors prior to UV/AOP, which is necessary as a polishing step. The 2017 and 2018 UV product samples had NDMA FP reductions of 69% and 85%, respectively, from the preceding sampling point. The NDMA FP concentration signifies that despite the applied advanced treatment processes, not all NDMA precursors are removed and may still form relevant NDMA concentration once injected into the subsurface.

2.3.3 NDMA Formation Potential of Reconstituted Precursor Extracts

For the 2017 and 2018 events, NDMA precursor extraction was performed by SPE and samples sent to the University of Colorado, Boulder for LC-QTOF/MS analysis. The analysis aimed at identifying NDMA precursors and is outlined in Chapter 2.3.6. Extracted precursor samples were reconstituted into Milli-Q water and subjected to NDMA FP tests. Analysis of the chloraminated reconstituted extracted samples allowed for precursor recovery calculation. A modified reconstitution method was applied on the 2018 ROP sample to minimize precursors already in the SPE cartridges from eluting into samples. Figure 2-9 shows the NDMA FP for both reconstitution methods.

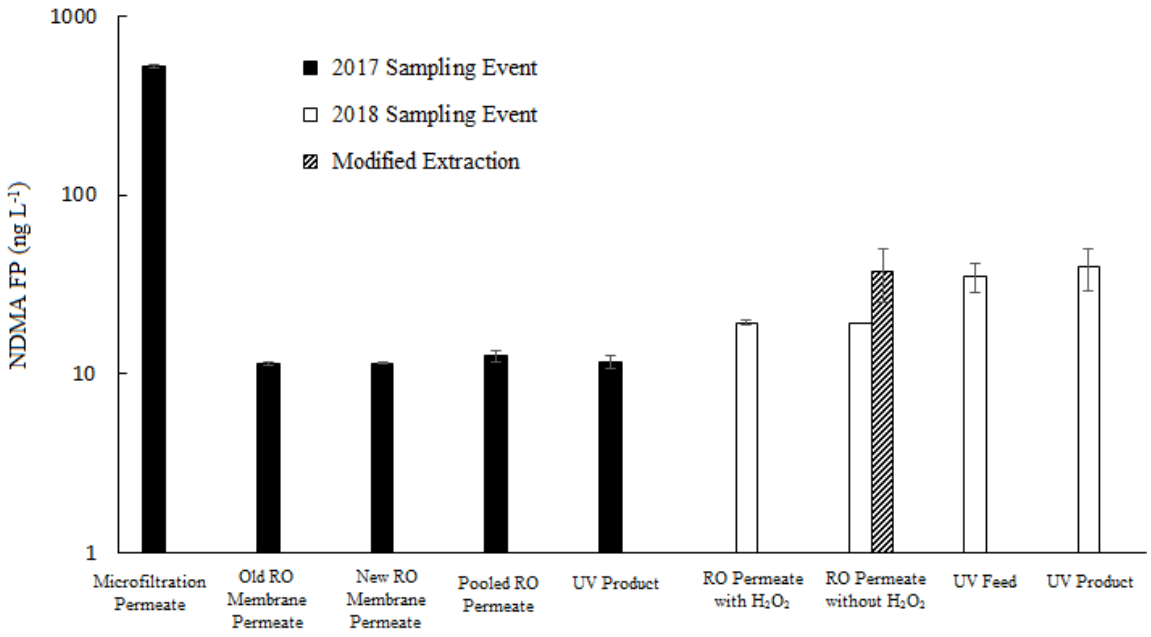


Figure 2-9 Reconstituted NDMA FP concentration for recharge utility processes including the modified extraction method from the 2017/18 events. Error bars represent individual samples (duplicates) with columns displaying average concentration

The 2018 reconstituted UV product had a higher NDMA FP concentration than either of the reconstituted RO permeates or UV feed. Similar to the original NDMA FP tests, this highlights that NDMA precursors are not completely removed during the advanced treatment process and can form significant amounts of NDMA up to 50 ng L^{-1} when isolated.

2.3.4 NDMA Precursor Recovery

Recovery was performed to determine the percentage of the original NDMA precursors that formed following NDMA FP tests. Equation 2-3 gives the calculation for NDMA precursor recovery and Figure 2-10 shows the recovery of selected processes from both sampling events.

Equation 2-3 $$\text{NDMA Precursor Recovery (\%)} = 100 * \left(\frac{\text{Reconstituted NDMA FP (ng L}^{-1})}{\text{NDMA FP (ng L}^{-1}) - \text{T}_0\ \text{NDMA (ng L}^{-1})}\right)$$

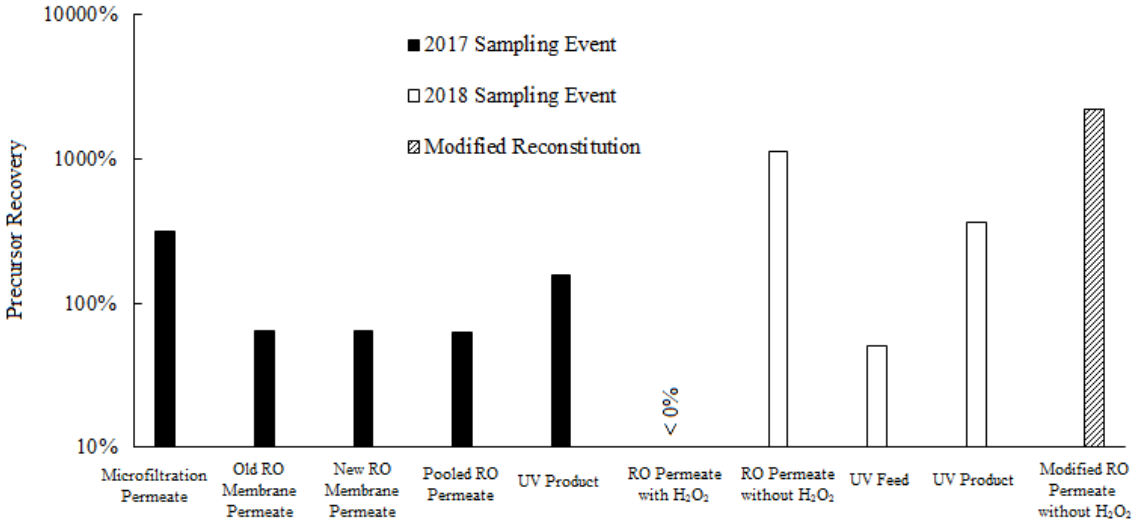


Figure 2-10 NDMA precursor recovery for recharge utility processes. <0% indicates negative recovery due to NDMA FP concentration being greater than NDMA concentration

NDMA precursor recovery was varied and ranged from 51% to greater than 100%. Recovery greater than 100% or less than 0% were potentially due to the low concentration of NDMA precursors that were present in the recharge utility. The impact of low NDMA precursor concentration signifies that a small variation can lead to a large calculation change in recovery. These variations were possible due to the large amount of sample manipulation performed during the process. Sample manipulation involved handling, FP tests, and extraction procedures. Additionally the presence of NDMA or NDMA precursors in the MCX cartridges or solvents could influence recovery if they elute during the extraction process. The modified extraction procedure aimed at limiting NDMA and NDMA precursor elution from the cartridges. Cartridges were conditioned with a base to elute any NDMA or NDMA precursors before being acidified to mimic the conditions in the samples.

The modified method removed the potential for NDMA or NDMA precursors to elute into samples and influence recovery. The recovery for the modified reconstitution process was

greater than 100%, indicating that recovery was probably influenced by the low NDMA precursor concentration. Ultimately, the sample manipulation and low concentration of NDMA precursors are the most likely culprits for poor recovery during the experiment.

2.3.5 NDMA Formation Potential of the Reverse Osmosis Cleaning Solution

A RO membrane cleaning solution is applied at the recharge utility every 9 to 14 months to extend the lifespan and increase membrane performance due to the high expense of replacement. The solution targets removal naturally occurring organic foulants. The solution was comprised of 2.00% weight sodium tripolyphosphate (STP) and 0.20% weight sodium dodecylbenzenesulfonate (Na-DDBS) in RO permeate water. Sodium hydroxide is added until the pH reaches 10.98. The solution component structures are shown in Figure 2-11.

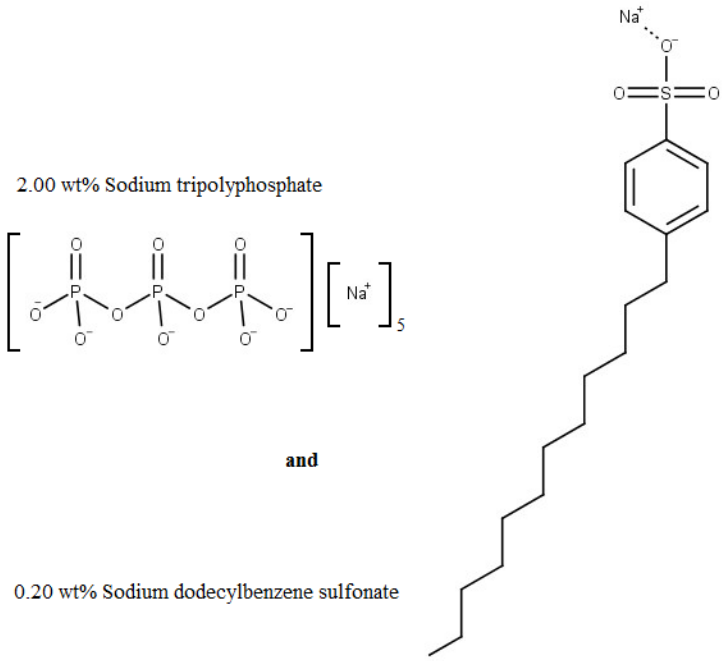


Figure 2-11 Chemical structures of the RO membrane cleaning solution components

The potential for the introduction of NDMA precursors in the cleaning process is dependent on the cleaning solution. Figure 2-12 shows the NDMA formation potential for three dilutions of the cleaning solution in Milli-Q water from the 2017 sampling event.

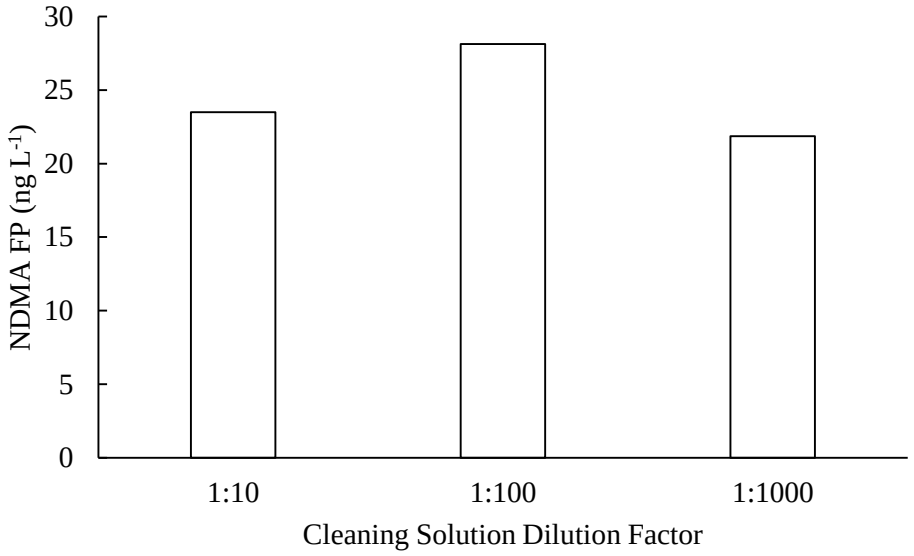


Figure 2-12 NDMA FP concentration for three dilution factors of the RO membrane cleaning solution in Milli-Q water

The cleaning solution components do not contain any secondary, tertiary, or quaternary amine functional groups according to Figure 2-11. Despite the lack of amine functional groups, NDMA FP concentration was within 22% of each dilution. This indicates that the cleaning solution may already contain NDMA precursors in the form of contaminants or unlisted/proprietary additives because the listed constituents should not contribute to NDMA formation based on structure. The dilution factor does not seem to substantially influence NDMA formation potential. This indicates that NDMA precursors may be unintentionally introduced during the FP test or during NDMA solid-phase extraction that markedly contribute to the NDMA FP concentration compared to the cleaning solution constituents.

2.3.6 NDMA Extracted Precursor Mass Spectrometric Analysis

NDMA precursors were identified by non-target mass spectrometric analysis using LC-QTOF/MS, performed by Dr. Imma Ferrer and Dr. E. Michael Thurman at the University of Colorado, Boulder, with results recently published (Roback et al., 2018). Briefly, 22 putative NDMA precursors were identified in RO feed water but none in the UV product. Five trace compounds were detected in the UV product. Three of these compounds (DEET, lamotrigine, and sulfamethoxazole) are not NDMA precursors, although DEET can form *N*-nitrosodiethylamine (NDEA), albeit at yields less than 1% (Shen & Andrews, 2011). The other two compounds were likely transformation products from UV/AOP treatment, but have an unknown NDMA FP.

2.4 NDMA in the Recharge Utility Conclusions

Water and cleaning solution samples from the recharge utility were investigated from two events to determine the concentration of NDMA formed and to identify its precursors. NDMA formation through the advanced treatment system was quantified to establish the efficacy of each treatment process to remove NDMA and its precursors. The following is a summary of the findings:

- NDMA concentration decreased through the recharge utility from 44 ng L^{-1} to 3 ng L^{-1} for the 2017 event and from 123 ng L^{-1} to < 2 ng L^{-1} for the 2018 event.
- NDMA FP concentration decreased through the recharge utility from 214 ng L^{-1} to 10 ng L^{-1} for the 2017 event and from 97 ng L^{-1} to 11 ng L^{-1} for the 2018 event.
- Permeate from older membranes contained 31% more NDMA than the newer membrane permeate. The NDMA FP decreased by 2.3% for the newer membranes, highlighting that they might have a slightly improved removal performance for NDMA precursors.
- The RO membrane cleaning solution had an NDMA FP of 22-28 ng L^{-1} with the dilution factor having no effect on NDMA formation.

2.5 NDMA in a Pilot Plant

2.5.1 NDMA Concentration in Pilot Plant Processes

NDMA concentration in the pilot plant was quantified to determine NDMA formation from ozonation as well as the effectiveness of BAC for NDMA and NDMA precursor removal. The WWTP feeding the pilot plant does not apply chlorine or ozone prior to water entering the pilot plant, thus limiting NDMA formation. Figure 2-13 shows the NDMA concentration in the pilot plant.

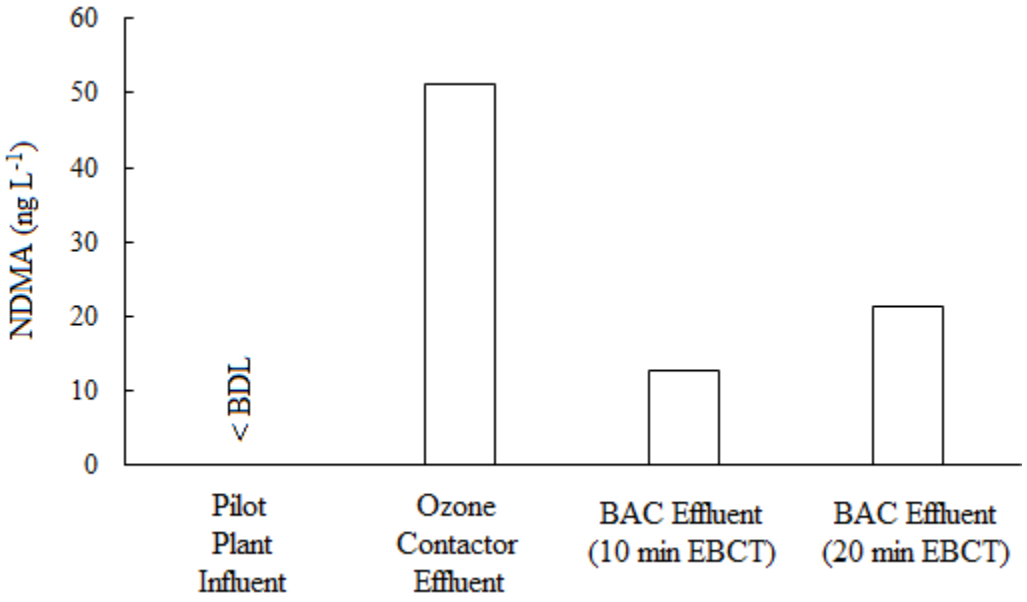


Figure 2-13 NDMA concentration from different processes in the pilot plant. BAC filters were operated in parallel and had different EBCTs. <BDL indicates that NDMA concentration was below the detection limit

The pilot plant influent did not contain NDMA above the detection limit of 2 ng L^{-1}. The ozone effluent water contained 51 ng L^{-1} NDMA. The high concentration of NDMA observed was due to ozone oxidation of organic material present in the secondary effluent. The applied ozone dose can also influence NDMA formation, with an increased dose leading to increased NDMA formation (Marti et al., 2015). Currently, the dose is regulated on a fixed ozone to total organic carbon (TOC) ratio, with a dose range of 6-20 mg L^{-1} O_3, but was not observed at the time of sampling. Thus, it is difficult to predict whether the typical NDMA concentration at the pilot plant is lower or higher.

Effluent of the BAC filters had an NDMA concentration of 13 ng L^{-1} for BAC 1 (8 gpm, 10 min EBCT) and 21 ng L^{-1} for BAC 2 (4 gpm, 20 min EBCT). This constituted a 75% and 58% reduction of NDMA from the ozone contactor, respectively. The increased NDMA removal efficiency of BAC 1 was surprising given that its EBCT is half that of BAC 2. The removal difference is likely due to variability between biomass communities in each filter. Additionally, Lagrangian sampling was not performed and thus the water composition was likely different.

Following pilot plant discharge, water is circulated back to the WWTP headworks. Effluent from the WWTP is reused or stored in a reservoir. Sunlight photolysis would therefore destroy any NDMA formed in the pilot plant, indicating that NDMA release is not an issue.

2.5.2 NDMA Formation Potential in the Pilot Plant

NDMA FP in the pilot plant was measured to determine the level of NDMA precursor loading, reduction of NDMA precursor concentration, and subsequent NDMA formation. Figure 2-14 shows the NDMA FP for each process

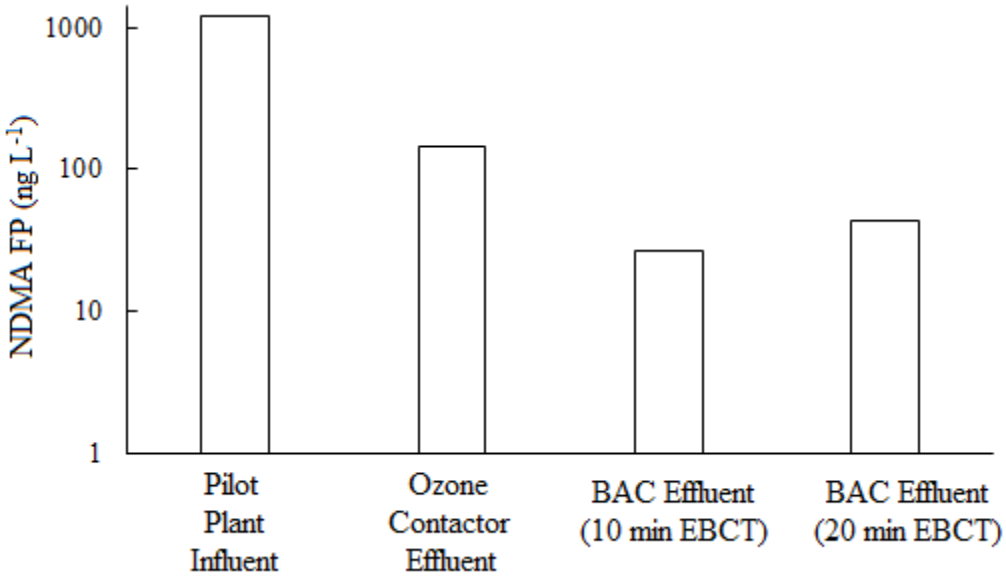


Figure 2-14 NDMA FP concentration from different processes in the pilot plant. BAC filters were operated in parallel and had different EBCTs

The pilot influent water had an NDMA FP of 1201 ng L^{-1} due to the large amount of reactive material in the secondary clarifier effluent. The NDMA FP of the ozone contactor effluent was 147 ng L^{-1}, an 88% reduction from the pilot influent water. The BAC filter effluents had an NDMA FP of 27 ng L^{-1} and 44 ng L^{-1}, respectively. On average, a 76% reduction was achieved by subjecting organic constituents in the wastewater to the BAC process. Again, the first BAC filter performed more effectively in removing NDMA precursors to limit formation despite having half the EBCT of the second filter. It was expected that the second filter would exhibit higher biodegradation and sorption of NDMA precursors.

Regardless, the FP tests confirmed the degradative ability of ozone contact and BAC on NDMA precursors. Ideally, multiple processes in series would be used to steadily degrade and remove NDMA precursors due to a single process not being sufficient for effective removal.

2.6 NDMA in the Pilot Plant Conclusions

NDMA and NDMA FP were quantified in water samples from a pilot plant. The following is a summary of the findings:

- NDMA was not detected in the pilot plant influent due to the lack of pre-chloramination or ozonation. The pilot plant influent had an NDMA FP concentration of 1201 ng L^{-1} due to NDMA precursors entering the pilot plant from the secondary clarifier effluent.
- The ozonation effluent had an NDMA concentration of 51 ng L^{-1} and an NDMA FP concentration of 147 ng L^{-1}. Ozonation of the secondary clarifier effluent reinforced the potential for ozonation to both form NDMA while simultaneously destroying NDMA precursors by 88%.
- The BAC columns decreased NDMA by 58-75% and NDMA FP by 70-82%. Higher NDMA and NDMA FP reduction was exhibited by the BAC column with a shorter EBCT.
- The pilot plant effluent had an average NDMA concentration of 17 ng L^{-1}. The NDMA formed in the pilot plant would be destroyed by sunlight photolysis following discharge from the WWTP.

Chapter 3 PPCP Uptake from Crop Irrigation using Reclaimed Wastewater

3.1 PPCPs in Crops Literature Review

3.1.1 PPCP Removal in Wastewater Treatment

Humans excrete 70% (±35%) of the parent compound and metabolites of PPCPs via urine and 22% (±25%) via feces (Lienert, Güdel, & Escher, 2007), after which many are poorly removed during conventional wastewater treatment (Heberer, 2002). Sludge retention time (SRT) has been investigated in lab-scale studies to determine the role it plays in influencing PPCP removal. A compound-dependent SRT of 25 days had greater than 80% removal of PPCPs (Oppenheimer, Stephenson, Burbano, & Liu, 2008). Conventional treatment has a limited scope for removal of PPCPs even if the SRT is increased significantly.

Alternative or advanced treatment technologies consisting of advanced oxidation, membrane filtration, and combined sequence reactors are effective at degrading or removing PPCPs. Due to the differing physicochemical properties of PPCPs, no single advanced treatment technology is a panacea for removal. Rather, a combination of processes can constitute thorough removal. Membrane filtration is effective for PPCP removal, however a combination of membrane filtration with advanced oxidation processes mitigates their respective disadvantages, such as membrane fouling and generation of toxic intermediates (Ganiyu, van Hullebusch, Cretin, Esposito, & Oturan, 2015). Advanced oxidation is an effective treatment option for destroying antibiotics (Homem & Santos, 2011), exhibiting a 99% reduction in amoxicillin resulting from ozonation (Marcelino, Leão, Lago, & Amorim, 2017). Similarly, Electro-Fenton treatment in tandem with sequencing batch reactors (SBRs) can degrade PPCPs in wastewater in less than two hours (Ganzenko et al., 2017).

Some PPCPs are recalcitrant and are difficult to remove even with advanced treatment. Carbamazepine removal was less than 10% through a variety of activated sludge processes including biotransformation, air stripping, sorption, and phototransformation (Zhang, Geissen, & Gal, 2008). Sucralose is resistant to a wide variety of treatment processes. Microbial degradation, hydrolysis, and soil sorption have been coupled with advanced treatment processes including chlorination, ozonation, activated carbon adsorption, and UV radiation to remove sucralose. Hydrolysis, ozonation, and microbial processes were effective at degrading sucralose yet only to a limited extent and not at conditions found within a treatment facility (Soh, Connors, Brooks, & Zimmerman, 2011). In some cases, adsorption to activated carbon has been effective at removing PPCPs at above 80%, but has produced a new residue (Homem & Santos, 2011). There is a wealth of information needed to further understand environmental treatment plant factors such as biodegradable dissolved organic carbon, redox mediators, catalytic surfaces, metal ions (Ghattas, Fischer, Wick, & Ternes, 2017), and how this pertains to biodegradation and PPCP removal. Bromide ion addition during UV/chlorine treatment of simulated drinking water has resulted in 1.6-23 times more removal for a wide range of PPCPs belonging to various classes (Cheng et al., 2018).

Removal of PPCPs in wastewater treatment does not encompass their environmental fate, given that they can be removed, degraded, or otherwise unaffected by treatment processes. There is currently not enough information regarding PPCP environmental accumulation after entering a treatment plant. For example, PPCPs treated with bromine ion addition may or may not release bromine-substituted compounds to the environment. PPCPs can also sorb to sludge in removal processes that are then sent to a landfill where leaching is possible (Dong et al., 2016). More information is required to determine the complete fate of PPCPs through the aquatic and terrestrial environment to complete a mass balance from consumer use to environmental release.

3.1.2 PPCP Fate in Soil

PPCP fate in soil is determined by factors including sorption, soil composition, and degradation. Sorption is one of the most important factors in determining the bioavailability of a PPCP with increased soil sorption leading to decreased uptake. Sorption primarily depends on pH, soil organic matter content, and PPCP concentration in the irrigation water. Sorption in relation to soil pH is particularly important when considering PPCP bonding to clay soils.

3.1.2.1 pH Effects

Sorption of PPCPs due to cation exchange has been primarily observed for antibiotics, anticonvulsants, and beta blockers. Antibiotics have predominantly been studied due to the prevalence of these compounds in the environment and in particular their interaction with the soil microbiome. Soil pH affects sorption by influencing PPCP charge, with acidic soil conditions having an increased amount of neutral and positively charged species that electrostatically bind to the soil (Ding et al., 2016; Park & Huwe, 2016). Sorption of tetracyclines, fluoroquinolones, trimethoprim, and sulfonamides indicate that cation exchange is the controlling process for acidic conditions (Gao & Pedersen, 2005; Jones, Bruland, Agrawal, & Vasudevan, 2005; Kodešová et al., 2015; Kulshrestha, Giese, & Aga, 2004; Kurwadkar, Adams, Meyer, & Kolpin, 2007; Wegst-Uhrich, Navarro, Zimmerman, & Aga, 2014). A pH range for typical crop-growing conditions of 4-8 exhibits maximum sorption potential (Park & Huwe, 2016), signifying that PPCPs are likely sorbed to soil following treated wastewater irrigation. Translocation of weakly acidic PPCPs can be increased due to the increase in soil pH following irrigation (Borgman & Chefetz, 2013). Acidic soil conditions typically result in greater sorption for antibiotics and is dependent on specific soil characteristics (Borgman & Chefetz, 2013; Gu, Karthikeyan, Sibley, & Pedersen, 2007; Kodešová et al., 2015; Kulshrestha et al., 2004; Kurwadkar et al., 2007; Park & Huwe, 2016; Zhang, Lin, Dai, Shi, & Zhou, 2014).

3.1.2.2 Organic Matter Content

Organic matter in soil influences PPCP sorption and mobility, and is typically made up of 40-60% carbon by mass (Schwarzenbach, Gschwend, & Imboden, 2003). Typically, soils rich with organic matter exhibit a higher sorption potential for a range of pharmaceutical classes than those with a low organic matter content (Chefetz, Mualem, & Ben-Ari, 2008; Revitt, Balogh, & Jones, 2015; Zhang et al., 2014). This is especially important for compounds of emerging concern and also for areas with historically low organic matter contents, such as semi-arid sites (Chefetz et al., 2008). Agricultural soil typically contains between 3-7% organic matter (FAO, 2017; Fenton, Albers, & Ketterings, 2008). Soil transport of PPCPs into the groundwater can thus be negated by increasing the organic matter content of the soil. It is especially important to retain PPCPs in the upper soil layers to reduce their capacity to enter the groundwater and to induce biotic and abiotic degradation processes. Sorption of PPCPs to organic matter typically involves van der Waals interactions and hydrogen bonding (Thiele-Bruhn, Seibicke, Schulten, & Leinweber, 2004). Due to these weak bond types, sorption of PPCPs can be reversible and is influenced by the irrigation solution chemistry (Borgman & Chefetz, 2013).

3.1.2.3 PPCP Degradation in Soil

Degradation of PPCPs with particular focus on antibiotics has been thoroughly investigated. The emphasis on antibiotics is due to the potential for antibiotic resistance proliferation in soil microbiota. Under field conditions, erythromycin and clarithromycin were on average 75 times less persistent in soil that had been exposed to environmentally reasonable antibiotic levels (0.1 mg kg^{-1}) and 86 times less persistent in soils exposed to unreasonably excessive levels (10 mg kg^{-1}) (Topp, Renaud, Sumarah, & Sabourin, 2016), highlighting that microbial degradation of antibiotics was promoted due to a history of exposure. Conversely, loading rates for five PPCPs and one antibacterial of 1 mg kg^{-1} resulted in inhibited microbial

activity and degradation compared to lower loading rates in a laboratory study (Xu, Wu, & Chang, 2009), indicating that prior soil loading of PPCPs and consequent degradation is concentration and compound dependent.

The interaction between PPCPs and soil microbiota primarily occurs in the top soil, with microbial degradation able to remove a wide range of PPCP classes including beta blockers, lipid regulators, anti-inflammatories, and antibiotics (Grossberger, Hadar, Borch, & Chefetz, 2014; Ternes, Bonerz, Herrmann, Teiser, & Andersen, 2007). Biotic and abiotic soil transformation processes have been studied in different agriculturally relevant soil types, with sterile soils leading to an increased half-life and decreased degradation rates of PPCPs compared to non-sterile soils (Xu et al., 2009; Yang et al., 2009). Abiotic factors such as chemical hydrolysis contribute to PPCP degradation wherein sulfadiazine was degraded in sterile soil (Yang et al., 2009). Loam soil has higher degradation rates of antibiotics compared to clay loam and loamy sand soil (Wu, Williams, Smith, Chen, & Kookana, 2012), indicating that higher organic matter content soils exhibit lower degradation rates (Xu et al., 2009).

3.1.2.4 Transformation Products

Transformation products (TPs) of PPCPs form from a mixture of physical, chemical, and biological processes (Dévier, Mazellier, Aït-Aïssa, & Budzinski, 2011). TPs have properties that are compound dependent, with toxic and stable products capable of forming (Ternes et al., 2007). In soil, the antibiotics clindamycin, sulfamethoxazole, and trimethoprim have been detected with 80% of their products being more persistent than the parent compounds (Koba, Golovko, Kodešová, Fér, & Grabic, 2017). Additionally, some TPs can revert back to the parent compound in the environment. Demethylation of methyl triclosan was observed using an environmentally relevant concentration of 1 mg L^{-1} found in active sludge and biosolids. Methyl triclosan can demethylate to triclosan in the roots and leaves of carrot and lettuce plants grown under

hydroponic conditions (Fu, Liao, Du, Schlenk, & Gan, 2018). Triclosan concentration was 11.5 ± 5.5 μg g^{-1} in lettuce and 3.7 ± 2.2 μg g^{-1} in carrot. Some unaccounted loss of triclosan was observed with sorption to soil or other media the most likely culprit. Reversion of a TP to its parent compound could pose an environmental risk in terms of persistence and exposure, especially for antibacterial compounds that may proliferate antibiotic resistance once reverted to the parent compound. Determining which types of PPCPs display reversion would be useful for field applications that have a wider range of environmental unknowns compared to more controlled hydroponic studies.

3.1.3 Plant Uptake of PPCPs

3.1.3.1 PPCP Uptake in Plant Components

PPCPs accumulate in plant fruits, leaves, roots, shoots, and stems following water uptake from soil, with PPCP internal translocation following the transpiration stream. PPCP internal translocation is continually driven as plants are irrigated (Wu, Spongberg, Witter, Fang, & Czajkowski, 2010), and maximum PPCP concentration occurs in plant leaves or roots, dependent on specific plant physiology and compound properties (Al Nasir & Batarseh, 2008; Calderón-Preciado, Renault, Matamoros, Cañameras, & Bayona, 2012; Eggen, Asp, Grave, & Hormazabal, 2011; Mathews, Henderson, & Reinhold, 2014; Shenker, Harush, Ben-Ari, & Chefetz, 2011; Tanoue et al., 2012; Wu et al., 2010; Wu, Conkle, Ernst, & Gan, 2014). Leaf accumulation is due to PPCPs translocating with the water stream, whereas root accumulation is due to an inability for compounds to transition across root membranes (Colon & Toor, 2016).

PPCP translocation has been observed in hydroponic and field studies using reclaimed wastewater sometimes spiked with environmentally relevant PPCP concentrations (Wu et al., 2014). Cucumbers are one of the most frequently studied plants, likely due to their ease of cultivation. Bioaccumulation factors of 500 have been determined for cucumber leaves spiked

with 1-3 µg L^{-1} carbamazepine (Shenker et al., 2011). However, roots for a range of plants (bell pepper, cabbage, carrot, celery, cucumber, eggplant, lettuce, maize, okra, onion, soybean, spinach, and tomato) typically have higher PPCP concentration than leaves (Al Nasir & Batarseh, 2008; Eggen et al., 2011; Mathews et al., 2014; Wu et al., 2014). Various governing factors for PPCP plant uptake make it difficult to apply a single rule that describes all uptake possibilities. However, there is evidence that PPCP uptake can be somewhat generalized with plants of the same family having similar trends and thus grouped accordingly (Al Nasir & Batarseh, 2008). This general rule has great potential for further study due to the number of plants and PPCPs that could interact through treated wastewater irrigation.

Common plant families include bulb vegetables (garlic, leek, and onion), cereal grains (corn, rice, wheat, and oilseed crops like soybean), cole crops (broccoli, cabbage, cauliflower, kale, mustard, radish, and turnip), curcubits (cantaloupe, cucumber, pumpkin, squash, and watermelon), fruiting vegetables (bell pepper, eggplant, and tomato), leafy vegetables (lettuce), and root and tuber vegetables (carrot) (Colon & Toor, 2016). Uptake trends between plants of the same family occur due to their physiological similarities, while marked uptake differences occur between plants from different families. A concurrent study of cucumber and tomato fruits found that both plants were able to uptake ionic (ibuprofen and clofibric acid) and neutral (carbamazepine, caffeine, and sulfamethoxazole) compounds from treated wastewater. Carbamazepine concentration in cucumber was 11 times greater than that of tomato, whereas multiple other compounds were quantified in cucumber but undetected in tomato (Goldstein, Shenker, & Chefetz, 2014). This is akin to other findings of fruiting vegetables taking up PPCPs but in markedly less concentration than other plant types (Mathews et al., 2014; Wu et al., 2014).

Investigation of PPCP translocation is valuable to implement introduction of cultivation practices that limit PPCP uptake to edible plant components, thereby reducing any health risks associated with consumption. Conversely, beneficial synergistic relationships between PPCPs and

plans regarding growth could constitute specific cultivation of target plants. Findings suggest that crops with edible stems and fruits, rather than leaves and roots should be cultivated under treated wastewater irrigation to limit the possibility of unwanted human uptake of PPCPs. The edibility of plant components is important to consider when investigating plant uptake. Accumulation of PPCPs in inedible plant components poses less of a health risk than accumulation in edible components. Limited information regarding the effects of cooking practices on PPCPs in edible plant components exists. Peeling root vegetables such as carrots was found to have no significant effects in reducing lamotrigine and epoxy-carbamazepine (CBZ-EP) concentration (Malchi, Maor, Tadmor, Shenker, & Chefetz, 2014). Cooking practices and plant component edibility are culturally and geographically diverse, demonstrating that there is no general rule governing worldwide consumption of PPCPs in treated wastewater irrigate crops.

3.1.3.2 Physicochemical Property Effects on Plant Uptake and Translocation

The octanol-water partitioning coefficient (log K_{ow}) is a reliable predictor for PPCP plant uptake and translocation (Briggs, Bromilow, & Evans, 1982). Log K_{ow} values roughly below 2 indicate hydrophilic compounds whereas values above 3 indicate hydrophobic compounds. PPCPs are typically hydrophilic or somewhat hydrophobic. Hydrophobic compounds have intermediate log K_{ow} values and exhibit diffusion across cell membranes, allowing transport into roots and translocation (Christou, Karaolia, Hapeshi, Michael, & Fatta-Kassinos, 2017; Engwall & Hjelm, 2000; Trapp, 2009). Hydrophilic compounds transport with the transpiration stream and can be taken up by plants, however highly hydrophilic compounds tend to accumulate in roots because they cannot permeate root membranes (Tanoue et al., 2012). Small, hydrophilic compounds have increased translocation efficiency due to being readily transported by xylem sap, which acts as a water and nutrient conveyor (Boxall et al., 2006; Briggs et al., 1982; Dettenmaier, Doucette, & Bugbee, 2009; Hyland, Blaine, Dickenson, & Higgins, 2015; Hyland, Blaine, &

Higgins, 2015). Log K_{ow} values cannot solely be used to describe PPCP uptake, due to weak acidic and weak basic compounds having the potential to be ionized by the pH of the soil and plant component (Goldstein et al., 2014).

Uptake and translocation of neutral and ionic compounds depends on the potential to cross cell membranes and plant physiology (Bromilow, Chamberlain, & Avis, 1990). Negatively charged plant cells repel ionic PPCPs (Tanoue et al., 2012). Cell membrane electrostatic rejection thus results in improved translocation for neutral compounds compared to ionic compounds (Edgington, 1981). Carbamazepine has accumulated five and 100 times greater in cucumber and tomato leaves, respectively, than lamotrigine, despite both compounds having similar log K_{ow} values. Accumulation discrepancies were due to partial ionization of lamotrigine and a subsequent inability to cross cell membranes (Goldstein et al., 2014). Carbamazepine has also been taken up by ryegrass approximately 600 times more than the ionic compounds diclofenac, fluoxetine, and propranolol (Carter et al., 2014), further indicating that charge rejection is the controlling factor for uptake. Ionic compounds that cross root membranes can be trapped in plant phloem, resulting in lower leaf concentration and higher fruit concentration. This suggests that fruits with high water contents have the potential for PPCP accumulation (Bromilow et al., 1990).

3.1.3.3 Impact on Biomass Growth

Plant growth inhibition from PPCP uptake may present a challenge for the applicability of treated wastewater irrigation. Plant roots have been predominantly studied because they are the first point of contact during uptake. Root growth and number are typically examined along with other factors like seed germination, photosynthesis, chlorophyll content, suppression of free branching, and reproduction rate (Bártíková, Podlipná, & Skálová, 2016).

Antibacterials have been predominantly studied to determine their impact on growth inhibition. Statistically significant differences of promotion and inhibition in wheat grown with tetracyclines has been determined. Root length promotion of 18% was found at a chlortetracycline concentration of 0.125 mg L^{-1} and a mitotic index promotion of 7% was found at a concentration of 0.25 mg L^{-1}. Inhibition was statistically significant at 25 mg L^{-1} for seed germination, root length, and mitotic index with decreases of 10%, 14%, and 6%, respectively. The antibacterial nature of chlortetracycline and improved uptake of nutrients into wheat is a possible explanation of promotion at a concentration below 0.25 mg L^{-1} (Xie, Zhou, He, & Bao, 2010). Wheat grown with oxytetracycline resulted in statistically significant root activity promotion of 16% at 5 mg L^{-1} and inhibition of 11% at 9 mg L^{-1}. Root number was also significantly inhibited by 57% at 5 mg L^{-1} (Li, Xie, Zhang, & Liang, 2011). Alfalfa grown with oxytetracycline in concentrations greater than 0.9 mg L^{-1} resulted in statistically significant shoot and root biomass inhibition of 60% and 80%, respectively. The alfalfa shoots wilted at 4.6 mg L^{-1} and leaves became weakly green at 9.2 mg L^{-1} (Kong et al., 2007).

Studies involving PPCPs from classes other than antibiotics have been performed. Ciprofloxacin, metformin, and narasin produced inhibition of carrot growth and development when spiked with 10 mg kg^{-1} of compound. This effect was most pronounced for narasin with the difference in biomass between the control and the spiked carrot root being approximately 30g. The carrot leaf also observed a biomass decrease of about 10g between the control and the spiked plant (Eggen et al., 2011). Acetaminophen spiked into mustard plants at 1 mM has resulted in inhibited plant growth. Additionally, detrimental visible changes also occurred after 1 week of exposure including leaf bleaching, lesions, and brownish discoloration (Bartha, Huber, Harpaintner, & Schröder, 2010). This is a sign of oxidative stress in the plant and results in irreversible damage.

In contrast, no observable growth inhibition was found for lettuce spiked with clofibric acid, hydrocinnamic acid, ibuprofen, naproxen, tonalide, and triclosan at a concentration of 0.1 mg L^{-1} (Calderón-Preciado et al., 2012). Similarly, radish and ryegrass have displayed no observable growth inhibition when grown with carbamazepine, diclofenac, fluoxetine, propranolol, sulfamethazine, and triclosan at an environmentally relevant level of 1 mg kg^{-1} (Carter et al., 2014). Another study involving ryegrass spiked with carbamazepine at a concentration range of 202-426 μg kg^{-1} displayed no growth inhibition (Winker, Clemens, Reich, Gulyas, & Otterpohl, 2010).

The findings highlight that growth inhibition of plants is concentration dependent, with higher concentration leading to an increased probability for impacted growth. For growth promotion, the interaction is concentration, compound, and plant specific, with antibiotics seemingly promoting plant growth more so than other PPCP classes.

3.1.3.4 Hydroponic Versus Field Studies

Plant uptake of pharmaceuticals has been extensively studied in greenhouses yet there is a lack of field-based data. There are a number of factors that make field-based studies more difficult such as weather, soil microbial activity, and wildlife interference. Due to the poorly controlled growing environment, PPCPs are typically taken up in smaller concentrations and can be absent in field studies while being substantially taken up by plants in greenhouses (Wu et al., 2010; Wu et al., 2014). Fluoxetine has been readily taken up in greenhouse studies yet absent in field studies. This is most likely due to the ionic and somewhat hydrophobic properties of fluoxetine, that increases sorption tendency to negatively charged soil particles (Wu et al., 2014), highlighting that field soil properties can also impact uptake. Another cause of PPCP absence in field studies is due to biotic degradation. Acetaminophen, a widely used analgesic, has also not been taken up by an array of plants in field conditions (Wu et al., 2014). Acetaminophen is

neutral, weakly sorbs to soils, and should therefore be readily available for plant uptake. However, acetaminophen is easily degraded by microorganisms in soils (Li, Ye, & Gan, 2014), highly reducing its uptake. Conversely, there are instances in which there were no statistical differences in PPCP uptake between field and greenhouse-grown plants. Benzotriazole has been taken up in similar amounts by greenhouse and field grown strawberries which were irrigated using similar exposure levels of benzotriazole (LeFevre et al., 2017). Although benzotriazole is a corrosion inhibitor and not a PPCP, it is interesting to see similar uptake levels from both types of studies.

3.1.4 Human Health Risk

3.1.4.1 Threshold of Toxicological Concern

For plant uptake of PPCPs, human health risk has typically not been quantitatively evaluated. A common method to determine exposure risk is the threshold of toxicological concern (TTC). The method involves risk characterization for compounds that do not have available toxicity data and provides an approximation of the exposure level for any compound of potential toxicity. Exceeding the TTC level indicates that further toxicity data is needed. Cramer et al., (1976) and Kroes et al., (2004) categorized compounds as Class I, II, III, or potentially genotoxic compounds, in relation to the TTC. Class III and potentially genotoxic compounds have a TTC value of 1500 ng kg^{-1} and 2.5 ng kg^{-1} of body weight per day, respectively, due to reactive functional groups and potential DNA interaction. Although PPCPs themselves are not genotoxic, some carbamazepine metabolites can be genotoxic (Bleeker et al., 1999; Leclercq et al., 2008), indicating that investigation of PPCPs is still important. Table 3-1 shows dry mass PPCP concentration in plants and importance, based off Cramer and Kroes' categorization and daily intake.

Table 3-1 Plant uptake of PPCPs and importance. Studies conducted in the field with treated wastewater irrigation

Compound	Concentration in Irrigation Water	Concentration (ng g^{-1} dry mass)	Importance	Reason
Bezafibrate	1.19 µg L^{-1} (Malchi et al., 2014)	Carrot leaves (3.49-5.93), roots (1.5-5.91)	LOW	Class III ionic compound. Limited plant uptake, unrealistic daily consumption based on TTC
Caffeine	1.55 µg L^{-1} (Malchi et al., 2014)	Carrot leaves (4-7.5)	LOW	Class III neutral compound. Unrealistic daily consumption based on TTC
	0.25 µg L^{-1} spiked (Wu et al., 2014)	Sweet potato leaves (5.5-6), roots (1-2) Mature carrot root (0.43±0.06) Celery stem (0.17±0.04)		
Carbamazepine	1.7 µg L^{-1} (Riemenschneider et al., 2016)	Arugula leaves (60.7), roots (37.6), shoots (7.5) Cabbage fruits (9.8), leaves (79), roots (61.4) Carrot leaves (61.2), roots (13.9) Eggplant fruits (32.2), leaves (77.6), roots (192.6), shoots (14) Parsley leaves (90.6), roots (40.8) Lettuce leaves (215.7), roots (26.7) Pepper fruits (8.3), roots (40), shoots (30.2) Potato leaves (173.1), roots (76.6), shoots (59.6) Tomato fruits (5), roots (26.7), shoots (40.9) Zucchini fruits (6.8), leaves (41.9), roots (69), shoots (9.3)	LOW	Class III neutral compound. Unrealistic daily consumption based on TTC despite increased and widespread uptake compared to other compounds
	0.25 µg L^{-1} spiked (Wu et al., 2014)	Mature cucumber fruit (0.02±0.02) Premature cabbage leaf (0.04±0.01) Premature celery stem (0.01±0.01) Premature and mature lettuce leaf (0.02±0.03, 0.04±0.01) Premature and mature spinach leaf (0.01±0.02, 0.01±0.02)		
	1.35 µg L^{-1} (Malchi et al., 2014)	Carrot leaves (13-22), roots (6-8) Sweet potato leaves (3-5), roots (0.5-1)		
Epoxy-carbamazepine	0.5 µg L^{-1} (Riemenschneider et al., 2016)	Arugula leaves (33.5), roots (22.4), shoots (6.5) Cabbage fruits (4.5), leaves (18.6), roots (12.8) Carrot leaves (53.5), roots (7.7) Eggplant fruits (11.8), leaves (45.4), roots (22.1), shoots (14.5) Lettuce leaves (89.4), roots (10.1) Parsley leaves (21), roots (24.9) Pepper roots (3.5) Potato leaves (138.1), roots (14.1), shoots (5.3) Tomato roots (3.3), shoots (12.3)	HIGH	Potentially genotoxic compound and more toxic than parent compound. TTC exceeded for a 70kg adult by the daily consumption of 1 potato (100g) or half an eggplant (177g). TTC exceeded for a 25kg child by the daily consumption of sweet potato leaves (90g) or carrot leaves (25g). Commonly eaten in Asia/Africa
	1.35 µg L^{-1}as CBZ prior to plant metabolization (Malchi et al., 2014)	Zucchini fruits (7.1), leaves (25.8), roots (43.6), shoots (5.5) Sweet potato leaves (14.78-65.81), roots (0.09-2.7) Carrot leaves (14.78-65.81), roots (0.09-2.7)		
Carbamazepine-dihydroxide	6.4 µg L^{-1} (Riemenschneider et al., 2016)	Carrot leaves (20.3), roots (7.4) Lettuce leaves (41.5), roots (19.1) Parsley leaves (11), roots (24.8) Potato leaves (13.6), roots (4.7), shoots (3.4)	LOW	Class III compound that has a limited uptake in plants compared to other metabolite CBZ-EP, unrealistic daily consumption based on TTC
	1.35 µg L^{-1} as CBZ prior to plant metabolization (Malchi et al., 2014)	Carrot leaves (0.31-2.91) Sweet potato leaves (0.31-2.91)		
Ciprofloxacin	0.3 µg L^{-1} (Riemenschneider et al., 2016)	Cabbage fruits (6.7) Carrot roots (12)	HIGH	Potentially genotoxic compound. TTC exceeded for a 70kg person by the daily consumption of 1 potato (100 g/day) or half an eggplant (177 g/day)
Clofibric acid	0.94 µg L^{-1} (Malchi et al., 2014)	Carrot leaves (0.43-2.43), roots (<0.8) Sweet potato leaves (0.43-2.43), roots (<0.8)	LOW	Class III ionic compound. Unrealistic daily consumption based on TTC
DEET	0.25 µg L^{-1} spiked (Wu et al., 2014)	Premature carrot root (2.8±0.2)	LOW	Neutral ingredient in insect repellent. Unrealistic daily consumption based on TTC

Dilantin	0.25 µg L^{-1} spiked (Wu et al., 2014)	Mature lettuce leaf (0.11±0.19) Spinach leaf (0.08±0.13)	LOW	Basic compound. Lack of reactive functional groups and genotoxic abilities leads to an unrealistic daily consumption based on TTC
Gabapentin	1.7 µg L^{-1} (Riemenschneider et al., 2016)	Arugula leaves (36.3) Carrot roots (10.1) Parsley leaves (22.1), roots (29) Potato leaves (32.4)	LOW	Class III zwitterionic compound. Unrealistic daily consumption based on TTC
Gemfibrozil	0.74 µg L^{-1} (Malchi et al., 2014) 0.25 µg L^{-1} spiked (Wu et al., 2014)	Sweet potato leaves (0.1-0.53) Not detected in any edible plant tissue	LOW	Ionic compound. Lack of reactive functional groups and genotoxic abilities leads to an unrealistic daily consumption based on TTC
Lamotrigine	1.52 µg L^{-1} (Malchi et al., 2014)	Carrot leaves (6-19), roots (2.5-8)	HIGH	Potentially genotoxic compound. TTC can be reached for a 25 kg child at a daily consumption of half a carrot (60g), 70 kg adult at two carrots a day (180g)
Metoprolol	0.65 µg L^{-1} (Malchi et al., 2014)	Sweet potato leaves (0.4-0.5)	LOW	Class III compound. Unrealistic daily consumption based on TTC. Compound mostly sorbed or degraded in soil
Primidone	0.25 µg L^{-1} spiked (Wu et al., 2014)	Cabbage leaf (0.3±0.31) Lettuce leaf (0.11±0.19) Premature celery stem (0.45±0.33)	LOW	Basic compound. Lack of reactive functional groups and genotoxic abilities leads to an unrealistic daily consumption based on TTC
Sildenafil	0.54 µg L^{-1} (Malchi et al., 2014)	Carrot leaves and roots (0.2-1.5) Sweet potato leaves (0.5-1)	LOW	Potentially genotoxic compound. Unrealistic daily consumption based on TTC
Sulfamethoxazole	0.025-0.055 ng/L (Christou et al., 2017) 0.75 µg L^{-1} (Malchi et al., 2014) 0.25 µg L^{-1} spiked (Wu et al., 2014)	Tomato fruits (5.26) Carrot roots (0.05-0.24) Sweet potato roots (0.05-0.24) Not detected in any edible plant tissue	LOW	Potentially genotoxic compound. Unrealistic daily consumption based on TTC. Compound mostly sorbed or degraded in soil
Sulfapyridine	0.58 µg L^{-1} (Malchi et al., 2014)	Carrot leaves and roots (<0.5)	LOW	Potentially genotoxic compound. Unrealistic daily consumption based on TTC. Compound mostly sorbed or degraded in soil
Trimethoprim	0.022-0.073 ng L^{-1} (Christou et al., 2017) 0.25 µg L^{-1} spiked (Wu et al., 2014)	Tomato fruits (3.4) Not detected in any edible plant tissue	LOW	Zwitterionic compound. Unrealistic daily consumption based on TTC

CBZ-EP, ciprofloxacin, and lamotrigine have high importance. CBZ-EP is a bioactive metabolite of carbamazepine that is environmentally stable, mobile, and has similar pharmacological properties to the parent compound (Miao, Yang, & Metcalfe, 2005). Ciprofloxacin and lamotrigine have high importance compared to other compounds due to their uptake in plants and potential to exceed their respective TTCs. A lamotrigine metabolite (lamotrigine-N^2-glucuronide) accounts for 76-90% of lamotrigine derived compounds in

wastewater (Zonja, Pérez, & Barceló, 2016), but was not evaluated for its TTC. There is limited information available on the ecotoxicological risk of pharmaceutical metabolites despite compounds like CBZ-EP retaining their pharmacological activity. This is especially an issue in terms of antibiotic resistance proliferation if active metabolites of antimicrobials are released through wastewater effluent.

3.1.4.2 Hazard Index Method

Another method to define health risk of consumption of plants irrigated with treated wastewater has been thoroughly reviewed (Prosser & Sibley, 2015). The hazard index method estimates hazard quotients to define risk by approximating adverse health or carcinogenic effects over a lifetime of exposure (USEPA, 2011). Furthermore, individual hazard quotients are often combined to create a more accurate representation of the health risk. The majority of the hazard quotients for PPCPs in edible plant components in the field at environmentally relevant levels were less than 0.1, signifying a *de minimis* risk to human health.

There is still a lack of knowledge regarding the synergistic and antagonistic relationships between PPCPs and how these interactions affect the environment. Synergistic relationships between carbamazepine and clofibric acid that acted according to non-polar narcosis have been observed. The relationship between the pair followed a concentration addition trend, indicating that measured effects were much stronger than the concentration responsible for singly measured effects (Cleuvers, 2003). Similar findings were found for 4-tert-nonylphenol and estradiol that resulted in an additive reaction (Thorpe et al., 2001). These combination effects are an issue because toxicity data for individual compounds would need to be reevaluated to account for environmental cocktail effects (Vasquez, Lambrianides, Schneider, Kümmerer, & Fatta-Kassinos, 2014). Another point to consider is the mixture data results of PPCPs that have similar and dissimilar mechanisms of action that relate to their biochemical interaction with organisms. For

human health risk assessments, PPCP mixtures in plants could result in potential human health risks in a scenario where individual hazard quotients of compounds are additive (Prosser & Sibley, 2015).

For compounds of emerging concern such as lamotrigine and CBZ-EP, the potential additive effects of these compounds with others needs to be investigated to ascertain if there is an ecotoxicological or human health risk. There is also the necessity to understand indirect human health risks that come from antibiotic resistance, given that environmentally relevant concentrations of antibiotics have been detected in carrot and lettuce (Azanu et al., 2016). Although these levels and corresponding estimated daily intake were several thousand times lower than the acceptable daily intake, the risks associated with antibiotics are not confined to direct toxicity. Rather, antibiotic compound concentrations found in plants and subsequent consumption could contribute to antibiotic resistance of microbiota inside humans. Due to the limited number of studies defining a quantitative human health risk, it can be concluded that more research needs to be completed on this topic.

3.1.5 PPCP Uptake from Crop Irrigation using Reclaimed Wastewater Research Objectives

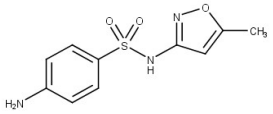
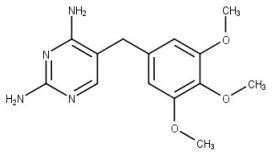
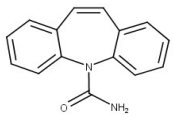
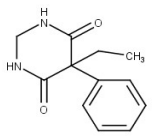
The objectives of the PPCP study were to quantify the dry mass concentration of PPCPs in field-grown alfalfa irrigated with treated wastewater to determine what fraction of PPCPs accumulate in crops from reclaimed wastewater irrigation. Dry mass concentration of PPCPs in market-sourced and groundwater-irrigated crops were also quantified.

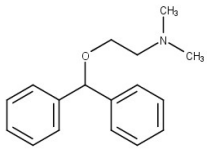
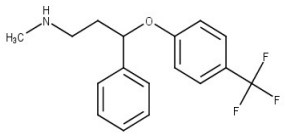
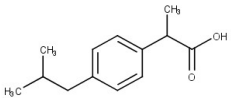
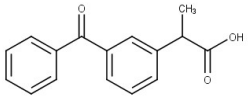
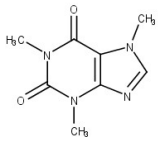
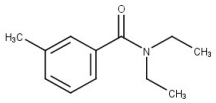
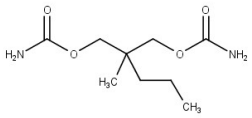
3.2 PPCPs Materials and Methods

3.2.1 Target PPCPs

11 compounds from multiple pharmacological classes were chosen for analysis. The compounds included commonly used, over-the-counter drugs (DEET, diphenhydramine, and ibuprofen) prescribed pharmaceuticals (carbamazepine, fluoxetine, ketoprofen, meprobamate, and primidone), prescribed antimicrobials (sulfamethoxazole and trimethoprim), and a common stimulant (caffeine). Table 3-2 shows each compound, their CAS number, registered trade name, classification, formula, structure, pK_a, and log K_{ow}.

Table 3-2 Target PPCPs and related physicochemical properties

Compound & CAS Number	Trade Name	Classification	Structure	pK_a	log K_{ow}
			$C_{10}H_{11}N_3O_3S$ 253 g mol^{-1}		
Sulfamethoxazole 723-46-6	Bactrim®	Antibacterial		1.60, 5.70	0.89
			$C_{14}H_{18}N_4O_3$ 290 g mol^{-1}		
Trimethoprim 738-70-5	Primsol®, Bactrim®	Antibacterial		7.12	0.91
			$C_{15}H_{12}N_2O$ 236 g mol^{-1}		
Carbamazepine 298-46-4	Tegretol®	Anticonvulsant		13.9	2.45
			$C_{12}H_{14}N_2O_2$ 218 g mol^{-1}		
Primidone 125-33-7	Mysoline®	Anticonvulsant		11.8	0.91

			$C_{17}H_{21}NO$ 255 g mol^{-1}		
Diphenhydramine 58-73-1	Benadryl®	Antihistamine		8.98	3.27
			$C_{17}H_{18}F_3NO$ 309 g mol^{-1}		
Fluoxetine 2-84-9	Prozac®	Antidepressant		9.80	4.05
			$C_{13}H_{18}O_2$ 206 g mol^{-1}		
Ibuprofen 15687-27-1	Advil®	Anti-Inflammatory		4.91	3.97
			$C_{16}H_{14}O_3$ 254 g mol^{-1}		
Ketoprofen 22071-15-4	Frotek®	Anti-Inflammatory		4.45	3.12
			$C_8H_{10}N_4O_2$ 194 g mol^{-1}		
Caffeine 58-08-2		Stimulant		14.0	-0.07
			$C_{12}H_{17}NO$ 191 g mol^{-1}		
DEET 134-62-3		Topical Agent		-0.95	2.18
			$C_9H_{18}N_2O_4$ 218 g mol^{-1}		
Meprobamate 57-53-4	Miltown®	Tranquilizer		15.5	0.70

The 11 compounds were selected due to different physicochemical properties. The PPCPs have a range of log K_{ow} values from the very hydrophilic caffeine to the hydrophobic fluoxetine.

3.2.2 Preliminary Health Impact Estimate

The health impact from the acceptable daily intake (ADI) over a person's lifespan was estimated for market-sourced produce (lettuce, tomato, carrot, cucumber, and potato) and PPCPs using a published method (Prosser & Sibley, 2015). Briefly, ADI values for PPCPs were estimated by dividing the lowest daily therapeutic dose for adults by a safety factor of 1000 and a body weight of 70 kg (WHO, 2012). The safety factor was comprised of three factors of 10 to account for different pharmacological responses between humans, sensitivity for population subgroups like toddlers, and the lowest daily therapeutic dose not being a level that represents no effect (Defra, 2007; NHMRCA, 2008; WHO, 2012). This safety factor was applied for diphenhydramine, fluoxetine, primidone, sulfamethoxazole, and trimethoprim. The ADI was incorporated with the maximum PPCP concentration quantified in the market produce as well as body mass. Equation 3-1 describes the necessary intake of a target plant for an adult or toddler that could exceed the ADI for the target compounds.

Equation 3-1 $$\text{Necessary Daily Intake to Exceed ADI} = \frac{\text{ADI}\left(\frac{\mu g}{kg \cdot day}\right) * \text{m (kg)}}{C_{food}\left(\frac{ng}{g}\right)}$$

C_{food} represents the determined dry mass concentration (ng g^{-1}) for edible plant tissue

m represents the average mass (kg) of an adult (20 to < 65 yrs), i.e., 70.0 (WHO, 2012), or a toddler (1 to < 4 yrs), i.e., 15.4 (Richardson, 2013)

The estimated daily intake (EDI) of lettuce, tomato, carrot, cucumber, and potato was found using Equation 3-2.

Equation 3-2 $$EDI = \frac{C_{food} * IR_{veg.} * \beta_{g/cup} * \beta_{ww/dw}}{m}$$

IR_{veg} is 2.80 cup equivalents of vegetables per day, which represents the 95th percentile for vegetable intake reported by the US National Health and Nutrition Examination Survey (NCI, 2005)

$\beta_{g/cup}$ represents the mass of a cup of fresh plant tissue diced to ≤ 0.5 cm^3

$\beta_{ww/dw}$ is 0.085 and represents the mean wet-to-dry conversion factor used by the USEPA for plant tissue in the development of soil screening values (USEPA, 1996)

3.2.3 Alfalfa Crop Sampling Procedure

Alfalfa is a perennial flowering plant that is harvested annually in early Fall at UNR Farms. Water from the local WWTP prior to dechlorination was irrigated onto the field-grown alfalfa crop, with a section utilized for harvesting and PPCP analysis. Crops are baled with a portion transported to Saudi Arabia to be used as racehorse feed due to the high quality of the crop. The remainder is used as cattle feed. The main alfalfa root remains intact in the ground between harvesting to allow for consistent regrowth in spring and summer. Alfalfa enters dormancy throughout winter at UNR Farms and survives with the aid of a strong taproot that can penetrate 6 m deep or more (CFIA, 2012). Figure 3-1 shows the growth and anatomical characteristics of the alfalfa plant.

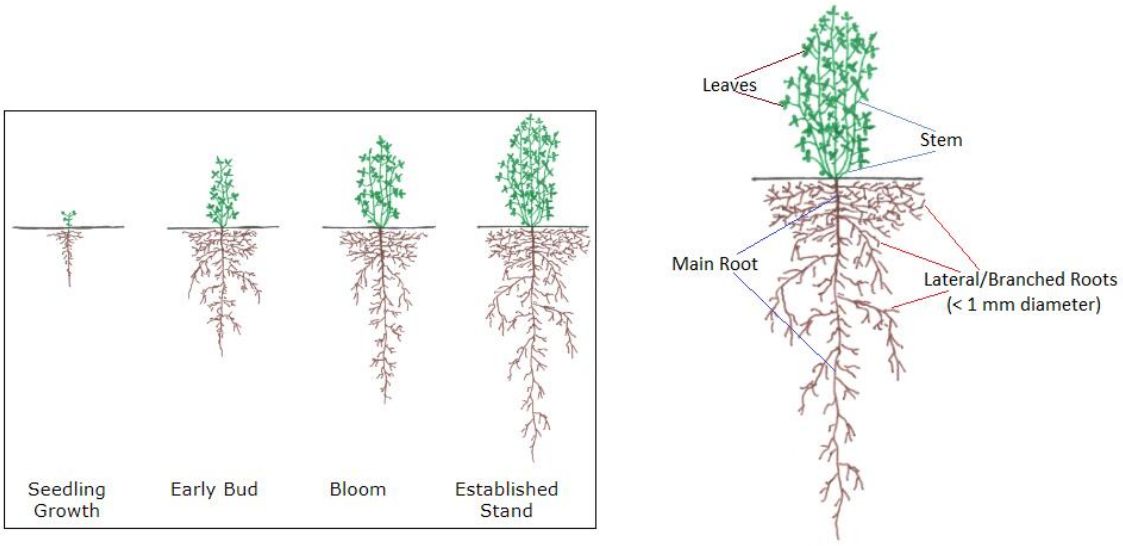


Figure 3-1 Alfalfa growth development in stages and enlarged established stand displaying specific anatomical characteristics (adapted from UCD (2013))

Alfalfa crops were sampled from the UNR Farms near the Wolf Pack Meats station twice during the growing season of June through September to determine leaf and shoot uptake of PPCPs. The first harvest occurred in early July 2018 with leaves and shoots gathered. The second harvest occurred on 6th September 2018, with only leaves gathered. Harvested samples were washed with DI water, shaken to remove soil and other organic material, and placed in the freezer until extraction. Figure 3-2 shows the schematic of UNR Farms and sampling location.

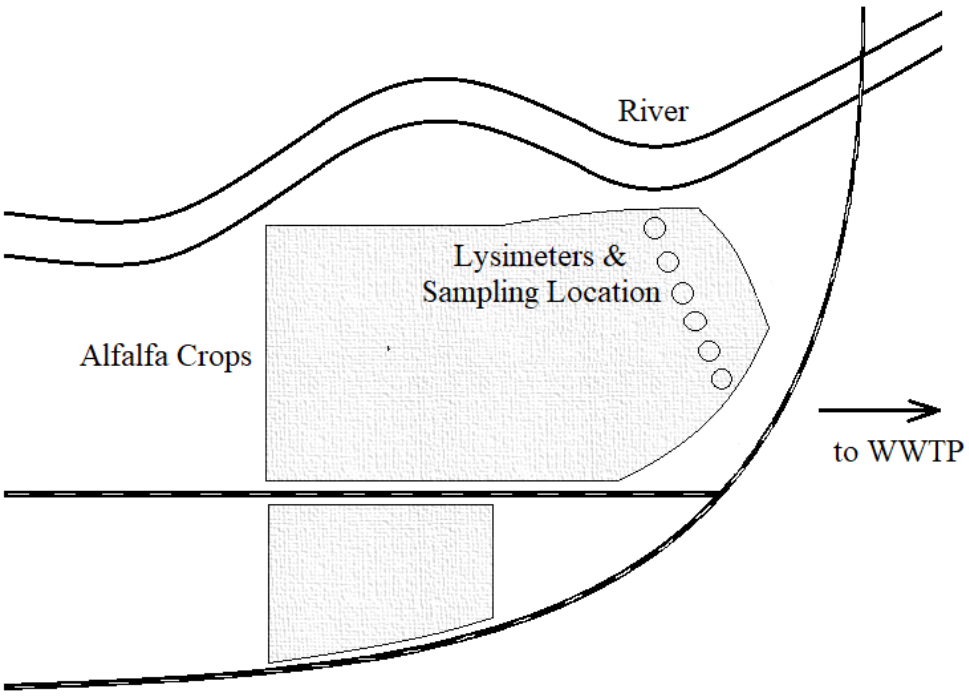


Figure 3-2 Schematic of UNR Farms reclaimed wastewater-irrigated alfalfa plots. Alfalfa was sampled from the lysimeter locations

A section near the edge of the crop was used for alfalfa sampling. The sampling location was set apart from the main crop to reduce interference with agricultural operations.

3.2.4 Fractional PPCP Uptake as a Function of Land Application

The fraction of PPCPs that accumulated in alfalfa leaves in comparison to the mass of PPCPs irrigated onto the field was determined using Equation 3-3.

Equation 3-3 $$\text{PPCP Fraction in Alfalfa Leaves} = 100\% * \left(\frac{\text{PPCP Leaf Concentration} \left(\frac{\text{ng}}{\text{g}}\right) * \text{Annual Harvest} \left(\frac{\text{g}}{\text{m}^2}\right)}{\text{PPCP Irrigation Concentration} \left(\frac{\text{ng}}{\text{L}}\right) * \text{Irrigation Amount} \left(\frac{\text{L}}{\text{m}^2}\right)} \right)$$

PPCP leaf concentration represents an upper estimate of PPCP accumulation in alfalfa, given that leaf accumulation is likely higher than shoot accumulation. The annual harvest of dry alfalfa matter was about 3.6 tons acre^{-1} (or 807 g m^{-2}). The average PPCP concentration in the irrigation water was selected to represent typical PPCP concentrations exposed to the field during growing season. The irrigation amount was 1200 L m^{-2}.

3.2.5 Market Produce and Groundwater Irrigated Crop Sampling

Market-sourced fresh fruit and vegetables were obtained from three locations. Cucumber, lettuce, tomato, and watermelon samples were bought from Trader Joe's store #82, Reno. Carrot and potato samples were sourced from Raley's on Keystone Ave, Reno. Strawberries were sourced fresh from a roadside market in Salinas Valley, California. Bell pepper and zucchini were sourced from soil plots irrigated with groundwater whereas cherry tomato and tomato were grown hydroponically with groundwater. The groundwater irrigated plants were sourced from Auburn, California. The geographical range of the produce is presented in Figure 3-3.

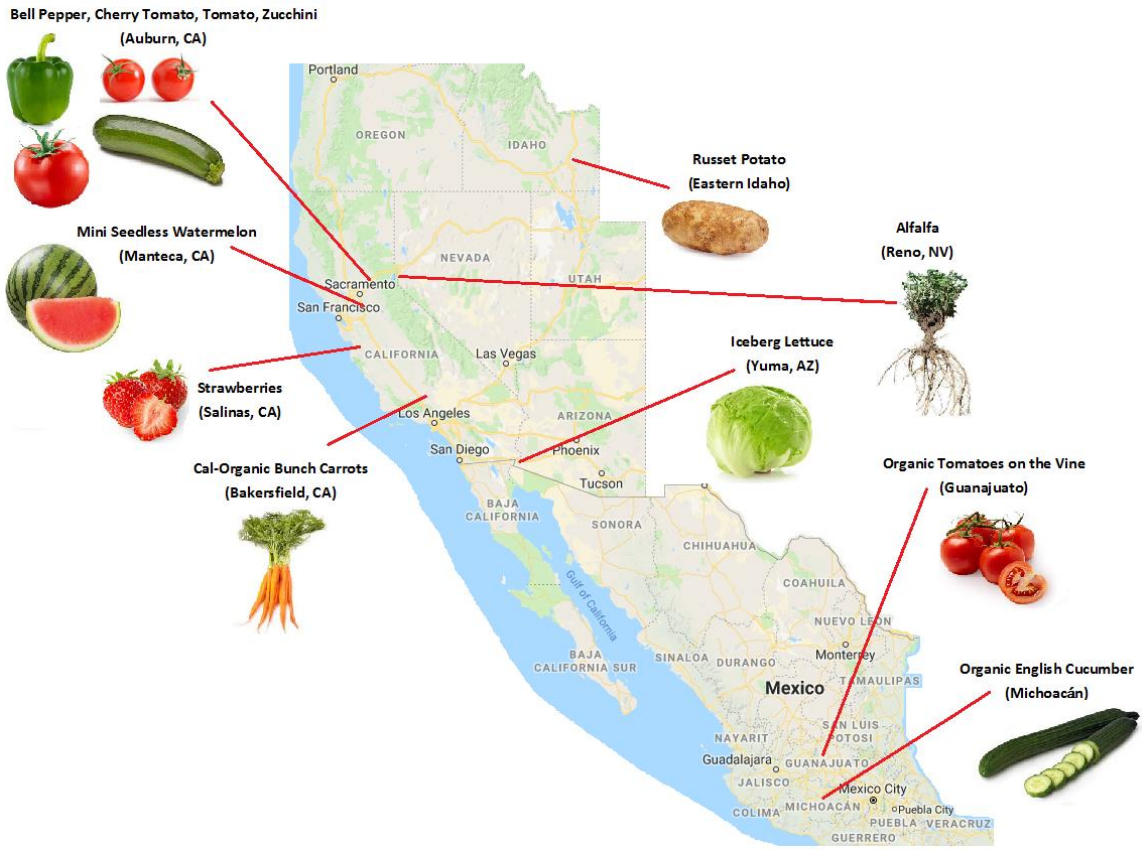


Figure 3-3 Geographical distribution of sampled fruits and vegetables

3.2.6 PPCPs in Plants Extraction

The standard operating procedure for PPCP extraction from plants is outlined in the Appendices. Plants were separated into their respective components (roots, shoots, leaves, and fruits). Samples were thoroughly rinsed with deionized (DI) water to remove any dirt or other organic matter. Larger plant components (fruits) were diced into pieces having an approximate volume of 1 cm^3 whereas smaller components (roots, shoots, and leaves) were chopped into thin strips to maximize surface area exposure before being frozen overnight. Fibrous material (roots and shoots) were cut to approximately 5 mm long with a 1 mm diameter to improve grinding efficiency. A value of 2 mm was used to separate fine and coarse roots. Fine roots were selected

for analysis due to their tendency to transpire water more effectively than coarse roots (Camiré, Côté, & Brulotte, 1991) which primarily provide structural stability for the plant in soil.

Frozen plant material was transferred into freeze-dryer vials and placed in a FreeZone 4.5 Liter freeze-dryer system (Labconco Corporation, Missouri, USA) for 72 hr. The freeze-dryer was set at -50°C and a 0.1 mBar vacuum as suggested by the manufacturer for vegetable tissue. Plant material was removed from the freeze-dryer and ground to powder using mortar-and-pestle or a conical burr coffee grinder (Capresso, New Jersey, USA) at the finest setting. Fibrous material was more amenable to grinding with the coffee grinder whereas leafy material or high-sugar content plant components (watermelon fruit) was more amenable to grinding with mortar-and-pestle. Ground material was sieved with a US Standard #60 (250 micron) sieve and kept in vials.

0.2 g of ground material was placed into a 50 mL centrifuge tube before adding 20 mL methyl *tert*-butyl ether (MTBE) and spiked with isotopes at 5 µg L^{-1} (25 ng g^{-1}). Fluoxetine-d_5 was purchased from Cayman Chemical Company (Michigan, USA); DEET-d_{10}, Primidone-d_5, Sulfamethoxazole-d_4, Trimethoprim-d_3 were purchased from Santa Cruz Biotechnology (Texas, USA); Caffeine-$^{13}C_3$, Carbamazepine-d_{10}, Diphenhydramine-d_3, Ibuprofen-d_3, Ketoprofen-d_3, Meprobamate-d_3 were purchased from Sigma-Aldrich (Missouri, USA). Isotopes were spiked into the liquid solution rather than onto the dry powder to limit syringe tip sample loss. Samples were sonicated for 20 min to disturb cell walls and transfer PPCPs into solution. Samples were then centrifuged at 1000 RCF for 20 min to separate solid matter from the liquid solution. The supernatant was then decanted into a separate 50 mL centrifuge tube. The sonication, centrifugation, and decanting step was then repeated on the original tube using acetonitrile (ACN). The combined decantate was then evaporated to near dryness under a gentle UHP N_2 gas stream in the TurboVap. The residue was re-dissolved with 20 mL Milli-Q water and 1 mL

MeOH. If any plant residue was left on the centrifuge tube walls then the samples were sonicated until the residue re-entered the solution.

SPE was performed following the method described by (Wu, Conkle, & Gan, 2012) using Oasis HLB 6 cc/200 mg cartridges (Waters Corporation, Massachusetts, USA). Cartridges were conditioned with 5 mL MeOH and Milli-Q water before samples were loaded at 3 mL min^{-1} to reduce sample input line clogging. Cartridges were then dried with UHP N_2 gas for 60 min before being eluted with 5 mL MeOH. Samples were transferred into 10 mL glass conical centrifuge tubes using pasteur pipettes and evaporated in the TurboVap under a gentle UHP N_2 gas stream to near dryness. Samples were then reconstituted with 1 mL MeOH, 50 µL ACN, and derivatized with 50 µL *N*-*tert*-butyldimethylsilyl-*N*-methyltrifluoroacetamide with 1% *tert*-butyldimethylchlorosilane (MTBSTFA + 1% TBDMSCl) (Sigma-Aldrich, Missouri, USA) if they were to be analyzed by GC-MS/MS. If not, then only 1 mL MeOH was added. All samples were pushed through 0.2 µm PTFE filters (Cole-Parmer, Illinois, USA) to remove all potential remaining plant material for instrument preservation. Collection vials were then firmly capped and placed in the oven for 1 hr at 80°C to facilitate the derivatization reaction if they were to be analyzed by GC-MS/MS. All samples were then transferred into 2 mL amber vials and placed in the freezer. The full procedure is displayed in Figure 3-4.

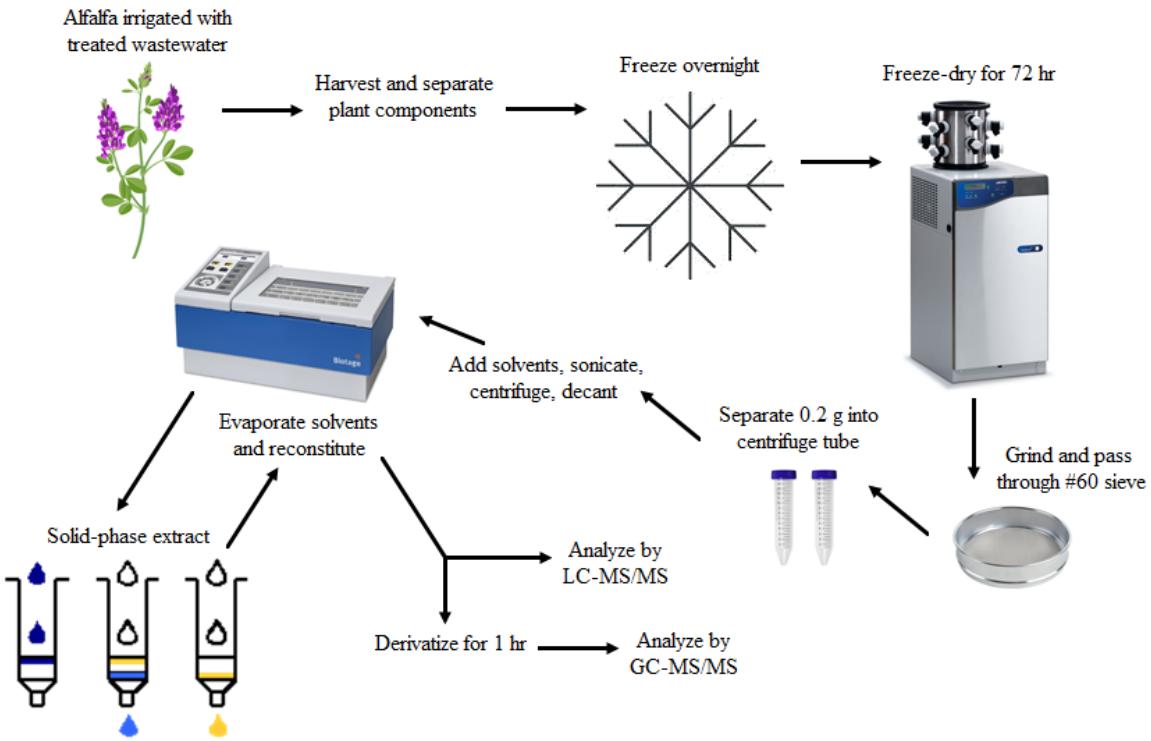


Figure 3-4 General extraction procedure for transferring PPCPs accumulated in plants to a liquid solution

3.2.7 PPCP Derivatization

Derivatization was used to increase the volatility of PPCPs to make them amenable to GC-MS analysis. MTBSTFA + 1% TBDMSCl was used to perform silylation derivatization due to its applicability with a range of functional groups. The hydrogen bound to a functional group (A) in the target compound is replaced with a *tert*-butyldimethylsilyl (TBDMS) group and results in the structural change shown in Figure 3-5.

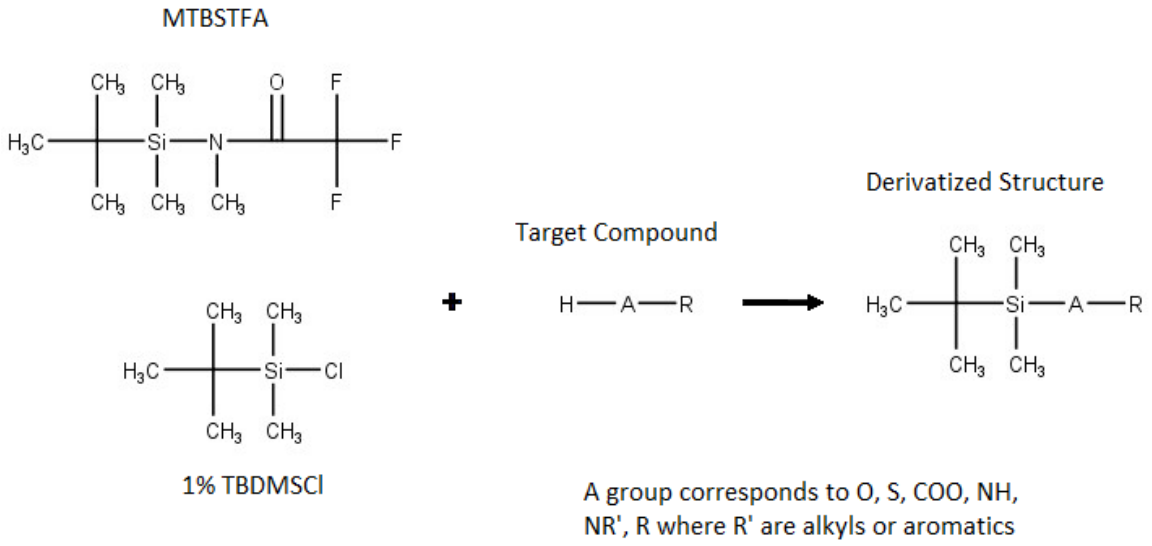


Figure 3-5 Structural change of a target compound from the derivatization reaction with MTBSTFA + 1% TBDMSCl (adapted from Orata (2012), Stenerson (2011))

3.2.8 GC-MS/MS Positive Electron Impact Analysis

Samples were analyzed by GC-MS/MS using an Agilent 6890 gas chromatograph (Agilent Technologies, California, USA) with a Waters Micromass Quattro micro GC mass detector (Waters Corporation, Massachusetts, USA). Separation was achieved on a HP-5MS (30 m x 0.25 mm x 0.5 µm) capillary column (Agilent J&W, CA, USA) with UHP helium as the carrier gas (1.4 mL min^{-1}). 1 µL samples were injected at splitless mode at an injection temperature of 250°C into an HP 5062-3587 single taper 2 mm I.D. injection sleeve (Hewlett-Packard, CA, USA). This inlet liner was used to limit organic matter buildup and consequent sleeve and column blockage. The temperature program of the GC oven was initially set at 65°C, held for 1 min and then ramped at 15°C min^{-1} to 120°C, at 6°C min^{-1} to 160°C, at 9°C min^{-1} to 180°C, at 6°C min^{-1} to 220°C, at 8°C min^{-1} to 315°C and held for 7 min with a 4 min equilibrium time post-run. The MS was operated in EI+ ionization mode at 70 eV. Initial identification of

derivatives was made in scan mode using a single quadrupole and monitoring the following ibuprofen ions: m/z (161, 177, 117, 220). The collision cell and second quadrupole were utilized to perform multiple reaction monitoring (MRM) on the most abundant precursor ion (m/z 161). UHP argon at 6V was used as the collision gas with the following fragmentation ions monitored: m/z (119, 105). For both scan and MRM modes, the most abundant ion was used for quantification purposes with the second most abundant ion used for confirmation. Ibuprofen was quantified from the ratio of the peak area of the fragmented analyte (m/z 119) to the fragmented internal standard (m/z 122).

3.3 GC-MS/MS Method Development and Ibuprofen Uptake Results and Discussion

3.3.1 Method Development

A GC-MS/MS method capable of analyzing PPCPs in plants was developed. Initially, 18 compounds were tested to determine their compatibility with GC-MS analysis. Compounds were derivatized with MTBSTFA + 1% TBDMSCl, which is selective for hydroxyl, amine, and thiol functional groups. Derivatization increases Henry's Law constants and thus lowers the boiling points of PPCPs to allow gas phase transfer. Initial tests determined that 11 compounds were unsuitable due to poor derivatization or ionization. Further tests identified six compounds that had low sensitivity. Table 3-3 shows the list of compounds and reasons for exclusion.

Table 3-3 Compounds tested during GC-MS/MS method development and exclusion reason

Compound	Included in Study	Exclusion Reason
Ibuprofen	Yes	
Carbamazepine	No	Discrete peaks due to incomplete derivatization
Lamotrigine Primidone Fenoprofen Ketoprofen Diclofenac Naproxen	No	Poor sensitivity
Sucralose Clofibric acid Mefenamic acid Tolfenamic acid Triclosan Gemfibrozil	No	No ionization
Phenacetin Sulfamethoxazole Trimethoprim Oxazepam	No	Poor derivatization or ionization

Carbamazepine had two discrete peaks, indicating that some fraction of the compound was not derivatized yet still transferred to the gas phase and interacted with the column. Compounds with carboxylic acid functional groups tended to ionize better than ones without. Fenoprofen, ibuprofen, and ketoprofen had the best analysis potential based on their similar structures and consequent amenability to derivatization. However, fenoprofen and ketoprofen were not sensitive enough for trace compound analysis and were thus discarded. Derivatization of 16 PPCPs has previously been performed, with retention times and fragment ions determined (Reddersen & Heberer, 2003). Fragment ion intensity from the study rarely matched determined ions from this analysis, indicating that GC-MS analysis for PPCPs is somewhat instrument specific.

Multiple inlet liners were tested to improve peak shape through chromatography optimization. Inlet liners having small internal diameters of 0.75 mm were deemed unsuitable. An injection temperature of 280°C coupled with organic material not removed during sample preparation caused blockage in these inlets as well as charring of the column tip that impeded compound transfer into the column. A 2 mm internal diameter inlet liner was chosen to minimize organic matter buildup and allowing complete transfer of the compound into the column. Split injection mode to further minimize inlet liner blockage was considered however it was deemed inappropriate due to the trace analysis.

Ibuprofen demonstrated consistent performance, however GC-MS analysis was not sufficient. Samples contained organic matter that ionized and often coincided with ibuprofen fragment ions at similar retention times, obscuring peaks and making analysis problematic. As such, GC-MS/MS was utilized to isolate ibuprofen and reject other compounds. Following chromatographic separation, gas molecules were ionized by collisions with high-energy electrons from a heated filament, with ibuprofen molecules selected for using the first quadrupole. The fragmented molecule was further fragmented through collision with argon gas in the collision

cell. Figure 3-6 shows the proposed structural change of ibuprofen through the GC-MS/MS process. Primary ions were used for quantification while secondary ions were used for confirmation.

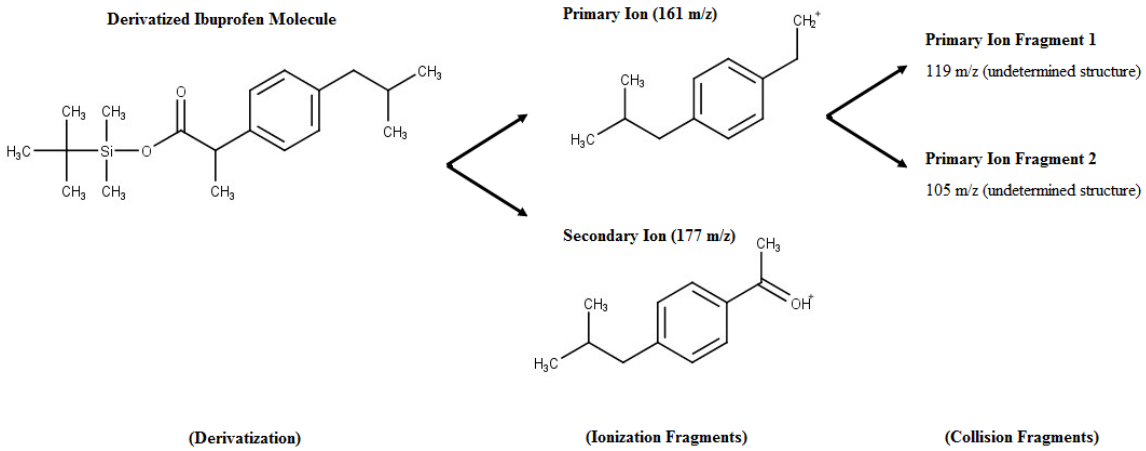


Figure 3-6 Proposed ibuprofen fragmentation from derivatization, ionization, and collision during GC-MS/MS analysis

Ionization in the source led to fragmentation at the carboxylic acid functional group and production of the primary ion. Further fragmentation produced two collision fragment ions of indeterminate structure.

3.3.2 Plant Uptake of Ibuprofen

Alfalfa crops irrigated with treated wastewater, market-sourced fruits and vegetables, and groundwater irrigated crops were quantified for ibuprofen uptake by GC-MS/MS. The method detection limit was approximately 1.5 ng g^{-1} dry mass concentration, based on a signal-to-noise ratio of 3:1. Figure 3-7 shows plant uptake of ibuprofen.

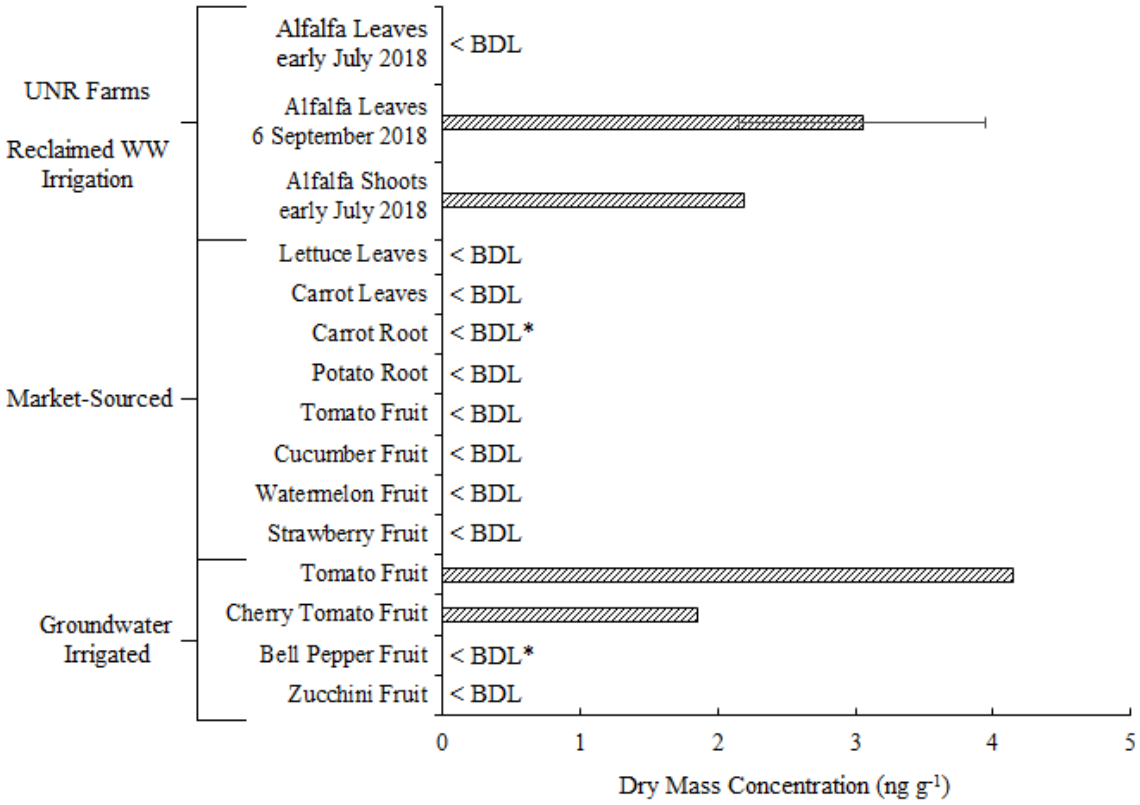


Figure 3-7 Ibuprofen concentration in three sets of plants from different sampling procedures. Error bars represent individual samples (duplicates) with bars displaying the average concentration. <BDL indicates that the dry mass concentration was below the method detection limit whereas asterisks indicate that peaks were detected but not quantified due to being below the 3:1 signal-to-noise ratio

Ibuprofen was detected in four of the 15 samples. Alfalfa irrigated with treated wastewater had a shoot concentration of 2.19 ng g^{-1} and below the detection limit for alfalfa leaves from the first harvest in early July 2018. Alfalfa leaves from the second harvest on 6th September 2018 had a mean concentration of 3.05 ng g^{-1}. The first harvest highlighted that ibuprofen was able to cross root membranes and enter the alfalfa plant, despite being weakly acidic. Approximately two months later during the second harvest, ibuprofen was detected in the leaves. Concentrations were 39% higher from the initial shoot harvest to the final leaf harvest.

Edible fruit and vegetable components sourced from markets had an ibuprofen concentration below the detection limit. An ibuprofen peak for carrot root was detected but not quantified because the peak was not clearly distinguishable from the baseline. The irrigation water type was also typically unknown due to proprietary reasons. All plant types were likely irrigated with treated wastewater based on the growing region. Concentration below the detection limit signifies that although ibuprofen may be present, it is not so in elevated concentrations.

The region surrounding the groundwater-irrigated crops has considerable farmland and agricultural activity, which could influence PPCP release to the groundwater. A nearby WWTP also discharged to a local creek that could leech PPCPs to the groundwater. Ibuprofen concentration in tomato and cherry tomato fruit were 4.14 and 1.85 ng g^{-1}, respectively. Ibuprofen was detected in bell pepper but not quantified for the same reason discussed as the carrot root. No ibuprofen peaks were detected for zucchini fruit, indicating that plant specific uptake of ibuprofen may be a controlling factor. Additionally, both tomato plants were grown hydroponically compared to bell pepper and zucchini, which were grown in soil plots. Hydroponic growth allows for transfer of nutrients and other compounds into the plant without any soil interference relating to degradation or sorption. Uptake of ibuprofen in the tomato plants is likely due to the hydroponic conditions compared to the plants grown in soil. Furthermore, the groundwater used in the hydroponic system was recirculated for both tomato plants, increasing uptake potential.

3.4 Method Development and Ibuprofen Uptake Conclusions

A GC-MS/MS method initially developed to analyze a range of PPCPs was reduced to solely quantify ibuprofen. Ibuprofen uptake in 15 plant samples from different sources and irrigation procedures was determined by the analysis. The following is a summary of the findings:

- 17 of the 18 PPCPs were unsuitable for plant uptake analysis due to derivatization, ionization, or sensitivity issues. GC-MS/MS analysis was required due to peak overlap from organic matter in the samples.
- PPCPs containing carboxylic acid functional groups such as ibuprofen were more amenable to silylation derivatization with MTBSTFA + 1% TBDMSCl than PPCPs containing other functional groups.
- Ibuprofen accumulated in alfalfa shoots and leaves, with dry mass concentration 39% higher in the final leaf harvest compared to the initial shoot harvest. Hydroponically-grown tomato took up ibuprofen in the fruit, whereas uptake was below detection limit for market-sourced plants.

3.5 LC-MS/MS Analysis Results and Discussion

Extracted plant samples from the procedure in Chapter 3.2.6 were analyzed by LC-MS/MS in the Nevada Proteomics Center at University of Nevada, Reno. Samples were analyzed by Priyam Sharma. Collection and extraction were performed by the author.

3.5.1 PPCP Concentration in a Local WWTP

PPCP concentration was measured in a local WWTP to determine PPCP degradation and release to UNR Farms. Treated wastewater is diverted to UNR Farms after chlorine disinfection and prior to dechlorination. Figure 3-8 shows the average PPCP concentration from the three points over four sampling events conducted in 2018 from 13th March to 16th April.

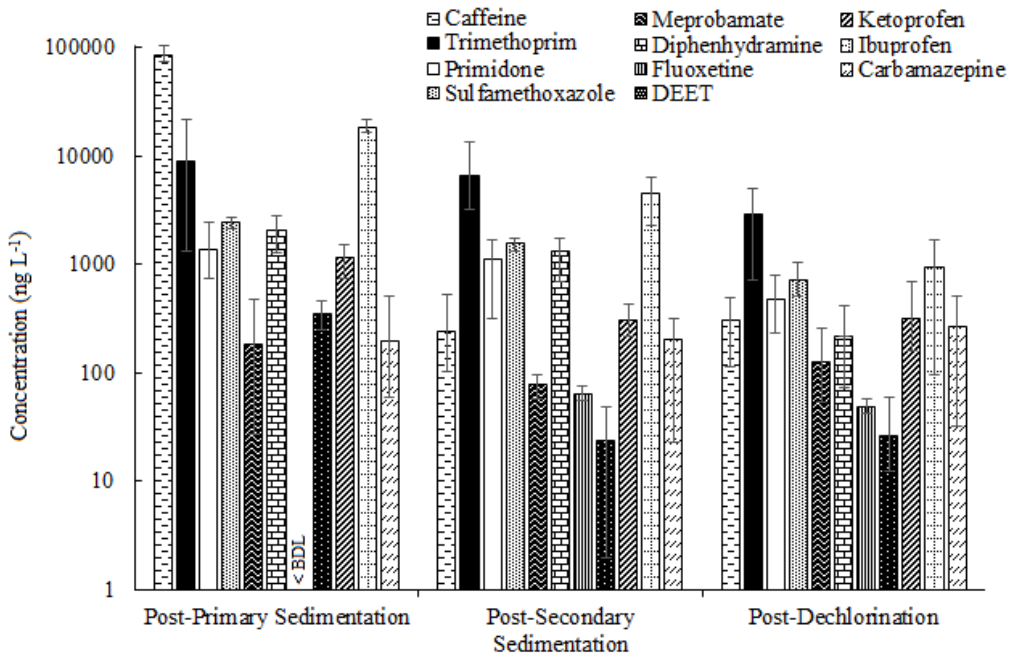


Figure 3-8 PPCP concentration in water after primary sedimentation, secondary sedimentation, and dechlorination in a local WWTP. Error bars represent individual samples (duplicates) with columns displaying the average concentration. <BDL indicates that PPCP concentration was below the detection limit

Caffeine was present at a concentration approximately one order of magnitude higher than other compounds with a mean concentration of 83 μg L^{-1}. This was not surprising given the widespread consumption of caffeinated beverages in the USA. Ibuprofen was measured at a mean concentration of 18 μg L^{-1}. Interestingly, fluoxetine was not detected after the primary treatment stage, yet was measured after the secondary treatment stage. Fluoxetine non-detection was most likely caused by extraction issues and matrix effects, due to the high level of organic and inorganic constituents in the water matrix after primary treatment that could act as interference.

PPCP concentration decreased after biological treatment and settling between 19.6-99.7%. Caffeine and DEET had the highest concentration reduction of 99.7% and 93.2%, respectively, likely due to degradation in the aeration basin by aerobic microorganisms. Aeration has previously removed PPCPs, including caffeine (Matamoros, Arias, Brix, & Bayona, 2007). Primidone had the least reduction of 20%, supported by other studies having a low biodegradation potential (Margot, 2015). Sulfamethoxazole and trimethoprim were reduced by 31%, likely due to their antibacterial properties and consequent resistance to biotic degradation. Fluoxetine was also measured at a mean concentration of 85 ng L^{-1}.

Tertiary treatment was relatively ineffective in reducing concentrations of caffeine, DEET, ketoprofen, and meprobamate. Other PPCP concentrations decreased between 43-84%. Overall, PPCP concentration reduction through the WWTP was between 31.2-99.6%. Caffeine and ibuprofen had the highest concentration reduction of greater than 95%, supported by other studies exhibiting their increased tendency for degradation, transformation, and sorption (Kim et al., 2014).

The analysis indicated that PPCPs can persist through tertiary treated wastewater treatment plants. The relatively high concentration of trimethoprim after tertiary treatment are concerning due to the potential for antibiotic resistance proliferation (Eliopoulos & Huovinen, 2001). Pharmaceutical metabolites from humans and PPCP TPs formed during treatment were not

quantified, indicating that the compounds detected may only incorporate a fraction of the discharged anthropogenic compounds.

3.5.2 PPCP Uptake in Field-Grown Alfalfa Irrigated with Treated Wastewater

Dry mass concentration of the 10 PPCPs in alfalfa leaves and shoots irrigated with local reclaimed wastewater were determined using LC-MS/MS analysis and are shown in Figure 3-9.

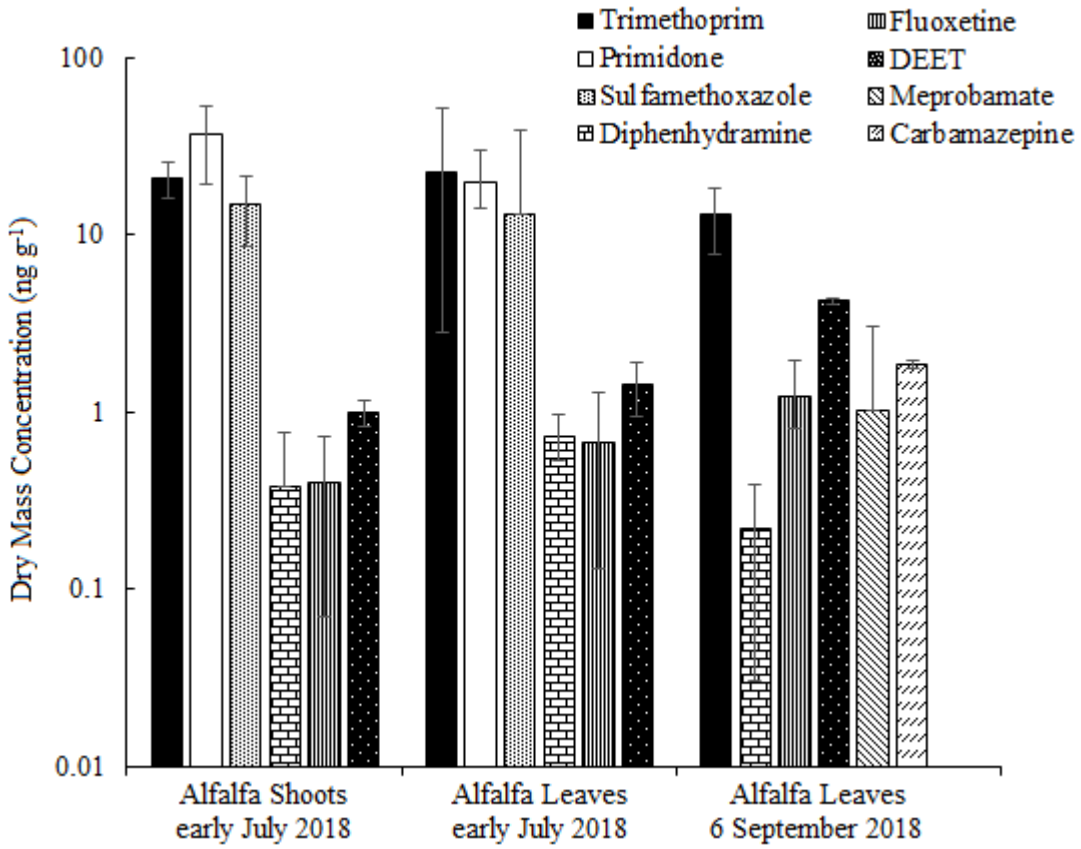


Figure 3-9 PPCP concentration in field-grown alfalfa leaves and shoots irrigated with treated wastewater. Alfalfa was sampled from two events in early July and September, 2018. Error bars represent individual samples (duplicates) with columns displaying the average concentration. Ibuprofen was below the detection limit (3 ng g^{-1}) for each sample

Eight compounds were quantified in alfalfa leaves and shoots from July to September. For the July harvest, concentrations of trimethoprim, diphenhydramine, fluoxetine, and DEET were typically higher in leaves than shoots, but not markedly so.

Primidone, sulfamethoxazole, and trimethoprim are hydrophilic and neutral at environmental pH. They were measured at a concentration one order of magnitude greater than other compounds for the July harvest. Neutral compounds are not charge rejected by root membranes and can translocate with the water stream through the plant (Goldstein et al., 2014). In contrast, fluoxetine is ionized at environmental pH which reduced root permeation due to charge rejection, and thus had shoot and leaf concentration of less than 1 ng g^{-1}. DEET was detected in the irrigation water, however there is contamination potential from workers applying insect repellant at the site.

Concentration of trimethoprim and diphenhydramine in alfalfa leaves decreased by 41.3% and 70.0%, respectively, from July to August. Conversely, concentration of fluoxetine and DEET in alfalfa leaves approximately doubled and tripled, respectively. Additionally, carbamazepine and meprobamate were detected at approximately 1 ng g^{-1} each, having not been detected in the July harvest.

Molecular weight (MW) and size was unlikely to influence differences in PPCP uptake for the target PPCPs, given that compounds with MW <500 are commonly taken up compared to larger compounds (Kumar, Gupta, Baidoo, Chander, & Rosen, 2005a).

3.5.3 Fractional PPCP Uptake as a Function of Land Application

The fraction of PPCPs that accumulated in alfalfa leaves in comparison to the mass of PPCPs irrigated onto the field was determined and is shown in Figure 3-10.

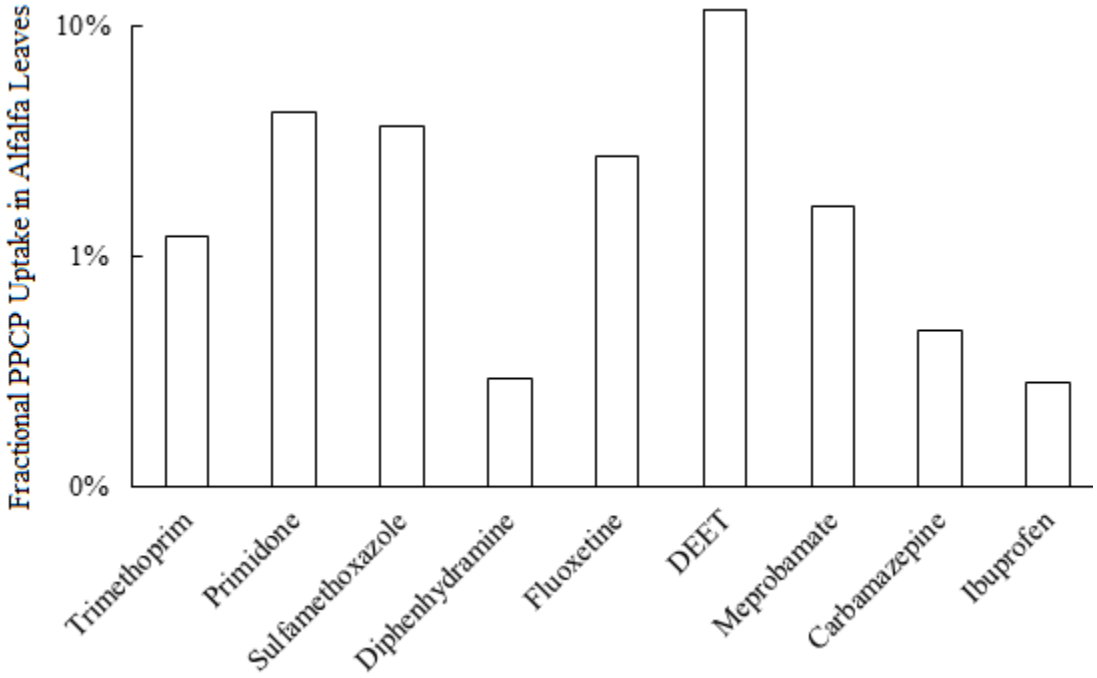


Figure 3-10 Upper estimate of the PPCP fraction that accumulated in alfalfa leaves from the total mass of PPCPs irrigated onto the crop

The transfer of PPCPs from reclaimed wastewater irrigation into alfalfa leaves compared to the total amount irrigated onto the crop was limited. DEET had the highest fraction of 11.4% due to the low concentration in irrigation water and comparative high uptake. However, contamination from workers applying insect repellent containing DEET at the site has the potential to influence this fraction. For the remaining compounds, transfer into alfalfa leaves was less than 5%. This indicated that PPCP uptake into crops from reclaimed wastewater irrigation constitutes a small fraction of PPCP release into the environment.

3.5.4 PPCP Uptake in Groundwater-Irrigated Crops

PPCP uptake in groundwater-irrigated crops was determined and is shown in Figure 3-11. The region surrounding the groundwater-irrigated crops has considerable farmland and agricultural activity, which could influence PPCP release to the groundwater. A nearby wastewater treatment plant also discharges to a local creek that could transport PPCPs to groundwater. Local growers confirmed that groundwater was used for irrigation.

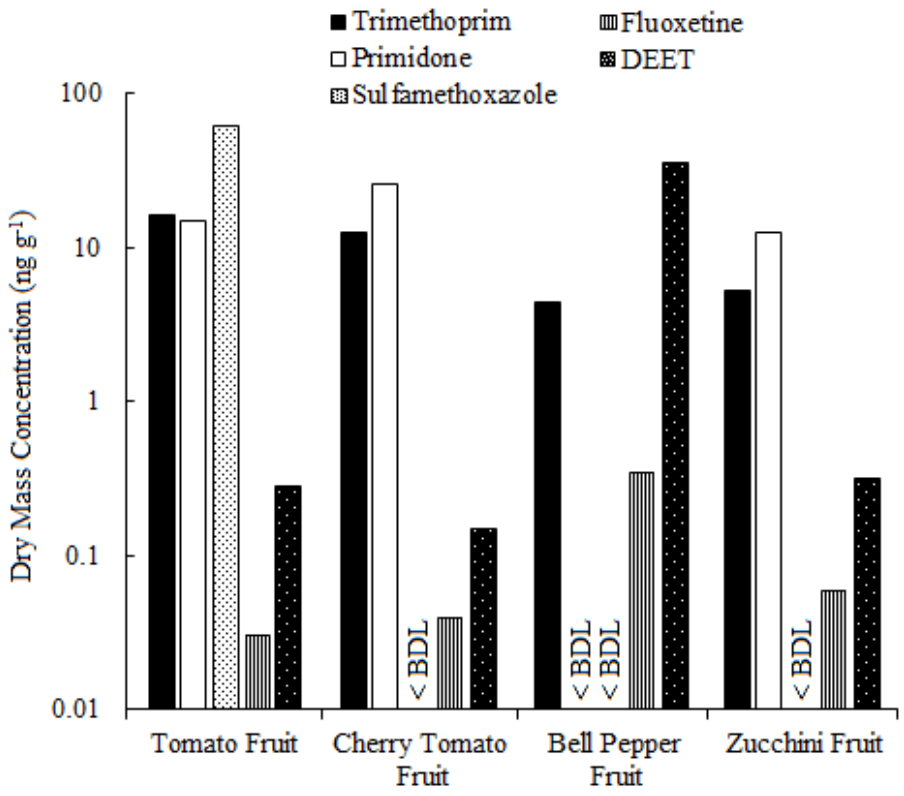


Figure 3-11 PPCP concentration in groundwater-irrigated crops. Both tomato plants were grown hydroponically whereas bell pepper and zucchini were grown in soil plots. Error bars represent individual samples (duplicates) with columns displaying the average concentration. <BDL indicates that PPCP concentration was below the detection limit. Diphenhydramine and ibuprofen were below the detection limit (0.25 ng g^{-1} and 3 ng g^{-1}, respectively) for each sample

Five compounds were quantified for the four plant types. Both tomato fruits took up the widest range of PPCPs compared to bell pepper and zucchini fruits, likely because they were grown hydroponically and thus avoided plant-soil interactions. Additionally, concentration of trimethoprim was 2-3 times higher in the hydroponically-grown plants than the soil-grown plants.

3.5.5 PPCP Concentration in Market-Sourced Produce

PPCP concentration for various market-sourced fruits and vegetables was determined and presented in Figure 3-12. All plant components are edible and commonly ingested. To the author's knowledge, this is the first analysis investigating PPCPs in market produce. Limited data was available for the irrigation water.

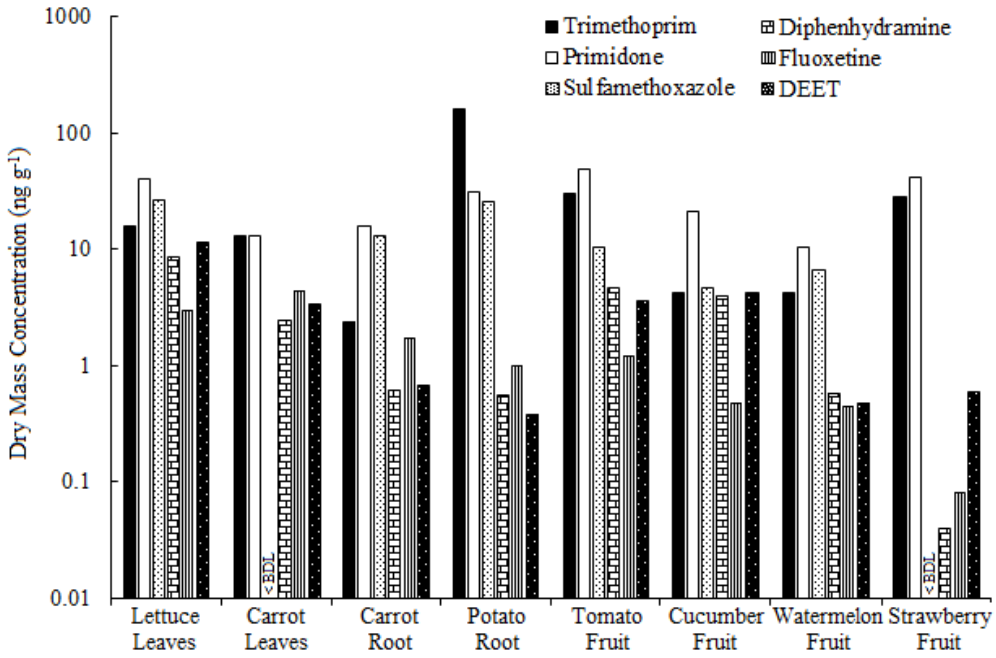


Figure 3-12 PPCP concentration in market-sourced produce. Error bars represent individual samples (duplicates) with columns displaying the average concentration. <BDL indicates that PPCP concentration was below the detection limit. Ibuprofen was below the detection limit (3 ng g^{-1}) for each sample

Primidone, sulfamethoxazole, and trimethoprim root concentration was up to 2 orders of magnitude greater than compounds ionized at environmental pH, indicating that charge rejection of ionic compounds limits translocation. Diphenhydramine and fluoxetine are such compounds that have difficulty permeating multiple membranes to translocate into the fruit (Hyland et al., 2015; Wu et al., 2010). Potato roots typically had higher PPCP uptake than carrot roots, which was likely because plants have different internal mechanisms that affect uptake. Lettuce leaves typically had higher PPCP concentration than carrot leaves, likely due to specific plant physiology. Lettuce is primarily composed of leaves compared to carrots, signifying that translocation into lettuce leaves not have to pass through as many root structures.

3.5.6 Ingestion Health Impact for Market Produce

The potential health impact from ingestion of market produce was estimated. Intake values to exceed the ADI are given in Table 3-4. The ADI and EDI for adults and toddlers is located in Appendix D.

Table 3-4 Necessary ingestion of target plants sourced from markets to exceed the ADI for five PPCPs for humans and toddlers

Plant		Necessary Plant Intake to Exceed PPCP ADI (kg d^{-1})					Health Impact
		DPH	**FLX**	**PMD**	**SMX**	**TMP**	
Lettuce	Adult	2.94	3393	1.2	15	6.4	ADI of PMD could be reached for about 2.5 lettuce heads
	Toddler	0.65	747	0.27	3.3	1.4	ADI of PMD could be reached for about half a lettuce head
Tomato	Adult	5.3	8342	1	39	3.3	ADI of PMD could be reached for about 7 tomatoes
	Toddler	1.2	1835	0.22	8.5	0.72	ADI of PMD could be reached for about 1.5 tomatoes
Carrot	Adult	40	5720	3.1	30	42	Negligible
	Toddler	8.9	1258	0.69	6.6	9.2	Negligible
Cucumber	Adult	6.4	20854	2.4	84	24	ADI of PMD could be reached for about 6 cucumbers
	Toddler	1.4	4588	0.52	19	5.2	ADI of PMD could be reached for about 1.5 cucumbers
Potato	Adult	45	10010	1.6	15	0.62	ADI of TMP could be reached for about 4 potatoes
	Toddler	9.8	2202	0.35	3.4	0.14	ADI of TMP could be reached for about 1 potato

DPH: diphenhydramine, FLX: fluoxetine, PMD: primidone, SMX: sulfamethoxazole, TMP: trimethoprim

The ADI of primidone was typically the controlling factor for health impact, due to its higher uptake in market-sourced produce compared to other compounds. Generally, the health impact for adults from ingestion of produce was unlikely, but still possible. Toddlers exhibit

lower necessary intake to exceed the ADI compared to adults, yet the health impact is still typically unlikely due to less food ingested. For potatoes, the ADI of trimethoprim could be reached for both adults and toddlers from ingestion of approximately 4 and 1 medium-sized potato, respectively.

Some factors not taken into consideration in this preliminary health impact estimate that could lower the intake to exceed the ADI are transformation products from human and plant metabolism as well as exposure to cocktail mixtures of PPCPs from the same plant. This was a preliminary risk analysis but appears to present an unlikely risk from ingestion of market-sourced produce.

3.6 LC-MS/MS Analysis and Ingestion Health Impacts Conclusions

PPCP uptake in a range of plants was analyzed by LC-MS/MS. The following is a summary of the findings:

- Alfalfa crops took up eight PPCPs throughout the growing season. Uptake of compounds that are neutral at environmental pH was greater than uptake of ionic compounds.
- PPCP concentration was typically greater in hydroponically-grown, groundwater-irrigated tomato fruits compared to the soil-grown plants. Market-sourced plants took up greater concentrations of neutral compounds compared to ionic compounds, highlighting that electrostatic rejection at root membranes is the likely PPCP uptake and translocation inhibitor.
- Despite the presence of PPCPs in supermarket-sourced produce, the health risk is typically unlikely for adults and toddlers. The full health risk for ingestion of affected plants needs to include transformation products from metabolism of PPCPs as well as cocktail effects from PPCP mixtures.

Chapter 4 PPCP Transport from Wastewater Treatment Plants

4.1 PPCP Transport Methods and Data Collection

The environmental fate estimation program EPI Suite was used to predict PPCP transport after treated wastewater irrigation. EPI Suite provided estimations using chemical structure and predicted percent removal in WWTPs, soil adsorption coefficients (log K_{oc}), and soil half-lives. 36 PPCPs shown in Table 4-1 were chosen based on human use and structural differences. The contrast agents (diatrizoic acid and iopamidol) were included because they contain iodine. The antibacterials triclosan and triclocarban were included due to potential health concerns stemming from their antimicrobial properties. The aliphatic solvent (methanol) and surfactants (PFOA and PFOS) were chosen to verify predictions, because they are easily degradable and recalcitrant, respectively (Howard, Boethling, Jarvis, Meylan, & Michalenko, 1991; USEPA, 2017).

Table 4-1 Target PPCPs chosen for the EPI Suite transport estimation

Classification	Compound	CAS Number
Analgesic	Acetaminophen	103-90-2
Antibacterial	Sulfamethoxazole	723-46-6
	Triclocarban	101-20-2
	Triclosan	3380-34-5
	Trimethoprim	738-70-5
Antibiotic	Azithromycin	83905-01-5
	Erythromycin	114-07-8
Anticonvulsant	Carbamazepine	298-46-4
	Primidone	125-33-7
Antidepressant	Fluoxetine	2-84-9
Anti-inflammatory	Aspirin	50-78-2
	Diclofenac	15307-86-5
	Ibuprofen	15687-27-1
	Ketoprofen	22071-15-4
	Naproxen	22204-53-1
Beta Blocker	Atenolol	29122-68-7
	Metoprolol	37350-58-6
	Propranolol	525-66-6
Contrast Agent	Diatrizoic acid	117-96-4
	Iopamidol	60166-93-0
Estrogen Hormone	17α-Ethinylestradiol	57-63-6
	Estradiol	50-28-2
	Estriol	50-27-1
	Estrone	53-16-7
Lipid Regulator	Bezafibrate	41859-67-0
	Gemfibrozil	25812-30-0
Sedative	Diazepam	439-14-5
Stimulant	Caffeine	58-08-2
Synthetic Fragrance	Galaxolide	1222-05-5
	Tonalide	1506-02-1
Topical Agent	DEET	134-62-3
	Octocrylene	6197-30-4
	Salicylic acid	69-72-7
Solvent	Methanol	67-56-1
Surfactant	PFOA	335-67-1
	PFOS	1763-23-1

4.1.1 PPCP Transport Parameters

PPCP percent removal in conventional wastewater treatment applying activated sludge secondary treatment was estimated. The removal processes were volatilization, biodegradation, sorption to sludge, and loss in final effluent. The most uncertain variable was the biodegradation rate, which is treatment plant specific and dependent on biomass concentration. Due to EPI Suite limitations, aspects such as influent water conditions, extra treatment processes, and factors affecting biodegradation (recycle rate and microbial culture) were not considered.

Soil adsorption coefficients were determined using a molecular connectivity index method. Maximum and minimum soil partitioning coefficients (K_d) were determined from Equation 5-1, using a range of values for the fraction of organic carbon (f_{oc}) in agricultural soil. K_d values for each compound were estimated to determine the extent of soil partitioning. A threshold K_d value of 100 was applied to determine if compounds will primarily sorb to soils (K_d > 100) or if compounds will transport through soil (K_d <100) (ECETOC, 2014).

Equation 5-1 $$K_d = K_{oc} * f_{oc}$$

Soil half-life values were determined from K_{oc} values and a Level III Fugacity model in EPI Suite that estimated partitioning into different environmental compartments. Compounds with half-lives of 30 days or less were classified as non-persistent, 30-100 days were moderately persistent, and over 100 days were persistent (Kerle, Jenkins, & Vogue, 1994). Model limitations meant that the estimated maximum possible half-life was 360 days. Limitations also applied to factors such as precipitation rate, aerosol deposition, soil water runoff, and diffusion mass transfer coefficients.

The transport parameters and corresponding calculations are tabulated in Appendix E.

4.2 PPCP Transport Results and Discussion

4.2.1 PPCP Removal in Conventional Wastewater Treatment

EPI Suite estimations for percent removal of PPCPs in conventional wastewater treatment are shown in Figure 4-1.

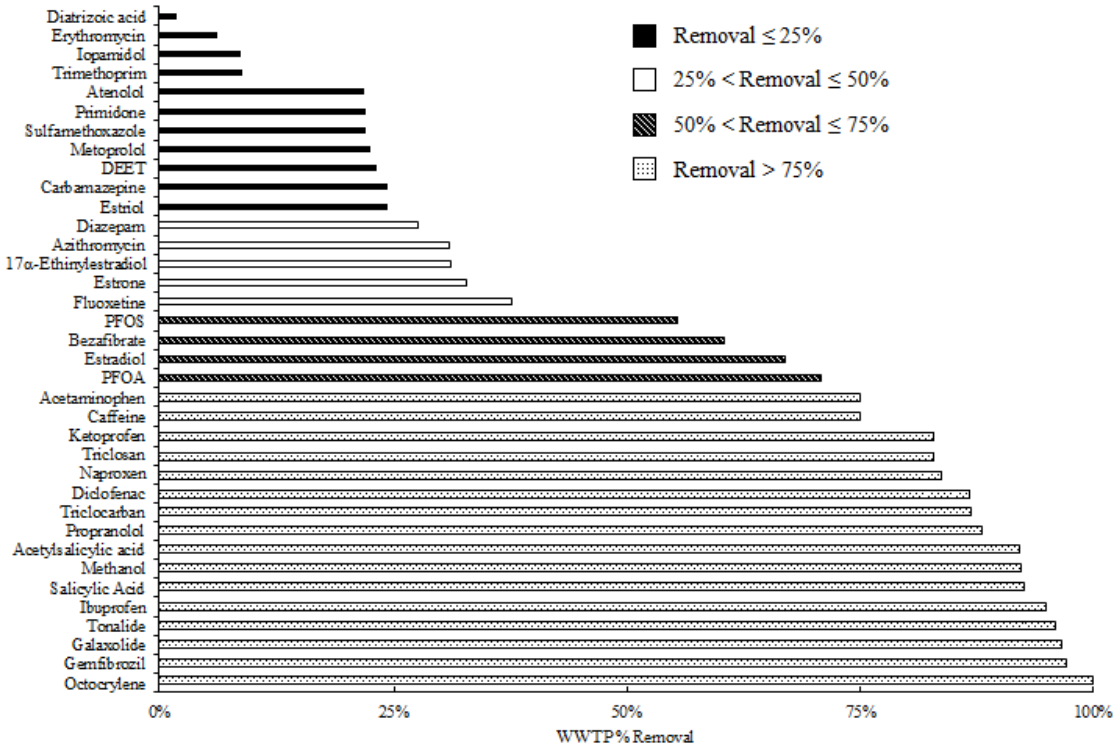


Figure 4-1 EPI Suite estimate of percent removal for target PPCPs from conventional wastewater treatment applying activated sludge. Compounds were grouped by percent removal

The majority of each compound was estimated to be removed by biodegradation and sludge adsorption. Volatilization was limited due to the low Henry's Law constants of most PPCPs. Removal rates differed from 1.94% (diatrizoic acid) to 99.9% (octocrylene), with a mean removal of 56.2%. Compounds were grouped at 25% removal intervals to determine if there were any structural similarities correlating with removal. Halogenated compound removal ranged from

1.94% (diatrizoic acid) to 86.9% (triclocarban), indicating that halogenated compound removal was diverse. Non-halogenated antimicrobials (azithromycin, erythromycin, sulfamethoxazole, and trimethoprim) had removal of 6.23-31.0%, likely due to biodegradation resistance. The estimation highlighted the wide variety of PPCP removal in conventional WWTPs.

4.2.2 PPCP Sorption Potential

A range of soil partitioning coefficients for each compound to estimate environmental transport are shown in Figure 4-2.

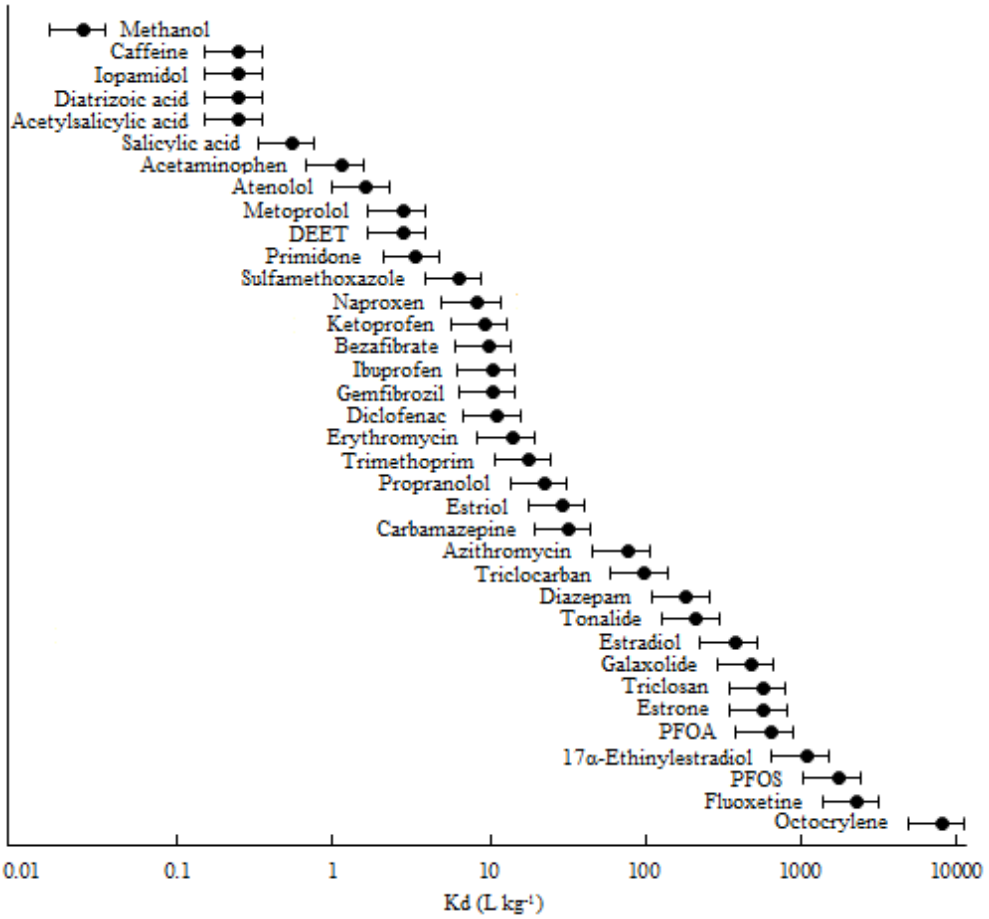


Figure 4-2 Estimated PPCP soil partitioning coefficients from EPI Suite. Markers represent average values and error bars represent upper and lower K_d estimates

Iopamidol, diatrizoic acid, and caffeine have average K_d values below 1 and could transport to groundwater if they are resistant to biodegradation. These compounds thus represent potential environmental markers for reclaimed wastewater release that can transition into groundwater. Primidone, sulfamethoxazole, naproxen, bezafibrate, ibuprofen, gemfibrozil, diclofenac, trimethoprim, and carbamazepine have K_d values between 1 and 100 and thus somewhat sorb to soil. These compounds have been readily detected in plants because they do not strongly bind to soil and can be present in the transpiration stream depending on respective hydrophilicity. Additionally, transport to groundwater is possible because of the relative lack of soil sorption, especially if these compounds are resistant to biodegradation like sulfamethoxazole. Compounds with K_d values greater than 100 strongly sorb to soils and have restricted transport to groundwater and plants, particularly compounds with K_d values approaching 10000. Additionally, these compounds could be targeted for WWTP removal using activated carbon. The estrogen hormones generally had a high sorption potential, which limits interactions with macrobiota. PFOA and PFOS had average K_d values of approximately 1000, indicating that these surfactants have limited transport to groundwater.

4.2.3 PPCP Soil Half-Lives

Soil half-lives were predicted to determine how long a compound can persist in soil when subjected to biotic and abiotic degradation. Figure 4-3 shows predicted soil half-lives and classifies compounds as non-persistent, moderately persistent, or persistent.

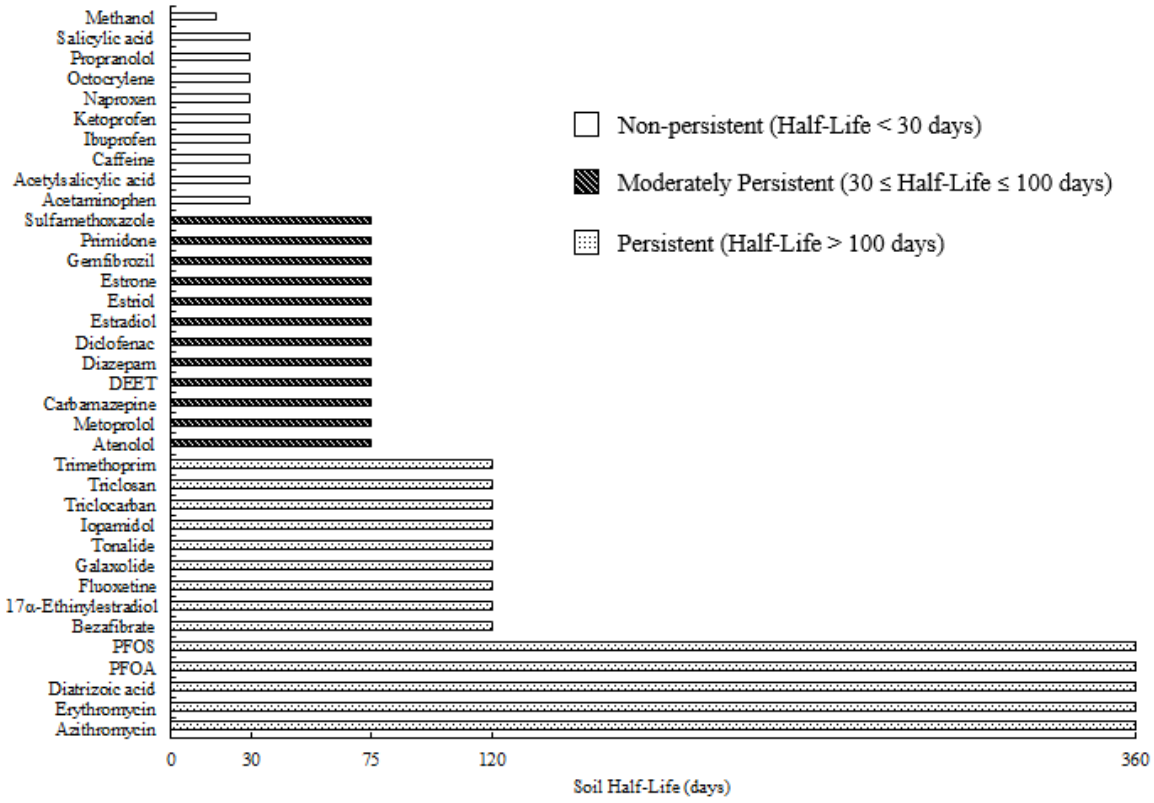


Figure 4-3 Estimated soil half-life values from EPI Suite. The maximum half-life estimate from EPI Suite was 360 d. Compounds were grouped by persistence

61% of compounds were moderately persistent or non-persistent. All halogenated compounds were persistent. PFOA and PFOS could be further classified as recalcitrant, and likely have a half-life a lot longer than 360 days. Azithromycin and erythromycin have considerably

larger molecules (>730 Da) than the other PPCPs, and could also be classified as recalcitrant. Most antibiotics were also predicted to be persistent due to their biodegradation resistance.

4.3 PPCP Transport Conclusions

PPCP transport to environmental compartments was determined from EPI Suite by predicting WWTP removal, sorption potential, and soil half-lives. The following is a summary of the findings:

- Diatrizoic acid, azithromycin, and erythromycin could transport to the groundwater due to low WWTP removal, sorption potential, and long half-lives.
- Trimethoprim, sulfamethoxazole, primidone, and carbamazepine could persist in the environment and either transport to groundwater, remain in the soil, or be taken up by plants due to intermediate sorption potential.
- Halogenated compounds (diatrizoic acid, fluoxetine, iopamidol, PFOA, PFOS, triclocarban, and triclosan) are all classified as persistent and can sorb to soils or transport to groundwater.

Chapter 5 Synthesis and Conclusions

The use of reclaimed wastewater for ASR and crop irrigation has risen in arid areas due to global climate change and population growth reducing freshwater supplies. Trace anthropogenic compounds not removed during conventional wastewater treatment have been released to a variety of environmental compartments. Quantification of these compounds in ASR recharge utilities and crops irrigated with reclaimed wastewater helps to elucidate if reclaimed wastewater use constitutes a safe practice for the public. The related findings are presented in context of individual research goals from each chapter. The central research objective was to quantify trace anthropogenic compounds (NDMA and PPCPs) in reclaimed wastewater. Figure 5-1 lists the individual research goals and Figure 5-2 illustrates the interconnectivity of NDMA and PPCPs in reclaimed wastewater.

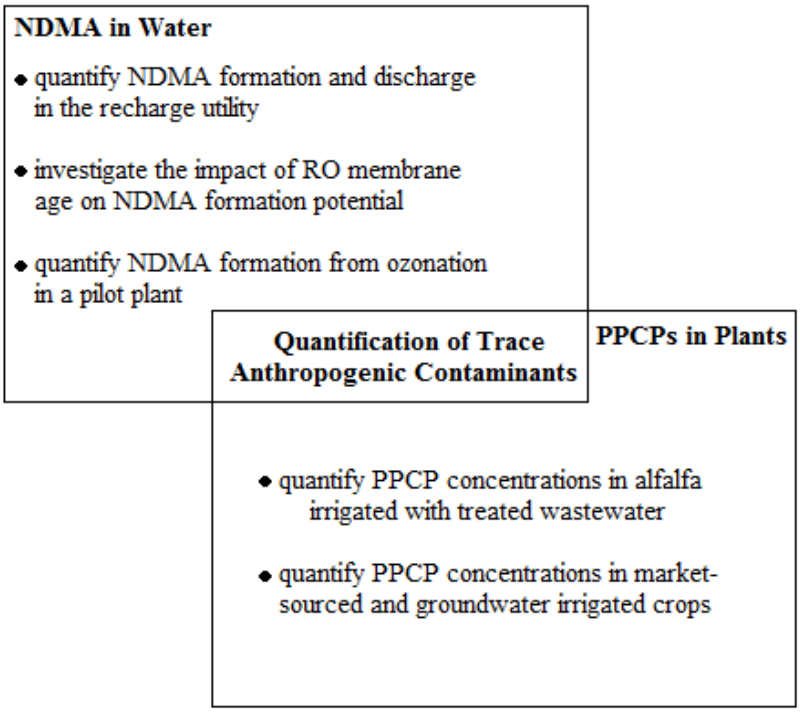


Figure 5-1 Research objectives from both studies used to quantify trace anthropogenic compounds in reclaimed wastewater

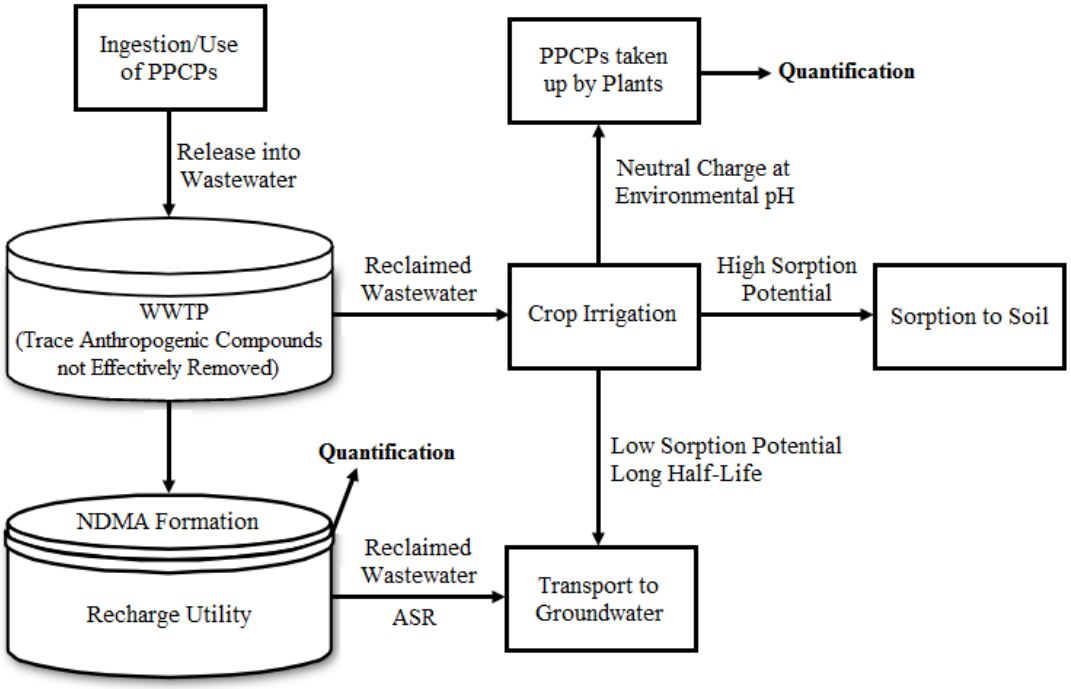


Figure 5-2 Interconnectivity of NDMA and PPCPs in reclaimed wastewater applications

NDMA and PPCPs are formed and present prior to reclaimed wastewater use, respectively, with their commonality being the potential for groundwater transport. NDMA formed during wastewater treatment can be discharged to groundwater from ASR, whereas PPCPs that have low sorption potential and long half-lives could transport to groundwater from crop irrigation. Additionally, PPCPs like ranitidine (active component in the antacid Zantac®) that contain a tertiary amine can form NDMA from chloramination (Liu, Selbes, Zeng, Zhong, & Karanfil, 2014). As such, removal of PPCPs like ranitidine could limit NDMA formation.

5.1 NDMA in Reclaimed Wastewater

NDMA can be formed in WWTPs applying chloramination or ozonation. NDMA and NDMA precursors were quantified in the recharge utility applying ASR. Advanced treatment (microfiltration, RO, and UV/AOP) are effective for NDMA and NDMA precursor removal. UV radiation cleaves the N-N bond in the NDMA molecule, thereby limiting discharge. The 2017 event had a UV product NDMA concentration of 3 ng L^{-1} whereas NDMA was not detected in the UV product for the 2018 event. NDMA precursor concentration was reduced on average by 84% for RO and 77% for UV/AOP. Overall NDMA and NDMA precursor concentration decreased through the utility after microfiltration by 93% and 89%, respectively.

NDMA formation from ozonation, as well as NDMA and NDMA precursor removal using BAC were quantified in a pilot plant. NDMA concentration after ozone contact was 51 ng L^{-1}. Removal of NDMA and NDMA precursors using BAC was between 58-75% and 70-82%, respectively, with greater removal corresponding to a lower EBCT. Human health concerns from NDMA transport in reclaimed wastewater from ASR or discharge to surface water is unlikely due to natural attenuation in groundwater and sunlight photolysis in surface water. However, low NDMA concentration could transport through groundwater and transition into wellheads, especially if ASR water is injected in close proximity to the wellhead.

5.2 PPCPs in Reclaimed Wastewater

PPCPs enter WWTPs through excretion or from washing off the applied site. Reclaimed wastewater contains PPCPs not removed during conventional treatment. Crop irrigation of reclaimed wastewater releases PPCPs to soil, where they can be taken up by plants, sorb to soil, transport to groundwater, or biodegrade. Quantification of PPCPs in plants irrigated with reclaimed wastewater found nine PPCPs taken up by a variety of plants. PPCP physicochemical properties in terms of ionization were likely the defining factor that limited uptake. Compounds ionized at environmental pH had limited uptake due to charge rejection at root membranes, whereas neutral compounds were readily taken up. Field-grown alfalfa had a concentration range of 0.03-54 ng g^{-1}, groundwater-irrigated crops had a range of 0.03-62 ng g^{-1}, and market-sourced plants had a range of 0.04-162 ng g^{-1}. Human health impacts were generally unlikely due to the low PPCP concentration present in market-sourced plants. PPCP sorption to soil and transport to groundwater was estimated using EPI Suite. Compounds with low sorption potential and long half-lives were predicted to transport to groundwater whereas compounds with intermediate to high sorption potential were more likely to be taken up by plants or remain in the soil. Reclaimed wastewater use involving crop irrigation is likely an effective reuse scheme due to the low concentration of PPCPs taken up by plants, as well as transport limitations to groundwater.

5.3 Summary of Trace Anthropogenic Compounds in Reclaimed Wastewater

NDMA and PPCPs can be present in reclaimed wastewater and transport to different environmental compartments. Table 5-1 summarizes the research objectives and conclusions reached from quantification of the compounds.

Table 5-1 Summary of research objectives and conclusions

Research Objective	**Conclusion**
Quantify NDMA formation and discharge in the recharge utility	NDMA and NDMA precursor concentration decreased through the utility due to advanced treatment by greater than 93% and 89%, respectively
Investigate the impact of RO membrane age on NDMA formation potential	Newer membranes reject 31% more NDMA more than older membranes
Quantify NDMA formation from ozonation in a pilot plant	NDMA forms from ozone contact and is removed by 58-75% using BAC columns
Quantify PPCP concentration in alfalfa irrigated with treated wastewater	Field-grown alfalfa takes up PPCPs between 0.03-54 ng g^{-1}, mostly dependent on physicochemical properties
Quantify PPCP concentration in market-sourced and groundwater irrigated crops	Market-sourced and groundwater irrigated crops contained PPCPs between 0.03-162 ng g^{-1}

The research conclusions indicate that NDMA and PPCPs can be quantified from their respective reclaimed wastewater applications. They are somewhat removed prior to reclaimed wastewater use depending on the applied treatment processes, however, incomplete removal indicates that they can transport to groundwater or irrigated fields from ASR and crop irrigation.

Chapter 6 Recommendations for Future Research

Chapter 2 – NDMA

NDMA and NDMA FP were quantified in a recharge utility and a pilot plant. NDMA formed from chloramination or ozone contact, with NDMA concentration decreasing through each system due to advanced treatment application. Recommendations for future work include:

- Elucidation of NDMA formation pathways from chloramination and ozone contact. This would make NDMA removal in advanced treatment systems clearer and instigate implementation of direct potable reuse applications without fear of NDMA discharge.

Chapter 3 – PPCPs

PPCPs were quantified in plants irrigated with treated wastewater, groundwater, and sourced from markets. Plants took up PPCPs primarily based on physicochemical properties. Recommendations for future work include:

- Field studies of PPCP uptake in reclaimed wastewater-irrigated plants at large-scale facilities that supply wholesale. Potential health impacts from ingestion of plants can then be outlined for a realistic scenario of ingestion of reclaimed wastewater-irrigated crops.
- Investigation and quantification of PPCP transformation products in WWTPs and crops to resolve uncertainties regarding health impacts from transformation products.

Chapter 4 – PPCP Transport from Wastewater Treatment Plants

PPCP transport from reclaimed wastewater irrigation was estimated using EPI Suite. Compounds with intermediate to high sorption potential and high half-lives were estimated to remain in the soil or be taken up by plants. Compounds with low sorption potential and high half-lives could transport to groundwater. Recommendations for future work include:

- Analysis incorporating a variety of WWTP processes and inputs, rather than theoretical values. This allows for modeling and mass balance analysis to predict PPCP transport to different environmental compartments.

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Appendix A: NDMA Concentration SOP

1. Prepare a 100 µg L^{-1} NDMA-d_6 isotope solution with Milli-Q water in an amber bottle. This solution can remain in the fridge and be reused for a few months provided it is securely closed and kept out of sunlight.

2. Spike 1 mL of the isotope solution into each 500 mL water sample.

3. Perform solid-phase extraction. First, run a clean Milli-Q water sample to rinse the input lines. Run Method 1, "Clean Sample Path" with blank cartridges. Then run Method 2, "Nitrosamines in Water 500 mL" using EPA Method 521 cartridges. DCM, MeOH, and Milli-Q water are attached to solvent ports 4, 2, and 5, respectively. Once complete, run a clean sample path again to rinse.

4. Push the DCM eluate through anhydrous sodium sulfate cartridges into 10 mL glass conical centrifuge tubes to remove any water.

5. Evaporate samples to just less than 1 mL under a gentle UHP N_2 gas stream in the TurboVap LV. The water temperature should be approximately 23°C.

6. Add DCM until the sample volume is 1 mL.

7. Transfer samples into 2 mL amber vials using pasteur pipettes and place in the freezer until analysis.

Appendix B: NDMA Formation Potential SOP

1. Prepare a 1 M borate buffer solution by dissolving 8.5046 g sodium tetraborate (borax) and 56.3086 g boric acid into 1 L Milli-Q water. Make sure that the solution is constantly stirred and heated to approximately 30°C.

2. Check that the pH is 8 in a 1:1000 diluted solution of the buffer.

3. Add 10 mL of a 5.65-6% sodium hypochlorite solution to 240 mL Milli-Q water to make a chlorine solution.

4. Dilute the chlorine solution 2000 times using Milli-Q water and add the contents of a DPD Free Chlorine Reagent powder pillow pack to the diluted 10 mL mixture.

5. Lightly swirl the mixture for 3 min to dissolve the powder.

6. Zero the reading for Program 80 on the DR 6000 UV-VIS spectrophotometer and ensure that the sides of the 10 mL diluted mixture vial are wiped clean.

7. Measure the free chlorine concentration using Program 80 on the DR 6000 UV-VIS spectrophotometer.

8. Apply the following equation to find the required ammonium chloride (NH_4Cl) addition, where (X) is the Cl_2 readout from the spectrophotometer.

$$\text{g } NH_4Cl = \frac{1.2 \text{ mol N}}{\text{mol } Cl_2} * 2000 \text{ (dilution factor)} * \frac{1 \text{ mmol } Cl_2}{71 \text{ mg } Cl_2} * \frac{\text{(X) mg } Cl_2}{\text{L}} * \frac{\text{mmol } NH_4Cl}{\text{mmol N}} * \frac{53.5 \text{ g } NH_4Cl}{\text{mmol } NH_4Cl} * \frac{1 \text{ g}}{1000 \text{ mg}} * 0.5 \text{ L} = \frac{\text{(X) } \frac{\text{mg}}{\text{L}} \text{ } Cl_2}{2.212}$$

9. Add the required NH_4Cl mass to 245 mL Milli-Q water and 5 mL of the 1 M borate buffer solution in a 500 mL amber bottle.

10. Pass the 250 mL chlorine solution through a burette into the rapidly stirred buffered ammonia solution. Chlorine solution should be slowly dripping out of the bottom of the burette.

11. Leave this monochloramine stock solution in the dark for 1 hr to equilibrate.

12. Add 5 mL of the buffer solution to each 500 mL water sample and measure the pH to ensure that it is 8.

13. Zero the reading for Program 66 on the spectrophotometer and ensure that the sides of the 10 mL mixture vial are wiped clean.

14. Measure the monochloramine concentration by adding the contents of a Monochlor F Reagent powder pillow pack.

15. Add the necessary volume of monochloramine solution to each 500 mL water sample using the following equation, where (Y) is the monochloramine concentration in the stock solution.

$$\text{Added volume} = \frac{18\ \frac{\text{mg}}{\text{L}}\ \text{Cl}_2\ *\ 500\ \text{mL sample}}{(\text{Y})\ \frac{\text{mg}}{\text{L}}\ \text{Cl}_2}$$

16. Store water samples at room temperature in the dark for 72 hr to facilitate NDMA formation.

17. Prepare a 0.5 M (88 g L^{-1}) ascorbic acid solution in Milli-Q water.

18. Quench water samples with 5 mL of the ascorbic acid solution.

19. Add 1 mL of a 100 µg L^{-1} NDMA-d_6 isotope solution in Milli-Q water to each sample. This gives an isotope concentration of 0.2 µg L^{-1}.

20. Perform solid-phase extraction. First, run a clean Milli-Q water sample to rinse the input lines. Run Method 1, "Clean Sample Path" with blank cartridges. Then run Method 2, "Nitrosamines in Water 500 mL" using EPA Method 521 cartridges. DCM, MeOH, and Milli-Q water are attached to solvent ports 4, 2, and 5, respectively. Once complete, run a clean sample path again to rinse.

21. Push the DCM eluate through anhydrous sodium sulfate cartridges into 10 mL glass conical centrifuge tubes to remove any water.

22. Evaporate samples to just less than 1 mL under a gentle UHP N_2 gas stream in the TurboVap LV. The water temperature should be approximately 23°C.

23. Add DCM until the sample volume is 1 mL.

24. Transfer samples into 2 mL amber vials using pasteur pipettes and place in the freezer until analysis.

Appendix C: PPCPs in Plants Extraction SOP

Sample Preparation

1. Use a knife to separate plants into respective components (roots, shoots, leaves, and fruits). Dice large plant components (fruits) to approximately 1 cm^3. Chop small plant components (roots, shoots, and leaves) into thin strips. Roots and shoots should be chopped to approximately 5 mm long with a 1 mm diameter. Rinse all plants components thoroughly with DI water to remove any organic matter.
2. Put plant components in separate freeze-dryer glass flasks and place in the freezer overnight.
3. Attach vials to ports on the Labconco FreeZone 4.5 L freeze-dryer system and leave for 72 hr. The freeze-dryer system temperature is set at -50°C and 0.1 mBar vacuum.
4. Detach vials and remove plant matter. Grind individual plant matter to powder. Use mortar-and-pestle for leafy material or high-sugar content material (watermelon fruit). Use a conical burr coffee grinder on the highest setting for fibrous material (roots and shoots).
5. Sieve ground plant matter with a US Standard #60 sieve into 1000 mL glass beakers. Ensure that at least a teaspoon of ground material is collected per sample. Transfer sieved plant matter into individual 10 mL glass vials and place in the fridge until ready for extraction.

PPCP Extraction

6. Weigh 0.2 g of plant matter using the Ohaus balance. Transfer the weighed material into plastic 50 mL centrifuge tubes.
7. Add 20 mL MTBE to each tube. Spike with PPCP isotopes at 5 μg L^{-1}.
8. Sonicate tubes for 20 min.
9. Centrifuge tubes at room temperature for 20 min at 1000 RCF.
10. Decant supernatant separately into new 50 mL centrifuge tubes and cap.
11. Add 20 mL ACN to the original tubes containing plant matter. Repeat the sonication and centrifugation steps. Decant supernatant into the new tubes, now containing 40 mL of

solution. Use pasteur pipettes to transfer any remaining liquid into the new tubes and dispose the original tubes.

12. Evaporate the combined decantate to near dryness under a gentle UHP N_2 gas stream in the TurboVap LV. The water temperature should be set to approximately 40°C.
13. Reconstitute with 20 mL Milli-Q water and 1 mL MeOH, ensuring that liquid is dispersed on the sides of the tubes to re-dissolve residue. If any plant residue is left on the tube walls, sonicate for 10 min and leave in the fridge overnight to allow residue to enter the solution.
14. Perform solid-phase extraction. First, run a clean Milli-Q water sample to rinse the input lines. Run Method 1, "Clean Sample Path" with blank cartridges. Then run Method 6, "PPCPs in Plants" using Oasis HLB 6 cc/200 mg cartridges. MeOH and Milli-Q water are attached to solvent ports 2 and 5, respectively. Once complete, run a clean sample path again to rinse.
15. Transfer eluate into 10 mL glass conical centrifuge tubes using pasteur pipettes.
16. Evaporate to near dryness under a gentle UHP N_2 gas stream in the TurboVap LV.
17. For samples being analyzed by GC-MS/MS, reconstitute with 1 mL MeOH and 50 µL ACN.
18. For samples being analyzed by LC-MS/MS, reconstitute with 1 mL MeOH.
19. Push all samples through 0.2 µm Cole-Parmer PTFE filters into 2 mL amber vials.
20. Add 50 µL MTBSTFA with 1% TBDMSCl into GC-MS/MS analysis vials. Firmly cap and ensure that no holes or gaps are present before placing them in the oven for 1 hr at 80°C.
21. Place all samples in the freezer until analysis.

GC-MS/MS Analysis

22. Ibuprofen quantification requires tandem MS/MS analysis in positive electron impact (EI+) mode using Argon as the collision gas.
23. The inlet method is "PPCP Uptake in Plants". The MS method is "MRM selected Ibuprofen CE 6V between 11-15 min". The injection volume is 10% (1 µL).

Appendix D Adult and Toddler Intake to Exceed the ADI

PPCP	Plant	Max C_{food} (ng/g dw)	IR_{veg}	$\beta_{g\text{-}cup}$	$\beta_{ww/dw}$	Mass Adult (kg)	Mass Toddler (kg)	Lowest Daily Therapeutic Dose (mg/day)	ADI (µg/kg-d)	Adult EDI (ng/kg)	Adult Intake to Exceed ADI (kg/day)	Toddler EDI (ng/kg)	Toddler Intake to Exceed ADI (kg/day)
Diphenhydramine	Lettuce	8.51	2.8	218.6	0.085	70	15.4	25	0.357	6.32	2.94	28.7	0.646
	Tomato	4.74		176.0						2.84	5.27	12.9	1.16
	Carrot	0.62		134.9						0.284	40.3	1.29	8.87
	Cucumber	3.93		174.2						2.33	6.36	10.6	1.40
	Potato	0.56		147.8						0.281	44.6	1.28	9.82
Fluoxetine	Lettuce	2.95	2.8	218.6	0.085	70	15.4	10	0.143	2.19	3.39	9.97	0.746
	Tomato	1.2		176.0						0.718	8.33	3.26	1.83
	Carrot	1.75		134.9						0.803	5.71	3.65	1.26
	Cucumber	0.48		174.2						0.284	20.8	1.29	4.58
	Potato	1		147.8						0.503	10.0	2.28	2.20
Primidone	Lettuce	40	2.8	218.6	0.085	70	15.4	50	0.714	29.7	1.25	135	0.275
	Tomato	49.3		176.0						29.5	1.01	134	0.223
	Carrot	15.9		134.9						7.29	3.14	33.1	0.692
	Cucumber	21.2		174.2						12.6	2.36	57.1	0.519
	Potato	31.4		147.8						15.8	1.59	71.7	0.350
Sulfamethoxazole	Lettuce	26.4	2.8	218.6	0.085	70	15.4	400	5.71	19.6	15.2	89.2	3.33
	Tomato	10.3		176.0						6.16	38.8	28.0	8.54
	Carrot	13.3		134.9						6.10	30.1	27.7	6.62
	Cucumber	4.75		174.2						2.81	84.2	12.8	18.5
	Potato	26.1		147.8						13.1	15.3	59.6	3.37
Trimethoprim	Lettuce	15.7	2.8	218.6	0.085	70	15.4	100	1.43	11.7	6.37	53.0	1.40
	Tomato	30.6		176.0						18.3	3.27	83.2	0.719
	Carrot	2.4		134.9						1.10	41.7	5.00	9.17
	Cucumber	4.2		174.2						2.49	23.8	11.3	5.24
	Potato	161.7		147.8						81.3	0.618	369	0.136

Appendix E: PPCP Transport Table of Values

Compound	Classification	CAS Number	pKA	log D at ph 6.0	K_H (atm-m^3/mol)	EPI Suite log K_{oc}	K_{oc} (L/kg)	Min. f_{oc}	Max. f_{oc}	Min. f_{oc}	Max. f_{oc}	Min. K_d (L/kg)	Max. K_d (L/kg)	WWTP Removal (%)	Ultimate Biodeg. Timeframe	Primary Biodeg. Timeframe	Ready Biodeg. Prediction	Mass Amount in Water (%)	Mass Amount in Soil (%)	Soil Half-Life (days)
Acetaminophen	Analgesic	103-90-2	9.38	0.91	6.42E-13	1.654	45.1	0.03	0.07	0.015	0.035	0.68	1.6	75.1	Weeks	Days	No	5.82	94.2	30
Sulfamethoxazole	Antibacterial	723-46-6	1.60, 5.70	0.60	9.56E-13	2.412	258	0.03	0.07	0.015	0.035	3.9	9.0	22.1	Weeks-Months	Days-Weeks	No	2.13	97.8	75
Triclocarban	Antibacterial	101-20-2	12.7	4.93	4.52E-11	3.608	4055	0.03	0.07	0.015	0.035	61	142	86.9	Months	Weeks	No	0.18	99.8	120
Triclosan	Antibacterial	3380-34-5	7.90	4.97	4.99E-09	4.369	23388	0.03	0.07	0.015	0.035	351	819	83.1	Months	Weeks	No	0.03	99.9	120
Trimethoprim	Antibacterial	738-70-5	7.12	0.27	2.39E-14	2.857	719	0.03	0.07	0.015	0.035	11	25	8.83	Months	Days-Weeks	No	0.96	99.0	120
Azithromycin	Antibiotic	83905-01-5	8.74	-3.64	5.30E-29	3.496	3133	0.03	0.07	0.015	0.035	47	110	31.0	Recalcitrant	Weeks-Months	No	0.29	99.6	360
Erythromycin	Antibiotic	114-07-8	8.88	0.25	5.42E-29	2.754	568	0.03	0.07	0.015	0.035	8.5	20	6.23	Recalcitrant	Weeks-Months	No	1.53	98.4	360
Carbamazepine	Anticonvulsant	298-46-4	13.9	2.77	1.08E-10	3.123	1327	0.03	0.07	0.015	0.035	20	46	24.5	Weeks-Months	Days-Weeks	No	0.44	99.5	75
Primidone	Anticonvulsant	125-33-7	11.8	1.12	1.94E-10	2.140	138	0.03	0.07	0.015	0.035	2.1	4.8	22.1	Weeks-Months	Days	No	3.76	96.2	75
Fluoxetine	Antidepressant	2-84-9	9.80	1.04	8.90E-08	4.971	93541	0.03	0.07	0.015	0.035	1403	3274	37.8	Months	Days-Weeks	No	0.01	99.9	120
Atenolol	Beta Blocker	29122-68-7	9.60	-2.84	1.37E-18	1.825	66.8	0.03	0.07	0.015	0.035	1.0	2.3	22.0	Weeks-Months	Days	No	6.90	93.1	75
Metoprolol	Beta Blocker	37350-58-6	9.67, 14.1	-1.34	1.40E-13	2.057	114	0.03	0.07	0.015	0.035	1.7	4.0	22.7	Weeks-Months	Days-Weeks	No	4.45	95.5	75
Propranolol	Beta Blocker	525-66-6	9.42	-0.52	7.98E-13	2.955	902	0.03	0.07	0.015	0.035	14	32	88.1	Weeks	Days-Weeks	No	0.39	99.6	30
Diatrizoic acid	Contrast Agent	117-96-4	2.17	-0.46	2.81E-18	1.000	10.0	0.03	0.07	0.015	0.035	0.15	0.35	1.94	Recalcitrant	Weeks	No	28.5	71.4	360
Iopamidol	Contrast Agent	60166-93-0	10.7	-1.35	1.14E-25	1.000	10.0	0.03	0.07	0.015	0.035	0.15	0.35	8.78	Months	Days-Weeks	No	23.8	76.1	120
17α-Ethinylestradiol	Synthetic Estrogen	57-63-6	10.5	3.90	7.94E-12	4.650	44668	0.03	0.07	0.015	0.035	670	1563	31.2	Months	Weeks	No	0.02	99.9	120
Estradiol	Estrogen	50-28-2	10.4	3.75	3.64E-11	4.186	15346	0.03	0.07	0.015	0.035	230	537	67.0	Weeks-Months	Days-Weeks	No	0.04	99.9	75
Estriol	Estrogen	50-27-1	10.4	2.67	3.64E-11	3.082	1208	0.03	0.07	0.015	0.035	18	42	24.5	Weeks-Months	Days-Weeks	No	0.48	99.5	75
Estrone	Estrogen	53-16-7	10.3	4.31	3.80E-10	4.375	23714	0.03	0.07	0.015	0.035	356	830	32.9	Weeks-Months	Weeks	No	0.03	99.9	75
Bezafibrate	Lipid Regulator	41859-67-0	3.83	1.83	2.12E-15	2.617	414	0.03	0.07	0.015	0.035	6.2	14	60.6	Months	Days-Weeks	No	1.63	98.3	120
Gemfibrozil	Lipid Regulator	25812-30-0	4.42	2.80	1.19E-08	2.636	433	0.03	0.07	0.015	0.035	6.5	15	97.2	Weeks-Months	Days-Weeks	No	1.31	98.7	75
Diclofenac	NSAID	15307-86-5	4.15	2.26	4.73E-12	2.661	458	0.03	0.07	0.015	0.035	6.9	16	86.6	Weeks-Months	Days-Weeks	No	1.24	98.7	75
Ibuprofen	NSAID	15687-27-1	4.91	2.67	1.52E-07	2.626	423	0.03	0.07	0.015	0.035	6.3	15	94.9	Weeks	Days	No	0.82	99.2	30
Ketoprofen	NSAID	22071-15-4	4.45	1.51	2.12E-11	2.586	385	0.03	0.07	0.015	0.035	5.8	13	82.9	Weeks	Days	No	0.89	99.1	30
Naproxen	NSAID	22204-53-1	4.15	1.18	3.39E-10	2.525	335	0.03	0.07	0.015	0.035	5.0	12	83.7	Weeks	Days	No	1.02	99.0	30
Acetylsalicylic acid	NSAID	50-78-2	3.49	-1.30	1.30E-09	1.000	10.0	0.03	0.07	0.015	0.035	0.15	0.35	92.1	Weeks	Days	Yes	13.7	86.3	30
Diazepam	Sedative	439-14-5	3.40	3.08	3.64E-09	3.875	7499	0.03	0.07	0.015	0.035	112	262	27.7	Weeks-Months	Days-Weeks	No	0.08	99.9	75
Caffeine	Stimulant	58-08-2	14.0	-0.55	3.58E-11	1.000	10.0	0.03	0.07	0.015	0.035	0.15	0.35	75.1	Weeks	Days-Weeks	No	13.7	86.3	30
Galaxolide	Synthetic Fragrance	1222-05-5	NA	4.72	1.32E-04	4.294	19679	0.03	0.07	0.015	0.035	295	689	96.6	Months	Weeks	No	0.04	99.9	120
Tonalide	Synthetic Fragrance	1506-02-1	NA	4.96	4.22E-05	3.938	8670	0.03	0.07	0.015	0.035	130	303	96.0	Months	Weeks	No	0.05	99.9	120
DEET	Topical Agent	134-62-3	-0.95	2.50	2.08E-08	2.055	114	0.03	0.07	0.015	0.035	1.7	4.0	23.4	Weeks-Months	Days-Weeks	No	4.48	95.5	75
Octocrylene	Topical Agent	6197-30-4	NA	6.21	3.00E-09	5.520	331131	0.03	0.07	0.015	0.035	4967	11590	99.9	Weeks	Days	No	0.00	100	30
Salicylic acid	Topical Agent	69-72-7	2.98, 13.6	-1.06	1.42E-08	1.336	21.7	0.03	0.07	0.015	0.035	0.33	0.76	92.6	Weeks	Days-Weeks	Yes	9.45	90.5	30
Methanol	Solvent	67-56-1	15.3	-0.52	4.27E-06	0	1.00	0.03	0.07	0.015	0.035	0.015	0.035	92.1	Days-Weeks	Days	Yes	14.9	83.7	17
PFOA	Surfactant	335-67-1	-0.5	1.58	NA	4.419	26242	0.03	0.07	0.015	0.035	394	918	70.8	Recalcitrant	Weeks-Months	No	0.01	95.1	360
PFOS	Surfactant	1763-23-1	-3.3	3.05	3.10E-09	4.855	71614	0.03	0.07	0.015	0.035	1074	2507	55.5	Recalcitrant	Months	No	0.01	99.7	360