Published in final edited form as:

Sci Total Environ. 2017 March 01; 581-582: 705–714. doi:10.1016/j.scitotenv.2016.12.185.

Pharmaceuticals in a temperate forest-water reuse system

Andrew D. McEachran^{a,*}, Damian Shea^b, and Elizabeth Guthrie Nichols^a

^aNorth Carolina State University, Department of Forestry and Environmental Resources, College of Natural Resources, Campus Box 8008, Raleigh, NC 27695, USA

^bNorth Carolina State University, Department of Biological Sciences, College of Sciences, Campus Box 7614, Raleigh, NC 27695, USA

Abstract

Forest-water reuse systems infiltrate municipal, industrial, and agricultural wastewaters through forest soils to shallow aquifers that ultimately discharge to surface waters. Their ability to mitigate regulated nutrients, metals, and organic chemicals is well known, but the fate of non-regulated chemicals in these systems is largely unstudied. This study quantified 33 pharmaceuticals and personal care products (PPCPs) in soils, groundwaters, and surface waters in a 2000-hectare forest that receives ~1200 mm/year of secondary-treated, municipal wastewater in addition to natural rainfall (~1300 mm/year). This forest-water reuse system does contribute PPCPs to soils, groundwater, and surface waters. PPCPs were more abundant in soils versus underlying groundwater by an order of magnitude (5–10 ng/g summed PPCPs in soil and 50–100 ng/L in groundwater) and the more hydrophobic chemicals were predominant in soil over water. PPCP concentrations in surface waters were greater at the onset of significant storm events and during low-rainfall periods when total summed PPCPs were >80 ng/L, higher than the annual average. With few exceptions, the margins of exposure for PPCPs in groundwater and surface waters were several orders of magnitude above values indicative of human health risk.

Graphical Abstract

*Corresponding author. admceach@ncsu.edu (A.D. McEachran), d_shea@ncsu.edu (D. Shea), egnichol@ncsu.edu (E.G. Nichols).
Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.scitotenv.2016.12.185>.

Keywords

Water reuse; Forests; PPCPs; Human health risk

1. Introduction

Climate change and population pressures are expected to increase the scarcity and diminish the quality of water resources (Ingram et al., 2013). While significant attention has been paid to more arid regions of the world, temperate climates are also experiencing water availability shortages and competition globally (Ingram et al., 2013). As such, managing water security through water re-use will become increasingly important as urbanization and human population growth continues. One strategy to improve water quality and regulate water

availability is the use of forest-water reuse systems (Braatz and Kandiah, 1996; Isosaari et al., 2010). Globally, forests are crucial to water resource capacity for 30% of the major cities in the world (Dudley and Stolton, 2003). Worldwide, forest water-reuse systems treat municipal wastewater through land application of wastewater to managed tree plantations as well as to natural forest stands (Nichols, 2016).

Forest water-reuse systems are slow-rate land application systems that treat municipal, industrial, and agricultural wastewaters via soil infiltration and groundwater recharge prior to surface water discharge (Crites, 1984; Pound and Crites, 1973). Slow-rate irrigation is the most ubiquitous and oldest wastewater land application technology and can be designed for different natural and managed landscapes such as crop lands, golf courses, and forest ecosystems (Crites, 1984; McKim et al., 1982). Relative to other land application technologies, slow-rate infiltration systems are designed to treat the greatest amount of wastewater on a given amount of land by using irrigation rates in excess of crop needs (Crites et al., 2014). In temperate regions, forest slow-rate infiltration systems enable year-round wastewater treatment, nutrient storage, and intermittent soil saturation without known adverse impacts on forest integrity and water quality. When compared to traditional wastewater treatment plants (WWTP) of similar wastewater volume treatment capacity, these systems are more cost-effective and energy efficient. Forest-water reuse systems provide ecosystem services such as provisioning wood products, biodiversity, and carbon storage that conventional wastewater treatment systems cannot provide (Shifflett et al., 2014). Under proper management and design, these systems effectively mitigate regulated nutrients, metals, and organics to acceptable water quality criteria levels for groundwater and surface waters (Crites, 1984; Crites et al., 2014; Hutchins et al., 1985), which is another important ecosystem regulating service. However, very little is known about the fate and effects of non-regulated wastewater contaminants in these water-reuse systems and studies are needed to understand the extent to which these systems regulate water quality.

Contaminants of emerging concern, specifically pharmaceuticals and personal care products (PPCPs), are non-regulated contaminants that have been routinely reported in the environment (Barnes et al., 2008; Boyd et al., 2003; Kim et al., 2007; Kolpin et al., 2002). These contaminants can elicit reproductive (Bringolf et al., 2010; Panter et al., 1998), behavioral (Weinberger Ii and Klaper, 2014), and developmental (Olmstead and LeBlanc, 2000) effects on aquatic organisms. While the environmental input of PPCPs has been documented from many sources (i.e. animal waste, landfill leachate, etc), municipal wastewater release to surface waters represents the largest source as most wastewater treatment technologies do not completely remove them prior to discharge to surface water bodies (Metcalf et al., 2010; Papageorgiou et al., 2016; Ternes et al., 2004). Various studies have reported concentrations of PPCPs in surface waters (de Jongh et al., 2012) and groundwaters (Meffe and de Bustamante, 2014) at levels far below acceptable daily intake doses for humans, but human health risks may exist when pharmaceuticals remain in water sources through drinking water intake. Exposure to unregulated pharmaceuticals is often calculated relative to acceptable intake values in adult humans to assess risk (Simazaki et al., 2015; Webb et al., 2003), and margins of exposure are rarely exceeded in drinking water (de Jongh et al., 2012). To date, PPCPs in forest-water reuse systems have yet to be evaluated relative to human health risks.

This study reports on the monthly occurrence, concentration, and human health risk of 33 PPCPs in applied wastewater, soils, groundwaters, and surface waters with seasonal changes for a full year. This temperate forest-water reuse system has been irrigated with secondary treated, municipal wastewater for two decades. Previous research has documented that this system effectively manages regulated nutrients for groundwater and surface water protection (Shifflett et al., 2014). A recent hydrological study of this system found that municipal wastewater comprised 50–76% of groundwater and 23% of surface water in irrigated catchments (Birch et al., 2016). Additionally, select PPCPs were identified in forest groundwater and surface water leaving the irrigated subwatershed during a preliminary investigation to ascertain if PPCPs were present (McEachran et al., 2016).

This work expands on the previous preliminary investigation by extending the sampling period to one year and addressing the seasonal differences in PPCP concentrations to better assess ecosystem and water regulating services for this system given the biological functioning of both built (reservoir lagoons) and natural (forest and soils) components. Preliminary research also did not address PPCP presence and concentrations in soils, an important compartment for PPCP mitigation and transport to groundwater. The occurrence and concentrations of PPCPs in soils and waters were evaluated using physiochemical parameters (log K_{ow}, K_{oc}), and margins of exposure (MOE) of PPCPs in groundwater were calculated to evaluate human health exposure potential via drinking water, which has not been previously assessed in forest-water reuse systems. Communities in this area utilize groundwater for drinking water resources, and quantifying PPCP human health risks is warranted to ensure that forest-water reuse systems are designed and implemented as an environmentally safe and sustainable water reuse technology.

2. Materials and methods

2.1. Study area and sampling

The majority of the study area of interest has been previously described (Birch et al., 2016; McEachran et al., 2016; Shifflett et al., 2014). Briefly, the study site is a 2000 ha, wastewater land-application facility which services a municipality of 70,000 defined by a large military presence and young (average age 22.8 years) population (United States Census Bureau, 2015). After a 7–14-day residence time in open reservoirs, secondary-treated wastewater is land-applied onto 930 ha of forested land in the 2000 ha watershed using one meter irrigation risers with weekly application rates of 25–75 mm. The 930-hectare land-application area receives approximately 1200 mm of wastewater and 1300 mm of precipitation annually (Birch et al., 2016; Shifflett et al., 2014) (see Supplementary material Fig. S2). Regulatory permits require that wastewater is applied only when conditions support infiltration of wastewater into soils; wastewater pooling and run-off at the soil surface is not allowed (Pound and Crites, 1973) and was not observed throughout the sampling period, even during periods of extreme rainfall when application still occurred under permit to reduce reservoir water levels.

Wastewater, groundwaters, and surface waters were collected over 12 consecutive months from August 2014 to July 2015 for analysis of PPCPs. Prior data were included from August 2014 to January 2015 (McEachran et al., 2016) and are identified in the tables and figures

below. Wastewater was collected from a central distribution spigot within the irrigation network and reflects wastewater after secondary treatment and storage in open reservoirs. Surface water samples were collected from Southwest Creek upstream of the land-application facility (Upstream site), at a small tributary within the site (TA SW sites), and at the subwatershed outlet on Southwest Creek (Outlet site) shown in Supplementary Material Fig. S1. Groundwater samples were collected along two separate gradients in two separate catchments, Transect A (TA 1–2, Well 3) and Transect B (TB 1–2), and from a reference groundwater well in a forested area that is not irrigated with wastewater (Reference). Surface and groundwater sampling procedures followed USGS field manual protocols (Wilde et al., 1999) and have been previously described (McEachran et al., 2016). One-liter amber glass sampling bottles were cleaned, solvent rinsed with acetone, and baked at 300 °C for 24 h before use. All water samples were, transported to the laboratory on ice and stored at 4 °C until extraction, within 7 days of sampling. A separate surface water sampling event took place during a 24-hour storm event in July 2015. The stage of the watershed outlet surface water was continuously monitored during the event while seven surface water samples were collected in order to evaluate how PPCPs are transported during high flow periods.

Soil samples were collected in two consecutive months (June and July 2015) concurrent with water sampling events at each groundwater sampling location along each transect (Transects A and B, see Fig. S1) at two depths (0–5 cm and 60–65 cm) in order to gain insight into PPCP migration through the vadose zone to groundwater. At each location and depth, approximately 100 g of soil (wet weight) were collected from four locations surrounding the groundwater sampling well. Samples were thoroughly mixed and quartered in the field following US EPA protocols for soil sampling (Simmons et al., 2014). 500 mL amber glass soil sampling bottles were cleaned, solvent rinsed with acetone, and baked at 300°C for 24 h before use. After collection all soil samples were transported to the laboratory on ice and stored at 4 °C until extraction, within 7 days of sampling. Soils ranged from sandy loam to fine sand and were fully characterized before subsequent analysis (see Supplementary Material, Table S1). The percent dry material was measured in each sample and ranged from 86 to 93% (see Supplementary Material, Table S1).

2.2. Sample extraction and analysis

2.2.1. Water samples—Extraction and pre-concentration of PPCPs in water samples has been previously described (McEachran et al., 2016) and is based on previously published methods (Cahill et al., 2004; Klosterhaus et al., 2013). All water samples were spiked with 50 ng of [^{13}C] carbamazepine before extraction. Briefly, Oasis® HLB solid phase extraction (SPE) cartridges were used for extraction and pre-concentration of pre-filtered surface water, groundwater, and wastewater samples followed by evaporation and reconstitution into LC-MS vials with 50 ng of reference stable isotope labeled (SIL) internal standards ([^{13}C] caffeine and [^{13}C] ibuprofen) for quantitation.

2.2.2. Soil samples—Soil samples were extracted via mechanical shaking following previously published methods with minor amendments (Karnjanapiboonwong et al., 2011; Walker et al., 2012; Williams and Adamsen, 2006). All samples were both water and solvent extracted to define fractionation of PPCPs within the soil. Briefly, 10 g wet-weight of

homogenized soil was manually mixed with individual spatulas with 15 mL of deionized water in 50 mL Oak Ridge Teflon® tubes to create a slurry. 50 ng of [¹³C] carbamazepine was spiked into every soil sample before extraction to evaluate recovery and matrix effects and an additional 10 mL of deionized water was added and the mixture was shaken horizontally on a New Brunswick Scientific Platform Shaker for 4 h. Tubes were centrifuged for 15 min at 2000 × *g* (Thermo Scientific IEC Centra CL2), the water fraction was decanted off, and the process was repeated. Water fractions were kept separate and stored at 4 °C until SPE cleanup. Proceeding with the solvent extraction, 25 mL of acetonitrile was added to the same Oak Ridge Teflon® tube and shaken for 4 h, centrifuged, and the solvent decanted off. The process was repeated with 10 mL of methanol plus 15 mL acetonitrile. Solvent extracts were combined, evaporated to 10 mL under a nitrogen stream, and mixed with 200 mL deionized water for SPE cleanup. Cleanup and pre-concentration followed the same method as the water samples and has been previously documented (McEachran et al., 2016).

2.2.3. Targeted analysis of PPCPs—Thirty-three PPCPs were targeted in the method (Table 1) and include steroid hormones, antibiotics and antimicrobials, prescription and non-prescription drugs, and personal care products including plasticizers, insect repellants, caffeine, and nicotine metabolites (see Supplementary Material Table S2 for more details). The targeted analytes were selected due to their ubiquity in wastewater (Kolpin et al., 2002; Papageorgiou et al., 2016; Sun et al., 2016) and high usage in the USA (Kolpin et al., 2002). All soil and water sample extracts were analyzed in the same manner (McEachran et al., 2016). Two separation and instrument methods (positive and negative electrospray) were used to identify and quantify all targeted compounds on a Thermo Scientific TSQ Quantum Ultra triple-quadrupole mass spectrometer configured with a Waters Acquity UPLC separation system. Targeted PPCPs were quantified using stable-isotope labeled (SIL) internal standard quantitation following similar previously published methods (Hilton and Thomas, 2003; McEachran et al., 2016; Roberts and Thomas, 2006; Tlili et al., 2016).

2.3. Data quality assurance and statistics

Data quality assurance and controls consisted of field duplicates, method blanks, method recovery spikes, and SIL internal standards. One field duplicate sample was collected for every sampling event throughout the study period. With every set of samples, a deionized water blank and method recovery spike were extracted and analyzed to determine possible sample contamination and method recoveries of all targeted pharmaceuticals, respectively. A surrogate recovery standard with an intermediate log Kow, [¹³C] carbamazepine, was spiked into every sample (soil and water) before extraction to evaluate extraction efficiency and matrix interferences. Average recovery of [¹³C] carbamazepine was 105% in all water samples and 86% in all soil samples. Method recovery of targeted compounds was within the range of other similar studies (Klosterhaus et al., 2013; McEachran et al., 2016), and the average for all targeted compounds was 69% in water samples and 42% in soil. Low recovery in multi-residue methods of complex environmental media is not unusual (Hilton and Thomas, 2003), and those compounds with unreasonably low recovery (<20%) were excluded from data analysis. Method quantitation limits ranged from 0.75 ng/L to 7.5 ng/L in surface water, groundwater, and wastewater samples and were 0.075 ng/g wet weight in soil. Matrix effects of wastewater with respect to PPCP quantitation have been well

described (Gros et al., 2006; Petrovic et al., 2006). As only one extraction surrogate was used for this suite of compounds, the data presented are likely underestimates of actual concentrations (Gros et al., 2006).

To evaluate the hypotheses that forest-water reuse systems contribute pharmaceuticals to the forest-water reuse system, to explain spatial and temporal variations, and to determine relationships between physicochemical properties (log Kow and log Koc) and PPCP concentration, statistical differences and relationships in concentrations were determined using, where appropriate, one-way analysis of variances (ANOVA), Student's *t*-tests, and Pearson's product-moment correlation coefficient. Data that did not fit assumptions of normality were analyzed using non-parametric statistics, specifically the Kruskal-Wallis Rank Sum, Wilcoxon Rank Sum tests, and Spearman's rank order correlation test as denoted. All analyses were conducted in R Computing Software (R Team Core, 2016).

3. Results and discussion

3.1. Wastewater

Pharmaceutical input, removal efficiencies, and seasonal variation of PPCPs in conventional wastewater treatment systems is increasingly well documented (such as Yu et al. (2013); Fairbairn et al. (2016); Papageorgiou et al. (2016)). However, information on seasonal PPCP occurrence in forest water reuse systems (open-air reservoirs, soils, groundwater, and surface waters) is limited but needed to evaluate the water regulating services provided by these green infrastructure systems. Overall, the most abundant PPCPs in wastewater were predominated by the prescription and over-the-counter drug, non-steroidal anti-inflammatory drug (NSAID), and antibiotics/antimicrobials chemical groups (Table 1, Fig. 1). Average concentrations of individual PPCPs in the irrigated wastewater ranged from <1 ng/L to 900 ng/L; the most abundant PPCPs by greatest average concentration were valsartan (878 ng/L), fluoxetine (618 ng/L), gemfibrozil (615 ng/L), tri-methoprim (571 ng/L), and diphenhydramine (441 ng/L). Average concentrations of valsartan have been reported at 350 ng/L in conventional wastewater effluent (Kasprzyk-Hordern et al., 2008), substantially lower than concentrations in this study in wastewater. Average concentrations of caffeine were 170 ng/L in this study and have ranged from 100 to 1000 ng/L in conventional systems (Sui et al., 2010) and fluoxetine concentrations in this study were higher than previously reported average concentrations in conventional treatment systems (200 ng/L (Metcalf et al., 2010) to 600 ng/L (Radjenović et al., 2009)). The insecticide DEET was found to be ubiquitous throughout the study site and throughout the sampling period at concentrations up to 300 ng/L in wastewater (see Supplementary Material, Table S2), therefore DEET was not included in figure presentation and subsequent analysis in this study due to its ubiquity dominating figures and potentially masking trends.

Seasonally, total summed concentrations of all PPCPs in wastewater decreased significantly with increasing daily temperatures (as monthly mean daily temperature) for spring and summer (Fig. 1, $r = -0.74$, $p = 0.003$). Individual PPCPs representative of high, middle, and low log Kows also decreased in the warmer months of the year (Fig. 2). Lower total PPCP concentrations with warmer daily temperatures may reflect chemical, biological, and physical PPCP dissipation in the open-air reservoirs due to enhanced photodegradation

through increased sunlight intensity, algal growth, and microbial activity. Specifically, sulfamethoxazole and carbamazepine concentrations in wastewater decreased in warmer months of the year (SMX - 500 ng/L to 200 ng/L and CMZ - 100 ng/L to 50 ng/L, see Fig. 2A) and their likelihood to photodegrade has been documented (Lam and Mabury, 2005). Likewise, higher temperatures could lead to higher rates of hydrolysis, volatilization, and microbial degradation. Enhanced algal growth during warmer months may also promote uptake, sorption, and biodegradation of PPCPs in the wastewater lagoons during the 7–14 day residence time before irrigation. Many PPCPs are also used seasonally (i.e. cold medicines, allergy medications, etc.) and can result in seasonal peaks of use and fluctuating presence in wastewater. Finally, variations in reservoir volumes due to rainfall may decrease PPCP concentrations due to dilution effects, but no significant correlation between rainfall and total PPCP concentration in wastewater was documented ($p > 0.05$). While exact mechanisms remain unknown and were beyond the scope of this study, PPCP occurrence and concentrations decreased in the open-air reservoirs during the warmer months of the year, indicating potential removal mechanisms.

3.2. Soils

The forest-water reuse system treats wastewater by soil infiltration; consequently, forest soils are critical to PPCP and nutrient removal to protect groundwater and surface water quality (Crites, 1984; Isosaari et al., 2010; Pound and Crites, 1973). Total summed PPCP concentrations were greater in irrigated forest soils than the reference, non-irrigated forest soil, and PPCP concentrations were greater in irrigated surface soils compared to irrigated deeper soils (Fig. 3A, B). Concentrations of PPCPs ranged from <1 ng/g to 5 ng/g wet weight (or up to 6 ng/g dry weight) for irrigated soils. Carbamazepine (0.7 ng/g), meprobamate (0.9 ng/g), bisphenol-A (1.4 ng/g), and 17- α ethynyl estradiol (2.0 ng/g) were the most abundant PPCPs in soils (Table S2), and their concentrations were similar to PPCP concentrations in soils irrigated with reclaimed wastewater (1–15 ng/g, dry weight) (Kinney et al., 2006) or amended with biosolids (<1 ng/g, dry weight) (Wu et al., 2010a). In this study, PPCP soil concentrations were lower than predicted based on the 20-year duration of irrigation in this system. Half-lives of PPCPs targeted in this study vary substantially in the literature, but many predicted biodegradation half-lives were less than two weeks (US EPA, 2016; Mansouri et al., 2016; Walters et al., 2010). Organic matter and microbial activity can cause dramatic changes to dissipation of PPCPs in soils resulting in increases and decreases in dissipation rate (Dodgen and Zheng, 2016). Thus the contribution of organic matter to soils from wastewater irrigation may have enhanced PPCP biodegradation and sequestration in forest-water reuse soils (Dalkmann et al., 2014) thus lowering observed PPCP concentrations.

Surface soils for Transect A had twice the organic carbon content as their deeper soils (Table S1) and greater amounts of total PPCPs. These surface soils had greater concentrations of PPCPs with higher log Kow values than deeper soils as observed by chemical group (Fig. 3A). Despite similar irrigation volumes between the transects (Birch et al., 2016), these trends were not observed for more sandy Transect B soils where surface and deeper soils had similar organic carbon content, PPCP amounts, and PPCP distribution. Sorption of many PPCPs in soil is driven by organic carbon content (Casey et al., 2003; Drillia et al., 2005),

and similar organic carbon contents would result in similar PPCP concentrations throughout the soil column. More antibiotics and antimicrobials were quantified in Transect A soils than Transect B soils while Transect B soils contained more prescription and over-the counter drugs (Fig. 3A). Physicochemical differences in soil quality likely contribute to differences in PPCP profiles in these different soils.

PPCP concentrations in soils were an order of magnitude higher than PPCP concentrations in groundwater (Fig. 3B and C). Total summed PPCP concentrations in soil were >6 ng/g while total PPCP concentrations in underlying groundwater ranged from 60 to 120 ng/L. PPCP concentrations, both grouped and individual concentrations, were analyzed for correlations against log Kow and log Koc to determine the effect of physicochemical properties on presence in soil versus water. PPCPs with larger log Kow values were found at greater concentrations in soils versus groundwater; as hydrophobicity (as average log Kow) of PPCPs within chemical groups increased, the relative abundance of those chemical groups in soils vs underlying groundwater also increased ($r = 0.65$, Fig. S3). However, no significant relationship between grouped PPCP concentration in soil and grouped log Koc existed. Furthermore, PPCPs were re-grouped by log Kow instead of compound class and the same trends were observed; a greater proportion of the total concentration in soil was made up of medium to high log Kow chemicals while a greater proportion of the total in groundwater was comprised of low log Kow chemicals (Fig. S4A, S4B). Individual chemical concentrations increased in soil as log Koc increased at all sampling locations except TA2 (all $p < 0.05$, $r > 0.35$), indicating that concentration is significantly correlated to a chemicals potential for sorption to organic carbon. These data provide preliminary insight as to the role of soil with respect to PPCPs in forest water reuse systems.

3.3. Groundwater and surface water

The irrigation of forest soils with wastewater provides a viable pathway for PPCP input to groundwater and surface waters and human exposure through drinking water supplies. Concentrations of PPCPs in groundwater ranged from <1 ng/L to >50 ng/L throughout the year (Table S2). The most abundant PPCPs in groundwater were cotinine, caffeine, valsartan, and carbamazepine which generally have lower log Kow values and greater water solubilities than the other targeted PPCPs indicating increased likelihood of movement towards groundwater (Table 1). Cotinine, caffeine, valsartan, and carbamazepine all have biodegradation half-lives <15 days (United States Environmental Protection Agency, 2016), indicating that long-term irrigation and soil penetration to groundwater is occurring despite rapid degradation. Total summed concentrations varied significantly by groundwater sampling location (Kruskal-Wallis, $p = 0.03$, Fig. 4A, differences denoted by letters), and groundwater in irrigated forest areas had significantly greater total PPCP concentrations than the non-irrigated, reference groundwater (Wilcoxon Rank Sum test, all $p < 0.05$) except for well TA 2 (Wilcoxon Rank Sum test, $p = 0.38$). The most upland groundwater wells (Well 3, TA 1) had higher total PPCP concentrations than groundwater well TA2, which is down gradient (Fig. 4A and Fig. S1), indicating potential degradation or sorption in groundwater during movement along the gradient.

PPCP concentrations in groundwater were at least one order of magnitude lower than concentrations in irrigated wastewater. For example, both valsartan and fluoxetine concentrations in groundwater were <10 ng/L, and caffeine was <20 ng/L while concentrations in wastewater were >1000, 700, and 150 ng/L, respectively. As the volume of precipitation and wastewater irrigation increased, total PPCP concentrations in groundwater also increased (TA1 $p = 0.07$, $r = 0.44$, TA2 $p = 0.02$, $r = 0.59$; Fig. 4B). Groundwater with the greatest total PPCP concentrations were dominated by chemical groups with the lowest mean log Kow values, indicating that these PPCPs migrated from soils to groundwater more so than the more hydrophobic PPCPs. The same trends were observed when chemicals were grouped according to log Kow; low log Kow chemicals (log Kow < 2.0) were predominant in groundwater relative to other sample types (Fig. S4B). Ionization potential and low biodegradability of these chemicals in particular are indicative of increased migration to groundwater (Avisar et al., 2009). Comparing representative chemicals across the span of log Kows resulted in a similar pattern in groundwater (Fig. 2B). Sulfamethoxazole (log Kow = 0.89) was generally present throughout the sampling period at higher concentrations in groundwater than representative chemicals with medium and high log Kows (Fig. 2B).

Surface waters entering the irrigated forest area did contain PPCPs (Fig. 5A and B). Several PPCPs, including atenolol, acetaminophen, paroxetine, and gemfibrozil, were quantified in upstream surface waters but not observed in irrigated wastewater. Some PPCPs (e.g. ibuprofen, atenolol) were present at similar concentrations both upstream and downstream of irrigated forest areas (see Supplementary Material, Fig. S5). In general, PPCP concentrations in surface waters in the irrigated forests were greater than upstream of the irrigated forest area (Fig. 5B), and concentrations of PPCPs were greatest at the watershed Outlet (t -test, $p < 0.001$, Fig. 5B). The most abundant PPCPs at the Outlet were lincomycin, cotinine, caffeine, DEET, fluoxetine, and valsartan while the most abundant PPCPs in upstream surface waters were atenolol, caffeine, and cotinine (Fig. S5). Concentrations of PPCPs in surface waters were similar to and often lower than previously reported values for PPCPs in surface waters (Supplementary Material, Table S3) (Kolpin et al., 2002; Loraine and Pettigrove, 2006; Pedersen et al., 2005; Sun et al., 2016). Individual chemicals with lower log Kows were predominant in the Outlet, and gemfibrozil, a prescription drug with a high log Kow (4.77), was rarely detected in surface water samples (Fig. 2C). The same pattern is observed when chemicals are grouped by log Kow; the lowest log Kow chemicals when grouped together increase in surface water throughout the system to the Outlet (Fig. S4C). Many factors contribute to transport and presence in surface water, and the chemicals most likely to remain in surface water have a combination of substantial presence in land-applied wastewater, are not likely to ionize, and do not biodegrade rapidly. Gemfibrozil, for example, is likely to be ionized ($pK_a = 4.5$) and is hydrophobic, indicating a low likelihood of transport from wastewater to groundwater or surface water. Carbamazepine and sulfamethoxazole are less likely to ionize and are less hydrophobic, resulting in a greater presence in water (Fig. 2C). These results suggest that only the most water soluble PPCPs present in land-applied wastewater are likely to end up in surface water sources.

Monthly irrigation volumes or seasonal rainfall did not significantly affect PPCP concentrations in surface water; however, concentrations at the watershed Outlet did vary significantly with respect to precipitation ($r = -0.54$, $p = 0.05$). As precipitation increased,

the total summed concentration decreased due to dilution by non-irrigated catchments within the watershed. PPCPs were quantified in surface waters collected at several time points throughout a major storm event in July 2015 (Fig. 4C). As expected, the Southwest Creek stage increased at the watershed outlet in two pulses (Das, 2008). Total PPCP concentrations increased until after the first crest of stream stage and then steadily decreased as rainfall continued and a second rise in stage occurred (Fig. 4C). Declining PPCP concentrations during the second stage pulse follows expected dilution effects from rainfall contributions across the entire subwatershed while initial PPCP spikes in the first stage represent initial mobilization and “first flush” of groundwater containing PPCPs. These observations are unique and important to understanding how forest water reuse systems can contribute PPCPs to surface waters, particularly with expected increased storm intensities due to climate change.

3.4. Human health risk estimation

Potential human health risk includes exposure to PPCPs via groundwater and surface waters used for drinking sources. In this study, concentrations of the most abundant PPCPs in groundwater and surface water were an order of magnitude below guideline values indicated in human health risk assessments previously conducted for individual PPCPs in drinking water (de Jongh et al., 2012; Schriks et al., 2010). Further, margins of exposure (MOE) were calculated based on the ratio between reported human health exposure levels and the estimated daily intake (EDI) from groundwater, as groundwater is the primary source of drinking water in this region of NC (Table 2). With the exception of four PPCPs, Acceptable Daily Intakes (ADIs) were used as exposure end-points for risk assessment (de Jongh et al., 2012; Murray et al., 2010; Schwab et al., 2005; Snyder et al., 2008; Versteegh and Dijkman, 2007). When unavailable, therapeutic or clinical doses were used and a safety factor of 1000 was applied (Collier, 2007; Vulliet and Cren-Olivé, 2011; Webb et al., 2003). Estimated Daily Intake was calculated based on consumption of two liters of water per day and the average concentrations of PPCPs in groundwater (Table 2). ADIs were gleaned from a variety of sources and were converted to uniform units (mg/day) before calculation. MOEs were calculated following Simazaki et al. (2015): ADI (or therapeutic dose) divided by the estimated daily exposure (EDI). Conservatively, MOEs <1000 are considered to be of concern according to the US EPA (United States Environmental Protection Agency, 2000). Only two PPCPs (estradiol and estrone) had MOEs <1000 (Table 3). Estrogenic compounds have high potency in risk assessment; despite the low concentrations present in groundwater (<5 ng/L), the MOEs for these estrogens are within the range of risk to human health via drinking water exposure. There is substantial uncertainty with regards to risk assessment in drinking water without appropriate toxicological studies, but on a conservative estimate 31 out of 33 PPCPs targeted in potential drinking waters were outside of the range of concern (DEET was removed from the risk assessment). Cumulative human health risk of mixtures of PPCPs, however, were not investigated in this study and remain under-investigated in literature. Finally, ecological risk in forest-water reuse systems has yet to be evaluated but exposure scenarios do exist for terrestrial and aquatic wildlife in this system. Ecological risk will be evaluated in future studies on this system.

4. Conclusions

Forest-water reuse systems are one option for sustainable wastewater treatment of nutrients and regulated chemicals such as metals and organics when systems are properly designed and managed. This study shows that most of the non-regulated organic contaminants of concern in this study were mitigated below levels considered harmful to human health. This temperate forest system has been in operation for 20 years, and it does contribute PPCPs to irrigated soils, groundwater, and surface waters. However, relative to concentrations in land-applied wastewater, substantial percentages (>90% concentration) of PPCPs were removed through the forest-soil system before reaching groundwater and the watershed outlet. Individual concentrations observed in groundwater were calculated to have low human health risks. These findings are important to the potential utility of these systems to provide sustainable water reuse alternatives to conventional municipal wastewater treatment for temperate landscapes. Concentrations of PPCPs in soil can help inform risk evaluation for wastewater irrigation onto human food crops. Although forested systems do not pose a human health risk from ingestion of plant material, exposure to PPCPs via ingestion of wastewater-irrigated crops can occur (Paltiel et al., 2016; Wu et al., 2010b) and uptake of PPCPs into plant material has not been completely characterized.

Our findings suggest that land application of municipal wastewater in forest-water reuse systems presents a feasible option for water reuse and wastewater treatment with minimal risk to human health. Other ecosystem benefits can be derived from these systems such as provisioning wood products, regulating soil and biodiversity, and provisioning water availability for surrounding areas. The benefits and tradeoffs of ecosystem services from forest water re-use systems merits investigation to understand their potential utility in both built and rural landscapes now and for the future.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors would like to thank L. Collins and W. Bodnar at the UNC Biomarker Mass Spectrometry Center for instrument use and technical assistance and A. Birch, S. Shifflett, and N. Harbordt for field and technical assistance. The authors would also like to sincerely thank the reviewers for providing suggestions and feedback that improved this manuscript. This study was supported with funding from the North Carolina State University Department of Forestry and Environmental Resources, the North Carolina Department of Agriculture & Consumer Services Bioenergy Research Initiative (G40100278314RSD), the UNC Center for Environmental Health and Susceptibility (P30ES010126), the National Institute of Environmental Health Sciences (NIEHS) Superfund Basic Research Program (Grant 5 P42 ES005948), and the NSF Research Experience for Undergraduates (REU): Basic and Environmental Soil Science Training (Grant 1358938).

References

- Avisar D, Lester Y, Ronen D. Sulfamethoxazole contamination of a deep phreatic aquifer. *Sci. Total Environ.* 2009; 407:4278–4282. [PubMed: 19403159]
- Barnes KK, Kolpin DW, Furlong ET, Zaugg SD, Meyer MT, Barber LB. A national reconnaissance of pharmaceuticals and other organic wastewater contaminants in the United States—I groundwater. *Sci. Total Environ.* 2008; 402:192–200. [PubMed: 18556047]

- Birch AL, Nichols EG, James AL, Emanuel RE. Hydrologic impacts of municipal wastewater irrigation to a temperate forest watershed. *J. Environ. Qual.* 2016
- Boyd GR, Reemtsma H, Grimm DA, Mitra S. Pharmaceuticals and personal care products (PPCPs) in surface and treated waters of Louisiana, USA and Ontario, Canada. *Sci. Total Environ.* 2003; 311:135–149. [PubMed: 12826389]
- Braatz, S., Kandiah, A. The use of municipal waste water for forest and tree irrigation. Food and Agriculture Organization of the United Nations; 1996. p. 45-51.
- Bringolf RB, Heltsley RM, Newton TJ, Eads CB, Fraley SJ, Shea D, et al. Environmental occurrence and reproductive effects of the pharmaceutical fluoxetine in native freshwater mussels. *Environ. Toxicol. Chem.* 2010; 29:1311–1318. [PubMed: 20821574]
- Cahill JD, Furlong ET, Burkhardt MR, Kolpin D, Anderson LG. Determination of pharmaceutical compounds in surface-and ground-water samples by solid-phase extraction and high-performance liquid chromatography–electrospray ionization mass spectrometry. *J. Chromatogr. A.* 2004; 1041:171–180. [PubMed: 15281266]
- Casey FXM, Larsen GL, Hakk H, Šim nek J. Fate and transport of 17 β -estradiol in soil–water systems. *Environ. Sci. Technol.* 2003; 37:2400–2409. [PubMed: 12831024]
- Collier AC. Pharmaceutical contaminants in potable water: potential concerns for pregnant women and children. *Ecohealth.* 2007; 4:164–171.
- Crites RW. Land use of wastewater and sludge. *Environ. Sci. Technol.* 1984; 18:140A–147A.
- Crites, RW., Middlebrooks, EJ., Bastian, RK. Natural wastewater treatment systems. CRC Press; 2014.
- Dalkmann P, Siebe C, Amelung W, Schloter M, Siemens J. Does long-term irrigation with untreated wastewater accelerate the dissipation of pharmaceuticals in soil? *Environ. Sci. Technol.* 2014; 48:4963–4970. [PubMed: 24702276]
- Das, G. Hydrology and Soil Conservation Engineering: Including Watershed Management. PHI Learning Pvt. Ltd; 2008.
- de Jongh CM, Kooij PJ, de Voogt P, ter Laak TL. Screening and human health risk assessment of pharmaceuticals and their transformation products in Dutch surface waters and drinking water. *Sci. Total Environ.* 2012; 427:70–77. [PubMed: 22551934]
- Dodgen LK, Zheng W. Effects of reclaimed water matrix on fate of pharmaceuticals and personal care products in soil. *Chemosphere.* 2016; 156:286–293. [PubMed: 27179428]
- Drillia P, Stamatelatos K, Lyberatos G. Fate and mobility of pharmaceuticals in solid matrices. *Chemosphere.* 2005; 60:1034–1044. [PubMed: 15993150]
- Dudley, N., Stolton, S. Running Pure: the Importance of Forest Protected Areas to Drinking Water. World Bank Publications; 2003.
- Fairbairn DJ, Arnold WA, Barber BL, Kaufenberg EF, Koskinen WC, Novak PJ, et al. Contaminants of emerging concern: mass balance and comparison of wastewater effluent and upstream sources in a mixed-use watershed. *Environ. Sci. Technol.* 2016; 50:36–45. [PubMed: 26605430]
- Gros M, Petrovi M, Barceló D. Development of a multi-residue analytical methodology based on liquid chromatography–tandem mass spectrometry (LC–MS/MS) for screening and trace level determination of pharmaceuticals in surface and wastewaters. *Talanta.* 2006; 70:678–690. [PubMed: 18970827]
- Hilton MJ, Thomas KV. Determination of selected human pharmaceutical compounds in effluent and surface water samples by high-performance liquid chromatography–electrospray tandem mass spectrometry. *J. Chromatogr. A.* 2003; 1015:129–141. [PubMed: 14570326]
- Hutchins SR, Tomson MB, Bedient PB, Ward CH, Wilson JT. Fate of trace organics during land application of municipal wastewater. *Crit. Rev. Environ. Sci. Technol.* 1985; 15:355–416.
- Ingram, KT., Dow, K., Carter, L., Anderson, J. Climate of the Southeast United States: Variability, Change, Impacts, and Vulnerability. Springer; 2013.
- Isosaari P, Hermanowicz SW, Rubin Y. Sustainable natural systems for treatment and disposal of food processing wastewater. *Crit. Rev. Environ. Sci. Technol.* 2010; 40:662–697.
- Karnjanapiboonwong A, Suski JG, Shah AA, Cai Q, Morse AN, Anderson TA. Occurrence of PPCPs at a wastewater treatment plant and in soil and groundwater at a land application site. *Water Air Soil Pollut.* 2011; 216:257–273.

- Kasprzyk-Hordern B, Dinsdale R, Guwy A. Multiresidue methods for the analysis of pharmaceuticals, personal care products and illicit drugs in surface water and wastewater by solid-phase extraction and ultra performance liquid chromatography–electrospray tandem mass spectrometry. *Anal. Bioanal. Chem.* 2008; 391:1293–1308. [PubMed: 18253724]
- Kim SD, Cho J, Kim IS, Vanderford BJ, Snyder SA. Occurrence and removal of pharmaceuticals and endocrine disruptors in South Korean surface, drinking, and waste waters. *Water Res.* 2007; 41:1013–1021. [PubMed: 16934312]
- Kinney CA, Furlong ET, Werner SL, Cahill JD. Presence and distribution of wastewater-derived pharmaceuticals in soil irrigated with reclaimed water. *Environ. Toxicol. Chem.* 2006; 25:317–326. [PubMed: 16519291]
- Klosterhaus SL, Grace R, Hamilton MC, Yee D. Method validation and reconnaissance of pharmaceuticals, personal care products, and alkylphenols in surface waters, sediments, and mussels in an urban estuary. *Environ. Int.* 2013; 54:92–99. [PubMed: 23527629]
- Kolpin DW, Furlong ET, Meyer MT, Thurman EM, Zaugg SD, Barber LB, et al. Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999–2000: a national reconnaissance. *Environ. Sci. Technol.* 2002; 36:1202–1211. [PubMed: 11944670]
- Lam MW, Mabury SA. Photodegradation of the pharmaceuticals atorvastatin, carbamazepine, levofloxacin, and sulfamethoxazole in natural waters. *Aquat. Sci.* 2005; 67:177–188.
- Loraine GA, Pettigrove ME. Seasonal variations in concentrations of pharmaceuticals and personal care products in drinking water and reclaimed wastewater in Southern California. *Environ. Sci. Technol.* 2006; 40:687–695. [PubMed: 16509304]
- Mansouri K, Grulke CM, Richard AM, Judson RS, Williams AJ. An automated curation procedure for addressing chemical errors and inconsistencies in public datasets used in QSAR modelling. *SAR QSAR Environ. Res.* 2016; 27:911–937. [PubMed: 27885861]
- McEachran AD, Shea D, Bodnar W, Nichols EG. Pharmaceutical occurrence in groundwater and surface waters in forests land-applied with municipal wastewater. *Environ. Toxicol. Chem.* 2016; 35:898–905. [PubMed: 26297815]
- McKim, HL., Sopper, WE., Cole, D., Nutter, W., Urie, D. Wastewater Applications in Forest Ecosystems. DTIC Document; 1982.
- Meffe R, de Bustamante I. Emerging organic contaminants in surface water and groundwater: a first overview of the situation in Italy. *Sci. Total Environ.* 2014; 481:280–295. [PubMed: 24602913]
- Metcalfe CD, Chu S, Judt C, Li H, Oakes KD, Servos MR, et al. Antidepressants and their metabolites in municipal wastewater, and downstream exposure in an urban watershed. *Environ. Toxicol. Chem.* 2010; 29:79–89. [PubMed: 20821422]
- Murray KE, Thomas SM, Bodour AA. Prioritizing research for trace pollutants and emerging contaminants in the freshwater environment. *Environ. Pollut.* 2010; 158:3462–3471. [PubMed: 20828905]
- Nichols, EG. Current and future opportunities for forest land application systems of wastewater. In: Ansari, AA.Gill, SS.Gill, R.Lanza, GR., Newman, L., editors. *Phytoremediation Management of Environmental Contaminants Volume III*. 2016.
- Olmstead AW, LeBlanc GA. Effects of endocrine-active chemicals on the development of sex characteristics of *Daphniamagna*. *Environ. Toxicol. Chem.* 2000; 19:2107–2113.
- Paltiel O, Fedorova G, Tadmor G, Kleinstern G, Maor Y, Chefetz B. Human exposure to wastewater-derived pharmaceuticals in fresh produce: a randomized controlled trial focusing on carbamazepine. *Environ. Sci. Technol.* 2016
- Panther GH, Thompson RS, Sumpter JP. Adverse reproductive effects in male fathead minnows (*Pimephales promelas*) exposed to environmentally relevant concentrations of the natural oestrogens, oestradiol and oestrone. *Aquat. Toxicol.* 1998; 42:243–253.
- Papageorgiou M, Kosma C, Lambropoulou D. Seasonal occurrence, removal, mass loading and environmental risk assessment of 55 pharmaceuticals and personal care products in a municipal wastewater treatment plant in Central Greece. *Sci. Total Environ.* 2016; 543(Part A):547–569. [PubMed: 26613513]

- Pedersen JA, Soliman M, Suffet IH. Human pharmaceuticals, hormones, and personal care product ingredients in runoff from agricultural fields irrigated with treated wastewater. *J. Agric. Food Chem.* 2005; 53:1625–1632. [PubMed: 15740050]
- Petrovic M, Gros M, Barcelo D. Multi-residue analysis of pharmaceuticals in wastewater by ultra-performance liquid chromatography–quadrupole–time-of-flight mass spectrometry. *J. Chromatogr. A.* 2006; 1124:68–81. [PubMed: 16759662]
- Pound, CE., Crites, RW. Wastewater treatment and reuse by land application. Vol. 1. Office of Research and Development, US Environmental Protection Agency; 1973.
- R Team Core. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2016.
- Radjenovi J, Petrovi M, Barceló D. Fate and distribution of pharmaceuticals in wastewater and sewage sludge of the conventional activated sludge (CAS) and advanced membrane bioreactor (MBR) treatment. *Water Res.* 2009; 43:831–841. [PubMed: 19091371]
- Roberts PH, Thomas KV. The occurrence of selected pharmaceuticals in wastewater effluent and surface waters of the lower Tyne catchment. *Sci. Total Environ.* 2006; 356:143–153. [PubMed: 15936058]
- Schriks M, Heringa MB, van der Kooi MME, de Voogt P, van Wezel AP. Toxicological relevance of emerging contaminants for drinking water quality. *Water Res.* 2010; 44:461–476. [PubMed: 19766285]
- Schwab BW, Hayes EP, Fiori JM, Mastrocco FJ, Roden NM, Cragin D, et al. Human pharmaceuticals in US surface waters: a human health risk assessment. *Regul. Toxicol. Pharmacol.* 2005; 42:296–312. [PubMed: 15979221]
- Shifflett SD, Hazel DW, Frederick DJ, Nichols EG. Species trials of short rotation woody crops on two wastewater application sites in North Carolina, USA. *Bioenergy Res.* 2014; 7:157–173.
- Simazaki D, Kubota R, Suzuki T, Akiba M, Nishimura T, Kunikane S. Occurrence of selected pharmaceuticals at drinking water purification plants in Japan and implications for human health. *Water Res.* 2015; 76:187–200. [PubMed: 25835589]
- Simmons, K., Deatrick, J., Lewis, B. SESD Operating Procedure for Soil Sampling. USEP, A., editor. Athens, GA: 2014.
- Snyder, S., Lei, H., Wert, E., Westerhoff, P. Yoon Y. Removal of EDCs and Pharmaceuticals in Drinking Water. Water Environment Research Foundation; 2008.
- Sui Q, Huang J, Deng S, Yu G, Fan Q. Occurrence and removal of pharmaceuticals, caffeine and DEET in wastewater treatment plants of Beijing, China. *Water Res.* 2010; 44:417–426. [PubMed: 19674764]
- Sun Q, Li M, Ma C, Chen X, Xie X, Yu C-P. Seasonal and spatial variations of PPCP occurrence, removal and mass loading in three wastewater treatment plants located in different urbanization areas in Xiamen, China. *Environ. Pollut.* 2016; 208(Part B):371–381. [PubMed: 26552527]
- Ternes TA, Joss A, Siegrist H. Peer reviewed: scrutinizing pharmaceuticals and personal care products in wastewater treatment. *Environ. Sci. Technol.* 2004; 38:392A–399A.
- Tlili I, Caria G, Ouddane B, Ghorbel-Abid I, Ternane R, Trabelsi-Ayadi M, et al. Simultaneous detection of antibiotics and other drug residues in the dissolved and particulate phases of water by an off-line SPE combined with on-line SPE-LC-MS/MS: method development and application. *Sci. Total Environ.* 2016;563–564. 424–433. [PubMed: 26896585]
- United States Census Bureau. State and County Quickfacts. Jacksonville, NC: 2015.
- United States Environmental Protection Agency. OSP Risk Characterization Handbook. Washington, D.C.: Office of Science Policy; 2000.
- United States Environmental Protection Agency. CompTox Chemistry Dashboard. 2016. <https://comptox.epa.gov/dashboard>
- Versteegh, J., Dijkman, E. Geneesmiddelen in drinkwater en drinkwaterbronnen. 2007.
- Vulliet E, Cren-Olivé C. Screening of pharmaceuticals and hormones at the regional scale, in surface and groundwaters intended to human consumption. *Environ. Pollut.* 2011; 159:2929–2934. [PubMed: 21570166]
- Walker CW, Watson JE, Williams C. Occurrence of carbamazepine in soils under different land uses receiving wastewater. *J. Environ. Qual.* 2012; 41:1263–1267. [PubMed: 22751070]

- Walters E, McClellan K, Halden RU. Occurrence and loss over three years of 72 pharmaceuticals and personal care products from biosolids-soil mixtures in outdoor mesocosms. *Water Res.* 2010; 44:6011–6020. [PubMed: 20728197]
- Webb S, Ternes T, Gibert M, Olejniczak K. Indirect human exposure to pharmaceuticals via drinking water. *Toxicol. Lett.* 2003; 142:157–167. [PubMed: 12691710]
- Weinberger Ii J, Klaper R. Environmental concentrations of the selective serotonin reuptake inhibitor fluoxetine impact specific behaviors involved in reproduction, feeding and predator avoidance in the fish *Pimephales promelas* (fathead minnow). *Aquat. Toxicol.* 2014; 151:77–83. [PubMed: 24210950]
- Wilde, FD., Radtke, DB., Gibs, J., Iwatsubo, RT. National Field Manual for the collection of Water-quality Data—Collection of Water Samples: US Geological Survey Techniques of Water-Resources Investigations book 9. chap. 1999.
- Williams C, Adamsen F. Sorption–desorption of carbamazepine from irrigated soils. *J. Environ. Qual.* 2006; 35:1779–1783. [PubMed: 16899748]
- Wu C, Spongberg AL, Witter JD, Fang M, Ames A, Czajkowski KP. Detection of pharmaceuticals and personal care products in agricultural soils receiving biosolids application. *Clean (Weinh).* 2010a; 38:230–237.
- Wu C, Spongberg AL, Witter JD, Fang M, Czajkowski KP. Uptake of pharmaceutical and personal care products by soybean plants from soils applied with biosolids and irrigated with contaminated water. *Environ. Sci. Technol.* 2010b; 44:6157–6161. [PubMed: 20704212]
- Yu Y, Wu L, Chang AC. Seasonal variation of endocrine disrupting compounds, pharmaceuticals and personal care products in wastewater treatment plants. *Sci. Total Environ.* 2013; 442:310–316. [PubMed: 23178835]

HIGHLIGHTS

- Forest-water reuse systems sustainably treat and manage wastewaters through land-application to natural forests.
- Fate and effects of wastewater contaminants remain uninvestigated in these systems.
- 33 pharmaceuticals were quantified in wastewater, groundwater, surface water, and soil.
- Land application of municipal wastewater contributes pharmaceuticals to the forest-water reuse system.
- Pharmaceutical concentrations observed do not pose a significant risk to human health.

Fig. 1. Total summed concentrations of PPCPs by chemical group in wastewater (bars) and average monthly daily temperature (filled circles). Chemical groups are indicated by color and are ordered by decreasing mean log Kow of the group. August–January concentrations have been previously reported in preliminary findings of this system (McEachran et al., 2016).

Fig. 2.

Mean concentrations and standard error of the mean (SEM) of individual PPCPs throughout the sampling period in wastewater (A), groundwater (B), and the subwatershed outlet (C). PPCPs are individually representative of low (sulfamethoxazole), medium (carbamazepine), and high (gemfibrozil) log Kows. August–January concentrations have been previously reported in preliminary findings of this system (McEachran et al., 2016).

Fig. 3.

(A) Average concentrations and SD of PPCPs in chemical groups for soils at a non-irrigated location (Ref) and at two irrigated transects (TA 1–2 and TB 1–2) at two soil depths (0–10 cm and 60–65 cm below surface). Chemical groups are indicated by color and are ordered by decreasing mean log Kow of the group. (B) Average concentrations and SD of PPCPs by group in combined surface and deep soils by location. (C) Average PPCP concentrations and SD by chemical group in groundwater at a non-irrigated location (Ref) and at two irrigated transects (TA 1–2 and TB 1–2). August–January PPCP concentrations of groundwater at locations TA1, TA2, and TB1 were previously reported in preliminary findings of this system (McEachran et al., 2016). Error bars are mean values $\pm$ on standard deviation.

Fig. 4.

(A) Box plots of summed ΣPPCP concentrations at six groundwater sampling locations for one year ($n = 12$). Significant differences of ΣPPCP concentrations between locations are denoted by letter (when $p < 0.05$). Boxplots denote the median, 25th percentile, and 75th percentile with whiskers extending to the 5th and 95th percentile. (B) Monthly ΣPPCP concentrations by chemical group with monthly precipitation plus irrigation volumes for irrigated wells TA 1 (top) and well TA 2 (bottom- downgradient of TA 1). August–January PPCP concentrations of groundwater at locations TA1, TA2, and TB1 were previously reported in preliminary findings of this system (McEachran et al., 2016).

Fig. 5.

(A) Locations of surface waters collected upstream of irrigated areas, within the forest-water reuse site, and at the sub-watershed outlet. (B) Average PPCP concentrations by chemical group at surface water locations. (C) Total summed PPCP concentrations by chemical group at seven sampling times throughout the duration of a storm event in July 2015. The stage (mm) of Southwest Creek is denoted by a black line throughout the duration of the storm event (22 h). August–January PPCP concentrations at location TASW and the Outlet only were previously reported in preliminary findings of this system (McEachran et al., 2016).

Table 1

Pharmaceuticals and personal care products (PPCPs) included in analysis by chemical group and physicochemical properties.

PPCP	log K _{ow} ^a	log K _{oc} ^b	pK _a ^a	Mean log K _{ow} ^a	Mean log K _{oc} ^b
<i>Steroid hormones</i>					
Estriol	2.45	3.08	10.54	3.32	3.54
Estrone	3.43	2.99	10.7		
Testosterone	3.25	3.30	19.0		
17- α Ethynylestradiol	3.67	5.52	10.3		
Progesterone	3.87	3.4	18.9		
17- β Estradiol	3.28	2.94	10.3		
<i>Plasticizer</i>					
BPA	3.32	2.8	9.6		
<i>Prescription/non-prescription drugs</i>					
Atenolol	0.16	2.47	9.60	2.61	2.97
Meprobamate	0.70	1.80	15.0		
Triamterene	0.98	1.90	6.20		
Carbamazepine	2.45	2.70	13.9		
Diltiazem	2.70	2.91	8.06		
Diphenhydramine	3.40	2.60	8.98		
Valsartan	3.65	4.00	5.51		
Paroxetine	3.95	4.00	9.60		
Fluoxetine	4.65	4.70	10.1		
Gemfibrozil	4.77	2.60	4.50		
<i>NSAIDs</i>					
Acetaminophen	0.46	1.30	9.38	2.21	2.48
Salicylic acid	2.26	2.60	2.98		
Naproxen	3.18	2.50	4.15		
Ibuprofen	3.97	3.50	4.91		
<i>Antibiotics and antimicrobials</i>					
Sulfamethazine	0.14	2.30	7.65	1.94	2.675

PPCP	log K _{ow} ^a	log K _{oc} ^b	pK _a ^a	Mean log K _{ow} ^a	Mean log K _{oc} ^b
Lincomycin	0.20	1.80	7.60		
Sulfamethoxazole	0.89	1.90	5.70		
Trimethoprim	0.91	1.90	7.12		
Tylosin	1.63	3.70	7.70		
Erythromycin	3.06	2.80	8.90		
Azithromycin	4.02	3.50	8.74		
Triclosan	4.76	3.50	7.90		
<i>Caffeine and metabolite</i>					
Caffeine	-0.07	3.50	10.4		
Paraxanthine	-0.2	2.01	10.8		
<i>Nicotine metabolite</i>					
Cotinine	0.07	2.10	8.80		
<i>DEET</i>					
<i>N,N</i> -diethyl-meta-toluamide	2.02	2.50			

^a log K_{ow} and pK_a values compiled from the Hazardous Substances Data Bank, Bethesda (MD); National Library of Medicine (US) [last revised 2016-03-17]. Available from <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>

^b log K_{oc} values compiled from the US EPA's CompTox Chemistry Dashboard (<https://comptox.epa.gov/dashboard>) and Mansouri et al. (2016).

Table 2

Margins of Exposure (MOE) from consumption of groundwater were estimated based on screening levels in the literature (cited in the footnote). Acceptable Daily Intake (ADI) values were preferred for all targeted pharmaceuticals when available but when unavailable therapeutic doses (MTD) were used. Average concentrations in groundwater from across the forest water reuse system were used to estimate daily intake per PPCP based on consumption of 2 L of water per day. Margins of Exposure were calculated as ADI/Estimated Daily intake per Simazaki et al. (2015).

PPCP	ADI or MTD (mg/day)	Avg conc GW (ng/L)	Estimated daily intake from GW (mg/day)	Margin of exposure
<i>Steroid hormones</i>				
17- β Estradiol ¹	1.19E-03	1.38E+01	2.77E-05	4.30E+01
Estrone ¹	9.10E-04	2.31E+00	4.63E-06	1.97E+02
17- α Ethynylestradiol ⁸	1.00E-02	0.00E+00	0.00E+00	N/A
Estriol	N/A	1.00E+00	2.01E-06	N/A
Testosterone	N/A	3.91E-03	7.82E-09	N/A
Progesterone ⁸	1.00E+02	1.26E-01	2.52E-07	3.97E+08
<i>Plasticizer</i>				
BPA ¹	5.00E-02	2.61E+00	5.23E-06	9.57E+03
<i>Prescription/non-prescription drugs</i>				
Fluoxetine ²	2.00E-01	8.92E+00	1.78E-05	1.12E+04
Valsartan	2.31E-01	3.70E+00	7.40E-06	3.12E+04
Meprobamate ⁵	7.50E-03	1.17E-01	2.35E-07	3.20E+04
Paroxetine ²	2.00E-01	7.86E-01	1.57E-06	1.27E+05
Carbamazepine ³	1.12E+00	3.08E+00	6.16E-06	1.82E+05
Gemfibrozil ²	3.85E+00	2.39E+00	4.79E-06	8.04E+05
Atenolol ³	5.00E-01	3.08E-01	6.16E-07	8.11E+05
Diltiazem ²	9.80E-01	8.51E-02	1.70E-07	5.76E+06
Diphenhydramine ⁷	2.50E+01	1.43E-01	2.85E-07	8.77E+07
Triamterene	N/A	8.10E-02	1.62E-07	N/A
<i>NSAIDs</i>				
Ibuprofen ²	7.70E+00	4.61E-01	9.22E-07	8.35E+06
Acetaminophen ²	2.38E+01	6.93E-01	1.39E-06	1.72E+07
Salicylic acid ⁴	3.00E+03	1.94E+00	3.88E-06	7.73E+08
Naproxen ⁵	5.70E-01	1.29E+00	2.58E-06	2.21E+05
<i>Antibiotics and antimicrobials</i>				
Triclosan ⁵	7.50E-02	2.93E+00	5.87E-06	1.28E+04
Trimethoprim ²	2.94E-01	2.07E-01	4.14E-07	7.09E+05
Sulfamethoxazole ²	9.10E+00	4.47E+00	8.93E-06	1.02E+06

PPCP	ADI or MTD (mg/day)	Avg conc GW (ng/L)	Estimated daily intake from GW (mg/day)	Margin of exposure
Azithromycin	2.52E+01	1.36E+00	2.73E-06	9.24E+06
Erythromycin ²	2.80E+00	2.08E-02	4.15E-08	6.74E+07
Lincomycin ²	1.75E+00	2.83E-05	5.65E-11	3.09E+10
Sulfamethazine ⁵	2.00E+00	0.00E+00	0.00E+00	N/A
Tylosin	N/A	0.00E+00	0.00E+00	N/A
<i>Caffeine and metabolite</i>				
Caffeine ⁶	3.00E+01	1.30E+01	2.60E-05	1.15E+06
Paraxanthine	N/A	3.80E+00	7.60E-06	N/A
<i>Nicotine metabolite</i>				
Cotinine	N/A	7.38E+00	1.48E-05	N/A

^{1, 2, 3, 5, 6} Acceptable Daily Intakes (ADIs) (de Jongh et al., 2012; Murray et al., 2010; Schwab et al., 2005; Snyder et al., 2008; Versteegh and Dijkman, 2007).

⁴ Minimum therapeutic dose (Webb et al., 2003).

⁷ Clinical dose (Collier, 2007).

⁸ Therapeutic dose (Vulliet and Cren-Olié, 2011).