A Review of Uptake and Translocation of Pharmaceuticals and Personal Care Products by Food Crops Irrigated With Treated Wastewater

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Abstract

Due to the detection of PPCPs in agricultural lands, research has recently focused on assessing the uptake and translocation of PPCPs into edible parts of crops. This is because PPCPs can be transferred to food crops through the application of reclaimed water from wastewater treatment plants. To better understand how PPCPs are taken up by food crops, 28 plant uptake studies relevant to food crops and reclaimed water application were identified and reviewed. This included crops such as bulb vegetables, cole crops, cucurbits, cereal grains, fruiting and leafy vegetables, herbs and spices, and roots and tuber vegetables. Of the 28 studies, 22 were carried out in controlled or greenhouse settings and 6 were field studies with reclaimed water. Based on the studies evaluated, it is evident that PPCPs can be taken up and translocated into edible parts of food crops at detectable levels. Therefore, human exposure of PPCPs from food crops is expected to be low based on studies performed. However, only a limited number of field studies have been conducted using reclaimed water to irrigate crops. Because reclaimed water use is anticipated to increase to help meet agriculture water demands, additional field studies are needed to better understand the uptake of PPCPs by crops over multiple growing seasons.

1.0 Introduction

We live in a chemical world, where numerous compounds are daily used in households for a variety of reasons from preventive medications to betterment of our lives. Among these chemicals, pharmaceuticals and personal care products (PPCPs) have received considerable attention in the last few years. For example, research on the occurrence of PPCPs in the environment began as early as the 1960s, but it wasn't until the 1990s that real concerns emerged regarding their potential ecological and human health effects. Since then, an abundance of studies have been published on a variety of PPCP-related topics, including the origin, source, occurrence, fate, and exposure of these contaminants. Most recently, research has been focused to investigate the transfer of PPCPs to the environment and then to food crops through the use of manure and sewage sludge (biosolids) as soil fertilizer, and irrigation with treated wastewater (hereafter referred to as reclaimed water) from wastewater treatment plants (Eggen and Lillo 2012). Because PPCPs have been detected in reclaimed water used for agricultural purposes and it is expected that the use of reclaimed water will double or triple in the near future (Wu et al. 2015), concerns have increased on their potential for uptake into food crops and effects to human health. While only a limited number of field studies have been published on the uptake of PPCPs by food crops irrigated with reclaimed water, laboratory and greenhouse studies have shown that PPCPs are taken up by plants. The objectives of this review are to summarize the current state of science on the plant uptake and translocation of PPCPs by food crops, discuss the approaches and challenges in managing PPCPs, and future research needs to protect human health risks.

2.0 PPCPs as Emerging Contaminants

Several terms have been used in the literature to describe the emerging contaminants. These include contaminants of emerging concern, microconstituents, micropollutants, and trace organic chemicals. In general, they are defined as a chemical or microorganism that has been detected in the environment and has the potential to cause adverse human health and ecological effects, yet their risk are not fully understood (USGS 2015; Drewes and Shore 2001; Younos 2005). This includes contaminants that have been released in the environment for many years but were not identified as a potential or known risk until recently, either because the technology did not exist to detect them or changes in the use and disposal of existing chemicals occurred, creating a new source (USGS 2015; DoD 2006). Because the potential health and environmental effects of emerging contaminants may not be known or little scientific information exists to characterize their risk, most of these contaminants are not regulated.

The PPCPs have been classified as emerging contaminants because of their widespread presence in the environment, particularly in surface water and groundwater (Daughton and Ternes 1999; Daughton, 2004). Although it is believed that PPCPs have been released into the environment for as long as these chemicals have been manufactured, it was not until recently, with new developments in technology that researchers have been able to detect and better understand the abundance and impacts of PPCPs in the environment. For instance, the U.S. Geological Survey (USGS) conducted a study using five newly developed analytical methods to detect organic wastewater contaminants (veterinary and human pharmaceuticals, personal care products, hormones, and plasticizers) in water samples from 139 streams across the United States and found that one or more contaminants were detected in 80% of the samples (Koplin et al. 2002). Since then, a plethora of studies have found PPCPs in various environmental matrices.

PPCPs have also been detected in reclaimed used for agricultural irrigation. This is of concern because PPCPs in reclaimed water may be transferred to crops from soil through root uptake. It is also anticipated that the use of reclaimed water will increase in order to meet irrigation demands, particularly in water-stressed areas. As a result, scientists have been focusing on better detecting PPCPs in reclaimed water and determining their potential uptake in food crops.

2.1 Early Signs of PPCPs in the Environment

Research on PPCPs in the environment began as early as the 1960s, when it was first reported by researchers from Harvard University that steroid hormones (estradiol and estrone) are not completely eliminated during wastewater treatment (Stumm-Zollinger and Fair, 1965; Snyder 2008). Other studies on the biodegradation of human hormones in wastewater were published in the 1970s (Tabak and Brunch 1970; Norpoth et al., 1973) and in general, concluded that not all hormones are fully biodegraded and further investigations were needed to understand their fate. Additional studies were published in the 1970s and 1980s, including a study in which concentrations of chlorophenoxyisobutyrate (metabolite of the widely used hypolipidemic drug, clofibrate) and salicylic acid (metabolite of aspirin) were detected in effluent samples from a wastewater treatment plant in Kansas City, Missouri (Hignite and Azarnoff, 1977). Despite these early signs of PPCPs being detected in the environment, little attention was given to these compounds until the 1990s. This may have been due to the heavy focus on other contaminants that were investigated during the 1970s and 1980s, including polychlorinated biphenyls (PCBs), heavy metals, volatile organics, polycyclic aromatic hydrocarbons (PAHs), and pesticides (Jones-Lepp et al., 2011; Kummerer, 2001).

Since the 1990s, the number of studies published on PPCPs in the environment has significantly increased. Recently, the U.S. Environmental Protection Agency (USEPA) developed the *PPCPs Bibliographic Citation Database*, which is a publically accessible listing of literature citations that are relevant to PPCPs in the environment (Daughton and Scuderi, 2015). The database covers a variety of topics on PPCPs and includes research published in journal articles, books, proceedings, databases, web pages, reports, etc. As of April 2015, over 21,000 citations have been added to EPA's database. This is a major increase from the number of citations available in December 2008, which consisted of 6,440 records. The number of citations available in EPA's bibliographic database by year are shown in Figure 1. The majority of these articles appear to be focused on the origins and sources of PPCPs as well as water treatment technologies for treating PPCPs. This is not a surprise, given that most of the research on PPCPs has been targeted on understanding how contaminants are released into the environment, particularly from wastewater treatment plants. However, limited research has been conducted on the uptake and translocation of these contaminants in plants, specifically food crops.

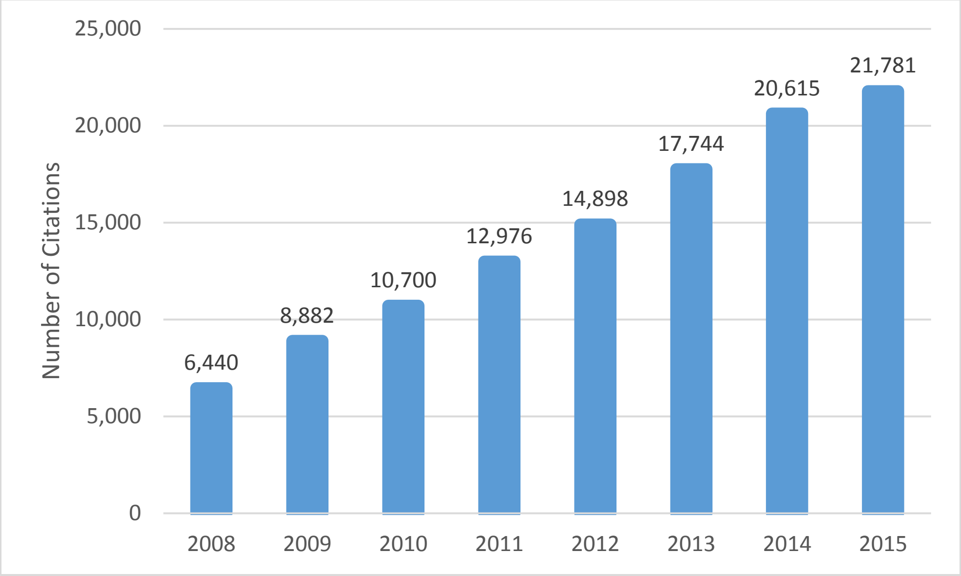

Figure 1: PPCPs Citations by Year in EPA's *PPCPs Bibliographic Citation Database*

Adapted from Daughton and Scuderi, (2015)

2.2 Types of PPCPs

PPCPs include pharmaceutical drugs (e.g., prescription, over-the-counter, illicit, therapeutic, and veterinary drugs), food supplements (e.g., nutraceuticals), and chemicals found in personal care products such as soap, detergents, fragrances, sunscreen, and cosmetics (Daughton, 2001). Pharmaceuticals are primarily used to treat illnesses, diseases, and medical conditions in both human and animals, while personal care products are used in consumer products and are typically applied to the human body (Daughton and Ternes, 1999).

3.0 Use of Reclaimed Water for Agricultural Irrigation

The reuse of treated wastewater has become an effective mechanism for solving water resource problems, particularly in arid and semi-arid regions such as the southwestern United States, where access to water supplies is limited. Also, with urban water demands expected to rise due to population growth, water reclamation and reuse have been considered a key in providing relief to water-stressed areas such as California (Wu et al. 2009; Wu et al. 2015). For example, in California alone, over 669,000 acre-feet (~218 billion gallons) of reclaimed water was used in 2009, with about 54% being used for agricultural and landscape irrigation (SWRCB 2009) and this is expected to increase 2-3 times in the near future (Wu et al. 2015). The distribution of reclaimed water in California is shown in **Figure 2**.

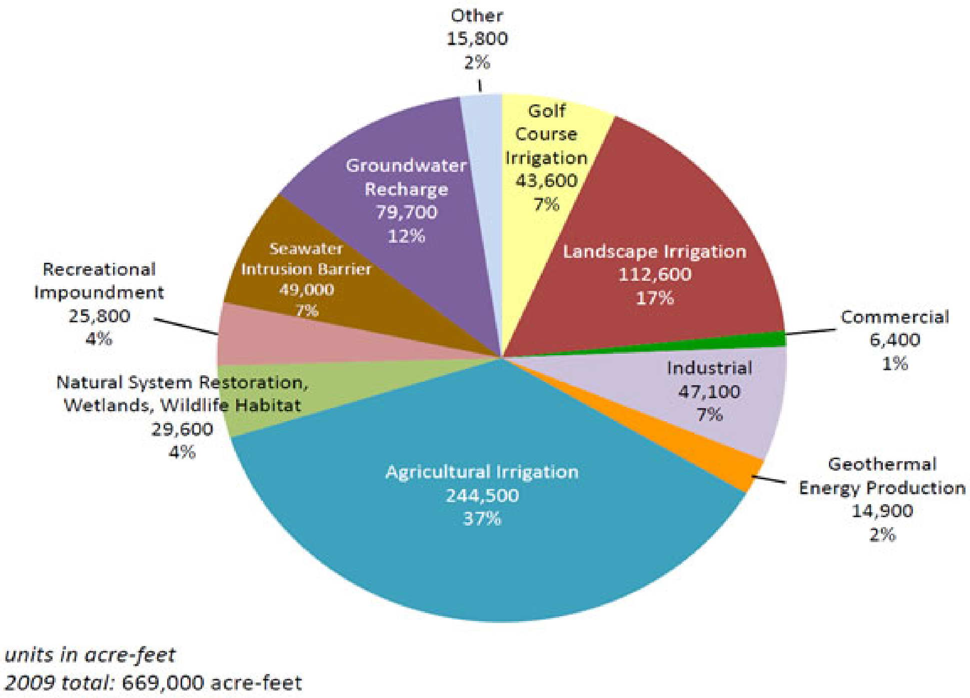

Figure 2: 2009 Distribution of Reclaimed Water in California

Source: SWRCB 2009

Florida is also one of the largest users of reclaimed water in the United States, with 63 of its 67 counties having utilities with reclaimed water systems. Although Florida is not a state one would associate with having a need for reclaimed water due to the high rainfall it receives, periodic droughts occur resulting in water shortages (Martinez and Clark 2009). Most of the state's reclaimed water (55%) is used for irrigating public access areas (e.g., residential areas, golf courses, parks, etc.), with about 10% being used for agriculture irrigation (FDEP 2015). Other states such as Arizona, Colorado, Nevada, New Mexico, Oregon, Texas, Virginia, and Washington are also relying more and more on reclaimed water to meet their water demands (USEPA 2012).

Use of reclaimed water on agricultural lands not only provides crops with the water needed for growth, but has also been shown to improve soil conditions due to the presence of nutrients, micronutrients, and organic matter that remain in wastewater after treatment. For instance, two sites in Beijing and California with a known history of long-term reclaimed water irrigation were compared to sites irrigated with tap water (Chen et al. 2013). Results indicated that the soil microbial biomass carbon had increased and soil enzymes were enhanced at the sites irrigated with reclaimed water. In addition, this study found that reclaimed water may supply a considerable portion of nutrient demand due to the presence of nitrogen and phosphorus in reclaimed water, reducing the need for fertilizers. Reclaimed water also provides farmers with a more reliable and economical water source.

Although there are multiple benefits associated with reclaimed water, there are also potential risks and challenges which are important to note. It has been found that the salinity level in reclaimed water is about 1.5 to 2 times higher than tap water, which may impact the soil quality and affect plant growth (Chen et al. 2013). Specifically, the accumulation of salts in soil can be toxic to sensitive plants species, resulting in poor root growth and water uptake by plants (Lewis and Wright 2011). Salt accumulation can also impact soils by making them less permeable.

In addition, there are concerns about environmental impacts from contaminants (e.g. PPCPs and heavy metals) and pathogens (e.g. viruses and parasites) present in reclaimed water, which may pose a threat to the environment as the use of reclaimed water increases (Chen et al. 2013). Some of the most commonly detected PPCPs in treated wastewater include pharmaceuticals such as acetaminophen, caffeine, meprobamate, atenolol, carbamazepine, sulfamethoxazole, diclofenac, fluoxetine, and others (Wu et al. 2014). *N,N-diethyl-metatoluamide* (DEET), triclosan, and triclocarban are among the most commonly detected personal care products in reclaimed water. A summary of benefits and risks associated with the use of reclaimed water is provided in **Table 1**.

Table 1: Benefits and Risks Associated with the Use of Reclaimed Water

Benefits	Risks
Reliable and economical source of water	Salts may be toxic to sensitive plants
Improves soil conditions	Decrease in soil permeability from salts
Reduces the need for fertilizers	Presence of contaminants and pathogens

4.0 Plant Uptake of PPCPs

Concerns regarding the presence of PPCPs in food crops have been increased following the evidence that plants are able to take up and accumulate these contaminants, not only in roots but in edible parts of the plant (Bartha et al., 2010). Although the measured concentrations found in food crops have been generally low, a little is known about the long-term effects of these compounds to human health (Boxall et al. 2006).

In general, factors that affect uptake of contaminants into plants include the compounds physicochemical properties (water solubility, vapor pressure, molecular weight, octanol-water partition coefficient), environmental characteristics (temperature, soil type, and water content in soil, agricultural practices), and plant characteristics (root system, shape and size of leaves, and lipid content) (Paterson et al., 1990; Trapp and Legind, 2011).

Some of the challenges faced when studying the uptake of PPCPs in plants is that there is a large variability in plant characteristics, with about 7,000 species having been cultivated for consumption throughout the world (FAO 2015). Additionally, the number and broad range of PPCPs manufactured and released into the environment makes it difficult to predict the uptake of these contaminants into plants.

4.1 Plant Uptake Processes

To better understand how PPCPs in the environment enter plant cells, it is important to discuss the major pathways and processes involved with the uptake and translocation of organic contaminants. Contaminants may be taken up by plants through the root system from the soil and its component soil solution (Paterson et al., 1990). The movement of contaminants across a cell membrane is achieved through passive diffusion (Trapp and Legind, 2011; Calderon-Preciado et al., 2012). Diffusion is the simplest type of passive transport as it does not require the cell to use energy. In contrast, active transport requires energy to move nutrients and contaminants across the cell membrane. Some hormone-like contaminants have been observed to be transported via active uptake, however, it is not believed to play a major role in the uptake of organic contaminants (Trapp and Legind, 2011). Once the contaminants are taken up by plants from the root system, compounds are transported to the aerial parts of the plant through the xylem of the vascular system. The xylem is responsible for moving water and nutrients upwards from the roots to the upper plant parts. A diagram showing the main uptake pathways in plants is shown in **Figure 3.**

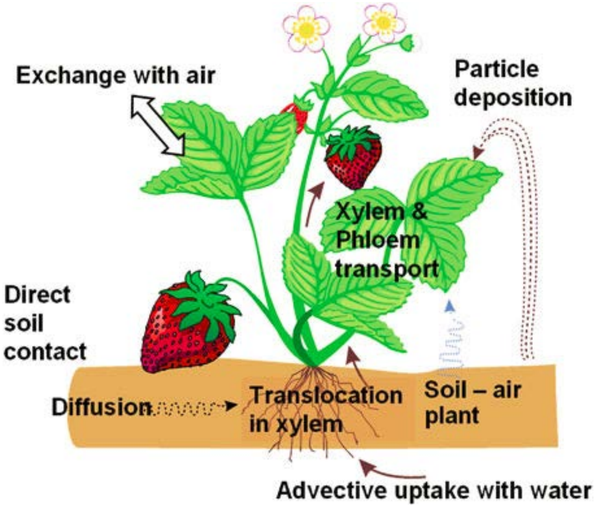

Figure 3: Plant Diagram Showing Main Uptake Pathways

Source: Trapp and Legind, 2011

Contaminants may also enter plants from the atmosphere as free gas molecules. This process occurs through the stomata, which are small pores on the surface of leaves and provide an entry for carbon dioxide and other atmospheric gases (Paterson et al., 1990). Once the gas molecules enter the stomata, they can be translocated by the phloem into other parts of plant tissues, including the root system (Calderon-Preciado et al., 2012). Contaminants in the vapor phase may also be taken up from the soil air by plant roots (O’Connor, 1996) or may dissolve in water droplets or sorb to particles that are deposited on plant surfaces and subsequently diffused into the plant (Hellstrom, 2004). Contaminants that have a high vapor pressure and high Henry’s law constant such as volatile organic compounds affect the uptake of contaminants from the air due to their large gaseous concentrations (Paterson et al. 1990). Uptake from air is also influenced by other factors such as temperature, plant species, contaminant concentration, and the chemical’s hydrophobicity.

Most available studies on plant uptake of PPCPs have been focused on root uptake as the pathway. This is because uptake of contaminants from irrigation with reclaimed water is expected to be the greatest through the roots than foliar uptake. As a result, the subsequent subsections focus on uptake of PPCPs through the root system.

4.2 Factors Influencing Plant Uptake of PPCPs

4.2.1 Chemical-Specific Factors

One of the characteristics generally recognized to influence the uptake of organic contaminants in plants is the octanol-water partition coefficient (K_{ow}). The K_{ow} is a quantitative parameter and is used as a relative indicator of the tendency of an organic compound to adsorb to soil (USEPA, 2009). Because PPCPs include a wide range of chemicals and physicochemical properties, their log K_{ow} values vary greatly from extremely hydrophilic (polar contaminants with low K_{ow}) to highly hydrophobic (lipophilic contaminants with high K_{ow}). Studies on pesticides have reported that translocation of organic contaminants occurs when the log K_{ow} is between 1 to 4 (Calderon-Preciado et al., 2013; Redshaw et al., 2008). This can be represented by the Gaussian distribution, where the maximum translocation of chemicals is observed at a log K_{ow} of ~1.78 (Briggs et al., 1982). Thus, if a contaminant is too hydrophilic, it will not be able to pass through lipid membranes of roots, while hydrophobic compounds will not be translocated because they tend to bind strongly to root tissues (Calderon-Preciado et al., 2013).

However, the use of K_{ow} as the primary factor affecting uptake of contaminants should only be considered for neutral PPCPs. This is because ionic PPCPs (usually more polar and water soluble) have been observed to behave differently than neutral PPCPs (Trapp and Ligand, 2011). For neutral PPCPs such as carbamazepine, a positive relationship between the root uptake and log K_{ow} (2.5) was observed (Carter et al., 2014), suggesting that hydrophobicity was a primary factor in the uptake of carbamazepine. However, this model cannot be applied to ionic PPCPs because additional mechanisms such as electrical attraction or repulsion, and ion trap may affect accumulation in the roots (Wu et al., 2015). Thus, the uptake of ionic compounds may be poorly related to the chemical's hydrophobicity. For example, Zhang et al. (2012) found that uncharged compounds such as caffeine are easily taken up by aquatic plants, whereas negatively charged compounds such as diclofenac are not taken up (Calderon-Preciado et al., 2013). This might be attributed to the plant cells having a negative electrical potential at the cell membrane, which leads to a repulsion of the negatively charged anions (Calderon-Preciado et al., 2011).

It has also been observed that contaminants must be stable within the soil system for a sufficient period of time in order for uptake to occur in plants. Specifically, contaminants with half-lives of more than 14 days are more likely to be taken up by plants (O'Connor, 1996). This is because degradation may occur for less stable compounds (half-life<14 days) during the wastewater treatment or transportation/storage process. For example, one study examined the levels of PPCPs in reclaimed water stored in an outdoor 6,000-

gallon polyurethane tank (Bondarenko et al., 2012). They showed that unstable compounds such as atenolol, trimethoprim, meprobamate, naproxen and gemfibrozil were decreased by as much as 41 to 82% prior to the application of reclaimed water to turfgrass plots. Another study found that concentrations of diclofenac and sulfamethazine were undetected in soil after 3-days of exposure, which is likely due to their corresponding half-life values of 0.5 and 0.99 days, respectively (Carter et al., 2014).

4.2.2 Plant-Specific Factors

In addition to the contaminant-specific pathways, the uptake of contaminants can vary depending on the plant species. For example, uptake of contaminants from soil is likely to be higher in root vegetables (e.g., carrots) than tree fruits (e.g., apples). This is because root crops are in close contact to soil, while tree fruit are not. However, uptake of contaminants directly from air is expected to be higher for tree fruits than root crops (Trapp and Ligand, 2011). Other plant-specific parameters include root system, transpiration rate, shape and size of leaves, and lipid content.

4.3 Uptake of PPCPs by Various Crop Types

As part of this review, plant uptake studies relevant to PCPPs were evaluated and summarized below and in **Table 2.** While there are other studies that have investigated the uptake of PCPPs by plants, these were selected because of their relevance to food crops and reclaimed water application. Using these criteria, a total of 28 plant uptake studies were identified, with 22 of them being carried out in controlled or greenhouse settings and 6 consisting of field studies with reclaimed water. Several studies were conducted under hydroponic conditions, which is a method used to quickly screen and identify PPCPs that have a high potential for plant uptake. However, this may not be representative of field conditions due to the complex processes of PPCPs in soils (Wu et al. 2015). For instance, fluoxetine was found to accumulate in plants grown under hydroponic conditions (Wu et al. 2013), but was not found in soybean plants grown in soils (Wu et al. 2010) perhaps due to sorption to soil (Wu et al. 2015). Therefore, caution should be taken when using hydroponic studies to predict plant uptake of PPCPs. Additionally, because of the different plant-growth methods used, it is difficult to compare the results found in each of the studies.

Table 2: List of Uptake Studies on PPCPs Relevant to Food Crops and Reclaimed Water Application

Crop Name	Growth Medium	Growth Conditions	Use of Reclaimed Water (Y/N?)	Source
Bulb Vegetables				
Onion	Nutrient solution	Controlled	No	Mathews et al. 2014
Cole Crops (Brassica)				
Broccoli	Nutrient solution	Controlled	No	Mathews et al. 2014
Cabbage	Nutrient solution	Controlled	No	Herklotz et a. 2009
Cabbage	Nutrient solution	Controlled	No	Mathews et al. 2014
Cabbage	Soil (coarse-loamy, alluvial)	Field-grown	(Continued)	Wu et al. 2014
Cabbage	Soil	Greenhouse	No	Li et al. 2013
Cauliflower	Artificial media	Controlled	No	Redshaw et al. 2008
Indian Mustard	Nutrient solution	Greenhouse	No	Bartha et al. 2010
Radish	Soil	Controlled	No	Carter et al. 2014
Watercress	Soil (sandy soil)	Controlled	No	Chitescu et al. 2013
Cucurbits				
Cucumber	Nutrient solution	Controlled	No	Mathews et al. 2014
Cucumber	Nutrient solution and soil	Greenhouse	Yes	Shenker et al. 2011
Cucumber	Nutrient solution	Controlled	No	Tanoue et al. 2012
Cucumber	Nutrient solution	Greenhouse	No	Wu et al. 2013
Cucumber	Soil (sandy soil, aeolian sand, alluvial soil)	Greenhouse	Yes	Goldstein et al. 2014
Cucumber	Soil	Controlled	No	Lillenberg et al. 2010
Cucumber	Soil (coarse-loamy, alluvial)	Field-grown	Yes	Wu et al. 2014
Cantaloupe	Soil (loam)	Field-grown	Yes	Jones-Lepp et al. 2010
Watermelon	Soil (loam)	Field-grown	Yes	Jones-Lepp et al. 2010

Table 2: List of Uptake Studies on PPCPs Relevant to Food Crops and Reclaimed Water Application

Crop Name	Growth Medium	Growth Conditions	Use of Reclaimed Water (Y/N?)	Source
Cereal Grains and Oilseed Crops				
Barley	Soil (loamy sand)	Greenhouse	No	Eggen and Lillo 2012
Barley	Soil (sandy soil)	Greenhouse	No	Eggen et al. 2011
Barley	Soil	Controlled	No	Lillenberg et al. 2010
Maize	Soil	Controlled	No	Marsoni et al. 2014
Maize	Soil (silt loam)	Controlled	No	Michelini et al. 2012
Maize Seedlings	Nutrient solution	Controlled	No	Card et al. 2012
Oat	Soil (loamy sand)	Greenhouse	No	Eggen and Lillo 2012
Oily Seeds (rape)	Soil (loamy sand)	Greenhouse	No	Eggen and Lillo 2012
Soybean	Nutrient solution	Greenhouse	No	Wu et al. 2010
Wheat	Soil (loamy sand)	Greenhouse	No	Eggen and Lillo 2012
Fruiting Vegetables				
Bell Pepper	Soil (coarse-loamy, alluvial)	Field-grown	Yes	Wu et al. 2014
Okra	Nutrient solution	Controlled	No	Mathews et al. 2014
Tomato	Soil (loamy sand)	Greenhouse	No	Eggen and Lillo 2012
Tomato	Soil (sandy soil, aeolian sand, alluvial soil)	Greenhouse	Yes	Goldstein et al. 2014
Tomato	Nutrient solution	Controlled	No	Mathews et al. 2014
Tomato	Soil (coarse-loamy, alluvial)	Field-grown	Yes	Wu et al. 2014
Herbs and Spices				
Pepper	Soil (loam)	Field-grown	Yes	Jones-Lepp et al. 2010
Pepper	Soil (loam)	Field-grown	No	Jones-Lepp et al. 2010
Pepper	Nutrient solution	Controlled	No	Mathews et al. 2014
Pepper	Nutrient Solution	Greenhouse	No	Wu et al. 2013

Table 2: List of Uptake Studies on PPCPs Relevant to Food Crops and Reclaimed Water Application

Crop Name	Growth Medium	Growth Conditions	Use of Reclaimed Water (Y/N?)	Source
Leafy Vegetables				
Arugula	Soil	Controlled	No	Marsoni et al. 2014
Celery	Nutrient solution	Controlled	No	Mathews et al. 2014
Celery	Soil (coarse-loamy, alluvial)	Field-grown	Yes	Wu et al. 2014
Lettuce	Soil (loamy sand)	Controlled	No	Boxall et al. 2006
Lettuce	Culture medium	Controlled	No	Calderon-Preciado et al. 2012
Lettuce	Soil	Greenhouse	Yes	Calderón-Preciado et al. 2013
Lettuce	Soil	Greenhouse	No	Jones-Lepp et al. 2010
Lettuce	Soil (loam)	Field-grown	Yes	Jones-Lepp et al. 2010
Lettuce	Soil (loam)	Field-grown	No	Jones-Lepp et al. 2010
Lettuce	Soil	Controlled	No	Lillenberg et al. 2010
Lettuce	Nutrient solution	Greenhouse	No	Wu et al. 2013
Lettuce	Soil (coarse-loamy, alluvial)	Field-grown	Yes	Wu et al. 2014
Spinach	Soil	Greenhouse	No	Jones-Lepp et al. 2010
Spinach	Soil (loam)	Field-grown	Yes	Jones-Lepp et al. 2010
Spinach	Soil (loam)	Field-grown	No	Jones-Lepp et al. 2010
Spinach	Nutrient solution	Greenhouse	No	Wu et al. 2013
Spinach	Soil (coarse-loamy, alluvial)	Field-grown	Yes	Wu et al. 2014
Legume Vegetables				
Asparagus	Nutrient solution	Controlled	No	Mathews et al. 2014
Beans	Soil (loamy sand)	Greenhouse	No	Eggen and Lillo 2012
Green Bean	Soil	Greenhouse	Yes	Calderón-Preciado et al. 2013
Pea	Nutrient solution and soil	Controlled	No	Tanoue et al. 2012
Pinto Bean	Sand and soil (sandy loam)	Controlled	No	Karnjanapiboonwong et al. 2011

Table 2: List of Uptake Studies on PPCPs Relevant to Food Crops and Reclaimed Water Application

Crop Name	Growth Medium	Growth Conditions	Use of Reclaimed Water (Y/N?)	Source
Root and Tuber Vegetables				
Beet	Nutrient solution	Controlled	No	Mathews et al. 2014
Carrot	Soil (loamy sand)	Controlled	No	Boxall et al. 2006
Carrot	Soil	Greenhouse	Yes	Calderón-Preciado et al. 2013
Carrot	Soil (loamy sand)	Greenhouse	No	Eggen and Lillo 2012
Carrot	Soil (sandy soil)	Greenhouse	No	Eggen et al. 2011
Carrot	Soil	Greenhouse	No	Jones-Lepp et al. 2010
Carrot	Soil (loam)	Field-grown	Yes	Jones-Lepp et al. 2010
Carrot	Soil (loam)	Field-grown	No	Jones-Lepp et al. 2010
Carrot	Soil	Controlled	Yes	Malchi et al. 2014
Carrot	Soil (coarse-loamy, alluvial)	Field-grown	Yes	Wu et al. 2014
Potato	Soil (loamy sand)	Greenhouse	No	Eggen and Lillo 2012
Potato	Nutrient solution	Controlled	No	Mathews et al. 2014
Sweet Potato	Soil	Controlled	Yes	Malchi et al. 2014

4.3.1 Bulb Vegetables

Bulb vegetables consist of crops such as onions (dry bulb), green onions, garlic, and leeks. These crops are commonly used for flavoring a wide variety of dishes, although some have also been used for medicinal purposes (NOA 2015; Boriss 2014). Onions are one of the most harvested crops and it is estimated that the United States produces about 6.2 billion pounds of onions a year, which accounts for 4% of the world's annual supply (NOA 2015).

Surprisingly, only one study was identified that investigated the uptake of personal care products in bulb vegetables. In this study by Mathews et al. (2014), onions were grown in a hydroponic solution spiked with triclocarban and triclosan, which are two antimicrobials commonly used in personal care products. After four weeks of exposure, accumulation of triclocarban and triclosan was observed in onion roots, shoots, and bulbs. Triclocarban and triclosan concentrations in onion roots (851 and 277 mg/kg, respectively) were substantially greater than onion shoots (0.24 and 0.12 mg/kg, respectively) and onion bulbs (25.6 mg/kg and 16.4 mg/kg, respectively). These results showed that antimicrobials are concentrated mostly in the roots and not the edible portions of onions.

4.3.2 Cole Crops (Brassica)

Cole crops include broccoli, cabbage, cauliflower, collards, kale, mustard, turnips, and radishes. They are known for their nutritional benefits because they are high in carotenoids, vitamins A and C, calcium, iron, magnesium, and dietary fiber (Guerena 2006). Cole crops also contribute a substantial amount of protein to the diet.

A total of eight studies investigating the uptake of PPCPs by Cole crops were identified, four of which were on cabbage and the others were on broccoli, cauliflower, Indian mustard, radish, and watercress. Two of the cabbage studies were conducted under hydroponic conditions and assessed the uptake of two antimicrobials (triclocarban and triclosan) (Mathews et al. 2014) and four pharmaceuticals (carbamazepine, salbutamol, sulfamethoxazole, and trimethoprim) (Herklotz et al. 2009). Mathews et al. (2014) observed that out of the Cole crops investigated, cabbage accumulated the highest concentrations of triclocarban and triclosan in the shoots and roots. Similarly, all four pharmaceuticals investigated by Herklotz et al. (2009) were taken up and translocated in cabbage.

The other two cabbage studies assessed the uptake of PPCPs from soil under controlled conditions (Li et al. 2013) and field conditions (Wu et al. 2014). Specifically, Li et al. (2013) investigated the uptake of three types of sulfonamides antibiotics (sulfadiazine, sulfamethazine, and sulfamethoxazole) by pakchoi cabbage and found that all three sulfonamides were taken up by the crop. Wu et al. (2014) studied the uptake of 19 PPCPs by eight crops from soil irrigated with disinfected, tertiary treated reclaimed water. This is one of six studies identified that assessed the uptake of PPCPs under field conditions. The field experiments were conducted in Irvine, CA, and weres divided into two sections, with one section receiving tertiary-treated reclaimed water and the other receiving PPCP-fortified (spiked) reclaimed water. In cabbage, four PPCPs (meprobamate, primidone, carbamazepine, and naproxen) were found in samples irrigated with reclaimed water and one additional pharmaceutical (dilantin) was found in samples irrigated with the reconstituted reclaimed water. With exception to naproxen, the PPCPs taken up by cabbage were neutral (carbamazepine) or basic (meprobamate, primidone, dilantin) chemicals, indicating that acidic chemicals are likely to be taken up less by plants due to the fact that anions tend to be repulsed by negatively charge of plant cells.

In the broccoli, Mathews et al. (2014) reported that triclocarban and triclosan were taken up and translocated in broccoli roots and shoots, but concentrations were substantially lower compared to cabbage. In cauliflower, Redshaw et al. (2008) assessed the potential uptake of fluoxetine hydrochloride (antidepressant, also known by the trademark Prozac) into different parts of cauliflower plants. After 12 weeks growth in artificial media, the roots, stems, leaves, and curds of tissue cultures of cauliflower were sampled and concentrations of fluoxetine were detected in the stems (0.49 µg/g wet weight) and leaves (0.26 µg/g wet weight). These concentrations are low but nevertheless, it indicates that translocation of fluoxetine occurred.

Another study investigated the uptake and translocation of acetaminophen (pain reliever and a fever reducer) in Indian mustard hydroponically grown for 4-weeks under greenhouse conditions (Bartha et al., 2010). They collected root and leaf samples after 1, 3, 7 days of treatment and results showed that after 1 day of exposure, acetaminophen was detected in the root (1.15 µmol/g FW) and leaf tissues (0.3 µmol/g FW). Results also showed a strong decrease in acetaminophen in both root and leaf samples collected after 1-week, suggesting the existence of an effective metabolism pathway in plants. Additionally, bleaching and dot-like lesions on the leaves were observed in samples treated with acetaminophen whereas the control plants did not have any visual stress symptoms.

In radishes, Carter et al. (2014) assessed the uptake of five pharmaceuticals (carbamazepine, diclofenac, fluoxetine, propranolol, sulfamethazine) and a personal care product (triclosan) grown in soils spiked with these PPCPs. Five of the six PPCPs were detected in the bulbs and leafy parts of the radish, with carbamazepine being taken up to the greatest extent (52 µg/g dwt) in radish leaf. Sulfamethzine was the only contaminant not taken up in detectable quantities.

Watercress plants, which are commonly used as a salad green or garnish in dishes, were also investigated to determine the uptake of three pharmaceuticals (sulfamethoxazole, oxytetracycline, and ketoconazole) used in veterinary and human practices (Chitescu et al. 2013). Uptake of sulfamethoxazole and ketoconazole was observed in plants, while oxytetracycline was not detected in any sample, which may be due to its ability to form strong complexes with metal cations, thus being strongly adsorbed to soils.

4.3.3 Cucurbits

The cucurbits group includes a variety of crops such as cucumber, cantaloupe, squash, pumpkin, and watermelon. In the United States, most of the cucurbits are grown in Florida, North Carolina, Michigan, Texas, California, and Georgia. In particular, Florida has been the leader in fresh market production of cucumber, squash, and watermelon (Cantliffe et al. 2007).

In reviewing the literature, eight studies on the uptake of PPCPs by cucurbits crops were identified. Seven of these studies were conducted using cucumber, making it one of the most commonly studied vegetables next to carrots (root and tuber group) and lettuce (leafy vegetable group), likely due to its high uptake of water (Tanoue et al. 2012). Of these seven studies, four were conducted under hydroponic conditions, including a study by Mathews et al. (2014) in which triclocarban and triclosan were translocated in cucumber roots and shoots. Another study evaluated the uptake of 13 pharmaceuticals in cucumber xylem sap, including acetaminophen, carbamazepine, crotamiton, cyclophosphamide, diclofenac, and sulfonamides (Tanoue et al. 2012). Of these 13 pharmaceuticals, 10 were detected in cucumber with carbamazepine, crotamiton, and cyclophosphamide being taken up in the highest concentrations. Wu et al. (2014) also evaluated the uptake of 20 PPCPs (16 pharmaceuticals, 3 personal care products, and 1 herbicide) by cucumbers grown in greenhouse conditions and results showed that 17 PPCPs were detected in cucumber leaves and stems. Concentrations of diuron, fluoxetine, and carbamazepine were the highest compared to other PPCPs. Carbamazepine was also shown to be taken up by cucumber in hydroponic experiment in a study conducted by Shenker et al., (2011).

PPCPs were also successfully translocated by cucumber under soil conditions. The pharmaceuticals carbamazepine, enrofloxacin, and ciprofloxacin were taken up by cucumber, although ciprofloxacin was only detected in samples with the highest spiked concentration of 500 µg/g (Lillenberg et al., 2010; Shenker et al., 2011). The remaining two cucumber studies were conducted under field conditions using reclaimed water. The first field study found that nonionic PPCPs (sulfapyridine, caffeine, lamotrigine, and carbamazepine) and a positively charged PPCP (metoprolol) were taken up more in cucumber fruit and leaves than acidic PPCPs (bezafibrate, clofibric acid, gemfibrozil, ibuprofen, ketoprofen, naproxen, and sulfamethoxazole) (Goldstein et al., 2014). In the other field experiment in which 19 PPCPs were measured, only carbamazepine was found in cucumber fruit irrigated with reclaimed water, but primidone, carbamazepine, dilantin, and naproxen were detected in samples with PPCP-fortified reclaimed water.

In addition to cucumber, a study evaluated the uptake of various pharmaceuticals in cantaloupe and watermelon irrigated with reclaimed water (Jones-Lepp et al. 2010) but only *N,N’*-dimethoxyphenethylamin (DMPEA) was detected in crops (53 ng/g and 180 ng/g, respectively).

4.3.4 Cereal Grains and Oilseed Crops

Cereal grains are edible seeds of specific grasses and make up a substantial part of the human diet. It is estimated that more than 50% of world daily caloric intake is derived directly from the consumption of cereal grains (Awika, 2011). Corn, wheat, and rice account for most of the world's grains and the majority of these grains are produced in the United States, China, and India (EPI, 2015). Oilseed crops are also an important component of the food industry and the use of vegetable oils has been steadily increasing. Soybean is one of the most important oilseed crops (also a legume) and the United States is the leading producer of soybean.

A total of eight studies assessed the uptake of PPCPs by cereal grains and oilseed crops. Across the eight studies, three experiments were conducted on barley, three were on maize, and the other crops included oat, oil seeds of rape, soybean, and wheat. One study investigated the uptake and translocation of metformin (antidiabetic drug) by multiple crops (barley, oat, oil seeds of rape and wheat) grown in soil under greenhouse conditions (Eggen and Lillo 2012). While metformin was detected in all four crops, metformin was taken up the highest in oil seeds of rape, followed by oat, barley, and wheat (bioaccumulation factor (BCF) of 21.72, 1.35, 0.91, and 0.29, respectively). Similarly, the uptake of metformin and two other pharmaceuticals (ciprofloxacin and narasin) by barley (root, leaf, seed) were assessed and results showed that all pharmaceuticals were found in samples, with the higher concentrations being in plant roots compared to aerial parts of the plant (Eggen et al., 2011).

Another study reported that enrofloxacin and ciprofloxacin were taken up by barley but the pharmaceutical concentrations in the spiked solution were higher than what has been detected in the environment (Lillenberg et al., 2010). Therefore, these results may not be representative of field conditions.

In maize, uptake of sulfadiazine was observed but the antibiotic remained mostly in the roots (Michelini et al. 2012). Another study evaluated the uptake of two naturally occurring estrogens and two synthetic estrogen mimics by maize seedlings (Card et al., 2012). Results showed that estrogen was quickly removed from hydroponic solution to maize seedlings, likely because they are moderately hydrophobic (K_{ow} values between 3.5 and 4.1). Also, all four estrogens were detected in root tissues while only two estrogens were detected in shoots.

Uptake studies have also been performed on soybean plants. Wu et al. (2010) evaluated the uptake of three pharmaceuticals (carbamazepine, diphenhydramine, fluoxetine) and two personal care products (triclosan and triclocarban) by soybean plants. During the experiment, two treatments were applied to the soybean plants to simulate biosolids application and wastewater irrigation. Results showed that carbamazepine, triclosan, and triclocarban were detected in root tissues and translocated into aerial parts of the plant. However, the accumulation of diphenhydramine and fluoxetine was limited, as it was mostly detected in soil samples and not translocated into the plant.

4.3.5 Fruiting Vegetables

The major fruiting vegetables include tomato, bell pepper, and eggplant. Tomatoes are the second most consumed vegetable in the United States, behind potatoes, and two-thirds of fresh-market tomatoes are grown in California and Florida (Naeve 2015). California and Florida also produce about two-thirds of bell peppers grown in the United States (Correll and Thornsbury 2013).

A total of six studies were identified that evaluated the uptake of PPCPs in fruiting vegetables and included four on tomatoes, one on bell peppers and one on okra. Of the four studies on tomatoes, two consisted of field experiments using reclaimed water from a wastewater treatment facility and included the Goldstein et al. (2014) study in which various pharmaceuticals were taken up by tomatoes. This included nonionic (carbamazepine, caffeine, and lamotrigine) and ionic (ibuprofen, dofibric acid, metoprolol, and sildenafil) pharmaceuticals. However, when compared to results from cucumber plants, concentrations in tomato were substantially lower. In the other field study with reclaimed water, carbamazepine was the only PPCP detected (out of 19) in tomato and the concentrations were very small.

In the other two tomato studies conducted under greenhouse conditions, PPCPs were shown to be taken up by tomatoes but at lower concentrations than other crops, which is consistent with the field studies (Eggen and Lillo 2012 and Mathews et al. 2014). In okra and bell peppers, PPCPs were translocated in plants but concentrations were lower than in tomatoes (Mathews et al. 2014 and Wu et al. 2014).

4.3.6 Leafy Vegetables

Several studies have demonstrated the uptake and translocation of PPCPs into aerials parts of leafy vegetables, particularly lettuce. Lettuce is one of the most common crops used in uptake studies, likely because it is found worldwide, grows relatively fast, and can be cultivated in a sterile medium spiked with contaminants (Calderon-Preciado et al., 2012). One study assessed the uptake of 10 veterinary pharmaceuticals in lettuce and carrot crops grown in soil under controlled conditions (Boxall et al., 2006). Target chemicals included amoxicillin, diazinon, enrofloxacin, florfenicol, levamisole, oxytetracycline, phenylbutazone, sulfadiazine, trimethoprim, and tylosin. Amoxicillin, sulfadiazine, and tylosin were not taken up by lettuce likely due to their significant degradation by the time plants were harvested (90% dissipation). However, results showed that florfenicol, levamisole, and trimethoprim were detected in lettuce leaves.

Calderon-Preciado et al. (2012) assessed the uptake of four pharmaceuticals (clofibric acid, naproxen, ibuprofen, and triclosan) and two fragrances (tonalide and hydrocinnamic acid) by lettuce in a culture medium. The culture medium was analyzed after 30 day of incubation and results showed that target analytes were depleted by 85-99%, which suggested the rapid uptake of PPCPs by lettuce. Lettuce plant tissues were also analyzed at 5, 8, 15, 22, and 64 days and results revealed that all target analytes except for hydrocinnamic acid were detected. Bleaching or necrotic spots did not appear on lettuce, indicating that the crop was tolerant of the target analytes and the concentrations used. Also, no growth differences were observed between control and treated lettuces.

Another study investigated the uptake of 20 microcontaminants (pharmaceuticals, biocides, fragrances, antioxidants, flame retardants, and pesticides) in lettuce, carrots, and green beans irrigated with groundwater and reclaimed water (secondary and tertiary effluents) (Calderon-Preciado et al., 2013). The crops were grown under greenhouse conditions and harvested after 3 months. Samples showed that 18 of the 20 target compounds were detected in lettuce. The PPCPs detected in the highest concentrations included the three fragrances ambrettolide (309 ng/g), galaxolide (270 ng/g), and tonalide (124 ng/g), and the pharmaceutical naproxen (113 ng/g). Also, out of the three crops studied, lettuce had the highest concentrations of the compounds.

4.3.7 Root and Tuber Vegetables

In addition to investigating the uptake of veterinary pharmaceuticals by lettuce, Boxall et al. (2006) assessed the uptake of these same compounds by carrots (whole carrot and carrot peel). Results showed that diazinon, enrofloxacin, florfenicol, and trimethoprim were detected in carrot roots. Also, it was observed that with the exception of trimethoprim, concentrations were higher on the outer layer of the carrot, suggesting that translocation to the inner parts of the carrot is limited (Wu et al., 2011).

Calderon-Preciado et al. (2013) investigated the uptake of PPCPs and other microcontaminants in carrots and found that the fragrance ambrettolide was detected in the highest concentration (336 ng/g), followed by carbamazepine (52 ng/g), which is a chemical used in pharmaceuticals.

5.0 Current Issues and Future Research Needs to Reduce Risk to Humans

Recent advances in analytical techniques have allowed researchers to detect the presence of PPCPs in the environment. In particular, research has recently focused on assessing the uptake and translocation of PPCPs into edible parts of crops. This is because PPCPs can be transferred to food crops through the application of reclaimed water from wastewater treatment plants. To better understand how PPCPs are taken up by food crops, 28 plant uptake studies relevant to food crops and reclaimed water application were identified and reviewed. Of the 28 studies, 22 were carried out in controlled or greenhouse settings and 6 were field studies with reclaimed water. Based on the studies evaluated, it is evident that PPCPs can be taken up and translocated into edible parts of food crops at detectable levels. While the levels have been low that it does not raise immediate human health concerns, uncertainties remain regarding the effects of these contaminants. However, only a limited number of field studies have been conducted using reclaimed water to irrigate crops. Because reclaimed water use is anticipated to increase to help meet agriculture water demands, additional field studies are needed to better understand the uptake of PPCPs by crops over multiple growing seasons.

Several studies have estimated the potential human health risk associated with the consumption of plants contaminated with PPCPs. For instance, Wu et al. (2013) estimated an individual's annual exposure using data from the leafy vegetables lettuce and spinach. The annual exposure values ranged from 0.08 to 150 µg for lettuce and 0.04 to 350 µg for spinach. Wu et al. (2014) also calculated the annual exposure of seven

PPCPs from the consumption of mature crops irrigated with PPCP-fortified reclaimed water and determined the exposure value to be 3.69 µg per capita. These exposure values are much smaller than found in a single medical dose, which is typically around 20-200 mg (Wu et al., 2015). Another study estimated daily intake of PPCPs for an adult and toddler from residues reported in the scientific literature (Prosser et al., 2015). The authors concluded that the concentrations of the majority of PPCPs in edible parts of the plants represented a *de minimis* risk to humans. Other studies have also reported similar findings (Boxall et al., 2006; Malchi et al., 2014).

An area where much progress has been made by researchers, is understanding the mechanism that affect uptake of PPCP by food crops. This includes chemical-specific factors such as the log K_{ow}, chemical's charge (positive, negative, or neutral), and half-life value. The type of plant species is also important in estimating potential human health risk. For example, in the case of cucumber and lettuce, uptake of PPCPs is anticipated to be higher than some other crops due to their high water uptake. However, one of the challenges faced is that there is a broad range of PPCPs that are released into the environment, making it is difficult to predict the uptake of these contaminants into plants. Even when comparing the same PPCPs and crops, other factors may produce accumulation differences in plants such as growing period, climatic conditions, and irrigation regime (Goldsetin et al. 2014). Therefore, caution should be taken when using the available results to predict uptake in crops and estimate potential human health risks.

Although human exposure to PPCPs from the consumption of food crops is low based on studies performed, there are still uncertainties regarding their long-term risks of these low-level exposures. Also, the potential risk of exposure to mixtures of PPCPs in plants have not been well studied. It is also difficult to compare the current studies available due to the large variability of methods used in the experiments. For example, some experiments were conducted under hydroponic conditions while others were conducted using soil as the growth medium. The types of food crops and concentration of PPCP-spiked solution also varied. There is also a limited number of data available from studies conducted under field conditions, which would allow for more representative exposure estimates. In particular, this is important for crops irrigated with reclaimed water because irrigation can occur over the entire life cycle of the plants, which means there is more opportunity for PPCPs to accumulate (Prosser et al. 2015).

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