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Soil–Plant Transfer of Pharmaceuticals and Personal Care Products

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Abstract

Purpose of Review Land application of organic wastes such as sewage effluent, biosolids, and animal wastes can introduce pharmaceuticals and personal care products (PPCPs) into soils. Food plants grown in soils receiving organic wastes may take up PPCP contaminants and accumulate them in the edible tissues. The purpose of this review is to summarize the latest findings on root uptake of PPCPs and their transfer in soil–plant systems, aiming to identify potential risks associated with organic waste application in crop production systems.

Recent Findings The processes and mechanisms of root uptake of PPCPs and their subsequent transfer in plants are intensively discussed in the present review. Soil properties, PPCP physicochemical properties, and plant species are demonstrated as the most important factors influencing the uptake and transfer of PPCPs in soil–plant systems. The metabolism processes and mechanisms of PPCPs in plant tissues are further elucidated with exemplification of commonly used PPCPs. The estimated daily intake is employed to assess the potential risks of consuming PPCP-containing foods based on their accumulation in edible plant tissues. Two innovative treatment techniques are proposed as cost-effective practices to reduce PPCP transfer into plants from organic wastes.

Summary Accumulation of PPCPs in edible plant tissues is governed by the combined processes of their root uptake, translocation, and metabolism in plants. This paper reviews the latest research advances in understanding the transfer of PPCPs in soil–plant systems, proposes mitigation practices to minimize PPCP entry into food chains, and identifies research challenges.

Keywords Pharmaceuticals and personal care products (PPCPs) · Organic wastes · Root uptake and translocation · Metabolism · Accumulation · Mitigation practice

Introduction

Pharmaceuticals and personal care products (PPCPs) refer to chemicals that are used by individuals for personal health or cosmetic reasons or used in animal feeding operations to enhance the growth or health of livestock. Common PPCPs include human and veterinary drugs (such as anesthetics, antibiotics, anti-inflammatory medicines, anticonvulsants, hormones, pain relievers, and their metabolites), preservatives, disinfectants, fragrances, and sunscreen agents. More than 2×10^7 tons of PPCPs are produced every year [1]. Moreover, the demand for PPCPs continues to grow as a result of the increasing consumption in our daily lives and the expanding needs in large-scale aquaculture and livestock farming. Because of the wide use and relatively high persistence, PPCPs have unintentionally and ubiquitously occurred in aquatic environments [2–7]. In the USA, for example, a nationwide reconnaissance conducted by the US Environmental Protection Agency (USEPA) and the US Geological Survey (USGS) reported that 118 pharmaceuticals were detected in samples collected from 25 US drinking water treatment plants [4, 5].

The widespread occurrence of PPCPs in the environment has increased concern about their potential risks to human and ecosystem health [8–10]. These emerging contaminants are usually detected in the environment at parts-per-trillion levels (i.e., ng/L or ng/kg), far below their therapeutic dose and typical use. However, chronic exposure to multiple

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PPCP contaminants at the same time through water supplies, even at low concentration levels, may result in synergistically negative impacts and thereby imperil public health [11, 12]. Certain pharmaceutical residues at as low as 0.1 μg/L in water could cause serious allergies or toxicity to susceptible individuals [12]. Some PPCPs are classified as highly potent endocrine-disrupting chemicals (EDCs), which may interfere with the normal function of the endocrine systems of humans and animals. Some pharmaceuticals (e.g., antibiotics) may jeopardize their continued effectiveness due to the emergence of bacterial resistance to the drugs [13–15].

In addition to drinking water, the dietary uptake of PPCPs through contaminated vegetables and fruits has raised considerable attention over the last decade. Currently, the increasing use of organic wastes (e.g., reclaimed wastewater, biosolids, and animal wastes) as fertilizers facilitates the introduction of PPCPs into field soils, where these emerging contaminants may subsequently be taken up by plants and thereby enter food chains. In particular, nontraditional water (e.g., sewage effluent or reclaimed wastewater) in arid and semi-arid regions is becoming an important water source for agricultural irrigation. Using nontraditional water to irrigate crop fields is often considered a win–win strategy to apply valuable nutrients and augment available water sources for agriculture. However, this practice may load contaminants including PPCPs into agro-food systems [16••]. Numerous studies have reported that PPCPs have been frequently detected in root and above-ground tissues of food plants grown in soils treated with reclaimed wastewater and biosolids [16••, 17, 18••, 19], posing potential risks to public health.

A variety of research studies using hydroponic, greenhouse, and field experiments and trials have been conducted to explore the plant uptake, transfer, and accumulation of PPCPs, as evidenced from many peer-reviewed publications documented in literature in the past decade [16••, 17, 18••, 19–21, 22•, 23••]. Compared to plants grown in soils, a hydroponic system is more convenient and controllable to demonstrate the processes and mechanisms of PPCP uptake and transfer in plants [20]. However, hydroponic systems do not manifest the complexity of soil environments and cannot represent the real soil conditions of cultivation agriculture [21, 22•]. Root uptake of PPCPs by plants grown in soils is significantly influenced by an array of factors including the contaminant sorption on soils and degradation by soil microorganisms. Compared to hydroponic systems, relatively few studies have examined the soil–plant transfer of PPCPs, especially for the uptake of PPCP contaminants in plants grown in field soils receiving wastewater effluent, biosolids, or animal wastes [22•].

This review aims to summarize the recent research findings of PPCP uptake and transfer in soil–plant systems by surveying the relevant scientific publications in the past 5 years and synthesizing our own research results. In this review paper, the sources of PPCP contaminants and their residues in soils are first introduced. Second, the mechanisms of uptake of PPCPs by roots and their transfer to above-ground plant tissue are illustrated. The effects of soil types, PPCP physicochemical properties, and plant species on contaminant uptake and transfer in soil–plant systems are emphasized. Third, the metabolism processes and mechanisms of PPCPs after they are taken up by plants are elucidated. Fourth, our experimental results are incorporated to better understand the accumulation of PPCPs in plants and assess the potential risks of human exposure to PPCPs from consuming contaminated food products. Fifth, potential mitigation strategies for preventing or reducing PPCP contaminant uptake and transfer in plants are proposed, especially focusing on two innovative treatment techniques (oil capture and biochar sorption). Finally, the needed areas for future research are identified and recommended.

PPCP Contamination Sources and Their Residues in Soils

Residues of PPCPs end in domestic sewage water and animal excreta after human individuals and livestock animals use or are administered with PPCP-containing products. Wastewater treatment plants (WWTPs) and concentrated animal feeding operations (CAFOs) are major sources for loading PPCP contaminants into soils through land application of organic wastes, including treated wastewater/effluent, biosolids, and animal wastes (Fig. 1). Although PPCPs may be partially treated in WWTPs, most of them cannot be entirely eliminated since the common WWTPs are not designed to remove these emerging contaminants. PPCP residues have been frequently detected in sewage effluents and biosolids [24, 25]. In CAFOs, most administered veterinary pharmaceuticals are not fully metabolized in animal digestive systems and are excreted shortly after medication, resulting in 30 to 90% of the dosed medicines in manure wastes being either parent compounds or metabolites [26, 27••]. Unlike WWTPs, CAFOs do not require additional treatments as long as animal wastes are not discharged directly into surrounding watersheds, resulting in the presence of a fair amount of veterinary pharmaceutical residues (e.g., 18.9 to 56.7 million kg of antibiotics per year) in manure and manure-containing wastewater [27••].

Since WWTP effluent, biosolids, and animal wastes contain high levels of nutrients and organic matters, their land application provides multiple economic and environmental benefits (e.g., improving soil fertility and quality, recycling waste products, and reducing the demand for synthetic fertilizers). In the USA, more than 50% of municipal biosolids are applied to agricultural lands as fertilizers [28]. In

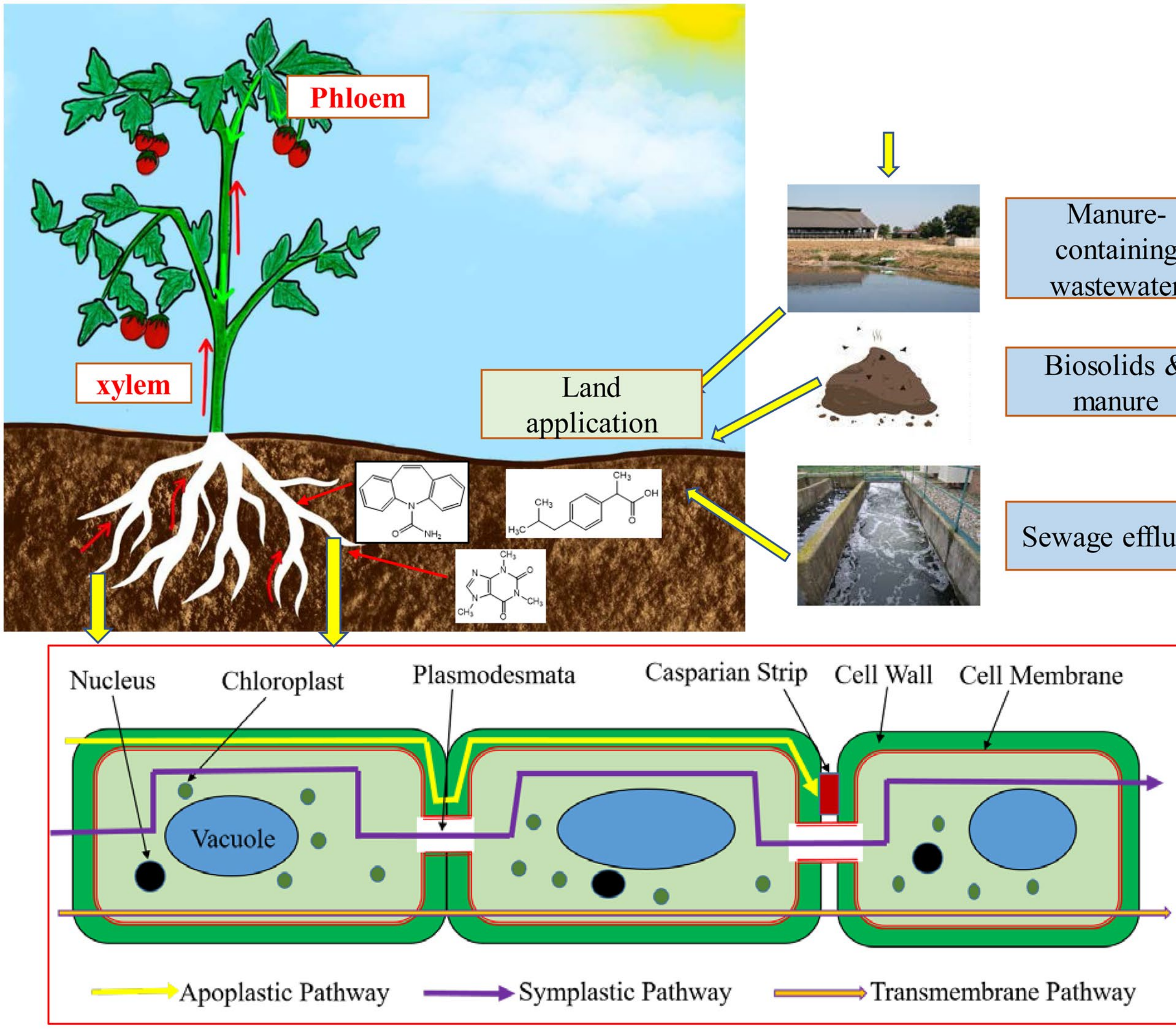

Fig. 1 Diagram of potential uptake and transfer of PPCPs in the soil–plant system through the transmembrane, symplastic, and apoplastic pathways within plant root cells

water-stressed regions (e.g., arid and semi-arid areas), the use of WWTP effluent and manure-containing wastewater can not only supplement increasingly scarce water sources for crop irrigation, but also decrease the amounts of wastewater directly discharged into watersheds. However, these practices result in the loading of many contaminants including PPCPs into agricultural soils, which may subsequently be taken up by plants and thereby enter food chains. In addition, PPCP contaminants can also be introduced into soils via direct effluent discharging from industries, hospitals, and households (e.g., septic tanks) [24, 29].

Concentrations of PPCPs vary widely in biosolids, animal manure, and reclaimed wastewater, ranging from a few micrograms to milligrams per kilogram dry solids or per liter [25, 30]. After PPCPs are introduced into soils with these organic wastes, they may bind to the soil solids, undergo a series of biotic and abiotic transformation, or migrate to surface water via runoff and to groundwater via leaching [23••, 27••]. These processes result in PPCP residues in soils being several orders of magnitude less than their waste origins [23••, 27••, 31]. Recently reported concentrations of residual PPCPs in soils receiving different organic wastes are summarized in Table 1. The detected levels of PPCP residues in these impacted soils range from parts-per-trillion to parts-per-billion (Table 1), which is much lower than those in organic wastes (i.e., parts-per-billion to parts-per-million) [23••, 31]. In addition, field studies have also confirmed that the measured concentrations of pharmaceutics in soils after organic waste land application were lower than the predicted levels as a result of degradation, sorption to soil constituents, and/or leaching [25, 32] However, repeated application of biosolids or long-term irrigation with reclaimed wastewater may elevate the concentrations of PPCPs in the receiving soils [25, 33].

Table 1 Reported concentrations of PPCP residues in soils receiving organic wastes

PPCPs	Concentration range in soils (μg kg^{-1})	Sources of organic wastes	References
Ibuprofen	n.d.–76	WWTP effluent	[76]
Alprazolam	n.d.–67		
Lorazepam	n.d.–62		
Sulfamethoxazole	1.31	Reclaimed wastewater	[77]
Trimethoprim	0.05		
Chloramphenicol	2.68		
Ibuprofen	1.71		
Triclosan	25.51		
Caffeine	1.74–25.44	Wastewater	[78]
Diclofenac	1.25–12.46		
Salicylic acid	6.17–76.07		
Triclosan	1.59–7.34		
Bisphenol A	3.87–45.25	Wastewater	[79]
Diclofenac	n.d–12.46		
Ibuprofen	n.d–59.57		
Triclocarban	n.d–1.91		
Metformin	n.d.–0.67		
Sulfamethazine	39–69		
Salicylic acid	< LOD–27	Manaure from poultry farms	[80]
Carbamazepine	< LOD–0.70		
Acetaminophen	n.d.–5.95	Reclaimed wastewater	[81]
Diclofenac	n.d.–5.06		
Mefenamic acid	0.08–1.97		
Phenazone	n.d.–0.36		
Carbamazepine	0.08–1.36		
Caffeine	0.51–3.21		
Flumequine	n.d.–5.31		
Hydrochlorothiazide	0.38–1.20		
Flecainide	0.06–14	Reclaimed wastewater	[82]
Irbesartan	0.02–5.8		
Methadone	0.01–0.44		
N-Desmethylcitalopram	0.38–21		
Nicotinamide	8.9–50		
O-Desmethyltramadol	1.6–40		
Sulpiride	0.06–7.4		
Telmisartan	1.5–713		
Carbamazepine	< LOQ–4.4	Wastewater	[83]
Caffeine	< LOQ–2.9		
N,N-diethyl-meta-Toluamide	< LOQ–0.68		
Trimethoprim	< LOQ–1.5		
Bezafibrat	< LOQ–1.5		
Chloramphenicol	< LOQ–2.7		
Diclofenac	< LOQ–0.98		
Gemfibrozi	< LOQ–1.7		
Ofloxacin	0.3–8.6	Sludge/biosolids	[25]
Ciprofloxacin Hydrochloride	0.6–8.7		
Carbamazepine	0.01–0.2		
Norfloxacin	2.0–9.4		
Carbamazepine	0.1–0.8	Reclaimed wastewater	[84]

Transfer Processes and Mechanisms of PPCPs in Soil–Plant Systems

In soils, PPCPs are either adsorbed on soil solids or dissolved in soil pore water, depending on the physiochemical properties of the chemicals and the soils. Root uptake of PPCPs from soil pore water into food plants is a major exposure route for these emerging contaminants [16••]. Miller et al. has aptly demonstrated the major mechanisms of solute root uptake in a dicot vascular plant [34]. In general, water is considered as a primary driver for root uptake and translocation of chemicals in plants. Chemical compounds with molecular weights < 500 g mol^{-1} can be carried by water and pass through the root epidermis. If chemicals cannot cross through the root epidermis, they are not able to enter the roots, resulting in accumulation predominately on the surface of the roots. Once in the epidermis, chemicals can cross the cortex and endodermis to reach the vascular tissues in roots. Only those compounds that can transport to the vascular tissues are able to translocate to above-ground tissues [23••, 34]. If chemicals cannot reach the vascular tissues, they will predominantly accumulate in plant roots.

Figure 1 shows three potential routes for chemicals to move from soil pore water to vascular tissues within plant root cells: the apoplastic pathway, the symplastic pathway, and the transmembrane pathway. The apoplastic pathway provides the movement of chemicals along cell walls through the intercellular spaces (Fig. 1). The transport of chemicals through the apoplastic pathway can be interrupted by the Casparian strip in roots, by the air spaces between plant cells, and by the plant cuticle. The Casparian strip, composing primarily of lignin and lamellar suberin, functions as a hydrophobic barrier to prevent chemicals from passing through the endodermis via the apoplastic pathway [34, 35]. The symplastic pathway provides the movement of chemicals between cells through interconnecting plasmodesmata (Fig. 1). The transmembrane pathway involves the movement of chemicals between root cells through cell walls and membranes (Fig. 1). These three pathways are not mutually exclusive, and some chemicals may use more than one route for transport within plant root cells. Presently, it does not have any studies to directly show PPCP transport in these pathways. However, PPCPs, like other solutes or dissolved minerals, may reach vascular tissues via these similar pathways [23••, 34].

Once PPCPs reach the vascular tissue in plant roots, they can be translocated to above-ground tissues (i.e., shoots, leaves, and fruit), primarily driven by transpiration and diffusion. In general, xylem and phloem are the two main transport tissues in vascular plants. The basic function of xylem is to transport water and nutrients from the roots to the upper surface of the plants, driven by transpiration. Phloem typically transports the products of photosynthesis (such as sucrose and amino acids) from leaves to various parts of the plant. Thus, xylem represents a main translocation pathway for those PPCPs taken up by roots to other plant parts (Fig. 1).

Generally, most PPCP residues in soil are polar organic compounds with low volatility and high persistence. The uptake of PPCPs by crop plants may be affected by a variety of biotic (e.g., plant physiology and genotype) and abiotic (e.g., soil environment and climatic conditions) factors [18••]. In controlled environmental conditions, the physicochemical properties of both soils and PPCPs strongly influence root uptake and translocation of the contaminants in plants. In addition, plant species may have strong impacts on the uptake and transfer of PPCPs in soil–plant systems.

Effect of Soil Properties on Root Uptake of PPCPs

In soil–plant systems, soil sorption affinity and abiotic/biotic degradations of PPCPs are two major factors impacting their availability in the soil pore water for root uptake [36]. PPCP sorption on soil solids could decrease their concentrations in the soil pore water and thereby significantly diminish their accessibility for uptake by plant roots [36]. In general, the sorption affinity of PPCPs to soils is closely related to the soil organic matter (SOM) and mineral surfaces [34], which are the most important soil properties dominating the sorption capacities of PPCPs in soils [27••, 34]. The plants grown in soils with high organic matter and clay contents typically have less PPCP uptake when compared to plants in sandy soils [37], since organic matter and clay-rich soils have higher sorption affinity for PPCPs and thereby reduce the contaminant availability in the soil pore water for plant uptake. Some studies reported that the concentrations of PPCPs in vegetable roots were negatively correlated to their sorption coefficients in soils [38, 39], suggesting soil sorption of PPCPs could restrict their plant uptake.

Residues of PPCPs in soils may undergo a series of abiotic and biotic transformations or degradation [23••, 27••], impacting the root uptake of these contaminants by decreasing their concentrations in the soil pore water. In most cases, the degradation of PPCPs in soils will convert parent compounds to lower molecular weight and more hydrophilic metabolites. Although the degradation products may be less toxic than their parent compounds, certain metabolites raise equal or even greater health concerns. For instance, the metabolites of cephalosporins are more toxic and more persistent than the parent compounds [40]. These degradation products could be more readily taken up by plant roots with water flow since most of them have lower molecular weights. Compared to abiotic degradation (e.g., hydrolysis, photolysis, and redox transformation), biotic degradation by soil microorganisms is a more important process governing the PPCP residues in soil. In particular, plant root exudates can improve biotic degradation of PPCPs by increasing microbial activity, which may alter their potential for root uptake in the rhizosphere. For example, the transformation of cephalexin in root enzyme extracts could influence its uptake and accumulation in vegetables [20].

In addition, other soil constituents such as heavy metals and macronutrients (P and K) can interact with PPCPs and thereby influence their uptake by plants. For example, the interactions of the four PPCPs (clarithromycin, metoprolol, carbamazepine, and trimethoprim) with heavy metals or macronutrients in soils were found to be antagonistic: the occurrence of heavy metals and macronutrients in soils decreased the uptake of PPCPs by a common beet [41].

Effect of PPCP Physicochemical Properties on Their Transfer in Soil–Plant Systems

The root uptake potential of different PPCPs and the subsequent translocation within plants vary with their physicochemical properties such as molecular size and weight, charged speciation, and lipophilicity. In general, the transpiration stream is a main driving force for plants to take up and transfer water and nutrients from roots to other parts. Only chemicals with low molecular weights can be carried by water and thereby enter plant tissues; large molecules are usually blocked from passively crossing the root cell membrane. Chuang et al. reported that small-sized PPCPs (e.g., caffeine and carbamazepine) with molecular weight < 300 g mol^{-1} were readily taken up by roots and transported to plant shoots [42•]. By contrast, large-sized PPCPs (e.g., lincomycin, monensin sodium, and tylosin) with molecular weight > 400 g mol^{-1} were excluded from cell membranes, resulting in the predominant accumulation in lettuce roots [42•, 43]. Although PPCPs with high molecular weight (> 500 g mol^{-1}) may not be easily taken up by plant roots [34], the potential uptake of degradation products still needs to be considered, given that these contaminants are readily degraded to small-sized compounds in soils.

Thousands of PPCPs are currently in use. These chemicals are highly diverse in structure, existing as neutral, cationic, anionic, or zwitterionic species. Moreover, these chemical contaminants may demonstrate differently charged forms under dissimilar pH conditions in soils and plant tissues. The speciation of PPCPs strongly affects their ability to passively cross the root cell membrane. In general, ionic PPCP species are less favorable for root uptake than nonionic compounds [42•]. Cationic PPCPs can be trapped on the negatively charged root surface via electrical attraction, limiting their further transfer from the root exterior into the root cortex. Accordingly, it is expected that cationic PPCPs mostly accumulate on the peels of roots and have low uptake and transfer rates. In contrast, anionic PPCPs are repelled by negatively charged cell walls due to their electrical repulsion, resulting in less accessibility to root cells. Compared to the ionic forms, nonionic PPCPs are able to cross the root cell membrane relatively easily and therefore, possess a higher potential to be taken up by the roots [16••, 34]. In addition, nonionic PPCPs are expected to be translocated preferentially in the xylem compared to in the phloem, suggesting that these nonionic compounds can be readily transferred to above-ground plant tissues.

Lipophilicity is another important property that governs the root uptake and transfer of PPCPs in plants. The root uptake pathways depend mainly on the chemical ability to cross the cell membrane [34]. The lipophilicity of PPCPs strongly affects their ability to passively cross root cell membranes. Molecules of PPCPs with high lipophilicity may rapidly diffuse across lipid membranes to enter the xylem. For nonionic PPCPs, their root uptake and translocation can be accurately predicted by their K_{OW} values [16••], which represent the tendency of an organic compound to partition between lipids and membrane permeability.

Effect of Plant Specificity on PPCP Transfer in Soil–Plant Systems

Accumulating evidence shows that the uptake of PPCPs by food plants may be affected by the plant itself (including the variety and cultivar, the genotype, and physiological state of the plant) [18••, 38]. Christou et al. estimated the potential of crop plants for PPCP uptake decreases following the order: leafy vegetables (e.g., lettuce and cabbage) > root vegetables (e.g., carrot and radish) > cereals and fodder crops (e.g., maize and wheat) > fruit vegetables (e.g., tomato and cucumber) [18••]. A recent study showed that the accumulation of cephalexin in vegetable roots followed the rank as lettuce > celery > radish [20], confirming that leafy vegetables have a higher potential for PPCP uptake compared to root vegetables. However, the uptake of PPCPs by fruit trees such as citrus, apple, and other fruit-bearing trees has not yet been evaluated. In addition, plant roots can release exudates in the rhizosphere, subsequently impacting soil properties and alter the availability of PPCPs to plant uptake [34].

Metabolism and Detoxication of PPCPs in Plants

Similar to liver metabolism of organic chemical contaminants, the metabolism of PPCPs in plants may involve a three-phase process [44, 45]. In the first phase of metabolism (Phase I), PPCP compounds are usually transformed to more reactive products with the introduction of functional groups (such as -OH, $-NH_2$, or SH) through oxidation, reduction, and/or hydrolysis. In the second phase of metabolism (Phase II), the activated products from Phase I are often conjugated with polar molecules such as sugar, amino acid, glutathione, or sulfate. These conjugation processes usually increase the hydrophilicity of compounds and thus allow them to diffuse into the vacuole via sequestration. The sequestration of PPCP conjugates is an energy-dependent process and provides an additional bioaccumulation mechanism [34]. The third phase of metabolism (Phase III) involves the conversion of Phase II metabolites into secondary conjugates in the vacuole.

There are few studies on the plant metabolism of PPCPs in comparison with their plant uptake and accumulation. Only several common PPCPs such as carbamazepine and caffeine have been well-investigated owing to their frequent detection in agricultural products. Carbamazepine can be extensively metabolized in plant tissues, even though it is recalcitrant to biotic and abiotic degradations in soils. A total of 21 Phase I metabolites of carbamazepine in tomato plant leaves were identified, corresponding to 33% of the parent compound taken up [44]. Ten Phase II transformation products were further identified in the same study, likely comprising another 12% of the plant uptake of carbamazepine [44]. According to the identified metabolites, a transformation pathway of carbamazepine in intact plants has been proposed, which involves a series of metabolism mechanisms, e.g., epoxidation, hydrolysis, hydroxylation, ring contraction, or loss of the carbamoyl group, followed by conjugation to glucose or cysteine as well as reduction [44]. Similarly, Chuang et al. identified eight caffeine metabolites in the shoots after the pharmaceutical was taken up by lettuce plants [46]. The main metabolism pathways for caffeine in plant tissues included demethylation, oxidization, and hydroxylation. In addition, eight metabolites of clarithromycin and two metabolites of sulfadiazine were identified in both leaves and roots of lettuce after the two antibiotics were taken up by the plants [47]. The metabolites of clarithromycin included Phases I and II transformation products, while only Phase II metabolites of sulfadiazine were detected. Currently, the mechanisms and transformation pathways of most PPCPs in plants still remain largely unclear, warranting further study [46].

In general, the metabolism of PPCPs in plant tissues is a detoxication process [48–50]. Particular plants such as *Phragmites australis* are often used in phytoremediation to clean contaminated soils and water [51, 52]. A study reported that acetaminophen was quickly conjugated with glutathione (GSH) to form GSH-acetaminophen in cucumber roots and leaves once the pharmaceutical was taken up by the plant. The GSH-mediated conjugation is considered as a crucial process to minimize the phytotoxicity of acetaminophen and other PPCPs in plants [48]. Similarly, the pharmaceutical ibuprofen in plant tissues could be first detoxicated by Cytochrome P450 monooxygenase, and then conjugated by glycosyltransferase and sequestrated into vacuoles or cell walls. Although four intermediate metabolites of ibuprofen were detected, no significant phytotoxicity was observed [51]. However, some metabolites may manifest similar or equivalent bioactivity compared to their parent compounds. For example, one of the carbamazepine metabolites is 10,11-epoxycarbamazepine, a potentially genotoxic compound that is more toxic than the parent chemical [21]. Some metabolites, especially those degraded from antibiotics, may have the ability to increase or acquire the antibacterial activity compared to the parent compounds [47]. Therefore, the metabolism of PPCPs in plants can impact health risk assessments that rely only on the accumulation concentrations of the parent compounds in edible plant tissues.

Accumulation of PPCPs in Plants and Risk Assessment

The accumulation levels of PPCPs in each part of the plant are governed by the combined processes of their root uptake, translocation, and metabolism. For those PPCPs that can accumulate in aerial tissues, a bioaccumulation factor (BAF) and exposure modeling approach are often employed to assess likely exposure concentrations in PPCP-contaminated soils [21, 53, 54]. The BAF values are defined as the accumulation mass of targeted compounds in plant tissues relative to their initial total concentrations in soil.

$$\mathrm{BAF} = \frac{\text{Concentration of PPCP in plant tissue}\left(\mu\text{g kg}^{-1},\ \text{dw}\right)}{\text{Concentration of PPCP in soil}\left(\mu\text{g kg}^{-1},\ \text{dw}\right)} \quad (1)$$

The BAF values are useful to evaluate the accumulation potential of different PPCPs in various plant parts. The BAF values mainly depend on the physicochemical properties of PPCPs, the total concentration of each contaminant in soils, soil properties, exposure time, and plant species [34]. For example, Li et al. reported that the BAF values of carbamazepine in three ready-to-eat vegetable tissues (i.e., carrot, celery and pak choi) grown in biosolid-amended soils ranged from 1.28 to 37.69 [28]. The BAF values of PPCPs in different plant parts may also vary widely [55]. Some PPCPs such as triclocarban, triclosan, sulfamethoxazole, and metformin have high BAF values in plant roots [53, 55], suggesting these contaminants have a high potential to accumulate in roots. By contrast, some PPCPs like carbamazepine and caffeine have higher BAF values for leaves than for roots [53–55], posing a potential risk to public health through the consumption of leafy vegetables. Carbamazepine and caffeine are small-sized and highly lipophilic molecules. They readily diffuse across root cell membranes to enter the xylem and thereby readily transfer to aerial plant parts from plant roots. Undoubtedly, PPCPs can be transferred into the crop plants if the agricultural fields are applied with PPCP-containing effluent, biosolids, and animal wastes. Previous studies reported that the levels of most PPCPs detected in plants grown in soils amended with organic wastes were below the suggested dosage for the therapeutic purpose [21, 23••, 56], indicating a minimal risk to human health. However, this simple estimation using PPCP accumulation concentration in the edible parts of plants may not well address chronic toxicity effects such as carcinogenicity [57]. Here, we use some of our research results [54] to assess the potential risk for PPCP accumulation in food crops (i.e., lettuce and tomato) by comparing acceptable daily intake (ADI) with estimated daily intake (EDI) [23••]. ADI is defined as the maximum amount of a contaminant in food or drinking water that can be ingested daily over a lifetime with no-observable-adverse-effect. EDI are calculated based on an average per capita consumption of 0.23 g (wet weight or ww) lettuce leaves and 0.72 g (ww) tomato fruit per kg (body weight) per day [58].

Table 2 shows EDI and ADI values of seven targeted PPCPs for a 65-kg human individual. ADI values of the selected PPCPs range from 0.0065 to 37,050 μg d^{-1} for a 65-kg individual [54, 57, 59]. Please note that the highest detected concentrations of each PPCP contaminant (Table 2) in lettuce leaves and tomato fruits were used to calculated EDI values. It is noteworthy that these calculations represent a "worst case" exposure estimation, as the plants were irrigated with very high PPCP concentration-containing water (0.5 mg L^{-1}). Worst case estimations are useful because they err toward human safety and allow further scrutiny to be focused on compounds that exceed these protective limits. Except carbamazepine and ethinylestradiol in lettuce, EDI values of all targeted PPCPs in both lettuce leaves and tomato fruits are much less than ADI values. The potential PPCP exposure to human health associated with the consumption of contaminated vegetables could be determined by the risk quotient (RQ), which is derived from the ratio between EDI and ADI. Some studies suggested that it could be considered as a negligible human risk when the value of RQ < 0.01, a considerable human risk if RQ > 0.01, and a distinct human risk of the value of RQ > 0.05 [23••, 60]. Table 2 shows that most RQ values for targeted PPCPs are less than 0.01. However, the RQ values of carbamazepine in both lettuce and tomato as well as ethinylestradiol in lettuce are more than 0.05, exceeding the threshold level of distinct human risk. In addition, these calculations are for average consumption. An individual who consumes more than average amounts of the vegetables would have greater exposure to these emerging compounds. Also, humans are likely exposed to PPCPs from multiple sources including food crops, drinking water, and home and work environments. When all inputs are summed, it is possible for humans to be exposed to greater amounts of PPCP contaminants than those are allowed by the ADI.

The frequent detection of PPCP contaminants in food plants has raised public concern about organic waste applications in agricultural fields [21, 56]. However, it does not have solid evidence to show whether long-term consumption of vegetables contaminated with low concentration PPCP mixtures could negatively impact human health [22•]. Further research is needed to develop thresholds for accumulation of PPCPs in food crops associated with the agricultural application of organic wastes [16••]. In addition, feasible and effective mitigation practices need to be developed to reduce the loading of these emerging contaminants into agricultural fields.

Table 2 ADI, EDI, and RQ values for a 65-kg human individual by ingestion of lettuce leaves and tomato fruits highly contaminated with PPCPs

Compound	ADI (μg d^{-1}) [54, 57, 59]	Highest detected concentrations in lettuce leaves (μg kg^{-1}, dry weight)	EDI for lettuce leaves (μg d^{-1})[a]	RQ for lettuce leaves	Highest detected concentrations in tomato fruits (μg kg^{-1}, dry weight)	EDI for tomato fruits (μg d^{-1})[b]	RQ for tomato fruits
Caffeine	1248	30,943	23.13	1.85×10^{-2}	19.3	0.063	5.05×10^{-5}
Carbamazepine	22.1	77,940	58.26	2.64	2764	9.05	4.10×10^{-1}
Ethinylestradiol	0.0065	109	0.082	12.6	0	0	0
Gemfibrozil	26.65	241	0.18	6.75×10^{-3}	54.9	0.18	6.75×10^{-3}
Ibuprofen	1625	30.8	0.023	1.42×10^{-5}	13.4	0.044	2.71×10^{-5}
Naproxen	37,050	281	0.21	5.67×10^{-6}	63.8	0.21	5.67×10^{-6}
Sulfamethoxazole	33,150	4977	3.72	1.12×10^{-4}	60.4	0.20	6.03×10^{-6}

[a] Exposure based on lettuce leave intake of 0.23 $g_{wet\ weight}/kg_{body\ weight}$/day

[b] Exposure based on tomato fruit intake of 0.72 $g_{wet\ weight}/kg_{body\ weight}$/day

RQ = EDI/ADI

Mitigation Practices to Reduce PPCP Plant Uptake and Transfer

To prevent the contaminants from entering the food chain, mitigation practices are needed to control the uptake and accumulation of PPCPs in the edible parts of food crops, especially those grown in soils receiving PPCP-containing organic wastes (i.e., sewage effluent, biosolids, and animal wastes). A series of treatment techniques and remediation practices have been proposed to limit PPCP transfer from waste-amended soils to food crops. One mitigation strategy is to develop best management practices (BMPs) to ensure that organic wastes are applied to the right cropping systems in the right place at the right time [27••, 31]. For example, these BMPs include (i) avoiding the use of PPCP-containing organic wastes during harvest seasons of food crops; (ii) avoiding the direct contact of organic wastes with seeds and seedlings because some PPCP can negatively affect seed germination and plant development; (iii) applying organic wastes on soils with high SOM and clay constituents, which can reduce the concentrations of PPCPs in the soil pore water; and (iv) co-applying with inorganic fertilizers to promote microbial degradation of PPCPs and thereby reduce their availability for plant uptake [27••, 31].

The other remediation strategy is to develop cost-effective and efficient technologies to remove or eliminate PPCP residues in organic wastes prior to the agricultural application [61]. For PPCP-containing solid wastes, anaerobic digestion and composting are two cost-effective techniques that can help to decompose certain amounts of PPCP residues in biosolids and animal manure. For PPCP-containing wastewater, some advanced treatment techniques such as physical adsorption, membrane separation, and advanced chemical oxidation have been proposed to directly remove PPCPs from municipal sewage effluents [62, 63]. However, these advanced techniques are overall costly and difficult to apply on a large scale. Recently, we proposed two innovative and cost-effective treatment techniques (oil capture and designer biochars) to remove hydrophobic PPCPs from sewage effluents [27••, 64].

Oil Capture to Remove PPCPs from Wastewater

Dodgen et al. successfully used vegetable oils to capture hormones from wastewater prior to field irrigation [64]. Compared to granular activated carbon (GAC) adsorption, which is the most common and effective approach for PPCP removal, the oil extraction technique has several advantages [27••]. (1) The cost of GAC ranges from \$1500 to \$3000/ton. By contrast, most fresh soybean or corn oil is < \$1000/ton, and the used oil is even less (< \$500/ton). (2) After treatment, the spent GAC is usually disposed of in a landfill. However, the spent oil after the oil capture treatment can be reused as a biofuel feedstock for bioenergy, a process that also eliminates the adsorbed contaminants. (3) GAC can simultaneously adsorb desirable inorganic nutrients (such as ammonium and phosphate ions) and organic contaminants, but oils only extract the hydrophobic contaminants. After the effluent is treated with oil capture, the reclaimed water can still provide nutrients to crop plants. Therefore, oil extraction is an economically feasible treatment to remove hydrophobic PPCPs such as estrogenic hormones [64]. More research is needed to explore the removal efficiency and feasibility of other PPCPs from wastewater using this oil capture technique. Overall, using the treated wastewater for irrigation would reduce PPCP loading to field soils and mitigate their entry into food crops.

Biochar Application to Reduce PPCP Plant Uptake and Accumulation

Biochar is a carbon-rich material produced from the thermal conversion of biomass under an oxygen-limited condition. Similar to activated carbon, biochar has a high-sorption affinity for organic contaminants, especially for hydrophobic PPCPs. Biochar is usually produced from forest and agricultural residues, making it a less expensive sorbent (e.g., \$100 ~ 200/ton) compared to GAC. Some studies have recommended biochar as a viable alternative to GAC for PPCP removal from wastewater [65–67].

The application of biochar into soils has a series of benefits including carbon sequestration, soil amelioration, and contaminant immobilization or mitigation [68, 69]. Compared to SOM, biochar has a greater affinity for organic compounds due to its highly carbonaceous and aromatic nature and relatively high surface area. Thus, applying biochar to soils can enhance the adsorption of PPCPs and reduce their accessibility to plant roots [70]. For example, the average PPCP concentrations in lettuce roots and leaves decreased by 34 ~ 48% and 23 ~ 55%, respectively, in the biochar-amended soils in comparison with the soils without biochar amendment [71]. Similarly, the accumulation of 11 PPCPs in radishes, grown in soils amended with biochar, decreased significantly by 33.3 ~ 83.0% compared to radishes grown in the unamended control soils [72].

In addition, a previous study showed that biochar application could increase the degradation of chemical contaminants in soils and thereby reduce their availability for plant root uptake [73]. In contrast, some studies revealed that biochar could inhibit the microbial degradation of certain organic chemical compounds including PPCPs (e.g., ibuprofen) in soils [71]. Interestingly, this decrease in biodegradation of PPCPs did not lead to higher concentrations in plant tissues because the PPCPs adsorbed on the biochar were unavailable for both soil microbial and plant access [71]. Thus, biochar as a soil amendment is likely an effective management practice for reducing the bioavailability of PPCPs and decreasing their potential for plant uptake from contaminated soils [74].

In addition to biochar soil amendment, adding biochar into solid wastes (i.e., biosolids and manure) is another mitigation practice to reduce the potential uptake and accumulation of PPCPs in plants. Biochar as a cost-effective sorbent can bind and immobilize PPCP contaminants in solid wastes and thereby limit their introduction into agricultural soils. A recent study revealed that a co-amendment of a walnut shell biochar and biosolids could not only improve soil fertility, but also minimize the uptake of biosolids-derived antibiotics by lettuce and carrot plants [75]. This study showed that the biochar reduced the concentrations of two antibiotics, ciprofloxacin and triclocarban, in lettuce leaves and resulted in a 67% reduction of triclocarban in carrot roots [75], suggesting this co-amendment practice could reduce the potential transfer and accumulation of biosolids-derived PPCPs in the edible plant parts.

Outlook and Recommendations for Future Studies

In the last decade, scientific studies on the uptake of PPCPs and their accumulation in plants have been continuously increasing because PPCPs are frequently detected in soils, especially in fields receiving organic wastes. Although many studies indicated that the concentrations of PPCP residues in edible plant tissues were far below their therapeutic dose, the public acceptance for consuming food plants growing in agricultural fields receiving PPCP-containing organic wastes (e.g., WWTP effluent) remains a great concern. More research is needed to fill the knowledge gap and provide solid evidence to accurately address this concern. The needed areas of future research that merit attention are proposed as follows:

- Fruit trees: There are limited studies on the uptake of PPCPs by fruit trees such as apple, bananas, citrus, and other fruit-bearing trees. These fruit trees may possess moderate to high potential for PPCP uptake (similar to that of vegetables) [18••]. Research on different kinds of fruit trees growing in different types of PPCP-contaminated soils needs to be conducted.
- Long-term application of organic wastes: Frequent application of organic wastes in agricultural fields can increase PPCP residues in the receiving soils, which may enhance the potential of their uptake by food plants. Moreover, some antibiotics can induce antimicrobial-resistant bacteria. Thus, the effect of long-term application of organic waste on PPCP uptake and accumulation in food plants needs to be assessed.
- Metabolism: The metabolism mechanisms of PPCPs in plants have been well recognized. However, the metabolites in the edible plant tissues are seldom identified, and their potential toxicities are usually unknown [34]. The conjugated metabolites are generally considered less or not at all bioactive, but it is largely unknown whether they may deconjugate to toxic compounds in human and animal digestion systems.
- Biosolids and animal manure: It has been a trend that solid wastes (e.g., biosolids) are increasingly applied to agricultural fields instead of landfill or incineration disposal. Eliminating residual PPCPs in biosolids and animal manure prior to land application is essential, which minimizes the contaminant loading into the soils and thereby reduces their uptake by plants. Composting is a cost-effective practice for the on-farm operation treatment of biosolids and manure. Optimization of the composting practices to promote decomposition and immobilization of PPCPs should be a focus of future research.
- Assessment of mitigation techniques: Many treatment techniques and mitigation strategies have been proposed to reduce the PPCP entry into food plants. These practices need to be further assessed in efficiency, cost-effectiveness, and feasibility for preventing PPCPs from loading into food plants. For the land application of organic wastes, standard protocols are required to achieve safe use, with special food safety considerations.

Conclusion

PPCPs have been used worldwide to improve quality of life and protect the health of humans and livestock. Due to extensive use and relatively high stability, a variety of PPCP contaminants have become very prevalent in the environment. In particular, the increasing application of organic wastes including WWTP effluent, biosolids, and animal wastes to cropland has introduced notable amounts of PPCP residues into agricultural soils. This review summarized recent studies concerning PPCP uptake, translocation, metabolism, and accumulation in food plants grown in PPCP-contaminated soils and soils receiving organic wastes. The potential of root uptake by PPCPs and their accumulation in edible plant parts may be influenced by a variety of biotic and abiotic factors. The main biotic factors include plant species and soil microorganisms which transform PPCPs to make them less available for root uptake. The physiochemical properties of soils (e.g., SOM, clay, and macronutrients) and PPCPs (e.g., molecular size and weight, charged speciation, and lipophilicity) are the main abiotic factors that govern the potential of PPCPs for plant uptake and translocation. The metabolism processes and mechanisms of common PPCPs after plant uptake are discussed in detail. Although the metabolism of most PPCPs in plant tissues is generally a detoxication process, the main metabolites that can accumulate in edible plant tissues need to be identified since some of them may have similar or equivalent bioactivity as the parent compounds. The accumulation of PPCPs in edible plant tissues is a collective consequence, depending on their root uptake, translocation, and metabolism in plants. The accumulation concentrations of PPCPs in food plants could be used to calculate EDI, which is a valuable parameter to assess the potential risk of consuming PPCP-containing foods. To minimize the entry of PPCPs into the food plants, several mitigation strategies for preventing or reducing the uptake and transfer of PPCPs in plants were proposed, focusing on the two innovative treatment techniques (oil capture and biochar sorption).

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

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