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Current Opinion in Environmental Science & Health

Translocation of pharmaceuticals and personal care products after land application of biosolids

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Abstract

Pharmaceuticals and personal care products (PPCPs) are common components of the municipal waste stream and well documented to be present in the final products of wastewater treatment including biosolids, which are commonly land applied in agricultural settings and at reclamation sites. Biosolids are therefore an identified source of PPCPs into environments, where biosolids are applied. Here, we review the current understanding of the potential for uptake and translocation of PPCPs within plants and consider knowledge gaps related to PPCP in plants and beyond them. Identified gaps include knowledge related to translocation of PPCPs beyond plants, the importance of transformation products for total exposure/uptake of PPCP, and the role of rhizosphere microorganisms in plant uptake.

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Current Opinion in Environmental Science & Health 2020, **14**:23–30

This review comes from a themed issue on **Environmental Pollution: Biosolids**

Edited by **Rolf U. Halden** and **Arjun K. Venkatesan**

For a complete overview see the Issue and the Editorial

https://doi.org/10.1016/j.coesh.2019.11.004

Keywords

Pharmaceuticals, Personal care products, Uptake, Plants, Translocation.

Introduction

Globally the production and use of pharmaceuticals and personal care products (PPCPs) is substantial. For example, global annual antibiotic consumption is estimated to be on the order of $1-2 \times 10^8$ kg [1]. In addition to human use, pharmaceuticals also find widespread use for veterinary purposes and livestock production. Wastewater and livestock production are widely regarded as the primary sources of PPCPs into the environment. Wastewater end products include treated wastewater, which is commonly discharged into surface water and increasingly used as a source of nonpotable water for irrigation of agricultural lands, and solid or semisolid sewage sludge. Organic carbon–rich sewage sludge that meets regulatory requirements can be classified as biosolids, which is commonly applied to agricultural soils as a nutrient-rich soil amendment. Biosolids derived from a variety of wastewater treatment technologies are documented to contain a diverse array of PPCPs in varying concentrations [2–4]. As a result, biosolids can serve as an important source of PPCPs into agricultural environments. For instance, as much as 28,000 kg of the antibiotic ciprofloxacin and 150,000 kg of the disinfectant triclocarban have been land applied in biosolids in the United States on an annual basis [4]. Data on the presence, distribution in the wastewater treatment process, and concentrations of PPCPs in biosolids can be accessed through a number of literature sources and previous reviews [2–5]. The concentrations of PPCPs in biosolids typically range from the ng/g to µg/g dry weight with use patterns, treatment technologies, and physicochemical properties influencing the resulting concentration of PPCPs in final biosolids.

The fate of PPCPs in biosolids after land application can vary by compound based on physicochemical properties of the PPCPs, the treatment process used to generate the biosolids, and soil properties (e.g. pH and organic carbon), as well as vary by agricultural practice and climate [5–9]. Organic compounds including steroid hormones and some personal care products present in biosolids can be mobilized during rainfall events after land application being detected in both the dissolved phase, as well as associated with suspended particulates [10,11]. Gottschall et al. [12] reported the presence of PPCPs in agricultural tile drainage and ground water after application of dewatered biosolids. Dissipation of many PPCPs in biosolids-amended soils occurs within the first few months after application, however some PPCPs including those in biosolids aggregates incorporated into soil can still be detected for more than 1 year after biosolids application [12]. Downward migration of PPCPs with irrigation or precipitation events appears to be limited [6,13]. The high organic matter content of biosolids can limit the bioavailability of PPCPs and other organic contaminants in biosolids-amended soils compared with soils not amended with biosolids, and therefore, limit uptake of PPCPs in plants, as well as

limit degradation/dissipation rates of PPCPs [14–16]. Although sorption to organic carbon–rich biosolids may limit bioavailability of PPCPs in amended soils, reports of the uptake of such contaminants in biosolids-amended soil into a variety of organisms including plant species exist [17–22].

Uptake and monitoring PPCPs in plants

Release of PPCPs into agricultural environments

Wastewater end products are commonly introduced into agricultural systems resulting in the exposure of plants (crops) to the PPCPs present in these products. In the United States and Europe, several million dry tons of biosolids are produced annually with about 50% of the biosolids produced in these biosolids being land applied [23–25]. The use of reclaimed treated wastewater as an irrigation source is expected to grow as the demands for potable water increase, especially in arid regions. The fraction of reclaimed wastewater used for irrigation of agricultural lands is more than 40% in California and Florida in the United States, about 71% in Spain, and about 85% in Israel meaning that reclaimed wastewater constitutes 50% of agricultural irrigation water in Israel [26–28].

Factors influencing uptake and translocation

The physicochemical properties of the PPCPs, plant physiology and growth conditions, environmental conditions, and soil properties have all been determined to be factors in the extant of the translocation of PPCPs into and within plant tissue [29]. Overall, the charge of the pharmaceutical and the hydrophobicity have been shown to have the greatest effect on translocation distance, where compounds with greater water solubility will have the greatest translocation and higher concentrations found in leaf tissue as compared with other tissues within a plant. Compounds with log K_{OW} values between 1 and 3.5 and neutral and cationic compounds have also been found in the leaves, indicating solubility is extremely important [28,57]. Therefore, pK_a and log K_{OW} values help explain the fate of the compound during original absorption and its ability to travel in the transpiration stream, and the translocation and ultimate concentration of the PPCP in leaf tissue is fundamentally affected by the transpiration rate of the plant.

Plants usually take up PPCPs through passive absorption of soil water through the epidermal layer of the root and into the root tissue cortex. Transportation of the chemicals into and within different tissues of the plant (aerial portions, leaves, fruit, stems) occurs by both simple diffusion, bulk water flow driven by transpiration through the xylem, and potentially transport within the relatively organic molecule–rich phloem vessels. Water evaporation through leaves drives transpiration resulting in unidirectional flow within the xylem. Phloem, on the other hand, uses differences in cell turgor pressure to create flow, allowing transport of organic-rich phloem sap in any direction.

The overall charge of the PPCP and the interaction of the molecule with the soil matrix can affect uptake. Multiple authors have observed that weakly acidic compounds had lower uptake values because of a probable interaction with soil organic matter, as well as being repelled by negatively charged plant cell walls and cytosol and therefore unavailable for translocation [19,28,30–33]. Neutral and cationic pharmaceuticals are likely to accumulate in leaves, whereas anionic ones remain in roots. For example, sulfamethoxazole with a relatively low pK_a value was easily deprotonated in hydroponic conditions, leading to increased translocation [34].

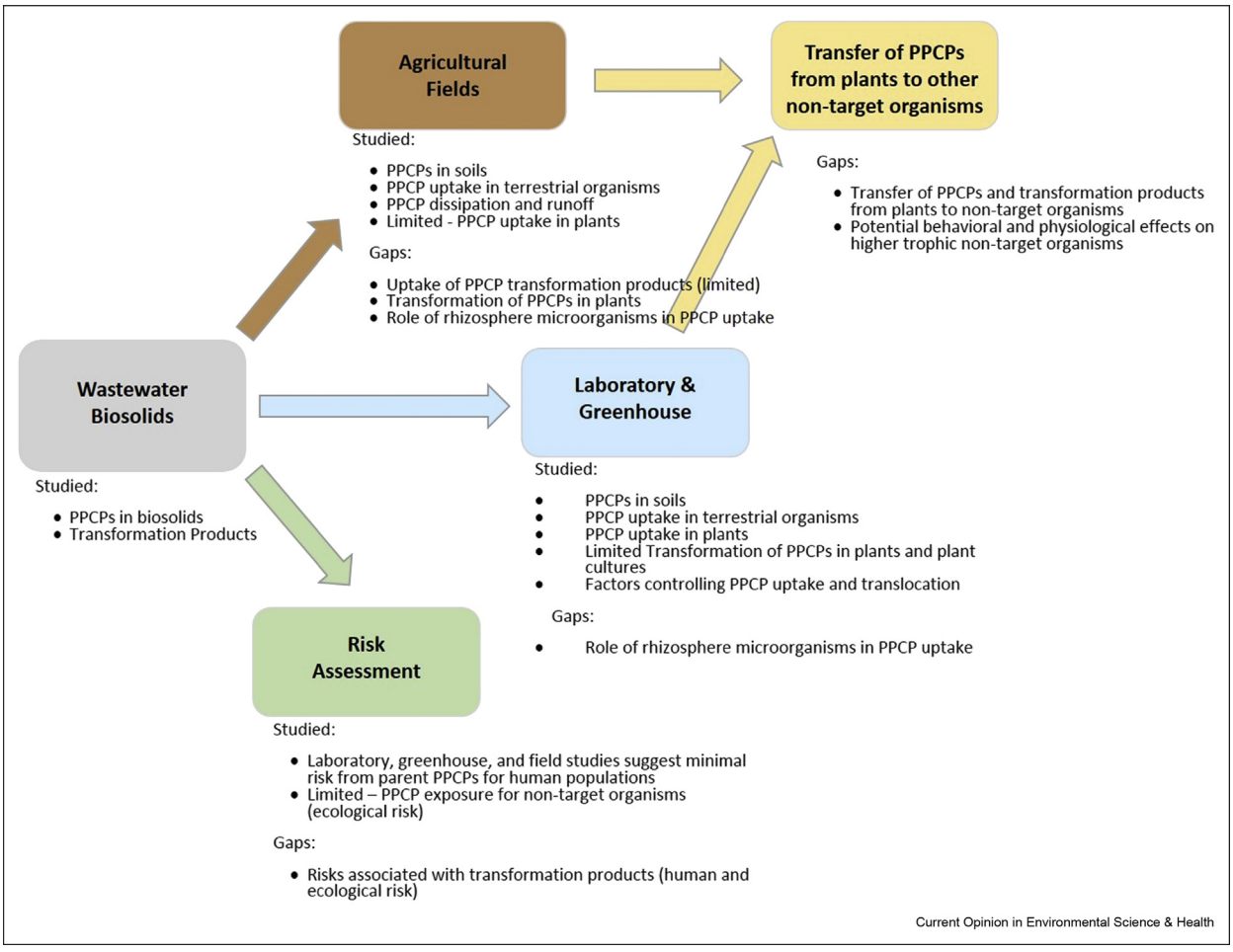
The hydrophobicity of individual compounds has also shown to be important in uptake patterns. Certain compounds with low log K_{OW} values have been shown to accumulate in leaves as compared with root or stem tissue, indicating transport within the transpiration stream. Compounds like carbamazepine, meprobamate, and dilantin were the most translocated when compared with atorvastatin, ibuprofen, and sulfamethoxazole [35,36]. Further, nonionic pharmaceuticals (carbamazepine, caffeine, and lamotrigine) were detected at significantly higher concentrations than ionic pharmaceuticals [35,37].

Although charge and hydrophobicity play a significant role in uptake and translocation of PPCPs in plants, it is important to point out that identical PPCPs have shown different uptake patterns in different species of plants [38,39], thought to be because of the concentrations and physicochemical characteristics (e.g., water solubility, polarity, and hydrophobicity) of the contaminants [40]. Uptake patterns for the same PPCPs were different for two aquatic plants, *Echinodorus horemanii* and *Eichornia crassipes* [40], and highly hydrophilic compounds trimethoprim and sulfonamides have been shown to accumulate heavily in leaves [28] and roots [41].

Potential for PPCP uptake in plants

The concern that use of wastewater end products could lead to uptake of PPCPs into plants and subsequently human exposure to these compounds have led to a variety of studies to better understand the potential for PPCP uptake, accumulation, and translocation in plants (Figure 1). Many early studies used hydroponic systems as a simplified model to better understand the potential for uptake and distribution of PPCPs in plants [30,34,42,43]. Hydroponic systems have value when screening PPCPs for potential accumulation and for considering the potential for translocation of PPCPs within the plant, especially to the edible portions of

Figure 1



Highlights of current understanding related to PPCPs in biosolids and plant uptake of PPCPs along with key knowledge gaps identified.

plants [30,34,43], yet these comparatively simple systems do not accurately represent widespread crop production and the complex factors that can influence PPCP behavior in soil systems.

Increasingly, studies of PPCP uptake in plants grown in soils amended directly with PPCPs [44,45], biosolids [15,19,46], or fortified biosolids [20,21] have been reported. Complimentary studies involving irrigation with a fortified aqueous solution or reclaimed wastewater are also available in the literature [15,20,28,30]. Among these existing studies, uptake of PPCPs and translocation within the plants is widely reported, thus demonstrating that PPCPs in soil systems can accumulate in plants, translocate within the plants, and in many cases end up in the edible portions of plants; however, most of these studies have been conducted at the laboratory or greenhouse scale. Few studies have investigated PPCP accumulation in crops under realistic crop production conditions, especially with biosolids as the source of the PPCPs.

Gottschall et al. [12] monitored PPCPs in soils, groundwater, tile drainage, and wheat grain after a single (22 Mg dw ha^{-1}) application of dewatered municipal biosolids. Although some of the PPCPs were detected in the soil, tile drainage, and groundwater at 2-m depth, none of the PPCPs studied were detected in the wheat grain. In another study, Sabourin et al. [47] reported results for uptake of PPCPs and other organic contaminants in tomatoes, carrots, potatoes, and sweet corn after application of biosolids complying with regulations appropriate for location of the field site (Ontario, Canada). A few of the PPCPs including atenolol, caffeine, ciprofloxacin, 4-epianhydrotetracycline, glyburide, naproxen, progesterone, and trimethoprim were detected in some of the vegetables from the treated sites at concentrations greater than the control sites at the time of harvest, but in general

the results were highly variable, including variable detection in replicate samples and controls. The results from these two cited studies [12,47] suggest that the risk of human exposure to PPCPs from commercial production of produce in biosolids-amended soils is low.

Transformation of PPCPs in plants

The presence of transformation products of PPCPs in wastewater end products has been reported and can result from human metabolism, biotic, and/or abiotic transformations during wastewater treatment, leading to the presence of transformation products in biosolids [48–50]. Recently, researchers have reported substantial metabolism of select PPCPs in plants after exposure [51–56]. Many transformation products are biologically active and may possess toxicity that can exceed that of the parent compound [57,58]. Transformation of PPCPs in plants can be categorized into three phases: activation (phase-I), conjugation with biomolecules (phase-II), and incorporation/storage of residues (phase-III) resulting in nonextractable residues [51,52]. Transformation of PPCPs by plants is not ubiquitous among compounds studied with those PPCPs containing carbonyl, phenolic, and N-aryl amine groups being most susceptible to transformation [53,55]. Transformation of PPCPs can occur rapidly in plants and plant cultures with 50% dissipation times from less than an hour to a few hours [55,56]. Although some identified transformation products are among those that were previously known and for which analytical standards are available, many of the observed products must be identified and elucidated using advanced analytical techniques such as accurate mass analysis (e.g. quadrupole time-of-flight or Orbitrap mass spectrometers) and nuclear magnetic resonance spectroscopy [53,54].

Macherius et al. [53] reported the formation of triclosan conjugates in carrot cell cultures such that the quantity of conjugates exceeded the amount of parent triclosan by a factor of 5. Mordechay et al. [15], reported extensive epoxidation of carbamazepine in the leaves of multiple plant species exposed to the pharmaceutical. Many transformation products can result in nonextractable residues, which have been reported using radio-labeled compounds that otherwise go undetected using traditional extraction and analysis techniques [56,59]. In the absence of monitoring for transformation products and accounting for nonextractable residues, total exposure and uptake is likely underestimated. Conjugated transformation products can be deconjugated by biotic and abiotic process, resulting in the parent compound or other potentially biologically active compounds [53,55,60]. Although field studies considering the transfer of PPCPs from biosolids into plants suggest limited uptake of PPCPs [12,47], the absence of nontarget analysis for phase-II transformation products or consideration of nonextractable residues, may have resulted underestimation of total uptake and potential exposure.

Risk assessment

Human risk assessment

The occurrence of PPCPs in edible portions of plants could pose a risk to humans through consumption of contaminated food products. Multiple studies have shown that concentrations of pharmaceuticals in plants are relatively low, suggesting that individuals would consume much less than a prescribed daily dose for more than a year of contaminated crop consumption [61–63]. In addition, field experiments following normal practices for biosolids applications during agricultural production observed the presence of a very limited quantity of PPCPs in plant tissues [12,47]. It is important to point out that, owing to growing demand for water and fertilizer, more reclaimed water and biosolids are expected to be used in agriculture, increasing the potential exposure through human consumption [45]. Furthermore, the lack of inclusion of PPCP transformation products in most previous studies likely underestimates potential exposure to biologically active contaminants.

Ecological risk assessment

Biosolids release their nutrients slowly in the rhizosphere of growing plants and demonstrate continued measurable positive effects on biomass production several years after application [64,65]. This is especially important in efforts to rehabilitate severely disturbed ecosystems that would otherwise have to proceed slowly through primary succession. Biosolids application on reclamation sites and forest land can be 5 to 50 times greater than on agricultural land. Similarly, these sites are more nutrient poor to begin with, thus can accommodate a greater nutrient loading than agricultural land. But with increased application comes increased PPCP load. Negative effects of some pharmaceuticals on plants have been documented in literature [66–70]. The specific effects on each plant species depend on the class of the pharmaceutical drug, drug concentration, and plant species exposed to the drug [71], but decreased root growth, leaf malformation and discoloration, inhibited shoot growth, and decreased seed germination have been reported in the presence of common PPCPs.

Gaps in understanding

Field-scale experiments, transformation products, and study compounds

To date, limited field-scale experiments of the uptake of PPCPs from biosolids into plants that also account for agricultural best practices exist [12,47]. Existing field experiments primarily focus on the presence and uptake of parent PPCPs, yet mounting evidence suggests that transformation products of PPCPs generated before biosolids application and within exposed organisms may

be as important as or more important than the parent compound to overall exposure in some cases [53–56]. Inclusion of transformation products in studies is hampered by the lack of available standards and thus requires time-intensive use of nontarget analysis to account for the presence of many transformation products. Many transformation products are biologically active themselves or can be transformed back to biologically active compounds, especially true for conjugated products [53,55,60]. In general, available literature in this area of study includes a relatively limited number of analytes per study, and the impact of future research may be more significant if a wider range of parent PPCPs and transformation products are incorporated.

The role of rhizosphere microorganisms

To date, there have been very few studies exploring how PPCPs affect the microorganisms that inhabit the rhizosphere, or how these organisms may modulate uptake into plants. Owing to the nature of the symbiotic relationship of these microorganisms to increase and enable nutrient uptake by the plant, the study of how these organisms may serve as a potential mechanism for enhancing or inhibiting the uptake of these compounds is pertinent. The interactions by these organisms are so important that between 5 and 21 percent of fixed carbon by the plant is then excreted to the bacteria as root exudate [72–75]. *Pseudomonas*, a genus of microorganisms that includes known plant growth–promoting bacteria, has been studied for its ability to remove compounds such as hydrocarbons and naphthalene [76,77] and carbamazepine [78,79]. Schilling [80] found that some known plant growth–promoting bacteria significantly increased uptake of carbamazepine, whereas other bacteria inhibited uptake of carbamazepine. Further exploration of the modulation of uptake of PPCPs by plant growth–promoting bacteria and known rhizosphere microorganisms is warranted.

Translocation beyond plants

Aside from the potential for human consumption, there is little knowledge on the movement of PPCPs and their transformation products to higher tropic levels. Because they are still active, pharmaceuticals may have negative effects on the organisms that also consume the plants or have a mutualistic relationship with them [4]. Common herbivores or known pests that use crop fields during their natural life processes and eat the plant material can potentially bioaccumulate pharmaceuticals in their tissues. Kinney et al. [18] has shown pharmaceutical uptake in earthworms from biosolids-amended soils. Bartolo [81] has preliminary data suggesting transfer of carbamazepine from tomato plants to tomato hornworm larvae and adult hawk moths. These compounds are not intended for organisms such as hornworms, and therefore when nontarget organisms are exposed to pharmaceuticals such as carbamazepine, there is potential for negative effects on exposed individuals. This can potentially change their behavior, disrupting their natural life cycle [82]. Transfer of the compound can potentially go even further up the food chain to higher tropic levels. Sherburne et al. [22] showed transfer of the antimicrobial compounds, triclosan and triclocarban, being passed along from primary to secondary and tertiary consumers at a site amended with biosolids. Such concerns may be magnified in settings, where biosolids are used for reclamation and can be applied at a higher rate than agricultural systems. Further research is needed to understand the translocation of PPCPs and their transformation products beyond those initially exposed (e.g. plants and earthworms) to PPCPs from biosolids.

Conclusions

Researchers investigating the uptake of wastewater-derived PPCPs in plants have facilitated a growing understanding of the potential for and occurrence of accumulation of PPCPs in plant tissues and factors influencing uptake and translocation of PPCPs within plants. This has allowed researchers to identify some concerns related to potential human and ecological risks associated with environmental release of PPCPs via wastewater end products. However, there is a paucity of data from field-scale studies employing realistic crop production practices involving biosolids as the source of PPCPs. In those field-scale studies using application of biosolids under realistic conditions that exist, the results suggest human exposure to parent PPCPs in exposed crops is of little concern. More recently, a limited number of studies have demonstrated the occurrence of extensive transformation of select PPCPs in plants and plant cultures. More information is needed on the importance of the production of PPCP transformation products after environmental release of these compounds, the potential for further translocation of PPCPs and transformation products beyond plants, especially among nontarget organisms consuming exposed plants, and further study of the role of environmental factors such as rhizosphere microorganisms may play in uptake and transformation of PPCS in the environment is required.

Conflict of interest statement

Nothing declared.

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** of outstanding interest

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