Uptake of Pharmaceutical and Personal Care Products by Soybean Plants from Soils Applied with Biosolids and Irrigated with Contaminated Water

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Many pharmaceuticals and personal care products (PPCPs) are commonly found in biosolids and effluents from wastewater treatment plants. Land application of these biosolids and the reclamation of treated wastewater can transfer those PPCPs into the terrestrial and aquatic environments, giving rise to potential accumulation in plants. In this work, a greenhouse experiment was used to study the uptake of three pharmaceuticals (carbamazepine, diphenhydramine, and fluoxetine) and two personal care products (triclosan and triclocarban) by an agriculturally important species, soybean (*Glycine max* (L.) Merr.). Two treatments simulating biosolids application and wastewater irrigation were investigated. After growing for 60 and 110 days, plant tissues and soils were analyzed for target compounds. Carbamazepine, triclosan, and triclocarban were found to be concentrated in root tissues and translocated into above ground parts including beans, whereas accumulation and translocation for diphenhydramine and fluoxetine was limited. The uptake of selected compounds differed by treatment, with biosolids application resulting in higher plant concentrations, likely due to higher loading. However, compounds introduced by irrigation appeared to be more available for uptake and translocation. Degradation is the main mechanism for the dissipation of selected compounds in biosolids applied soils, and the presence of soybean plants had no significant effect on sorption. Data from two different harvests suggest that the uptake from soil to root and translocation from root to leaf may be rate limited for triclosan and triclocarban and metabolism may occur within the plant for carbamazepine.

Introduction

Pharmaceuticals and personal care products (PPCPs) have been extensively used for decades for both personal health and cosmetic reasons as well as for veterinary purposes. They are members of a group of chemicals of emerging concern as increasing evidence suggests their ubiquity in the environment and potential adverse effects on nontarget organisms and humans (*1*−*3*). One major pathway that PPCPs enter the environment is through municipal wastewaters. In cities, where the abundance of most PPCPs are utilized, wastewater is commonly treated in wastewater treatment plants (WWTPs) before discharge into the environment. As a result, much of the previous work has been devoted to understanding the fate and behavior of PPCPs during wastewater treatment and in receiving natural waters. The removal efficiency of PPCPs has been found to be compound specific and affected by the treatment technique and operating conditions. During wastewater treatment many PPCPs have limited biodegradability, resulting in only partial removal from the water phase, and often partition into sewage sludge instead of breaking down (*4*−*6*). As a result, considerable amounts of PPCPs remain in WWTPs effluents and treated sewage sludges (commonly termed biosolids). PPCP residuals have been found at concentrations up to $\mu g\ L^{-1}$ levels in effluent and up to mg kg^{-1} levels in biosolids (*7*), and as a result discharge of effluents has led to the contamination of receiving waters (*8, 9*).

Treated wastewater (commonly referred to as reclaimed or recycled water) and biosolids are commonly reused worldwide. In the United States, there have been over 3000 wastewater application sites. In order to meet the increasing water demand over $400 \times 10^6\ m^3$ of reclaimed water is used yearly in the state of California, with $239 \times 10^6\ m^3$ used for agricultural irrigation alone (*10*). The land application of biosolids has been practiced for decades and still is the most common method of disposal. In the United States and Europe, millions of dry tons of biosolids are generated every year with over 50% being reused (*11, 12*). Following the land application of reclaimed water and biosolids, PPCPs can enter the terrestrial environment. In soils irrigated with reclaimed water, pharmaceuticals have been detected with typical concentrations ranging from 0.02−15 $\mu g\ kg^{-1}$ (*13*). Pharmaceuticals and other anthropogenic organic contaminants have also been reported in agricultural soils amended with biosolids, several compounds being detected in earthworms from applied sites, with the highest bioaccumulation factor of 27 being found for triclosan (*14*).

Once in soil, PPCPs are subjected to transport and degradation. Compounds with strong sorption and recalcitrant to degradation remain in surface soils and have the potential to subsequently be uptaken by plants. However, very limited information is currently available. Previous research has focused primarily on plant uptake of veterinary pharmaceuticals that are associated with animal waste, that is, manures, and demonstrated their potential to accumulate in plants (*15*−*17*). Recently, uptake of human pharmaceuticals in plants grown hydroponically or in nutrient solution has also been reported (*18, 19*). In this work, the uptake of five PPCPs by soybean plants grown in soils was studied in a greenhouse setting. Selected compounds (Table 1) have a high occurrence in wastewater effluent and biosolids and show potential to persist in the terrestrial environment (*20*). Wastewater irrigation and biosolids application as two major pathways introducing PPCPs into soils were investigated. The effect of soybean plant on the fate of PPCPs in soil was examined as well.

Materials and Methods

Chemicals and Materials. Carbamazepine (CBZ), diphenhydramine (DIP), fluoxetine (FLU), triclosan (TCS), and triclocarban (TCC) standards were provided by Sigma-Aldrich (St. Louis, MO). Carbamazepine-D_{10} (CBZ-D_{10}) and triclosan-$^{13}C_{12}$ (TCS−$^{13}C_{12}$) were obtained from Cambridge Isotope

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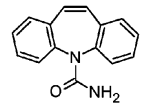
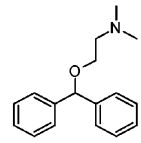
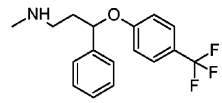
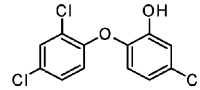
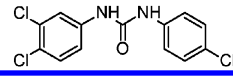
TABLE 1. Selected Physico-chemical Properities of Target Compounds

Compound (CAS number)	Application	Structure	Acid/base	pK_a	Log K_{ow}	K_d (L kg^{-1})
Carbamazepine (298-46-4)	anticonvulsant		neutral	2.3[a]	2.45[a]	12.6-19.8[b]
Diphenhydramine (58-73-1)	antihistamine		very weak base	9.08[c]	3.44[c]	61[d]
Fluoxetine (54910-89-3)	antidepressant		weak base	10.09[c]	4.61[c]	785-12,546[e]
Triclosan (3380-34-5)	antimicrobial		weak acid	7.9[f]	4.8[f]	178-264[g]
Triclocarban (101-20-2)	antimicrobial		weak acid	12.7[f]	4.9[f]	763-1187[g]

[a] Ref *37*. [b] Ref *30*. [c] Ref *36*. [d] Unreported data for the same soil from our lab. [e] Ref *38*. [f] Ref *39*. [g] Ref *29*.

Laboratories (Andover, MA), fluoxetine-D_5 (FLU-D_5) was purchased from Ceriliant (Round Rock, TX). Diphenhydramine-D_5 (DIP-D_5) and triclocarban-D_5 (TCC--D_5) were from CDN isotopes (Pointe-Claire, Quebec, Canada). Other chemicals and solvents were supplied by Fisher Chemicals (Fair Lawn, NJ). Stock standard solutions were prepared by dissolving certain amounts of standard in methanol. Working standard solutions were prepared and diluted from stock standard solutions.

A sandy soil (Lamson series, an Aeric Haplaquepts, with 9.7% clay, 3.2% silt, and 87.1% sand) with a pH of 5.1 and 2.7% organic matter was collected from the Stranahan Arboretum, a University of Toledo field research station located in Toledo, OH. The soil was air-dried and sieved to less than 2 mm. Biosolids (Class B) containing 19 g L^{-1} solid were collected from the Oregon wastewater treatment plant (Oregon, OH). Detailed information on the plant has been described previously (*21*).

Nursery pots (10 L) were used for plant growth. Each pot was filled with 8.7 kg soil. For biosolids application treatments, 3.2 L of biosolids were spiked with the mixed standard solution (approximately 10 mg kg^{-1}, dry weight) and mixed with 8.7 kg soil by adding incrementally, roughly equivalent to a field application rate of five dry tons per acre. The theoretical concentration in amended soil was 0.07 mg kg^{-1} for each compound without considering the background residual in biosolids. Compared to the results from a recent National Sewage Sludge Survey in the United States (*22*), this spiked concentration is comparable for TCC and TCS. For CBZ, DIP, and FLU the concentrations are about 10−100 times higher than average reported values but still within the same order of magnitude compared with the maximum reported values. The biosolids applied soil was allowed to dry for two weeks before use in the experiment. Homogeneity and concentration after drying of the soil/biosolids mixture were tested in each treatment replicate, and found to be close to the theoretical concentration values, with relative standard deviations generally low (9−30%). The soil pH and organic matter content increased from 5.1 to 5.6 and 2.7 to 2.9%, respectively.

Experimental Setup. Soybean (*Glycine max* (L.) Merr.) was used for the uptake study. Soybean seeds were obtained from Pioneer Hi-Bred International (Johnston, IA). Two treatments and a blank control were used, each consisting of nine containers. Each pot was planted with four seeds, and at least three seeds germinated from each pot. A plant-free control was also used for the biosolids application treatment (three pots) to examine the effect of plants on PPCPs dissipation. All pots were kept in a glass green house set at 24/21 °C day/night temperatures with 25−50% humidity. Photoperiod was 16 h using a 1:1 ratio of high-pressure sodium and metal halide lamps with minimum light levels of 200 μmol m^{-2} s^{-1}. Each pot was watered with modified Hoagland's nutrient solution adjusted to pH 6.5 (*23*) two to three times a week. Less water was used for biosolids application treatment due to the increase of water retention as a result of the biosolids application. For the irrigation treatment, water was spiked at 10 μg L^{-1} with mixed standard solution immediately before irrigation. This spiked concentration was 2−3 orders of magnitudes higher than typical concentration found in reclaimed water (*13*). This higher concentration was used to allow for the detection of PPCPs in soil and plant and was determined by the sensitivity of the analytical method. After the first harvesting (60 days), the irrigation solution was switched to tap water, previously found to have no detectable concentration of the target compounds.

Harvesting. The first set of samples was collected after 60 days, when the soybean plants entered the sixth node (V6) stage. Three pots were withdrawn from each treatment along with a blank control. Plants from each pot were separated from soil into root, stem and leaf. Thoroughly mixed subsamples of soil were taken from each pot after plant harvesting. The second set of samples was harvested after 110 days, when the plants entered the full seed (R6) stage. Again three pots were withdrawn from each treatment, a

TABLE 2. Concentration (ng g^{-1}, Dry Weight) of Target Compounds Detected in Soil and Plant

	first harvesting (60 days)				second harvesting (110 days)				
compound	soil	root	stem	leaf	soil	root	stem	leaf	bean
	irrigation treatment				irrigation treatment				
CBZ	0.7 ± 0.2	3.3 ± 0.6	1.37 ± 0.75	3.4 ± 1.1	1.1 ± 1.4	2.4 ± 0.6	0.6 ± 0.1	1.9 ± 0.4	nd
DIP	0.8 ± 0.2	2.0 ± 0.1	nd[a]	nd	0.9 ± 0.4	1.8 ± 0.2	nd	nd	nd
FLU	0.8 ± 0.3	nd	nd	nd	0.5 ± 0.4	nd	nd	nd	nd
TCS	nd	16.9 ± 2.6	10.1 ± 3.3	13.7 ± 2.0	nd	24.2 ± 21.3	58.0 ± 29.6	80.1 ± 5.6	35.8 ± 20.2
TCC	1.4 ± 0.2	7.4 ± 0.4	7.06 ± 2.05	5.9 ± 0.9	2.4 ± 2.2	7.1 ± 2.6	4.8 ± 1.7	14.9 ± 1.6	4.0 ± 1.5
	biosolids application treatment				biosolids application treatment				
CBZ	49.0 ± 2.3	153 ± 46	27.3 ± 0.3	216 ± 75	44.2 ± 1.1	127 ± 30	33.5 ± 6.8	110 ± 25	nd
DIP	43.3 ± 8.0	26.2 ± 5.3	7.8 ± 3.1	6.3 ± 1.7	46.6 ± 4.8	17.8 ± 4.2	4.8 ± 2.5	7.2 ± 0.6	nd
FLU	40.5 ± 5.6	22.2 ± 5.3	8.1 ± 0.8	nd	47.8 ± 2.8	20.4 ± 4.08	nd	nd	nd
TCS	12.8 ± 1.9	28.9 ± 6.1	10.9 ± 0.9	17.1 ± 3.3	13.2 ± 1.5	76.8 ± 3.1	136 ± 66	120 ± 37	12.6 ± 2.3
TCC	73.9 ± 8.7	126 ± 31	35.5 ± 25.0	7.1 ± 1.8	82.5 ± 8.8	168 ± 34	16.5 ± 14.0	37.6 ± 9.9	2.6 ± 0.3

[a] nd = not detected.

blank control and additionally a plant-free control. Plants were then separated into root, stem, leaf, and bean. Subsamples of soil were also collected. Plant samples were rinsed with deionized water after harvesting. All samples were then freeze-dried and stored in sealed plastic bags at −20 °C until analysis.

Chemical Analysis. Plant and soil samples were spiked with stable isotope labeled surrogate standards and extracted by pressurized liquid extraction (PLE) using a Dionex ASE200 system (Sunnyvale, CA). The extracts were further cleaned and concentrated using Biotage Evolute ABN solid phase extraction (SPE) cartridges (Charlottesville, VA). Prepared samples were separated using a Luna C8(2) end-capped column (100 × 4.6 mm 3 μm particle size) with a Security-Guard column (Phenomenex, Torrance, CA) and analyzed using a Varian 1200 L (Walnut Creek, CA) liquid chromatography-tandem mass spectrometer with electro-spray ionization interface (LC-ESI-MS/MS). Details of sample preparation and analysis are described in the Supporting Information.

Data Analysis. Reported concentrations and bioconcentration factor were calculated based on dry weight and are presented as mean and standard deviation of three replicates. Student's *t* test or one-way ANOVA (significant level = 0.05) were used to evaluate PPCP accumulation in plants from the two treatments and dissipation in soil with and without plants. All statistical analyses were performed using SPSS 17.0 software.

Results and Discussion

Soybean Uptake of PPCPs. Concentrations of target analytes detected in soils and plant samples from two treatments at two harvestings are listed in Table 2. All compounds presented the ability to transfer into plant tissues from soils but their uptake behavior was compound specific and affected by treatment. After 60 days' growth, CBZ, TCS, and TCC had accumulated in roots and translocated into above ground parts. TCS (16.9 ± 2.6 ng g^{-1}) was detected with the highest concentration in root from the irrigation treatment whereas CBZ (216 ± 75 ng g^{-1}) in leaf had the highest concentration from the biosolids application treatment. DIP and FLU were detected in root tissues at very low concentrations and their translocation from root to above ground tissues was limited. After 110 days, TCS (80.1 ± 5.6 ng g^{-1}) was detected with the highest concentration in leaf from the irrigation treatment and TCC (168 ± 34 ng g^{-1}) in root was the highest from biosolids application treatment. Concentrations of PPCPs in samples from the biosolids application treatment were generally higher, likely due to a higher loading of the PPCPs into the soils (a total of 0.07 and 0.61 mg of each compound was added into each pot by irrigation and biosolids, respectively). After 110 days, only TCS and TCC were detected in beans. The absence of CBZ in beans is unexpected, since it was accumulated in leaf tissues. This implies that metabolism may be occurring within the bean.

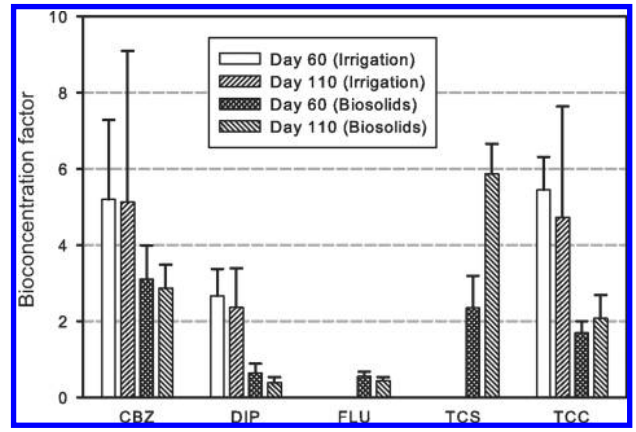


FIGURE 1. Bioconcentration factors (BCF) between root and soil.

The bioconcentration factor (BCF) between root and soil is calculated as the ratio of root concentration to soil concentration and is presented in Figure 1. The BCF was not calculated for FLU and TCS from the irrigation treatment as FLU was not detected in root and TCS was not detected in soil. Generally, BCF was higher for CBZ, TCS, and TCC compared to that of DIP and FLU. The root uptake of nonionic organic chemicals from soil solution is considered to be a partition related process and generally increases with the increase of a compound's hydrophobicity (*24*). The uptake of ionizable compounds is more complicated and can be affected by hydrophobicity as well as pK_a and substrate pH conditions (*25, 26*). Among tested compounds, CBZ is a very weak base and TCS and TCC are weak acids. With soil pH's ranging between 5 and 6 during the experimental period, they existed predominantly in neutral form. Whereas, DIP and FLU are weak bases, and exists as cation in tested soils. For ionizable organic compounds, their neutral form generally favors the root uptake, whereas ionization can reduce their bioaccumulation in plants (*27*).

Sorption to soil particles can also affect the plant uptake potential of the compound. For neutral organic compounds, distribution between soil and water (K_d) is highly correlated to the organic carbon fraction in soils while the distribution between organic carbon and water (K_{oc}) is correlated to their octanol−water partition coefficient (K_{ow}) (*28*). As both root uptake and K_d increase with the increase in K_{ow} of the

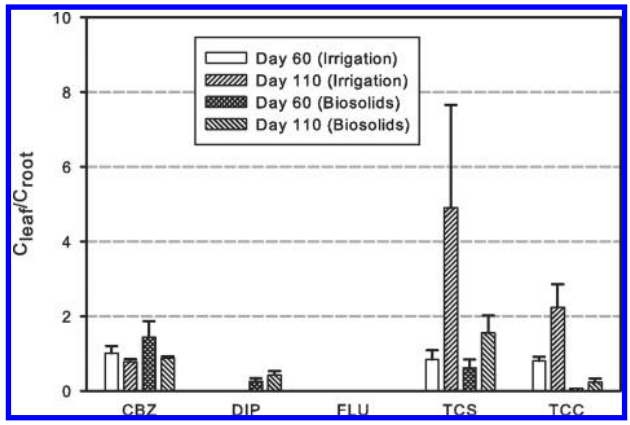


FIGURE 2. Leaf to root concentration ratios (C_{leaf}/C_{root}).

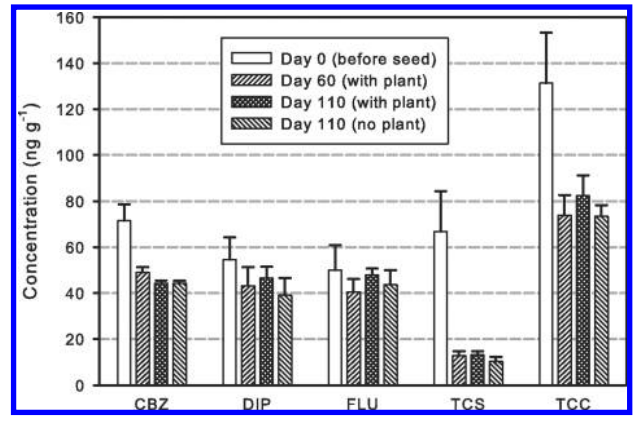


FIGURE 3. Dissipation of target PPCPs in biosolids spiked soil with or without plants.

compound, the BCF will be determined by the overall effect of two processes. Based on modeled results from Trapp (*27*), BCF between root and soil will generally decrease with the increase in K_{ow}. For the three PPCPs existing in neutral form here, their BCF trend generally agrees with the prediction based on their K_{ow}. However, the BCF of TCS in biosolids amended soil from day 110 was much higher that that of CBZ and TCC, which might suggest that other uptake mechanisms other than partition are involved. Mechanisms for the sorption of ionized organic compounds such as ionic binding can be more important than hydrophobic interaction. Therefore, increased sorption of ionized compounds will reduce their root uptake potential. Both DIP and FLU have relatively strong sorption capacity (Table 1), especially FLU, which results in low BCF values.

Comparing the two treatments, irrigation had a higher average BCF for CBZ, DIP and TCC, but only statistically significant for DIP (t test, $p < 0.01$) due to high variation. This result suggests that these compounds are more available for root uptake when introduced by irrigation. This is possibly because freshly added compounds have less time to interact with soil particles whereas compounds added through biosolids application had a longer soil contact time and the resulting aging process reduces their bioavailability. Biosolids application also increased soil organic matter content and possibly increased the PPCPs sorption (*29, 30*), thus reducing their root uptake. Other than TCS (t test, $p < 0.01$), no statistically significant differences from day 60 and day 110 were observed for BCF, suggesting that equilibrium between soil and root was likely reached. However, in biosolids application treatment, the BCF of TCS from day 110 was more than doubled compared to BCF from day 60, indicating that the uptake of TCS from soil to root might be rate limited.

Leaf to root concentration ratio (C_{leaf}/C_{root}) was calculated to evaluate translocation of PPCPs from root to above ground parts (Figure 2). The C_{leaf}/C_{root} was not calculated for DIP from irrigation treatment and for FLU from both treatments as their leaf concentrations were below LOD. Comparing the two treatments, a higher average C_{leaf}/C_{root} was observed in the irrigation treatment for TCS (t test, $p = 0.19$) and TCC (t test, $p < 0.01$). This result suggests that irrigation might also increase the translocation potential of certain compounds. This is possibly due to higher water transpiration in plants from this treatment, as a result of more frequent watering, but this explanation cannot be verified as no transpiration measurements were performed. When comparing the two harvesting times, C_{leaf}/C_{root} decreased for CBZ (t test, $p < 0.04$), increased for TCS and TCC (t test, $p < 0.02$), with no significant change for DIP. The decrease of C_{leaf}/C_{root} for CBZ is likely due to metabolism within the leaf, whereas the increase of C_{leaf}/C_{root} for TCS and TCC suggests that their translocation rate from root to leaf was rate limited, likely due to their high hydrophobicity (*31*).

Dissipation in Soil. The dissipation of selected PPCPs in biosolids applied soil with and without plants over time is illustrated in Figure 3. No dissipation was observed for DIP and FLU (ANOVA, $p > 0.26$) in soil containing plants within the 110 day experimental period. The persistence of DIP and FLU in soils has also been observed previously (*32, 33*). The concentration of CBZ, TCS, and TCC decreased significantly by 38, 80, and 37%, respectively. The loss of compounds occurred predominantly within the first 60 days, with the concentration of CBZ only dropping 10% between day 60 and day 110 and TCS and TCC showing no testable difference in that same period. This is possibly due to the reduced biodegradation availability of these compounds over time. These compounds are polar and nonvolatile, so degradation and plant uptake can be the major pathways for dissipation. Sorption to container may also occur but considering the surface area of the pot is much smaller than that of the soil, loss by sorption to container should not be significant. The dry biomass from each pot averaged 15.4 g, whereas the amount of PPCPs mass accumulated in plant was less than 1.0 μg. Thus, loss by plant uptake from the soil is negligible compared with the amount present in soils (0.4−1.1 mg). Therefore, degradation was a more important removal mechanism. Previously, biodegradation has been found to be responsible for the loss of TCS and TCC in soils (*34*) and could be a likely mechanism here. A comparison of compound residual in soil with and without plants after 110 days provided no statistically significant differences (t test, $p > 0.14$), suggesting that the soybean plants had no major effect on the dissipation of selected compounds either by uptake or by stimulating biodegradation.

Environmental Relevance. This study demonstrates the ability of plants to uptake PPCPs from soils that have been applied with biosolids or irrigated with PPCPs contaminated water. The plant uptake of PPCPs depends on their physicochemical properties such as pK_a and K_{ow}, interaction with the substrate, and introducing pathways. The potential for PPCPs to enter the plant presents concerns for their phytotoxicity. Negative effects to plants have been observed for several pharmaceuticals at environmentally relevant concentrations (*35, 36*). Accumulation of PPCPs through the food chain could also pose potential risks to species consuming plant parts, including humans.

Acknowledgments

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D. Dwyer, B. Fink, B. Harrington, S. Khuder, A. Kumar, S. Milz, A. Spongberg, R. Vincent, and V. Sigler) for their support.

Supporting Information Available

Details of soil and plant extraction methods, parameters for the instrumental analysis, quality assurance and quality control information. This material is available free of charge via the Internet at http://pubs.acs.org.

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