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Pharmaceutical and Personal Care Products (PPCPs) in the environment: Plant uptake, translocation, bioaccumulation, and human health risks

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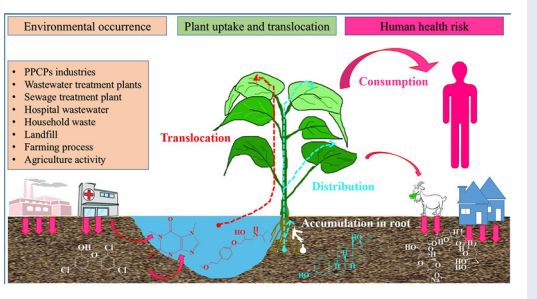
ABSTRACT



Pharmaceutical and personal care products (PPCPs) are considered as emerging contaminants (ECs) in the environment due to their known or suspected adverse ecological effects and human health risks. Wastewater, compost, and manure application release PPCPs into the agricultural soil systems. Since the plants can take up such ECs, they are considered as a primary window of human exposure to the PPCPs via the route of consumption of contaminated plants. This may lead to deleterious human health effects. However, as PPCPs are of various kinds, differential uptake and bioaccumulation in the plant have recently received research interest. Therefore, the present article reviewed the occurrence of PPCPs as antibiotics, anti-inflammatory drugs, hormones, cytostatic drugs, contrast media, β-blockers, blood lipid regulators, antiepileptic drugs, antimicrobials, ultra-violet filters, preservatives, insect repellents, and synthetic musks in the environment by assembling the literature. Moreover, plant uptake and translocation under the realistic and greenhouse condition, and the factors influencing the uptake and translocation through the plants are explicitly demonstrated in this review. Also, the human risk connected with the consumption of the contaminated plants and the research gap areas were investigated with future perspectives.

KEYWORDS Endocrine disruptors; emerging contaminants; soil amendment

1. Introduction

Pharmaceuticals and Personal Care Products (PPCPs) are a group of chemical substances that are being widely used for human health, cosmetic,

agriculture, and veterinary purposes. They are ubiquitously found in the water and soil environment throughout the world and have been implied for causing deleterious effects on human and non-target organisms (Liu & Wong, 2013; Wu et al., 2010). Recently, numerous studies have reported the presence of PPCPs in wastewater (Yang et al., 2017), groundwater (Balakrishna et al., 2017), surface water (Balakrishna et al., 2017), drinking water (Odendaal et al., 2015), soil (Boxall et al., 2006) and sludge (Cortés et al., 2013) arising from the usage of wastewater irrigation, biosolids, and manure application to agricultural soils which may result in the uptake of PPCPs into crops (Christou et al., 2019; Madikizela et al., 2018). Various sources have been identified for contributing PPCPs to the environment, including effluent from the wastewater and sewage treatment plants, household and hospital wastewater discharge, agricultural manure application, and farming activities (Evgenidou et al., 2015; Tasho & Cho, 2016). Most recently, the first nationwide investigation on surface water bodies in Sri Lanka reported 41 PPCPs in the range of 5.49 and 993 ng/L in water sources that abstract drinking water for the general public (Guruge et al., 2019).

In recent years, research publications have focused their special attention on plant uptake, translocation, and accumulation of PPCPs due to the inability of conventional water treatment systems to remove those ECs. Increased emphasis on biosolid and compost application to improve soil quality and urban and rooftop farming further provided opportunities for uptake of PPCPs by plants (Ahmed et al., 2015; Madikizela et al., 2018; Tasho & Cho, 2016; Wu et al., 2014; Zhang et al., 2017). Wastewater irrigation may introduce the PPCPs into the agricultural farmlands. For instance, the wastewater irrigation as a source of PPCPs loaded significant quantity of PPCPs including carbamazepine (4.4 μg/kg), chloramphenicol (2.7 μg/kg), gemfibrozil (0.98 μg/kg), N,N-diethyl-meta-toluamide (DEET) (0.68 μg/kg), and caffeine (2.9 μg/kg) to the soil surface (Ma et al., 2018).

Recently, sorption, plant uptake, and metabolism of benzodiazepines by *Raphanus sativus* and *Beta vulgaris* have been documented by Carter et al. (2018). Moreover, Ben Mordechay et al. (2018) have presented the data on uptake, translocation, and metabolism of carbamazepine by tomato, wheat, and lettuce. A contemporary hydroponic study detected sulfamethoxazole and trimethoprim at various concentrations in tomato fruit cultivated under controlled conditions (Christou et al., 2019). Similarly, another hydroponic study was undertaken by Chuang et al. (2019) to investigate the uptake and translocation of PPCPs in lettuce. Furthermore, some research articles assessed plant uptake of PPCPs (Ben Mordechay et al., 2018; Bhalsod et al., 2018; Riemenschneider et al., 2017). For example, the uptake, translocation, and transformation of pharmaceuticals in hydroponically grown intact tomato plants have been investigated (Riemenschneider

et al., 2017). A case study has been reported the effect of treated wastewater and composted biosolids on plant uptake of PPCPs (Ben Mordechay et al., 2018). The accumulation of pharmaceuticals in greenhouse lettuce have been investigated under the overhead and soil surface irrigation with pharmaceuticals contaminated water (Bhalsod et al., 2018). Further, the translocation of PPCPs in tomato plant irrigated with reclaimed water and its human risk was assessed under the field condition (Martínez-Piernas et al., 2019).

The dietary intake of PPCPs contaminated vegetables and fruits can cause a potentially harmful impact on human health. The daily consumption of PPCPs (especially antibiotics) contaminated vegetables can develop antibiotic-resistant pathogens in the human body, leaving humans at high risk of complex health complications. Further, some other medical issues, such as a weak estrogenic activity, immediate systemic hypersensitivity reactions, and inhibition of the enzyme responsible for the activity of the central nervous system have also been reported (Stuart et al., 2012). The plant uptake of PPCPs from the environment has created special attention over a decade. Only a limited number of reviews have been published, and the uptake data presented are limited to specific groups of PPCPs by plants (Al-Farsi et al. 2017; Madikizela et al., 2018; Tasho & Cho, 2016; Wu et al., 2015). These reviews are more focused on pharmaceuticals; however, lack of data is reported on personal care products (PCPs) and, together, lack of risk assessment data resulting in a vast knowledge gap.

Furthermore, the data on the plant uptake of personal care products have been on track recently due to their emerging concerns in the research area, which accounts the gap between this review and the previous works. Although PPCPs are essential in the modern life of the human, they pose serious environmental problems owing to their use, misuse, overuse, and uncontrolled disposal. It is essential to feed the knowledge and sensitize the ordinary people about the environmental implications and human health risks arising from the usage of PPCPs. The usage and the discharge of PPCPs into the environment have been increasing day by day with mounting environmental concerns. Therefore, the present paper attempts a comprehensive review based on the recently published peer-reviewed review and research articles, which reported the environmental occurrence, plant uptake and translocation, and human risk of PPCPs. Thus, the goals of this review are, to point out the occurrence of various groups of PPCPs in the environment, and their uptake, translocation, and bioaccumulation in the plant issues under the simulated greenhouse and realistic environmental conditions. Further, the human health effects of PPCPs exposure through ingesting the contaminated crops and vegetables are discussed here. Besides, the analysis methods to determine the PPCPs in the plant tissues and the current issues and future scope also discussed.

2. Types of pharmaceutical and personal care products

PPCPs including pharmaceutical products, for instance, antibiotics, anti-inflammatory drugs, hormones, cytostatic drugs, contrast media, β-blockers, blood lipid regulators, and antiepileptic drugs, and personal care products (PCPs), such as antimicrobials, ultra-violet filters, preservatives, insect repellents, and synthetic musks are the collection of chemical substances used in daily activities of human life (Liu & Wong, 2013). Antibiotics are being used as animal and human therapeutic medicines for the prevention and treatment of bacterial diseases; hence these are biologically active compounds (Pan & Chu, 2017). Recently antibiotics are being considered as emerging contaminants in the environment, and it is frequently reported because of the fact that the occurrence of antibiotics in the environment is a major threat for human and animal health as it may often lead to the development of antibiotic-resistant bacteria. These are mainly classified into many categories including tetracyclines (tetracycline, oxytetracycline, and chlortetracycline), sulfonamides (sulfachlorpyridazine, sulfadimidine, sulfadiazine, etc.), quinolone (ciprofloxacin, enrofloxacin, etc.), macrolide (erythromycin, tylosin, etc.), trimethoprim, thiamphenicol, chloramphenicol, lincomycin, and clindamycin (Jiang et al., 2014; Pan & Chu, 2017).

Anti-inflammatory drugs (such as Ibuprofen, Diclofenac, Acetaminophen, Indomethacin Aspirin, Naproxen, Nimesulide, Phenazone, and Ketoprofen) are also widely used as pharmaceutical products, and they are frequently found in the environment due to their unwarranted use (Lonappan et al., 2016; Veras et al., 2019). Further, the synthetic hormones (for instance, ethinylestradiol) (Gogoi et al., 2018), cytostatic drugs (examples, ifosfamide, and cyclophosphamide) (Liu & Wong, 2013), contrast media (iopromide, iomeprol, and diatrizoate) (Wang & Wang, 2016) are widely used pharmaceutical products detected in the environment. The β-blockers, including atenolol, metoprolol, nadolol, pindolol, acebutolol, and propranolol prescribed worldwide, also detected in the environment frequently. Moreover, the blood lipid regulators (such as Gemfibrozil) (Yang et al., 2017), antiepileptic drugs (such as Dilantin, Primidone, and Carbamazepine) (Madikizela et al., 2018), stimulant drugs (caffeine) also observed in the environment from ten of μg/L to thousands of ng/L.

The PPCPs including antimicrobials (triclocarban and triclosan), UV-filters (Oxybenzone, Enzacamene, and Sulisobenzone) (Aparicio et al., 2018; Ebele et al., 2017) are used in the daily lifespan to improve the quality of life. These reported in the environment due to the lack of technology to remove from the wastewater. Moreover, the preservatives (butylparaben, methylparaben, and propylparaben) (Yang et al., 2017), are widely applied to preserve the cosmetics, food, and pharmaceutical products also detected in the environment. Also, the insect repellents (DEET) (Murray et al., 2010), synthetic

musk (divided into nitro musks and polycyclic musks; polycyclic musks such as galaxolide (HHCB) being applied more frequently in a recent year than nitro musks) found in the environment in a range of few μg/L to ng/L. Another widely available PCPs is plasticizers, which are primarily used in cosmetics, shampoo, hair spray and gel, and plastic bottled water. Phthalate compounds such as bis(2-ethylhexyl)phthalate (BEPH) and di-n-butylphthalate (DBP) are the mostly used plasticizers (Saeidnia & Abdollahi, 2013). The artificial sweeteners, for, instance sucralose, saccharin, and acesulfame are another type of PCPs which are utilized to enhance the taste food during the food manufacturing process (Subedi et al., 2015). The perfluoroalkyl substances (PFASs) such as perfluorooctanesulfonate (PFOS), perfluorooctanoate (PFOA), perfluoropentanoate (PFPeA), perfluorohexanoate (PFHxA), perfluorodecanoate (PFDA), etc. are used as a surface activator used in the packaging, textiles, and paper industries, household-cleaning products, agricultural activities, cosmetic products, medical devices, etc. due to their hydrophilic and hydrophobic behaviors (Li et al., 2020; Shigei et al., 2020). The types of PPCPs and their physicochemical properties are displayed in Table 1.

3. Occurrence and persistence of PPCPs in the environment

The water and soil system are the critical reservoirs of PPCPs in the environment. As demonstrated in Figure 1, the introduction of PPCPs into the environment occurs through domestic and commercial sources. The domestic sources include landfills of urban solids, disposal of household wastes, animals, and human excretions (Madikizela et al., 2018; Yang et al., 2017), agricultural application of PPCPs laden manure. The commercial source includes effluent of water and sewage treatment plants, drug manufacturing processes, pharmaceutical companies (Tasho & Cho, 2016), and hospital wastes and effluents (Evgenidou et al., 2015), which may add an enormous quantity of PPCPs into the aquatic and soil ecosystem. The sewage treatment plants and water treatment plants are the primary pathway that introduces the PPCPs in the environment. Recently different types of PPCPs, including antibiotics, anti-inflammatory drugs, β-blockers, hormones, lipid regulators, were detected in the effluent from the sewage and water treatment plants (Hong et al., 2019; Tarpani & Azapagic, 2018; Yang et al., 2017). Moreover, PPCPs are frequently entered into bodies of humans and animals and are subjected to metabolic transformations. However, they do not undergo the complete metabolism, and are, therefore, excreted to the environment as either metabolites or unchanged form of PPCPs through the urine and feces (Tasho & Cho, 2016; Zhou et al., 2013). Furthermore, usage of life enhancement products, such as cosmetics, detergents, soap, sun-creams, toothpaste, perfumes, etc. leads to the

Table 1. Physiochemical profile of selected PPCPs.

PPCPs	Molecular weight, g/mol	Chemical formula	Degradation half-life	Solubility mg/L	log Kow[s]	pka
Antibiotics						
Tetracycline[a]	444.43	$C_{22}H_{24}N_2O_8$	19 days[x]	231	−1.3	3.3
Oxytetracycline[a]	460.43	$C_{22}H_{24}N_2O_9$	17 days[x]	313	−0.9	3.27
Chlortetracycline[a]	478.88	$C_{22}H_{23}ClN_2O_8$	18 days[x]	288	−0.62[q]	–
Sulfachlorpyridazine[b]	284.72	$C_{10}H_9ClN_4O_2S$	–	133	1.30[r]	–
Sulfamethazine[c]	278.33	$C_{12}H_{14}N_4O_2S$	576 h[v]	1500	0.89	7.59
Sulfamethoxazole[b]	253.28	$C_{10}H_{11}N_3O_3S$	2 days[u]	610	0.89[r]	5.7[a]
Sulfadiazine[b]	250.28	$C_{10}H_{10}N_4O_2S$	42 h[y]	77	0.39[r]	6.36
Ciprofloxacin[b]	331.34	$C_{17}H_{18}FN_3O_3$	378 h[v]	<1mg/mL	0.28[r]	6.09
Enrofloxacin[b]	359.40	$C_{19}H_{22}FN_3O_3$	77 days[x]	53.9 μg/mL[q]	0.44[r]	–
Difloxacin[b]	399.40	$C_{21}H_{19}F_2N_3O_3$	06 days[x]	–	0.89[q]	–
Flumequine[b]	261.25	$C_{14}H_{12}FNO_3$	–	–	1.6[q]	6.5[q]
Norfloxacin[b]	319.33	$C_{16}H_{18}FN_3O_3$	363 h[v]	1.78E + 005	0.46[r]	6.34, 8.75[q]
Ofloxacin[b]	361.37	$C_{18}H_{20}FN_3O_4$	06 days[x]	28.3	−0.39[r]	5.97, 9.28[q]
Pefloxacin[b]	333.36	$C_{17}H_{20}FN_3O_3$	–	11.4	0.27	–
Roxithromycin[d]	837.05	$C_{41}H_{76}N_2O_{15}$	2.4–10 days[w]	0.0189	2.75[r]	–
Tylosin[d]	916.10	$C_{46}H_{77}NO_{17}$	–	–	1.63[q]	7.73[q]
Erythromycin[d]	733.93	$C_{37}H_{67}NO_{13}$	2.4–10 days[w]	2000	3.06[q]	8.88
Clarithromycin[e]	747.95	$C_{38}H_{69}NO_{13}$	–	0.33	3.16[r]	8.99
Trimethoprim[f]	290.32	$C_{14}H_{18}N_4O_3$	**/**[v]	400	0.79[r]	7.12
Thiamphenicol[e]	356.22	$C_{12}H_{15}Cl_2NO_5S$	–	–	−0.27[q]	–
Chloramphenicol[g]	323.13	$C_{11}H_{12}Cl_2N_2O_5$	–	2500	1.14	–
Lincomycin[h]	406.54	$C_{18}H_{34}N_2O_6S$	–	927[h]	0.56	7.6[q]
Clindamycin[h]	424.98	$C_{18}H_{33}ClN_2O_5S$	–	30.6	2.16	7.6[q]
Anti-inflammatory drugs						
Ibuprofen[i]	206.28	$C_{13}H_{18}O_2$	01 day[u]	21	3.97	5.3
Diclofenac[i]	296.15	$C_{14}H_{11}Cl_2NO_2$	3 or 4 days[u]	2.37	4.51	4.15
Acetaminophen[i]	151.16	$C_8H_9NO_2$	674 h[v]	1.4E + 004	0.91	9.38[q]
Aspirin[i]	180.16	$C_9H_8O_4$	–	4600	1.18	3.5
Indomethacin[i]	357.79	$C_{19}H_{16}ClNO_4$	–	0.937	4.27	4.5
Naproxen[i]	230.26	$C_{14}H_{14}O_3$	**[v]	15.9	3.18	4.15
Nimesulide[i]	308.31	$C_{13}H_{12}N_2O_5S$	–	–	2.6	–
Phenazone[i]	188.23	$C_{11}H_{12}N_2O$	–	5.19E + 004	0.38	1.4
Ketoprofen[i]	254.28	$C_{16}H_{14}O_3$	**[v]	51	3.12	4.45
Synthetic hormone						
Ethinylestradiol[j]	296.40	$C_{20}H_{24}O_2$	–	11.3	3.67	1.7[a]
Stimulant drug						
Caffeine	194.19	$C_8H_{10}N_4O_2$	**[v]	2.17 g/100 mL	−0.07	14
Cytostatic drugs						
Ifosfamide[k]	261.09	$C_7H_{15}Cl_2N_2O_2P$	–	3780	0.86c	–
Cyclophosphamide[k]	261.09	$C_7H_{15}Cl_2N_2O_2P$	–	1–5 g/100 mL	0.8	–
Contrast media						
Iopromide[i]	791.11	$C_{18}H_{24}I_3N_3O_8$	–	–	−2.05[q]	>10.6[t]
Iomeprol[i]	777.09	$C_{17}H_{22}I_3N_3O_8$	–	–	−2.79[q]	>11.3[t]
Diatrizoate[i]	613.91	$C_{11}H_9I_3N_2O_4$	–	–	3.3	1.13, 7.95[q]
β-blockers						
Atenolol[i]	266.34	$C_{14}H_{22}N_2O_3$	**[v]	1.33E + 004	0.16	9.6
Metoprolol[i]	267.36	$C_{15}H_{25}NO_3$	861 h[v]	–	2.15	9.7
Nadolol[i]	309.40	$C_{17}H_{27}NO_4$	2 or 3 days[u]	8330	0.81	9.67
Pindolol[i]	248.32	$C_{14}H_{20}N_2O_2$	–	7880	1.75	9.25
Acebutolol[i]	336.43	$C_{18}H_{28}N_2O_4$	–	259	1.71	–
Propranolol[i]	259.34	$C_{16}H_{21}NO_2$	255 h[v]	61.7	3.48	9.42
Sotalol[i]	272.36	$C_{12}H_{20}N_2O_3S$	–	5510	0.24[q]	–
Blood lipid regulators						
Gemfibrozil[g]	250.33	$C_{15}H_{22}O_3$	4 or 3 days[u]	10 mg/mL	3.4	4.5[q]
Antiepileptic drugs						
Dilantin[a]	252.27	$C_{15}H_{12}N_2O_2$	–	32	2.47	8.33
Primidone[a]	218.25	$C_{12}H_{14}N_2O_2$	–	500	0.91	12.3[q]
Carbamazepine[a]	236.27	$C_{15}H_{12}N_2O$	**[u, v]	17.7	0.91	13.9[q]

(*continued*)

Table 1. Continued.

PPCPs	Molecular weight, g/mol	Chemical formula	Degradation half-life	Solubility mg/L	log Kow[s]	pka
Antimicrobials						
Triclocarban[l]	315.58	$C_{13}H_9Cl_3N_2O$	**[v]	Insoluble	4.34[q]	12.7[q]
Triclosan[l]	289.54	$C_{12}H_7Cl_3O_2$	866 h[v]	–	4.76[q]	7.9
UV-Filters						
Oxybenzone[m]	228.24	$C_{14}H_{12}O_3$	–	–	3.79	7.1[q]
Sulisobenzone[m]	308.30	$C_{14}H_{12}O_6S$	–	10 μg/mL	0.37[q]	−2.4, 7.6[q]
Enzacamene[n]	254.37	$C_{18}H_{22}O$	–	Poorly soluble		–
Preservatives						
Propylparaben[g]	180.20	$C_{10}H_{12}O_3$	–	–	3.04[q]	8.5[q]
Butylparaben[g]	194.23	$C_{11}H_{14}O_3$	–	–	3.57[q]	8.47[q]
Methylparaben[g]	152.15	$C_8H_8O_3$	–	–	1.96[q]	8.5[q]
Insect repellants						
DEET[o]	191.27	$C_{12}H_{17}NO$	–	–	2.18[q]	–
HHCB[p]	258.41[q]	$C_{18}H_{26}O_3$	–	1.75[q]	5.90[q]	–
Plasticizer						
BEPH	390.60	$C_{24}H_{38}O_4$	–	0.27[q]	–	–
DBP	282.37	$C_{16}H_{22}O_4$	–	–	–	–
Artificial sweeteners						
Sucralose	397.60	$C_{12}H_{19}C_{l3}O_8$	–	22700[q]	−1.00[q]	–
Saccharine	183.19	$C_7H_5NO_3S$	–	4000[q]	0.91[q]	1.31[q]
Acesulfame	163.15	$C_4H_5NO_4S$	–	270g/L[q]	−1.33[q]	2.0[q]
Surface activators (PFASs)						
PFOS	499.09	$C_8F_{17}SO_3^-$	–	–	–	0.14
PFOA	413.08	$C_7F_{15}CO_2^-$	–	–	–	−0.21
PFPeA	263.05	$C_4F_9CO_2^-$	–	–	–	−0.10
PFHxA	313.06	$C_5F_{11}CO_2^-$	–	–	–	−0.17
PFDA	513.10	$C_9F_{19}CO_2^-$	–	–	–	−0.22

a: (Madikizela et al., 2018); b: (Lee et al., 2019), c: (Prosser & Sibley, 2015), d: (Jiang et al., 2014), e: (Xie et al., 2019), f: (Kumar et al., 2019), g: (Yang et al., 2017), h: (Subedi et al., 2014), i: (Wang & Wang, 2016), j: (Gogoi et al., 2018), k: (Liu & Wong, 2013), l: (Colon & Toor, 2016), m: (Aparicio et al., 2018) n: (Ebele et al., 2017) o: (Zhang et al., 2016) p: (Zeng et al., 2007) q: https://pubchem.ncbi.nlm.nih.gov r: (Liu et al., 2017), s: https://www.drugbank.ca/, t: (Riemenschneider et al., 2016), u: (Biel-Maeso et al., 2019), v: (Baena-Nogueras et al., 2017), w: (Batchu et al., 2014), x: (Liu et al., 2019), y: (Li & Zhang, 2010), ** No degradation.

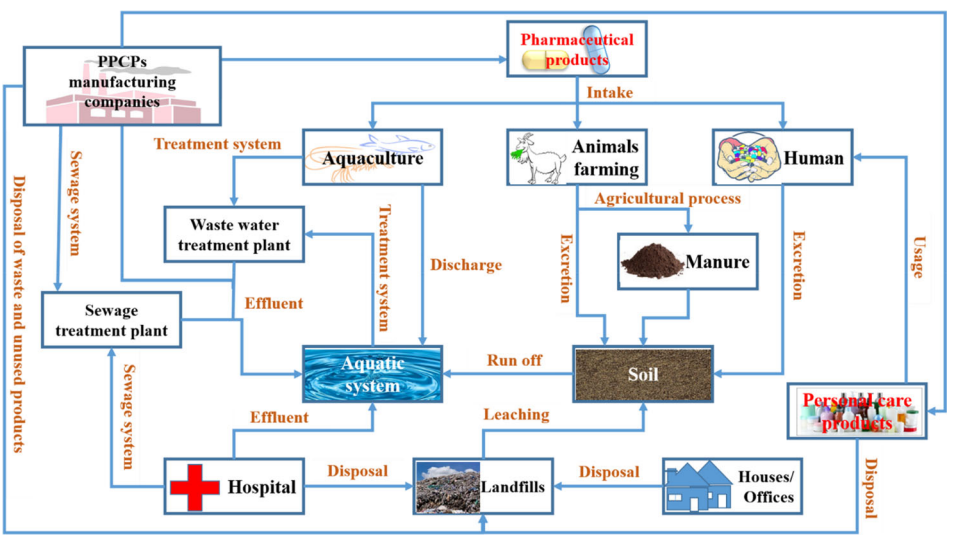


Figure 1. Sources of PPCPs in the environment.

persistence of personal care products into the environment (Yang et al., 2017). Moreover, the improper disposal of unused and expired PPCPs such as medicines and cosmetics products in landfills may introduce them into the land and water bodies (Al-Farsi et al., 2017). Finally, the stability and environmental metabolism of PPCPs are other essential factors that can regulate the occurrence and functional states of PPCPs in the environment (Al-Farsi et al., 2017). The state of the knowledge on the existence of selected PPCPs in the environment is presented in Table 2.

The assessment of PPCPs persistence is the most critical aspect which helps to understand the fate of PPCPs in the environment. The persistence of PPCPs in the environment is governed by many environmental facets, for instance, biodegradation, photolysis, redox reactions, and hydrolysis (Yamamoto et al., 2009). The persistence of PPCPs in the environment depends on the environmental conditions, such as temperature, sunlight exposure, microbial activity, redox status and the medium (soil/sediment/air/water) (Bu et al., 2016). Usually, the persistence of PPCPs is determined by the respective half-life of the individual compound in the medium. The half-lives of chlortetracycline in soil have been reported as >30 days. The half-life of oxytetracycline has been reported as 150 days in the marine sediment. The half-lives of fluoroquinolones and sulfonamides in sediment have been reported >30, and >40 days, respectively. A minimum degradation of ciprofloxacin after 40 days exposure to the environment has also been reported (Brooks et al., 2008). The half-lives of naproxen, bisphenol A, ibuprofen, clofibric acid, diclofenac, and triclosan vary within the range of 5.68–16.82, 0.81–5.5, 0.91–6.09, 4.52–18.48, 3.07–20.44, and 12.65–15.68 days, respectively, in four types of agricultural soil (Xu et al., 2009). Similarly, the aerobic biodegradation of 13 PPCPs including sulfamethoxazole, gemfibrozil, carbamazepine, and sulfamethizole in soils with 30 days incubation was investigated by Biel-Maeso et al. (2019), and 12 PPCPs except carbamazepine were reported as biodegraded in the range of 36–100% with half-lives range 1–30 days, while carbamazepine behaved as a recalcitrant with no biodegradative decay after 30 days incubation (Biel-Maeso et al., 2019). The half-life of a few PPCPs is provided in Table 1. However, the persistence of all groups of PPCPs in the environment is not well understood.

4. Uptake of PPCPs by plants

Since the PPCPs are frequently encumbered into the environment through many pathways as already elaborated in Figure 1, the uptake of PPCPs by the plants is widespread which has been recently reported by many researchers (Carter et al., 2018; Knight et al., 2018). This review presents

Table 2. Types of PPCPs, and their environmental occurrence.

Categories of PPCPs	Compounds	Country	Source	Quantity	References
Antibiotics	Tetracycline	Spain	Manure	0.9 mg/kg	(Conde-Cid et al., 2018)
	Oxytetracycline	Spain	Manure	28 mg/kg	(Conde-Cid et al., 2018)
	Chlortetracycline	Spain	Manure	4.0 mg/kg	(Conde-Cid et al., 2018)
	Sulfachloropyridazine	Jordan	WWTP influent	<0.005 μg/L	(Al-Mashaqbeh et al., 2019)
	Sulfamethazine	China	Soil	0.11 μg/kg	(Liu et al., 2020)
	Sulfamethoxazole	China	Soil	1.31 μg/kg	(Liu et al., 2020)
	Sulfadiazine	Bangladesh	River water	0.58 ng/L	(Hossain et al., 2018)
	Ciprofloxacin	Sri Lanka	Surface water	36.2 ng/L	(Guruge et al., 2019)
	Enrofloxacin	Vietnam	Wastewater	2869 ng/L	(Tran et al., 2019)
	Difloxacin	Argentina	wastewater	14.2 μg/L	(Teglia et al., 2019)
	Flumequine	France	WWTP influent	<4.6 ng/L	(Miossec et al., 2019)
	Norfloxacin	France	WWTP influent	<3.4 ng/L	(Miossec et al., 2019)
	Ofloxacin	Vietnam	Wastewater	2867 ng/L	(Tran et al., 2019)
	Pefloxacin	China	Wastewater	0.127 ng/mL	(Wang et al., 2019)
	Roxithromycin	Sri Lanka	Surface water	0.63 ng/L	(Guruge et al., 2019)
	Tylosin	Bangladesh	River water	16.68 ng/L	(Hossain et al., 2018)
	Erythromycin	Sri Lanka	Surface water	21.6 ng/L	(Guruge et al., 2019)
	Clarithromycin	Sri Lanka	Surface water	119 ng/L	(Guruge et al., 2019)
	Trimethoprim	China	Soil	0.05 μg/kg	(Liu et al., 2020)
	Thiamphenicol	China	Manure	32.8 μg/kg	(Qian et al., 2016)
	Chloramphenicol	China	Soil	2.68 μg/kg	(Liu et al., 2020)
	Lincomycin	Sri Lanka	Surface water	3.08 ng/L	(Guruge et al., 2019)
	Clindamycin	Vietnam	Wastewater	29 ng/L	(Tran et al., 2019)
Anti-inflammatory drugs	Ibuprofen	China	Soil	1.71 μg/kg	(Liu et al., 2020)
	Diclofenac	Sri Lanka	Surface water	80.0 ng/L	(Guruge et al., 2019)
	Acetaminophen	Mexico	WWTP influent	14900 ng/L	(Rivera-Jaimes et al., 2018)
	Aspirin	India	River water	0.777 μg/L	(Mutiyar et al., 2018)
	Indomethacin	Sri Lanka	Surface water	3.18 ng/L	(Guruge et al., 2019)
	Naproxen	Mexico	WWTP influent	4210 ng/L	(Rivera-Jaimes et al., 2018)
	Nimesulide	Portugal	Tap water	9.24 ng/L	(Paíga & Delerue-Matos, 2016)
	Phenazone	France	WWTP influent	<0.91 ng/L	(Miossec et al., 2019)
	Ketoprofen	India	River water	107 ng/L	(Sharma et al., 2019)
Synthetic hormone	Ethinylestradiol	Spain	Sewage sludge	97.8 μg/kg	(Martín et al., 2015)
Stimulant drug	Caffeine	Canada	Effluent	14200000 ng/L	(Kleywegt et al., 2019)
Cytostatic drugs	Cyclophosphamide	France	WWTP influent	<0.06 ng/L	(Miossec et al., 2019)
Contrast media	Iopromide	Korea	STP influent	2462 ng/L	(Hong et al., 2019)
	Iomeprol	Spanish	Wastewater	2093 μg/L	(Mendoza et al., 2015)
	Diatrizoate	China	Surface water	19.6 ng/L	(Xu et al., 2017)
β-blockers	Atenolol	Mexico	Surface water	32 ng/L	(Rivera-Jaimes et al., 2018)
	Metoprolol	France	WWTP influent	192 ng/L	(Miossec et al., 2019)
	Nadolol	Spain	WWTP influent	103 ng/L	(Biel-Maeso et al., 2018)
	Propranolol	Sri Lanka	Surface water	2.64 ng/L	(Guruge et al., 2019)
Blood lipid regulators	Gemfibrozil	Sri Lanka	Surface water	25.6 ng/L	(Guruge et al., 2019)
Antiepileptic drugs	Dilantin	Korea	Surface water	4.3 ng/L	(Kim et al., 2007)
	Carbamazepine	Sri Lanka	Surface water	71.2 ng/L	(Guruge et al., 2019)
Antimicrobials	Triclocarban	Sri Lanka	Surface water	41.0 ng/L	(Guruge et al., 2019)
	Triclosan	China	Soil	25.51 μg/kg	(Liu et al., 2020)
UV-filter	Oxybenzone	Canada	Effluent	8160 ng/L	(Kleywegt et al., 2019)
Preservatives	propylparaben	Poland.	Landfill leachate	0.77 μg/L	(Kapelewska et al., 2018)
	Butylparaben	Sri Lanka	Surface water	0.25 ng/L	(Guruge et al., 2019)
	Methylparaben	Sri Lanka	Surface water	12.9 ng/L	(Guruge et al., 2019)
Insect repellant	DEET	Sri Lanka	Surface water	202 ng/L	(Guruge et al., 2019)
Synthetic musks	HHCB	USA	Effluent	1.86 μg/L	(Sun et al., 2014)
Plasticizer	BEPH	China	Drinking water	6.35 μg/L	(Liu et al., 2014)

(*continued*)

Table 2. Continued.

Categories of PPCPs	Compounds	Country	Source	Quantity	References
	DBP	China	Drinking water	1.52 μg/L	(Liu et al., 2014)
Artificial sweetener	Sucralose	India	Sludge	1870 ng/g	(Subedi et al., 2015)
	Saccharine	India	Sludge	17900 ng/g	(Subedi et al., 2015)
	Acesulfame	India	Sludge	8.81 ng/g	(Subedi et al., 2015)
Surface activators	PFOS	Uganda	River water	3.89 ng/L	(Dalahmeh et al., 2018)
	PFOA	Uganda	River water	3.90 ng/L	(Dalahmeh et al., 2018)
	PFPeA	Jordan	River water	8.1 ng/L	(Shigei et al., 2020)
	PFHxA	Jordan	River water	2.4 ng/L	(Shigei et al., 2020)
	PFDA	Jordan	River water	2.3 ng/L	(Shigei et al., 2020)

the uptake of PPCPs under two conditions; one is the uptake of PPCPs by plants under the greenhouse condition, and another is the uptake of PPCPs by plants in the natural environment. Here, uptake means the transfer of PPCPs into the plant tissues (especially roots) from the plants' environmental media (Wu et al., 2013; Zheng et al., 2014). The experiment under the greenhouse conditions is usually carried out in the laboratory with controlled light-period, relative-humidity, temperature, etc. (Bhalsod et al., 2018), whereas the natural environment means the realistic agricultural farming system with less controlled conditions (Riemenschneider et al., 2016). The greenhouse condition include hydroponic experiment where the experiment plant grows into the nutrient solution with the known spiked amount of PPCPs and pot experiment where the experiment plants subjected to the soil (Kodešová et al., 2019) or manure amended soil (Dolliver et al., 2007) or coconut fiber substrate (González García et al., 2019) or sewage sludge (Cortés et al., 2013). The bioavailability of PPCPs in the greenhouse condition relatively higher than realistic field conditions since the photo exposure, microorganisms play a major role in the persistence of PPCPs in the environment. Therefore, this review has gathered existing knowledge under both greenhouse and field condition separately.

4.1. Uptake of PPCPs by plants under greenhouse conditions

The uptake of PPCPs by plants under the greenhouse conditions has been investigated by different authors around the world (Ahmed et al., 2015; Bassil et al., 2013). In a greenhouse experiment, the plants are grown in the known quantity of PPCPs spiked media, either soil or water, for a particular period of time. Finally, PPCPs are extracted from the experimental plants and preconcentrated for the determination of PPCPs. There are several greenhouse investigations on the uptake of PPCPs by different plants, and their main facets and findings are presented in Table 3. The removal percentages of sulfamethoxazole (73%), trimethoprim (59%), and metronidazole

Table 3. Uptake of PPCPs under the greenhouse condition.

Groups of PPCPs	Compounds	Plant samples	Spiked amount	Grown media	Root concentration	References
Anti-inflammatory drug	Acetaminophen	Cucumber (*Cucumis sativus*)	5.0 mg/L	Nutrition solution	1.7 μmol/g	(Sun et al., 2019)
Antibiotic	Clarithromycin	Lettuce (*Lactuca sativa*)	1.0 mg/L	Hydroponic	4977 μg/Kg	(Tian et al., 2019)
Antibiotic	sulfadiazine	Lettuce (*Lactuca sativa*	1.0 mg/L	Hydroponic	24599 μg/Kg	(Tian et al., 2019)
Psychoactive	Carbamazepine	Spinach (*Spinacia oleracea*)	100 μg/L	Hydroponic	>5 μg/g	(Nason et al., 2019)
Psychoactive	Carbamazepine	Spinach (*Spinacia oleracea*)	1 μg/L	Hydroponic	>0.5 μg/g	(Nason et al., 2019)
Psychoactive	Carbamazepine	Lettuce (*Lactuca sativa*)	210 μg/L	Coconut fiber substrate irrigated with spiked treated waste water	∼ 550 ng/g	(González García, Fernández-López, Polesel, et al., 2019)
Anti-inflammatory drug	Ketoprofen	Lettuce (*Lactuca sativa*)	210 μg/L	Coconut fiber substrate irrigated with spiked treated waste water	∼ 560 ng/g	(González García, Fernández-López, Polesel, et al., 2019)
Anti-inflammatory drugs	Ibuprofen	Lettuce (*Lactuca sativa*)	210 μg/L	Coconut fiber substrate irrigated with spiked treated waste water	∼ 800 ng/g	(González García, Fernández-López, Polesel, et al., 2019)
Anti-inflammatory drugs	Naproxen	Lettuce (*Lactuca sativa*)	210 μg/L	Coconut fiber substrate irrigated with spiked treated waste water	∼ 2000 ng/g	(González García, Fernández-López, Polesel, et al., 2019)
Antimicrobials	Triclocarban	Cucumber (*Cucumis sativus*)	05 μg/L	Hydroponic	2000 ng/g	(Sun et al., 2018)
Anti-inflammatory drug	Naproxen	Cucumber (*Cucumis sativus*)	05 μg/L	Hydroponic	690 ng/g	(Sun et al., 2018)
Antimicrobials	Triclosan	Cucumber (*Cucumis sativus*)	05 μg/L	Hydroponic	490 ng/g	(Sun et al., 2018)
Antibiotic	Sulfamethoxazole	Cucumber (*Cucumis sativus*)	05 μg/L	Hydroponic	460 ng/g	(Sun et al., 2018)
Stimulant drug	Caffeine	Cucumber (*Cucumis sativus*)	05 μg/L	Hydroponic	450 ng/g	(Sun et al., 2018)
Blood lipid regulators	Gemfibrozil	Cucumber (*Cucumis sativus*)	05 μg/L	Hydroponic	420 ng/g	(Sun et al., 2018)
Antibiotic	Tetracycline	Carrot (*Daucus corota*) Lettuce (*Lactuca sativa*)	0.1–15 mg/L	Soil irrigated with antibiotics spiked water	4.4–28.3 ng/g 12.0–36.8 ng/g	(Azanu et al., 2016)
Antibiotic	Amoxicillin	Carrot (*Daucus corota*) Lettuce (*Lactuca sativa*)	0.1–15 mg/L	Soil irrigated with antibiotics spiked water	13.7–33.6 ng/g 14.3–45.2 ng/g	(Azanu et al., 2016)
β-blockers	Atenolol	Reddish (*Raphanus sativus*) Lettuce (*Valerianella locusta*) Spinach (*Spinacia oleracea*) Arugula (*Eruca sativa*)	1 mg/L	Soil irrigated with PPCPs contaminated water	10 ng/g 430 ng/g 160 ng/g 420 ng/g	(Kodešová, Klement, Golovko, Fér, Nikodem, et al., 2019)
Antibiotic	Sulfamethoxazole	Reddish (*Raphanus sativus*) Lettuce (*Valerianella locusta*) Spinach (*Spinacia oleracea*) Arugula (*Eruca sativa*)	1 mg/L	Soil irrigated with PPCPs contaminated water	230 ng/g 1100 ng/g 1200 ng/g 1000 ng/g	(Kodešová, Klement, Golovko, Fér, Nikodem, et al., 2019)
Antiepileptic drug	Carbamazepine	Reddish (*Raphanus sativus*) Lettuce (*Valerianella locusta*)	1 mg/L	Soil irrigated with PPCPs contaminated water	2600 ng/g 1900 ng/g	(Kodešová, Klement, Golovko, Fér, Nikodem, et al., 2019)

(*continued*)

Table 3. Continued.

Groups of PPCPs	Compounds	Plant samples	Spiked amount	Grown media	Root concentration	References
		Spinach (*Spinacia oleracea*)			1500 ng/g	
		Arugula (*Eruca sativa*)			1800 ng/g	
Antibiotic	Tylosin	Lettuce (*Lactuca sativa*)	50 ng/mL	Hydroponic	~ 309.38 ng/g	(Chuang et al., 2019)
Antimicrobial	Triclosan	Lettuce (*Lactuca sativa*)	50 ng/mL	Hydroponic	5.59 ng/g	(Chuang et al., 2019)
Antibiotic	Sulfamethazine	Lettuce (*Lactuca sativa*)	5 mg/kg	Soil spiked with antibiotic	0.32 mg/kg	(Rajapaksha et al., 2014)
Antibiotic	Sulfamethazine	Lettuce (*Lactuca sativa*)	50 mg/kg	Soil spiked with antibiotic	0.62 mg/kg	(Rajapaksha et al., 2014)
Surface activator	PFOS	Chicory (*Cichorium intybus*)	62.5 μg/L	Hydroponic	3158.5 ng/g	(Gredelj et al., 2020)
	PFOA	Chicory (*Cichorium intybus*)	62.5 μg/L	Hydroponic	653.0 ng/g	(Gredelj et al., 2020)
	PFDA	Chicory (*Cichorium intybus*)	62.5 μg/L	Hydroponic	4945.9 ng/g	(Gredelj et al., 2020)
	PFPeA	Chicory (*Cichorium intybus*)	62.5 μg/L	Hydroponic	105.8 ng/g	(Gredelj et al., 2020)
Plasticizer	BEPH	Lettuce (*Lactuca sativa*)	500 μg/kg	Soil	852.17 μg/kg	(Sun et al., 2015)
		Strawberry (*Fragaria x ananassa*) Carrot (*Daucus corota*)			967.86 μg/kg 1343.87 μg/kg	
	DBP	Lettuce (*Lactuca sativa*)	500 μg/kg	Soil	351.57 μg/kg	(Sun et al., 2015)
		Strawberry (*Fragaria x ananassa*) Carrot (*Daucus corota*)			1286.02 μg/kg 2385.12 μg/kg	

(96%) after 24 days exposure, and cefadroxil (100%) after 14 days of exposure to the experimental solution using duckweed (*Lemna minor*) from the aquatic environment were reported (Iatrou et al., 2017). A similar study was carried out by Gatidou et al. (2017) with duckweed using five types of benzotriazoles, and it reported 26–72% removal of benzotriazoles by the duckweed from the wastewater. An interesting study investigated the uptake of PPCPs by greenhouse lettuce grown with the soil base and over-head irrigation of PPCPs contaminated water. The authors reported that over-head irrigation increased the uptake of PPCPs in lettuce plants (Bhalsod et al., 2018). Very recently, Rosa et al. (2019) made a study on the uptake of oxytetracycline by seaweed *Ulva* sp. under laboratory condition by exposing to the oxytetracycline spiked natural seawater solution containing two different initial concentrations of oxytetracycline (0.040 and 0.120 mg/L). After 24 h exposure, they detected 40 and 100 ng/g of oxytetracycline in the seaweed, respectively.

4.2. Uptake of PPCPs by plants in the natural environment

Many researchers have investigated the plant uptake of PPCPs under the laboratory conditions, but studies on the plant uptake under the natural environment or field condition are minimal. Nuel et al. (2018) conducted an interesting study on the role of local plants, such as sedge (*Carex caryophyllea*), callitriche (*Callitriche palustris*), yellow flag *(Iris pseudacorus*), soft rush (*Juncus effusus*), and white willow (*Salix alba*) of surface flow treatment wetland in the mitigation of PPCPs from the effluent of the wastewater treatment system. Moreover, authors investigated the seasonal variation on the plant uptake of PPCPs, suggested the removal efficiency of PPCPs was well improved in the summer than those in the winter (Nuel et al., 2018). Another study investigated the uptake of 141 PPCPs in plants sweet corn, potato, carrot, and tomato under the normal farming conditions but reported no PPCPs found in the plants above the limit of detection. This study reported, eight of 141 PPCPs, including atenolol, DEET, ibuprofen, lincomycin, and sulfamerazine were found in the range of 0.33–6.25 ng/g in dry weight (Sabourin et al., 2012). It suggested that the uptake of PPCPs in the plant was quite smaller under the rational/realistic farming conditions (Sabourin et al., 2012).

In another field experiment, Christou et al. (2017) detected the presence of diclofenac, sulfamethoxazole, and trimethoprim at 11.63, 5.26, and 3.40 µg/kg, respectively, in tomato fruits which was irrigated for long-term under the regular farming conditions with wastewater from municipal wastewater treatment plant (Christou et al., 2017). Riemenschneider et al. (2016) reported, 12 types out of 28 micropollutants were found in the

field-grown plants including potato, lettuce, carrot, and zucchini irrigated with Zarqa River in Jordan, with a concentration range of 1.7–216 ng/g in dried weight (Riemenschneider et al., 2016). Ben Mordechay et al. (2018) explored the uptake of carbamazepine and its metabolism by tomato, wheat, and lettuce with an introduction of treated wastewater and soil amended with biosolids in the realistic farming scenario. The same authors reported that the introduction of treated wastewater in the agricultural activity led to plant uptake of carbamazepine as a representative of PPCPs in a significantly higher than the introduction of biosolids (Ben Mordechay et al., 2018).

Very recently, a study reported the occurrence of PPCPs such as carbamazepine, methylparaben, and caffeine in seaweeds obtained from the Saudi red sea at 1.7, 44.3, and 41.3 ng/g, respectively (Ali et al., 2018). Further, phytoremediation study assessed the use of aquatic plants, including *Ipomoea aquatica, Phragmites australis, Typha latifolia*, *Azolla caroliniana, Lemna minor,* and *Salix atrocinerea* for the removal of PPCPs from the wastewater, which achieved 70–90% removal efficiency (Dhir, 2019). Moreover, a systematic analysis of the accumulation of 11 PPCPs, including sulfamethoxazole, ibuprofen, trimethoprim, triclosan, chloramphenicol, and sulfamethazine with long term reclaimed water irrigation (20, 30, and 40 years) in agriculture lands was reported by Liu et al. (2020). The authors stated that PPCPs were detected in eggplant, cucumber, wheat, and long bean at the range of 0.02–28.01 µg/kg (Liu et al., 2020). Table 4 provides a few studies conducted in realistic environmental conditions. However, the scientific investigation on the plant uptake of PPCPs in realistic field condition still remains very limited to this date.

5. Translocation of PPCPs in plants

The translocation of PPCPs can be referred to as the passage of PPCPs from the roots to the areal parts of the plants, such as leaves, stems, fruits and rhizomes (Cui & Schröder, 2016; Dodgen et al., 2015) as shown in Figure 2. The translocation of PPCPs in plants can be expressed by the translocation factor (TF), which is calculated by the ratio between the concentrations of PPCPs in areal parts and those in roots of the plants (Dodgen et al., 2015) (Eq. (1)).

$$TF = \frac{Concentration\ of\ PPCPs\ in\ areal\ part}{concentration\ of\ PPCPs\ in\ root} \tag{1}$$

Moreover, the translocation of PPCPs depends on several factors, such as physicochemical properties of PPCPs (pKa, log K_{ow}, molecular size, etc.), properties of soil (soil pH, temperature, organic carbon content, etc.), and

Table 4. Plant uptake of PPCPs in realistic environment.

PPCPs	Source of PPCPs	Plant	Country	Concentration in plant	References
Diclofenac	Wastewater	Tomato (*Lycopersicon esculentum*)	Cyprus	11.62 μg/kg	(Christou et al., 2017)
Sulfamethoxazole	Wastewater	Tomato (*Lycopersicon esculentum*)	Cyprus	5.26 μg/kg	(Christou et al., 2017)
Trimethoprim	Wastewater	Tomato (*Lycopersicon esculentum*)	Cyprus	3.40 μg/kg	(Christou et al., 2017)
Carbamazepine	Treated wastewater	Tomato (*Solanum lycopersicum*) Wheat (*Triticum aestivum*) Lettuce (*Lactuca sativa*)	Israel	29.30 ng/g 9.25 ng/g 69.72 ng/g	(Ben Mordechay et al., 2018)
Carbamazepine	Biosolid application	Tomato (*Solanum lycopersicum*) Wheat (*Triticum aestivum*) Lettuce (*Lactuca sativa*)	Israel	6.65 ng/g 3.80 ng/g 1.83 ng/g	(Ben Mordechay et al., 2018)
Atenolol	Effluent of WWTP	Cabbage (*Brassica oleracea*)	Saudi Arabia	55 ng/g	(Picó et al., 2019)
Caffeine	Effluent of WWTP	Cabbage (*Brassica oleracea*)	Saudi Arabia	125 ng/g	(Picó et al., 2019)
Gemfibrozil	Effluent of WWTP	Cabbage (*Brassica oleracea*) Eggplant (*Solanum melongena*) Green beans (*Phaseolus vulgaris*)	Saudi Arabia	72 ng/g 34 ng/g 45 ng/g	(Picó et al., 2019)
Malathion	Effluent of WWTP	Cabbage (*Brassica oleracea*) Chili plant (*Capsicum frutescens*) Tomato (*Solanum lycopersicum*)	Saudi Arabia	1000 ng/g 84 ng/g 85 ng/g	(Picó et al., 2019)
Naproxen	Effluent of WWTP	Cabbage (*Brassica oleracea*)	Saudi Arabia	38 ng/g	(Picó et al., 2019)
Triclosan	Reclaimed water	Eggplant (*Solanum melongena*) Long bean (*Vigna unguiculate*) Wheat (*Triticum aestivum*) Cucumber (*Cucumis sativus*)	China	6.77 μg/kg 18.46 μg/kg 12.83 μg/kg 13.39 μg/kg	(Liu et al., 2020)
Sulfamethazine		Eggplant (*Solanum melongena*) Long bean (*Vigna unguiculate*) Wheat (*Triticum aestivum*) Cucumber (*Cucumis sativus*)	China	0.03 μg/kg 0.01 μg/kg 0.08 μg/kg 0.36 μg/kg	(Liu et al., 2020)
Trimethoprim		Eggplant (*Solanum melongena*) Long bean (*Vigna unguiculate*) Wheat (*Triticum aestivum*) Cucumber (*Cucumis sativus*)	China	0.02 μg/kg ND 0.05 μg/kg 0.08 μg/kg	(Liu et al., 2020)
Ibuprofen		Eggplant (*Solanum melongena*) Long bean (*Vigna unguiculate*) Wheat (*Triticum aestivum*) Cucumber (*Cucumis sativus*)	China	0.78 μg/kg 0.75 μg/kg 1.21 μg/kg 13.82 μg/kg	(Liu et al., 2020)
Sulfamethoxazole		Eggplant (*Solanum melongena*) Long bean (*Vigna unguiculate*) Wheat (*Triticum aestivum*) Cucumber (*Cucumis sativus*)	China	0.05 μg/kg 0.08 μg/kg 0.16 μg/kg 0.90 μg/kg	(Liu et al., 2020)

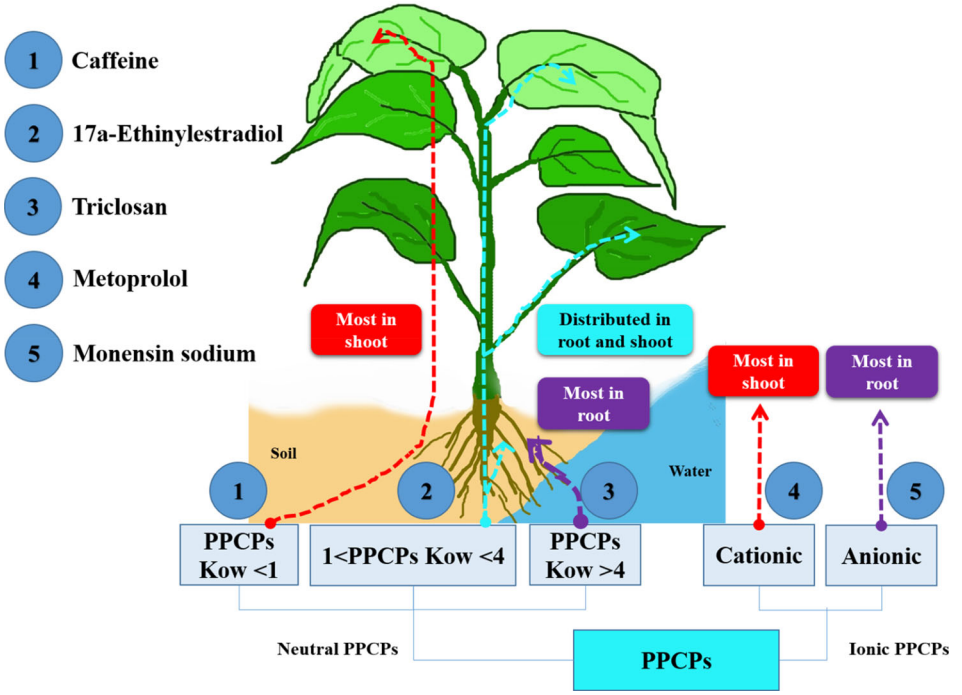


Figure 2. Plant uptake and translocation of PPCPs from the environment to different aerial parts. The examples are based on Chuang et al. (2019), He et al. (2017), Christou et al. (2016), and Goldstein et al. (2014).

environmental conditions (temperature, relative humidity, photo-period, etc.) (Madikizela et al., 2018). The effect of these factors on the plant uptake PPCPs has explained in the later section. This current study has reviewed the translocation of PPCPs in two ways; (1) the translocation of PPCPs in plants under the greenhouse/laboratory conditions, and (2) the translocation of PPCPs in plants in realistic environmental condition. Hence, the translocation of PPCPs may vary with environmental conditions, variety of plants, and physicochemical properties of PPCPs.

5.1. Translocation of PPCPs in plants under greenhouse conditions

Until recently, there is plenty of work which studied on the translocation of PPCPs from roots to the areal part of the plant once it is taken up (Li et al., 2018; Madikizela et al., 2018). A recent hydroponic study on lettuce reported that small-sized PPCPs such as carbamazepine and caffeine showed low affinity to roots, which was expressed by sorption coefficient (Kp) below 0.05 L/g while molecular weight (MW) below 300 g/mol showed high translocation to the areal parts of lettuce. The small-sized PPCPs such as trimethoprim, and lamotrigine with relatively high Kp above 12 L/g

showed high translocation to areal pieces of lettuce. Large-sized PPCPs such as tylosin, monensin sodium, and lincomycin with MW above 400 g/mol showed higher accumulation ability in lettuce roots (Chuang et al., 2019). Small-sized PPCPs took up with water through the symplast pathway could allow the passage of them across the Casparian strip to xylem, whereas large-sized PPCPs enter into root through the apoplast pathway, which blocked at the Casparian strip (Chuang et al., 2019). A comparatively higher concentration of PPCPs was detected in the plant roots and shoots under the greenhouse condition. He et al. (2017) reported very low translocation of triclosan in water spinach, penny grass, purple perilla, rice, cress, and cane shoot, and it might be due to its high hydrophobic nature (log K_{ow}; 4.76) and high affinity to the roots. Similarly, the high accumulation of triclosan was observed in the lettuce root (Chuang et al., 2019). Moreover, higher TFs of carbamazepine were observed (Table 5) in reddish (4.8), and arugula (6.8) than those in lettuce (0.6), and spinach (0.7) (Kodešová, Klement, Golovko, Fér, Nikodem, et al., 2019). The same authors detected higher translocation of atenolol in reddish (2.1), and spinach (4.6) than those in lettuce (0.2), and arugula (0.7). Recently investigated data on the translocation of PPCPs in the plant is assembled in Table 5.

5.2. Translocation of PPCPs in plants in the natural environment

Investigations on the translocation of PPCPs in the plant under the field condition are scarce. However, some studies reported a limited number of PPCPs and their translocation to the areal parts of the plant. Martínez-Piernas et al. (2019) found 17 PPCPs in the realistic field-grown tomato leaves irrigated with reclaimed water in the concentration range of 0.04–32 ng/g. Similarly, the long-term application of manure under the realistic farming condition introduced the antibiotics to the peanut plants as investigated by Zhao et al. (2019). Based on their results, sulfamethoxazole shows the highest TF, followed by enrofloxacin, erythromycin, and chlortetracycline, whereas ciprofloxacin shows the lowest TF (Table 6). This account, the PPCPs with less TF value, have the highest affinity toward the root, which led to the accumulation of them in root cell. Different TF values of carbamazepine, in cabbage, lettuce, and zucchini and caffeine in potato, and zucchini might indicate that the translocation of these compounds depends on the crop type (Riemenschneider et al., 2016). However, comparatively less concentration of PPCPs was detected in plant roots and shoots under the realistic field condition than those under the greenhouse condition.

Table 5. Translocation of PPCPs under the greenhouse condition.

PPCPs	Plant	Spiked amount	Concentration in roots	Concentration in shoot	TF*	References
Caffeine	Lettuce (*Lactuca sativa*)	50 ng/mL	~ 42.75 ng/g	~ 70.02 ng/g	1.6379	(Chuang et al., 2019)
Carbadox	Lettuce (*Lactuca sativa*)	50 ng/mL	~ 48.21 ng/g	~ 3.85 ng/g	0.0799	(Chuang et al., 2019)
Carbamazepine	Lettuce (*Lactuca sativa*)	50 ng/mL	~ 84.83 ng/g	~ 240.39 ng/g	2.8338	(Chuang et al., 2019)
Estrone	Lettuce (*Lactuca sativa*)	50 ng/mL	~ 13.28 ng/g	~ 7.38 ng/g	0.5557	(Chuang et al., 2019)
Lincomycin	Lettuce (*Lactuca sativa*)	50 ng/mL	~ 128.2 ng/g	~ 10.27 ng/g	0.0801	(Chuang et al., 2019)
Trimethoprim	Lettuce (*Lactuca sativa*)	50 ng/mL	~ 349.54 ng/g	~ 49.35 ng/g	0.1412	(Chuang et al., 2019)
Lamotrigine	Lettuce (*Lactuca sativa*)	50 ng/mL	~ 80.66	~ 14.49	0.1796	(Chuang et al., 2019)
Diclofenac	Alfalfa (*Medicago sativa*)	10 μg/L	162.83 μg/kg	ND	–	(Christou et al., 2016)
Sulfamethoxazole	Alfalfa (*Medicago sativa*)	10 μg/L	52.46 μg/kg	3.48 μg/kg	0.0663	(Christou et al., 2016)
Trimethoprim	Alfalfa (*Medicago sativa*)	10 μg/L	311.90 μg/kg	23.52 μg/kg	0.0754	(Christou et al., 2016)
17a-ethinylestradiol	Alfalfa (*Medicago sativa*)	10 μg/L	28.85 μg/kg	28.26 μg/kg	0.9795	(Christou et al., 2016)
Acetaminophen	Cucumber (*Cucumis sativus*)	5.0 mg/L	1.7 μmol/g	0.5 μmol/g	0.2941	(Sun et al., 2019)
Atenolol	Reddish (*Raphanus sativus*) Lettuce (*Valerianella locusta*) Spinach (*Spinacia oleracea*) Arugula (*Eruca sativa*)	1 mg/L	53 ng/g	110 ng/g	2.0755	(Kodešová, Klement, Golovko, Fér, Nikodem, et al., 2019)
			2400 ng/g	390 ng/g	0.1625	
			130 ng/g	600 ng/g	4.6154	
			390 ng/g	280 ng/g	0.7179	
Sulfamethoxazole	Reddish (*Raphanus sativus*) Lettuce (*Valerianella locusta*) Spinach (*Spinacia oleracea*) Arugula (*Eruca sativa*)	1 mg/L	120 ng/g	48 ng/g	0.40	(Kodešová, Klement, Golovko, Fér, Nikodem, et al., 2019)
			580 ng/g	23 ng/g	0.0397	
			800 ng/g	300 ng/g	0.3750	
			1600 ng/g	75 ng/g	0.0469	
Carbamazepine	Reddish (*Raphanus sativus*) Lettuce (*Valerianella locusta*) Spinach (*Spinacia oleracea*) Arugula (*Eruca sativa*)	1 mg/L	3100 ng/g	15000 ng/g	4.8387	(Kodešová, Klement, Golovko, Fér, Nikodem, et al., 2019)
			2400 ng/g	1400 ng/g	0.5833	
			2800 ng/g	1900 ng/g	0.6786	
			3400 ng/g	23000 ng/g	6.7647	
Triclosan	Water spinach (*Ipomoea aquatica*) Penny grass (*Hydrocotyle vulgaris*) Purple perilla (*Prilla frutescens*) Rice (*Oryza sativa*) Cress (*Oenanthe javanica*) Cane shoot (*Zizania latifolia*)	0.042 μg/mL	59.34 μg/g	0.143 μg/g	0.0024	(He et al., 2017)
			60.43 μg/g	0.107 μg/g	0.0017	
			09.39 μg/g	0.040 μg/g	0.0043	
			33.75 μg/g	1.061 μg/g	0.0314	
			63.71 μg/g	0.209 μg/g	0.0033	
			14.04 μg/g	0.201 μg/g	0.0143	
Diclofenac	Chicory (*Cichorium intybus*)	1 mg/L	3.9 μg/100g	2.6 μg/100g	0.6667	(Podio et al., 2020)
PFOS	Chicory (*Cichorium intybus*)	65.2 μg/L	3158.5 ng/g	168.4 ng/g	0.0533	(Gredelj et al., 2020)
PFOA	Chicory (*Cichorium intybus*)	65.2 μg/L	653.0 ng/g	230.7 ng/g	0.3533	
PFDA	Chicory (*Cichorium intybus*)	65.2 μg/L	4945.9 ng/g	204.1 ng/g	0.0413	
PFPeA	Chicory (*Cichorium intybus*)	65.2 μg/L	105.8 ng/g	460.0 ng/g	4.3478	
BEPH	Lettuce (*Lactuca sativa*) Strawberry (*Fragaria x ananassa*) Carrot (*Daucus corota*)	500 μg/kg	852.17 μg/kg	667.59 μg/kg	0.7834	(Sun et al., 2015)
			967.86 μg/kg	695.92 μg/kg	0.7190	
			1343.87 μg/kg	1220.08 μg/kg	0.9079	
DBP	Lettuce (*Lactuca sativa*) Strawberry (*Fragaria x ananassa*) Carrot (*Daucus corota*)	500 μg/kg	351.57 μg/kg	123.80 μg/kg	0.3521	(Sun et al., 2015)
			1286.02 μg/kg	180.47 μg/kg	0.1403	
			2385.12 μg/kg	548.81 μg/kg	0.2301	
DBP	*Brassica rapa var. perviridis*	0.5 mg/L	6.89 mg/kg	0.05 mg/kg	0.0073	(Li et al., 2020)

*TF was calculated.
ND: not detected.

Table 6. Translocation of PPCPs under the realistic environmental condition.

PPCPs	Plant	Concentration in roots, ng/g	Concentration in shoot, ng/g	TF*	References
Acetaminophen	Tomato (*Solanum lycopersicum*)	NR	2	–	(Martínez-Piernas et al., 2019)
Antipyrine	Tomato (*Solanum lycopersicum*)	NR	1	–	(Martínez-Piernas et al., 2019)
Caffeine	Tomato (*Solanum lycopersicum*)	NR	0.7	–	(Martínez-Piernas et al., 2019)
Carbamazepine	Tomato (*Solanum lycopersicum*)	NR	5	–	(Martínez-Piernas et al., 2019)
Propranolol	Tomato (*Solanum lycopersicum*)	NR	0.3	–	(Martínez-Piernas et al., 2019)
Trimethoprim	Tomato (*Solanum lycopersicum*)	NR	2	–	(Martínez-Piernas et al., 2019)
Venlafaxine	Tomato (*Solanum lycopersicum*)	NR	2	–	(Martínez-Piernas et al., 2019)
Carbamazepine	Cabbage (*Brassica oleracea*)	61.4	79.0	1.29	(Riemenschneider et al., 2016)
Carbamazepine	Lettuce (*Lactuca sativa*)	26.7	215.7	8.08	(Riemenschneider et al., 2016)
Carbamazepine	Zucchini (*Cucurbita pepo*)	69.0	41.9	0.61	(Riemenschneider et al., 2016)
10,11-epoxide carbamazepine	Carrot (*Daucus corota*)	7.7	53.5	6.95	(Riemenschneider et al., 2016)
Acesulfame	Cabbage (*Brassica oleracea*)	72.3	56.0	0.77	(Riemenschneider et al., 2016)
Caffeine	Potato (*Solanum tuberosum*)	30.3	61.8	2.04	(Riemenschneider et al., 2016)
Caffeine	Zucchini (*Cucurbita pepo*)	169.0	23.7	0.14	(Riemenschneider et al., 2016)
2-hydroxy carbamazepine	Zucchini (*Cucurbita pepo*)	42.2	6.9	0.16	(Riemenschneider et al., 2016)
3-hydroxy carbamazepine	Zucchini (*Cucurbita pepo*)	34.9	3.8	0.11	(Riemenschneider et al., 2016)
Carbamazepine	Lettuce (*Lactuca sativa*)	1	1.4	1.40	(Wu et al., 2014)
Meprobamate	Spinach (*Spinacia oleracea*)	ND	0.03	–	(Wu et al., 2014)
Dilantin	Spinach (*Spinacia oleracea*)	0.32	0.27	0.84	(Wu et al., 2014)
Naproxen	Cabbage (*Brassica oleracea*)	0.31	0.26	0.84	(Wu et al., 2014)
Carbamazepine	Cabbage (*Brassica oleracea*)	0.74	0.18	0.24	(Wu et al., 2014)
Tetracycline	Peanut (*Arachis hypogaea*)	6.38	7.08	1.11	(Zhao et al., 2019)
Oxytetracycline	Peanut (*Arachis hypogaea*)	22.73	ND	–	(Zhao et al., 2019)
Chlortetracycline	Peanut (*Arachis hypogaea*)	8.33	21.84	2.62	(Zhao et al., 2019)
Norfloxacin	Peanut (*Arachis hypogaea*)	9.37	0.99	0.11	(Zhao et al., 2019)
Ciprofloxacin	Peanut (*Arachis hypogaea*)	3.35	0.07	0.02	(Zhao et al., 2019)
Enrofloxacin	Peanut (*Arachis hypogaea*)	0.50	4.26	8.52	(Zhao et al., 2019)
Sulfamethoxazole	Peanut (*Arachis hypogaea*)	0.12	3.10	25.83	(Zhao et al., 2019)
Sulfamethazine	Peanut (*Arachis hypogaea*)	3.19	2.35	0.74	(Zhao et al., 2019)
Erythromycin	Peanut (*Arachis hypogaea*)	1.16	3.41	2.94	(Zhao et al., 2019)
Tylosin	Peanut (*Arachis hypogaea*)	0.27	0.17	0.63	(Zhao et al., 2019)

*TF was calculated.
NR: not reported; ND: not detected.

6. Factors affecting the uptake and translocation of PPCPs in the plant

There are several factors that influence the plant's uptake and translocation of PPCPs from planted media to roots and areal parts. Biological characteristics of plants (lipid and carbohydrate content of plant roots), physiochemical properties of PPCPs (molecular size, K_{ow}, and pKa), and environmental conditions of media are the primary categories that influence the plant uptake of PPCPs (Zhang et al., 2017). Lipid and carbohydrate content of root cell walls and permeability of root cell membranes are the dominant plant biological factors that play a strong influence on the uptake of PPCPs from external media to roots (Chen et al., 2009; Zhang et al., 2017; Zhang and Zhu, 2009). Moreover, the physicochemical parameters of PPCPs such as molecular weight, hydrophobicity parameter (K_{ow}; partition coefficient of PPCPs between octanol and water), and ionic nature of PPCPs, either cationic or neutral or anionic (Zhang et al., 2017) also affect the uptake and translocation of PPCPs significantly from the surrounding environment to the plants (Al-Farsi et al., 2017; Zhang et al., 2017). These physicochemical properties of selected PPCPs are provided in Table 1. The PPCPs which have a molecular weight less than 1000 g/mol can be efficiently accumulated by the plant (Öztürk et al., 2016). The volatile and low molecular weight compounds can be taken by roots and shoot easily. However, the nonvolatile, higher molecular weight, and hydrophobic compounds can only be accumulated in roots (Zhang et al., 2017). Besides, the K_{ow} of PPCPs is an essential quantitative parameter that shows the remarkable effect on the PPCPs uptake by the plant; the PPCPs with significantly higher log K_{ow} (>4) are considered as highly hydrophobic compounds. Usually, these compounds do not translocate through the plant since it has expressed strong interaction with soil or root tissues. The PPCPs with lower log K_{ow} (<1), considered as highly hydrophilic compounds, and these compounds have a low tendency to move across the phospholipid membrane of root tissues. The PPCPs which have log K_{ow} between 1 and 4, can be readily translocated in plant parts (Colon & Toor, 2016). The ionic nature of PPCPs is another factor that influences the uptake of PPCPs. For neutral PPCPs such as caffeine, carbamazepine, and estrone (Chuang et al., 2019), the K_{ow} phenomena can be applied. In the case of ionic PPCPs, because of the repulsion or attraction between the ionized PPCPs, either anionic or cationic and negatively charged cell membrane of roots, the uptake and translocation of PPCPs by plant might be affected (Colon & Toor, 2016). The anionic PPCPs are likely to accumulate in the roots, whereas the neutral and cationic PPCPs are likely to translocate in areal parts of plant either leaves, or steams, or fruits (Madikizela et al., 2018). It was reported by Goldstein et al. (2014), that the positively charged PPCPs such as metoprolol was

found in the cucumber and tomato leaves at quite high concentration compared to negatively charged PPCPs, probably as a result of the attraction of positively charged metoprolol with negatively charged cell membranes. The negatively charged PPCPs such as, ibuprofen, ketoprofen, gemfibrozil, and sulfamethoxazole are preferentially accumulated in the root cells since such weak acidic PPCPs undergo the dissociation into anionic forms in the cytosol once entered inside, which are repels by cell walls (Goldstein et al., 2014). Similarly, Christou et al. (2016) stated that being weak acidic property in nature, the diclofenac and sulfamethoxazole are accumulated at high concentration in the root but very less in leaves. In contrast, the trimethoprim as a basic PPCPs shows more accumulation in roots and high translocation to leaves when compared to the weak acidic PPCPs (Christou et al., 2016). The same author reported that the neutral PPCPs such as 17a-ethinylestradiol show almost quantitatively equal accumulation in roots and leaves. The environmental conditions such as the concentration of PPCPs in soil, pH of outside media, temperature, the concentration of available organic carbon in the soil also affect the plant uptake of PPCPs (Zhang et al., 2017).

7. Mechanism of uptake and translocation of PPCPs in the plant

Plants take up water along with dissolved solute such as minerals, organic compounds like PPCPs through the roots from the rhizosphere by passive diffusion. Generally, the passage of PPCPs through the plant starts at root hairs. Once PPCPs enter into root hairs, PPCPs reach the xylem/phloem through cortex, endodermis, and Casparian strip (Miller et al., 2016). The movement of PPCPs from root hair to xylem/phloem has been demonstrated by several pathways. (1) the movement of water and solute occurs through the space outside the cell membrane (apoplastic movement), (2) flux of water along with solute occurs through the cell cytoplasm (symplastic movement), and (3) the water and solute flow occurs via the vacuoles in cells (vacuolar movement) (Öztürk et al., 2016; Zhang & Zhu, 2009). Mainly, hydrophobic PPCPs move toward the xylem/phloem via the apoplastic movement, whereas the movement of hydrophilic PPCPs occurs via the symplastic movement (Zhang & Zhu, 2009). However, the apoplastic movement gets stopped at the Casparian strip because the deposition of lignin and suberin on the Casparian strip cell walls blocks the passive movement of water and solute. At this point, the flux of water and solute via apoplastic movement is forced into the symplastic movement (Cui & Schröder, 2016). Once the PPCPs reach the xylem/phloem, they get translocated upward to the aerial parts of the plant, such as stems, leaves, or fruits. Mainly, the water and PPCPs are pulled toward the leaves by the

combined action of transpiration steam, capillary action, and root pressure. Apart from this, the hydrophobic PPCPs are translocated to the shoot via the xylem sap, which contains latex-like-proteins which bind with hydrophobic PPCPs (Goto et al., 2019). The solubility enhancement of triclocarban and endosulfan in zucchini and soybean xylem sap was observed when those solubilities are compared with deionized water (Garvin et al., 2015).

Apart from the root uptake, there is another possibility of PPCPs uptake by the plant through stomata on the leaf surface, which function as an inlet for carbon dioxide and an outlet for water vapor. The gaseous contaminants can be taken up into the plant along with carbon dioxide through stomata (Colon & Toor, 2016). The recent study of Khuman and Chakraborty (2019) detected the occurrence of endosulfan, hexachlorocyclohexane, and dichlorodiphenyltrichloroethane in the air with a concentration of 429, 888, and 1689 pg/m^3. Therefore, it is now possible to identify the plant uptake of PPCPs through leaves and their uptake and translocation mechanism.

8. Human health exposure and risks of PPCPs through consumption of contaminated plants

The PPCPs as endocrine-disrupting contaminants enter into the human body through the consumption of the contaminated crops, vegetables and fruits. These PPCPs may cause several harmful effects on human health, especially in children. Recently, more than two PPCPs were found in the edible crops such as potato, lettuce, carrot, tomato, and zucchini (Christou et al., 2017; Riemenschneider et al., 2016). The consumption of two or more PPCPs at the same time may create interactive concerns in humans which cases were narrated in a review paper by Wu et al. (2015) showing 500 ng/day of each compound was ingested simultaneously through intake of the vegetable crops irrigated with PPCPs contaminated water. Daily exposure of PPCPs, especially antibiotics, will cause resistance to antimicrobial activity in humans, and it can increase the probability of risk of death. In a review on the risk assessment of personal care products, Stuart et al. (2012) showed that parabens suppressed the estrogenic activity and induced immunologically mediated, immediate systemic hypersensitivity reactions, while DEET inhibited the enzyme responsible for the operation of the central nervous system. However, Verslycke et al. (2016) found a large margin of safety for the exposure of triclosan through all routes, including biosolids – soil-plant – human, and they drew an inference that the contaminant could pose a minimal risk to human health. Furthermore, the human risk associated with exposure to PPCPs is determined in terms of risk quotient (RQ) and cumulative health hazard index (HI). The RQ is derived

from the ratio between estimated daily intake (EDI) and acceptable daily intake (ADI) (Liu et al., 2017) (Eq. (2)).

$$RQ = \frac{EDI\left(ngkg^{-1}day^{-1}\right)}{ADI\left(ngkg^{-1}day^{-1}\right)} \tag{2}$$

where the EDI value will be calculated by the equation expressed by Eq. (3).

$$EDI = \frac{Daily\ intake\ rate\ \left(g\ person^{-1}day^{-1}\right) * PPCPs\ in\ vegetable\ \left(ng\ g^{-1}\right)}{person\ average\ weight\ \left(kg\ person^{-1}\right)} \tag{3}$$

and the value of HI is estimated by the tally of RQ of each PPCPs detected in a vegetable (Zhao et al., 2019), which mathematically expressed by Eq. (4).

$$HI = \sum_{j=1}^{n} RQ_i \tag{4}$$

It is considered as a negligible human risk when the value of RQ and HI < 0.01, as a considerable human risk if RQ and HI > 0.01, and as a distinct human risk if the value of RQ and HI > 0.05 (Liu et al., 2017; Zhao et al., 2019). Zhao et al. (2019) reported that PPCPs presence in human bodies living in both rural and urban areas was traced by ingesting PPCPs contaminated peanut kernels, where the RQ value for enrofloxacin, exceeded the threshold level of distinct human risk (RQ > 0.05), and for ofloxacin, norfloxacin, ciprofloxacin, and clarithromycin the RQ values reached the threshold level of considerable human risk (Zhao et al., 2019). Moreover, human health risk assessments through calculations of human exposure to the PPCPs are warranted when human exposure to PPCPs occurs concurrently via multiple pathways. Generally, human exposure (HE) of PPCPs is calculated using the mathematical equation expressed in Eq. (5),

$$HE = C * D * W * T \tag{5}$$

where C is the concentration of PPCPs in vegetables (ng/kg wet weight), D is the average daily consumption of vegetables (g wet weight/kg body weight/day), W is the human body weight, and T is the exposure time (day) (Wu et al., 2013). Typically, the acceptable annual human exposure range of PPCPs is 20–200 mg. Many laboratory experiments suggested that the human exposure of PPCPs, including carbamazepine, sulfamethazine, fluoxetine, and diclofenac through ingesting the contaminated plants, was much lower than the accepted range of 20–200 mg (Carter et al., 2014; Wu et al., 2013). However, to the best of the knowledge of the authors, no such

investigation is available in the literature about the human risks associated with the consumption of the contaminated vegetables.

9. Instrumental analysis methods to determine the PPCPs in plant tissues

The extraction of PPCPs in the plant tissues is a bit challenging task when compared to those in water and soil. The occurrence of primary and secondary metabolites, pigments, and other cellular compounds in plant tissues can interfere with PPCPs during the analysis. Therefore, the PPCPs extraction procedure from the plant tissue is essential in order to achieve accurate analysis. Previous studies have utilized various extraction techniques for the extraction of PPCPs from the plant tissues, for instance, solid-phase extraction (Petrie et al., 2017; Rajapaksha et al., 2014), liquid-liquid extraction (Loos et al., 2013), accelerated solvent extraction (Azanu et al., 2018), QuEChERS (**Qu**ick, **E**asy, **Ch**eap, **E**ffective, **R**ugged, and **S**afe) extraction (Podio et al., 2020). The QuEChERS method is frequently used by researchers nowadays due to the diversification in the physiochemical properties of PPCPs.

Moreover, many instrumental analyses (gas and liquid chromatography) have been employed in the quantification of PPCPs in the plant tissues after the extraction process. Mostly, the combination of liquid chromatography (LC) with mass spectroscopy (MS) can be used to quantify the various PPCPs accurately in the plant tissue extraction. The detection sensitivity of instruments toward the various PPCPs further increased in the liquid chromatography-tandem MS system. Many researchers have used different instruments, for instance, liquid chromatography-tandem mass spectroscopy (LC-MS/MS), high-performance liquid chromatography coupled mass spectroscopy (HPLC-MS/MS), and ultra-performance liquid chromatography coupled mass spectroscopy (UPLC-MS/MS) with electrospray ionizer. Further, the mobile phases and their flow gradient also crucial during the analysis of PPCPs in plant tissue extraction. Mostly, acetonitrile, formic acid, ultra-pure water, and methanol used as mobile phase solvents during the analysis. The different mobile phases composition with different flow gradients were reported in previous studies. The ultra-pure water as mobile phase A and acetonitrile as mobile phase B with 35–90% flow gradient of B were used in Liu et al. (2020). Similarly, 0.3% of formic acid as mobile phase A and 0.3% of formic acid with 65/35 v/v of acetonitrile and methanol as mobile phase B, with 40–100% gradient of B were used by Chuang et al. (2019). Table 7 provided commonly used analytical methods for PPCP analysis with preconcentrated techniques.

Table 7. Analysis methods of PPCPs in plant tissues.

PPCPs	Plants	Grown media	Pre-concentration and clean up	Instrument	Reference
Diclofenac	Chicory *(Cichorium intybus)*	Soil	QuEChERS extraction	HPLC-MS/MS	(Podio et al., 2020)
Carbamazepine and Diclofenac	Lettuce *(Lactuca sativa)*	Coconut fiber	SPE extraction	UPLC	(González García, Fernández-López, Bueno-Crespo, et al., 2019)
4 PPCPs	Spinach (*Spinacia oleracea*)	Hydroponic	Accelerated solvent extraction	LC-MS	(Nason et al., 2019)
Chlorotetracycline, sulfamethoxazole, and sulfathiazole	Maize (*Zea mays*)	Hydroponic	SPE extraction	HPLC-MS/MS	(Zhang et al., 2019)
Diclofenac, sulfamethoxazole, and trimethoprim	Tomato (*Solanum lycopersicum*)	Silica sand	SPE extraction	UPLC-MS/MS	(Christou et al., 2019)
Atenolol, sulfamethoxazole and carbamazepine	Spinach (*Spinacea oleracea*)	Sludge amended soils	–	Hybrid quadrupole - orbital trap -MS	(Kodešová, Klement, Golovko, Fér, Kočárek, et al., 2019)
5 PPCPs	Beetroot (*Beta vulgaris*)	Soil	QuEChERS extraction	LC-MS	(Papaioannou et al., 2019)
11 PPCPs	4 plants including Cucumber (*Cucumis sativus*)	Real agricultural land	SPE extraction	HPLC-MS/MS	(Liu et al., 2020)
Clarithromycin and sulfadiazine	Lettuce (*Lactuca sativa*)	Nutrient solution	SPE extraction	UPLC-MS/MS	(Tian et al., 2019)
12 PPCPs	Lettuce (*Lactuca sativa*)	Farming land	Accelerated solvent extraction and SPE	LC-MS/MS	(Azanu et al., 2018)
Chlortetracycline, enrofloxacin, and sulfathiazol	Reddish (*Raphanus sativus*)	Soil	QuEChERS extraction	LC-MS/MS	(Chung et al., 2017)

10. Contemporary issues and future scope

We have briefly explained the available groups of PPCPs and respected compounds come under each group. The physicochemical properties of each compound play a significant role in their uptake by the plant. It has been identified that the bioavailability of PPCPs under the realistic field condition is scarcer than those under the greenhouse condition, and the translocation of PPCPs from root to shoot occurs along with the water flow though they are influenced by several factors: plant types, and physiochemical properties of PPCPs. Based on the literature, the authors suggested, human exposure and risk were minimal through the consumption of contaminated crops/vegetables. However, the research on human risk and exposure is premature due to the lack of comprehensive studies.

Several recent studies have investigated the accumulation of PPCPs in the edible plants such as water spinach, cucumber, and spinach under the greenhouse condition (Kurade et al., 2019; Nason et al., 2019; Sun et al., 2019). In a field study, Christou et al. (2017) reported uptake of diclofenac, sulfamethoxazole, and trimethoprim in tomato fruits, which were irrigated with wastewater from municipal wastewater treatment plant for long-term under the realistic farming conditions. However, the investigation on the plant uptake of PPCPs under the practical field conditions is minimal. Therefore, researchers should strive to explore more about the uptake and transformations of PPCPs under real-life environmental scenarios. Furthermore, there are very few studies reported so far on the occurrence of anti-viral drugs in the urban water cycle (Funke et al., 2016). Nevertheless, there is no such study conducted yet on the uptake of an anti-viral medication in the plants, neither in the laboratory nor under outdoor environmental conditions. Therefore, it leaves an ample opportunity for conducting experiments to explore such issues and put some insight into the future.

The PPCPs undergo the biodegradation process once they are taken up by the plants. Recently, several studies have found some metabolites of respective PPCPs in the plant system, which are resulted from the metabolic transformation of the xenobiotics in the individual plant's body. Tian et al. (2019) detected eight metabolites of clarithromycin, and two metabolites of sulfadiazine in lettuce (*Lactuca sativa*). Similarly, Kurade et al. (2019) reported five metabolites of sulfamethoxazole in water spinach (*Ipomoea aquatica*). These metabolites may produce more adverse health issues than their corresponding parent compounds. Therefore, it is urgently required in the future to appraise the human health risks of the metabolites of important PPCPs along with their parent counterparts since health risks for parent compounds only are mostly estimated in such toxicological studies. On the other hand, further mechanistic understanding of uptake,

toxicity, and persistence of all groups of PPCPs needs to be elucidated evidently by future research.

Studies have established that the mechanism of plant uptake of PPCPs depends on the physicochemical properties of PPCPs, and environmental conditions. Goto et al. (2019) showed that the translocation of polychlorinated biphenyls to the shoot via the xylem sap involves latex-like-proteins, which bind with hydrophobic PPCPs. Therefore, further investigation needs to be carried out on other groups of PPCPs how they are translocated to different aerial parts of the plants employing a suite of biochemical working horses. Although several studies have reported the plant uptake and translocation of PPCPs, most of them have studied well about pharmaceutical products. Only a few studies have reported the PCPs such as triclosan, triclocarban, caffeine, and phthalate. Therefore, this study suggested, plant uptake of PCPs should be carried out in future research since the use and misuse of PCPs have increased in the modern world.

Apart from the root uptake, stomata are the minuscule 'windows' on the surface of plant leaves, which can allow the intake of volatile organic compounds from the air. A greenhouse experiment by Bhalsod et al. (2018) elaborated how the over-head irrigation using PPCPs contaminated water could increase the accumulation of PPCPs, which even exceeded the root uptake in lettuce (*Lactuca sativa*). Although the research on the uptake of PPCPs through the plant leaves remains in a nascent stage in the mostly unexplored territory. Future research investigations need to be directed toward the plants' uptake of PPCPs through their leaves since PPCPs such as endosulfan, dichlorodiphenyltrichloroethane, and hexachlorocyclohexane are found in the air and enter into the plant system through stomata. However, this route of exposure with associated risks remains entirely ignored without drawing its due attention to date.

11. Conclusion

The pathways which loaded the PPCPs in the environment, plant uptake and translocate of PPCPs under the greenhouse condition and realistic field condition, and the mechanism of plant uptake of PPCPs are discussed in detail. Currently, PPCPs are reported in plant parts, which may end up in the human bodies. The uptake of PPCPs under the greenhouse condition comparatively higher than those under the field condition. Furthermore, only a few studies have investigated the human health issues by ingesting the contaminated vegetables showed that the human exposure of these PPCPs is much lower than the accepted intake margin. More research is needed on personal care products whereas pharmaceuticals have been well studied.

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