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Factors driving PPCPs uptake by crops after wastewater irrigation and human health implications

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ABSTRACT

Currently, water scarcity affects more than three billion people. Nevertheless, the volume of treated wastewater discharged into the environment is estimated to exceed 100 m^3 per inhabitant/year. These water resources are regularly used in agriculture worldwide to overcome water shortages. Such a practice, however, entails the uptake of waterborne pollutants, such as pharmaceuticals and personal care products (PPCPs), by crops and their further access to the food web, constituting an additional route of human exposure to PPCPs, with potential health outcomes.

In this study, the occurrence of 56 PPCPs in tomatoes, lettuce, and carrot, together with soil and irrigation water, was evaluated using a QuEChERS-based methodology for extraction and LC-MS/MS for analysis. The influence of the selected cultivation conditions on the plant uptake levels of PPCPs was assessed. Two irrigation water qualities (secondary and tertiary treatment effluents), two soil compositions (sandy and clayey), two irrigation systems (dripping and sprinkling), and three crop types (lettuce, tomato, and carrot) were tested. Carrots showed the highest load of PPCPs (7787 ng/g dw), followed by tomatoes (1692 ng/g dw) and lettuces (1248 ng/g dw). The most translocated PPCPs were norfluoxetine (fluoxetine antidepressant main metabolite) (521 ng/g dw), and the anti-inflammatory diclofenac (360 ng/g dw). Nine PPCPs, are reported to be accumulated in crops for the first time. Water quality was the most important factor for reducing PPCPs' plant uptake. Overall, the best conditions for reducing PPCP uptake by crops were irrigation with reclaimed water by sprinkling in soils with higher clay content. The risk assessment performed revealed that the crops' consumption posed no risk to human health. This study serves as the first comprehensive assessment of the relevance of diverse cultivation factors on PPCPs' plant uptake under field agricultural practices.

1. Introduction

Thousands of tons of pharmaceuticals and personal care products (PPCPs) are consumed annually as a consequence of the increasing world population and life expectancy. PPCPs include a wide range of chemical compounds intended to prevent or treat human and animal diseases and improve quality of life (Rajapaksha et al., 2019). PPCPs are considered contaminants of emerging concern (CECs) due to their persistence, potential toxicity, and bioaccumulation in the environment. Indeed, they are considered "pseudo-persistent" because they are continually released into the environment (Tong et al., 2022). Many studies have shown that continuous exposure to some of these compounds contributes to the dissemination of antibiotic resistance genes (ARG) in the environment (Tadić et al., 2021) and poses health risks to living organisms, including humans (Boberg et al., 2010; Cavus et al., 2008; Liang et al., 2017; Rosenfeld and Feng, 2011; Zhao et al., 2013).

Wastewater treatment plants (WWTPs) play an essential role in the spread of these contaminants because conventional wastewater treatments are not intended to remove these pollutants from wastewater. Nevertheles, given the current climatic emergency with important periods of drought, the use of this treated wastewater constitutes a necessary practice to supply agri-food to the growing world population.

However, a wide range of PPCPs has been reported in wastewater effluents (Golovko et al., 2021). Additional treatment steps (e.g. advanced oxidation or phytoremediation) have demonstrated to enhance the removal of specific PPCPs (Dayana Priyadharshini et al.,

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2021; Krishnan et al., 2021; Vassalle et al., 2020a), but are still far from removing them completely. Nevertheless, the use of the treated wastewaters in that way as irrigation water could lead to the uptake of PPCPs by crops, and therefore, their subsequent access to the food web, constituting an additional route of human exposure to PPCPs, with potential health implications (Ben et al., 2022b).

Several studies addressed the translocation of pollutants from treated wastewater and reclaimed water by plants (Christou et al., 2017; Margenat et al., 2017; Palese et al., 2009). However, only a few have evaluated the extent of PPCP uptake depending on the type of plant and culture conditions (Kovačič et al., 2023; Libutti et al., 2018; Palese et al., 2009). Furthermore, most studies were carried out under hydroponic or greenhouse conditions (Goldstein et al., 2014; Kodešová et al., 2019b).

Some of the most important factors affecting crop growth and yield are the nutrient absorption capacity of the plant, water availability, and soil fertility. Therefore, certain cultivation factors may significantly impact the plant growth process, as well as the accumulation of contaminants during the growth period (Al-Farsi et al., 2017). The contaminants concentrations in irrigation water have been reported as a key factor in the uptake of contaminants by crops (Ben Mordechay et al., 2021). Under real field cultivation practices, other factors such as soil composition or irrigation system may also affect the final uptake.

Many countries in the world, notably Israel, already use large volumes of reclaimed water in agriculture (Ben et al., 2022b). In Spain, for example, 8.1% of water supply comes from reclaimed water, which is mainly used for agriculture (62%) (Asociación Española de Abastecimientos de AguaSaneamientos, 2022.) Therefore, it is crucial to determine the key aspects driving the uptake of PPCPs by crops when irrigated with reclaimed water, as well as the possible implications for human health derived from this. Specifically, it is necessary to identify the factors that direct this translocation under real field agricultural practices and the types of crops that can play a key role in minimizing the transfer of contaminants (Keerthanan et al., 2021).

In a previous study, we developed a methodology based on QuEChERS extraction and liquid chromatography tandem-mass spectrometry (HPLC-MS/MS) for the analysis of PPCPs (Sunyer-Caldú and Diaz-Cruz, 2021) in lettuce grown in experimental plots in field that received different water qualities and using drip and sprinkler irrigation systems in soils of different nature. Subsequently, in another work (Sunyer-Caldú et al., 2022), the transfer of PPCPs and pathogens to lettuce was evaluated, demonstrating the significant influence of crop variables on accumulation. However, since only one type of culture was investigated, the processes involved in uptake were not fully understood.

In the present study, these plots were used to identify the agricultural conditions that minimize crop uptake of 56 selected PPCPs by lettuce, tomato, and carrot, proxies of leaves, roots, and fruit as raw edible parts of the crop. The role and influence of PPCPs' physicochemical properties and crop physiological features (Wei et al., 2023) were used to explain the different accumulation patterns and behaviors observed. The PPCPs' concentrations measured in the crops were used to perform a risk assessment based on a Mediterranean diet to identify associated human health risks. This study unveils novel insights into accumulation patterns and behavior, ultimately supporting a safe reclaimed water use in agriculture.

2. Materials and methods

2.1. Standards and reagents

The 56 PPCPs selected for this study encompassed different families of substances (anti-inflammatories, antibiotics, analgesics, antidepressants, UV filters, UV blockers, and parabens, among others) that are usually detected in WWTP effluents. Their physicochemical properties are listed in Table S1 and information regarding their purity and purchase brands is provided in **Section S1** of the Supplementary Information (SI).

2.2. Agricultural plots and crops description

The experimental agricultural plots constructed were located on the northeast Spanish Mediterranean coast, at the WWTP of Palamós (Girona). The wastewater treatment includes pre-treatment, primary and secondary biological treatments (activated sludge). A pilot water reclamation plant treating WWTP secondary effluent was installed in this facility. It consisted of a soil-aquifer treatment (SAT) complemented with natural-based reactive barriers to improve pollutants degradation and pathogen retention. Further details about this tertiary treatment can be found elsewhere (Valhondo et al., 2020).

Two agricultural plots were constructed next to the SAT and WWTP secondary treatments (Fig. 1). One plot was designed to be irrigated with secondary effluent (**W water**), and the other with reclaimed water from the SAT (**B water**). To investigate the effect of soil composition and irrigation system on PPCPs plant uptake, each plot was divided into two subplots containing sand (**S soil**) the same soil to which clay was added up to 10% content (**C soil**), and two irrigation systems (dripping (**D**) and sprinkling (**S**)). These factors were evaluated in three types of crops with different edible parts: lettuce (leaf), carrot (root), and tomato (fruit). Fig. 1 represents concisely the SAT pilot system and the agricultural plots. Additional information about the plots' design, installed sensors, and other related parameters can be found elsewhere (Sunyer-Caldú et al., 2022).

2.3. Samples

Three vegetables were selected as investigated crops; carrots from *Daucus carota sativus* species, tomatoes from *Solanum Lycopersicum* species, and lettuce from *Chicorium intybus* species (red oak leaf lettuce). Crops were grown between September 2018 and September 2019 at their corresponding cultivation periods for the Mediterranean climate: September–December (lettuce), March–May (carrots), and June–September (tomatoes). They were collected when they reached market sale size. For the analysis, ten specimens from each subplot were randomly harvested, shaken to remove soil particles, and stored in zip bags. Only the edible parts of each crop were used for the analysis. Further information regarding the sampling and storage conditions is provided in **Section S2**.

2.4. Sample pre-treatment and HPLC-MS/MS analysis

PPCPs were extracted from lettuce, carrot, tomato, and soil by optimizing our QuEChERS-based method previously developed for lettuce analysis (Sunyer-Caldú and Diaz-Cruz, 2021). A slight modification (5 g of the sample instead of 1 g) was required for soil analysis. Details of the HPLC-MS/MS analysis are provided in Table S2. Information on the optimization and validation of the methodology for tomatoes, carrots, and soil is included in **Section S3**. An example of the ion chromatograms of the compounds detected in the BCS sample of tomatoes is shown in Fig. S1.

The analyses of the irrigation waters were carried out following our previously developed method based on online solid-phase extraction and HPLC-MS/MS analysis (Vassalle et al., 2020b).

The performance of the methods including linearity ranges, coefficients of determination, and limits of detection (LODs) and quantification (LOQs) of tomatoes, carrots, soils, and waters is provided in Tables S3, S4, S5, and S6.

2.5. Human health risk assessment

To evaluate the risk posed by the consumption of vegetables irrigated with treated and reclaimed wastewater, hazard quotients (HQs) were estimated according to Eq. 3

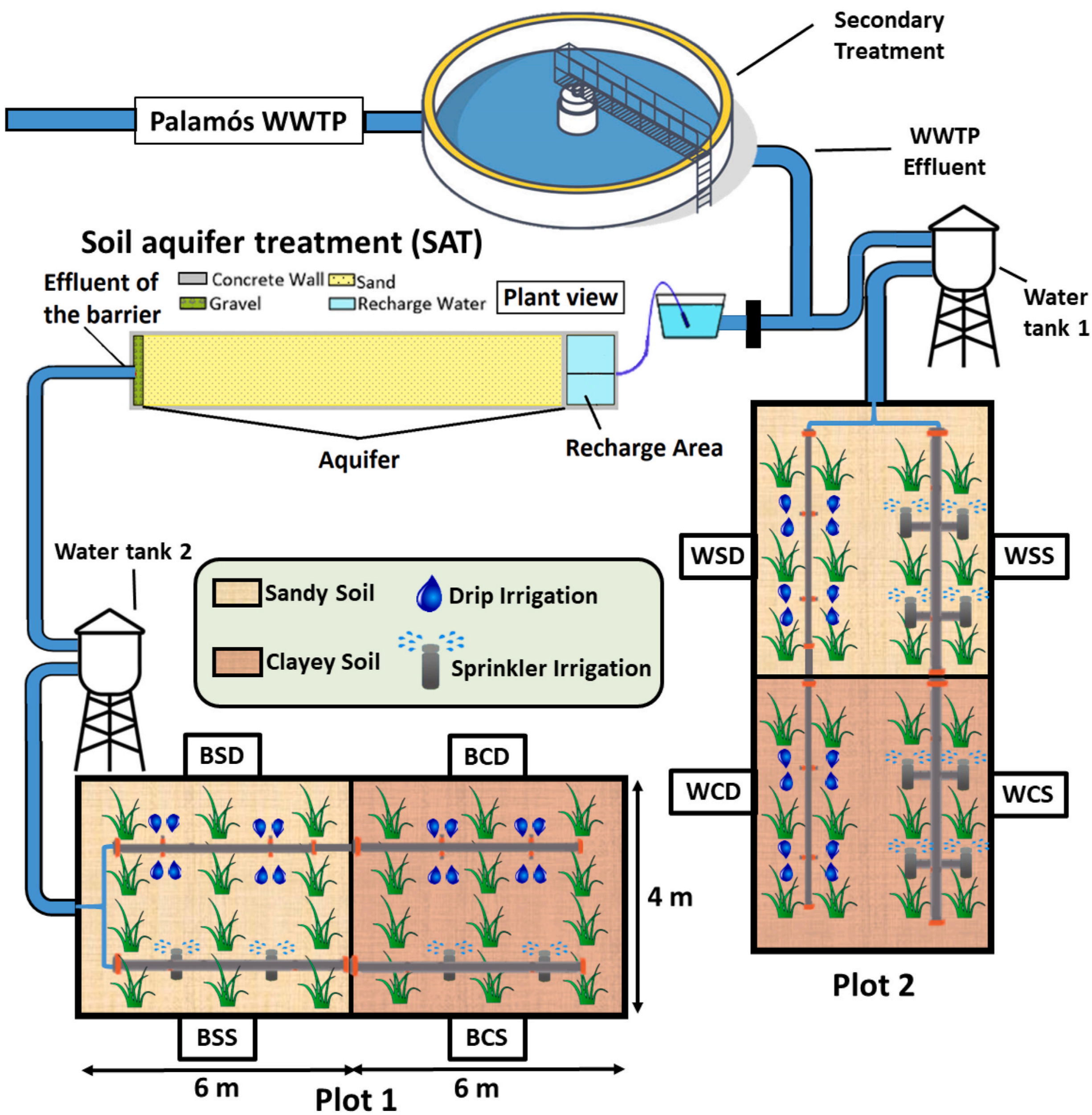

Fig. 1. Experimental plots located in the Palamós WWTP. BSD: Barriers irrigation, sandy soil, drip irrigation; BCD: Barriers irrigation, clayey soil, drip irrigation; BSS: Barriers irrigation, sandy soil, sprinkler irrigation; BCS: Barriers irrigation, clayey soil, sprinkler irrigation; WSD: Wastewater irrigation, sandy soil, drip irrigation; WCD: Wastewater irrigation, clayey soil, drip irrigation; WSS: Wastewater irrigation, sandy soil, sprinkler irrigation; Wastewater irrigation, clayey soil, sprinkler irrigation.

$$HQ = \frac{EDI}{ADI} \tag{3}$$

where ADI is the *acceptable daily intake* obtained from the literature (Ben et al., 2022; LeFevre et al., 2017; Shahriar et al., 2021; Silva et al., 2017; Wang et al., 2021). When the ADI was not available, it was calculated by dividing the no observed adverse effect level (NOAEL) by a factor of 1000, as stated by the World Health Organization (WHO) (2011). EDI is the estimated daily intake calculated using Eq. 4

$$EDI = \frac{DI \cdot C_e}{BW} \tag{4}$$

where C_e is the average compound concentration and DI is the daily intake, obtained from surveys conducted by the Spanish Agency for Consumption and Food and Nutrition Safety (AECOSAN) (Marcos Suarez et al., 2015).

Finally, using a linear approach, the hazard index (HI), considered the cumulative risk posed by all compounds present in the sample, was calculated using Eq. 5

$$HI = \Sigma HQ \tag{5}$$

2.6. Data analysis

Principal component analysis (PCA) was performed in R software (v. 4.2.2) using RStudio (v. 2022.12.0 + 353) to evaluate the data and compare variables and matrices. The package used for PCA was Factoextra (v. 1.0.7), and information regarding the process and scripts are described in **Section S4**.

3. Results and discussion

3.1. PPCPs in irrigation water

To compare the influence of water quality on PPCPs crop uptake, a WWTP effluent (W water) and a tertiary treatment effluent (B water) were used as irrigation water sources. The concentrations of PPCPs detected in W and B waters are listed in Table S7.

All irrigation water samples contained PPCPs, and 42 of the 56 target contaminants were detected in at least one sample. The cumulative concentrations in the water after both treatments are shown in Fig. 2. The differences in the contaminants concentrations of each water demonstrate the good performance of a SAT system in the PPCP removal process. This behavior was previously reported in the same (Sunyer-Caldú et al., 2023a) and other SAT systems that include infiltration of secondary treated wastewater through natural materials (Ben et al., 2022a).

The pharmaceuticals showed the highest concentrations in the irrigation waters, both in the W and B waters, with accumulated concentrations of up to 16383 ng/L and 6720 ng/L, respectively. In this group, 26% of the total concentration corresponded to antibiotics (4302 ng/L). PBs was the group with the lowest concentrations, as expected from the high removal rate of PBs reported in conventional wastewater treatments (Haman et al., 2015). The highest average concentrations for W water, 1673 ng/L, corresponded to the UV filter benzophenone-4 (BP4), followed by diclofenac (DCF) at 1503 ng/L, ofloxacin (OFX) at 1106 ng/L, and gemfibrozil (GFZ) at 1104 ng/L. In contrast, DCF at 912 ng/L, benzotriazole (BZT) at 482 ng/L, methyl-benzotriazole (MeBZT) at 402 ng/L, and BP4 at 372 ng/L showed the highest average concentrations in B water. BP4 is one of the most commonly used UVFs in the formulation of sunscreens and other products with UV light protection (Fenni et al., 2022), and BZT is another frequently used UVF with multiple industrial uses (Shi et al., 2019). DCF, GFZ, and OFX are recalcitrant pharmaceuticals commonly reported in wastewater (Rueda-Márquez et al., 2021). Similar concentrations of these contaminants have been reported in waste and reclaimed water (Shi et al., 2019).

3.2. PPCPs in soil

Soil features influence the uptake of contaminants by crops (Kodešová et al., 2019a). The accumulation of PPCPs in the soil is difficult to predict because they are subject to microbial degradation, oxidation, and photodegradation. However, those with the capacity to accumulate in the soil will be suitable candidates for bioaccumulation in crops, and the levels found can help to understand plant uptake mechanisms. The PPCPs concentrations measured in the sandy (S) and clayey (C) soils are listed in Table S8. Because C soils have a larger surface area than S soils, C soils are expected to accumulate higher concentrations of contaminants, as has been previously reported (Goldstein et al., 2014). However, as shown in Fig. S2, the accumulated PPCPs concentrations in the S and C soils were similar. The pharmaceuticals showed the highest levels in both soil types. As aforementioned caffeine (CFF) was present in all water samples probably due to the widespread use of coffee and other similar products, but also to certain pharmaceuticals which also contain caffeine. In soils, however, it was never detected. This fact could be explained by the mineralization of CFF to CO_2 (Topp et al., 2005) or the metabolization through N-demethylation to more easily degradable compounds (Quandt et al., 2013).

The anti-inflammatory DCF was the most accumulated compound in soils (45 ng/g dw average), far from the second most accumulated (salicylic acid (SCY) at 14 ng/g dw). This result agrees with the levels found in irrigation water, where DCF was present at high average concentrations. Similar and even higher levels of DCF (90 ng/g) and SCY (47 ng/g) have been previously reported in agricultural soils in Spain after pond (Azzouz and Ballesteros, 2012) and wastewater irrigation (Aznar et al., 2014) when cultivating rice, cereal, potatoes, and cabbage, among other crops. Surprisingly, SCY was not detected in water but was detected at substantial concentrations in the soil. SCY is an endogenous compound in plants, involved in regulating plant stress (Thompson et al., 2017). Thus, we hypothesize that the SCY present in the soil is excreted by plants during the growing process in periods of stress. SCY is easily conjugated with small molecules forming an inactive SCY form, which can be easily transported (Thompson et al., 2017), facilitating the crop-soil transfer.

The pollutants present in irrigation water have a significant impact

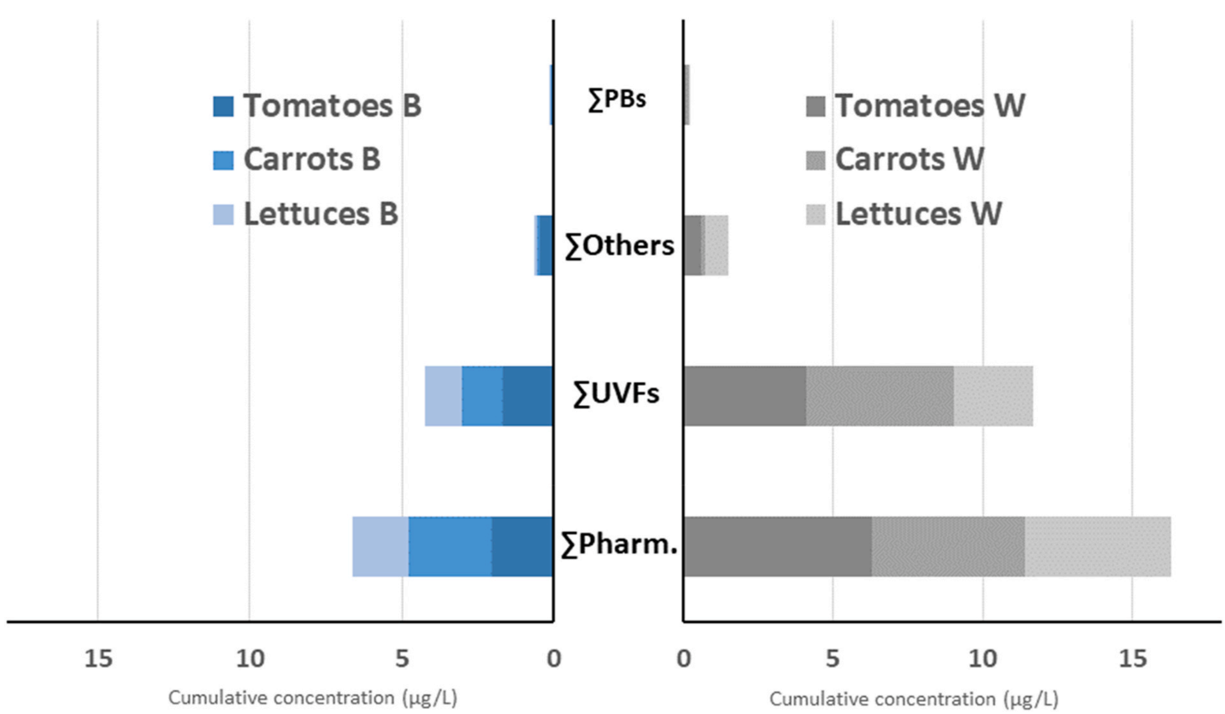

Fig. 2. Comparison of accumulated concentrations (∑) of pharmaceuticals, UVFs, caffeine (others), and PBs in B (left) and W (right) irrigation waters.

on soil contamination (Maddela et al., 2022), as confirmed by the higher concentrations measured in soils irrigated with W water. This supports the importance of a tertiary treatment after the secondary in the WWTP. Nevertheless, different accumulation trends in the same type of soil were observed, depending on the crop cultivated (Fig. S2). Similar trends have been reported before by Aznar et al., 2014. They observed higher accumulated values in soils from rice fields, probably because of prolonged direct contact with irrigation water. In this study, the highest average PPCPs concentration in soils was found after tomato cultivation (482 ng/g dw), followed by lettuce (281 ng/g dw) and carrot (160 ng/g dw). This could be explained by the intrinsic properties of each crop; for example, because of carrots (root crops) are in direct contact with the soil, the surface area of exposure to contaminants is greater. Therefore, contaminants easily reach them, whereas, in lettuce and tomatoes, a higher load remains in the soil. This could also be explained by the different water requirements of each crop type. Because irrigation was automatically controlled to avoid hydric stress in the crops, the irrigation water volumes disposed of in the soil varied among cultivations. According to Mekonnen and Hoekstra (2011), it takes 214 L to produce 1 kg of tomato, while 237 L/kg and 195 L/kg are needed for lettuces and carrots, respectively. Thus, lower water volumes were disposed of when cultivating carrots, which could also explain the lower accumulated levels.

3.3. Plant uptake

The concentrations of PPCPs determined in lettuce, tomatoes, and carrots are listed in Tables S9, S10, and S11 and are depicted in Figs. S3, S4, and S5. Overall, carrots showed the highest uptake, followed by tomatoes and lettuces, as shown in Fig. 3. Pharmaceuticals and UVFs had the highest concentrations. In lettuce, UVFs showed a higher uptake, but in tomatoes and especially in carrots, pharmaceuticals were more accumulated. PBs and CFF showed low concentrations. Forty out of the 56 target compounds were taken up by at least one of the crops. SCY was the compound detected at the highest average concentration (1356 ng/g dw carrot, 95 ng/g tomato) as a result of the secretion of the plant itself, followed by the anti-depressant norfluoxetine (norFXT) (264 ng/g dw; carrot), DCF (231 ng/g dw; tomato), BP4 (68 ng/g dw; tomato), the analgesic acetaminophen (APP, paracetamol) (62 ng/g dw; carrot), CFF (62 ng/g dw; carrot), the BP3 metabolite 4-hydroxy benzophenone (4HB) (61 ng/g dw; lettuce), and the β-blocker atenolol (ATL) (59 ng/g dw, carrot).

UVFs: Ultraviolet filters; Pharm: Pharmaceuticals; PBs: Paraben preservatives; Others: Caffeine.

SCY, as already mentioned, is naturally produced in crops and plants (Lefevere et al., 2020) during stress periods, which could explain the high levels found in crops. Besides, it is a metabolite of acetylsalicylic acid (aspirin), one of the most consumed analgesics worldwide. It is also found in various over-the-counter products such as topical anti-acne products. However, this input cannot be considered in our case because SCY was not present in any irrigation water.

NorFXT is the main metabolite of fluoxetine, a highly prescribed serotonin reuptake inhibitor that is used to treat depression, obsessive-compulsive disorder, and bulimia. Fluoxetine (FXT) is a widely consumed antidepressant in Spain (Carballa et al., 2008). In contexts of crisis and complexity such as those we have experienced in recent years; its consumption has multiplied. According to the Spanish Pharmacists Association (FEFE) (2022), in 2021 (compared to 2020) the sale of antidepressant drugs increased by 10% and that of antipsychotics by 7%. This could explain why norFXT was detected in all irrigation waters, except in B water for lettuce cultivation, ranging between 11 and 174 ng/L. The highest concentrations in the water were found for carrot cultivation, which probably favoured the uptake in this crop (264 ng/g dw). However, it was not detected in the soils. Since FXT and norFXT are very persistent in soil and are resistant to biodegradation (Redshaw et al., 2008), the absence of norFXT suggests that it was fully

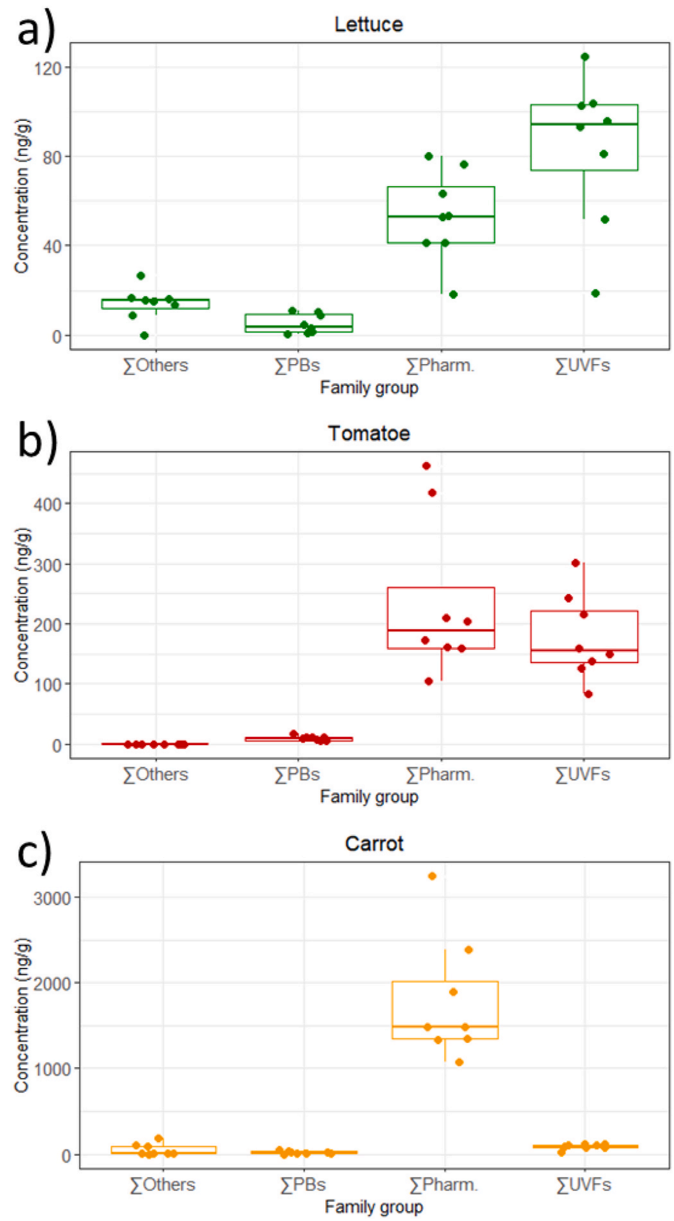

Fig. 3. Box plots of the concentrations found in lettuces (a), tomatoes (b), and carrots (c).

translocated by crops. The lipophilicity of non-ionic organic compounds has been correlated with their uptake rates in plants (Li et al., 2019). This can explain norFXT (log octanol-water partition constant (log Kow >3)) uptake at high concentrations (up to 407 ng/g dw in carrot). Uptake of FXT in crops has been reported in cauliflower (Redshaw et al., 2008) and radish (Carter et al., 2014), between 3 and 200 ng/g dw. However, to the best of the author's knowledge, this is the first report of norFXT uptake by lettuce, tomatoes and carrot.

DCF is an anti-inflammatory agent commonly used to relieve pain and is prescribed for arthritis (Jaramillo and Restrepo, 2017). It is a pharmaceutical that is usually included in pollutant translocation studies owing to its persistence and ubiquity in aquatic environments. In this work, it was present in all irrigation waters at large concentrations (>640 ng/L) and was the compound with the highest concentration in soils (426 ng/g dw). This explains the high uptake levels observed in crops. Previous studies have reported that DCF uptake was more effective in tomatoes when irrigated with wastewater (Kovacs et al., 2021), as observed in this study, where the highest concentrations were found in tomatoes (360 ng/g dw average). However, Christou et al. (2017) reported lower uptake values (12 ng/g dw) than those reported here. Other studies found similar values in lettuce (Dodgen et al., 2013; Prosser and Sibley, 2015), but DCF uptake in carrots have not been previously reported in the literature, even though a few studies have focused on this crop. Kovacs et al. (2021) reported DCF to have a high bioconcentration factor in different crops, which also supports the levels found in this work.

As aforementioned, BP4 is a common UVFs used in the formulation of sunscreens and similar products, while 4HB is a metabolite of oxybenzone (BP3), which is another widely used UVF. The presence of both compounds in aquatic ecosystems has been well-studied (Díaz-Cruz et al., 2019; Jurado et al., 2014). BP4 showed high concentrations in tomatoes (up to 140 ng/g dw), but low uptake by carrots and lettuce. The metabolite 4HB was also present in the three matrices, lettuces being the crop that showed the highest uptake (84 ng/g dw). The large concentrations of BP4 in crops measured can be explained by the high concentrations of this compound in irrigation waters since due to its high solubility in water and hydrophilicity is poorly removed in conventional wastewater treatments. In the case of 4HB, its occurrence in the crops can be associated with partial degradation of BP3, which was also present in irrigation waters and soils. No data on these compounds have been reported before in the literature for similar matrices.

The analgesic APP and the β-blocker ATL also accumulated in carrots at considerable concentrations (>58 ng/g dw) and similar to those reported by Beltrán et al. (2020), but were barely detected in tomatoes and lettuce. Both pharmaceuticals were present in the irrigation water and were not detected in the soils, since they are polar (log Kow <0.5). We hypothesize that they tend to accumulate in carrots because they are root crops and the contact between the soil and irrigation water is more direct, which favours plant uptake. Indeed, ATL has been reported to accumulate more in roots than in other parts of plants (Kodešová et al., 2019b), and a previous study pointed out the higher APP stability in carrots compared with that in soil and lettuce (Dickman et al., 2021).

To the best of the author's knowledge, the UVFs 4,4′-dihydroxy benzophenone (DHB), 2,2′-dihydroxy-4-methoxybenzophenone (DHMB), avobenzone (AVO), and enzacame (4-methyl benzylidene camphor (4MBC)), and the PBs methylparaben (MePB) and propylparaben (PrPB) are reported to be uptaken by lettuce, tomato and carrot for the first time.

3.4. PPCPs plant uptake patterns

Different behaviours and PPCPs uptake patterns have been observed depending on the nature and physiology of the crop. For example, although the UVFs were detected at similar concentrations in carrots and tomatoes irrigation waters, UVFs largely accumulated only in tomatoes (Fig. 3). BP3 and all its metabolites (4HB, benzophenone-1 (BP1), 4,4′-dihydroxy benzophenone (DHB), and 2,2′-dihydroxy-4-methoxy benzophenone (DHMB)) were detected at significant concentrations (2.6–77.5 ng/g dw), and other UVFs, i.e. benzophenone-2, BP4, AVO and 4MBC, were also present. We hypothesize that these differences are based on soil pH and pKa values of the compounds. All the target UVFs (except BP4) have similar pKa values (7–9.7). In the soil environment (pH ~ 7.5), UVFs are present in their neutral form because the soil pH < compound pKa. Non-ionized species tend to cross membranes and are transported predominantly in the direction of the transpiration stream (Goldstein et al., 2014), which could explain the UVFs preference for tomatoes (fruit). Pharmaceuticals have lower pKa values (<4.5), and thus they will be present in their ionic form. Ionic compounds have a lower potential for translocation by plants because of the repulsive forces exerted by the negatively charged root epidermis (Miller et al., 2016). Thus, we hypothesize that root vegetables, such as carrots, have a higher uptake and accumulation capacity for ionized compounds; they are in direct contact with the bioavailable fraction of the pharmaceuticals present in soil pore water, enabling them to easily penetrate these tissues (Malchi et al., 2014). However, in tomatoes, these compounds must translocate through different parts of the plant to reach the fruit. Therefore, non-ionized compounds display a high capacity to cross membranes and are therefore uptaken by plants more efficiently (Christou et al., 2019). ATL, norFXT, and CFF are exceptions because of their high pKa values (>9.5). However, their hydrophobicity is very low, which could explain their ability to reach carrots that are in direct contact with the soil, but not tomatoes.

Although the contaminant concentration in water is the key factor in lowering the uptake (Fig. 4 a), soil composition is another critical factor controlling the retention of PPCPs in soil. Previous works reported S soils producing higher crop uptake than C soils (Goldstein et al., 2014; Malchi

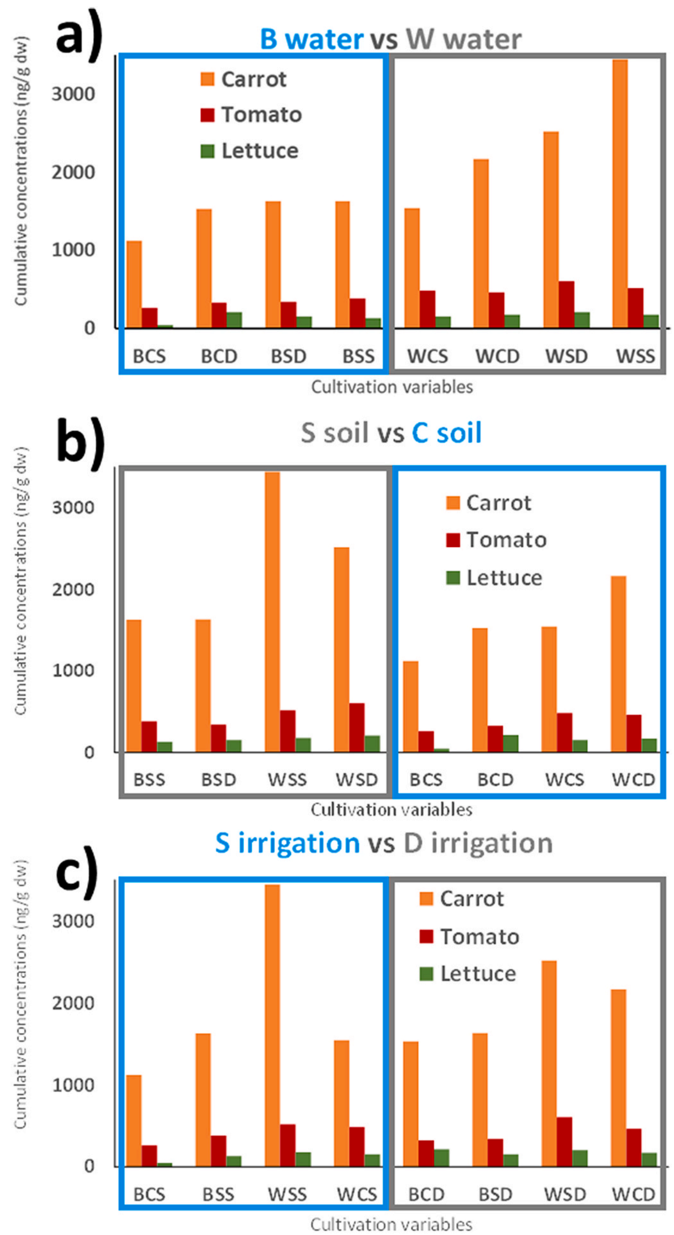

Fig. 4. Cumulative PPCPs concentrations in crops comparing irrigation water quality (a), soil composition (b), and irrigation system (c). BSD: Barriers irrigation, sandy soil, drip irrigation; BCD: Barriers irrigation, clayey soil, drip irrigation; BSS: Barriers irrigation, sandy soil, sprinkler irrigation; BCS: Barriers irrigation, clayey soil, sprinkler irrigation; WSD: Wastewater irrigation, sandy soil, drip irrigation; WCD: Wastewater irrigation, clayey soil, drip irrigation; WSS: Wastewater irrigation, sandy soil, sprinkler irrigation; WCS: Wastewater irrigation, clayey soil, sprinkler irrigation.

et al., 2014). This is in accordance with our results, as shown in Fig. 4 b. Crops grown in C soils showed a lower uptake, independently of the irrigation water, irrigation system, or crop type. C soils are porous and present a higher capacity to retain water. Therefore, this greater retention capacity probably applies to PPCPs, binding them more strongly to soil and lowering their tendency to reach the crop system.

Another factor reported to influence plant uptake is the irrigation system used. Theoretically, the use of drip irrigation is effective in avoiding contamination because it reduces the contact of water with the edible parts of crops (Mañas et al., 2009). Indeed, EU reuse regulations indicate that drip irrigation systems are the safest (Mendoza-Grimon et al., 2022). Our results show that the lower uptake was obtained by S irrigation, except for the tomatoes irrigated with W water, which showed a lower uptake by D irrigation (Fig. 4 c). We hypothesize that S irrigation favoured PPCPs degradation through aeration and dispersion, which led to a lower uptake in the crops. However, in tomatoes, S irrigation favoured direct contact between water and fruits, which resulted in a higher uptake. Scarce information on this topic is available in the literature using field cultivation practices; Yang et al. (2017) tested the influence of three types of drain fields (i.e. drip dispersal, gravel trench, and advanced system), demonstrating different dissipation rates of pollutants, and Palese et al. (2009) compared drip irrigation with unirrigated (rain field), and its influence on soil and crop microbiological contamination. Overall, combining C soil and irrigating with B water by sprinkling is the best combination of factors to minimize the uptake of PPCPs by crops.

3.5. Statistical analysis

A PCA analysis was performed to determine the main axes of variance within our dataset to identify the key variables driving the uptake of pollutants by the crops. Fig. 5 shows the scores plot (a), loadings plot (b), and biplot of our data.

The scores plot (Fig. 5 a) demonstrates large differences in PPCPs uptake among crops since each crop type forms a spatially differentiated cluster, independently of the irrigation water, soil composition, or irrigation system. No outliers were observed. This confirms that the nature and physiology of the plant enhanced or decreased the uptake of compounds. These different uptake trends are probably conditioned by the physicochemical properties of the compounds, such as log Kow and pKa, but also by the soil and water pH, which favour or hinder uptake depending on plant physiology (Fu et al., 2019).

In the loadings plot, we observed four groups, one in each quadrant. For example, BP3, BP1, 4DHB, and 4MBC formed a cluster in the lower left quadrant. All of these are UVFs, being BP1 and 4DHB metabolites of BP3, which explains the similar plant uptake trend. Another cluster is formed by SCY, norFXT, APH, ATL, CFF, and MePB, in the lower-right quadrant. Since these compounds were among the most accumulated in the crops (>51 ng/g dw), the loadings plot statistically differentiates them from other groups.

Finally, the biplot representing the scores and loadings plots together showed the variables with greater contributions to the samples. Therefore, in our dataset, the closer a compound is to a crop cluster (e.g. ATL

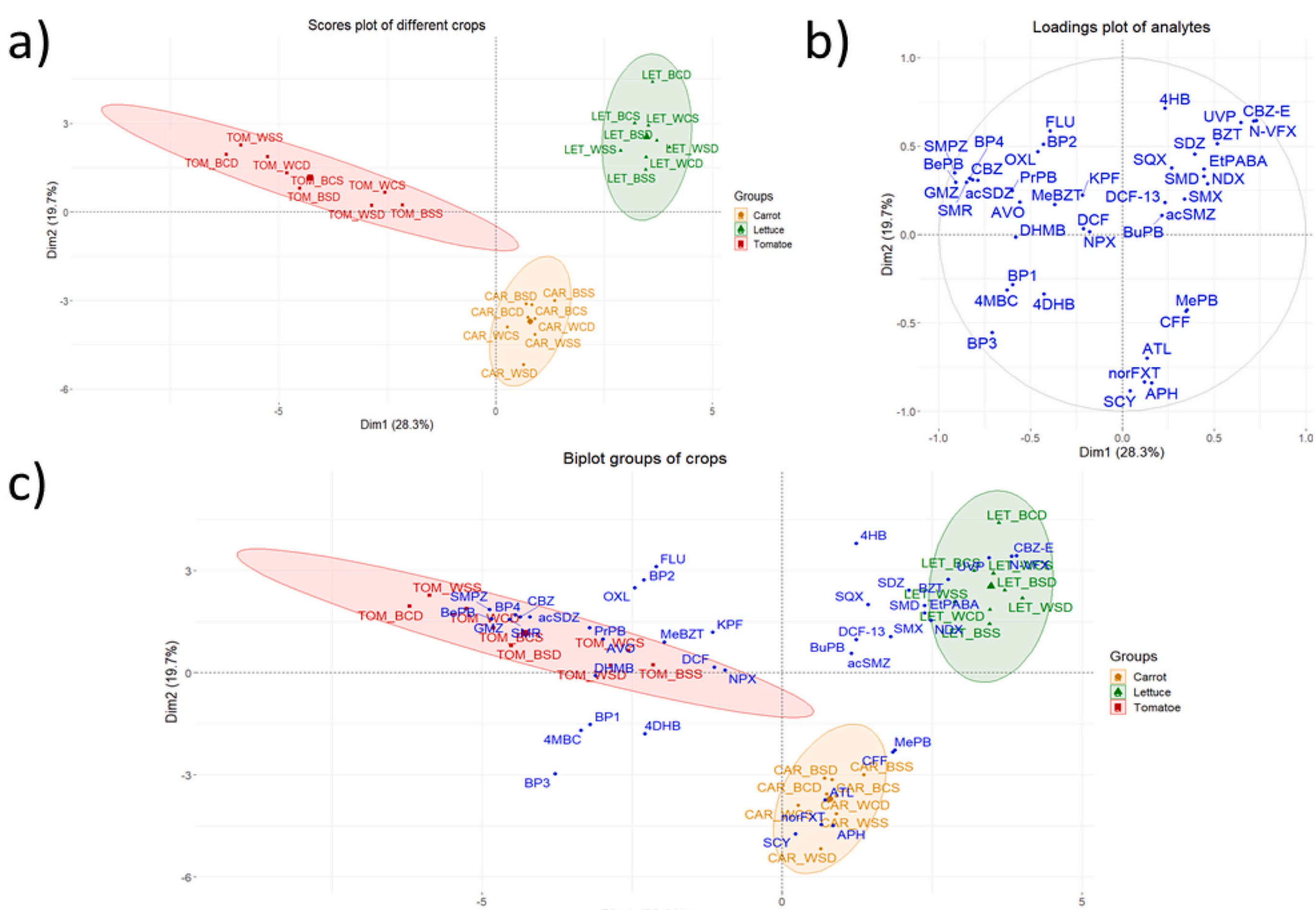

Fig. 5. Scores plot (a), loadings plot (b), and biplot (c) of the PPCPs accumulated concentrations. BSD: Barriers irrigation, sandy soil, drip irrigation; BCD: Barriers irrigation, clayey soil, drip irrigation; BSS: Barriers irrigation, sandy soil, sprinkler irrigation; BCS: Barriers irrigation, clayey soil, sprinkler irrigation; WSD: Wastewater irrigation, sandy soil, drip irrigation; WCD: Wastewater irrigation, clayey soil, drip irrigation; WSS: Wastewater irrigation, sandy soil, sprinkler irrigation; Wastewater irrigation, clayey soil, sprinkler irrigation.

and carrot cluster), the higher the affinity of the compound for this matrix. Compounds that are at a certain distance from any cluster have combined contributions (e.g., BP3, carrots and tomatoes) or non-significant contributions (e.g. BuPB). Indeed, the left-down cluster (BP3, 4MBC, BP1, 4DHB) is halfway between tomatoes and carrots, showing that both crops uptake PCCPs. Lettuces, however, appear to metabolize BP3 because they have a large contribution of 4HB (BP3 metabolite). 4HB is almost in a parallel line to this cluster, but in the opposite quadrant showing a negative correlation. This suggests that when BP3 is uptaken by the plant at high concentrations (tomatoes and carrots), 4HB is not present. However, when BP3 was absent (lettuces), 4HB was detected as a result of BP3 metabolism by the plant. The right-down cluster is strongly related to carrots (SCY, norFXT, APH, ATL, CFF, and MePB), which is explained by the high concentrations found in this crop.

A visual example of the information provided by PCA is the anti-epileptic carbamazepine (CBZ), known to be very recalcitrant to wastewater treatments, and usually translocated by plants (Beltrán et al., 2020). As reported in Tables S9–S11, it was mainly present in tomatoes but was not present in carrots and only slightly present in lettuce. However, its main metabolite, carbamazepine 10,11-epoxide (CBZ-E) was detected in all lettuce samples. Therefore, this suggests that in carrots CBZ was not uptaken, in tomatoes it was able to reach the fruit, and lettuces degraded it, producing its metabolite CBZ-E. Previous studies have reported high concentrations of CBZ-E in leafy crops (such as lettuce), whereas CBZ was only barely present (Kodešová et al., 2019b). This accumulation trend is observed in the PCA, where CBZ is in the main center of the tomatoes cluster, whereas CBZ-E is in the lettuce one, and no CBZ-related compound is close to the carrots' cluster.

Antibiotics generally showed higher uptake values in tomatoes and lettuce but considerably lower values in carrots. This accumulation trend (fruit > leaf > root) has been reported previously (Pan et al., 2014) and can be explained by the re-transport of the antibiotics in the transpiration stream within the xylem of the plants. It is observed in the PCA, where all detected antibiotics are close to the tomatoes (flumequine (FLU), oxolinic acid (OXL), N^4-acetylsulfadiazidine (acSDZ), sulfamerazine (SMR), and sulfamethoxypyridazine (SMPZ)) or lettuce clusters (sulfaquinoxaline (SQX), sulfadiazine (SDZ), sulfadiazine (SDZ), sulfamethoxazole (SMX), sulfamethoxazole (SMX), and nalidixic acid (NDX)), but none is close to the carrots one.

3.6. Exposure and risk assessment

The human health risks associated with the raw consumption of the crops included in this study were estimated for adults and children using HQ and HI. The HQ and HI values for all the compounds together with their ADI values are listed in Tables S12 and S13. The estimated values revealed that the concentrations found in crops do not constitute a risk to adults or children. The highest HQ values (all <0.016) were found for SCY (carrots), DCF (tomatoes), norFXT (carrots), ATL (carrots), and BZT (lettuce) (Table S12). The same applies to the HI values (Table S13), all of them were below 0.21, being carrots the crop with the highest risk. These results are in accordance with those reported in similar works considering typical scenarios of consumption (Ben et al., 2022a; Christou et al., 2017; Liu et al., 2020; Tadić et al., 2021).

Although the estimated risk suggests that crops are safe for human consumption, other factors that are not included in this estimation should be considered to achieve a comprehensive assessment. Such evaluation should consider the presence of a cocktail of contaminants in crops (which could result in unknown synergic effects), the uptake of unknown compounds not included in the target analysis, or the degradation capacity of the crops (which can generate multiple transformation products that can be even more toxic than the parent compound) (Sunyer-Caldú et al., 2023b). Furthermore, significant variations in the estimated risk could be observed depending on the concentration of the pollutants in the irrigation water, the region where the crops are grown, the consumption patterns (diet) of that region, and the hypersensitivity of certain individuals towards specific chemicals or during vulnerable periods of life such as pregnancy.

4. Conclusions

The increase in the world population and the prospect that this process will continue in the future makes it necessary to provide food like never before. Given this circumstance, and the current context of climate emergency, with long periods of drought, it is necessary to use alternative sources of water for agriculture. Reclaimed water, which provides a significant volume of water and a practically sure supply, can be a good tool to alleviate this lack of freshwater. However, this water contains traces of contaminants that can be translocated by plants.

This is the first work targeting a high number of multiclass chemicals (>50) in crops cultivated in a real field system. Furthermore, four factors (water origin, soil type, irrigation system, and type of crop) potentially affecting the transfer of contaminants from irrigation water to harvest have been evaluated.

All crops accumulated more than 15 PPCPs, which demonstrates that wastewater reuse is a direct pathway of contaminants to the crops, and to human. The type of crop conditioned the translocation of chemicals depending on their physicochemical properties (e.g. Kow). The highest transfer was found in carrot, followed by tomatoe and lettuce, suggesting the root > fruit > leaves trend. Pharmaceuticals showed higher affinity for carrots, while antibiotics and UVFs showed higher levels in tomatoes. The contaminants load in the irrigation water was the key factor driving the uptake, but soil composition and the irrigation system were also relevant; clay soils enhanced the retention of PPCPs, leading to a lower uptake, and sprinkling irrigation favoured PPCPs degradation through aeration and dispersion. Sprinkling irrigation with reclaimed water in clayey soils was the best factors combination to lower the translocation of pollutants.

This work reports for the first time the occurrence of many UVFs and PBs (BP4, 4HB, DHB, DHMB, AVO, 4MBC, MePB and PrPB) in crops. Considering the ubiquity of these chemical families in wastewater, further investigation of their presence in crops is warranted. Another relevant finding was the significant presence of metabolites in the cultures, probably triggered by the biodegradation processes taking place. This highlights the importance of using untargeted approaches that allow the identification of new transformation products, which may be even more toxic than the parent compounds. The rise in mental illnesses and eating disorders, was observed; the human metabolite of fluoxetine (Prozac), norFXT was the compound accumulated the most, ahead, of anti-inflammatory and analgesic drugs such as ibuprofen and paracetamol.

Despite the risk assessment concluded that the consumption of these vegetables did not pose a risk to human health, when we are exposed to multiple chemicals throughout the diet for long periods, joint effects cannot be discarded. Therefore, further analysis is needed to understand the effects of long-term exposure to PPCPs and to identify the mechanisms underlying plant uptake to guarantee safe reclaimed water use in agri-food production.

Author statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2023.116923.

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