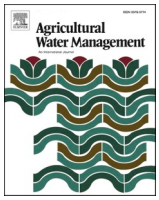
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Possible accumulation of emerging contaminants of concern in treated wastewater on the soil plant system of a processing tomato-wheat succession

Giuseppe Gatta [a,*], Federica Carucci [b], Anna Gagliardi [a], Michele Perniola [c], Michele Denora [c], Francesco De Mastro [d], Gennaro Brunetti [d], Sapia Murgolo [e], Cristina De Ceglie [e], Alfieri Pollice [e], Marcella Michela Giuliani [a]

[a] Department of Agricultural Sciences, Food, Natural Resources and Engineering (DAFNE), University of Foggia, Foggia 71122, Italy
[b] Department of Agricultural and Forestry scieNcEs (DAFNE), University of Tuscia, Viterbo 01100, Italy
[c] Department of European and Mediterranean Cultures, University of Basilicata, Via Lanera, Matera, Italy
[d] Department of Soil, Plant, and Food Science, University of Bari, Bari, Italy
[e] Water Research Institute (IRSA), National Research Council (CNR), Bari, Italy

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ABSTRACT

Treated wastewater (TWW) is increasingly recognized as a valuable resource for agriculture and water management in the Mediterranean region. However, its use can pose significant risks due to the potential presence of emerging contaminants of concern (ECCs), including personal care products, pesticides, food additives, and pharmaceuticals. This study aimed to evaluate the impact of irrigation with TWW on the accumulation of ECCs within the soil-plant system during a processing tomato (*Solanum lycopersicum* L.)-durum wheat (*Triticum turgidum* spp. durum) crop succession. The experiment was carried out on Petrocalcic Palexerolls soil. Over two experimental years, both crops were irrigated using two water sources: TWW and freshwater (FW) as a control. Of the 17 compounds detected in the TWW, only 8 were found in the soil (clarithromycin, carbamazepine, fluconazole, climbazole, flecainide, sitagliptin, telmisartan and venlafaxine). The use of TWW effluent led to a significant increase in the soil of carbamazepine up to 3.3 ± 0.5 ng g^{-1}, sitagliptin up to 9.4 ± 0.4 ng g^{-1}, flecainide up to 8.3 ± 1.6 ng g^{-1}, and clarithromycin up to 5.3 ± 0.6 ng g^{-1}, highlighting their potential accumulation during the two tomato-wheat cycles. Crop uptake varied depending on the specific ECC, with different levels detected in plant roots, leaves, and stems. Importantly, no ECCs were detected in the edible parts of either crop, with concentrations below the limit of quantification. These findings underscore the potential of using TWW for irrigation without compromising food safety in crops like tomatoes and durum wheat. However, continued monitoring and further research are essential to fully understand the long-term effects of ECCs on agricultural systems and ensure the protection of both human health and the environment.

1. Introduction

Treated wastewater is increasingly recognized as a valuable water resource (Lorite et al., 2018; Lavrnić et al., 2017) particularly in agriculture and water management. While it offers potential benefits, its use also presents some risks. Among these, the presence of trace organic contaminants in treated wastewater effluents, such as personal care products, pesticides, food additives, and pharmaceutical products, has garnered significant attention in recent years (De Mastro et al., 2023; Frascaroli et al., 2021; Gorovitis et al., 2020). They have been designated as emerging contaminants of concern (ECCs), whose impact on agroecosystems is not yet well-known and regulated (Rout et al., 2021; Ferreiro et al., 2020).

Traditional wastewater treatment plants (WWTPs) are not equipped to fully remove ECCs from wastewater effluents (Kumar et al., 2022). As a result, using treated effluents for crop irrigation can lead to potential issues regarding the fate of these contaminants in the soil-plant system, agricultural product quality, and human health. Over the past decade,

* Corresponding author.
E-mail address: giuseppe.gatta@unifg.it (G. Gatta).

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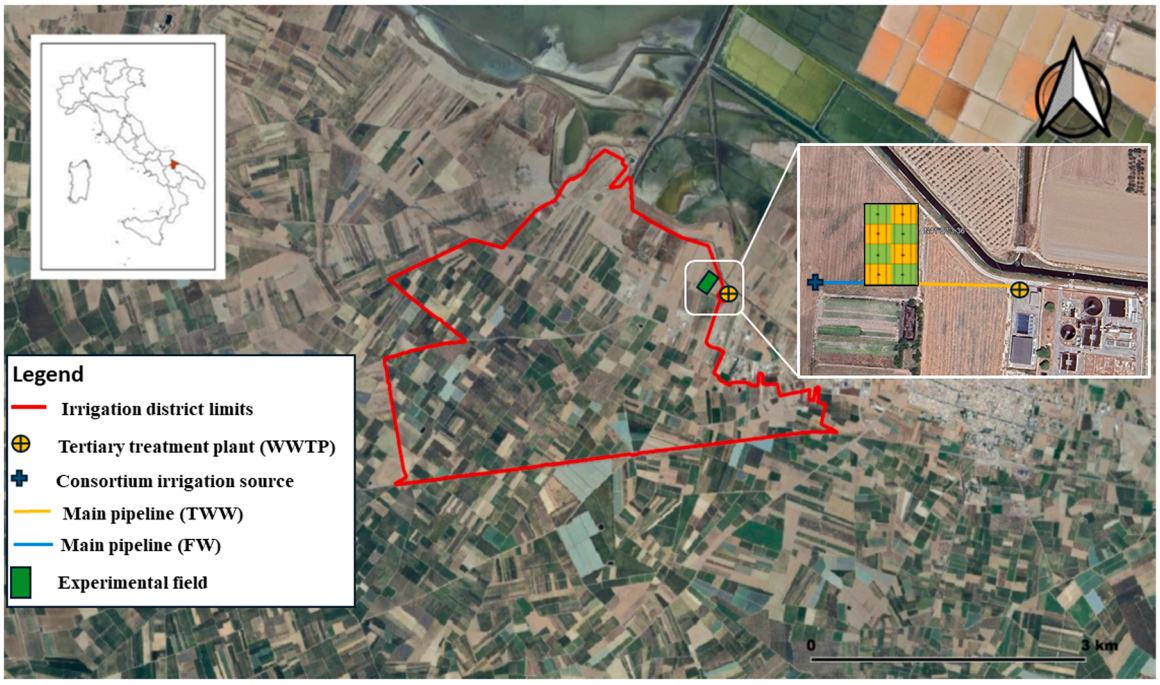


Fig. 1. Experimental field site.

concerns have grown over the accumulation of ECCs in soil, their possible uptake by plants, accumulation in the edible parts, and the subsequent entry into the food chain (Christou et al., 2017; González García et al., 2019). The behaviour of ECCs in soil is largely influenced by both their physico-chemical properties and the characteristics of the soil itself, determining whether they are retained in the topsoil, leached into groundwater, or run off into surface water. In some cases, these compounds may be degraded by microorganisms or other processes, but many are recalcitrant, persisting in the soil environment (Yang et al., 2012; Zhang et al., 2014; Miller et al., 2016, De Mastro et al., 2022a).

The extent of ECC sorption, retention, and desorption, depends heavily on clay content and soil organic matter, which also determine their potential transport in soil or bioavailability for degradation and plant uptake (Pan and Chu, 2016). Soil pH, particularly, plays a crucial role in the uptake of ionic ECCs over non-ionic ECCs (Mikes and Trapp, 2010).

Among the most studied ECCs, the anticonvulsant carbamazepine is highly resistant to microbial degradation in the soil (Maeng et al., 2011; Walters et al., 2010). In contrast, non-steroidal anti-inflammatory drugs naproxen, diclofenac and ibuprofen degrade more readily, with half-life time (DT_{50}) ranging from days to weeks (Xu et al., 2009).

The plant can take up ECCs released in agroecosystems and accumulate in the edible parts of the crop (Christou et al., 2017; Pan et al., 2014; Wu et al., 2014). Once taken up by roots, ECCs are transported through the vascular system, either via transpiration-driven mass flow, or through energy-dependent transporters (Miller et al., 2016). Several studies highlight the risks associated with ECC accumulation in edible plant parts. For example, Goldstein et al. (2014) found that ECCs, including carbamazepine metabolites, were primarily bioaccumulated in leaves and roots of vegetables such as carrot (*Daucus carota* L.) and sweet potato (*Ipomoea batatas* L.) irrigated with wastewater, while lamotrigine posed a public health threat due to its concentration in the edible roots. Mansilla et al. (2024) similarly reported high carbamazepine levels in leafy vegetables like lettuce (*Lactuca sativa* L), compared to root or fruit-bearing vegetables. Christou et al. (2017) also observed the uptake of pharmaceuticals such as diclofenac, sulfamethoxazole, and trimethoprim in tomatoes (*Solanum lycopersicum* L.) after prolonged irrigation with treated wastewater. Other ECCs, including triclosan and triclocarban, have been shown to be taken up by plant roots and subsequently translocated to stems, leaves, and fruits (Holling et al., 2012; Prosser et al., 2014; Wu et al., 2013).

In many Mediterranean countries, integrated systems for managing non-conventional water sources, including treated wastewater irrigation, are under evaluation. This is in line with EU Regulation 2020/741 (Official Journal of the European Union, 2020), which promotes sustainable and safe water reuse in agriculture. This regulation, which became effective in June 2023, establishes uniform minimum quality and monitoring standards for parameters such as Escherichia coli, Biochemical Oxygen Demand, Total suspended solids, and turbidity, with quality classes (A, B, C, and D) defined according to crop types and irrigation methods. Currently, the risk assessment related to ECCs is not mandatory, and there are no globally standardized regulations specifically addressing ECCs in vegetable food when they enter food chains via irrigation water. Therefore, assessing and monitoring the effect of ECCs on soil-plant systems when using treated wastewater for crop irrigation at the field scale is essential.

The present study aimed to evaluate the impact of irrigation with tertiary municipal wastewater (TWW) on the accumulation of the primary forms of different ECCs in the soil-plant system over two consecutive growing seasons in a processing tomato (*Solanum lycopersicum* L.)-durum wheat (*Triticum turgidum* spp. Durum) crop succession. Specifically, the study aimed to verify how the ECCs present in TWW influence soil and plant contaminant concentrations and the quality of the edible parts.

2. Materials and methods

2.1. Site description and agronomic conditions

The study was conducted in Trinitapoli, located in the Apulia Region of southern Italy (41°21' N; 16° 03' E; altitude 10 m a.s.l.). This area is part of an irrigation district that covers around 2000 ha (Fig. 1), and it is managed by the Capitanata Irrigation Consortium (https://www.bonificacapitanata.it/). The district mainly relies on irrigation water from the Capacciotti reservoir, which can hold up to 30 million cubic meters of water. Recently, a municipal WWTP has been constructed within the

Table 1
Main physico-chemical soil characteristics in the 0–0.9 m depth of the experimental site.

Parameter	Methods	Values
Physical parameters		
Sand (g/100 g dry weight)	ISO 11277:2020	39.4
Silt (g/100 g dry weight)	ISO 11277:2020	37.3
Clay (g/100 g dry weight)	ISO 11277:2020	23.2
Apparent Bulk Density (kg/dm^3)	-	1.21
Field Water Capacity (g/100 g dry weight)	Plate apparatus (- 0.03 MPa)	25.7
Wilting Point (g/100 g dry weight)	Plate apparatus (- 1.5 MPa)	11.9
Chemical parameters		
pH (-)	1:2.5 (w/v) aqueous soil extracts	8.5
Organic matter (g/100 g dry weight)	Walkley and Black (Walkley and Black, 1947)	1.1
Available phosphorus as P_2O_5 (mg kg^{-1})	Olsen method (Olsen et al., 1954)	240.0
Total potassium (g kg^{-1})	Coupled plasma optical emission spectrometer. Agilent. ICP-OES 720	11.2
N-NO_3^-(mg kg^{-1})	Keeney and Nelson (1982) procedure	3.7
N-NH_4^+ (mg kg^{-1})	Keeney and Nelson (1982)	3.3
Soil electrical conductivity (dS m^{-1})	1:2 (w/v) aqueous soil extracts	0.6

irrigation district; the plant can process up to 2 million cubic meters of wastewater per year, which may be used to enhance the district's water supply.

During the past ten years both fresh water from the Capitanata Consortium's irrigation distribution network and tertiary-treated wastewater deriving from the WWTP have been used for irrigating tomato (*Solanum lycopersicum* L.), artichoke (*Cynara scolymus* L.), cabbage (*Brassica oleracea* var. capitata), broccoli (*Brassica oleracea* var. botrytis), fennel (*Foeniculum vulgare* L.), and durum wheat (*Triticum turgidum* spp. Durum).

The area is characterised by low temperatures during winter and very high temperatures during summer (Figure S1); thus can be classified as "Hot-summer Mediterranean climate_Csa" according to the Koppen classification (Kottek et al., 2006). The average annual long-term rainfall is 590 mm, with precipitation unevenly distributed throughout the year. Most of the rainfall is concentrated between October and April (Caliandro et al., 2005). Throughout the field experiment, a nearby weather station recorded daily meteorological data, including maximum and minimum air temperature, maximum and minimum air relative humidity, wind speed, and precipitation. The experiment was carried out in a soil classified as Petrocalcic Palexerolls (USDA Soil Survey Staff. Keys to Soil Taxonomy, 2022), whose physicochemical properties are shown in Table 1.

During the two experimental years (2020–2021, Y_1 and 2021–2022, Y_2) processing tomato (*Solanum lycopersicum* L.) and durum wheat (*Triticum turgidum* spp. durum) were grown in succession. Processing tomato (cv. "Taylor") was transplanted on May 11th, and June 17th, in Y_1 and Y_2, respectively, in single rows (plant density 2.77 plants m^{-2}). Durum wheat (cv. "Saragolla") was sowed on November 15th, and December 10th, in Y_1 and Y_2, respectively, at a seeding rate of 350 germinable seeds m^{-2}.

2.2. Crop management and treatment

Two irrigation sources were compared in this study: tertiary treated wastewater (TWW) and freshwater (FW) as the control. Each treatment covered a plot of 75 m^2. The TWW was obtained from the full-scale municipal WWTP located near the experimental site. Here, municipal wastewater was treated with a conventional activated sludge process followed by sand filtration and disinfection. Final tertiary treatment based on membrane ultrafiltration ensured effluent quality, complying with the current standards for water reuse in irrigation (Lopez et al., 2010). Tertiary ultrafiltration is an effective way to polish treated wastewater effluents and remove residual suspended solids and colloids that may clog the irrigation lines and drippers. Furthermore, ultrafiltration provides an efficient barrier against faecal contamination indicators and parasites (e.g., Giardia, Cryptosporidium) that sometimes

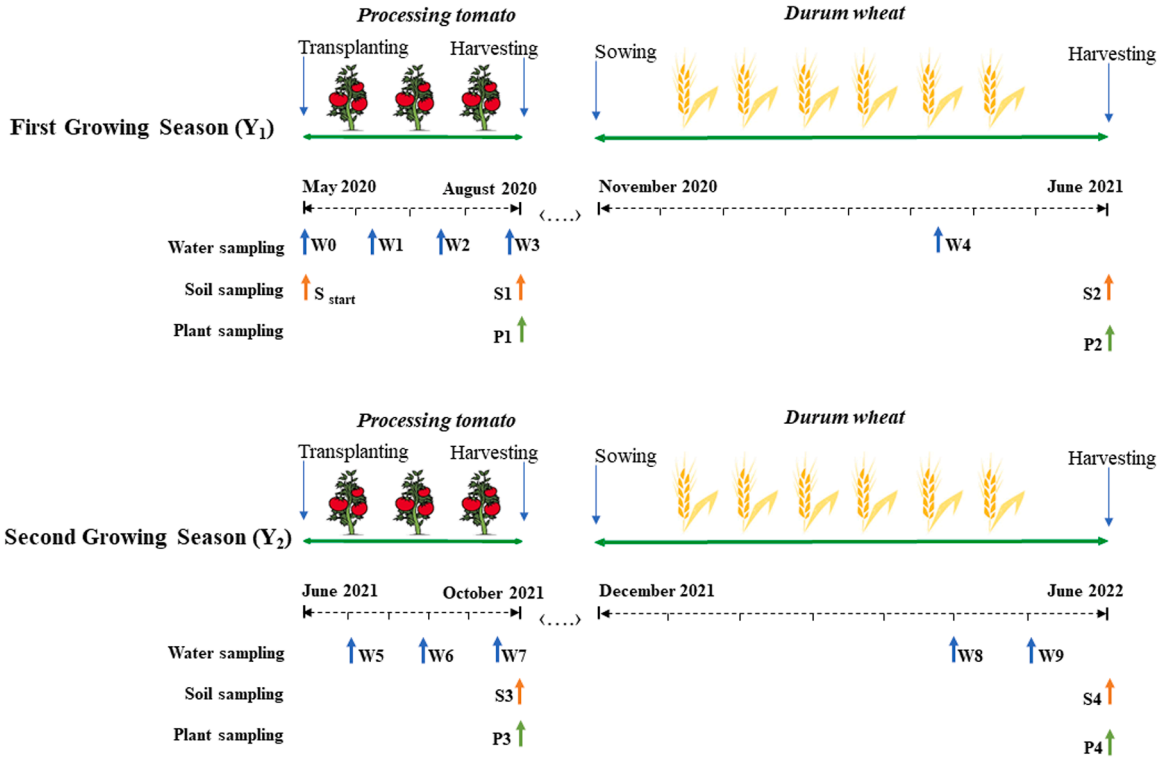


Fig. 2. Scheduling of the water, soil and plant sampling during the experimental trials.

overcome the normal disinfection steps adopted at municipal WWTP (Vergine et al., 2015, Lonigro et al., 2006). The FW was obtained from the irrigation network system that farmers typically use for crop irrigation. The physical-chemical and microbial parameters of the two irrigation water sources during the experimental trial are reported in Table S1.

A drip irrigation system was used for crop irrigation, with drippers at a 2 L h^{-1} flow rate spaced every 20 cm. A water flow meter installed on each pipeline determined the amounts of irrigation water applied at each irrigation event.

During the two growing seasons, the Bluleaf™ DSS model (Abi Saab et al., 2019; Buono et al., 2021) was utilized to aid in the daily irrigation scheduling for processing tomato crops. The model calculates daily crop evapotranspiration (ETc), soil water depletion, and net irrigation water requirements using the standard procedure proposed by FAO Paper n. 56. Daily weather data is utilized to determine the reference evapotranspiration (ETo) using the FAO Penman-Monteith equation. The model then estimates crop ETc using the single-crop coefficient (Kc) approach, following the standard FAO two-step procedure. The tomato crop was irrigated whenever the water lost by crop evapotranspiration (ETc) in the soil layer containing the roots reached a predetermined level (30 % of the available water depletion) with a watering volume that restores 100 % of the water lost (Carucci et al., 2023). During Y_1 and Y_2 tomato crops received 5900 m^3 ha^{-1} supplied in 25 watering events and 6800 m^3 ha^{-1} supplied in 33 watering events, respectively.

For the wheat irrigation scheduling, we followed the agronomic technique commonly used in the Mediterranean area known as "supplementary irrigation" (Si et al., 2023). In our experimental condition, the wheat crop needed 1100 m^3 ha^{-1} of irrigation only during the second year (Y_2) distributed through 3 watering events during March-May period of Y_2, when no rainfall occurred (Figure S1). The other agricultural techniques used on the two crops were carried out following standard management practices (Table S2).

2.3. Scheduling of water, soil, and plant sampling

Three months before starting the field experiment, water samples were collected monthly from the WWTP to determine the most common classes of ECCs and their concentration in tertiary effluents, and this information was used to guide subsequent analytical procedures. Moreover, water samples were collected and analysed ten times (W_0-W_9) during the two crop-growing seasons according to the sampling layout reported in Fig. 2.

In the first growing season, water samples were taken four times during the tomato crop cycle (W_0-W_3) and one time during the durum wheat crop cycle (W_4), while in the second growing season, three samples were taken during the tomato crop cycle (W_5-W_7) and two during the durum wheat crop cycle (W_8-W_9). Each water sample was collected from 3 emitters selected randomly in each irrigation treatment (water source), replicated 4 times using 100 mL sterile glass bottles, and stored at 4 °C before ECCs analysis. Moreover, before starting the experiment, soil samples (S_{start}) were taken from all plots to verify the initial soil-ECC concentration. Soil sampling was also conducted at the end of each crop cycle (S_1, S_2, S_3, and S_4, Fig. 2) at different depths, including D_1 (0–0.3 m), D_2 (0.3–0.6 m), and D_3 (0.6–0.9 m). For the two crops (tomato and wheat), D_1 and D_2 soil depth represent the high root density zone (top profile), while D_3 represents the deeper part of the root zone (bottom profile). The soil samples were air-dried and passed through a 2 mm sieve, and stored at − 20 °C, before the laboratory analysis.

The experimental treatments (irrigation sources and soil sampling depths) were arranged according to a split-plot design with four replicates where irrigation sources were the main plot and soil depths the sub-plot treatments.

Processing tomato harvesting took place on August 24th, and October 4th, in Y_1 and Y_2, respectively. Durum wheat harvesting occurred on June 7th, and June 11th, in Y_1 and Y_2, respectively.

To determine the ECCs concentration, whole plants (including roots, stems, leaves, grain and fruit) were collected from a sampling area (1 m x 1 m) within each experimental plot during the harvest dates (P_1-P_4, Fig. 2). After collecting the samples, they were separated into various fractions and stored at a temperature of– 20 °C.

2.4. Extraction and quantification of ECCs from soils and plant

To extract ECCs from soils, tomato and wheat plants, the modified QuEChERS method reported by De Mastro et al., (2022b) and Denora et al., (2023) were followed. Related to extracting ECCs from wheat plants, root was carefully washed with tap water to remove any soil residues. Afterwards, they were rinsed with deionized water and gently dried with a paper towel.

Roots, leaves, stems and marketable yield of the wheat crops were finely chopped and stored in a 50-mL centrifuge tube in the dark at– 20 °C until extraction. Briefly, 2 g of roots or 2 g of wheat leaves and stems or 5 g of milled wheat were placed in a 50 mL plastic centrifuge tube. 10 mL of water was added to the centrifuge tubes for all plant portions, except for roots for which 6 mL was added. Subsequently, the capped tubes were vortexed for 1 min. The samples were then thoroughly wetted, and 10 mL of acetonitrile was added. The centrifuge tubes were shaken by hand for 5 min. After this step only leaves and stems were left to rest for 15 min. The method was followed by a salting step with citrate buffer (4 g $MgSO_4$, 1 g NaCl, 0.5 g dibasic NaCitrate sesquihydrate, 1 g tribasic NaCitrate dihydrate). The tubes were again shaken vigorously by hand for 5 min. Samples were subsequently centrifuged (5 min, 3700 rpm), which resulted in a phase separation between the aqueous and organic solvents. The upper ACN layer (6 mL) was transferred into 15 mL tubes for the clean-up step. Tubes containing 900 mg $MgSO_4$ + 150 mg primary secondary amine (PSA) for roots, or 900 mg $MgSO_4$ + 150 mg PSA + 150 mg octadecyl (C18) for leaves and stems and milled wheat were vortexed for 1 min. After centrifugation (5 min, 4000 rpm), the supernatant was filtered through a membrane filter (PVDF, 0.22 μm), and 1.5 mL was transferred to a screw-cap vial for LC-MS/MS analysis.

The quantification of target compounds in the extracts was performed using an ultra-high pressure liquid chromatography system (UltiMate 3000 system, Thermo Fisher Scientific: https://www.thermofisher.com/us/en/home.html) interfaced to a high-resolution mass spectrometer (TripleTOF 5600 + system, AB Sciex: https://sciex.com) equipped with a duo-spray ion source operated in positive electrospray ionization mode (UHPLC-HR/MS/MS). The MS operating conditions were the following (arbitrary units): nebulizer gas 35, turbo gas 45, curtain gas 20, ion spray voltage 5500 V, temperature 500°C, declustering potential 80 V, collision energy voltage 35 V, collision energy spread voltage 15 V and *m/z* range 70–800 Da. The analytes were detected with an acquisition method based on both TOF-MS/IDA (Information Dependent Acquisition) experiments, in the mass scan range of 70–800 Da.

The chromatographic separation of analytes was achieved using a ZORBAX Eclipse Plus C18 column (150 × 2.1 mm, 1.8 μm) with 0.1 % (v/v) formic acid in water (solvent A) and 0.1 % (v/v) formic acid in acetonitrile (solvent B) as mobile phase. Before injection (100 μL) each sample was spiked with the internal standard at a level of 10 μg L^{-1} and eluted with the following gradient: 0 −2 min, 2 % solvent B; 2 −3 min, linear from 2 % to 20 % solvent B; 3 −17 min, linear from 20 % to 100 % solvent B; 17 −21 min, isocratic at 100 % solvent B; 21 −21.5 min, from 100 % to 2 % solvent B; 21.5 −25 min, column reconditioning. The column flow rate was set to 0.300 mL min^{-1} and the temperature to 40 °C. The analytes were quantified in the extracts by using a calibration curve in the range 0.1–10 μg L^{-1} (0.1, 0.2, 0.5, 1, 2, 5, and 10 μg L^{-1}) (De Mastro et al., 2023).

Table 2
Physicochemical properties (Molecular weight; Water Solubility; log K_{OW}, Octanol/Water Coefficient; pKa, Acid Ionization Constant; log D, it is refers to the water: octanol partition coefficient at a specific pH=7.4; DT_{50}, half-life) of the Selected ECCs (https://www·chemspider.com).

ECCs	Molecular weight g mol^{-1}	Chemical Structure	Chemical Class	Water Solubility (mg L^{-1}) at 25 °C	Log K_{OW}	pKa	Log D (pH 7.4)	DT_{50} (day)
Molecule target[†]								
Clarithromycin	748.0	$C_{38}H_{69}NO_{13}$	antibiotic	0.33	3.16	8.99	2.38	15.8[b]
Trimethoprim	290.3	$C_{14}H_{18}N_4O$	antibiotic	400.0	0.91	7.12	2[h]	120[h]
Sulfamethoxazole	253.2	$C_{10}H_{11}N_3O_3S$	antibiotic	610.0[†††]	0.89	1.60	1.3[i]	35–53[i]
Triclosan	289.5	$C_{12}H_7Cl_3O_2$	antibiotic	10	4.76	7.9	2.31	46
Fluconazole	306.2	$C_{38}H_{69}NO_{13}$	antifungal	335.5	0.25	2.27	0.70	360
Climbazole	292.7	$C_{15}H_{17}ClN_2O_2$	antifungal	8.2	3.76	6.49	3.32	120
Diclofenac	296.1	$C_{14}H_{11}Cl_2NO_2$	antinflammatory	4.5	4.51	4.00	1.37	75
Ketoprofen	254.2	$C_{16}H_{14}O_3$	antinflammatory	120.4	3.12	4.45	0.06	30
Naproxen	230.2	$C_{14}H_{14}O_3$	antinflammatory	15.9	3.18	4.15	-	6–19[c]
Metoprolol	267.3	$C_{15}H_{25}NO_3$	beta-blockers	4777.0	1.88	9.70	−0.25	75
Carbamazepine	236.2	$C_{15}H_{12}N_2O$	antiepileptics	17.6	2.45	13.9	2.28	355–1624[c]
Gemfibrozil	-	$C_{15}H_{22}O_3$	lipid-regulating					
Molecule target added[††]								
Sotalol	272.3	$C_{15}H_{25}NO_3$	beta-blockers	5513.0	0.37	0.24	−1.63	35[d]
Sulpride	341.4	$C_{15}H_{23}N_3O_4S$	antidepressant	2275.0	0.57	-	−0.99	120
Venlafaxine	277.4	$C_{17}H_{27}NO_2$	antidepressant	266.70	3.28	9.50	1.43	120
Flecainide	414.3	$C_{17}H_{20}F_6N_2O_3$	antiarrhythmic	1.47	3.78	9.30	1.01	360
Gabapentin	171.2	$C_9H_{17}NO_2$	antiepileptics	4491.0	−1.10	3.70	−1.40	30
Sitagliptin	407.3	$C_{16}H_{15}F_6N_5O$	antidiabetic	179.2	1.39	8.70	1.09	360
Telmisartan	514.6	$C_{16}H_{15}F_6N_5O$	antihypertensive	Insoluble in water[e]	-	3.80[g]	4.01	75[a]
Irbesartan	428.5	$C_{25}H_{28}N_6O$	antihypertensive	0.0599	5.31	-	1.24	75
Olmesartan	446.5	$C_{24}H_{26}N_6O_3$	antihypertensive	1.24	3.63	4.30[f]	−0.39	120
Valsartan	435.5	$C_{24}H_{29}N_5O_3$	antihypertensive	1.40	3.65	4.70	−0.89	30

[†] Molecule target defined by the international literature;
[††] Molecule added according to specific monitoring activity on effluents produced by municipal wastewater treatment plan;
[†††] Water Solubility (mg L^{-1}) at 37 °C.
[a] Mean value relate to the sartan group (irbesartan, olmesartan and valsartan).
[b] Topp et al., (2016) (https://doi.org/10.1016/j.scitotenv.2016.03.210).
[c] Gworek et al., (2021) (https://doi.org/10.1007/s11270-020–04954-8).
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[f] https://pubchem.ncbi.nlm.nih.gov
[g] Li et al., (2014) (https://doi.org/10.1016/j.watres.2022.119352);
[h] Rietra et al., (2024) (https://doi.org/10.1016/j.heliyon.2023.e23718);
[i] Shen et al. (2018) (https://doi.org/10.1016/j.chemosphere.2017.11.175).

2.5. Statistical analysis

The dataset was tested according to the basic assumptions for ANOVA analysis. The Shapiro-Wilk and Bartlett's tests were used to verify the experimental error's normal distribution and common variance, respectively. If required, Box-Cox transformations (Box and Cox, 1964) were applied before conducting the analysis. ECC's water and plant concentration data did not meet ANOVA assumptions, so we presented them by mean data ± standard error.

For soil data, the ANOVA procedure was conducted according to a split-plot design with four replicates where irrigation source was defined as the main plot treatment and soil depth as the plot treatment, both combined with sampling time (split-plot design over time). Irrigation source, soil depth and sampling time were considered as fixed factors, while replications were considered random. In addition, a multivariate approach (stepwise discriminant analysis, SDA) was used to statistically process the soil ECC concentrations, with the two experimental factors (sampling time and soil depth) as discriminating sources for each irrigation source (Rencher, 1992; Zhao et al., 2011). SDA was used to explain differences among treatments within each experimental factor and to evaluate the main variables (ECCs considered) responsible for those differences. Before performing the SDA, the values of each variable were correctly standardized. The stepwise procedure added variables (each ECC considered) to the model one by one, choosing at each step the variable that made the most significant additional contribution to the discrimination.

We used a cross-validation procedure to assess model performance to prevent overfitting in the stepwise discriminant analysis (SDA). Additionally, we implemented stringent criteria during the stepwise process by using a low significance level for Fisher's test ($p < 0.05$). This ensured that only statistically significant predictors (ECCs) were included in the analysis.

Once the relevant variables were selected, discriminant analysis was used to compute different discriminant functions (canonical axis, CAs). The first two canonical axes (CA_1 and CA_2) accounted for a significant portion of the data variability and were selected for further analysis. The chosen canonical axes were graphically represented by a biplot, in which the canonical scores were plotted as symbols, whereas standardized canonical coefficients related to the original variables (ECCs) were reported as vectors and used for interpretation.

ANOVA and SDA analyses were performed using the JMP software package, version 16.2 (SAS Institute Inc., Cary, NC, USA), and graphs were constructed using the SigmaPlot software (Systat Software, Chicago, USA).

3. Results and discussions

3.1. ECCs content in irrigation water

The ECCs evaluated and their main physicochemical properties, are reported in Table 2. We monitored a total of 22 target compounds, 12 of which were identified as the most common contaminants based on international literature, and 10 others were selected from based on preliminary monitoring activities conducted before the start of the field trials on the effluents used for the irrigation. The 22 target compounds represent ten drug class, including four antibiotics (clarithromycin,

Table 3
Concentrations of selected ECCs related to irrigation water used during the experimental trials. Mean values ± standard error, median value, range of variation and frequency of quantification (F, as % presence of the ECC in the detected water samples) are reported.

ECCs	Category	FW[†]				TWW[††]			
		Means[†††] (μg/L)	Median (μg/L)	Range (μg/L)	F (%)	Means (μg/L)	Median (μg/L)	Range (μg/L)	F (%)
Clarithromycin	Antibiotic	<LOQ				0.27 ± 0.04	0.07	0.01–1.13	100
Ketoprofen	Antiinflammatory	<LOQ				0.012 ± 0.02	0.04	0.01–0.44	50
Diclofenac	Antinflammatory	<LOQ				0.83 ± 0.07	0.75	0.21–1.62	100
Carbamazepine	Antiepileptics	<LOQ				0.29 ± 0.017	0.27	0.16–0.37	100
Gabapentin	Antiepileptics	<LOQ				0.23 ± 0.04	0.23	0.12–0.43	70
Metoprolol	Beta-blocker	<LOQ				0.08 ± 0.026	0.06	0.04–0.24	100
Sotalol	Beta-blocker	<LOQ				0.16 ± 0.021	0.14	0.05–0.26	100
Fluconazole	Antifungal	<LOQ				0.15 ± 0.08	0.13	0.04–0.28	100
Climbazole	Antifungal	0.011 ± 0.005	0.011	0–0.02	16	0.05 ± 0.009	0.04	0.01–0.13	93
Flecainide	Antiarrhythmic	0.04 ± 0.012	0.05	0.03–0.06	16	1.06 ± 0.132	0.92	0.5–2.32	100
Sitagliptin	Antidiabetic	<LOQ				0.52 ± 0.08	0.50	0.17–1.00	100
Venlafaxine	Antidepressant	<LOQ				0.19 ± 0.02	0.13	0.09–0.33	100
Sulpride	Antidepressant	<LOQ				0.14 ± 0.015	0.13	0.04–0.32	100
Olmesartan	Antihypertensive	<LOQ				5.10 ± 0.51	4.18	2.00–10.2	100
Irbesartan	Antihypertensive	<LOQ				1.35 ± 0.25	1.29	0.15–3.71	100
Telmisartan	Antihypertensive	<LOQ				0.55 ± 0.21	0.23	0.13–2.36	100
Valsartan	Antihypertensive	<LOQ				0.047 ± 0.01	0.05	0.02–0.09	59

[†] FW, Fresch water. The values reported are the range of variation (highest value minus the lowest value) of the ECCs target related to 40 irrigation water samples (10 sampling data x 4 replications).
[††] TWW, treated wastewater. The values reported are the range of variation (highest value minus the lowest value) of the ECCs target related to 40 irrigation water samples (10 sampling data x 4 replications).
[†††] below the quantification limit, <LOQ).

trimethoprim, triclosan and sulfamethoxazole), two antifungals (fluconazole and climbazole), three anti-inflammatories (diclofenac, ketoprofen and naproxen), two beta-blockers (sotalol and metoprolol), two antidepressants (sulpride and venlafaxine), one antiarrhythmic (flecainide), two antiepileptic (carbamazepine and gabapentin), one antidiabetic (sitagliptin), four antihypertensive (telmisartan, irbesartan, olmesartan and valsartan), and one lipid-regulating (gemfibrozil). Of these, three ECCs (trimethoprim, sulfamethoxazole, and naproxen) were below the quantification limit (Table S3), while two compounds, triclosan and gemfibrozil, were not detected.

Table 3 provide details on the ECCs detected in the FW and TWW irrigation sources along with their mean concentrations. In FW, climbazole (0.011 μg L^{-1}) and flecainide (0.04 μg L^{-1}) were detected in 16 % of the irrigation water samples analyzed during the two growing seasons. This finding aligns with previous reports (Castiglioni et al., 2018) suggesting that surface waters can receive pollutants such as ECCs from both point-based sources (e.g., municipal wastewater discharges) and diffuse sources (e.g., agricultural runoff and erosion) (Parra-Saldivar et al., 2021).

In TWW, the most frequently detected ECCs were antihypertensive drugs (sartans) including olmesartan, irbesartan, telmisartan, and valsartan. Among these, olmesartan had the highest concentration (5.10 ± 0.51 μg L^{-1}) and largest range of variation (2.00–10.20 μg L^{-1}). Mean concentrations of irbesartan, telmisartan and valsartan in TWW were 1.35 ± 0.25, 0.55 ± 0.21, and 0.047 ± 0.01 μg L^{-1}, respectively. The detection frequency (F) for the sartan group was 100 %, except for valsartan, which showed a detection frequency of 59 %.

Our findings align with those of Li et al. (2023), who reported that sartans (losartan, valsartan, irbesartan, and olmesartan) were present in wastewater effluents at concentrations ranging from the limit of detection up to 6 μg L^{-1}.

With respect to concentrations of antinflammatory (ketoprofen and diclofenac), beta-blocker (metoprolol and sotalol), antiepileptics (carbamazepine and gabapentin) and antifungal (fluconazole) groups, diclofenac had the largest concentration range (0.21–1.62 μg L^{-1}) while climbazole had the narrowest (0.01–0.13 μg L^{-1}) (Table 3).

As noted by numerous authors, comparing ECC concentrations in wastewater effluent across different investigations can be challenging due to variations in influent characteristics and the technology used at individual treatment plants (Roberts and Thomas, 2006; Margot et al., 2015; Helmecke et al., 2020; Parra-Saldivar et al., 2021). Therefore, the quality and quantity of ECCs can vary significantly depending on the specific site or geographical production area, highlighting the need for localized research. Under our experimental conditions, the TWW concentrations are comparable to those found in similar studies. In southern Italy, De Mastro et al. (2023) found tertiary wastewater concentrations of 0.54, 0.2, 0.07, and 0.03 μg L^{-1} for carbamazepine, ketoprofen, fluconazole and climbazole, respectively. Similarly, Petrie et al. (2015) reported concentrations of 0.016, 0.3 and 0.05 μg L^{-1} for ketoprofen, diclofenac and metoprolol, respectively. They also found that the concentrations of flecainide (antiarrthythmic), sitagliptin (antidiabetic) and clarithromycin (antibiotics) ranged from 0.5 to 2.32, 0.17–1.00, and 0.0–1.13 μg L^{-1}, respectively. Overall, the concentrations reported here are consistent with those found in literature, except for flecainide, which was found at a notably higher concentration in TWW (Ben Mordechay et al., 2021).

3.2. Soil-ECCs content

The soil accumulation of ECCs was significantly affected by sampling time, soil depth, irrigation water source, and their interactions ($p < 0.05$ of the Fisher's test). Among the 17 compounds identified in the TWW used for irrigation (Table 3), only 8 (i.e., clarithromycin, carbamazepine, fluconazole, climbazole, flecainide, sitagliptin, telmisartan, venlafaxine) were detected in the soil profile. These results are consistent with several studies which highlighted that not all the ECCs present in wastewater effluent accumulated in the soil at the same rate, due to processes such as soil adsorption, plant uptake, leaching, and biotransformation (Gibson et al., 2010; Brienza et al., 2021). Drillia et al. (2005) demonstrated that ECC mobility in soil, and thus the risk of groundwater contamination, depends on factors such as the ECC concentration in wastewater, rainfall intensity, and soil type. Recent studies (Manasfi et al., 2020; Gworek et al., 2021; Narain-Ford et al., 2022; De Mastro et al., 2023) have further explored how ECC physicochemical properties influence their behavior in the soil, emphasizing parameters such as octanol-water coefficient (log D) and half-life parameter (DT_{50}) to predict their mobility and persistence under various environmental conditions.

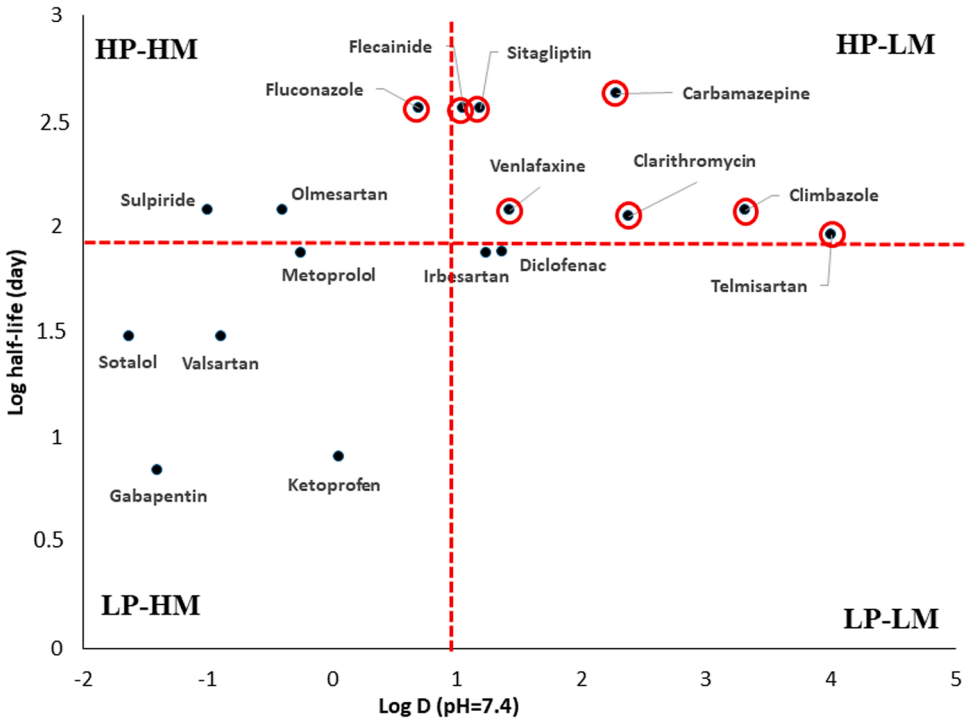


Fig. 3. ECCs classification based on their persistence (DT_{50}) and mobility (Log D) in the soil. The persistence-mobility categories have been defined using the 50_{th} percentile of DT_{50} and Log D values. The categories include HP-HM (high persistence and high mobility), HP-LM (high persistence and low mobility), LP-HM (low persistence and high mobility), and LP-LM (low persistence and low mobility). The red circle represents the ECCs detected both in the irrigation sources and soil profiles.

Based on the approach by Narain-Ford et al. (2022), we used log D and DT_{50} to categorize each soil-detected ECCs into four persistency-mobility categories: high persistency and high mobility (HP-HM), high persistency and low mobility (HP-LM), low persistency and high mobility (LP-HM), and low persistency and low mobility (LP-LM) (Fig. 3).

ECCs not detected in TWW-irrigated soil were positioned in the figure zones characterized by low persistence (diclofenac and irbesartan) or high mobility (olmesartan and sulpride) or both low persistence and high mobility (valsartan, gabapentin, ketoprofen, sotalol, and metoprolol).

Thus, these compounds' low persistence and/or high mobility do not allow their accumulation since they may have been rapidly leached into the soil profile and/or rapidly degraded into by-products with distinct chemical compositions (Manasfi et al., 2020; Denora et al., 2023). De Mastro et al. (2023) similarly reported that some ECCs (e.g., ketoprofen) were absent in TWW-irrigated soil due to potential leaching, a behaviour also observed for beta-blockers like metoprolol and sotolol, known for their high mobility and potential to reach groundwater (Maszkowska et al., 2014;Kodešová et al., 2015).

Figs. 4 and 5 present the mean ECC concentrations in soil across soil sampling (S_1-S_4) and soil depths (D_1-D_3) for the two irrigation sources. At the beginning of the experiment, the ECC concentrations in soil ranged from 5.54 ± 0.38 ng g^{-1} for climbazole at D_1 and 0.25 ± 0.08 ng g^{-1} for carbamazepine at D_3 (Table 4), likely resulting from prior use of treated wastewater or biosolids in the area.

The molecules found at S_{start} (Table 4) are characterized by high persistence (fluconazole) or low mobility (clarithromycin) or both (clarithromycin, climbazole, sitagliptin, flecainide, telmisartan, and venlafaxine) as reported in Fig. 3. Moreover, these detected compounds remained largely stable over the experimental period (approximately 700 days), despite irrigation with freshwater (FW). These results indicate that under the tested conditions, the half-life parameter (DT_{50}) for the evaluated ECCs may differ from values reported in the literature. This discrepancy is likely due to the influence of our specific environmental conditions; semi-arid climates, indeed, can affect key factors such as soil pH, organic matter content, water availability, and microbiological activity, all of which are closely related to the biodegradation of these compounds (Pérez Solsona et al., 2021). Interestingly, fluconazole and telmisartan were not detected under FW irrigation from S_3 and S_2, respectively (Figs. 4C and 5B).

During the first tomato crop (S_1) which received 5900 m^3 ha^{-1} of irrigation, significant differences between FW- and TWW-irrigated soils were observed for fluconazole at D_2 and D_3 (Fig. 4C) and flecainide at D_1 (Fig. 4D). Fluconazole's behaviour can be attributed to its high mobility (Fig. 3), while flecainide's high concentration at D_1 can be due to its high concentration in TWW (Table 3) and to the chemical properties of the molecule. At the most common pH in wastewater, the molecule is predominantly positively ionized. Thus, the flecainide's high concentration can be explained by the occurrence of electrostatic interactions with negatively charged soil surfaces at alkaline pH. The flecainide molecule can, therefore, interact with the extracellular matrix and clay minerals (Ramil et al., 2009) by cation exchange processes (Schaffer et al., 2012).

By S_2 (end of the first wheat cycle, without irrigation), the difference between TWW and FW-irrigated soil were not significant. However, significant differences reemerged by S_3 (end of the second tomato cycle, with 6800 m^3 ha^{-1} irrigation), particularly at D_1, for all ECCs considered, and at D_2 only for the fluconazole.

Similarly, the second wheat cycle (S_4), in which supplementary irrigation was carried out (1100 m^3 ha^{-1}), revealed significant increases in ECCs at in D_1, except for fluconazole, which during S_4 fell below detection limits (Fig. 3), likely due to its mobility (Pacholak et al., 2022).

Throughout the experiment (S_{start}-S_4), significant increases in carbamazepine, sitagliptin, and flecainide at D_1, and clarithromycin at D_1 and D_2 were observed in TWW-irrigated soil indicating their accumulation over the two tomato-wheat cycles.

The concentration of these compounds increased notably from the S_{start} (Table 4) to S_4 (Figs. 4 and 5) at D_1: 1.19 ± 0.16–3.3 ± 0.5 ng g^{-1}

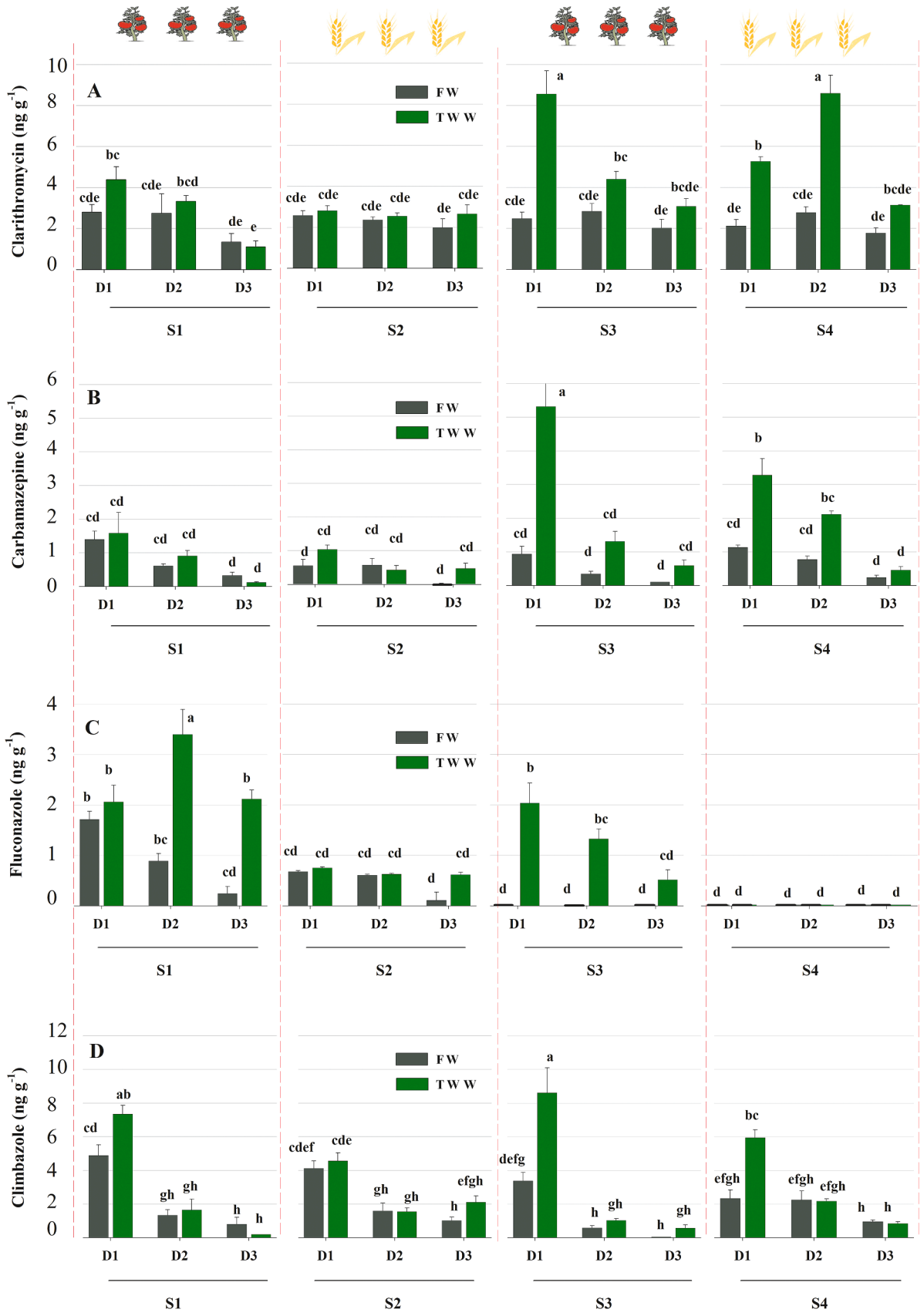


Fig. 4. Mean values of clarithromycin, carbamazepine, fluconazole and climbazole soil concentration at S_1-S_4 sampling time and D_1-D_3 soil depths for two irrigation water sources (freshwater, FW and tertiary wastewater, TWW) (interaction sampling time x soil depth x water sources). Different letters indicate statistically significant differences ($P \leq 0.05$, Tukey's test). Vertical bars indicate standard errors of four replicates.

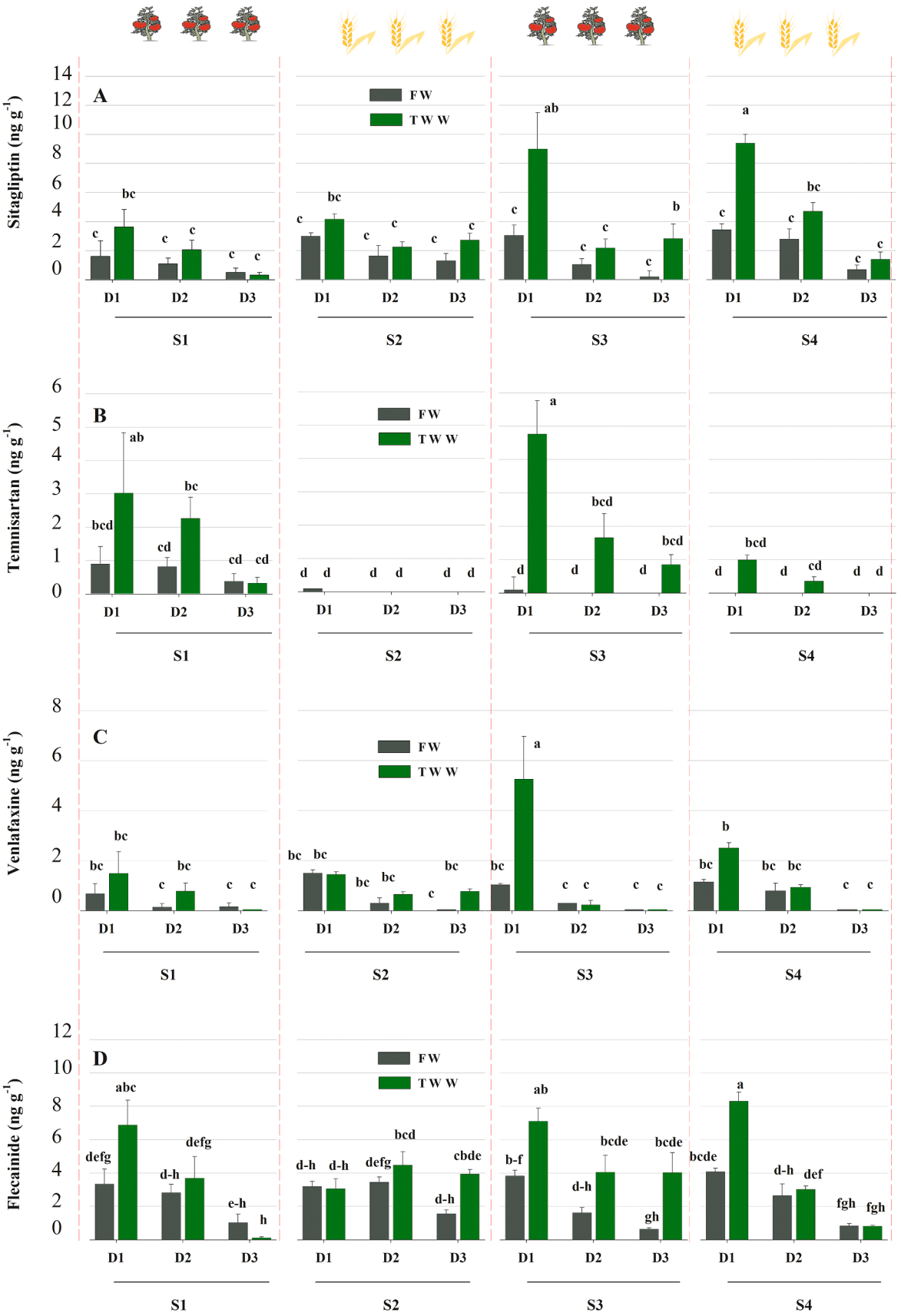


Fig. 5. Mean values of sitagliptin, telmisartan, venlafaxine and flecainide soil concentration at S_1-S_4 sampling time and D_1-D_3 soil depths for two irrigation water sources (freshwater, FW and tertiary wastewater, TWW) (interaction sampling time x soil depth x water sources). Different superscript letters indicate statistically significant differences ($P \leq 0.05$, Tukey's test). Vertical bars indicate standard errors of four replicates.

Table 4
The ECCs soil content (ng g^{-1}) at the beginning of the experimental trial (S_{start}).

ECCs	Soil depth†		
	D_1	D_2	D_3
Clarithromycin	1.96 ± 0.15	2.06 ± 0.34	1.86 ± 0.33
Carbamazepine	1.19 ± 0.16	0.55 ± 0.14	0.25 ± 0.08
Fluconazole	2.14 ± 0.19	0.71 ± 0.16	0.26 ± 0.08
Climbazole	5.54 ± 0.38	1.53 ± 0.56	0.95 ± 0.15
Sitagliptin	1.50 ± 0.57	1.20 ± 0.38	1.36 ± 0.13
Telmisartan	0.95 ± 0.36	0.97 ± 0.37	0.91 ± 0.29
Venlafaxine	0.71 ± 0.20	-	-
Flecainide	3.94 ± 0.99	2.57 ± 0.25	1.75 ± 0.27

† D_1, 0.0–0.30 m; D_2, 0.30–0.60 m and D_3, 0.60–0.90 m. The values are mean of 4 field replications ± standard error.

for carbamazepine, 1.50 ± 0.57–9.4 ± 0.4 ng g^{-1} for sitagliptin, and 3.94 ± 0.99–8.3 ± 1.6 ng g^{-1} for flecainide; clarithromycin increased from 1.96 ± 0.15–5.3 ± 0.6 ng g^{-1} for D_1 and from 2.06 ± 0.34–8.6 ± 0.3 ng g^{-1} for D_2.

Our experimental results are in accordance with a study conducted by Biel-Maeso et al. (2018), which examined the presence of pharmaceuticals in soils irrigated with reclaimed wastewater. This study found that analgesics and antinflammatory drugs were the most prevalent, followed by antibiotics and antiepileptics (among which carbamazepine) in topsoils (0–20 cm deep). All detected concentrations of pharmaceuticals ranged from 2 to 15 ng g^{-1}, with the highest levels identified for carbamazepine.

No significant differences were found at the deeper soil layer (D_3, 0.6–0.9 m) throughout the experiment. Clarithromycin's concentration in TWW-irrigated soils aligns with Kodešová et al. (2016) who reported half-life for this compound ranging from 112 to 1000 days, depending on soil type. However, these findings contrast with Topp et al. (2016), who observed rapid clarithromycin dissipation (DT_{50} of 36 days) under controlled laboratory conditions, highlighting the influence of environmental factors like field versus laboratory conditions.

Carbamazepine, a well-known recalcitrant compound, was consistently detected in both TWW- and FW-irrigated soils. Its accumulation predominantly in the topsoil (D_1) is consistent with previous research (Walker et al., 2012; Grossberger et al., 2014; Ben Mordechay et al., 2021, 2022) and is influenced by factors such as soil organic carbon content, which has been shown to limit leaching and increase retention in clay-rich soils (Filipović et al., 2020).

3.2.1. *Multivariate statistical analysis of ECC Soil contents*

The ANOVA results showed the effects of the experimental factors (sampling time, irrigation source, and soil depth) on the individual soil-ECCs' concentration. To enhance these findings, a multivariate statistical procedure, specifically stepwise discriminant analysis (SDA), was employed. This method evaluated which of the ECCs analysed simultaneously played an important role in separating sampling time and soil depth within each irrigation source (FW and TWW).

Based on SDA results, significant differences ($P < 0.0001$) were observed for the two experimental factors, sampling time and soil depth, across the selected irrigation sources (Table S4). To identify, the ECCs significantly contributing to these differences, a stepwise procedure was applied.

For TWW-irrigated soil (Table S5A), SDA by the sampling time identified six ECC (clarithromycin, carbamazepine, fluconazole, sitagliptin, telmisartan, and venlafaxine) which showed the highest discrimination across the sampling periods (S_{start}-S_4). Fluconazole and telmisartan were the first ECC to be added to the SDA model (F ratio=19.1 and 15.7, respectively; $P < 0.0001$), while carbamazepine was the last (F ratio=4.12; $P < 0.005$). Likewise, the same ECCs showed the greatest discrimination across the different soil depths (D_1-D_3).

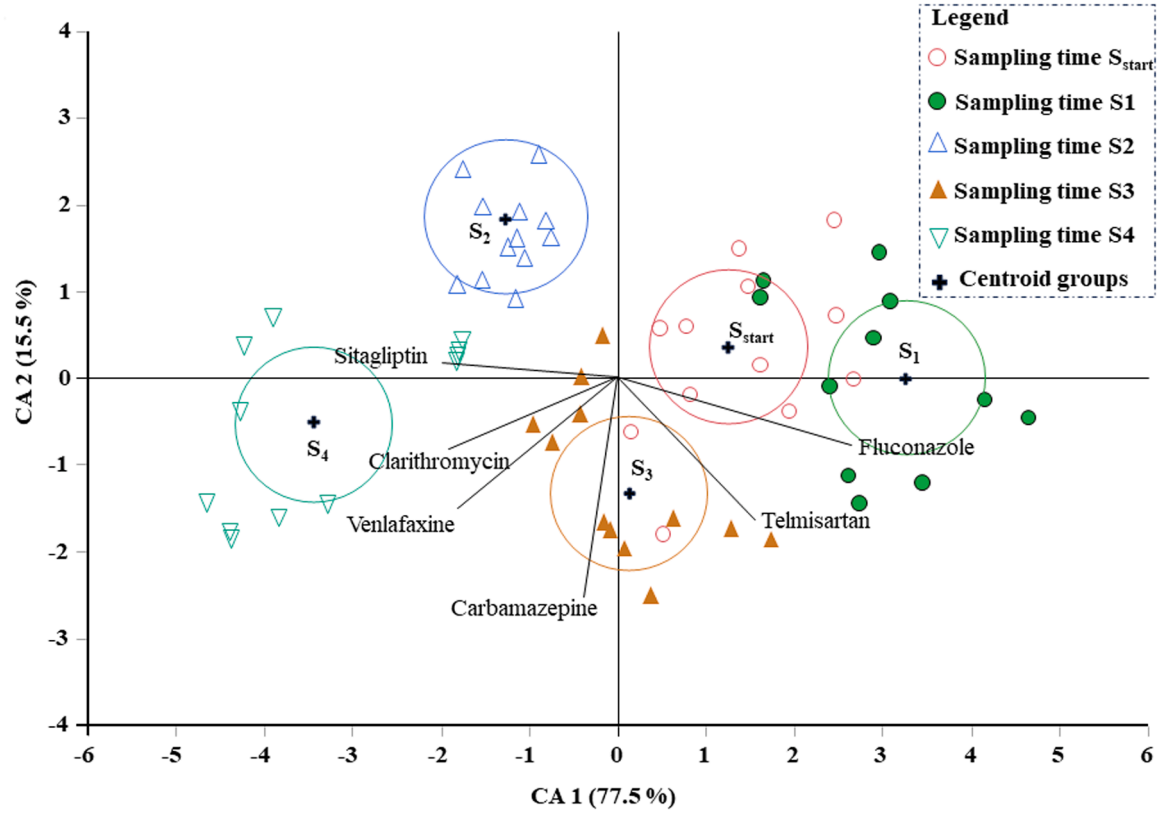


Fig. 6. Biplot of the SDA relative to TWW-irrigated soil and performed by the sampling time. Different rays represent the covariates (selected ECCs). The 95 % confidence level ellipse is plotted for each sampling time. Non-intersecting ellipses indicate significant differences between ECCs soil content, related to different sampling times.

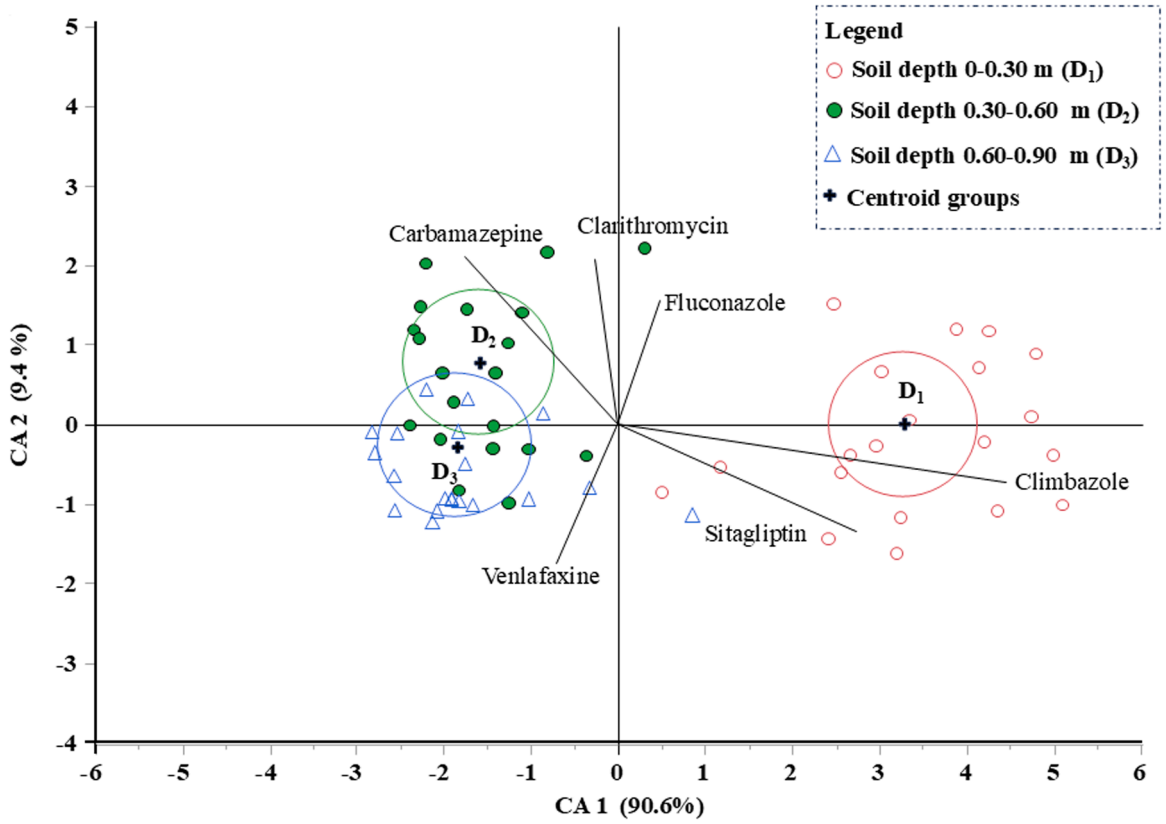


Fig. 7. Biplot of the SDA relative to TWW-irrigated soil and performed by the soil depth. Different rays represent the covariates (selected ECCs). The 95 % confidence level ellipse is plotted for each soil depth. Non-intersecting ellipses indicate significant differences between ECCs soil content, related to different soil depths.

Climbazole was the first added in the model for soil depth (F ratio=84.1; $P < 0.0001$), and venlafaxine was the last (F ratio=2.37; $P < 0.047$).

In FW-irrigated soil (Table S5B), SDA by sampling time selected six ECC (clarithromycin, carbamazepine, fluconazole, telmisartan, venlafaxine, and flecainide), while for soil depth, the selected ECC included clarithromycin, carbamazepine, climbazole, venlafaxine, flecainide, and telmisartan.

A more detailed interpretation of the effects of each selected ECC in TWW-irrigated soil can be gained by considering the canonical biplot graph and the relative length and direction of the vectors (Figs. 6 and 7).

The canonical variables CA_1 and CA_2 explained for 77.5 % and 15.5 % of the total variance, respectively, representing two dimensions that maximized the separation among sampling time groups (S_{start}-S_4). Fluconazole played an important role in differentiating S_1, while clarithromycin and sitagliptin were critical in defining S_4. Carbamazepine and telmisartan were effective for separating S_3. For TWW-irrigated soil, significant differences among soil depths (D_1-D_3) were identified using six ECCs selected through SDA (Fig. 7). CA_1 and CA_2 explained 90.6 % and 9.4 % of the total variance, respectively. Climbazole and sitagliptin played an important role in differentiating the upper soil layer (D_1) from D_2 and D_3, which showed partial overlap.

Canonical biplots for FW-irrigated soil (Figures S2 and S3) demonstrated the limited ability of SDA to differentiate sampling periods. Most canonical scores were clustered near the origin, and the overlapping 95 % confidence ellipses suggested no significant differences between some sampling periods (S_2-S_4).

These multivariate results are in accordance with the univariate analysis (Figs. 4 and 5), where the initial soil content of clarithromycin, carbamazepine, flecainide and venlafaxine soil content (S_{start}) remained substantially unchanged throughout the field trial, highlighting high persistence and low mobility for these compounds. Conversely, fluconazole and telmisartan levels declined over time, falling below the quantification limit by S_3 and S_4 (Table S3), suggesting lower persistence and/or higher mobility (Fig. 3).

3.3. Plant-ECCs contents

The uptake of the soil-ECC content in the studied crops was selective and ECC concentration varied across plant parts, including roots, leaves, stems and the edible part (tomato fruit and wheat grain). The process of ECC uptake in plants is complex and dependent on the chemical-physical properties of the compounds, as well as the soil's properties such as pH and organic matter content (Goldstein et al., 2014; Miller et al., 2016; Christou et al., 2017; Goldstein et al., 2018; Denora et al., 2023).

Table 5 shows the concentration of ECCs in the plants and the edible parts such as tomato fruit and wheat grain. Among the 8 ECCs detected in the soil, 5 were found in the plants (carbamazepine, fluconazole, climbazole, venlafaxine and flecainide). These compounds were localized in roots, leaves and stems, but were undetectable in edible parts (values below the detection limit, Table S3). Several studies reported that transpiration is the primary physiological process responsible for the uptake and transport of ECCs from soil to plants (Dodgen et al., 2015; Ben Mordechay et al., 2021). Tomatoes, however, do not transpire water through their fruits, preventing the flow of water and solutes into the fruit (Goldstein et al., 2014). Under the tested experimental conditions, this physiological trait appears to prevent the ECCs accumulation (as a primary form) in tomato fruit, thus avoiding risks to human health. Similarly, there was no ECC accumulation was observed in the wheat grain, regardless of whether irrigation was used (Table 5).

These findings have significant implications for food safety in the Mediterranean region, where tomato and wheat crops are commonly grown in succession. The absence of ECC translocation to edible plant parts, as demonstrated in this study, underscores the opportunity to utilize wastewater for the irrigation of tomatoes, one of the most water-

Table 5
The mean content of ECCs (ng g^{-1} dry weight, dw) in the plant and in the edible part (fruit and grain) of tomato and wheat crops.

ECCs	Matrix	Irrigation Water[†]	Crop cycle[††]			
			Tomato 1	Wheat 1	Tomato 2	Wheat 2
Carbamazepine	Root	FW	-	-	-	-
		TWW	1.4 ± 0.2	-	1.9 ± 0.1	-
	Stem/Stalk	FW	-	-	-	-
		TWW	1.3 ± 0.2	-	1.1 ± 0.1	-
	Leaf	FW	6.1 ± 0.7	-	4.6 ± 0.6	-
		TWW	12.2 ± 3.9	-	16.9 ± 2.3	-
	Fruit/Grain	FW	-	-	-	-
		TWW	-	-	-	-
Fluconazole	Root	FW	-	-	-	-
		TWW	-	-	-	-
	Stem/Stalk	FW	-	-	-	-
		TWW	0.9 ± 0.05	-	1.9 ± 0.2	-
	Leaf	FW	29.3 ± 5.4	-	12.3 ± 0.8	-
		TWW	44.7 ± 16.9	-	58.4 ± 4.9	-
	Fruit/Grain	FW	-	-	-	-
		TWW	-	-	-	-
Climbazole	Root	FW	-	-	-	-
		TWW	-	-	-	1.7 ± 0.1
	Stem/Stalk	FW	-	-	-	-
		TWW	-	-	-	-
	Leaf	FW	-	-	-	-
		TWW	-	-	-	-
	Fruit/Grain	FW	-	-	-	-
		TWW	-	-	-	-
Venlafaxine	Root	FW	-	-	-	-
		TWW	-	-	-	1.0 ± 0.1
	Stem/Stalk	FW	-	-	-	-
		TWW	-	-	-	-
	Leaf	FW	-	-	-	-
		TWW	-	-	-	-
	Fruit/Grain	FW	-	-	-	-
		TWW	-	-	-	-
Flecainide	Root	FW	-	-	-	-
		TWW	0.9 ± 0.02	-	1.3 ± 0.2	1.6 ± 0.1
	Stem/Stalk	FW	-	-	-	-
		TWW	-	-	-	-
	Leaf	FW	1.5 ± 0.33	-	1.5 ± 0.3	-
		TWW	3.1 ± 0.63	-	4.3 ± 0.9	-
	Fruit/Grain	FW	-	-	-	-
		TWW	-	-	-	-

–ECCs content below to the Limit of Quantification (LOQ).
The values reported are the mean value ± standard error (four replications).
[†] Different water sources: FW, fresh water; TWW, tertiary treated wastewater.
[††] Tomato 1 -Tomato 2: first and second processing tomato crops; Wheat 1 and Wheat 2: first and second wheat crops.

demanding crops in the Mediterranean area. Our results showed that tomato plants absorbed carbamazepine, fluconazole, and flecainide through their roots, with the highest accumulation in leaves (Table 5). Specifically, carbamazepine levels in tomato leaves were 5.4 ng g^{-1} for FW and 14.6 ng g^{-1} for TWW (means of the two cycles). The fluconazole content in leaves was the highest (21.1 ng g^{-1} and 51.5 ng g^{-1} for FW and TWW, respectively), while the flecainide leaves content was the lowest (1.5 ng g^{-1} and 3.6 ng g^{-1} for FW and TWW, respectively).

The accumulation of ECCs in the tomato leaves under TWW treatment was higher in the second tomato cycle compared to the first (Table 5).

In a pilot-scale study in southern Italy, Denora et al. (2023) found that irrigation of processing tomatoes with tertiary wastewater spiked with 200 and 600 μg L^{-1} of 10 selected contaminants, including carbamazepine, fluconazole, climbazole, and flecainide, resulted in significant absorption of these contaminants by the plants. The accumulation in the plant was particularly significant in the spiked effluent with 600 μg L^{-1}, with leaves, roots, and fruits showing high contents. However, the study did not detect any climbazole and fluconazole in the tomato fruits, while the carbamazepine content was primarily found in leaves.

Differences between our findings and those of Ben Mordechay et al. (2018) and Denora et al. (2023) are likely due to the different tomato types (fresh *vs* processing), different experimental conditions (greenhouse *vs* open field) and different concentrations of ECCs applied.

To the best of the authors' knowledge, very little literature is available about the effects of ECC on wheat. Durum wheat, a typical Mediterranean crop, is traditionally cultivated in rainfed conditions, making this topic relevant particularly since durum wheat is often cultivated following high water -demanding crops, like processing tomatoes. In the first durum wheat cycle, in which no irrigation was applied, the content of ECCs was always under their quantification limit for all the plant's parts. This highlights that the content of ECCs in the soil from under the previous processing tomato crop, was insufficient to trigger uptake into the wheat roots and translocate to other parts (stalk, leaves, and grain). In contrast, during the second cycle with an irrigation of 1100 m^3 ha^{-1} of irrigation, low quantities of climbazole, venlafaxine, and flecainide were detected in the roots, but none were translocated to the leaves or grain.

4. Conclusion

Among the 22 ECCs analyzed, 17 were detected in the TWW used for crop irrigation, while only 8 were found in the corresponding irrigated soil (clarithromycin, carbamazepine, fluconazole, climbazole, flecainide, sitagliptin, and telmisartan). Notably, the application of TWW

resulted in a marked accumulation of carbamazepine, sitagliptin, flecainide, and clarithromycin in the soil throughout the two tomato-wheat succession cycles, highlighting their potential to persist in agricultural systems. Additionally, the half-life (DT_{50}) values of these contaminants varied from those reported in previous studies, likely due to the specific environmental conditions of our semi-arid study site. In terms of plant uptake, carbamazepine, fluconazole, and flecainide were detected in tomato leaves, stems and roots, while climbazole, flecainide, and venlafaxine were quantified only in the roots of durum wheat. Notably, no ECCs were detected in the edible portions of either crop during the course of the two-year trials, which holds important implications for food safety in the Mediterranean region, particularly for key food chains like tomato and durum wheat. Nonetheless, further research is necessary to deepen our understanding of ECC transport, uptake, and metabolism mechanisms within soil-plant systems under field conditions.

CRediT authorship contribution statement

Sapia Murgolo: Writing – original draft, Methodology, Formal analysis, Data curation. **Francesco De Mastro:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Gennaro Brunetti:** Writing – review & editing, Supervision, Resources, Methodology, Funding acquisition, Conceptualization. **Michele Perniola:** Writing – review & editing, Writing – original draft, Methodology, Conceptualization. **Michele Denora:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Federica Carucci:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Data curation, Conceptualization. **Anna Gagliardi:** Writing – original draft, Resources, Investigation, Data curation. **Marcella Michela Giuliani:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Giuseppe Gatta:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Cristina De Ceglie:** Writing – original draft, Investigation, Formal analysis, Data curation. **Alfieri Pollice:** Writing – review & editing, Writing – original draft, Methodology, Funding acquisition, Conceptualization.

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.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.agwat.2025.109305.

Data availability

Data will be made available on request.

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