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Linking conventional activated sludge treatment plant performances for micropollutants removal to environmental risk and SimpleTreat model assessment

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Abstract

The attention to the contaminants of emerging concerns or micropollutants is continuously rising, also stimulated by the new initiatives at European level. The present study focuses on the removal of target micropollutants in a conventional activated sludge wastewater treatment plant which is the most common system and considered a source of micropollutants to the environment. The aims were to evaluate the removal efficiency of different stages of the wastewater treatment plant and to conduct the Environmental Risk Assessment on the final effluent. As indicated by the European's guidelines on Environmental Risk Assessment, the SimpleTreat4.1 model was applied to this purpose: different values of the biodegradation constant, which represents the key factor for modelling, were applied, and the effects on the quality of prediction were evaluated. The evaluations were carried out thorough 3-year monitoring activity in a full-scale wastewater treatment plant on 10 micropollutants belonging to the classes of illicit drugs, pharmaceuticals and psychoactive. The model was found statistically not satisfactory for most of the investigated micropollutants. A better prediction was obtained when the biodegradation constant was calculated based on the full-scale data. Nonetheless, the results obtained in terms of risk were considered acceptable and comparable among each other.

Graphical abstract
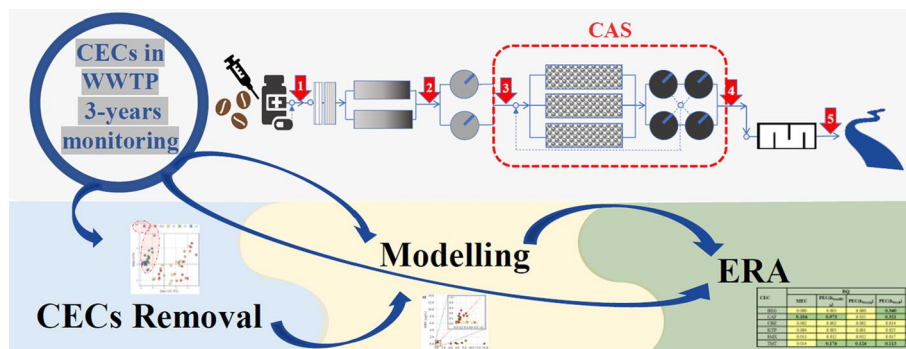
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Introduction

Contaminants of Emerging Concern (CECs) are a wide range of chemical compounds and their transformation by-products, either natural or synthetic, belonging to different

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classes such as pharmaceuticals and personal care products (PPCPs), endocrine-disrupting chemicals (EDCs), persistent organic pollutants (POPs), veterinary medicines, nanoparticles, microplastics, antibiotic resistant bacteria (ARB), antibiotic resistant genes (ARG) and, more recently, the SARS-CoV-2 virus (Chen et al. 2022; Brack et al. 2022).

The sources and routes of release of CECs in the aquatic environment are numerous. Among the point sources, the treated and untreated sewage (from combined and separate systems) is considered as the main responsible of CECs release in the environment. Indeed, CECs are present in the sewage as a consequence of human consumption and excretion; when the wastewater passes through the conventional wastewater treatment plants (WWTPs) for domestic sewage, they are not completely removed since the processes here present are designed and operated to remove other contaminants, such as suspended solids, nutrients and carbon compounds (Lautz et al. 2017; Borzooei et al. 2019; Kumar et al. 2022; Di Marcantonio et al. 2023). The European Parliament has started addressing the CECs in the wastewater, by issuing several measures from the Water Framework Directive to daughter directives such as 2008/105/EC and 2013/39/EU (The European Parliament and the Council of the European Union 2000; The European Parliament 2008; The European Parliament and the Council 2013).

The growing significance of CECs is not only within the scientific community but also among the general public and regulators (Dulio et al. 2020; Verlicchi et al. 2023). This increased attention is evident in the revision of the Urban Wastewater Treatment Directive (UWTD) and the introduction of a new Regulation outlining minimum water reuse requirements (The European Parliament and the Council of the European Union 2020; European Commission 2022a). The revised UWTD mandates additional treatments for urban wastewater, targeting a removal rate of over 80% for at least six specified substances, including carbamazepine, which is also an object of the present investigation (European Commission 2022b).

The operation of the WWTPs is facing an increasing complexity due to the effects of climate change, more stringent limits on the treated effluent to comply with, new contaminants to address such as CECs and rising energy costs. To cope with these new issues, the mathematical modelling represents a flexible tool for researchers and operators for the analysis and prediction of the behaviour of WWTPs under different operative and pollutant conditions (Pomiès et al. 2013; Delli Compagni et al. 2020). Both static and dynamic models might be used for this purpose. Even though they are based on the same mass balance equations; however, the aim of the user affects the model selection. For instance, the static models are limited by the regime type and usually are more suitable for the permanent regime simulation. On the other hand, dynamic models give better results in terms of

temporal variations of the influent pollutant concentration; however, they need more calibration data.

One type of the extensively employed models within this domain is represented by the Activated Sludge Models (ASMs) (Henze et al. 2015), which were built to simulate the behaviour and removal of traditional contaminants, such as organic carbon, nitrogen species and phosphorous. Recently, these models were updated to incorporate also the removal of xenobiotic compounds including pharmaceuticals (Li et al. 2023). However, numerous challenges persist in achieving a satisfactory model performance: a particular concern regards the influence of the operational parameters of WWTPs, which were proven to be of high relevance for CEC removal, and their interaction with specific kinetics processes strongly linked to the physicochemical characteristics of the contaminants (Gabrielli et al. 2022). Consequently, also due to the complexity of the characteristics of these contaminants, uncertainties continue to persist in modelling the fate, effects as well as transformation pathways and their products. In fact, it is worth noting that transformation products might exhibit higher ecotoxicity than their parent compounds, underscoring the pivotal importance of their inclusion within the modelling framework (Pomiès et al. 2013). Negative removal efficiencies have been observed at the full-scale for some CECs, e.g. for oxazepam, carbamazepine, sulfamethoxazole, trimethoprim, due to transformation products generation and/or parent compounds recombination, which are difficult to be simulated by the available models (Verlicchi et al. 2012; Di Marcantonio et al. 2020, 2021).

Modelling is of paramount importance also for the environmental risk assessment (ERA), which is recognized as a necessary tool to define the requirements to be achieved with the treatment in order to protect the environment from the effects of contamination (Brack et al. 2017). ERA process involves the evaluation of the physicochemical properties of the active substance to determine its fate and toxicity in a specific environment. A reference guideline for ERA was provided by the European Medicines Agency (EMA) in 2006 and then revised in 2018: "Guidelines on the Environmental Risk Assessment of Medicinal Products for Human Use" (European Medicines Agency 2018). This process comprises two key stages, i.e. Phase I and Phase II, to calculate finally the value of the risk quotient, RQ, as the ratio between the predicted (PEC) or measured (MEC) environmental concentration and the predicted no-effect concentration (PNEC). To date, SimpleTreat 4.1 model, developed by the Dutch National Institute of Public Health and the Environment for the chemicals (RIVM), is recommended for the prediction of chemical removal in WWTPs within the European regulatory context (European Medicines Agency 2018). It is also mentioned by the Registration,

Evaluation, Authorization and Restriction of Chemicals Legislation (REACH) for the Biocidal Products Regulation (BPR) and active pharmaceutical ingredients evaluations. The model simulates a wastewater treatment plant composed by a primary clarifier, an aerobic activated sludge tank followed by a secondary clarifier; the flux of chemicals is simulated in water, air and solid media (i.e. sludge). The model is considered suitable for estimating the effluent concentrations based on the actual WWTP conditions, even when scarce information are available (Lautz et al. 2017). However, empirical evidence suggests that simple models, like SimpleTreat, lack the necessary complexity to accurately simulate complex processes, such as deconjugation, which might occur within the plant (Douziech et al. 2018).

The present study focuses on the removal of target CECs in a Conventional Activated Sludge Process (CAS) of a WWTP in Central Italy for the Environmental Risk Assessment of the final effluent by following the EMA's guidelines. A 3-year monitoring activity (2019, 2020 and 2021) was carried out on 10 CECs belonging to the classes of illicit drugs, pharmaceuticals and psychoactive substances (European Commission 2019). The results from the full-scale investigation were compared with those provided by the application of SimpleTreat 4.1 model as suggested by the reference guidelines for ERA. The modelling procedure focused on the effects of the selection of the biodegradation rate constant on the quality of prediction of the effluent concentrations. The main novelty was the evaluation of the model through data from a long monitoring activity at a full-scale and the effects of the value of the biodegradation constant on the quality of prediction of each of the target CECs, considering the options proposed by the literature, OECD and historical data from the real plant's operation. Additionally, only few studies have been published about the validation of SimpleTreat, although it is suggested at EU level for the estimation of data need for environmental risk assessment (Fauser et al. 2003; Kah and Brown 2011; Lautz et al. 2017).

Materials and methods

Wastewater treatment plant and monitoring campaign

The WWTP object of the study serves a highly urbanized area in the Center of Italy. The authorized treatment capacity is 780,000 PE, corresponding to an average flow rate (Q_{WWTP}) of 2.9 m³/s. The treated final effluent of the plant is released into a surface water body with an average annual flow rate (Q_{rec}) of 165 m³/s. The plant is composed by two parallel identical lines. Each of them has a conventional water line layout (as shown in Fig. 1) made up by: pre-treatment consisting of bar screening and degreasing–degritting tanks, primary settlement tanks, secondary treatment by aerobic activated sludge reactors followed by secondary settlement tanks. Final disinfection is achieved by sodium hypochlorite addition (according to local legislation, it is operated only during the seaside season, i.e. from May to September). The average hydraulic retention time (HRT) of the plant is $\Theta_H = 11$ h. The present study focused on materials and methods, which has the more recent aeration system.

The target contaminants of the study were 10 CECs: cocaine (COC), methamphetamine (MET), benzoylecgonine (BEG), lincomycin (LCN), trimethoprim (TMT), sulfamethoxazole (SMX), sulfadiazine (SDZ), carbamazepine (CBZ), ketoprofen (KTP) and caffeine (CAF). Furthermore, 6 traditional water quality parameters (WQPs) were also monitored: total suspended solids (TSS), chemical oxygen demand (COD), ammonia and nitrate nitrogen (NH_4^+-N and NO_3^--N, respectively) and total phosphorous (P_{tot}).

The monitoring campaign was carried out along three years (2019, 2020 and 2021) according to the following schedule:

- The first phase was conducted in July 2019 and performed on two different days: at the beginning of the week (Monday) with the aim of assessing possible effects of the weekend activities of the population served by the plant, and at the mid-week (Wednesday) to investigate
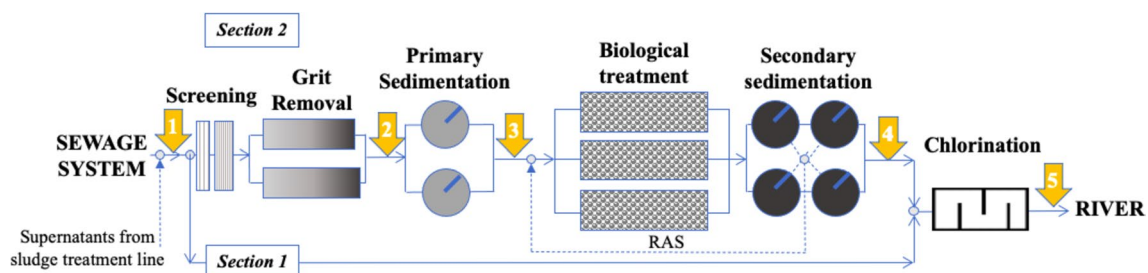

Fig. 1 WWTP layout and sampling points in 2020: (1) IN, (2) PRE, (3) PT, (4) ST, (5) CL

the occurrence and hourly and daily variability of CECs concentrations. Hourly samples were collected from the influent and effluent of the WWTP (i.e. points 1 and 5 of Fig. 1) along the day, using an auto-sampling device. Then, the samples were mixed two by two to create two-hour composite samples. During this phase, it was decided to consider only two representative CECs (i.e. CBZ and BEG) to perform a clear and simple analysis of the effects of the behaviours and habits of the population on the CECs load released to the sewage and then entering the plant with the wastewater. Along with CBZ and BEG were also measured COD, TSS and NH_4^+-N. CBZ and BEG were firstly chosen as target CECs, based on previous studies in the same geographical area (Di Marcantonio et al. 2020, 2021, 2023), because: (1) they have shown to be always present in the influent to the plants; (2) they possess completely dissimilar physicochemical characteristics and therefore are subjected to different removal and transformation processes; and (3) they are generated by different types of anthropogenic activities which affect the load released into the sewage networks and entering the plants. Based on these features, they were considered adequate to achieve the purposes of this stage o of the study.

- The second phase was conducted between June and December 2020 for a total of 11 sampling days. Grab samples were collected in the day when the highest influent concentrations occurred based on the results of the first phase. All the 10 CECs and the 6 WQPs abovementioned were monitored in the influent to the plant and in the effluent of each treatment unit in order to identify that one mostly contributing to the removal. In detail, the concentrations were monitored in the following points, as highlighted in Fig. 1: (1) influent to the plant, (2) effluent from pre-treatment (PRE), (3) effluent from primary settlement (PT), (4) effluent from secondary treatment (ST) and (5) effluent from chlorination (CL).

- The third phase was conducted in 2021, collecting one 24-hourly composite sample every month from the influent and effluent to the WWTP (i.e. 12 sampling days in points 1 and 5 of Fig. 1). The sampling was carried out in the day of the week when the highest influent concentrations occurred based on the results of the first phase.

- All samples were collected in Nalgene bottles, immediately transported to the laboratory and then stored at 4 °C until analysis.

Analytical methods

The water quality parameters were measured by following the standard methods: TSS through APAT CNR IRSA 2090 B Man 29/2003, COD through APAT CNR IRSA 5135 Man 29/2003, P_{tot} through M.U. 2252:08/1, $NH_4^+ - N$ and

$NO_3^- - N$ through Standard Methods 4500 2, 4500H and 4500 1, respectively (APAT IRSA-CNR 2003; APHA 2017).

The CECs were quantified using ultrahigh performance liquid chromatography coupled with tandem mass spectrometry. The analytical method was specifically developed by the research group in previous studies and validated by ACCREDIA for most analytes (Di Marcantonio et al. 2021). CECs standard solutions and internal standards Cocaine-d3 and carbamazepine-d10 were purchased from Sigma-Aldrich Company (Gillingham, UK) each at a concentration of 100 μg/ml in methanol. The Minimum Reporting Levels (MRL) were posed equal to the following values: 0.05 μg/L for KTP, 0.1 μg/L for CAF and 0.01 μg/L for the other contaminants.

SimpleTreat 4.1 modelling

SimpleTreat 4.1 is a steady-state multimedia box model which is used to estimate the PEC values for the environmental risk assessment of CECs in a wastewater treatment plant. The input data for the model are: the physicochemical properties of the contaminant, which were obtained from the literature; the operative conditions of the plant, provided by the managing company; and the biodegradation rate constant (k_{bio}) and the parameters which describe the emission scenario from the sewage network. Among the model outputs, the dissolved effluent concentration (μg/L) was selected for validation. The procedure focused on the effects of k_{bio} selection on this output. Particularly, three different types of k_{bio} were applied for each contaminant: (a) the value proposed in the literature ($k_{bio,lit}$), (b) the value experimentally determined based on the data collected during the 2020 monitoring campaign, calculated by Eq. 1 ($k_{bio,exp}$), (c) the value selected from the list provided in the SimpleTreat database and referred to OECD standard procedures ($k_{bio,OECD}$). For the $k_{bio,lit}$ and $k_{bio,exp}$, the temperature was set equal to 288.15 K (15 °C), as for the plant. More details about the model application procedure are reported in Supplementary materials (Section S.M. 1). The data from the third phase of the investigation (i.e. 2021) were used for the modelling with SimpleTreat 4.1 and to perform the environmental risk assessment since composite samples are considered more appropriate for this evaluation.

Calculation methods

The frequency of detection (Fd) and removal efficiency (R) were calculated as reported in Di Marcantonio et al. (2021).

The data of the second phase (2020) were processed also through principal component analysis (PCA) to obtain a further insight into the effects of the different treatment stages. The PCA was performed by applying the R package "FactoMineR" (Lê et al. 2008).

The experimental biodegradation rate constant, $k_{bio,exp}$, was calculated by applying the first order kinetic equation to the data of the second phase 2020 monitoring (Metcalf & Eddy 2015) (Eq. 1 below). The concentrations measured for each sampling day in the influent and effluent (C_0 and C_e, corresponding to points 3 and 4 of Fig. 1, respectively) and the hydraulic retention time of the biological reactor (θ_H) (equal to the volume of the reactor, V, divided by the average daily influent flow rate, Q) were used for the purpose:

$$k_{bio,exp}[1/h] = \frac{1}{\theta_H} \times \left(\frac{C_0}{C_e} - 1 \right) \tag{1}$$

The model's validation was carried out through a statistical comparison between the effluent concentrations provided by the model with the three values of k_{bio} as above outlined and the real data of the third monitoring phase of the study. Two formulations of the test are available and therefore used depending on the homoscedasticity of the groups, which were verified with the F-test. When the normality was not verified, the corresponding nonparametric test, i.e. the Wilcoxon test, was used. The Rpackage "stats" was applied to perform the aforementioned statistical tests (R Core Team 2021).

Environmental risk assessment (ERA)

The ERA was performed following the procedure proposed by the Environmental Medicine Agency (European Medicines Agency 2018). The risk quotient (RQ) was calculated for each contaminant using the following equation:

$$RQ[/] = \frac{(MEC \text{ or } PEC)/D}{PNEC} \tag{2}$$

where MEC and PEC represent the measured and the predicted environmental concentration, respectively, obtained through SimpleTreat, PNEC is the predicted no-effect concentration and D is the dilution factor of the treated effluent flow rate with the receiving river flow rate. If the RQ is < 1, the contaminant is unlikely to represent a risk to surface water. As PNEC, the lowest values found in the scientific literature for freshwater species were used (mainly collected from the open-access NORMAN Database System) (Norman Network 2022). They were: 2.46 for COC, 2.33 for BEG, 2.30 for MET (van der Aa et al. 2013), 0.03 for KTP, 2.00 for CBZ, 0.60 for SMX, 0.16 for TMT, 3.95 for LCN, 1.00 for SDZ and 0.10 for CAF.

The ERA was carried out on the data from 2021 (third phase of the study), using the 95th percentile of the effluent concentration (for both MEC and PEC), to consider a precautionary contamination scenario. The effluent concentrations were reduced by the dilution factor to consider the actual concentration of exposure for the ecosystem after

mixing of effluent and receiving river. The suggested value of D by EMA is equal to 10 (European Medicines Agency 2018); however, a site-specific estimation of D was also carried out to obtain a more accurate assessment of the environmental risk as already highlighted by previous works (Abily et al. 2021; Di Marcantonio et al. 2023). The site-specific D value was calculated as the sum of the average river flow rate (Q_{rec}) and the average WWTP effluent flow rate (Q_{WWTP}), divided by the WWTP effluent flowrate (European Commission 2003). The ERA was performed only for those CECs detected in more than 10% of the effluent samples, to have statistical reliability of the results.

Results and discussion

Hourly and daily variation of the concentrations

Figure 2 shows the statistical variation of BEG and CBZ in the influent and effluent of the WWTP in Monday and Wednesday.

Figure 2 highlights only a slight change in the influent and effluent concentrations between Monday and Wednesday for both CECs. In the case of BEG, this can reveal a pretty constant use during the week of COC which is its parent compound. Indeed, BEG can be excreted by the human body up to 96 h after consumption of COC (van Nuijs et al. 2009a, b). It is also reported the existence of a delay time between the excretion of pollutants to their occurrence in a WWTP, which depends on the characteristics of the sewage network (Metcalf & Eddy 2015). Therefore, the concentrations detected in a given day of the week can be attributed to the consumption of the substance even a few days earlier (Zuccato et al. 2008; van Nuijs et al. 2009a, b). The effluent BEG concentrations were lower than the LOQ, thus indicating a good removal achieved by the plant.

For CBZ, the similar concentrations in the influent of Monday and Wednesday confirm the non-occasional use of this pharmaceutical. The higher effluent concentrations than in the influent, observed on both Monday and Wednesday, have been previously reported in the literature and attributed to complex re-conjugation reactions occurring along the treatment train (Kumar et al. 2022). The CBZ occurred in all the samples ($F_D = 100\%$) as also reported by the OECD 2017 (Organization for Economic Cooperation and Development) (OECD 2020). The constant presence in the influent is documented as a consequence of the increasing consumption of the psychiatric drugs occurred in the last years (Paíga et al. 2019).

The hourly trend of influent concentration of BEG at the beginning of the week (Monday), reported in Figure S.M.1, shows a peak of 3.06 µg/L in the evening (7–9 pm) and a slight peak of 2.64 µg/L during the late night (3–5 am). This

Fig. 2 Daily variation of BEG and CBZ concentrations
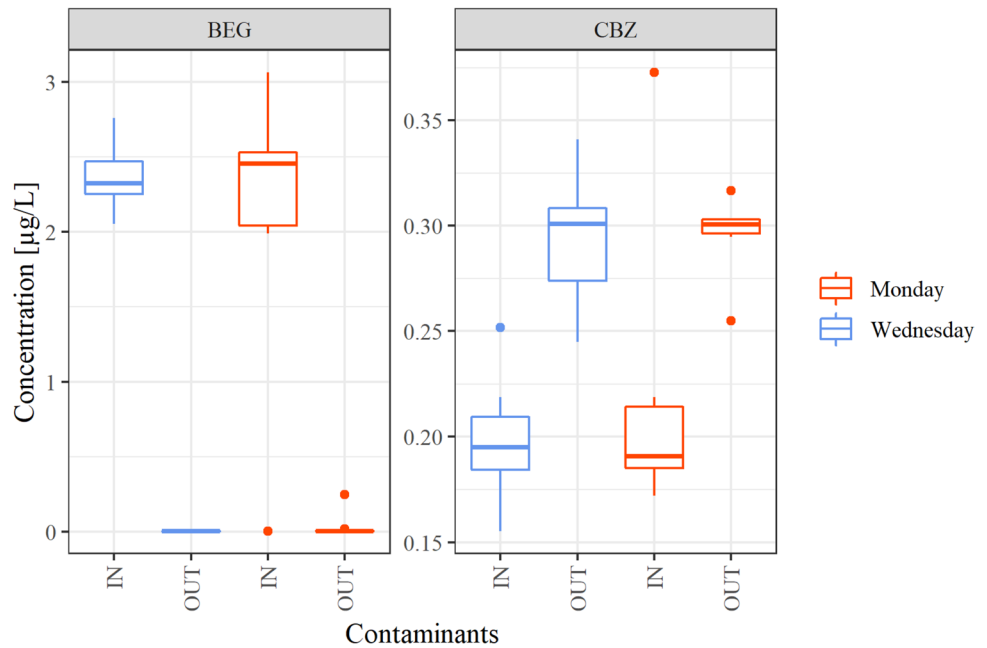
pattern was also observed in the COD concentration during the same day. The hourly trend becomes pretty constant in the middle of the week (Wednesday). As regards CBZ, the trends does not show any significant variation throughout the day and the week.

The low variation observed can be linked to the equalization effect due to the sewage network on the contaminant load in the wastewater before this reaches the inlet section of the plant, particularly when the concentrations are so low as in the case of CBZ.

Concentrations and removals along the WWTP

Influent concentrations

Table S.M.7 shows minimum, maximum and median CECs concentration measured in the different sampling points of the WWTP (i.e. IN, PRE, PT, ST and CL) along with the frequency of detection (F_D) during the second phase of the study. Table 1 lists the corresponding removal efficiency calculated based on the influent concentration to the plant

and the effluent from each treatment stage. Figure S.M. 2 highlights the relative statistical variation as boxplot.

All the CECs were detected in the influent to the plant (F_D always above 73%), whereas 8 contaminants out of 10 were also found in the effluent (only MET and SDZ gave F_D values of 0%). CAF was the contaminant measured at the highest concentration in the influent (53.69 μg/L as maximum value), followed by BEG and KTP (3.56 μg/L and 3.45 μg/L as maximum values, respectively). CAF is a psycho-active substance mainly consumed in coffee and related products and very widely used worldwide including Italy (Raj et al. 2021). Gracia-Lor et al. (2020) found 134.6 ± 43.6 mg/day/person as mean consumption. Human excretion through urine and coffee waste are considered as primary sources of CAF in the sewage (Raj et al. 2021). The unmetabolized CAF from human body is equal to 3–5% of the total intake, while the remaining fraction is released unchanged.

The higher influent concentrations of BEG than COC can be explained by the fact that the latter is largely excreted in urine as BEG (35–54%) and only a small fraction (1–9%) as an unmodified substance (Van Nuijs et al. 2009a, b; Ratola et al. 2012).

Table 1 Median removal efficiency (%) after each treatment stage

Treatment stage	BEG	COC	MET	SMX	TMT	LCN	SDZ	KTP	CBZ	CAF
PRE	5	2	10	2	− 3	− 14	8	11	5	13
PT	11	− 16	22	− 2	14	− 12	4	25	6	27
ST	99	96	91	28	46	− 40	70	96	2	99
CL	100	97	91	64	63	69	78	94	3	100

The values underlined are above the required removal efficiency sets by the proposal of the new UWTD (i.e. ≥ 80%)

SMX, CBZ, COC and TMT were detected at lower concentrations in the influent, with maximum values equal to 0.78 µg/L, 0.28 µg/L, 0.61 µg/L and 0.22 µg/L, respectively. The occurrence of SMX in wastewater is linked to its high use in clinical treatment: about 15% of this contaminant is excreted by the human body as an unaltered drug (Gao et al. 2012). TMT is often recommended in combination with SMX for the treatment of several diseases with a ratio of 1:5 (Thiebault 2020): this explains the higher concentration found for SMX as compared to TMT. The presence of CBZ, an antiepileptic drug, is related to the large quantities consumed worldwide, with an estimated growth from 742 tons in 1995 to 1214 tons in 2015 (Feijoo et al. 2022). After its oral administration, 72% is absorbed by the human body; up to a 99% is metabolized, while the residual is discharged into the sewage system (Feijoo et al. 2022).

The lowest concentrations in the influent samples were found for MET (0.11 µg/L as maximum), LCN and SDZ (0.04 µg/L and 0.05 µg/L as maximum, respectively). LCN and SDZ were revealed in the influent samples with F_D values above 82%, which can be explained by their widespread use. The presence of antibiotics in wastewater is also linked to the disposal of unused and expired drugs (Tran et al. 2016).

About KTP (anti-inflammatory drug), the high concentrations found in the wastewater are likely due to the elimination of 80% as an unmodified compound after consumption (Kermia et al. 2016).

The concentrations measured in the plant and shown in Table S.M.7 are close to the ranges reported by other studies of the scientific literature (Di Marcantonio et al. 2021; Khan et al. 2022).

Below a detailed analysis of the values was found in the different sampling points for each class of CECs.

In 2021, the influent concentrations for most of the contaminants were lower than in 2020 (data reported in Supplementary Materials in Table S.M.8). In both years, all the target CECs were detected in the influent at a frequency above the 50%, as also reported in a previous study by the same research group (Di Marcantonio et al. 2022). In the effluent, the frequency of detection in 2021 increased for every CEC except for COC.

Six were the CECs detected in around 50% of effluent samples of both years, i.e. BEG, KTP, SMX, TMT, CAF and CBZ. These CECs were used for model validation.

Removal by each treatment stage

Illicit drugs The median concentrations of illicit drugs did not change after PRE and PT, and the F_D values were the same as in the influent. Therefore, adsorption on suspended solids and sedimentation of solids, which are the main processes taking place through these units, are ineffective with respect to their removal. BEG was detected at a higher concentration (i.e. 2.52 µg/L) in the effluent of the pre-treatment than in the influent to the WWTP; an increase in the median concentration was also found for COC downstream PT. These behaviours can be explained by the occurrence of compounds, not monitored in the study, which are transformed back into the original compounds as a result of biological or physical–chemical reactions (Tiedeken et al. 2017). The highest decrease in the illicit drugs was due to the secondary treatment, in accordance with their chemical–physical properties: BEG, COC and MET have low octanol–water partition coefficients (log Kow equal to -1.32, 2.30 and 2.07, respectively) and a high solubility (1605 mg/L, 1298 mg/L and 13,300 mg/L, respectively, at 25 °C), which reveal a good affinity for the water phase and a higher biodegradability. In the final effluent (sampling point 5), COC and MET were found with median concentrations below MRL, while BEG was equal to 0.01 µg/L.

The highest removal efficiency, considering the entire treatment train, was recorded for BEG (equal to 100%) followed by COC and MET (97% and 91%, respectively). The disinfection unit did not contribute to the removal. These data agree with the removal efficiencies found in a previous study by the same research group (Di Marcantonio et al. 2021). It can be concluded that WWTPs equipped with the conventional activated sludge process are effective in the removal of illicit drugs.

Antibiotics Among the searched antibiotics, LCN and SDZ were found at the lowest concentrations downstream each sampling point. LCN has a hydrophilic behaviour (log Kow equal to 0.2) and can be mainly removed by biodegradation (Gao et al. 2012; Tran et al. 2016).

The low log Kow (equal to 0.73) of TMT would figure out a higher ease to biodegradation (Tran et al. 2016). Indeed, Michael et al. (Michael et al. 2013) indicated that nitrifying microorganisms appeared to be able to degrade TMT. However, in the present study only a slight decrease in the median concentration of TMT was observed after ST and a F_D equal to 100% was measured in the final effluent, which indicated an incomplete removal in the WWTP. No further reduction was observed through CL. Therefore, TMT can be considered among the persistent CECs (Yang et al. 2017).

The data showed a slight decrease in SMX after the activated sludge biological treatment and a further reduction downstream CL. It must be considered that about 50% of SMX is metabolized to N 4-acetylsulfamethoxazole which can be reconverted to the parent compound during the biological treatment (Gao et al. 2012). Its chemical–physical properties such as log Kow (equal to 0.89) indicate a limited affinity for suspended solids (Thiebault 2020). SMX is also one of the most frequently found antibiotics in the effluents

of WWTP. These data are in accordance with the findings of the present study (F_D was equal to 100%) (Yang et al. 2017).

Total removal percentages obtained in the WWTP for these 4 antibiotics ranged from 63 for TMT to 78% for SDZ. The pre-treatment units did not affect the removal, except for TMT which was reduced by 14% in the PT. The ST contributed differently on the removal, i.e. from 28 for SMX up to 46% for TMT and to 70% for SDZ, as reported in Table 1.

The scientific literature shows conflicting results for antibiotics. This can be due to both the wide range of influent concentration, because of varying consumption habits, and also the type of wastewater treatment plant. It is also reported that antibiotics in wastewater can induce toxic or inhibitory effects on bacteria of activated sludge by altering the microbial community, resulting in reduced removal efficiency (Yang et al. 2017). The low removal may be also due to the complex processes taking place during the treatment which are responsible of reconversion back into the parent compounds in the final effluents (Spataro et al. 2019).

Other pharmaceuticals and caffeine PRE and PT caused only a minimal reduction of KTP concentration, whereas disinfection did not provide any effect. The highest removal was achieved in the ST. Indeed, this behaviour can be attributed to its log Kow (equal to 3.12), proving a moderately hydrophilic behaviour and low affinity for sludge adsorption (Aydin et al. 2019). The removal rate of KTP increased from 25% downstream PT to 96% after ST. This finding agrees with other studies. For instance, Palli et al. (2019) measured removal efficiencies ranging between 78 and 93%. Disinfection, on the other hand, does not seem to be responsible of any improvement. The highest contribution to removal can be considered due to biodegradation, whereas adsorption on the sludge has a negligible effect as explained by the pKa value equal to 4.5 (Aydin et al. 2019).

A low reduction of CAF concentration was observed after PRE and PT. Differently, the biological process produced its significant decrease. Indeed, the removal increased from 27 after PT to 99% after ST, reaching 100% downstream CL. CAF is moderately polar (log Kow equal to -0.07) which makes it soluble in water and in polar organic solvents (Buerge et al. 2003).

CBZ concentration persisted almost at the same level in the effluent of each treatment stage, thus confirming the recalcitrant nature of this contaminant as widely reported (Palli et al. 2019). The low removal efficiency can be explained by its water-soluble nature: it has a low value of the solid–liquid partition constant (K_D of 1.2 L/Kg$_{SS}$) and a low value of log Kow (of 2.45). The occurrence of CBZ in the effluent from the plant can induce deleterious effects (changes in the antioxidant enzyme system and gene expression) in algae, crustaceans and fish (Zhang et al. 2008; Trombini et al. 2019).

Principal component analysis (PCA)

To better elucidate the effects of the different treatment stages, the PCA was applied to the concentrations of all the monitored compounds (i.e. CECs and WQPs) in all the sampling points (Fig. 3a).

The two main dimensions covered most of the variance of the data (i.e. 62.5%), indeed they can be used for the following evaluations. The individual plot (Fig. 3a) shows that the samples collected from the influent to the plant, from the effluent of the preliminary treatment (PRE) and of the primary settlement (PT) are heterogeneously distributed within the I, IV and III quadrants of the graph: this confirms the large variability of the concentrations in these sampling points which cannot be one from another. By contrast, the samples collected after the secondary treatment (ST) were grouped in the II quadrant with a significantly reduced variability. The same can be assessed for the samples collected downstream the chlorination (CL), i.e. the final effluent of the plant. This trend proves that the secondary treatment is responsible for the main removal of the monitored compounds and is able to achieve comparable concentrations among the different sampling days even if the influent is characterized by a high variability. This behaviour was also observed in a previous study on a WWTP made by a pre-denitrification process in addition to carbon oxidation and nitrification, as the WWTP monitored here (Di Marcantonio et al. 2021). Therefore, comparison among the two studies suggests that the aerobic biological treatment, which is present in both treatment layout, is the main responsible of the removal of the mix of target contaminants.

Due to the high relevance of the biological compartment, a further PCA was performed on the samples collected in the influent and effluent of this stage. The aim was to find out a possible correlation between the WQP removed by the biological process (i.e. COD, $NH_4^+ - N$ and P_{tot}) and the CECs considered biodegradable (i.e. removal in the biological reactor > 50%: BEG, COC, MET, SDZ, KTP, CAF). The results of this PCA, reported as correlation circles in Fig. 3b, show a very high direct correlation of KTP, CAF, BEG with $NH_4 + $-N and to a less extent with COD. A similar correlation was also observed in a previous study carried out on the influent and effluent of 8 WWTPs having different characteristics (Di Marcantonio et al. 2023).

Modelling activity

Biodegradation rate constant

This phase of the study aimed at evaluating how the selection of the value of the biodegradation rate constant, k_{bio}, can affect the results provided by the model (reported in Table 2). As described in details in previously, the values
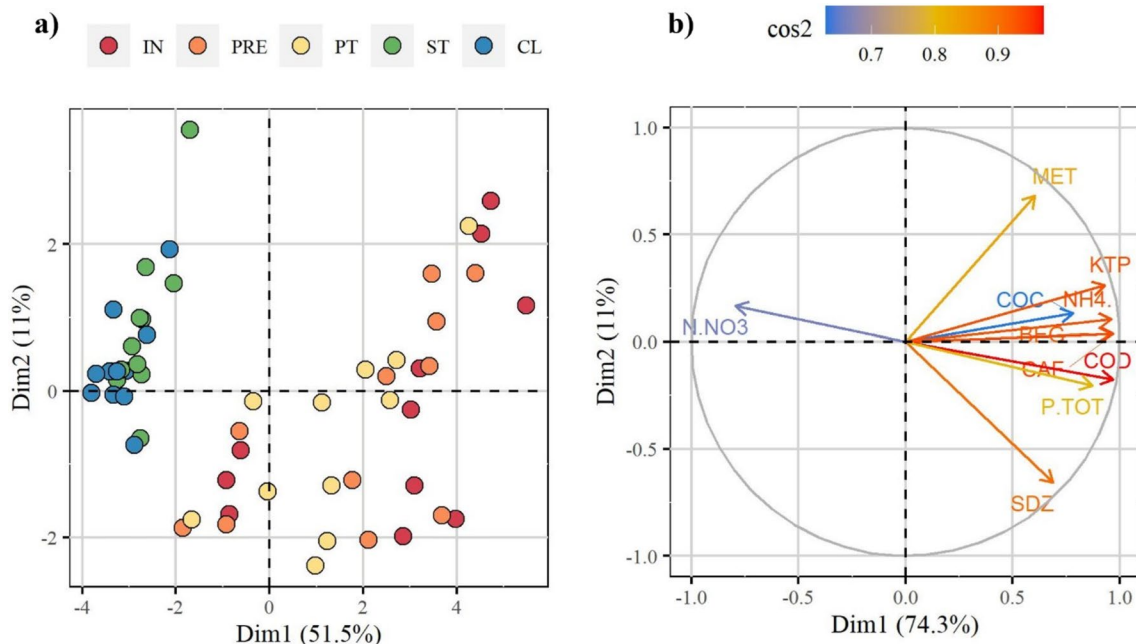
Fig. 3 PCA: **a** individuals plot of CECs and WQPs concentrations in all sampling points, **b** correlation cycle of influent and effluent concentrations of the secondary treatment for CECs here removed by more than 50%

Table 2 Comparison of the k_{bio} values (1/h) from: 2020 full-scale monitoring ($k_{bio,exp}$), scientific literature ($k_{bio,lit}$) and corresponding OECD categories ($k_{bio,OECD}$). n.a. stands for not available

CEC	$k_{bio,exp}$	$k_{bio,lit}$		$k_{bio,OECD}$
BEG	38.91	0.28	(Chiavola et al. 2019)	1 (readily biodegradable fulfilling)
CBZ	0.0	0.01	(Urase and Kikuta 2005)	0 (not biodegradable)
COC	5.49	n.a		1 (readily biodegradable fulfilling)
KTP	3.89	0.39	(Urase and Kikuta 2005)	1 (readily biodegradable fulfilling)
LCN	-0.01	0	(Bergheim et al. 2015)	0 (not biodegradable)
MET	1.14	0.04	(Boni et al. 2018)	0.3 (readily biodegradable not fulfilling)
SMX	0.08	0.07	(Plósz et al. 2010)	0.1 (inherently biodegradable)
TMT	0.08	0.22	(Xue et al. 2010)	0.3 (readily biodegradable not fulfilling)
CAF	36.94	0.38	(Xue et al. 2010)	1 (readily biodegradable fulfilling)
SDZ	0.38	n.a	0.3 (readily biodegradable not fulfilling)	

of $k_{bio,exp}$ were calculated by applying Eq. 1 to the data collected in the second phase 2020 monitoring. The values of $k_{bio,lit}$ were selected among the data available in the scientific literature and mainly obtained under laboratory conditions. The values of $k_{bio,OECD}$, reported in the third column of Table 2, were obtained by the list provided in the Simple-Treat database and referred to OECD standard procedures. Particularly, the specific value for each CECs was selected depending on the known characteristics of biodegradability of the pollutant with respect to the categories and criteria indicated by OECD, either readily biodegradable fulfilling, readily biodegradable not fulfilling, inherently biodegradable and not biodegradable (European Commission 2003).

BEG, COC, CAF, KTP and MET showed median removal in the plant of 99%, 96%, and 99%, respectively.

Therefore, they can be considered highly biodegradable using the OECD category. However, a wide difference can be observed between the values of $k_{bio,exp}$ and $k_{bio,lit}$ for all the CECs. For COC, although $k_{bio,lit}$ value is unavailable, the full-scale behaviour showed a readily biodegradability as confirmed by the high $k_{bio,exp}$ and the $k_{bio,OECD}$ category. These observations are also in agreement with previous studies (Xue et al. 2010; Boni et al. 2018).

MET, SDZ and TMT are classified as readily biodegradable not fulfilling according to OECD (European Commission 2003). However, the removal efficiency of TMT observed in the full-scale ST was lower than that of the MET and SDZ (i.e. 46% vs. 91%, 96% and 70%, respectively). The difference between the values of the biodegradation rate constant of TMT can be ascribed to the conditions used for their

determination. For instance, in the reference study by Xue et al. (2010) the biological compartment included an aerobic tank preceded by anaerobic and anoxic tanks. Since the latter compartments are known to be more effective on TMT degradation, they can be responsible of the greater overall removal rate. This explains the higher $k_{bio,lit}$ with respect to $k_{bio,exp}$ (0.22 vs 0.08 1/h). Therefore, it seems that the experimental value might fit better the specific performance of the treatment plant. This was evaluated by the application in the modelling activity.

The removal efficiencies of CBZ and LCN measured in the secondary treatment at full-scale were 2% and -40%, respectively. This is in accordance with the OECD classification which considers them as not biodegradable ($k_{bio,OECD}=0$).

SMX was classified as inherently biodegradable which is in agreement with the median removal of 28% measured at full-scale.

Comparison of measured and modelled data

The six CECs detected in more than 50% of the 2021 effluent samples were considered for model application and the environmental risk assessment. Indeed, for the scope of model validation, the $k_{bio,exp}$ used in the model was calculated based on the data collected in the monitoring carried out at the full-scale in 2020, whereas the comparison of the results obtained by the model was done with the data measured in 2021.

For each of the CECs, three values of the effluent concentration and removal efficiency were obtained by model simulation based on the different values of the biodegradation rate constant: PEC ($k_{bio,lit}$), PEC($k_{bio,OECD}$) and PEC($k_{bio,exp}$). The results are reported in detail in Table S.M.9 and Figure S.M.3 of Supplementary Materials. A

graphical representation is shown in Fig. 4 where the measured effluent concentrations (MEC) are compared with the model predicted values (PEC) for each CEC, along with the data obtained by the significance test. In the figure, the dotted red line indicates perfect model fitting and the symbols in the legends represent the significance of the difference between MEC and PEC for each CEC: $* = p$ value < 0.05, $** = p$ value < 0.01, $*** = p$ value < 0.001, $\wedge =$ no significant difference.

The SimpleTreat simulation always provided the best agreement for SMX; no matter was the value of k_{bio} used. It is worth noting that in this case the values of the k_{bio} from the different sources did not change significantly.

The quality of prediction, i.e. the number of CECs whose concentration was well simulated, improved changing the biodegradation rate constant value from $k_{bio,lit}$ to $k_{bio,OECD}$ and to $k_{bio,exp}$. In the last case, SMX, CBZ and CAF were represented with no significance difference with respect to the measured concentrations. Therefore, the value experimentally calculated for $k_{bio,exp}$ can be considered pretty suitable for predicting their concentrations in the effluent also in a different year. For KTP, a good agreement between modelled and real concentrations was achieved only using $k_{bio,OECD}$, whereas BEG and TMT behaviour were always predicted very badly. In general, it can be highlighted the wide difference of k_{bio} between the values reported by OECD and the literature for highly biodegradable CECs. This might affect negatively the quality of the prediction by the model in Fig. 4.

Environmental risk assessment (ERA)

The environmental risk assessment was finally carried out for the six modelled CECs using either the MEC values (corresponding to the 95th of the effluent concentrations
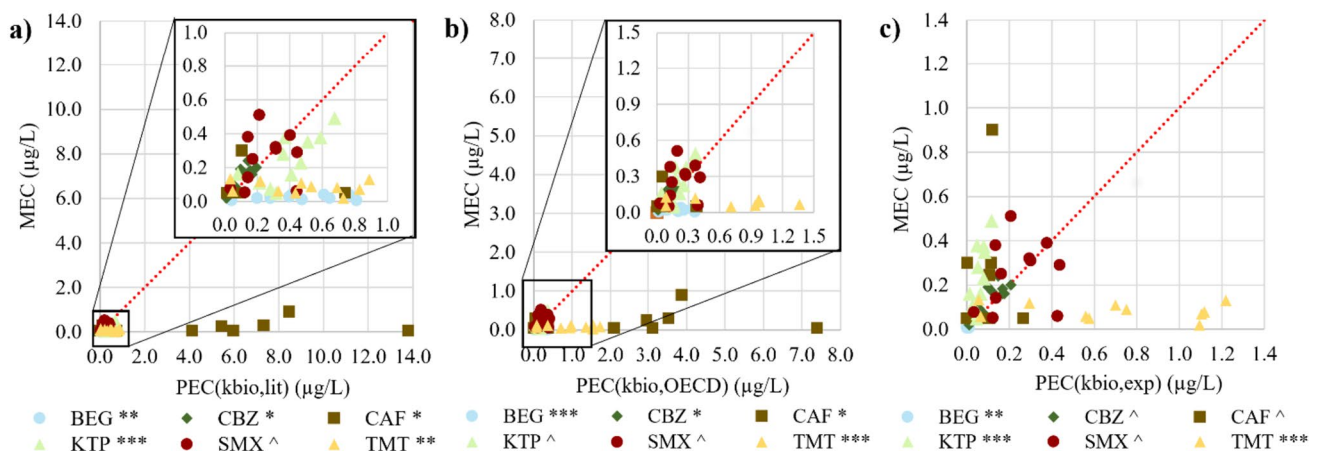

Fig. 4 Concentrations measured in the effluent (MEC) and concentrations modelled by SimpleTreat (PEC) using the different values of k_{bio}: **a** $k_{bio,lit}$; **b** kbio,OECD; and **c** $k_{bio,exp}$

measured in 2021) or the PEC obtained by using the three different values of k_{bio}(results reported in Table 3).

A low risk was found for all the CECs, except for CAF and TMT. Particularly, both MEC and most PEC gave a medium risk, still acceptable, for CAF. The risk was always medium using PEC for TMT. Comparable risks were obtained with MEC and PEC for CBZ, KTP and SMX.

Conclusion

The full-scale monitoring highlighted concentration peaks for illicit drugs (i.e. BEG) at the beginning of the week which might be a consequence of the higher consumption during the weekend. For the other CECs, there was not a significant difference between the values measured during the week and the day.

The CAS process resulted to be the most effective treatment stage within the plant for the majority of the investigated CECs: indeed BEG, COC, MET, KTP and CAF showed removal efficiency above 90%. For the other CECs, which presented a much lower removal, a slight reduction was though produced by the secondary treatment. Pretreatment and primary sedimentation as well as chlorination did not affect the concentration. The application of the PCA confirmed these trends. It also showed a relevant direct correlation between the biodegradable CECs removal and nitrification.

About modelling, it can be concluded that the application of SimpleTreat 4.1 does not seem to represent a good tool for the prediction of the effluent concentration of the investigated CECs on a routine basis. The quality of prediction slightly improved when the experimental k_{bio} was used instead of $k_{bio,lit}$ and $k_{bio,OECD}$, although the agreement was not always satisfactory. This result can be ascribed to the differences in the CECs concentration and behaviour in each plant and under real conditions (Di Marcantonio et al. 2022). Furthermore, these unsatisfactory results can be also due to the inability of the model to simulate the complex mechanisms occurring to some CECs within the treatment plant, such as back-transformation of conjugated metabolites into the parent compound or unexpected sorption, and also the variable operating conditions of the WWTPs as reported by many studies (Lautz et al. 2017; Deviller et al. 2020). Therefore, to improve the quality of prediction it would be needed to better understand the behaviour of each CECs in the activated sludge systems so as to implement the equations of the specific representative processes within the software.

Nonetheless, the current version of the model is roughly effective for the prediction of the environmental risk of most of the investigated CECs, especially when applying the experimental k_{bio}. Finally, it is important to emphasize that the environmental risk calculated under severe conditions (i.e. 95th percentile of the effluent concentrations measured and modelled) was always acceptable.

Declarations

Table 3 Environmental risk assessment for MEC and PEC obtained with the three values underlined high risk (RQ > 1), values in bold medium risk (1 > RQ > 0.1), other values low risk (RQ < 0.1)

CEC	RQ			
	MEC	PEC($k_{bio,OECD}$)	PEC($k_{bio,exp}$)	PEC($k_{bio,lit}$)
BEG	0.000	0.003	0.000	**0.340**
CAF	**0.104**	**0.973**	0.033	**0.321**
CBZ	0.002	0.002	0.002	0.014
KTP	0.004	0.003	0.001	0.025
SMX	0.013	0.012	0.012	0.017
TMT	0.014	**0.176**	**0.126**	**0.113**

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