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A year-long study of the occurrence and risk of over 140 contaminants of emerging concern in wastewater influent, effluent and receiving waters in the Republic of Ireland

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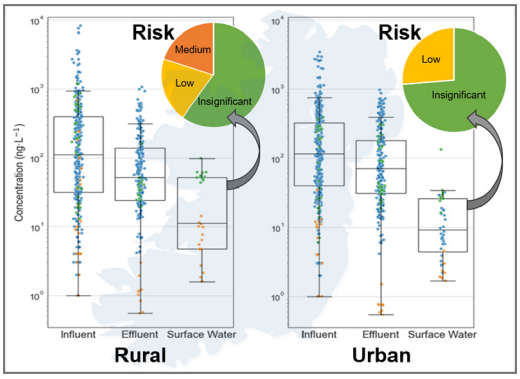
HIGHLIGHTS

- Largest monitoring campaign for 142 CECs in Irish wastewater and freshwater.
- 58 CECs detected with venlafaxine showing the highest concentration overall in influent.
- Less than ~50 % of CECs concentrations remained in wastewater effluent following treatment.
- On average, ≥93 % CEC dilution once entering the natural aquatic environment.
- Estimated risks for most CECs generally low or insignificant in Irish river waters.

GRAPHICAL ABSTRACT



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ABSTRACT

Despite being a developed country in the European Union (EU), knowledge of the nature and extent of contamination of water bodies with contaminants of emerging concern (CECs) in Ireland is limited. In this study, >140 CECs including pharmaceuticals, pesticides and personal care products were monitored in monthly samples of wastewater treatment plant (WWTP) influent, effluent and receiving surface waters at both an urban and a rural location (72 samples in total) in Ireland over a 12-month period in 2018–2019. In total, 58 CECs were detected, including several EU Water Framework Directive Watch List compounds. Of all classes, the highest concentrations were measured for pharmaceuticals across all media, i.e., propranolol in surface waters (134 ng·L^{-1}), hydrochlorothiazide in effluent (1067 ng·L^{-1}) and venlafaxine in influent wastewater (8273 ng·L^{-1}). Overall, high wastewater treatment removal was observed and a further reduction in CEC occurrence and concentration was measured via dilution in the receiving river environment. Lastly, an environmental risk assessment (ERA) was performed using risk quotients (RQ), which revealed that in surface waters, total RQ for all CECs was an order of magnitude lower than in effluents. The majority of CECs in surface waters posed a lower risk except E2 and EE2 which presented a medium risk (RQs of 3.5 and 1.1, respectively) in the rural area. This work represents the most comprehensive CEC monitoring dataset to date for Ireland which allowed for an ERA prioritisation to be performed for the first time.

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1. Introduction

Contaminants of emerging concern (CECs) have entered the environment for decades from a variety of primarily anthropogenic sources (Breton and Boxall, 2003; Oberg and Leopold, 2019). Due to their use in healthcare (e.g., pharmaceuticals), agriculture (e.g., selected groups of non-regulated pesticides), daily personal/household uses and lifestyle activities (Ng et al., 2020; Rapp-Wright et al., 2017), such contaminants can be transported into the aquatic environment where they can pose risks to aquatic ecosystems. In comparison to other European Union (EU) countries, the population of the Republic of Ireland is relatively low at 5,052,259 (2022 Census) and ranks 19th of 27 EU member states (1.1 % of total EU population) as of January 2020 (Eurostat Statistics, 2020). It has the fifth largest per capita gross domestic product in the world (The World Bank - GDP per capita, 2021) and has the highest share of population that reports being in good health in the EU (European Commission, 2019). It has growing and vibrant agricultural and industrial sectors (An Phríomh-Oifig Staidrimh (Central Statistics Office), 2020), inclusive of the pharmaceuticals industry, which is predominately based in more populated counties like Dublin and Cork. Currently, Ireland hosts manufacturing plants from 120 pharmaceutical companies, including nine of the 10 largest globally, and ~ 50 % of its exports derive from this sector (Irish Pharmaceutical Healthcare Association, 2021). Equally, there are large areas that are very rural and dominated by agricultural activity providing employment to ~167,000 people (Teagasc, 2018). Approximately 4,886,600 ha are devoted to agriculture in the Republic of Ireland (~ 70 % of total land) (Teagasc, 2018).

Wastewater treatment plants (WWTPs) have been identified as major point sources of CEC contamination via their treated effluent discharge points (Llamas-Dios et al., 2021). Many CECs survive the wastewater treatment process and, for combined systems in particular, sewer overflows of both treated and untreated wastewater have also been identified internationally as sources of aquatic CEC contamination, especially following heavy rainfall events (Munro et al., 2019). Receiving water CEC concentrations can range from ng·L^{-1} to μg·L^{-1} (Cantwell et al., 2018; Dogan et al., 2017; Letsinger et al., 2019), where CECs can have effects on living systems (Brumovský et al., 2017). In comparison to other EU countries, and despite marked rises in personal wealth and life expectancy, as well as indicators of higher medical interventions and reliance on pharmaceuticals (Lichtenberg, 2022), relatively little is known about the environmental occurrence and impact of CECs in the Irish aquatic environment. Thus far, most studies have focussed on small selections of pharmaceutical compounds (Lacey et al., 2008) and little/no environmental measurements of other CECs such as perfluorinated organic chemicals, microplastics and nanomaterials. Although river ecological health has historically been high or good on average, more recently it has been in decline, and just 51 % of Irish large urban areas' wastewaters met the EU standards in 2021 (Environmental Protection Agency, 2022). As an example, over the period 2013–2018, 4.1 % of samples from 144 monitored rivers tested positive for 14 priority pesticides, which affected the quality of 117 rivers (Environmental Protection Agency, 2019). In another study in 2014, a year-long study of pharmaceuticals in Galway Bay on the west coast revealed concentrations of five selected pharmaceuticals as high as 3.16 μg·L^{-1} in wastewater effluent and 1.41 μg·L^{-1} in receiving marine water (i.e., carbamazepine, an antipsychotic drug). In addition, three pharmaceutical residues were measured in marine mussels at concentrations up to 9.22 ng·g^{-1} (i.e. trimethoprim, an antibiotic) (McEneff et al., 2014). Most recently, a global study of river waters for pharmaceutical residues found only six compounds (out of 61 substances targeted) totalling 615 ng·L^{-1} in concentration at an Irish site in rural Co. Dublin on the River Liffey (Wilkinson et al., 2022). Taking pharmaceuticals as an example, several antibiotics presented higher concentrations in Autumn than in Spring in Ireland, which had the highest concentration on average in WWTP effluent when compared to other countries in Europe (Rodriguez-Mozaz et al., 2020).

In terms of transport, CECs arising from WWTP effluents can dilute rapidly depending on the size of the receiving river (Egli et al., 2021), but compounds such as ibuprofen, paracetamol and trimethoprim have been found up to 10 km downstream from WWTPs (Letsinger et al., 2019). Other compounds such as UV-filters have been reported at higher concentrations in river water globally, for example during the summer season in Korea (Ekpeghere et al., 2016), and occurrence therefore related to consumption habits (Carrao et al., 2021). Very little, if any literature exists on these compounds in Ireland, not least from carefully designed campaigns with appropriate resolution to understand transport and fate. Population density has been shown to have a correlation with CEC concentrations in wastewater and surface waters, as they are affected by urbanisation and industrialisation, allowing for defined environmental pollution point sources to be identified (Ashfaq et al., 2019; Gogoi et al., 2018; Llamas-Dios et al., 2021). An example of this are the higher concentrations or number of compounds found on geographical areas downstream WWTP effluent discharges (Yang et al., 2022). However, rural practices also influence the diffuse influx of CECs to the environment such as pesticides, agrichemicals and veterinary compounds which have been reported worldwide (Khan et al., 2022; Yang et al., 2022). To help improve knowledge of environmental contamination and risk in line with other EU member states and given that Ireland is a relatively small island nation with extremes of both rural and urbanised environments, temporal and spatial monitoring campaigns are required to study CECs in multiple matrices. Procuring analytical measurement of such compounds at scale can be challenging. Usually, large numbers of samples require concentration and clean-up and need to be coupled with relatively rapid, confirmatory and quantitative instrumental analytical methods to achieve sufficient throughput while ensuring data quality remains high. A recently developed, relatively fast quantitative analytical workflow for >100 CECs using direct-injection liquid chromatography-tandem mass spectrometry (DI-LC-MS/MS) in both influent wastewater and river water has been applied to international samples for CECs at the low ng·L^{-1} concentration level (Egli et al., 2021; Ng et al., 2020). This approach is suitable for broad, large-scale application, but may still require additional and potentially more selective extraction methods to concentrate ultra-trace concentrations (e.g., ≤ pg·L^{-1}) for some target species before analysis.

The hypothesis to be tested was that there are currently several unmonitored chemical residues in the Irish aquatic environment and that their risk to aquatic wildlife is similar to other developed EU states. In order to test this hypothesis (i) samples of influent wastewater, effluent wastewater and receiving river water on a rural and urbanised river catchment were collected monthly over a one-year period; (ii) a quantitative analysis of all samples using three analytical methodologies was then performed, i.e., a DI-LC-MS/MS for rapid analysis of >100 CECs and, for higher sensitivity requirements for a smaller set of CECs, two LC-MS/MS methods using solid phase extraction for CEC concentration and clean-up; and (iii) CECs were then prioritised in terms based on calculated risk quotients and compared with those reported in the literature. This paper represents the first comprehensive temporal assessment of a comparatively larger number of CECs at two Irish WWTPs and their receiving river water to assist with much needed environmental risk-based prioritisation in the country.

2. Materials and methods

2.1. Reagents, chemicals and consumables

LC-MS grade methanol and acetonitrile; analytical HPLC grade acetonitrile, methanol, dichloromethane and dichlorodimethysilane; and solids of ammonium acetate and ammonium fluoride were purchased from Sigma Aldrich (Steinheim, Germany). Hydrochloric acid (37 % *v/v*) and formic acid were obtained from Fisher Scientific (Loughborough, UK). Ultrapure water was supplied from a Millipore Milli-Q water purification system at 18.3 MΩ (Millipore, Bedford, MA, USA). All reference standards materials and stable isotope labelled internal standards (SIL-IS) with ≥ 98 % purity, are listed in the supplementary information (SI) (Section S1). Stocks were prepared at a concentration of 1 mg·L^{-1} or 0.1 mg·L^{-1} in methanol or acetonitrile, and 0.01 % formic acid (*v/v*) was added to ciprofloxacin stocks to improve dissolution. Stocks were stored in the dark at −20 °C in silanised amber vials for stability purposes. Multi-compound working solutions

were prepared weekly in methanol, or in acetonitrile:water (10:90, *v/v*) where appropriate, by dilution of the stocks and these were also stored under the same conditions as the stocks.

2.2. Instrumentation

Three different LC-MS/MS analytical methods were used depending on the analyte (refer to Fig. S1 for a workflow diagram of the methodology employed). For the vast majority of CECs, analysis was performed using a previously validated DI-LC-MS/MS method using a Shimadzu LCMS8060 instrument (Shimadzu Corporation, Kyoto, Japan) according to Ng et al. (2020) and Egli et al. (2021) (details in Section S1.1).

For hormones (E1, E2, EE2, β-estradiol-d2, and estrone-d4) and for erythromycin, amoxicillin, ciprofloxacin, triclosan, triclosan-d3, octinoxate, octocrylene, and benzophenone-4, LC-MS/MS analysis was carried out using two newly developed methods involving solid phase extraction (SPE) and analysis using a 1290 Infinity II LC system, consisting of a binary solvent manager, an Agilent Infinity II 1290, a 1290 high-speed pump, and a 1290 multi-column thermostat compartment, all coupled to an Agilent 6470A triple quadrupole mass spectrometer with the Agilent Jet Stream ion source (Agilent Technologies, Cork, Ireland). Further details are given in the SI (-Section S1.2).

2.3. Sampling locations

Irish Water estimates that ~66 % of the population is connected to public sewer systems in the Republic of Ireland. Locations for monitoring were selected in collaboration with Environmental Protection Agency (EPA) Ireland as a "worst case scenario", to gain insight into the likely maximum scale of CEC occurrence, frequency and fate. Grab samples were collected monthly from October 2018 to September 2019 from two WWTPs, one located in a rural area (<2000 population equivalent (PE)) and another one in an urban area (50,000–100,000 PE). Locations and details of both WWTPs and, by extension, precise river locations subject to effluent discharge cannot be disclosed due to confidentiality agreements. That said, the urban area selected for monitoring was located in the eastern midlands region and situated on the River Liffey, which has the largest total catchment population in Ireland of ~1,255,000 and is heavily urbanised across its length with multiple sources of WWTP effluent as well as significant industrial and agricultural activities (Environmental Protection Agency, 2021). The site selected was not immediately down-river from any major pharmaceutical, personal care product or pesticide manufacturing facilities. Interestingly, approximately 60 % of its water volume is abstracted to serve municipal water supply needs, including drinking water. The WWTP provides up to tertiary treatment of wastewater and 97 % connectivity with the local population and was upgraded in 2018 prior to this campaign. Information provided by Irish Water stated that the WWTP hydraulic capacity in 2019 was 85,500 $m^3 \cdot day^{-1}$ and had an annual average loading of 29,968 $m^3 \cdot day^{-1}$ (maximum loading = 54,082 $m^3 \cdot day^{-1}$). The rural site was located in a very small, remote town on the Northwest Coast of Ireland (population of <2000) with a river receiving effluent from only one Irish Water WWTP which was upgraded in 2017 (comprising primary and secondary treatment) and which had very limited urbanisation across its entire catchment length. Approximately 72 % of the residential population were connected to the sewer network. In addition, no major industry contribution to riverine discharge existed there. The hydraulic capacity of the WWTP in 2019 was 1704 $m^3 \cdot day^{-1}$, with an annual average hydraulic loading of 612 $m^3 \cdot day^{-1}$ (maximum = 1504 $m^3 \cdot day^{-1}$). Unfortunately, no riverine flow data was available for either location to determine dilution but receiving waters at both sites were classified by the EU-Water Framework Directive (WFD) as having "moderate" status.

2.4. Sample collection and preparation

At both sites, duplicate grab samples of 1 L of each of influent and effluent wastewater as well as down-stream receiving surface water (50 m away for the rural area and 1 km away for the urban area) were collected in amber Nalgene bottles and were transported chilled on ice. Upon arrival at the laboratory, one set of samples was left unacidified. The other set were acidified to pH <2, using HCl (37 % *v/v*). All samples were stored in the freezer at −20 °C until analysis. For correlation calculation purposes at both sites, average monthly surface air temperature (°C), calculated from the average daily data (Fig. S2), and daily rainfall (mm) data (Fig. S3) was obtained from open access historical data of meteorological monitoring performed by MET Éireann (The Irish Meteorological Service, https://www.met.ie/).

For direct injection LC-MS/MS analysis, unacidified samples were analysed immediately following shipment from Dublin to the laboratory in London, UK. Samples of 15 mL in centrifuge tubes were shipped frozen in a cool polystyrene box filled with icepacks to prevent degradation. Upon arrival ~30 h later, they were kept in the freezer (−20 °C) until further treatment and analysis. For preparation, PTFE membrane syringe filters of 4 mm, 0.2 μm (Whatman, UK) and 1 mL BD Plastipak™ syringes (Becton Dickinson S.A., Madrid, Spain) were used for filtering. Silanised LC amber vials (Agilent Technologies UK Ltd., Cheshire, UK) were used to store and prepare the samples, where 100 μL of a standard solution in methanol was added, including SIL-IS where needed, to a 900 μL fixed volume of sample in order to obtain a final volume of 1 mL using positive displacement pipettes. Matrix-matched calibration curves were prepared from 0 to 5000 $ng \cdot L^{-1}$ (n = 13) and a SIL-IS solution was added at a constant concentration of 500 $ng \cdot L^{-1}$ where required (see Ng et al. (2020) and Egli et al. (2021) for details).

For the other two analytical methods, where additional sensitivity was required for selected compounds, acidified samples were first defrosted and filtered under vacuum using Nalgene sterile disposable filters with 0.45 μm nylon membranes (Thermo Fisher Scientific, UK). Following this, SPE was then performed using a vacuum manifold (Phenomenex, Cheshire, UK) and Oasis HLB (200 mg, 6 mL barrel, 30 μm, Hertfordshire, UK) cartridges. They were conditioned with 4 mL of methanol and 4 mL of ultrapure water, then 100 mL of sample was loaded at a flow rate of ~1 mL/min. Next, a washing step was performed using 4 mL of methanol:water (5:95, *v/v*) followed by drying under vacuum for 20 min to remove excess water. Elution was completed with 4 mL of 5 mM ammonium acetate in acetonitrile:methanol (25:75, *v/v*) into a pre-silanised container. Solvent was then evaporated under nitrogen at room temperature and reconstituted to 1 mL of acetonitrile:water (10:90, v/v). Extracts were vortex-mixed for 30 s, sonicated for 10 min, and followed by vortex mixing again. They were further filtered using syringe filters of 0.20 μm nylon membranes (VWR, Dublin, Ireland) before transfer into capped amber silanised 1.5 mL LC-MS vials (Agilent Technologies, Cork, Ireland) and stored at −20 °C until analysis. Samples were spiked with standards where appropriate, including SIL-IS where required, prior to extraction. Matrix-matched calibration curves were prepared for both SPE LC-MS/MS methods ranging from 0 to 1000 $ng \cdot L^{-1}$ ($n \geq 5$) including a SIL-IS at a constant concentration of 100 $ng \cdot L^{-1}$ and 500 $ng \cdot L^{-1}$ for hormones and rest of analytes, respectively.

2.5. Method performance

The analytical performance of all methods was assessed in surface waters, WWTP influent and effluent wastewater according to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), 2005). Pooled samples of each matrix type were used to assess the validation parameters of linearity, range, limits of detection and quantification (LOD and LOQ, respectively), precision, accuracy, recovery, and matrix effects, where required. For analytes that were already present in the pooled sample, a subtraction of average peak areas in the unfortified sample (n = 3) was performed. To understand any potential analyte transformation or instability while in transit, pooled matrices (n = 3) of each type spiked with 500 $ng \cdot L^{-1}$ (including SIL-IS) and stored in the freezer (−20 °C) for

24 h. After freezing, n = 3 replicates were removed and left at room temperature for 48 h in the same sealed polystyrene box used for transportation. The time period studied represented 18 h beyond the maximum time for transportation. The relative % stability was calculated as the ratio of the peak areas measured in the room temperature and those in frozen matrices. Full method performance data can be found in the SI, Section S2.

2.6. Environmental risk assessment (ERA)

The environmental CEC risks were estimated using risk quotients (RQs) calculated in wastewater effluent and receiving river water by dividing the measured environmental concentration (MEC) in each matrix at each site by the lowest predicted no-effect concentration (PNEC) obtained from the NORMAN Ecotoxicology database (NORMAN Network). In order to calculate RQs, the highest concentration quantified for each compound per site was used as the MEC value for its determination (Rivera-Jaimes et al., 2018). If any CEC was detected below the LOQ, half of this concentration was used as the MEC (Mendoza et al., 2015). Classifications of risk for a CEC were assigned as follows: RQ < 0.1 = insignificant risk, 0.1–1.0 = low risk; 1.0–10 = medium risk; and >10 = high risk.

In order to understand the potential risk at the entire site from all CECs present, in both rural and urban areas, the total summed RQs (ΣRQ_{site}) were calculated. The same thresholds for risk classification were used as for individual compounds (Iturburu et al., 2019; Riva et al., 2018).

2.7. Statistical and data analysis

Microsoft® Office Excel (WA, USA), IBM® SPSS Statistics v27 (New York, USA), EPI Suite™ version 4.1 (US Environmental Protection Agency's Office of Pollution Prevention and Toxics and Syracuse Research Corporation (SRC)) and Python version 3.7.9 were utilised for statistical and data analysis. Linear statistical analysis was used for stablishing the correlations of CEC concentrations and weather data using Microsoft® Office Excel and correlations are expressed either as Pearson or Spearman coefficients, as specified. For the generation of molecular descriptors and physicochemical properties, ACD Labs Percepta (Advanced Chemistry Development Laboratories, ON, Canada) and Dragon version 7.0 (Kode Chemoinformatics, Pisa Italy) were used.

3. Results and discussion

3.1. Method performance

Method performance for the three methods was assessed in all three matrices as per Ng et al. (2020), details of which can be found in the SI (-Section S2). In summary, out of a total of 142 CECs included in this study across all three methods and matrices, coefficients of determination (R^2) were > 0.98 for the majority of compounds (≥76 % of total compounds across all matrices), indicating good linearity. However, some compounds displayed R^2 < 0.98 and therefore, these should be considered semi-quantitative (5 compounds in surface water, 16 in effluent wastewater and 20 compounds in influent). Overall, recoveries, precision and accuracy were acceptable. As perhaps expected, matrix effects varied depending on the compound and complexity of the sample. LODs and LOQs generally achieved at the low-sub ng·L^{-1} level were also acquired. Regarding instability of analytes within transit, the relative percent stability was 102 ± 15 %, 98 ± 17 % and 103 ± 12 % for surface water, wastewater influent and effluent, respectively. All individual data is presented in Table S10 (-Section S3). Only a few analytes showed significant instability (<50 % or >150 %): azelnidipine and cymoxanil in all matrices; fenoxaprop-ethyl, clodinafop-propargyl, ketoconazole in influent alone; and amiodarone in surface water alone. However, overall, method performance was considered good for this large set of compounds and generally fit for purpose for monitoring.

3.2. Occurrence of CECs in wastewater influent, effluent and receiving water

Qualitatively, of all 142 compounds, 58 CECs were detected in any matrix (Fig. 1(a) and (b)), with 19 compounds in common across all three matrices. Similar numbers of CECs were detected in both sites in each matrix: 45 and 49 (influent), 37 and 38 (effluent) and 10 and 19 (surface waters) in the rural and urban areas, respectively. The largest proportion of all CECs detected in influent or effluent wastewater were antibiotics, antidepressants and antihypertensives. In receiving water, the number of CECs detected was far lower than wastewater and different across sites, with the urban area reflecting the wastewater profile more closely. Over 50 % of CECs were detected with 100 % frequency in influent and effluent wastewater (Fig. 1(c) and(d)). Therefore, these two selected sites arguably represent extremes of urbanisation and potential for CEC occurrence, and a promising result in terms of environmental CEC contamination in general. All occurrence data is presented in Tables S11–13.

Quantitatively, and across the year in influent wastewater, 46 and 39 compounds were quantifiable up to 8273 (venlafaxine) ng·L^{-1} and up to 3476 ng·L^{-1} (valsartan) for rural and urban areas, respectively (Fig. 2). For effluent, a total of 33 and 32 compounds were quantifiable in rural and urban areas respectively up to 1067 ng·L^{-1} (hydrochlorothiazide) for rural areas and up to 976 ng·L^{-1} (mefenamic acid) for urban areas. CEC concentrations in surface waters were measured up to 99 and 134 ng·L^{-1} (both for propranolol) in surface waters in rural and urban areas, respectively. Only four CECs were detected at quantifiable concentrations in rural surface water and twelve compounds quantified in the urban river. All compounds detected in surface water were also identified in the effluent wastewater samples, except E2 in the rural area.

3.2.1. Pharmaceutical and personal care products (PPCPs)

From all 47 pharmaceuticals detected across all samples, 17 were present on the Top-100 most-prescribed drugs list from the General Medical Service (GMS) in Ireland, including atorvastatin and bisoprolol, which were ranked two and six respectively (see Table S14). Some of these pharmaceuticals are also included in the preferred list of drugs by The Medicines Management Programme (MMP), such as amlodipine, bisoprolol, citalopram, and venlafaxine (Statistical Analysis of Claims and Payments 2019, 2019).

Pharmaceuticals were found at higher concentrations than other CECs in influent wastewater samples with the antidepressant venlafaxine having the highest concentration in October in the rural area. Average venlafaxine concentrations across the year were 1133 (±2267) and 553 (±101) ng·L^{-1} for the rural and urban areas, respectively. This compound was ranked between positions 26–29 during the sampling period on the Top-100 most prescribed pharmaceuticals in Ireland (Table S14). It has been found in the environment elsewhere at concentrations higher than other antidepressants (Bisesi et al., 2014; Rice et al., 2020) which was also observed here. In the UK, venlafaxine has been quantified at higher-than-expected concentrations in wastewater when compared to the prescription data and has been previously considered an abused compound (Rice et al., 2020). It is also currently included in the EU-WFD "Watch List" of CECs along with its metabolite *o*-desmethylvenlafaxine. The antihypertensive medication, valsartan, followed with average concentrations detected across both sites in wastewater of 2894 (±2283) and 2423 (±821) ng·L^{-1} for rural and urban areas, respectively. It was ranked between 59 and 71 of the most prescribed pharmaceuticals during this sampling campaign. However, it was not detected in receiving waters, perhaps as a result of dilution and/or high wastewater treatment removal efficiency. Regarding the latter, and of most relevance to the urban site here, valsartan has been shown to be efficiently removed in WWTPs in other similarly equipped sites in the EU and often >90 % (Lopez et al., 2022; Styszko et al., 2021).Valsartan is usually co-prescribed with another Top-100 pharmaceutical, hydrochlorothiazide (Statistical analysis of claims and payments *2018*, 2018; Statistical analysis of claims and payments *2019*, 2019). Other compounds such as antipyrine, an analgesic, were detected at relatively high concentrations in influent wastewater (average of 1302

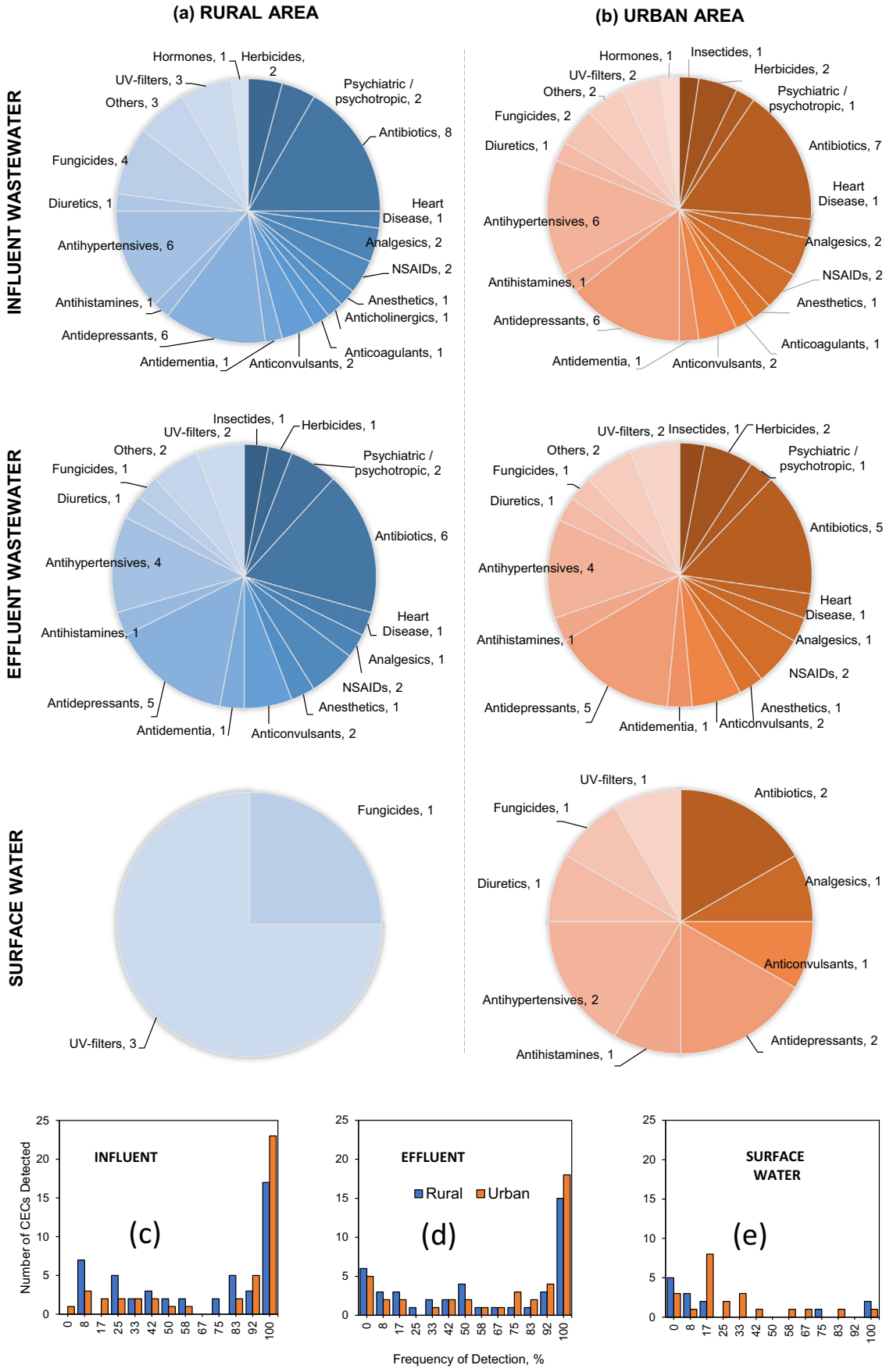

Fig. 1. Compound classification in the rural (a) and urban areas (b) for all detected analytes in wastewater influent (top) and effluent (middle) and surface waters (bottom) samples and frequency of detection in all matrices, i.e., wastewater influent (c), effluent (d) and receiving surface water (e).

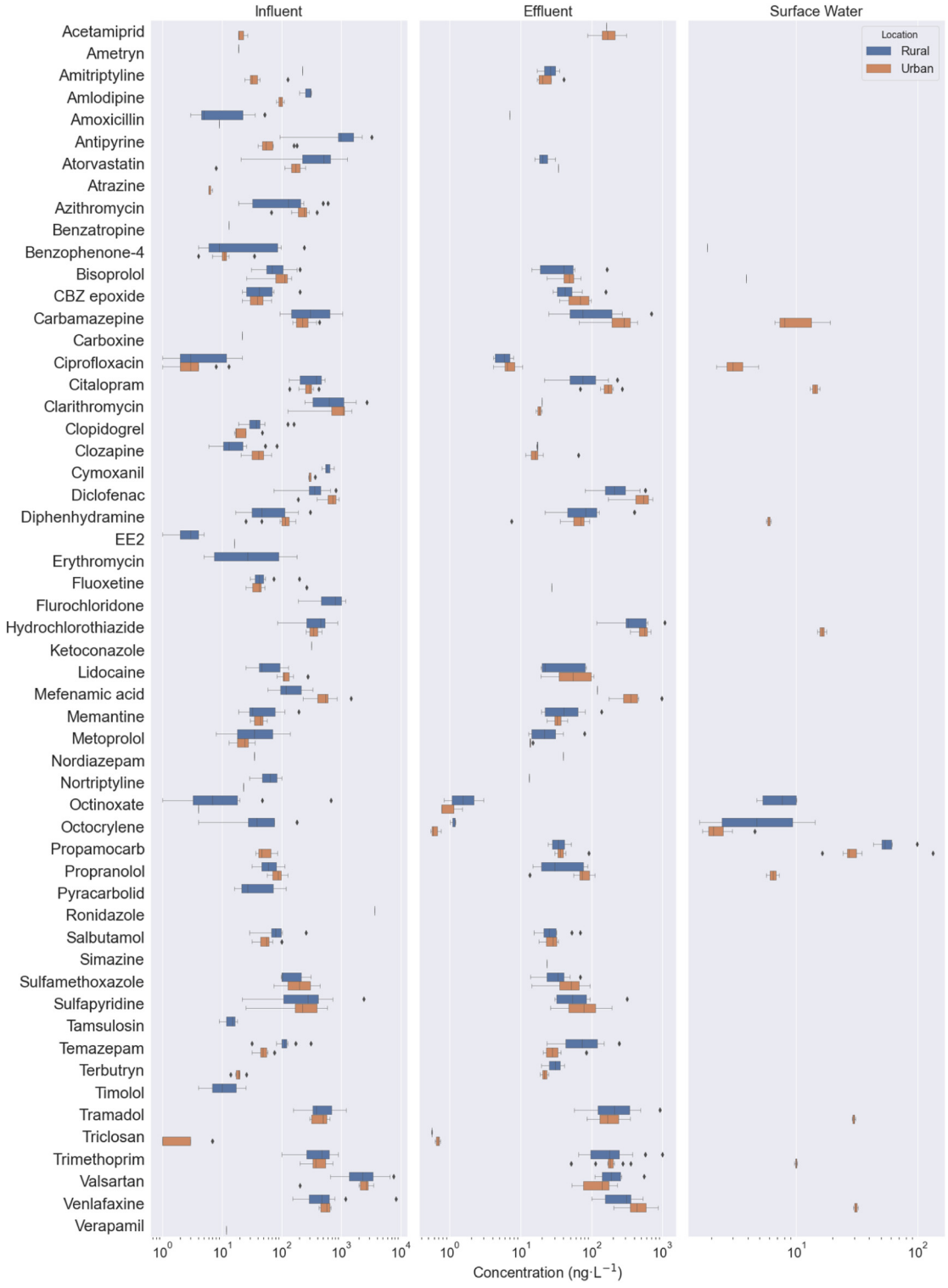

Fig. 2. Measured CEC concentrations in (a) wastewater influent, (b) effluent and (c) surface water in urban and rural sites across 12 months of sampling. Boxes represent the interquartile range (IQR), whiskers extend to points that lie within 1.5 IQRs of the lower and upper quartile and dots represent outliers. Raw data is given in Table S11–13.

(±826) ng·L^{-1} for the rural area) but were not in the Top-100 most prescribed list for Ireland. This pharmaceutical is commonly detected in the aquatic environment (Monteagudo et al., 2016), but its main use is in veterinary medicine (Rashid et al., 2008).

Although only grab samples were taken each month during this study, an obvious increase in the concentrations of UV-filters were observed in the sunnier months (May–July). In particular, octinoxate concentrations increased in the rural area and its detection has been correlated to seasonal use elsewhere (Carve et al., 2021; O'Malley et al., 2020). However, aside from its use in sunscreen products, octinoxate is also widely used in cosmetics, shampoos, and lotions as well as industrial products such as insecticides, plastics and detergents (Carve et al., 2021).

In wastewater effluent, the highest average concentrations across the year were quantified for hydrochlorothiazide at 444 (±251) and 547 (±99) ng·L^{-1} for both rural and urban areas, respectively. Other compounds that were present at concentrations >100 ng·L^{-1} in both areas included

diclofenac, carbamazepine, tramadol, trimethoprim, valsartan and venlafaxine. Interestingly, antibiotics represented a fifth of the number of pharmaceuticals detected, with sulfamethoxazole, sulfapyridine, trimethoprim and ciprofloxacin quantifiable at 44 (±23), 81 (±67), 228 (±197), and 6 (±2) ng·L^{-1}, respectively; 6 % of all compounds investigated.

In surface waters, pharmaceutical concentrations were generally very low or non-quantifiable and could be due to the dilution factor over the distance between the WWTP and the sampling point. Tramadol and carbamazepine concentrations in the urban area were the highest at 31 (±6) and 19 (±10) ng·L^{-1}, respectively, and have been shown globally to occur in several different types of environmental samples (Brumovský et al., 2017). Tramadol has also been measured in effluent and receiving water samples internationally (Munro et al., 2019; Santos et al., 2021). Regarding antibiotics, concentrations were very low or not quantifiable with only ciprofloxacin quantified in urban areas and only up to 5 (±26) ng·L^{-1}. In comparison to wastewater, concentrations were also low for antihypertension medications, including hydrochlorothiazide, which was quantified at a maximum concentration of 18 (±25) ng·L^{-1} in the urban area. In addition to these compounds, several others were or are included on the EU-WFD Watch Lists including amoxicillin, ciprofloxacin, E1, E2, EE2, erythromycin, sulfamethoxazole, trimethoprim, venlafaxine and octinoxate. Of these, only ciprofloxacin and venlafaxine were quantified in surface water in the urban area with a maximum concentration of 5 (±26) and 32 (±7) ng·L^{-1} respectively, while sulfamethoxazole was not detected in any sample. Octinoxate was measured at low concentrations (generally <10 ng·L^{-1}) in the rural surface water, but is likely to be more prevalent in suspended particular matter or in the solid phase (logKow = 5.80) (Proctor et al., 2021; Sang and Leung, 2016) and its highest concentrations were determined in influent at 682 (±153) ng·L^{-1} in the rural area in June. Aside from octinoxate, the remaining personal care products investigated were detected across all matrices with one exception. The highest concentration measured for benzophenone-4, a UV-blocker, was 242 (±95) ng·L^{-1} and it was detected in all except the rural site wastewater effluent. Lastly, triclosan, an antimicrobial agent found in cosmetics and hand-soaps, and which was banned for use in some products by the Food and Drug Administration (FDA) in 2016, was also quantified at low concentrations here with a maximum of 7 (±46) ng·L^{-1} in urban influent. It has been shown previously in Ireland to be removed by activated sludge treatment due to its hydrophobicity (Barron et al., 2009, Barron et al., 2008).

3.2.2. Pesticides

Across all samples analysed, 11 pesticides were detected in influent, six in effluent and one in surface waters. Only propamocarb was found in all matrices. Propamocarb is a systemic fungicide used to treat different diseases such as seedings, white tip, downy mildew and pythium. It is used to treat a variety of vegetables such as lettuce, onions, spinach and tomatoes (Hiemstra and de Kok, 2002; López-Ruiz et al., 2019). It is widely used in both agriculture in Ireland/Northern Ireland (afbi, 2020; Pesticide Control Division, 2021; Teagasc, 2021) and is widely available to the general public for use in gardening/plant protection. However, aquatic toxicity data on this compound is quite limited and it has been considered as a low toxicity chemical (Liu et al., 2020a). Nevertheless, it has shown a lipid metabolism disorder in the liver in zebrafish (Zhang et al., 2018) and toxic effects to different aquatic organisms have been suggested (Liu et al., 2020a). Occurrence frequencies were generally high for this compound in all matrices, but concentrations were relatively consistent and low overall, perhaps suggesting that this may have arisen from storm water and/or leachate (generally <50 ng·L^{-1}). It was also not clear in these locations what the usage patterns were across the year. A total of 26 out of the total 51 pesticides included in this analytical method are not approved by the EU Commission for plant protection products (EU Pesticides Database, European Commission; Official Journal of the European Union, 2009). Ametryn, atrazine, cyromazine, prometryn and terbutryn were detected mainly in wastewater influent, suggesting efficient removal during treatment. Only prometryn and terbutryn were further detected in effluents but not in surface waters. Simazine, another WFD priority substance, was detected in wastewater effluent samples but not in receiving surface water.

Neonicotinoids are among most widely used classes of insecticides in agriculture, though recent rulings policies have restricted their use among flowering crops (Wood and Goulson, 2017). They have been found at higher concentrations than the limits set by EU, and so were included in the first and second EU WFD Watch Lists (Pietrzak et al., 2020). From this group, acetamiprid was detected in urban influent samples with maximum concentrations of only 27 (±14) ng·L^{-1}. It is potentially toxic to several organisms, but use of acetamiprid has not yet to be prohibited (EU Pesticides Database, European Commission). Studies have showed its relation to reduced sperm density in birds, and it is claimed that agriculture contributes to the decline in farmland bird populations (Humann-Guilleminot et al., 2019). This pesticide is also associated with detrimental impacts for pollinators and ecosystem services (Camp et al., 2020). Acetamiprid was not found in surface waters which is consistent with other studies, where it has been infrequently detected and if so, with concentrations below LOQ; similar results have been found for this compound in biota (Miller et al., 2019). In summary, all pesticides appeared to be removed before discharge from these WWTPs to the natural environment apart from propamocarb.

3.3. Removal efficiency of wastewater treatment and effect of temperature

Given that the study only utilised grab samples of wastewater, all twelve months of data for both influent and effluent were combined to more reliably evaluate the efficiency of wastewater treatment for CECs. The effect of treatment was obvious overall in both areas with a significantly lower average concentration of CECs in effluent (Fig. 3). In the urban and rural areas respectively, a 48 % and 69 % overall reduction in average CEC concentration was calculated. In the urban area, ~98 % of the average measured CEC concentration remaining in the effluent were further reduced in surface waters, even after a short 1 km distance downstream of the outfall, whereas there was a ~93 % reduction in the rural area. This observation was similar to other recent work assessing environmental fate of these CECs in continental Europe (Egli et al., 2021). Unfortunately, at either site, it was not possible to assign the proportion of CEC sources in influent wastewater to industrial or domestic sectors (Naidoo and Olaniran, 2013).

For specific CECs in influent, wastewater treatment efficiency varied depending on the physicochemical properties of the individual molecules and the type of treatment performed, among other variables (Burns et al., 2018). Using the ratio of cumulative measured individual CEC concentrations across the year in both influent and effluent as a measure of WWTP efficiency, it was found that very high removal (>98 % of CEC present in influent only) in both areas was observed for nine compounds including amlodipine, antipyrine, azithromycin, benzophenone-4, clopidogrel, cymoxanil, EE2, clarithromycin and atorvastatin (Fig. 4 (a) and (b)). For some of these CECs, the frequency of detection was low in both matrices (<5 quantified data/year) and therefore some caution is advised against over-interpretation of their removal efficiency at this level (e.g., amlodipine, clopidogrel, cymoxanil and EE2). An additional 11 substances in the rural area alone were removed to a similar high extent, as well as four others in the urban area, but these were different between rural and urban areas. While logP was moderately high for some of these CECs, there was still no obvious correlation. For example, logP of antipyrine is 0.72 and removal during conventional treatment has been previously shown to be around 30 % (Monteagudo et al., 2016) and it also is relatively recalcitrant to biodegradation or transformation. However, other studies have reported wide ranging removal efficiency for this substance from 0 to 100 % based on the type of treatment employed (Li et al., 2019). Efficient removal of antipyrine has also been achieved via photodegradation (Li et al., 2019), but UV treatment was not employed at either WWTP studied here and yet removal was still high. Therefore, further consideration of the specific technologies at the WWTP for compound removal is necessary.

Two substances, notably the pesticide propamocarb, were predominantly present in wastewater effluent in both the rural and urban areas across all months at concentrations ≤51 ng·L^{-1} and ≤ 91 ng·L^{-1},

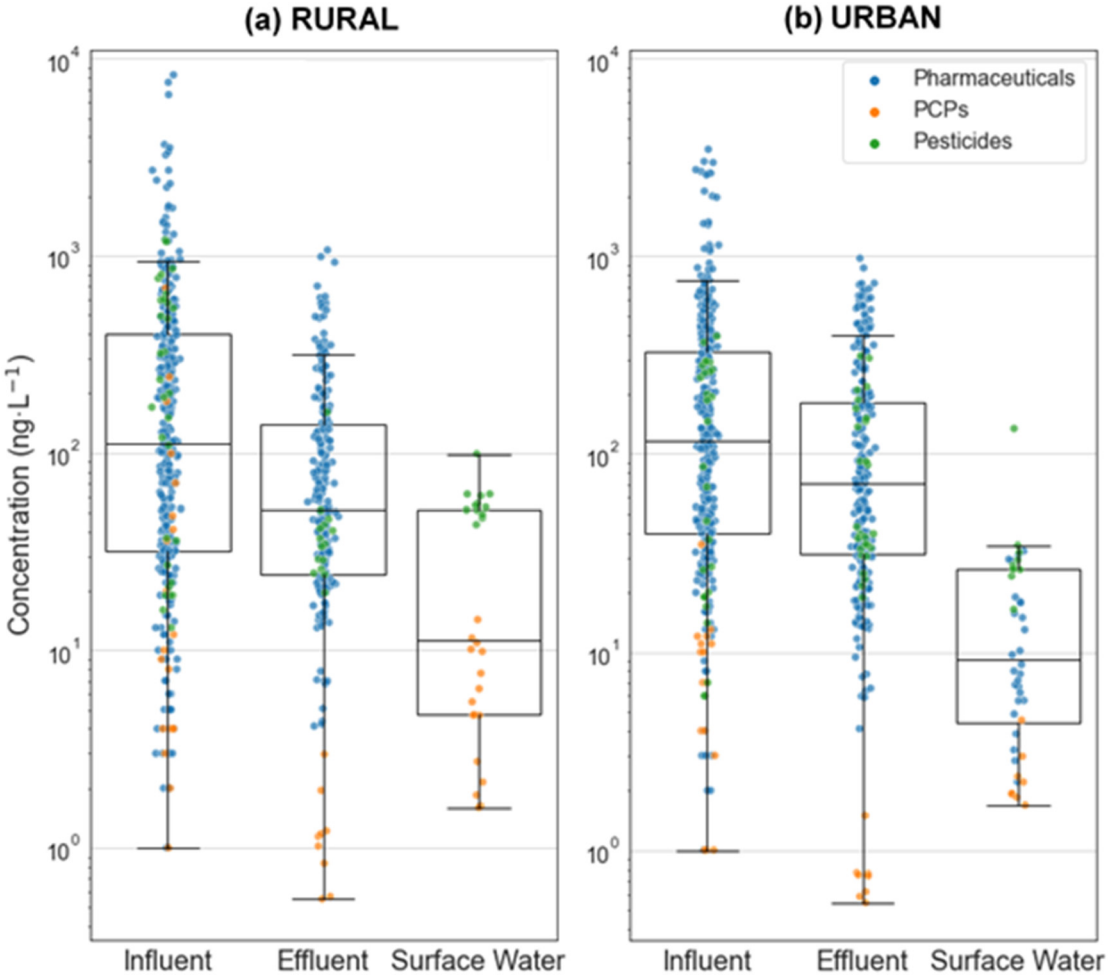

Fig. 3. Combined concentrations of all CECs (colour-coded by class) measured in the rural (a) and urban areas (b) across the year-long campaign.

respectively (no statistically significant difference in concentration data between sites). In addition, acetamiprid in the urban area was present at much higher concentrations in effluent (22 versus 183 ng·L^{-1} on average) and was of more concern given its toxicity. The reasons behind their increased frequency and/or concentration in effluent are unclear, but perhaps could be due to a decrease in matrix interference inhibiting reliable trace measurement (particularly for propamocarb) or potential metabolite transformation to the parent molecule during wastewater treatment, especially for unstable conjugates. Acetamiprid, however, has been shown to metabolise to *N*-desmethyl-acetamiprid and has been detected in human urine samples where no known source of exposure to acetamiprid itself (Ichikawa et al., 2019; Phogat et al., 2022; Ueyama et al., 2020). Using BioTransformer 3.0, N-glucuronidation of acetamiprid was predicted to occur via CYP450 enzymes in human Phase II metabolism and in the human gut. No environmental microbial conjugation of acetamiprid was predicted.

Aside from CEC dominance in either matrix, the remaining compounds showed a wide range of occurrence in either phase. Taking all data for all CECs, no appreciable correlations existed between relative CEC concentration in either matrix, except for a few compounds such as mefenamic acid in the urban area ($R^2 = 0.78$) with either logP or logD (pH of urban and rural influent was ~7.5 and 6.3, respectively). However, for CECs quantified in more than five samples in both wastewater influent and effluent at each site ($n = 21$ compounds) and on which to base a more confident comparison, a moderate correlation existed between sites (Pearson $r = 0.65$) indicating that there were some similarities in performance levels across the two different regional treatment works (Fig. 4 (c)). A brief evaluation of >1900 molecular descriptors for these molecules (using ACD Labs Percepta and Dragon version 7.0 software) revealed no significant correlations existed in general between CEC proportions in effluent/influent for molecular physicochemical properties, basic constitutional indices or functional group counts. However, some moderate correlations existed for a few descriptors including 2D autocorrelations (e.g., SpMax6_Bh(e), the largest eigenvalue n. 6 of Burden matrix weighted by Sanderson electronegativity, average $r = 0.52$ across sites); and Burden eigenvalues such as GATS5v (Geary autocorrelation of lag 5 weighted by van der Waals volume, $r = 0.49$). Whilst prediction of sorption behaviour of CECs to solid materials has been demonstrated in the past (Barron et al., 2009), such correlations did not provide a useful basis to develop predictive models on which to understand wastewater treatment efficiency here. Clearly, understanding the removal efficiency of specific mid-polarity CECs during wastewater treatment remains very complex and is not easily generalisable. Another hypothesis is the desorption of CECs from biological materials. Possible desorption of parent compounds could occur during biological treatment processes thereby changing the effluent CEC concentration (and variance thereof) (Angeles et al., 2020).

Furthermore, a brief investigation into any correlations between influent or effluent concentrations with meteorological parameters, such as air temperature and rainfall data, were performed using linear regression (see Section S4.1). A moderate correlation existed between the concentrations of some compounds and the monthly average air temperature (°C) at both locations. The best example of this was acetamiprid in the urban site, which in both influent and effluent samples, a high correlation ($R^2 = 0.72$ and 0.70, respectively) was observed (Fig. S4). A generalised linear model analysis combining the different weather parameters with higher statistical power to include other variables such as rainfall and humidity,

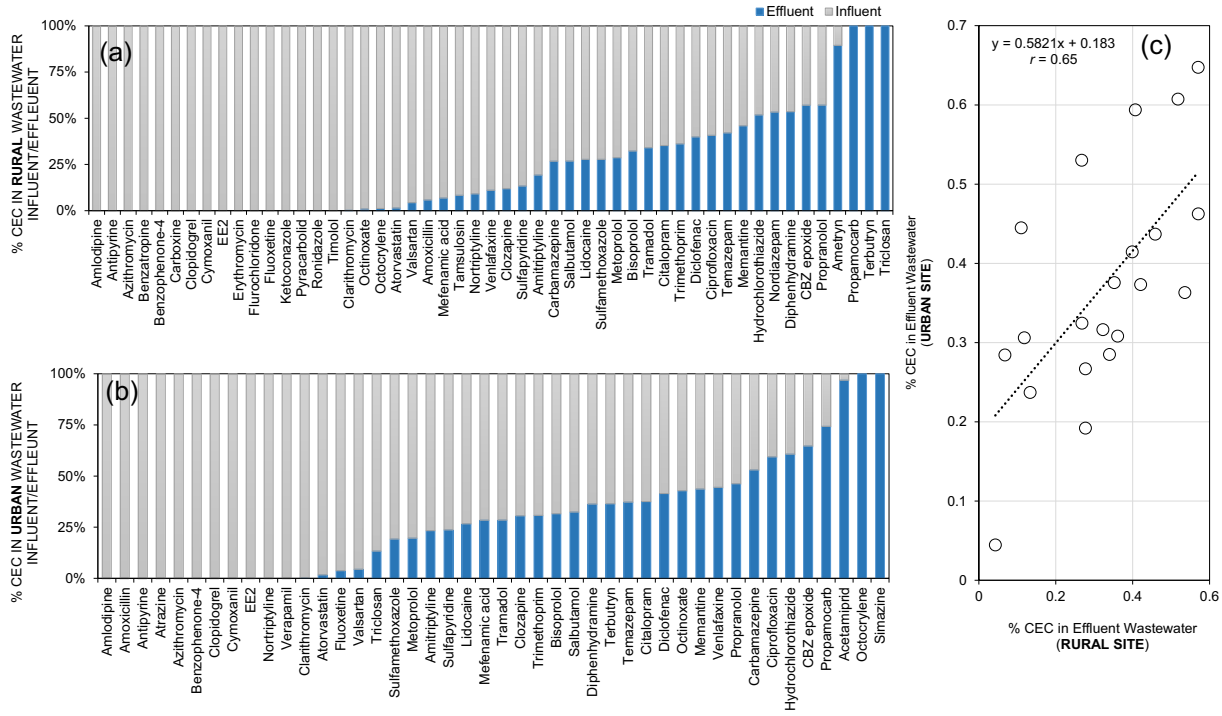

Fig. 4. Proportion of CEC in wastewater influent or effluent in the rural (a) and urban (b) area. Bars represent the ratio of cumulative concentrations for all twelve months of samples in either matrix. Panel (c) represents the correlation of average measured CEC concentrations in effluent wastewater between the rural and urban sites only for CECs present at both sites at a frequency at or greater than five months.

for example, is suggested for further investigation, especially to understand whether temperature significantly affects WWTP removal efficiency (Alisawi, 2020).

3.4. Environmental risk assessment (ERA)

All compounds detected in surface waters and effluent wastewater samples were subjected to an environmental risk assessment and RQs can be found in Table 1. Wastewater effluent discharge points, mainly used in urban populations, are often considered a worst-case scenario for CECs due to either higher concentrations, the number of compounds or a combination of the two (Kosma et al., 2014). The urban area in this study had a slightly higher calculated ΣRQ, which supports these previous findings. However, in this study, results derived from a small sewer-connected population and a paired Students *t*-test found that the risks of CECs at both sites in effluent were not statistically different to each other. Approximately one third of all compounds presented insignificant risks (RQs <0.1) in the rural site, whereas only half of all compounds had an RQ <0.1 in the urban site. Half of all CECs in rural effluent and a third of CECs in urban effluent presented low risks (0.1 < RQ < 1.0). In higher risk categories, there was a high degree of commonality in specific CECs presenting medium/high risk at both sites, including acetamiprid, atorvastatin and carbamazepine, whereas diclofenac, EE2, temazepam and venlafaxine. Some of these compounds have been demonstrated to cause negative effects on fish, such as venlafaxine, which has been shown to decrease brain serotonin concentrations which can affect fishes' locomotor activity and appetites (Bisesi et al., 2014). The only other substance presenting a medium risk was mefenamic acid and only in the urban area. On average across both sites, the top four CECs of high risk in effluents were EE2 (RQ = 27.9), venlafaxine (RQ = 18.4), diclofenac (RQ = 13.0) and carbamazepine (RQ = 11.5).

Compared to similar studies around the world, these sites presented lower RQs for particularly hazardous CECs (Table S15). Unlike this study, compounds such as metoprolol and fluoxetine presented high risks in wastewater effluents in Europe (Zhou et al., 2019), but risks were insignificant and low here, respectively. In this study, sulfamethoxazole was not detected in surface waters and presented a low risk in effluent samples in Ireland. This is consistent with several studies of surface waters in European countries where RQs ranged from 0 (Ireland, Portugal, Germany, Finland and Norway) to 0.02 (Cyprus) (Rodriguez-Mozaz et al., 2020). Although not many antibiotics result in high RQs due to their hydrophilicity, high risks have been reported in other countries such as China (RQ = 1955) (Liu et al., 2020b). For other antibiotics, RQs obtained were comparable to findings from different European countries: trimethoprim, clarithromycin and sulfapyridine showed no or low risk and ciprofloxacin and azithromycin presented moderate risks. Other studies have also reported that the dilution of the compound concentrations when reaching the natural aquatic environment led to lower risks. Compounds such as mefenamic acid and sulfamethoxazole had medium or high risks in wastewaters in Europe, but were minimal in surface waters (Ashfaq et al., 2019), which agrees with the results in this study.

In surface water, the ΣRQ was an order of magnitude lower at both sites compared to effluent and, again, individual CEC risks presented no statistical difference between sites following a paired Students *t*-test. Most CECs presented insignificant risks, with those presenting any risks mostly in the low-risk category apart from E2 and EE2 in the rural area (both medium risk) which were the main contributors to overall site risk with RQs of 3.5 and 1.1, respectively. The highest risk for the urban area was attributed to venlafaxine, with an RQ of 0.8. Interestingly, most substances displaying high risks in effluent wastewater were not quantifiable in surface water, indicating that their risks were successfully minimised, including compounds such as diclofenac. This is a promising result when compared to other studies, as diclofenac was on the top highest RQs obtained (RQ = 154) across 33 European countries (Zhou et al., 2019). That said, some compounds still posed a low-level risk in surface waters including E1, EE2, venlafaxine, ciprofloxacin and carbamazepine. The latter, an antiepileptic drug, belongs to one of the most frequently prescribed pharmaceuticals (Brumovský et al., 2017) and several studies have investigated its ecotoxicological effects, where Ferrari et al. (2003) found it to be the most dangerous tested compound for aquatic environment. Carbamazepine has also been classified

Table 1
Environmental risk assessment of CECs (as risk quotients) quantified in both effluent wastewater and surface waters at both sites. Risk quotients were calculated based on the highest concentration measured in each matrix and PNEC values based on acute (A) and chronic (C) data as specified, unless not stated (n.s.).

Class/compound	PNEC[a]		Risk Quotient, Matrix and Site[b]							
	($ng{\cdot}L^{-1}$)	Type	Rural Area				Urban Area			
			WW Effluent		Surface Water		WW Effluent		Surface Water	
Pesticides										
Acetamiprid	24	n.s.	6.7	M			13.0	H		
Propamocarb	1,000,000	A and C	<0.1	I	<0.1	I	<0.1	I	<0.1	I
Terbutryn	65	C	0.6	L			0.4	L		
Simazine	1000	n.s.	<0.1				<0.1	I		
Pharmaceuticals										
Amoxicillin	78	n.s.	<0.1	L	<0.1	I	<0.1	I		
Amitriptyline	140	n.s.	0.3	L			0.3	L		
Atorvastatin	10	n.s.	3.1	M			3.4	M		
Bisoprolol	3180	n.s.	<0.1	L			<0.1	I	<0.1	I
Carbamazepine	50	C	14.0	H			8.9	M	0.4	L
CBZ epoxide	2570	n.s.	<0.1	L			<0.1	I		
Ciprofloxacin	89	n.s.	<0.1	L			0.1	L	<0.1	L
Citalopram	16,000	C	<0.1	I			<0.1	I	<0.1	I
Clarithromycin	120	n.s.	0.2	L			0.2	L		
Clopidogrel	620	A	<0.1	I			<0.1	I		
Clozapine	180	C	<0.1	L			0.4	L		
Diclofenac	50	C	11.5	H			14.5	H		
Diphenhydramine	990	A	0.4	L			<0.1	L	<0.1	I
E1	3.6	C	0.5	L	0.7	L	0.5	L	0.7	L
E2	0.1	n.s.			3.5	M				
EE2	0.035	C	27.9	H	1.1	M	27.9	H		
Erythromycin	200	n.s.	<0.1	I			<0.1	I	<0.1	I
Fluoxetine	100	C	<0.1	L			0.3	L		
Hydrochlorothiazide	8380	n.s.	0.1	L			<0.1	L	<0.1	I
Lidocaine	4670	n.s.	<0.1	I			<0.1	I	<0.1	I
Lincomycin	3950	n.s.	<0.1				<0.1	I		
Mefenamic acid	200	n.s.	0.6	L			4.9	M		
Memantine	1840	n.s.	<0.1	L			<0.1	I		
Metoprolol	8600	C	<0.1	I			<0.1	I		
Nordiazepam	2630[c]	n.s.	<0.1	L						
Nortriptyline	190	A		L			<0.1	I		
Propranolol	410	C	0.2	L			0.3	L	<0.1	I
Salbutamol	17,100	n.s.	<0.1	I			<0.1	I		I
Sulfamethoxazole	600	C	0.1	L			0.2	L		
Sulfapyridine	1830	n.s.	0.2	L			0.1	L		
Tamsulosin	350	n.s.	<0.1	I						
Temazepam	71	C	3.5	M			1.2	M		
Tramadol	8650	n.s.	0.1	L	<0.1	I	<0.1	I	<0.1	I
Trimethoprim	100,000	n.s.	<0.1	I			<0.1	I	<0.1	I
Valsartan	560,000	C		I			<0.1	I		
Venlafaxine	38	C	13.9	H			22.9	H	0.8	L
Personal care products										
Benzophenone-4	3520	n.s.	<0.1	I	<0.1	I	<0.1	I	<0.1	I
Octinoxate	6000	A	<0.1	I	<0.1	I	<0.1	I	<0.1	I
Octocrylene	23	A	<0.1	I	0.6	L	<0.1	I	0.2	L
Triclosan	20	C	<0.1	L	<0.1	I	<0.1	L	<0.1	I
ΣRQ_{site}			83.9		5.9		99.3		2.1	

[a] PNEC data was sourced from the Norman Ecotoxicology Database.
[b] Data show risk quotients for each site (left) and risk level (right) as Insignificant (I), Low (L), Medium (M) or High (H).

as "R52/53 Harmful to aquatic organisms and may cause long-term adverse effects in the aquatic environment" (Jos et al., 2003). Only octocrylene displayed any risk (but low-level in both areas) in surface water where none was quantified in effluent, suggesting a difference source from WWTPs.

In summary, the final RQ varied depending not only on the concentration (such as season, weather conditions and WWTP treatment used) (Molnar et al., 2021), but also a country's demographics (population and substance use patterns), the exact geographical location, and the calculation methods (predicted effect concentrations (PEC) or measured concentrations (MEC)) (Bouissou-Schurtz, 2014). Countries reporting lower numbers of high-risk compounds could be due to low risks but also limited or no data available from monitoring campaigns (Zhou et al., 2019). This exemplifies the importance of performing comprehensive studies on unregulated chemicals as many of them have known risks to the environment and potentially to human health. Furthermore, the use of rapid multi-residue and fully quantitative analytical methods, such as DI-LC-MS/MS used in this study, can reduce the uncertainty in RQ calculation, and reduce the dependency on the reliability of variable input data used to make predictions, such as sales data, prescription data and drug-use patterns (Molnar et al., 2021).

4. Conclusions

For the first time, the temporal and spatial occurrence of >140 contaminants of emerging concern were monitored in the aquatic environment and WWTPs over a period of a year (12 months) at two sites in Ireland. The hypothesis was partly upheld in that there were several quantifiable and unmonitored chemical residues present in these study locations, but their risk to aquatic wildlife was lower in comparison to other developed states. Across all samples, 58 compounds were detected and ≥ 39, ≥32 and ≥4 were quantified at the $ng{\cdot}L^{-1}$ level in wastewater influent, effluent and surface waters, respectively. Maximum concentrations obtained were 134 (propranolol), 1067 (hydrochlorothiazide) and 8273 (venlafaxine) $ng{\cdot}L^{-1}$ (i.e., all pharmaceuticals). Contaminants decreased both in concentration after treatment and after they entered the natural environment, but the level of decrease varied by compound. A moderate correlation in CEC concentrations was seen between both WWTPs on a temporal basis. Preliminary findings suggested a moderate correlation existed between surface air temperature and concentrations of some wastewater CEC concentrations, but more data is required to better understand this dependency. Lastly, an environmental risk assessment was performed, where CECs in wastewater effluent presented higher RQs in total. However, in surface waters, ΣRQ was an order of magnitude lower and majority of compounds were in the low-risk category, suggesting a clear dilution effect in the environment. Although only ~66 % of the Irish population is connected to public sewers and this study monitored just two of Irish Water's 1000+ WWTPs, this work still represents the most comprehensive study of CECs in Irish wastewater and receiving waters to date, and which will enable risk-based prioritisation for future monitoring programmes.

CRediT authorship contribution statement

Helena Rapp-Wright: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Visualization. **Fiona Regan:** Conceptualization, Funding acquisition, Project administration, Supervision. **Blánaid White:** Conceptualization, Funding acquisition, Project administration, Supervision, Writing – review & editing. **Leon P. Barron:** Conceptualization, Funding acquisition, Project administration, Supervision, Visualization, Writing – original draft, Writing – review & editing.

Data availability

All data is available in the SI, however, WWTPs names are confidential.

Declaration of competing interest

We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2022.160379.

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