



Occurrence and mass flows of contaminants of emerging concern (CECs) in Sweden's three largest lakes and associated rivers

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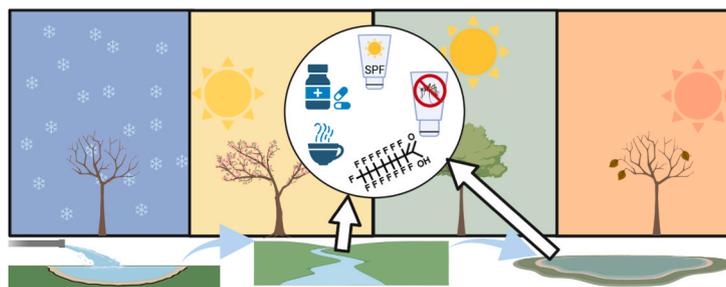
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HIGHLIGHTS

- Trace levels of CECs were found at all drinking water source area sites.
- Many CECs showed seasonal changes in concentrations.
- Riverine CEC concentrations were correlated to distance or discharge of WWTPs.
- Rarely investigated CECs were detected with potential PMT properties.

GRAPHICAL ABSTRACT



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ABSTRACT

Contaminants of emerging concern (CECs) are a concern in aquatic environments due to possible adverse effects on the environment and humans. This study assessed the occurrence and mass flows of CECs in Sweden's three largest lakes and 24 associated rivers. The occurrence and distribution of 105 CECs was investigated, comprising 71 pharmaceuticals, 13 perfluoroalkyl substances (PFASs), eight industrial chemicals, four personal care products (PCPs), three parabens, two pesticides, and four other CECs (mostly anthropogenic markers). This is the first systematic study of CECs in Sweden's main lakes and one of the first to report environmental concentrations of the industrial chemicals tributyl citrate acetate and 2,2'-dimorpholinylether. The \sum CEC concentration was generally higher in river water (31–5200 ng/L; median 440 ng/L) than in lake water (36–900 ng/L; median 190 ng/L). At urban lake sites, seasonal variations were observed for PCPs and parabens, and also for antihistamines, antidiabetics, antineoplastic agents, antibiotics, and fungicides. The median mass CEC load in river water was 180 g/day (range 4.0–4300 g/day), with a total mass load of 5000 g/day to Lake Vänern, 510 g/day to Lake Vättern, and 5600 g/day to Lake Mälaren. All three lakes are used as drinking water reservoirs, so further investigations of the impact of CECs on the ecosystem and human health are needed.

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1. Introduction

Contaminants of emerging concern (CECs) constitute a large and diverse group of chemicals, including pharmaceuticals, personal care products (PCPs), and perfluoroalkyl substances (PFASs) (Naidu et al., 2016; Naidu and Wong, 2013). CECs are widely used in industrial and consumer products, and can be released to the aquatic environment from various polluting sources such as wastewater treatment plants (WWTPs) (Ibáñez et al., 2017; Keller et al., 2014; Lindberg et al., 2010; Rostvall et al., 2018; Söregård et al., 2019), on-site sewage treatment facilities (OSSFs) (Blum et al., 2018), landfill leachate (Gobelius et al., 2018), and other sources (Ahrens et al., 2015). Thus, CECs are continuously released into the aquatic environment (Brausch and Rand, 2011; Chen and Ying, 2015; Godoy et al., 2015; Haman et al., 2015; Li, 2014; Meffe and de Bustamante, 2014; Merel and Snyder, 2016; Wilkinson et al., 2017), where they can have long-term adverse effects (Nilsen et al., 2019). Moreover, CECs in aquatic resources used as drinking water sources (Castiglioni et al., 2020) can affect drinking water quality (Karki et al., 2020; Valcárcel et al., 2011).

Earlier research has shown that seasonal variations occur in WWTP influent and effluent (Golovko et al., 2014), rivers (Daneshvar et al., 2010; Gago-Ferrero et al., 2017; Müller et al., 2020), and lakes (Maasz et al., 2019; Rehrl et al., 2020). Seasonal variations in WWTP influent might be attributable to consumption patterns (Golovko et al., 2014), but variations in aquatic systems are more complex (Kunkel and Radke, 2011; Li et al., 2016). Once CECs are released into the aquatic environment, their geochemical cycling can be affected by various processes (Rehrl et al., 2020). Seasonal variations in the environment can depend on physical (e.g., varying flow patterns and stratification), chemical (photolysis) (Batchu et al., 2014; Blum et al., 2017; Dodson et al., 2011; Trawiński and Skibiński, 2019) and biological (biodegradation) (Baena-Nogueras et al., 2017) factors. In lake systems, temporal variations can occur due to e.g., recreational activities and usage patterns of certain CECs (Mao et al., 2019), or to variations in photodegradation between seasons (Bonvin et al., 2011; Lindholm-Lehto et al., 2016). Spatial variations in lake systems can occur depending on proximity to large-scale WWTPs (Rehrl et al., 2020) and WWTP treatment efficiency (Golovko et al., 2021), or other pollution sources, e.g., landfill leachate (Gobelius et al., 2018). Spatiotemporal variations can occur due to fluxes of people, e.g., summer or winter tourism (Maasz et al., 2019; Mandaric et al., 2017). However, more research is needed to better understand the seasonal cycling of CECs in the aquatic environment.

The overall aim of this study was to assess the occurrence and mass flows of CECs in Sweden's three largest lakes and associated rivers. Specific objectives were to (i) evaluate the occurrence of CECs in lake and river waters, (ii) determine the variation between seasons, (iii) estimate the loads of CECs from rivers to the lakes, and (iv) assess the environmental impact of CEC loads. This was the first systematic study of CECs in the three largest lakes in Sweden.

2. Materials and methods

2.1. Standards, reagents, and chemicals

Standards, reagents and chemicals: Reference standards were purchased from Sigma-Aldrich (Sweden). Isotopically labelled internal standards were purchased from Wellington laboratories (Canada), Teknolab AB (Kungsbacka, Sweden), Sigma-Aldrich and Toronto Research Chemicals (Toronto, Canada). All analytical standards were of high analytical grade (>95%).

A total of 105 target CECs were selected for analysis, based on occurrence and distribution in the aquatic environment, and production and consumption patterns (Golovko et al., 2020a, 2020b, 2021; Örn et al., 2019; Rehrl et al., 2020). Detailed information about the target contaminants can be found in Table S1A and S1B in Supporting Information (SI) and detailed information about purchased standards,

reagents, and chemicals can be found in text in SI.

2.2. Study sites and sample collection

Lake Vänern, Lake Vättern, and Lake Mälaren are the three largest lakes in Sweden, with a respective area of 5450, 1890, and 1070 km² and a respective volume of 153, 73.5, and 14.3 km³ (Eklund et al., 2018). They are also among the largest lakes in Europe (European Environment Agency, 2018). Lakeshore areas of Lake Vänern, Vättern, and Mälaren have a population of 0.3, 0.2, and 3 million, respectively (Eklund et al., 2018). The water residence time is nine years, 60 years, and three years, respectively (Eklund et al., 2018). All three lakes are vital drinking water reservoirs (Eklund et al., 2018).

Rivers were selected for sampling based on their water flux to the lakes and expected high impact of urbanization or industry (Sonesten et al., 2013) (Table S2 in SI). The selected rivers for Lake Vänern were: Göta älv (R15 in Fig. 1), Ösan (R16), Tidan (R17), and Klarälven (R18-R20). Those for Lake Vättern were: Motåla ström (R21), Huskvarnaån (R22), the outlet from Munksjön (R23), and Lillån (R24), and those for Lake Mälaren were Svartån (R1), Kolbäckån (R2), Hedströmmen (R3), Arbogaån (R4), Eskilstunaån (R5), Sagån (R6), Enköpingsån (R7), Örsundaån (R8), Fyrisån (R9), Lövsån (R10), Märstaån (R11), Oxundaån (R12), Norrström (R13), and Köpingsån (R14) (Fig. 1).

Grab samples were collected in polypropylene (PP) or polyethylene bottles. Grab sampling was performed for two sampling events for rivers

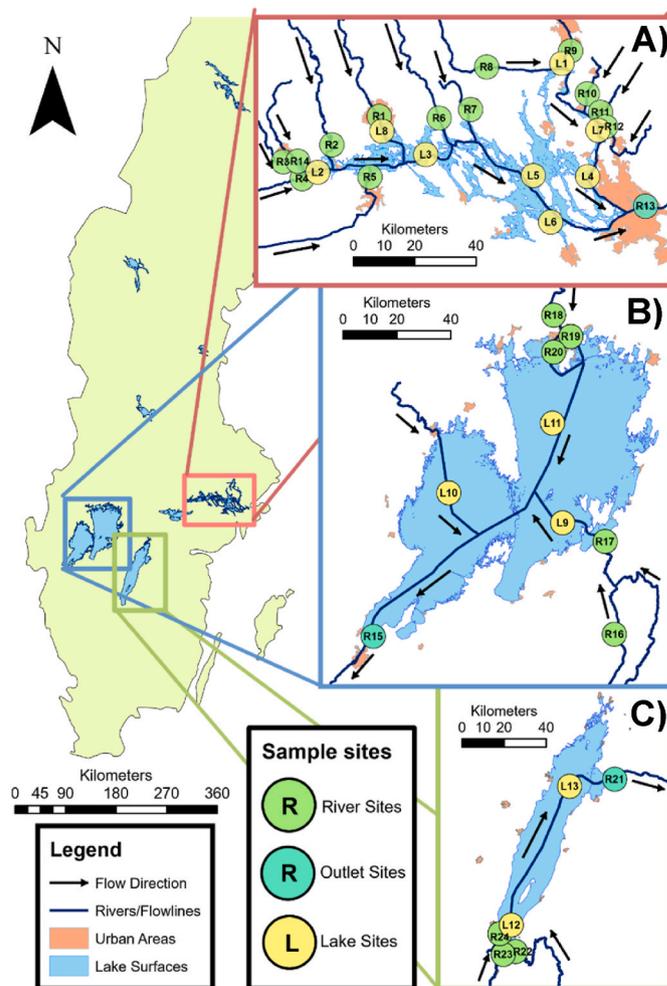


Fig. 1. Map showing surface water sampling locations in rivers (R) and lakes (L) (Lake Vänern (B), Lake Vättern (C), Lake Mälaren (A)) in Sweden.

(October 2019 and April 2020) (in total $n = 47$) and four sampling events for the lakes (Lake Vänern: July 2019, August 2019, October 2019, and April 2020; Lake Vättern: July 2019, September 2019, April 2020, and July 2020; Lake Mälaren: July 2019, September 2019, February 2020, and April 2020) (in total $n = 51$). The lake samples were collected at 0.5 m depth. Detailed information on sampling can be found in [Figure S1](#) in SI. After collection, the samples were stored frozen ($-20\text{ }^{\circ}\text{C}$) in darkness until extraction.

2.3. Sample preparation and UPLC-MS/MS analysis

Water samples (500 mL) from rivers ($n = 47$) and lakes ($n = 51$) were extracted by solid-phase extraction (SPE) using Oasis HLB-cartridges (6 mL, 200 mg, 30 μm) following the procedure described by [Söregård et al. \(2019\)](#). Samples were analyzed using a DIONEX UltiMate 3000 ultraperformance liquid chromatograph (UPLC) system (Thermo Scientific, Waltham, MA, USA) coupled to a triple quadrupole mass spectrometer (MS/MS) (TSQ Quantiva, Thermo Fischer Scientific, Waltham, MA, USA). The data were evaluated with Tracefinder 4.1 (Thermo Fischer Scientific, MA, USA). Detailed information regarding instrument configuration and analysis is described elsewhere ([Golovko et al., 2020a, 2020b, 2021](#); [Rehrl et al., 2020](#)).

2.4. Quality assurance and quality control

Method performance was evaluated with respect to blanks, precision, relative recovery, matrix effects, limit of quantification (LOQ), and linearity of the calibration curve ([Table S1](#) in SI).

Duplicate samples ($n = 13$) were prepared for every tenth sample. Fortified samples were prepared by spiking samples with internal and native standards (ISs and NSs respectively) before extraction. Fortified samples were prepared for minimum one lake sample and one river sample per season (in total $n = 22$). The calibration curves for individual substances (0.05–250 ng/L) generally had R-values >0.99 . The blanks consisted of Milli-Q water ($n = 9$) and were prepared and extracted in the same way as the samples and no target analytes were detected in method blanks. LOQ was calculated as one half of the lowest calibration point in the calibration curve where the relative standard deviation of the average response factor was $<30\%$. For all studied CECs, LOQs were in the range of 0.007–30 ng/L. The recoveries were on average 93% for the lake samples and 84% for the river samples. Matrix-matched standards were used to assess the matrix effect and were prepared from sample extract spiked with ISs and NSs at concentration levels equivalent to 20 ng/L and 100 ng/L, respectively. Matrix-matching samples were prepared for minimum one lake sample and one river sample per season (in total $n = 13$).

2.5. Statistical analysis

A Friedman test followed by a Tukey-Kramer post hoc test was performed, due to non-normal distribution of the data. Pearson correlation test was used to analyze the relationship between concentration and various parameters.

Data for total CEC concentration, flow, personal equivalents (PE) and distance were ranked from low to high numerical values. The corresponding ranks were then plotted pairwise. Spearman's rho was used to identify which pair of values had the highest observed rho when predicting the ranking of observed total concentration.

2.6. Data analysis

Mass flows of CECs were calculated for all rivers sampled, based on concentration and flow rate ([Söregård et al., 2019](#)), using the following equation:

$$m_{CECs,river} = \left(\sum_{i=1}^n C_{analyte(i)} (1 \pm \sigma) \right) \times Q_{river} (1 \pm (1 - NSE)) \times 8.64 \times 10^6$$

where $m_{CECs,river}$ [g/day] is the mass of quantified contaminants in sampled river, $C_{analyte}$ is the concentration of analyte in sample [g/L], σ is the standard deviation of analyte in chemical analysis, is the modeled river flow rate [m^3/s], NSE is the Nash Sutcliffe Efficiency coefficient, and the numerical values are conversion factors [$\text{L s m}^{-3} \text{ day}^{-1}$].

3. Results and discussion

3.1. Occurrence of CECs in river water

The \sum CEC concentrations in river water ranged between 31 and 5200 ng/L (mean 1100 ng/L, median 440 ng/L) ([Fig. 2](#), [Figure S2](#) in SI). Of the 105 target contaminants, 92 were detected at least once and 60 were detected in $>50\%$ of all samples ([Table S3](#) in SI). Numerous compounds were detected in all river samples analyzed, including desvenlafaxine (median concentration 11 ng/L; maximum concentration 150 ng/L), fexofenadine (7.8 ng/L; 200 ng/L), tributyl citrate acetate (ATBC) (5.4 ng/L; 29 ng/L), carbamazepine (5.0 ng/L; 91 ng/L), caffeine (4.3 ng/L; 880 ng/L), tris(2-butoxyethyl) phosphate (TBEP) (4.1 ng/L; 570 ng/L), nicotine (3.6 ng/L; 36 ng/L), and diethyltoluamide (DEET) (1.2 ng/L; 32 ng/L) ([Table S3](#) in SI). The highest concentrations were found for sucralose (1100 ng/L), caffeine (880 ng/L), tolyltriazole (750 ng/L), TBEP (570 ng/L), losartan (460 ng/L), sulisobenzene (BP-4) (420 ng/L), metoprolol (400 ng/L), and hydrochlorothiazide (HCTZ) (400 ng/L). On average, pharmaceuticals accounted for approximately 60% of \sum CEC concentrations, followed by other contaminants (20%), industrial chemicals (9%), PCPs (5%), pesticides (3%), PFASs (2%), and parabens (0.5%). The high percentage contribution by the group 'other contaminants' was due to high concentrations of the artificial sweetener sucralose (median concentration 74 ng/L; maximum concentration 1100 ng/L).

Some of the pharmaceuticals found in high concentrations, such as metoprolol and HCTZ, have been detected previously in river waters (e.g., [Čelić et al., 2019](#); [Maszkowska et al., 2014](#)). Carbamazepine has been detected in numerous studies (e.g., [Loos et al., 2009](#); [Tousova et al., 2017](#)), in median concentrations up to 15-fold higher than seen in this study. [Ruff et al. \(2015\)](#) analyzed three antiepileptic drugs in water from the river Rhine and reported a similar combined concentration as seen in the present study (median 64 ng/L; maximum concentration 244 ng/L). High detection frequency and high median concentration of beta-blockers in river water have been reported globally ([Maszkowska et al., 2014](#)), with concentrations in surface waters being highest for e.g., metoprolol ([Godoy et al., 2015](#)).

For industrial chemicals, except for tolyltriazole (median 15 ng/L), the concentrations were low compared with those reported in other European studies. [Wolschke et al. \(2011\)](#) compared concentrations in rivers in central Europe, where tolyltriazole was typically present in median concentration >100 ng/L and maximum concentration 470 ng/L. TBEP was found ubiquitously in the present study (median 4.1 ng/L), contradicting earlier findings in Sweden ([Gustavsson et al., 2018](#)), which could be due to lower LOQ in this study (0.072 ng/L) compared with the previous study (150 ng/L). ATBC was detected in low concentrations in this study (median 5.4 ng/L), whereas seven-fold higher concentrations have been found in Swedish rivers impacted by wastewater ([Golovko et al., 2021](#)). To the best of our knowledge, only three other studies have examined ATBC in freshwater environments ([Bolívar-Subirats et al., 2021](#); [Golovko et al., 2021](#); [Nagorka and Koschorreck, 2020](#)).

Among PCPs, BP-4 had a detection frequency (DF) of 83% in the present study (median 27 ng/L), whereas the other UV-filter products 3-(4-methylbenzylidene) camphor (4MBC) was not detected and oxybenzone (BP-3) had low DF (38%). The high DF for BP-4 supports previous findings of DF 93% in wastewater-impacted Swedish rivers ([Golovko et al., 2021](#)). Non-detection of 4MBC in this study is in contrast to findings in other studies in Sweden (DF 73%; median concentration

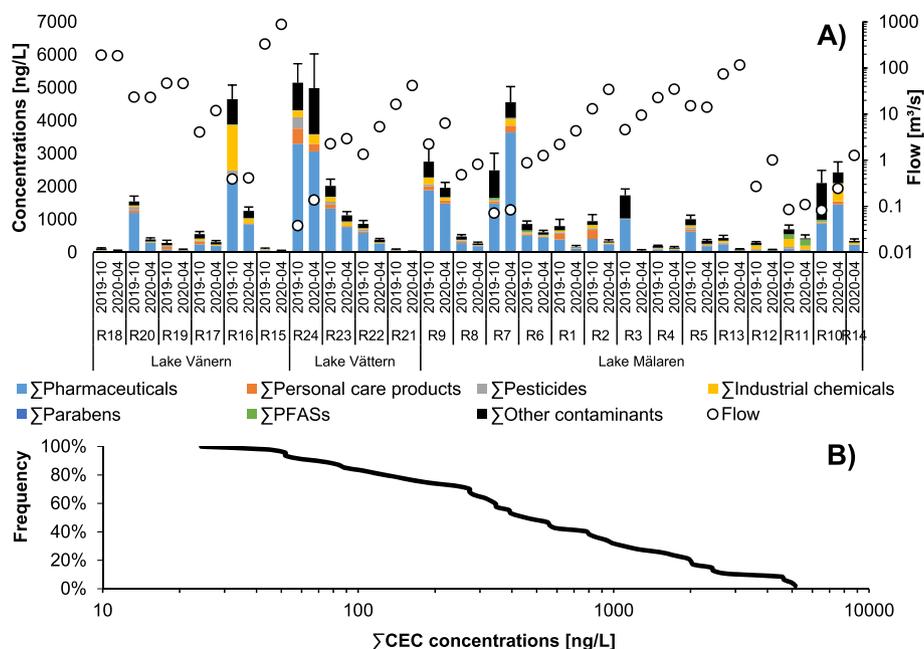


Fig. 2. Σ CEC concentrations in river water samples ($n = 47$). A) Σ CEC concentration and river flow rate; and B) reverse cumulative distribution as a function of Σ CEC concentration.

9.5 ng/L (Golovko et al., 2021), and internationally (DF 86%; median concentration 10 ng/L) (reviewed by Brausch and Rand, 2011).

Among the target pesticides, DEET had DF of 100%, which is similar to the level reported in other studies (e.g., DF 87% in Golovko et al., 2021; DF 94% in Tousova et al., 2017). However, both median and maximum concentration were lower in the present study (1.2 and 32 ng/L, respectively) than in the two earlier studies (23 and 180 ng/L; 17 and 490 ng/L, respectively).

The Σ PFASs concentration (median 8.2 ng/L) was slightly higher than observed by Nguyen et al. (2017) for sites R13, R15, and R21 (median 4.0 ng/L), but site R9 (11 ng/L) had only one-third of the Σ PFASs concentration detected by Nguyen et al. (2017) (33 ng/L). These differences could be due to seasonal variations and decreasing concentrations over time due to introduction of new regulations on PFASs (Gobelius et al., 2018), since samples for this study were collected more recently (2019–2020) than those analyzed by Nguyen et al. (2017) (collected 2013). In addition, C₈-based PFASs have been banned, which has resulted in decreasing concentrations in the environment (Gobelius et al., 2018). This can, for example, explain the low concentrations of PFOA (0.78 ng/L and 1.4 ng/L) and PFOS (1.6 ng/L and 3.1 ng/L) in this study (2019–2020) compared to a previous study on PFOA and PFOS (4.2 ng/L and 5.3 ng/L, respectively, 2013) (Nguyen et al., 2017) at site R9. Other contaminants were detected in similar concentrations to those reported previously, such as caffeine (median 4.3 ng/L) (e.g., 72 ng/L in Loos et al., 2009) and nicotine (median 3.6 ng/L) (e.g., 530 ng/L in Valcárcel et al., 2011). Sucralose was detected at higher concentrations in this study (median 100 ng/L, maximum 1100 ng/L) than in water from the river Rhine (range 20–170 ng/L in Ruff et al., 2015) and from major German rivers (range 60–80 ng/L) (Scheurer et al., 2009).

3.2. Factors impacting CEC concentrations in river water

Higher Σ CEC concentrations (range 1300–5200 ng/L) were found in wastewater-impacted rivers with low discharge (<0.5 m³/s) ($n = 8$) than in rivers with high discharge (typically >40 m³/s) (range 31–440 ng/L; $n = 10$). This indicates that low-discharge rivers are more impacted by point sources such as WWTP effluent (i.e., less dilution) than rivers with high discharge (higher dilution), which is in agreement with previous findings (Castiglioni et al., 2018; Golovko et al., 2021). A Pearson

correlation test was performed for wastewater-impacted rivers ($n = 14$ of 24 river sites), covering Σ CEC concentrations (ng/L) versus flow rate (m³/s), PE of upstream WWTPs, and distance (m) between the sampling point and upstream WWTP effluent (Table S2 and Figure S3 in SI). The Σ CEC concentrations were significantly negatively correlated with discharge ($r = -0.43$, $p = 0.0093$) (Figure S3A in SI), and with distance between the sampling point and WWTP ($r = -0.36$, $p = 0.036$) (Figure S3C in SI). River discharge determines the ratio between river water and effluent wastewater, resulting in a dilution factor (Li et al., 2016). The estimated dilution factor in Sweden is typically between 100 and 1000 (Keller et al., 2014). Decreasing concentrations with increasing distance from the polluting source have been reported previously (e.g., Kunkel and Radke, 2011). There was no correlation between Σ CEC concentration and PE ($r = -0.04$, $p = 0.85$; Figure S3B in SI). This could be explained by the strong impact of water flow, which resulted in dilution of Σ CEC concentrations independently of number of PE served by upstream WWTPs. When comparing all three factors (flow rate, PE, and distance between the sampling point and the upstream WWTP) against the Σ CEC concentrations, a significant correlation was found ($r = 0.49$, $p = 0.002$) (Fig. 3), but with two outliers (R7, both sampling seasons).

Without the outliers, the correlation was even higher ($r = 0.65$, $p = 0.00001$). Uncertainties relating to the modeled flow rate could not explain the outliers. The outlier location R7 could be due to potential underestimation of the distance between the sampling point and the upstream wastewater effluent, or the nonlinear relationship between Σ CEC concentrations and river discharge (Figure S3A in SI). Contrary to our expectations, neither distance to point nor PE equivalents showed significant correlations with CEC concentrations ($p > 0.05$). Water flow on the other hand revealed to have a rho of 0.71 ($p > 0.05$). This indicates that water flow is an important driver when sampling for CECs and changes of water flow needs to be taking into account when evaluating the risks of CECs to the environment. Mass fluxes, on the other hand, should rely on representative flow conditions instead of unrepresentative low flow events.

3.3. Occurrence of CECs in lake water

The cumulative concentration in lake water varied between 36 and

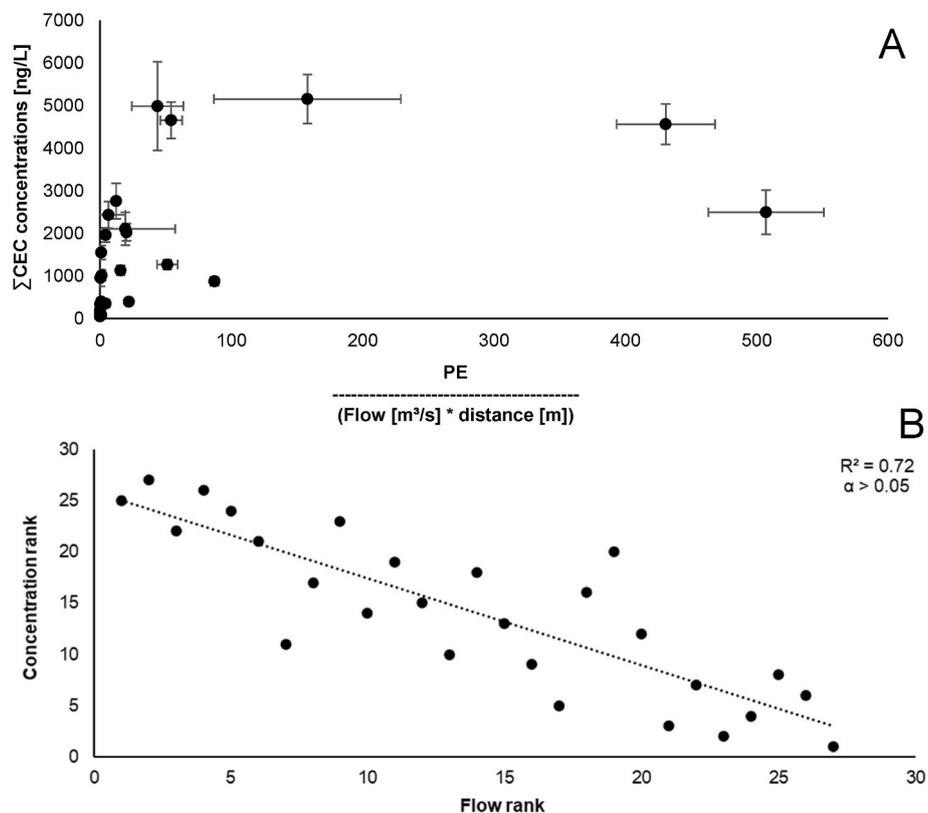


Fig. 3. A) Evaluation of \sum CEC concentrations vs PE and the inverse of flow and distance to WWTP. Vertical error bars: standard deviation of \sum CEC concentrations, horizontal error bars: model uncertainties of river discharge. B) Evaluation of \sum CEC concentrations vs riverine flow using ranked data.

900 ng/L, with a median value of 190 ng/L (Fig. 4, Figure S4 in SI). Of the 105 target CECs analyzed, 75 contaminants were detected at least once, 33 contaminants in >50% of the samples, and 11 contaminants in all samples (Table S4 in SI). On average, the category ‘other contaminants’ accounted for approximately 47% of the \sum CEC concentration, followed by pharmaceuticals (35%), industrial chemicals (7%), PCPs (3%),

pesticides (2%), PFASs (2%), and parabens (2%). \sum_1 artificial sweetener (other contaminants) was the group with the highest median concentration (72 ng/L; maximum concentration 370 ng/L), followed by \sum_2 stimulants (other contaminants; 21 ng/L; 91 ng/L), \sum_8 industrial chemicals (17 ng/L; 49 ng/L), \sum_4 antiepileptics (pharmaceuticals; 16 ng/L; 190 ng/L), \sum_8 antidepressants (pharmaceuticals; 4 ng/L; 65 ng/L)

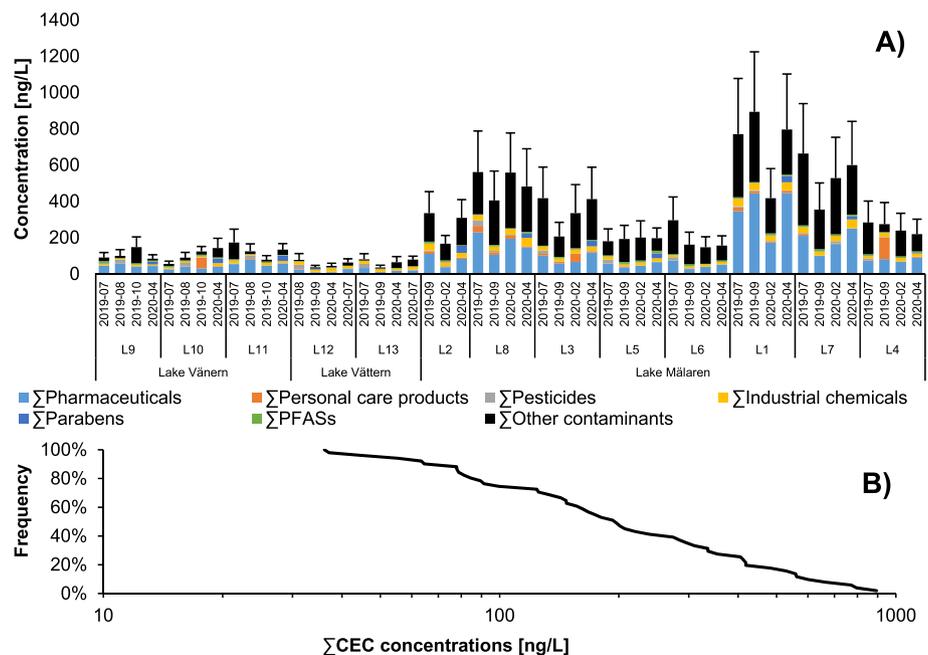


Fig. 4. \sum CEC concentrations in lake water samples ($n = 51$). A) \sum CEC concentration in samples L1-L8 from Lake Mälaren, samples L9-L11 from Lake Vänern, and samples L12-L13 from Lake Vättern; and B) reverse cumulative distribution as a function of \sum CEC concentration.

L), \sum_1 anesthetic (pharmaceuticals; 3.2 ng/L; 50 ng/L), and \sum_2 pesticides (2.9 ng/L; 31 ng/L).

Contaminants detected in all samples were caffeine (median concentration 20 ng/L; maximum concentration 91 ng/L), lamotrigine (9.6 ng/L; 150 ng/L), ATBC (8.3 ng/L; 32 ng/L), carbamazepine (5.0 ng/L; 37 ng/L), desvenlafaxine (3.9 ng/L; 19 ng/L), bicalutamide (2.4 ng/L; 19 ng/L), DEET (2.1 ng/L; 6.5 ng/L), fexofenadine (1.6 ng/L; 32 ng/L), PFOA (1.5 ng/L; 4.5 ng/L), metoprolol (1.2 ng/L; 24 ng/L), and triisopropanolamine (0.87 ng/L; 4.4 ng/L) (Table S4 in SI). The highest concentrations were found for sucralose (370 ng/L), lamotrigine (150 ng/L), laurilsulfate (120 ng/L), caffeine (91 ng/L), tramadol (59 ng/L), sulisobenzone (59 ng/L), HCTZ (54 ng/L), and lidocaine (50 ng/L). Lake Mälaren had higher median (340 ng/L) and maximum \sum CEC concentration (900 ng/L) than Lake Vänern (110 ng/L and 170 ng/L, respectively) and Lake Vättern (64 ng/L and 81 ng/L, respectively).

The dominant CECs detected in this study (i.e., lamotrigine, carbamazepine, bicalutamide, fexofenadine, metoprolol, tramadol, lidocaine, and DEET) showed similar patterns to those reported in previous studies (Golovko et al., 2020b; Maasz et al., 2019; Moschet et al., 2013; Rehr et al., 2020). HCTZ was not detected in lake water in a previous analysis (Moschet et al., 2013), but sampling in that study was performed during sun-intensive months (May–October 2009). HCTZ degradation is strongly dependent on photolysis (Baena-Nogueras et al., 2017), which could explain why the highest DF in this study was seen in April 2020 (33%, 50% and 63% in Lake Vänern, Vättern, and Mälaren, respectively, 54% overall), and the lowest in July 2019 (67%, 0%, and 29% in Lake Vänern, Vättern, and Mälaren respectively, 33% overall). Similar caffeine concentrations and DF values have been reported previously for Swedish surface waters (Rehr et al., 2020). However, higher concentrations of caffeine have been found lake water in other countries, e.g., in Lake Batalon, Hungary (Maasz et al., 2019). ATBC and triisopropanolamine were ubiquitously detected in lake waters in this study, but few previous studies have examined these chemicals. PFOA has previously been investigated in Swedish lakes in remote areas (Gobelius et al., 2018), with concentrations in the range <0.40–0.90 ng/L (DF 50%, $n = 10$), which is slightly lower than in this study (median 1.5 ng/L, DF 100%).

The largest variation in \sum CEC concentrations between seasons was observed for Lake Mälaren in July 2019 and February 2020 or April 2020 (Fig. 4A). These differences in \sum CEC concentrations (range 160–480 ng/L between seasons) were observed at sites L1–L3 and L7–L8, i.e., mostly urban lake sites. A Friedman test followed by a Tukey-Kramer post hoc test was performed for sites L1, L7, and L8 to evaluate seasonal variations at sites close to urban areas (viz. Fig. 1), using data for four seasons (Fig. 4). Of the major CEC groups, PCPs ($Q = 15.50$, $p = 0.00043$) and parabens ($Q = 15.50$, $p = 0.00043$) showed seasonal variations (Figure S5 in SI), the results for industrial chemicals ($Q = 17.00$, $p = 0.00020$) were inconclusive (Figure S5 in SI), and no variation was observed for the other major groups. PCPs showed seasonal variations between July 2019 and April 2020, and parabens showed seasonal variations between September 2019 and April 2020. Several pharmaceutical groups exhibited seasonal variations (Figure S5 in SI), including: antihistamines ($Q = 16.50$, $p = 0.00026$) between July 2019 and February 2020, antidiabetics ($Q = 15.88$, $p = 0.00036$) between July 2019 and April 2020, antineoplastic agents ($Q = 18.50$, $p = 0.00010$) between all seasons except February and April 2020, antibiotics ($Q = 18.50$, $p = 0.00010$) between all seasons except September 2019 and February 2020, and fungicides ($Q = 17.00$, $p = 0.00020$) between July 2019 and February 2020, and between July 2019 and April 2020.

Seasonal variations have been reported previously for PCPs (UV-filters) (reviewed by Mao et al., 2019), parabens (reviewed by Haman et al., 2015), antihistamines (Rehr et al., 2020), and antibiotics (Morano-González et al., 2014). To our knowledge, seasonal variations have not been reported previously for antidiabetics and antineoplastics. The results for antidiabetics could be a result of reduced biodegradation

(Straub et al., 2019). The results for antineoplastics are in contrast to Rehr et al. (2020), who reported that bicalutamide concentrations in lake water showed little annual fluctuation. The elevated concentrations of fungicides in lake water in July 2019 could possibly be due to increased use, as photolysis degrades fluconazole (Chen and Ying, 2015) and it undergoes negligible removal in WWTPs (Lindberg et al., 2010). Concentrations of the pesticides DEET and 2,6-dichlorobenzamide (BAM) did not show clear variations at the lake water sampling sites. The use of BAM's parent compound has been banned since 1990 (Ulén et al., 2002) and it is therefore suspected that leaching occurs independent of season. DEET is primarily used as an insect repellent during spring and summer (Merel and Snyder, 2016), however, DEET showed no temporal trends in surface waters in this study, which is supported by earlier studies (reviewed by Merel and Snyder, 2016).

3.4. Mass flows and seasonal variations in CEC concentrations in river water

The total mass of \sum CECs ($n = 105$) in the studied rivers ($n = 24$) had a median value of 180 g/day and a mean value of 610 ± 320 g/day (Fig. 5). The inlets corresponded to an estimated 16% (Table S5), 37% (Table S6), and 79% (Sonesten et al., 2013) of the total median river discharge into Lake Vänern, Lake Vättern, and Lake Mälaren, respectively. The average total mass load of CECs into the lakes was 5000 g/day (Lake Vänern, $n = 10$), 510 g/day (Lake Vättern, $n = 6$), and 5600 g/day (Lake Mälaren, $n = 24$). The outlets generally had high loads, Göta älv (Lake Vänern, R15, 3100 ± 2300 and 4300 ± 2700 g/day) Norrström (Lake Mälaren, R13, 2800 ± 1400 g/day), and Motala ström (Lake Vättern, R21, 120 ± 82 g/day).

The highest median loads in all rivers came from \sum_8 industrial chemicals, followed by \sum_1 artificial sweeteners (14 g/day), \sum_4 antiepileptics and \sum_8 antidepressants (both 11 g/day), \sum_6 beta blockers (9.3 g/day), \sum_2 analgesics (8.9 g/day), \sum_6 antihypertensives (8.1 g/day), \sum_2 diuretics (7.9 g/day), and \sum_6 NSAIDs (non-steroidal anti-inflammatory drugs) (6.1 ng/day) (Table S7). The top 10 substances with detection frequency >50% and with the highest median load were sucralose (40 g/day), BAM (8.9 g/day), acetaminophen (8.8 g/day), lamotrigine (8.4 g/day), venlafaxine (8.4 g/day), HCTZ (8.3 g/day), metoprolol (6.6 g/day), losartan (6.2 g/day), tolyltriazole (5.7 g/day), and sulisobenzone (5.5 g/day). High loads of anthropogenic markers, industrial chemicals, and pharmaceuticals in recipient waters have been reported in other studies (e.g., Castiglioni et al., 2018; Meffe and de Bustamante, 2014).

Variations in mass loads between seasons were observed for some compounds (Figure S6 in SI). During autumn, the antibiotic metronidazole, the UV-filters BP-3 and BP-4, the antipsychotic clozapine, the industrial chemical di-(2-ethylhexyl)phosphoric acid, the anti-asthmatic albuterol, the Alzheimer medicine memantine, and the antidepressant amitriptyline were typically found in higher loads at the sampled sites. During spring, the antibiotic erythromycin was typically found in higher loads.

Seasonal variations in concentrations of benzophenone-type UV-filters in river water are known, and their lower mass loads in spring could be due to their use in other PCPs (Mao et al., 2019). Clozapine degrades under direct photolysis (Trawiński and Skibiński, 2019). Seasonal variations in industrial chemicals were most likely due to their specific usages, as some such as motor vehicle antifreeze are used seasonally (Janna et al., 2011). While albuterol is expected to slowly photodegrade at environmentally-relevant pH (Dodson et al., 2011), its use in treating chronic-type diseases and its limited variations in the present study (Figure S6F in SI) make seasonal variation unlikely. Memantine is not affected by photolysis (Blum et al., 2017), and few reasons for seasonal use are expected (Golovko et al., 2014; Ibáñez et al., 2017). The increased loads of amitriptyline during autumn likely reflected an increase in use, as amitriptyline degrades by photolysis (Blum et al., 2017). In Greece, metronidazole was detected only in spring-time

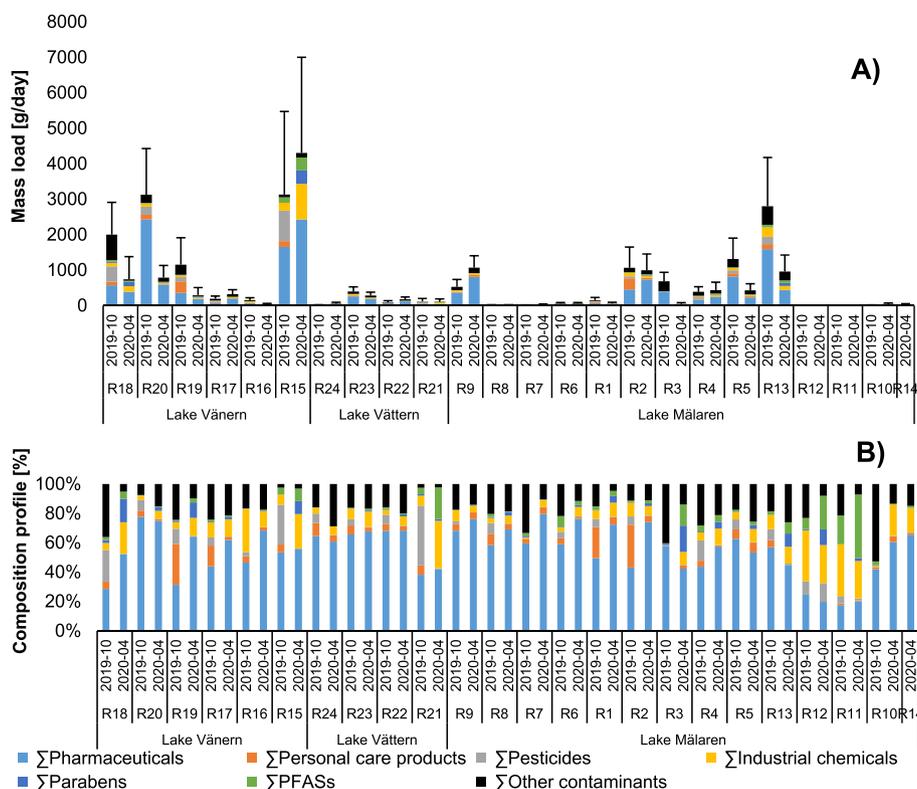


Fig. 5. Mass loads of target CECs in sampled rivers ($n = 47$). A) Overview of total mass load in all sampled rivers; and B) composition profile of sampled rivers.

(Papageorgiou et al., 2016), but in the present study metronidazole was detected in both autumn and spring (Figure S6A). In contrast with Papageorgiou et al. (2016), the highest mass loads were found in autumn. Data for erythromycin were not publicly available, but group-level data for macrolide antibiotics (category J01FA) show stable consumption throughout the year (Folkhälsomyndigheten, 2021). Macrolides have been shown to require days to photodegrade in environmental waters (Batchu et al., 2014).

3.5. Impact on the aquatic environment

The target CECs were detected in lake waters far from their point of emission. Thus the CECs showed high mobility and were transported via rivers and diffuse sources to the main Swedish lakes. The detected CECs also appeared to be persistent to degradation processes in the aquatic environment. Examples of persistent and mobile organic compounds (PMOCs) (Reemtsma et al., 2016) have been observed previously, e.g., metoprolol (reviewed by Godoy et al., 2015), or suspected, e.g., 2, 2'-dimorpholinyl-diethyl-ether (Schulze et al., 2018). This highlights the need for environmental monitoring of PMOCs, which are currently understudied (Reemtsma et al., 2016). It has been predicted that PMOC concentrations in (semi)enclosed water systems will increase over time as a result of their continued use in society (Hale et al., 2020). As the turnover time for Lake Vänern, Lake Vättern, and Lake Mälaren is nine years, 60 years, and three years, respectively, the CEC concentrations could persist or even increase over time. This is not only problematic for the environment (Galus et al., 2013; Kortenkamp et al., 2019), but possibly also for drinking water producers (Arp et al., 2017; Reemtsma et al., 2016), since the three Swedish lakes are all used as drinking water reservoirs. If PMOCs are also toxic (persistent, mobile, and toxic, PMT) (Schrenk et al., 2020; Vossen et al., 2020; Sangion and Gramatica, 2016), there are risks of long-lasting effects for humans and environment on an equivalent level of concern (ELOc) as reported for PBT substances (Hale et al., 2020; Richmond et al., 2018). Some CECs have been proven to be toxic at environmentally relevant concentrations (e.

g., Aguirre-Martínez et al., 2015), but mixtures of CECs are of most concern (Drakvik et al., 2020). A recent review of 10 years of experimental studies on CEC mixtures concluded that the default assumption should be of concentration addition for chemicals which produce a common toxic effect (Martin et al., 2021). Using the information on CEC composition in surface water provided in this study, CEC mixtures and concentrations can be assessed in hazard screening (Posthuma et al., 2019). The findings on seasonal variation in CECs provide additional information on the level of hazard, which might not be chronic but could be recurrent (Beckers et al., 2018; Nilsson et al., 2019).

4. Conclusions

The highest \sum CEC concentrations were found in wastewater-impacted Swedish rivers with low water flows. Of the parameters studied, river discharge was the best predictor of \sum CEC concentrations, followed by distance between the sampling point and upstream WWTP effluent in river water samples. The highest \sum CEC concentrations in lake water samples were found for Lake Mälaren. Three CEC groups, i.e., other contaminants, pharmaceuticals, and industrial chemicals, dominated the composition profiles in both lakes and rivers. Rivers were the main source of CECs in the lakes, supplying a median mass load of 180 g/day and a total mass load of 5600, 5000, and 510 g/day to Lake Mälaren, Lake Vänern, and Lake Vättern, respectively.

In river water samples, most CECs exhibiting seasonal variations had their highest load during autumn, whereas urban lake sites exhibited higher concentrations in winter and spring than in summer and autumn. In lake water samples, PCPs had their highest concentrations in summer and parabens in spring. The pharmaceutical groups fungicides, antihistamines, and antineoplastic agents exhibited their highest concentrations in summer, while antibiotic concentrations were highest in spring and summer. This shows that aquatic environments in Sweden are exposed to varying mixtures of CECs during the year.

A large number of CECs were detected and quantified in this study, some of which have scarcely been reported previously. It was shown that

some CECs were transported far from their point source in the fresh-water environment. Non-urban lake sites exhibited relatively stable concentrations between sampling occasions, showing persistence of some CECs. More studies are needed to estimate the hazard posed by CECs to the aquatic ecosystem.

Credit statement

Daniel Malnes: Formal analysis, Writing – Original & Draft, Sampling **Oksana Golovko:** Writing – Reviewing & Editing, Supervision, Methodology, Formal analysis, Data handling **Lutz Ahrens:** Writing – Reviewing & Editing, Supervision, Project administration **Stephan Köhler:** Sampling design, Supervision **Malin Forsberg:** Formal analysis, Sampling.

Declaration of competing interest

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

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.chemosphere.2022.133825>.

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