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# Pharmaceuticals in water and sediment of small streams under the pressure of urbanization: Concentrations, interactions, and risks

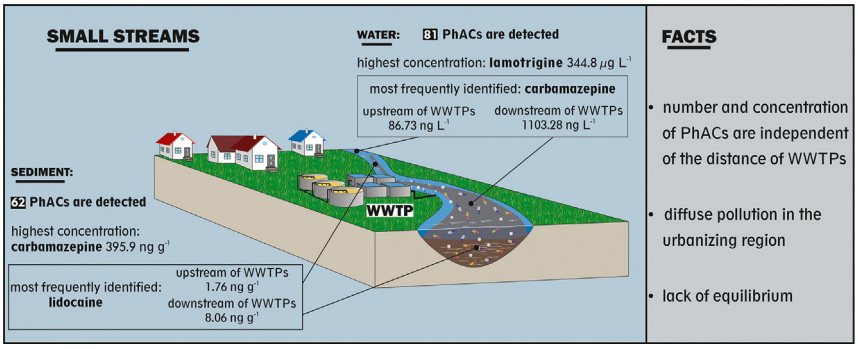
Attila Csaba Kondor [a], Éva Molnár [b], Gergely Jakab [a,c,d,*], Anna Vancsik [a], Tibor Filep [a], József Szeberényi [a], Lili Szabó [a,c], Gábor Maász [b,e], Zsolt Pirger [b], András Weiperth [f], Árpád Ferincz [f], Ádám Staszny [f], Péter Dobosy [g], Katalin Horváthné Kiss [h], István Gábor Hatvani [i], Zoltán Szalai [a,c]

[a] Geographical Institute, Research Centre for Astronomy and Earth Sciences, MTA Centre for Excellence, Budaörsi út 45, Budapest H-1112, Hungary
[b] Balaton Limnological Research Institute, Eötvös Loránd Research Network, Klebelsberg Kuno u. 3, Tihany H-8237, Hungary
[c] Department of Environmental and Landscape Geography, Eötvös Loránd University, Pázmány Péter sétány 1/C, Budapest H-1117, Hungary
[d] Institute of Geography and Geoinformatics, University of Miskolc, Egyetemváros, Miskolc H-3515, Hungary
[e] Soós Ernő Research and Development Center, University of Pannonia, Zrínyi Miklós Str. 18, Nagykanizsa H-8800, Hungary
[f] Department of Freshwater Fish Ecology, Institute of Aquaculture and Environmental Safety, Hungarian University of Agriculture and Life Sciences, Páter K. u. 1, Gödöllő H-2100, Hungary
[g] Institute of Aquatic Ecology, Centre for Ecological Research, Karolina út 29, Budapest H-1113, Hungary
[h] Aquaprofit Zrt., Krisztina krt. 32, Budapest H-1013, Hungary
[i] Institute for Geological and Geochemical Research, Research Centre for Astronomy and Earth Sciences, MTA Centre for Excellence, Budaörsi út 45, Budapest H-1112, Hungary

## HIGHLIGHTS

- A total of 111 PhACs were investigated in the water and sediment of small streams
- Eighty-one PhACs were detected in water and sixty-two were detected in sediment
- Number and concentration of PhACs were independent of the distance to WWTP outlets
- Water–sediment distribution coefficients suggested a lack of equilibrium
- High risks of diclofenac, E1, and the mixture of PhACs were determined

## GRAPHICAL ABSTRACT

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## ABSTRACT

Small streams are crucial but vulnerable elements of ecological networks. To better understand the occurrence of pharmaceutically active compounds (PhACs) in streams, this study focused on the occurrence, distribution, and environmental risk of 111 PhACs and 7 trace elements based on a total of 141 water and sediment samples from small streams located in the urbanizing region of Budapest, Hungary. Eighty-one PhACs were detected in the aqueous phase, whereas sixty-two compounds were detected in the sediment. Carbamazepine (CBZ) was the most frequently identified PhAC in water, and was found in 91.5% of all samples. However, the highest concentrations were measured for lamotrigine (344.8 $\mu g \cdot L^{-1}$) and caffeine (221.4 $\mu g \cdot L^{-1}$). Lidocaine was the most frequently occurring PhAC in sediment (73.8%), but the maximum concentrations were detected for CBZ (395.9 $ng \cdot g^{-1}$) and tiapride (187.7 $ng \cdot g^{-1}$). In both water and sediment, more PhACs were found downstream of the wastewater treatment plants (WWTPs) than in the samples not affected by treated wastewater, even though no relationship was observed between the total amount of treated wastewater and the number of detected PhACs. The PhAC concentrations were also independent of the distance from the WWTP effluents. PhAC-polluted samples were detected upstream of the WWTPs, thereby suggesting

* Corresponding author at: Geographical Institute, Research Centre for Astronomy and Earth Sciences, MTA Centre for Excellence, Budaörsi út 45, Budapest H-1112, Hungary.
*E-mail address:* jakab.gergely@csfk.org (G. Jakab).

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the relevance of diffuse emissions in addition to WWTP outlets. The most frequently detected PhACs in the sediment were usually also present in the water samples collected at the same place and time. The varying concentrations of PhACs and the fluctuating water–sediment properties resulted in a lack of correlation between the general chemical properties and the concentrations of PhACs, which makes it difficult to predict PhAC contamination and risks in urbanized small streams. The environmental risk assessment indicated that diclofenac had the highest risk in the sampling area.

## 1. Introduction

The occurrence of human pharmaceutically active compounds (PhACs) in aquatic ecosystems is of increasing concern worldwide (Li, 2014; López-Pacheco et al., 2019; Rosi-Marshall and Royer, 2012). The long-term presence of some PhACs with high ecotoxic potential and other toxic compounds, such as heavy metals, can cause considerable risks in aquatic environments with phenotypically and/or genotypically detectable damage (Bókony et al., 2018; Crane et al., 2006; Staszny et al., 2021). These can contribute to the degradation of ecosystems, thereby causing significant losses of global freshwater biodiversity and ecosystem services (Erős et al., 2018; Gál et al., 2019; Jourdan et al., 2018; Murdoch et al., 2020). Dendritic networks of smaller streams, which make up more than 88% of the global freshwater stream length and ensure habitat for many taxa (Maloney et al., 2020), are strongly subjected to contamination by PhACs because small, low-order streams (Strahler number 1–3; Strahler, 1957) are common recipients of treated and untreated wastewater (Casado et al., 2019; Ding et al., 2016; Mandaric et al., 2018; Sousa et al., 2019).

There has been growing recognition of the importance of small-sized and highly fragmented aquatic ecosystems (Di Sabatino et al., 2013), and more research has focused on the pollution of low-order streams both in urban and rural areas (Aleksander-Kwaterczak and Plenzler, 2019; Englert et al., 2013; Kienle et al., 2019; Liu et al., 2020; Proia et al., 2016; Szöcs et al., 2017). In smaller streams, it was observed that owing to the lower dilution compared with that in rivers with a higher water flow, the PhAC concentration may be related to the effluents of wastewater treatment plants (WWTPs) (Ebele et al., 2017; Maasz et al., 2019; Paíga et al., 2019). However, other agricultural or urban point sources (eg. fertilizers, leaking sewage infrastructure, septic-field leachate, untreated wastewater etc., (Battaglin et al., 2018; Bradley et al., 2016; da Silva et al., 2011; Fork et al., 2021; Kramulov et al., 2017; Verlicchi et al., 2012)) can also be primary sources of pollution. Polluted effluents and leachates can cause persistency or pseudo-persistency (Daughton, 2003) of several PhACs in the environment, such as endocrine disruptor hormones (e.g., EE2), beta-blockers [e.g., propranolol (PRP) and metoprolol (MTP)], anti-inflammatory drugs [e.g., paracetamol and diclofenac (DCL)], antiepileptic drugs [carbamazepine (CBZ)], antidepressants (citalopram), antibiotics, and illicit drug metabolites (aus der Beek et al., 2016; Bradley et al., 2020; Patel et al., 2019). The constant supply of treated or untreated wastewater can be responsible for the frequent occurrence of more biodegradable compounds in small streams [e.g., caffeine (CAF), (Buerge et al., 2003).

Stream sediments can adsorb PhACs from the water phase influencing PhACs concentrations in aqueous phase. The sorption potential of PhACs in sediments, which are governed by different mineralogical characteristics, is affected by several factors [pH, total organic carbon (TOC) content, redox potential, ionic interactions, and formation of PhAC aggregates, among others] (Al-Khazrajy and Boxall, 2016; Filep et al., 2021a, 2021b; Liu et al., 2019; Moreno-González et al., 2015; Vazquez-roig et al., 2012). The organic matter content and compounds in the solid phase also regulate the sorption capacity (Al-Khazrajy et al., 2018; Filep et al., 2021b). In smaller rivers, the outcome of the sorption processes of micropollutants may be unpredictable owing to the ever-changing circumstances and the absence of equilibrium (Patrolecco et al., 2010; Fairbairn et al., 2015).

Concentrations in urban streams can change considerably with variations in water discharge, wastewater effluent, the micropollutant removal capacity of WWTPs, the spatially different failures of the aging wastewater infrastructure, and seasonality (Alder et al., 2010; Fork et al., 2021; Liu et al., 2020; Luo et al., 2014; Mandaric et al., 2018; Yang et al., 2015; Yuan et al., 2020) In recent decades, the risks of PhACs are seriously exacerbated by other processes in urban stream networks, such as climate change and urban sprawl. Global climate change can cause extreme runoff events, and in many countries, extended low-water periods may increase the contamination of PhACs during the growing season (Wolff and van Vliet, 2021). Urban expansion, which results in the fragmentation of habitats by land-use conversion worldwide (Gardi, 2017; Zipperer et al., 2012), amplifies the risks of warming and reshapes the urban hydrosphere. The modified or sealed natural water pathways and the reduced water buffer capacity caused by urban sprawl lead to increased surface runoff, changing fluvial morphology, and rapid erosion of sediments during heavy precipitation events (Braud et al., 2013; Napieralski, 2020; Neller, 1988; Pizzuto et al., 2000; Verbunt et al., 2005). Fast runoff exacerbates water scarcity during dry periods when treated wastewater represents almost 100% of the total flow in small streams (Brus and Perrodin, 2017; Gosset et al., 2021; Osorio et al., 2012), and can change the physicochemical properties and adsorption capacity of sediments, resulting in a significant change in the level of risk.

Although some assessments of pharmaceutical effects and risks have already been performed for extended urban stream networks (Gosset et al., 2020, 2021; Tamura et al., 2017) and in U.S., for example, the Geological Survey (USGS) carried out a multi-region assessment of PhACs exposures with cumulative risk approach (Bradley et al., 2021, 2019), there are still limited data available on the spatiotemporal patterns of PhACs, the water-sediment interactions, and risks of PhACs both in aqueous and solid phases of urban stream systems. This study intends to show the sources, occurrence and distribution of 111 PhACs and 7 trace elements in water and sediments of small watercourses within a highly urbanized region in Hungary. The specific objectives were to i) determine the concentrations of contaminants in water and related sediment in a complex stream network, ii) analyze the spatial patterns of PhAC contamination and sediment–water interactions in relation to the WWTP outlets, and iii) assess the level of PhAC-associated risks both in water and sediment, based on ecotoxicological data from literature and own empirical distribution data. Our main hypothesis was that the concentrations fluctuate in water with space and time, and the locations of WWTPs effect on PhACs occurrence and concentrations.

## 2. Materials and methods

### 2.1. Study area and data collection

This study was performed in the highly urbanized area and commuting zone of Budapest, central Hungary, which comprises approximately 8200 $km^2$ and has more than 3.3 million inhabitants (population density: 400 people·$km^{-2}$). In the last three decades, land use conversion and the rate of urban sprawl have increased, and the proportion of artificial surfaces is now almost 20% (Kovács et al., 2019). In this research, 26 small streams were sampled at 75 sampling sites (Fig. 1**; Fig. S1**). The sampling frame was part of a larger research program aimed at exploring the PhACs contamination and its environmental and human risks of surface water (including the river Danube), groundwater, and drinking water in the Budapest metropolitan area (Kondor et al., 2021, 2020; Staszny et al., 2021). The average water discharge of the sampled perennial streams ranged from 0.01 $m^3 \cdot s^{-1}$ to 0.46 $m^3 \cdot s^{-1}$, but the average water flow of 19 streams did not reach 0.10 $m^3 \cdot s^{-1}$ (**Table S1**) (RBMPH, 2015). Most of these small

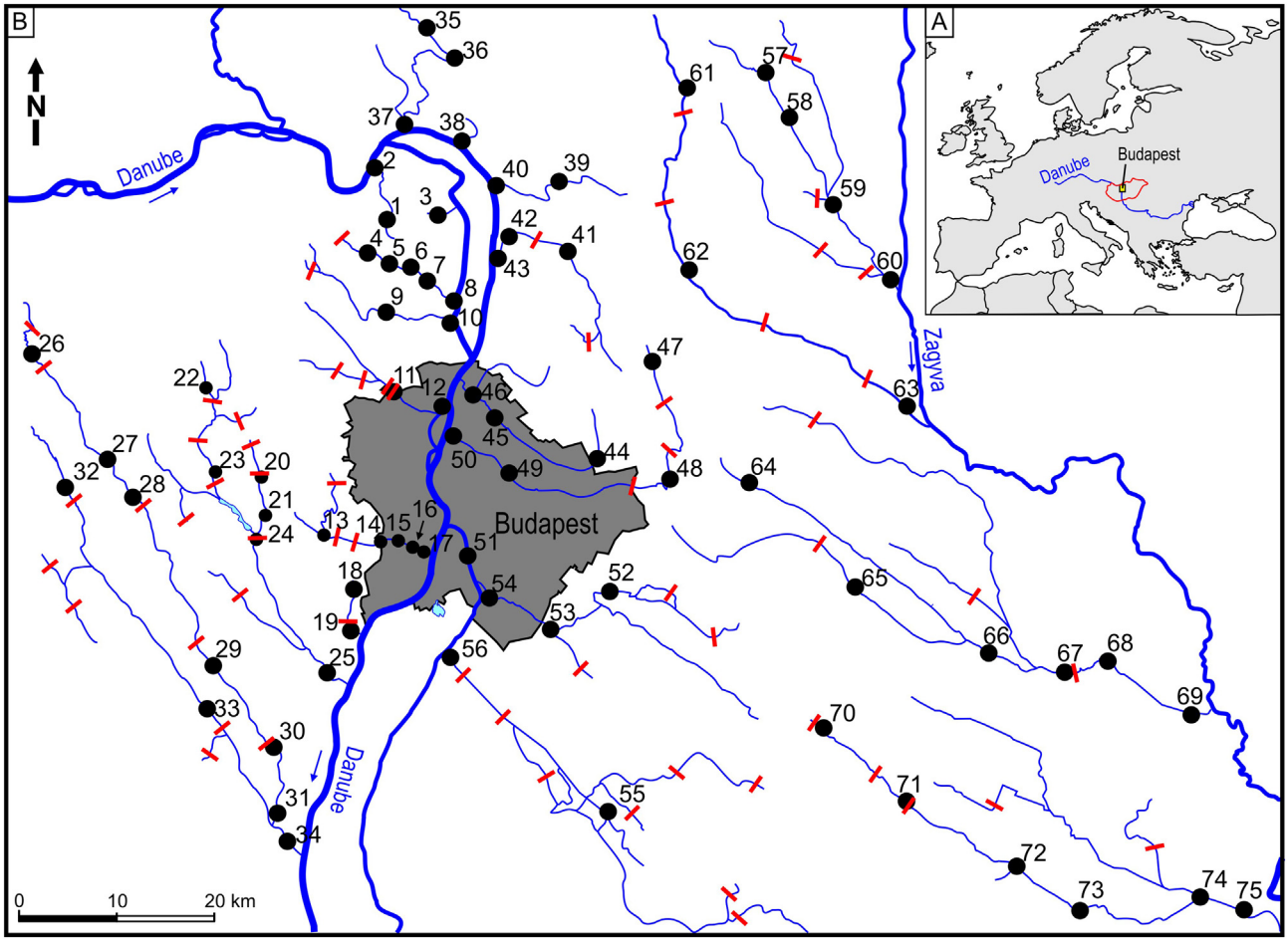


**Fig. 1.** Sampling area in the urbanizing region of Budapest, Hungary. Location of the study site in Europe (A) and location of the sampling sites (B). Red lines indicate the location of wastewater treatment plants.

catchments are connected to the Danube River basin, and six of the sampled streams flow partly through the city of Budapest. The Zagyva and Tisa rivers are the recipients of six streams, and these sub-catchments are also located in the suburban area of Budapest.

The area is mainly flat (100–200 m a.s.l.) with an elevated area in the northwest (**Table S2**). The average annual temperature is 10–12 °C and the average precipitation is 550–650 mm. More than 80% of the dwellings in the study area are connected to the public wastewater network. Sixty-two conventional WWTPs with different capacities produce approximately 30 million $m^3$ of treated wastewater per year in the study area without post-treatment (**Table S3**). Twenty-one sampling sites were located above WWTP discharges, from which thirty-five samples were collected. The outflows of the largest WWTPs of Budapest, which are responsible for 80% of the discharged wastewater in this region, flow directly into the Danube River (Kondor et al., 2020); thus, they were not covered by this study.

### 2.2. Sampling

To determine the degree and spatiotemporal processes of PhAC concentrations and trace elements, 141 water and sediment grab samples were collected at the same time and place in 2017 and 2018. One hundred and eleven PhACs with various physicochemical characteristics (**Table S4**) and seven heavy metals in both the aqueous and sediment phases were examined. The details of the applied water sampling methods, preparation processes, instrumental analytical approaches, validation parameters of measured PhACs, and data evaluation have been published in previous studies (Kondor et al., 2020; Maasz et al., 2019). Briefly, water sampling for strong anion and cation analyses was conducted by collecting a 500 mL water sample in a brown borosilicate glass container. For TOC and total nitrogen (TN) analyses, 50 mL water samples were collected in a white borosilicate container and acidified by adding 500 μL of 2 M hydrochloric acid (VWR International, Pennsylvania, USA). To determine the elemental concentration, a 15 mL water sample was filtered through metal residue-free centrifuge tubes using a 0.45 μm syringe filter, and then 100 μL of high-purity nitric acid (VWR International, Pennsylvania, USA) was added to the sample. Water samples (2.5 L) for PhAC analysis were collected a few minutes prior to sediment sampling by submerging clean amber borosilicate glass bottles (Thermo Fisher Scientific, Massachusetts, USA) into the stream to a depth of 10–20 cm, after which each sample was acidified by applying HPLC-grade formic acid (VWR International, Pennsylvania, USA) to a pH of 3.5–4.0. Water samples were refrigerated at 4 °C until processing, which was initiated 72 h after collection.

For sediment analysis, grab samples of surface river sediments (0–10 cm depth) were collected in amber borosilicate glass jars (100 mL) (Thermo Fisher Scientific, Massachusetts, USA) using a stainless-steel scoop at the same sampling sites as the water. The jars were transported at −30 °C using a portable fridge freezer and stored until processing to maintain the cold chain.

### 2.3. Analysis of the aqueous phase

For water sample analysis, TOC and TN concentrations were quantified using a Multi N/C 3100 TC/TN analyzer (Analytik Jena, Germany). Measurement of anions (fluoride, chloride, sulfate, bromide, and nitrate) and cations (ammonium, calcium, magnesium, sodium, and potassium) was conducted using a Dionex ICS 5000+ chromatography system (Thermo Fischer

Scientific, USA). Total hardness, alkalinity, phosphate, and nitrite were determined by applying standard titrimetric and spectrophotometric methods (American Public Health Association et al., 2005). Trace element concentrations were measured using a PlasmaQuant MS Elite inductively coupled plasma mass spectrometer (Analytik Jena, Germany). PhAC quantitative analysis was conducted using supercritical fluid chromatography (ACQUITY UPC2 system, Waters) coupled with tandem mass spectrometry (Xevo TQ-S Triple Quadrupole, Waters) (SFC-MS/MS). The samples were vacuum-filtered through a 0.7 μm glass microfiber filter (#516-0345, VWR) and spiked with internal standards (IS) (except in the case of sediment extract). The analytes were desalted and concentrated using an AutoTrace 280 automated solid-phase extraction system (Thermo Fischer Scientific, Massachusetts, USA) with Strata X-CW cartridges (#8B-S035-FCH, Phenomenex). The data were recorded using MassLynx software (V4.1 SCN950), and ion peak detection and evaluation were conducted using TargetLynx XS software (Waters). The 111 quantified PhACs, analytical parameters of the SFC-MS/MS method, limit of detection, limit of quantification (LOQ), and validation values are listed in **Table S5**.

### 2.4. Analysis of the solid phase

Sediment samples were air-dried and then kept in a sample incubator at 40 °C to eliminate water residue. The dried samples were ground and homogenized using a mortar and pestle and then sieved through a 500 μm sieve. For elemental analyses, the sediment samples were mineralized using a microwave-assisted acid digestion system (TOPWave, Analytik Jena, Germany); 300–500 mg sediment samples were digested in a mixture of 7 mL of 67% nitric acid (VWR International, Pennsylvania, United States) and 3 mL of 30% hydrogen peroxide (VWR International, Pennsylvania, United States). After this process, the digested solutions were filled up to 25 mL with deionized water, and then 20 $\mu g \cdot L^{-1}$ internal standards (Sc, Y, and In) were added. The elemental concentrations of the samples were measured using a PlasmaQuant MS Elite inductively coupled plasma mass spectrometer (Analytik Jena, Germany). To determine the PhAC contamination level, freeze-dried samples were stored in pre-cleaned glass bottles at −30 °C until extraction. One gram of dried sediment sample was spiked with IS (citalopram-d6, carbamazepine-d10, E2-13C3, and N-ethyloxazepam) to a final concentration of 5 $ng \cdot g^{-1}$ and incubated at 20 °C for 2 h to achieve complete drying. The extraction solution (50 mL of $H_2O$: MeOH, 75:25) was added to the spiked sediment sample and the PhACs were extracted by microwave extraction using ETHOS X (MLS GmbH, Germany) at 50 °C and 800 W for 30 min. After extraction, the sample was centrifuged at 1000 rpm for 10 min, and the supernatant was transferred to a new glass bottle. Concentrated extracts were diluted with water to reduce the methanol content (< 5 vol%) and processed further as water samples (da Silva et al., 2011).

### 2.5. Data management, evaluation, and visualization

The frequency of occurrence (FRO) was calculated as the ratio of samples > LOQ, to the total number of samples expressed as a percentage. The overlap ratio between sediment and water samples shows the overlap in the percentage of a given PhAC detected in water and sediment samples taken at the same place and time.

The distribution of pollutants between the aqueous and solid phases was assessed by the observed solid–water distribution coefficients (log $K_{d(obs)}$ variation; Fairbairn et al., 2015), as follows (Eq. (1)):

$$\log K_{d(obs)} = \frac{\log CC_{sed}\frac{ng}{g}}{\log CC_{water}\frac{ng}{L}} \times 1000 \quad (1)$$

where $K_{d(obs)}$ is the solid–water distribution coefficient, $CC_{sed}$ is the concentration observed in the sediment, and $CC_{water}$ is the concentration observed in the water.

Owing to the lack of a normal distribution of most properties investigated in this study, non-parametric tests were conducted, such as the Spearman's Rho test, to measure the correlation between the variables with a significance level of 95%. The Mann–Whitney *U* test (Mann and Whitney, 1947) was used to measure the differences between the number of PhACs identified (> LOQ) upstream and downstream of the WWTPs. All the statistical analyses were conducted using IBM SPSS Statistics for Windows (version 22; IBM Corp., Armonk, NY, USA).

The sampling points were recorded using a Magellan Professional Mobile Mapper CX GPS/GIS receiver (Magellan Systems Corporation, San Dimas, CA, USA). A GIS database was built to reveal the spatial distribution of the investigated parameters using ArcGIS v. 10.3. software (ESRI Inc., Redlands, CA, USA). For quantitative assessments, land coverage data were derived from the CORINE, 2018 database (CORINE, 2018). The fine-scale population, housing, and wastewater network data were derived from the Hungarian Central Statistical Office (HCSO, 2021) (for 2017 and 2018) (**Table S3**).

To assess whether significant differences can be found in the stream and sediment samples' PhACs content, a One-way Analysis of similarities (ANOSIM) was conducted on the censored sample data converted to a binary absence-presence matrix (0/1) following the procedures described in Helsel (2011) (Supplementary C).

### 2.6. Environmental risk assessment

To estimate the ecological risk levels of the PhAC concentrations measured in the aquatic environment, the risk quotient (RQ) was calculated. The RQ of each PhAC concentration in each sample can be determined as the ratio of the measured environmental concentration (MEC) to the predicted no-effect concentration (PNEC), as follows (Eq. (2)):

$$RQ = \frac{MEC}{PNEC} \quad (2)$$

Generally, RQ < 0.01 represents a negligible risk, 0.01 < RQ < 0.10 indicates a low risk, 0.10 < RQ < 1.00 denotes a medium risk, and RQ > 1.00 refers to a high risk to aquatic organisms.

Environmental risk assessment allows predicting the concentration of a compound below which adverse effects are unlikely to happen to ecological communities during acute or chronic exposure (Finizio and Vighi, 2014). PNEC is defined as the ratio of selected ecotoxicological data (median effective concentration (EC50), median lethal concentration (LC50), no observed effect concentration (NOEC), and hazardous concentration for 5% of the species (HC5)) to an assessment factor (AF) (Table S6). Therefore, PNEC depends on the available results of ecotoxicological tests on different organisms (a more detailed determination of PNEC calculation is described in our previous publication: (Molnar et al., 2020)).

Because ecotoxicological data are absent in the case of the sediment matrix, $PNEC_{water}$ values were applied to estimate $PNEC_{sediment}$ and to assess the risk levels of PhAC concentrations using the following previously published formula (Eq. (3)) (Liu et al., 2018; Peng et al., 2020):

$$PNEC_{sediment} = \frac{PNEC_{water}}{1000} \times \frac{K_{oc}}{\%TOC} \quad (3)$$

where $\%TOC$ represents the TOC content of sediment expressed as a percentage by weight and $K_{oc}$ denotes the estimated sediment organic carbon-water partitioning coefficient from the Chemical Aquatic Fate and Effects (CAFE) database (Bejarano et al., 2016). When empirical sediment and water concentrations were also available from the same place and time, $PNEC_{sediment}$ values were also determined using Eq. (4) (Ashfaq et al., 2017; Martín et al., 2012):

$$PNEC_{sediment} = PNEC_{water} \times K_{d(obs)} \quad (4)$$

In order to identify which PhAC posed the highest risk (RQ) in a sampling site the maximum value of RQs ($RQ_{max}$) was assessed in both phases.

To determine the risk order between the sampling sites separately for the two phases investigated, $RQ_{mix}$ was used. The $RQ_{mix}$ equation (Eq. (5)) is based on the concentration-addition method for risk assessment of mixtures (Backhaus and Faust, 2012; Gosset et al., 2020, 2021), and is defined as the sum of the RQ values derived from PhAC concentrations in the water and sediment phases.

$$RQ_{mix\ (water/sediment)} = \sum_{i=1}^{n} RQ_i \quad (5)$$

By summarizing the $RQ_{mix}$ values of the samples collected from the different phases at the same site and time, $RQ_{mix\ sum}$ was defined (Eq. (6)) to determine the riskiest sampling sites considering the results of the risk assessment of both phases.

$$RQ_{mix\ sum} = \sum_{i=1}^{n} RQ_{mix\ water} + \sum_{i=1}^{n} RQ_{mix\ sediment} \quad (6)$$

In this study, we aimed to provide information on the environmental risk of the PhACs with a high (> 25%) FRO in water and/or sediment samples; thus, the RQ was determined for the 32 PhACs. For 20 PhACs, the assessment was based on experimental ecotoxicity data (**Table S6**).

## 3. Results and discussion

### 3.1. Occurrence of PhACs and trace elements in water

Eighty-one of the one hundred and eleven targeted PhACs were detected in the aqueous phase of the small streams (**Table S7; Table S8**). The antiepileptic drug CBZ was the most frequently identified PhAC, which was found above the LOQ (FRO: 91.5%) in almost all samples. Another six PhACs [the local anesthetic lidocaine (LID), the morphine derivative tramadol, the antiepileptic lamotrigine (LTG), and three cardiovascular drugs, namely perindopril (PER), losartan (LOS), and MTP] were detected in at least 76% of the samples, and the frequency of 23 other substances exceeded 20% (Fig. 2). These frequent PhACs are a concern worldwide because of their universal use and low removal efficiency in WWTPs (Golovko et al., 2021).

The concentrations were extremely variable for most PhACs, as indicated by the standard deviation and coefficient of variation (CV). Sixty-three PhACs occurred in at least three water samples, of which twenty-five compounds had a maximum value more than twice the second-highest concentration. The antiepileptic LTG, the alkaloid CAF, and the antiepileptic CBZ were detected at the highest maximum concentrations of 344.8, 221.4, and 58.9 $\mu g \cdot L^{-1}$, respectively. The concentrations of LTG and CAF exceeded 1 $\mu g \cdot L^{-1}$ in 59 and 29 water samples, respectively, and the concentration of CBZ was higher than 500 $ng \cdot L^{-1}$ in 19 samples. These high concentrations exceeded most of the literature data on surface water, and were more typical of treated wastewater (Patel et al., 2019; aus der Beek et al., 2016). These PhACs are considered to be markers of adjacent anthropogenic contamination mainly due to the high proportion of treated/untreated wastewater (Chaves et al., 2020; König et al., 2017). This is reinforced by the CV values, which exceeded 500% in the cases of CAF, CBZ, and LTG.

Notable measured data also occurred in other groups of PhACs, which indicate a very low degree of dilution and the presence of inefficiently treated wastewater or raw wastewater. For non-steroidal anti-inflammatory drugs (NSAID)s, the 60% FRO of DCL was not notable (Johnson et al., 2013); however, the maximum concentration of DCL (2070 $ng \cdot L^{-1}$) was remarkable, with a further 39 samples exceeding 100 $ng \cdot L^{-1}$. Although the more degradable NSAID drug naproxen (NPX) (Radke and Maier, 2014) appeared much less frequently, the maximum value (4659.3 $ng \cdot L^{-1}$) was the fourth highest of all substances. Although the pseudo-persistency of the most widely used β-blockers (e.g., bisoprolol and PRP), SSRI antidepressants (e.g., citalopram), frequently prescribed benzodiazepines (e.g., alprazolam, cinolazepam, and nordiazepam), and illicit drugs (cocaine with its metabolite, BZE) has been confirmed by the literature (Huerta-Fontela et al., 2008; Loos et al., 2013; Maasz et al., 2019, 2021), their variance is characterized by smaller extremities (CV of approximately 100–200%). The presence of some natural and synthetic steroid estrogens with endocrine disruptive effects, such as E1 and EE2, was also detected in the investigated waters (FRO: E1 = 51.8%; EE2 = 17.0%); however, the appearance of progestogens [e.g., progesterone (PRG) and drospirenone], despite the low LOQ, was extremely rare or completely absent in water samples [e.g., levonorgestrel (LNG)].

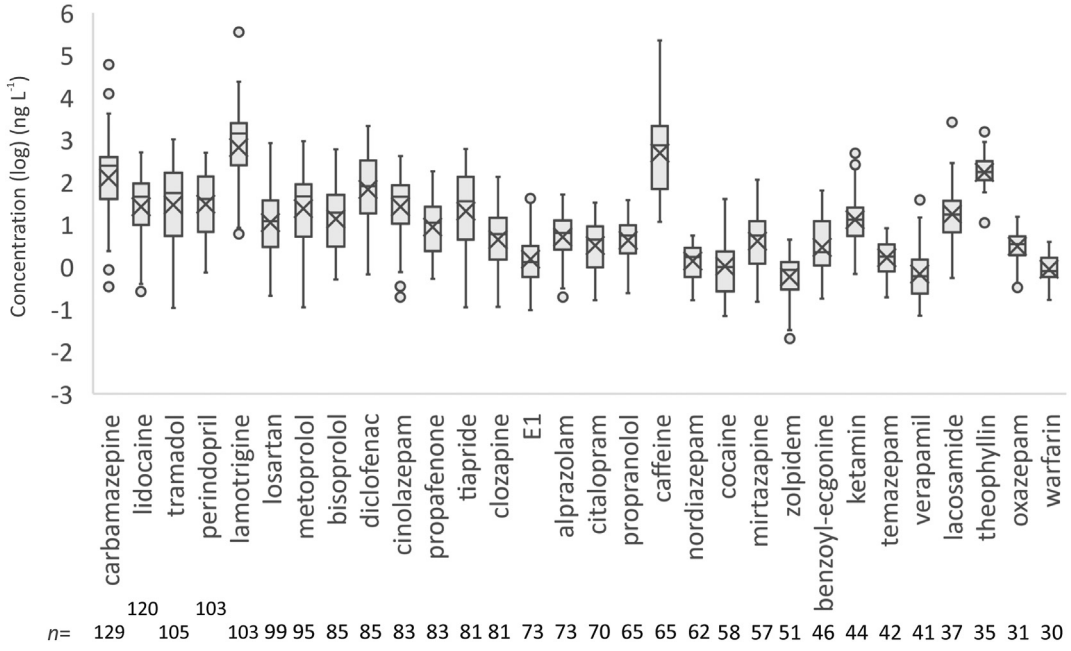


**Fig. 2.** Concentrations of the more frequent pharmaceutically active compounds (frequency of occurrence > 20%) in the water phase; concentrations run on a logarithmic scale; n: number of samples higher than the limit of quantification; the total number of samples: 141.

The number of PhACs found in water (81) was much higher than that found in the Danube River (52), which was sampled during the same period with the same methods around Budapest (Kondor et al., 2020). Although the FRO of the most persistent PhACs found in the Danube River was higher than that found in streams, the occurrence of less frequent PhACs was higher in small watercourses (**Table S9; Fig. S2**). This suggests that because of the longer travel time and high dilution capacity (König et al., 2017), some drugs cannot be detected in the Danube River, but the distribution of the most frequent pollutants from point sources with fluctuating concentrations will become more even.

Of the investigated non-essential metallic and semi-metallic trace elements, the concentrations of Zn and As were higher than the maximum allowable concentrations in 3 and 13 samples out of 144 (2% and 9%, respectively). In contrast, Hg exceeded the environmental standard in 83 water samples (57.6%). The concentrations of PhACs found in at least 25% of the water samples were not correlated with the measured water chemistry and trace element parameters (**Table S10**).

### 3.2. Occurrence of PhACs and trace elements in sediment

In the sediment samples, the concentrations of 62 PhACs were greater than the LOQ (**Table S11**). Twenty-five drugs were found in at least ten samples, but the FRO exceeded 20% for only eleven drugs (Fig. 3). LID was the most frequently occurring PhAC (73.8%) with higher concentrations (mean: 6.5 $ng{\cdot}g^{-1}$) and a higher maximum value (98.9 $ng{\cdot}g^{-1}$) than that described in the literature (< 0.3 $ng{\cdot}g^{-1}$; Ahrens et al., 2020; Yang et al., 2015). The less water-soluble CBZ and the antidepressant tiapride (TIP) were detected in more than 50% of the samples. CBZ has been detected in riverine sediments worldwide (Cardoso-Vera et al., 2021); however, to the best of our knowledge, TIP has not yet been detected in the sediments of small streams.

The mean concentrations of nine PhACs were more than 10 $ng{\cdot}g^{-1}$ above the LOQ, which also indicated the presence of untreated or poorly diluted treated wastewater in the streams. The maximum concentrations of five of these substances [olanzapine (OLZ), CBZ, CAF, TIP, and LTG] exceeded 100 $ng{\cdot}g^{-1}$. Although the antischizophrenic PhAC OLZ was detected in 25 water samples and has been found to occur at even higher concentrations in wastewater from psychiatric hospitals (Yuan et al., 2013), the outlier result from sediment sample site No. 30 (507.7 $ng{\cdot}g^{-1}$) might have been caused by significant pollution. The detected maximum concentrations of CBZ (395.9 $ng{\cdot}g^{-1}$) and CAF (153.6 $ng{\cdot}g^{-1}$) were also uncommon, but they have been described above 100 $ng{\cdot}g^{-1}$ in some sediments of various types of aquatic ecosystems regardless of their different chemical properties. The CBZ concentration in sediment exceeded the measured concentrations in the Ganga River (Chakraborty et al., 2019), a small stream in Doñana National Park, Spain (Camacho-Muñoz et al., 2013), and an urban pond from our sampling area (Bókony et al., 2018). CAF can also accumulate in sediment, as found by Matongo et al. (2015) in the very polluted Umgeni River near Durban, South Africa. TIP and LTG had similar maximum concentrations (187.7 $ng{\cdot}g^{-1}$ and 133.0 $ng{\cdot}g^{-1}$, respectively), but were not described in riverine sediments at all. In the case of substances with higher average concentrations, similar concentrations of NPX and DCL (NPX: < LOQ–20 $ng{\cdot}g^{-1}$; DCL: < LOQ–38 $ng{\cdot}g^{-1}$) were measured by Varga et al. (2010) in the Danube River sediments around Budapest. Six substances were detected only in the sediment, including the hormone LNG, which was found in 10 sediment samples. This may indicate limitations of grab sampling because episodic pollution cannot always be sampled in both matrixes (Chapin, 2015).

Among the trace elements, As exceeded the maximum allowable concentration in 17 sediment samples (11.8%). The environmental limits of the other elements were surpassed only in a few sediment samples. Similar to the water samples, no correlations were observed between the concentrations of PhACs found in at least 25% of the sediment samples and the parameters of water chemistry and trace elements (**Table S12**).

### 3.3. Spatiotemporal patterns of PhACs

In both water and sediment, significantly more PhACs were found below the WWTPs than in the 35 samples not affected by treated wastewater (Table S13). The average concentrations of each frequent compound were much lower in the water samples collected upstream of the WWTP effluents than those collected below the treated wastewater discharges (Table 1).

In the aqueous phase, there was only one water sample (ID 108 from site No. 58) above the WWTPs in which no PhACs were detected, but there were still 34 other water samples in which 1–28 PhACs were identified regardless of the fact that treated wastewater could not be found in the sampling site (Fig. S3a). There was a relationship ($r > 0.5$) between the total amount of effluent discharged upstream of the sampling sites and the number of detected PhACs, but no relationship could be detected between the total amount ($m^3{\cdot}y^{-1}$) of treated wastewater, and the sum of the PhAC concentrations ($ng{\cdot}L^{-1}$) (**Fig. S4a-e**). As our statistical model confirmed, there was no significant ($p < 0.05$) difference between the water and sediment samples closer or more distant from wastewater input sources. The presence of the PhACs is independent from the wastewater discharge and the treated wastewater/total flow ratio, especially in the case of the sediment

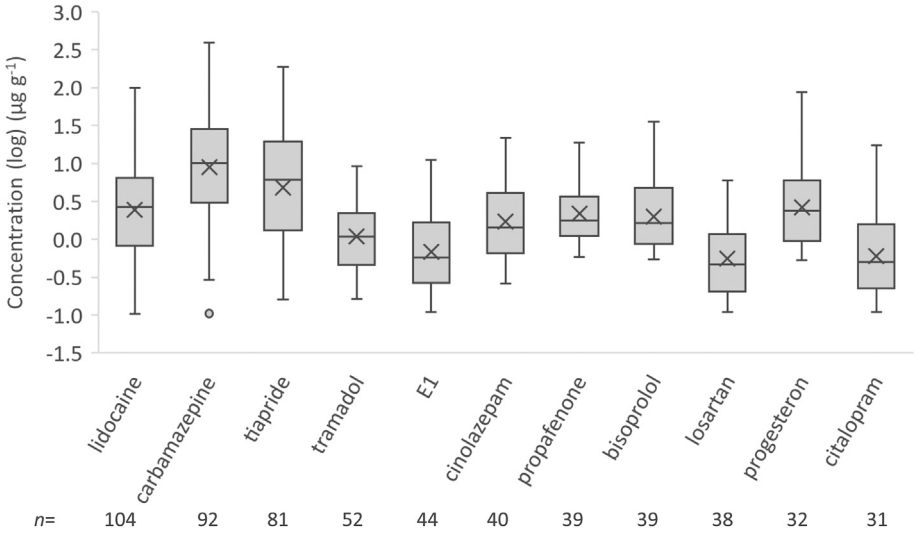


**Fig. 3.** Concentrations of more frequently occurring pharmaceutically active compounds (frequency of occurrence > 20%) in the sediment phase; concentrations run on a logarithmic scale; n: number of samples higher than the limit of quantification; the total number of samples: 141.

**Table 1**
Mean concentrations and standard deviations of the 10 most frequent PhACs in water (ng·L$^{-1}$) and sediment (ng·g$^{-1}$) (> limit of quantification) upstream and downstream of wastewater treatment plant (WWTP) discharges.

| Water phase | Upstream of WWTPs | Downstream of WWTPs | Solid phase | Upstream of WWTPs | Downstream of WWTPs |
|---|---|---|---|---|---|
| *Lidocaine* | 14.4 ± 18.8 | 81.4 ± 82.2 | *Lidocaine* | 1.76 ± 2.33 | 8.06 ± 14.1 |
| *Carbamazepine* | 86.7 ± 128 | 1100 ± 6070 | *Carbamazepine* | 4.63 ± 8.32 | 35.9 ± 61.1 |
| *Lamotrigine* | 306 ± 613 | 6430 ± 37,500 | *Tramadol* | 1.40 ± 2.47 | 1.91 ± 2.14 |
| *Tramadol* | 18.3 ± 45.5 | 166 ± 213 | *Bisoprolol* | 1.53 ± 1.83 | 4.13 ± 6.59 |
| *Metoprolol* | 23.2 ± 60.2 | 86.0 ± 128 | *Tiapride* | 1.22 ± 1.89 | 19.1 ± 29.5 |
| *Diclofenac* | 61.4 ± 140 | 249 ± 339 | *Propafenone* | 1.64 ± 0.10 | 3.77 ± 4.58 |
| *Perindopril* | 18.6 ± 37.8 | 99.6 ± 108 | *Cinolazepam* | 0.58 ± 0.13 | 3.49 ± 4.51 |
| *Losartan* | 11.7 ± 29.46 | 52.4 ± 113 | *Losartan* | 0.41 ± 0.32 | 1.25 ± 1.56 |
| *Bisoprolol* | 20.1 ± 35.4 | 48.2 ± 81.2 | *Progesterone* | 4.88 ± 4.49 | 7.17 ± 16.8 |
| *Cinolazepam* | 11.3 ± 23.4 | 77.5 ± 89.5 | *E1* | 1.23 ± 1.29 | 1.49 ± 2.21 |

samples (Supplementary C). Contrary to some of the literature (Fairbairn et al., 2015; Maasz et al., 2019; Tang et al., 2021; White et al., 2019) the absolute number and sum of detected PhACs in water were also independent of distance from the nearest effluent. In the case of the sediment samples, there were no PhACs in only two sediment samples above the WWTPs, and more PhACs were also detected in stream sections not containing treated wastewater (**Fig. S3b**). The spatial distribution of PhACs in the sediment samples was also not determined by the distance between the WWTPs and the amount of discharged wastewater ($r < 0.2$) (**Fig. S5a-e**).

The temporality of the PhACs was tested based on sampling sites from which more samples were available during the same growing season. No temporal change was detected in the concentration of each PhAC, and within a given watercourse, the concentrations varied differently between seasons. Repeated sediment sampling at the same location provided high temporal variability not only for the PhAC types and concentrations, but also for the particle size distribution and TOC content of the sediment. This suggests that the intensive mobility of sediment along creeks results in the continuous redistribution of adsorbed PhACs. Because of the dynamic environmental conditions (changes in precipitation, land use, and surface coverage), some parts of these small water courses may be highly affected by bank erosion and sedimentation (Lizaga et al., 2019; Neller, 1988; Russell et al., 2018), thereby causing the lack of correlation between PhAC concentrations and investigated environmental properties.

The spatiotemporal heterogeneity indicates the importance of other sources of contamination in urban streams (Bradley et al., 2016), and further local processes. The insufficient dilution of treated wastewater and the shorter travel time for biodegradation and photodegradation (Liu et al., 2020) compared with those in larger rivers might have been the primary factors contributing to the varying occurrence and concentrations of PhACs (Mandaric et al., 2018). However, some data (e.g., the presence of PhACs upstream of the WWTPs and the high variability of the drug concentrations regardless of the number of PhACs, yield, and vicinity of WWTP effluents) suggested that other processes also play a role in the variability of contamination. Because of the rapid suburbanization process and informal urban sprawl (Soós and Ignits, 2003; Tsenkova, 2008), many new dwellings are not connected to the wastewater network; therefore, the proportion of untreated wastewater in the investigated small streams may be higher than the official statistics suggest (Angyal et al., 2016). Because the capacities of wastewater networks and treatments are often inadequate in urbanizing watersheds (Salerno et al., 2018), the increased discharge of combined sewer overflows caused by increasing impervious surfaces may cause more pollution of local streams. Different point sources of pollution in an anthropized territory, such as private swimming pools (Moreno-González et al., 2015), different public and private institutions such as hospitals (Feitosa-Felizzola and Chiron, 2009), and baths (Jakab et al., 2020), can fundamentally change the spatiotemporal patterns of pollution.

Finally, the efficiency of conventional WWTPs is influenced by other factors, such as the maintenance of the activated sludge quality (Song et al., 2020) or the financial and legal background of the operation of WWTPs (Fischhendler, 2007). If the revenues of public water utility companies decrease, then according to the authors who analyzed the current situation in Hungary (Kovács and Rozsnyai, 2019), the efficiency of waste management services will be reduced. Together, these processes deteriorate the spatiotemporal regularity of PhAC concentrations.

### 3.4. Interactions between the aqueous and solid phases

An overlap was observed between the most frequent PhACs found in water and sediment, but different LOQ values (ng·L$^{-1}$; ng·g$^{-1}$) must be taken into account when comparing the results. PhACs found in at least 10% of the sediment samples were generally detected in water samples at the same time and location. Additionally, some sporadically observed substances in the sediments (e.g., PRP, cocaine, clonazepam, diazepam, and midazolam) occurred only where they also appeared in the water (Fig. 4). However, ketamine, lacosamide, theophylline, warfarin, and betaxolol found in at least 20% of the water samples were not detected over the LOQ in the sediment. In contrast, some PhACs with a range of chemical properties (e.g., the hormone PRG and the gastrointestinal stimulator domperidone), were detected in sediment but not in water.

The observed distribution of micropollutants between the aqueous and solid phases can be described by the log $K_{d(obs)}$ variation (Fairbairn et al., 2015; Čelić et al., 2019). Log $K_{d(obs)}$ was calculated for the 22 PhACs that were found in at least three water–sediment sample pairs. The observed distributions diverged from the equilibrium-based predicted values (log *P*), for hydrophilic (e.g., CAF) and hydrophobic (e.g., LOS and DCL) PhACs (Fig. 5). The log $K_{d(obs)}$ values typically range from 1.6 to 2.5; thus, drugs with similar log *P* had the smallest differences between the two indicators (e.g., MTP and BSP). As demonstrated by Fairbairn et al. (2015) for small streams, the ratio of the measured concentrations between the two phases is not only influenced by the solubility. In the investigated streams, the role of unbalanced local effects (e.g., fluctuations of contamination) deeply undermined the applicability of the equilibrium partition coefficients. As a result, there were much smaller differences between the log $K_{d(obs)}$ values of hydrophilic and hydrophobic PhACs than between their log *P* values.

### 3.5. Environmental risk assessment

Out of 141 water samples, the concentrations of 11 analyzed PhACs reached the high-risk level (RQ > 1), namely DCL (51% of all samples), E1 (30%), EE2 (12%), citalopram (11%), CAF (9%), E3 (5%), bE2 (3%), aE2 (1%), CBZ (1%), LTG (1%), and temazepam (1%) (**Table S14,** Fig. 6). At 18 of the 75 sampling sites, the RQ value of each PhAC was not higher than 1 at any of the sampling times. However, at two sites (Nos. 30 and 31), five PhAC concentrations exceeded the high-risk level in at least one water sample. In the sediment phase, if RQs were calculated based on estimated $K_{oc}$ values (Eq. (3)), the concentrations of only three PhACs reached the high-risk level, namely DCL (18% of all sediment samples), CAF (9%), and E1 (4%) (**Table S15,** Fig. 6). The concentrations of at least one PhAC reached the high-risk level at 28 sampling sites, of which at least two PhACs exceeded RQ = 1 at only 6 sites (Nos. 30, 34, 48, 59, 71, and 75). If RQs were determined based on empirical $K_{d(obs)}$

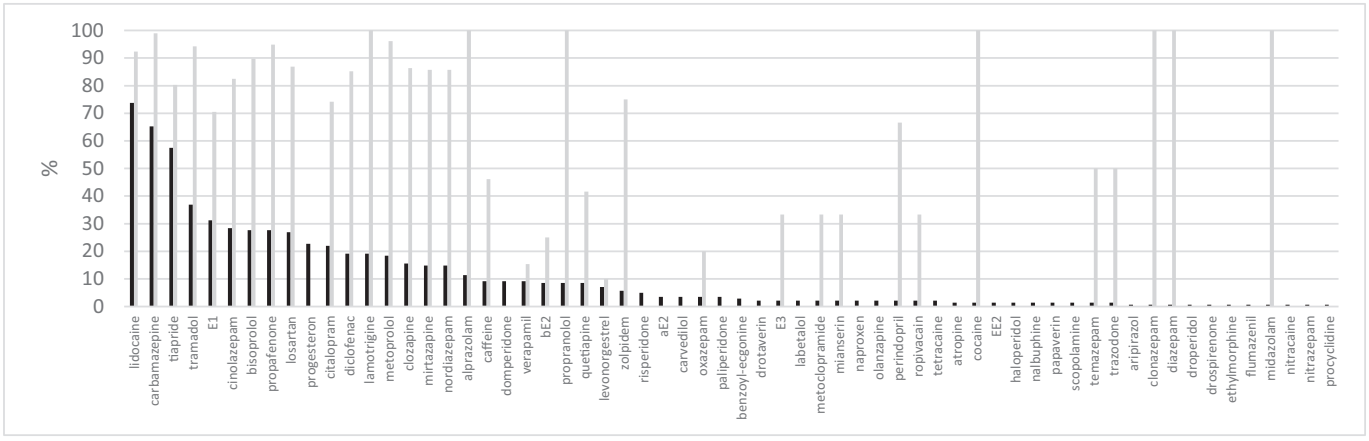


**Fig. 4.** Frequency of occurrence in sediment (black) and the overlap ratio (gray) of the occurrence of pharmaceutically active compounds in the sediment and water phases at the same place and time.

values (Eq. 4), six PhACs reached the high-risk level: E1 (17%), DCL (15%), citalopram (5%), CAF, bE2, and E3 (1%) (Table S16, Fig. 6). In this case, the concentrations of at least one PhAC posed a high-risk level at 33 sampling sites, and three PhACs exceeded the RQ = 1 value at sampling sites Nos. 30, 48, and 71 (Table S16). These values show that the risk levels may vary for some PhACs in the solid phase, and some other PhACs pose a major risk. Although the higher risks of DCL and E1 are also generally known in the environment, it should be noted that the values of RQ > 1 are rather exceptional in both matrices. Even though, extremely high RQ values can also be determined sporadically.

Based on the mixture risk approach, $RQ_{mix(water)} > 10$ was found in 52 water samples, and the $RQ_{mix(water)}$ values of 4 of the samples were higher than 100. In the sediment phase, $RQ_{mix(sediment)} > 10$ in the case of 10 samples based on estimated $K_{oc}$, and 18 ones on empirical $K_{d(obs)}$. Although there are some limitations to the interpretation of the $RQ_{mix}$ values (e.g., the overestimating effect of the additions; Gosset et al., 2020, 2021), these results indicate high risks. This is especially true for $RQ_{mix\ sum}$, which summarizes the RQs of sediment and water for each sample (**Table S17**). Considering the $RQ_{mix(sediment)}$ values based on $K_{oc}$, $RQ_{mix\ sum}$ exceeded 10 in 59 water and sediment samples collected from the same place and time (42% of all samples), and $RQ_{mix\ sum} > 100$ in 6 samples. Similar results were obtained when $K_{d(obs)}$ based $RQ_{mix(sediment)}$ was calculated: the distribution of $RQ_{mix\ sum}$ exceeded 10 in 56 water and sediment samples (40% of all samples), and $RQ_{mix\ sum} > 100$ in case of 11 samples. Considering the number of PhACs with high risk levels in both water and sediment samples and the $RQ_{mix\ sum}$ values, sampling point No. 30 was characterized by the highest risk in both calculation methods ($RQ_{mix\ sum}$ = 258, and 259) (**Table S17**).

In the water, the sampling points characterized by the highest risks were in sections in which treated wastewater inflow was present within 10 km. $RQ_{mix}$ only exceeded 100 where at least one WWTP effluent discharge could be found upstream of the sampling site. However, $RQ_{mix}$ exceeded 1 in 20 of the 35 water samples collected above the WWTPs, and DCL and estrogens posed a risk in many cases. These results confirm the necessity of broad scale approaches to prevent contamination (Bradley et al., 2016). In the solid phase, high risk was identified in five samples collected from stream sections not affected by WWTP effluents; however, unlike that in water, CAF posed a risk in four of these cases.

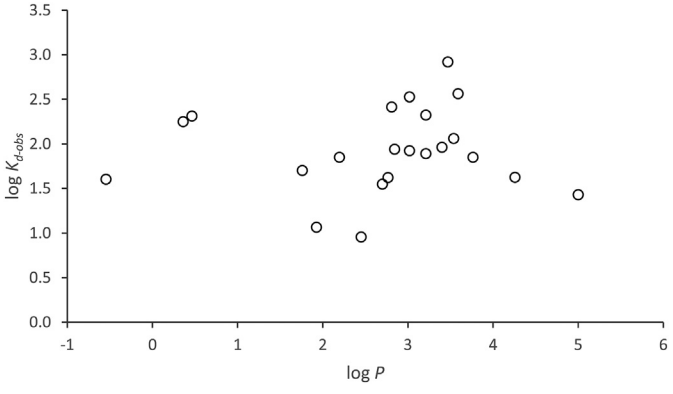


**Fig. 5.** Log $K_{d(obs)}$ and log $P$ for the 22 pharmaceutically active compounds detected in at least three water–sediment sample pairs.

## 4. Conclusions

Concentrations of PhACs detected in the investigated urban stream network fluctuated remarkably. Although WWTP effluents affected the spatial patterns of PhAC occurrence, many PhACs entered the small streams above the effluent discharge point, indicating the role of non-point contamination due to population growth. Our results indicate, that the presence of PhACs were independent of the distance and discharge from WWTP effluents especially in the case of the sediment samples. PhACs are also transferred to sediment in large quantities regardless of their physicochemical properties. The input of varying concentrations of PhACs and the rapidly fluctuating water–sediment properties resulted in a complex system in which there was no correlation between water and sediment concentrations owing to the limited natural attenuation processes. This confirms that it is difficult to estimate the extent of PhAC contamination and environmental risks in small urban streams regardless of WWTP effluents, thereby exacerbating the risks of global environmental change and urbanization. Although some micropollutants (e.g., DCL, CAF, E1, and EE2) present very high environmental risks in some samples, especially when the $RQ_{mix}$ values are considered, these RQ values fluctuate over space and time. This uncertainty need to be taken into account when modeling the ecological status and risks of a complex urban stream network.

## CRediT authorship contribution statement

**Attila Csaba Kondor:** Conceptualization, Writing – original draft, Writing – review & editing, Project administration, Methodology. **Éva Molnár:** Methodology, Formal analysis, Writing – original draft. **Gergely Jakab:** Methodology, Formal analysis, Writing – original draft, Writing – review & editing. **Anna Vancsik:** Data curation. **Tibor Filep:** Writing – original draft. **József Szeberényi:** Visualization. **Lili Szabó:** Data curation. **Gábor Maász:** Investigation. **Zsolt Pirger:** Methodology. **András Weiperth:**

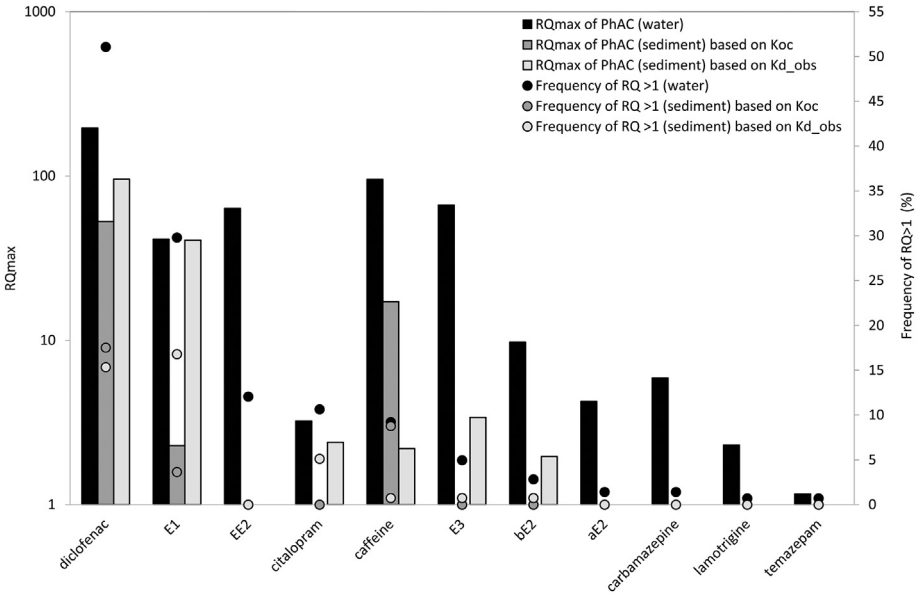


**Fig. 6.** $RQ_{max}$ values and frequency of RQ > 1 in both water and sediment.

Resources. **Árpád Ferincz:** Resources. **Ádám Staszny:** Resources. **Péter Dobosy:** Investigation. **Katalin Horváthné Kiss:** Methodology. **István Gábor Hatvani:** Methodology, Formal analysis, Writing – review & editing. **Zoltán Szalai:** Conceptualization, Methodology.

## 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 results presented 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.scitotenv.2021.152160.

## References

Ahrens, L., Golovko, O., Rehrl, A., Stephan, K., 2020. Chemosphere Organic micropollutants in water and sediment from Lake Ma Sweden. 258. https://doi.org/10.1016/j.chemosphere.2020.127293.

Alder, A.C., Schaffner, C., Majewsky, M., Klasmeier, J., Fenner, K., 2010. Fate of β-blocker human pharmaceuticals in surface water: comparison of measured and simulated concentrations in the Glatt Valley Watershed, Switzerland. Water Res. 44, 936–948. https://doi.org/10.1016/j.watres.2009.10.002.

Aleksander-Kwaterczak, U., Plenzler, D., 2019. Contamination of small urban watercourses on the example of a stream in Krakow (Poland). Environ. Earth Sci. 78, 1–13. https://doi.org/10.1007/s12665-019-8509-4.

Al-Khazrajy, O.S.A., Boxall, A.B.A., 2016. Impacts of compound properties and sediment characteristics on the sorption behaviour of pharmaceuticals in aquatic systems. J. Hazard. Mater. 317, 198–209. https://doi.org/10.1016/j.jhazmat.2016.05.065.

Al-Khazrajy, O.S.A., Bergström, E., Boxall, A.B.A., 2018. Factors affecting the dissipation of pharmaceuticals in freshwater sediments. Environ. Toxicol. Chem. 37, 829–838. https://doi.org/10.1002/etc.4015.

American Public Health Association, American Water Works AssociationWEF, 2005. Standard Methods for the Examination of Water and Wastewater. 21th ed. American Public Health Association.

Angyal, Z., Sárközi, E., Gombás, Á., Kardos, L., 2016. Effects of land use on chemical water quality of three small streams in Budapest. Open Geosci. 8, 133–142. https://doi.org/10.1515/geo-2016-0012.

Ashfaq, M., Noor, N., Saif-Ur-Rehman, M., Sun, Q., Mustafa, G., Faizan Nazar, M., Yu, C.P., 2017. Determination of commonly used Pharmaceuticals in Hospital Waste of Pakistan and evaluation of their ecological risk assessment. Clean Soil Air Water 45, 19–21. https://doi.org/10.1002/clen.201500392.

aus der Beek, T., Weber, F.A., Bergmann, A., Hickmann, S., Ebert, I., Hein, A., Küster, A., 2016. Pharmaceuticals in the environment-Global occurrences and perspectives. Environ. Toxicol. Chem. 35, 823–835. https://doi.org/10.1002/etc.3339.

Backhaus, T., Faust, M., 2012. Predictive environmental risk assessment of chemical mixtures: a conceptual framework. Environ. Sci. Technol. 46, 2564–2573. https://doi.org/10.1021/es2034125.

Battaglin, W.A., Bradley, P.M., Iwanowicz, L., Journey, C.A., Walsh, H.L., Blazer, V.S., 2018. Pharmaceuticals, hormones, pesticides, and other bioactive contaminants in water, sediment, and tissue from Rocky Mountain National Park, 2012–2013. Sci. Total Environ. 643, 651–673. https://doi.org/10.1016/j.scitotenv.2018.06.150.

Bejarano, A.C., Farr, J.K., Jenne, P.J., Chu, V., Hielscher, A., 2016. Hazard/Risk Assessment the Chemical Aquatic Fate and Effects Database (CAFE), a Tool That Supports Assessments of Chemical Spills in Aquatic Environments. 35, pp. 1576–1586. https://doi.org/10.1002/etc.3289.

Bókony, V., Üveges, B., Ujhegyi, N., Verebélyi, V., Nemesházi, E., Csíkvári, O., Hettyey, A., 2018. Endocrine disruptors in breeding ponds and reproductive health of toads in agricultural, urban and natural landscapes. Sci. Total Environ. 634, 1335–1345. https://doi.org/10.1016/j.scitotenv.2018.03.363.

Bradley, P.M., Journey, C.A., Button, D.T., Carlisle, D.M., Clark, J.M., Mahler, B.J., Nakagaki, N., Qi, S.L., Waite, I.R., VanMetre, P.C., 2016. Metformin and other pharmaceuticals widespread in wadeable streams of the southeastern United States. Environ. Sci. Technol. Lett. 3, 243–249. https://doi.org/10.1021/acs.estlett.6b00170.

Bradley, P.M., Journey, C.A., Berninger, J.P., Button, D.T., Clark, J.M., Corsi, S.R., DeCicco, L.A., Hopkins, K.G., Huffman, B.J., Nakagaki, N., Norman, J.E., Nowell, L.H., Qi, S.L., VanMetre, P.C., Waite, I.R., 2019. Mixed-chemical exposure and predicted effects potential in wadeable southeastern USA streams. Sci. Total Environ. 655, 70–83. https://doi.org/10.1016/j.scitotenv.2018.11.186.

Bradley, P.M., Journey, C.A., Button, D.T., Carlisle, D.M., Huffman, B.J., Qi, S.L., Romanok, K.M., van Metre, P.C., 2020. Multi-region assessment of pharmaceutical exposures and predicted effects in USA wadeable urban-gradient streams. PLoS One 15, 1–25. https://doi.org/10.1371/journal.pone.0228214.

Bradley, P.M., Journey, C.A., Romanok, K.M., Breitmeyer, S.E., Button, D.T., Carlisle, D.M., Huffman, B.J., Mahler, B.J., Nowell, L.H., Qi, S.L., Smalling, K.L., Waite, I.R., Van Metre, P.C., 2021. Multi-region assessment of chemical mixture exposures and predicted cumulative effects in USA wadeable urban/agriculture-gradient streams. Sci. Total Environ. 773, 145062. https://doi.org/10.1016/j.scitotenv.2021.145062.

Braud, I., Breil, P., Thollet, F., Lagouy, M., Branger, F., Jacqueminet, C., Kermadi, S., Michel, K., 2013. Evidence of the impact of urbanization on the hydrological regime of a medium-sized periurban catchment in France. J. Hydrol. 485, 5–23. https://doi.org/10.1016/j.jhydrol.2012.04.049.

Brus, A., Perrodin, Y., 2017. Identification, assessment and prioritization of ecotoxicological risks on the scale of a territory: application to WWTP discharges in a geographical area located in Northeast Lyon, France. Chemosphere 189, 340–348. https://doi.org/10.1016/j.chemosphere.2017.09.054.

Buerge, I.J., Poiger, T., Müller, M.D., Buser, H.R., 2003. Caffeine, an anthropogenic marker for wastewater contamination of surface waters. Environ. Sci. Technol. 37, 691–700. https://doi.org/10.1021/es020125z.

Camacho-Muñoz, D., Martín, J., Santos, J.L., Aparicio, I., Alonso, E., 2013. Distribution and risk assessment of pharmaceutical compounds in river sediments from doñana park (Spain). Water. Air. Soil Pollut. https://doi.org/10.1007/s11270-013-1665-3.

Cardoso-Vera, J.D., Elizalde-Velázquez, G.A., Islas-Flores, H., Mejía-García, A., Ortega-Olvera, J.M., Gómez-Oliván, L.M., 2021. A review of antiepileptic drugs: part 1 occurrence, fate in aquatic environments and removal during different treatment technologies. Sci. Total Environ. 768. https://doi.org/10.1016/j.scitotenv.2021.145487.

Casado, J., Brigden, K., Santillo, D., Johnston, P., 2019. Screening of pesticides and veterinary drugs in small streams in the European Union by liquid chromatography high resolution mass spectrometry. Sci. Total Environ. 670, 1204–1225. https://doi.org/10.1016/j.scitotenv.2019.03.207.

Čelić, M., Gros, M., Farré, M., Barceló, D., Petrović, M., 2019. Pharmaceuticals as chemical markers of wastewater contamination in the vulnerable area of the Ebro Delta (Spain). Sci. Total Environ. 652, 952–963. https://doi.org/10.1016/j.scitotenv.2018.10.290.

Chakraborty, P., Mukhopadhyay, M., Sampath, S., Ramaswamy, B.R., Katsoyiannis, A., Cincinelli, A., Snow, D., 2019. Organic micropollutants in the surface riverine sediment along the lower stretch of the transboundary river ganga: occurrences, sources and ecological risk assessment. Environ. Pollut. 249, 1071–1080. https://doi.org/10.1016/j.envpol.2018.10.115.

Chapin, T.P., 2015. High-frequency, long-duration water sampling in acid mine drainage studies: a short review of current methods and recent advances in automated water samplers. Appl. Geochemistry 59, 118–124. https://doi.org/10.1016/j.apgeochem.2015.04.004.

Chaves, M.de J.S., Barbosa, S.C., Malinowski, M.de M., Volpato, D., Castro, Í.B., Franco, T.C.R. dos S., Primel, E.G., 2020. Pharmaceuticals and personal care products in a Brazilian wetland of international importance: occurrence and environmental risk assessment. Sci. Total Environ. 734, 139374. https://doi.org/10.1016/j.scitotenv.2020.139374.

CORINE, 2018. Copernicus Land Monitoring Service, CORINE Land Cover (CLC) 2018. https://land.copernicus.eu/. (Accessed 8 September 2021).

Crane, M., Watts, C., Boucard, T., 2006. Chronic aquatic environmental risks from exposure to human pharmaceuticals. Sci. Total Environ. 367, 23–41. https://doi.org/10.1016/j.scitotenv.2006.04.010.

Daughton, C.G., 2003. Pollution from the combined activities, actions, and behaviors of the public: pharmaceuticals and personal care products. NorCal SETAC News 14, 5–15.

Di Sabatino, A., Coscieme, L., Vignini, P., Cicolani, B., 2013. Scale and ecological dependence of ecosystem services evaluation: spatial extension and economic value of freshwater ecosystems in Italy. Ecol. Indic. 32, 259–263. https://doi.org/10.1016/j.ecolind.2013.03.034.

Ding, J., Jiang, Y., Liu, Q., Hou, Z., Liao, J., Fu, L., Peng, Q., 2016. Influences of the land use pattern on water quality in low-order streams of the Dongjiang River basin, China: a multi-scale analysis. Sci. Total Environ. 551–552, 205–216. https://doi.org/10.1016/j.scitotenv.2016.01.162.

Ebele, A.J., Abou-Elwafa Abdallah, M., Harrad, S., 2017. Pharmaceuticals and personal care products (PPCPs) in the freshwater aquatic environment. Emerg. Contam. 3, 1–16. https://doi.org/10.1016/j.emcon.2016.12.004.

Englert, D., Zubrod, J.P., Schulz, R., Bundschuh, M., 2013. Effects of municipal wastewater on aquatic ecosystem structure and function in the receiving stream. Sci. Total Environ. 454–455, 401–410. https://doi.org/10.1016/j.scitotenv.2013.03.025.

Erős, T., O'Hanley, J.R., Czeglédi, I., 2018. A unified model for optimizing riverscape conservation. J. Appl. Ecol. 55, 1871–1883. https://doi.org/10.1111/1365-2664.13142.

Fairbairn, D.J., Karpuzcu, M.E., Arnold, W.A., Barber, B.L., Kaufenberg, E.F., Koskinen, W.C., Novak, P.J., Rice, P.J., Swackhamer, D.L., 2015. Science of the Total environment sediment – water distribution of contaminants of emerging concern in a mixed use watershed. Sci. Total Environ. 505, 896–904. https://doi.org/10.1016/j.scitotenv.2014.10.046.

Feitosa-Felizzola, J., Chiron, S., 2009. Occurrence and distribution of selected antibiotics in a small Mediterranean stream (Arc River, southern France). J. Hydrol. 364, 50–57. https://doi.org/10.1016/j.jhydrol.2008.10.006.

Filep, T., Szabó, L., Kondor, A.C., Jakab, G., Szalai, Z., 2021a. Evaluation of the effect of the intrinsic chemical properties of pharmaceutically active compounds (PhACs) on sorption behaviour in soils and goethite. Ecotoxicol. Environ. Saf. 215. https://doi.org/10.1016/j.ecoenv.2021.112120.

Filep, T., Szabó, L., Kondor, A.C., Jakab, G., Szalai, Z., 2021b. Evaluation of the effect of the intrinsic chemical properties of pharmaceutically active compounds (PhACs) on sorption behaviour in soils and goethite. Ecotoxicol. Environ. Saf. 215. https://doi.org/10.1016/j.ecoenv.2021.112120.

Finizio, A., Vighi, M., 2014. Predicted no effect concentration (PNEC). Encyclopedia of Toxicology: Third Edition, Third Edit. ed Elsevier https://doi.org/10.1016/B978-0-12-386454-3.00572-8.

Fischhendler, I., 2007. Escaping the "polluter pays" trap : Financing wastewater treatment on the Tijuana – San Diego border. 3. https://doi.org/10.1016/j.ecolecon.2006.12.012.

Fork, M.L., Fick, J.B., Reisinger, A.J., Rosi, E.J., 2021. Dosing the coast: leaking sewage infrastructure delivers large annual doses and dynamic mixtures of pharmaceuticals to urban rivers. Environ. Sci. Technol. 55, 11637–11645. https://doi.org/10.1021/acs.est.1c00379.

Gál, B., Szivák, I., Heino, J., Schmera, D., 2019. The effect of urbanization on freshwater macroinvertebrates – knowledge gaps and future research directions. Ecol. Indic. 104, 357–364. https://doi.org/10.1016/j.ecolind.2019.05.012.

Gardi, C. (Ed.), 2017. Urban Expansion, Land Cover and Soil Ecosystem Services - Google Books. Routledge.

Golovko, O., Örn, S., Sörengård, M., Frieberg, K., Nassazzi, W., Lai, F.Y., Ahrens, L., 2021. Occurrence and removal of chemicals of emerging concern in wastewater treatment plants and their impact on receiving water systems. Sci. Total Environ. 754, 142122. https://doi.org/10.1016/j.scitotenv.2020.142122.

Gosset, A., Polomé, P., Perrodin, Y., 2020. Ecotoxicological risk assessment of micropollutants from treated urban wastewater effluents for watercourses at a territorial scale: application and comparison of two approaches. Int. J. Hyg. Environ. Health 224, 113437. https://doi.org/10.1016/j.ijheh.2019.113437.

Gosset, A., Wiest, L., Fildier, A., Libert, C., Giroud, B., Hammada, M., Hervé, M., Sibeud, E., Vulliet, E., Polomé, P., Perrodin, Y., 2021. Ecotoxicological risk assessment of contaminants of emerging concern identi fi ed by " suspect screening" from urban wastewater treatment plant ef fl uents at a territorial scale. Sci. Total Environment 778. https://doi.org/10.1016/j.scitotenv.2021.146275.

HCSO, 2021. Hungarian Central Statistical Office, Dissemination database. https://statinfo.ksh.hu/Statinfo/themeSelector.jsp?&lang=en. (Accessed 8 September 2021).

Huerta-Fontela, M., Galceran, M.T., Martin-Alonso, J., Ventura, F., 2008. Occurrence of psychoactive stimulatory drugs in wastewaters in North-Eastern Spain. Sci. Total Environ. 397, 31–40. https://doi.org/10.1016/j.scitotenv.2008.02.057.

Jakab, G., Szalai, Z., Michalkó, G., Ringer, M., Filep, T., Szabó, L., Maász, G., Pirger, Z., Ferincz, Á., Staszny, Á., Dobosy, P., Kondor, A.C.A.C., 2020. Thermal baths as sources of pharmaceutical and illicit drug contamination. Environ. Sci. Pollut. Res. 27, 399–410. https://doi.org/10.1007/s11356-019-06633-6.

Johnson, A.C., Dumont, E., Williams, R.J., Oldenkamp, R., Cisowska, I., Sumpter, J.P., 2013. Do concentrations of ethinylestradiol, estradiol, and diclofenac in european rivers exceed proposed EU environmental quality standards? Environ. Sci. Technol. 47, 12297–12304. https://doi.org/10.1021/es4030035.

Jourdan, J., O'Hara, R.B., Bottarin, R., Huttunen, K.L., Kuemmerlen, M., Monteith, D., Muotka, T., Ozolinš, D., Paavola, R., Pilotto, F., Springe, G., Skuja, A., Sundermann, A., Tonkin, J.D., Haase, P., 2018. Effects of changing climate on european stream invertebrate communities: a long-term data analysis. Sci. Total Environ. 621, 588–599. https://doi.org/10.1016/j.scitotenv.2017.11.242.

Kienle, C., Vermeirssen, E.L.M., Schifferli, A., Singer, H., Stamm, C., Werner, I., 2019. Effects of treated wastewater on the ecotoxicity of small streams - unravelling the contribution of chemicals causing effects. PLoS One 14, 1–30. https://doi.org/10.1371/journal.pone.0226278.

Kondor, A.C., Jakab, G., Vancsik, A., Filep, T., Szeberényi, J., Szabó, L., Maász, G., Ferincz, Á., Dobosy, P., Szalai, Z., 2020. Occurrence of pharmaceuticals in the Danube and drinking water wells: efficiency of riverbank filtration. Environ. Pollut. 265. https://doi.org/10.1016/j.envpol.2020.114893.

Kondor, A.C., Molnár, É., Vancsik, A., Filep, T., Szeberényi, J., Szabó, L., Maász, G., Pirger, Z., Weiperth, A., Ferincz, Á., Staszny, Á., Dobosy, P., Horváthné Kiss, K., Jakab, G., Szalai, Z., 2021. Occurrence and health risk assessment of pharmaceutically active compounds in riverbank filtrated drinking water. J. Water Process Eng. 41. https://doi.org/10.1016/j.jwpe.2021.102039.

König, M., Escher, B.I., Neale, P.A., Krauss, M., Hilscherová, K., Novák, J., Teodorović, I., Schulze, T., Seidensticker, S., Kamal Hashmi, M.A., Ahlheim, J., Brack, W., 2017. Impact of untreated wastewater on a major european river evaluated with a combination of in vitro bioassays and chemical analysis. Environ. Pollut. 220, 1220–1230. https://doi.org/10.1016/j.envpol.2016.11.011.

Kovács, A.G., Rozsnyai, K.F., 2019. Price regulation of public water services and the consequences of its centralisation for Hungarian Municipalities. Lex Localis 17, 821–835. https://doi.org/10.4335/17.3.819-835(2019).

Kovács, Z., Farkas, Z.J., Egedy, T., Kondor, A.C., Szabó, B., Lennert, J., Baka, D., Kohán, B., 2019. Urban sprawl and land conversion in post-socialist cities: the case of metropolitan Budapest. Cities 92, 71–81. https://doi.org/10.1016/j.cities.2019.03.018.

Kramulov, B., Tauchen, J., Marsik, P., Rezek, J., Zidkov, M., 2017. Non-steroidal anti-in fl ammatory drugs in the watercourses of Elbe basin in Czech Republic. Chemosphere 171. https://doi.org/10.1016/j.chemosphere.2016.12.055.

Li, W.C., 2014. Occurrence, sources, and fate of pharmaceuticals in aquatic environment and soil. Environ. Pollut. 187, 193–201. https://doi.org/10.1016/j.envpol.2014.01.015.

Liu, K., Yin, X., Zhang, D., Yan, D., Cui, L., Zhu, Z., Wen, L., 2018. Distribution, sources, and ecological risk assessment of quinotone antibiotics in the surface sediments from Jiaozhou Bay wetland, China. Mar. Pollut. Bull. 129, 859–865. https://doi.org/10.1016/j.marpolbul.2017.10.010.

Liu, F., Nielsen, A.H., Vollertsen, J., 2019. Sorption and degradation potential of pharmaceuticals in sediments from a stormwater retention pond. Water (Switzerland) 11. https://doi.org/10.3390/w11030526.

Liu, Y., Zar, C., Basu, N.B., 2020. Modeling the Fate of Pharmaceuticals in a Fourth - Order River Under Competing Assumptions of Transient Storage Water Resources Research. https://doi.org/10.1029/2019WR026100.

Lizaga, I., Gaspar, L., Blake, W.H., Latorre, B., Navas, A., 2019. Fingerprinting changes of source apportionments from mixed land uses in stream sediments before and after an exceptional rainstorm event. Geomorphology 341, 216–229. https://doi.org/10.1016/j.geomorph.2019.05.015.

Loos, R., Carvalho, R., António, D.C., Comero, S., Locoro, G., Tavazzi, S., Paracchini, B., Ghiani, M., Lettieri, T., Blaha, L., Jarosova, B., Voorspoels, S., Servaes, K., Haglund, P., Fick, J., Lindberg, R.H., Schwesig, D., Gawlik, B.M., 2013. EU-wide monitoring survey on emerging polar organic contaminants in wastewater treatment plant effluents. Water Res. 47, 6475–6487. https://doi.org/10.1016/j.watres.2013.08.024.

López-Pacheco, I.Y., Silva-Núñez, A., Salinas-Salazar, C., Arévalo-Gallegos, A., Lizarazo-Holguin, L.A., Barceló, D., Iqbal, H.M.N., Parra-Saldívar, R., 2019. Anthropogenic contaminants of high concern: existence in water resources and their adverse effects. Sci. Total Environ. 690, 1068–1088. https://doi.org/10.1016/j.scitotenv.2019.07.052.

Luo, Y., Guo, W., Ngo, H.H., Nghiem, L.D., Hai, F.I., Zhang, J., Liang, S., Wang, X.C., 2014. A review on the occurrence of micropollutants in the aquatic environment and their fate and removal during wastewater treatment. Sci. Total Environ. 473–474, 619–641. https://doi.org/10.1016/j.scitotenv.2013.12.065.

Maasz, G., Mayer, M., Zrinyi, Z., Molnar, E., Kuzma, M., Fodor, I., Pirger, Z., Takács, P., 2019. Spatiotemporal variations of pharmacologically active compounds in surface waters of a summer holiday destination. Sci. Total Environ. 677, 545–555. https://doi.org/10.1016/j.scitotenv.2019.04.286.

Maasz, G., Molnar, E., Mayer, M., Kuzma, M., Takács, P., Zrinyi, Z., Pirger, Z., Kiss, T., 2021. Illicit drugs as a potential risk to the aquatic environment of a large freshwater Lake after a major music festival. Environ. Toxicol. Chem. 40, 1491–1498. https://doi.org/10.1002/etc.4998.

Maloney, K.O., Krause, K.P., Buchanan, C., Hay, L.E., McCabe, G.J., Smith, Z.M., Sohl, T.L., Young, J.A., 2020. Disentangling the potential effects of land-use and climate change on stream conditions. Glob. Chang. Biol. 26, 2251–2269. https://doi.org/10.1111/gcb.14961.

Mandaric, L., Mor, J., Sabater, S., Petrovic, M., 2018. Impact of urban chemical pollution on water quality in small, rural and effluent-dominated Mediterranean streams and rivers. Sci. Total Environ. 613–614, 763–772. https://doi.org/10.1016/j.scitotenv.2017.09.128.

Mann, H., Whitney, D., 1947. On a test of whether one of two random variables is stochastically larger than the other. Ann. Math. Stat. 18, 50–60.

Martín, J., Camacho-Muñoz, D., Santos, J.L., Aparicio, I., Alonso, E., 2012. Occurrence of pharmaceutical compounds in wastewater and sludge from wastewater treatment plants: removal and ecotoxicological impact of wastewater discharges and sludge disposal. J. Hazard. Mater. 239–240, 40–47. https://doi.org/10.1016/j.jhazmat.2012.04.068.

Matongo, S., Birungi, G., Moodley, B., Ndungu, P., 2015. Occurrence of selected pharmaceuticals in water and sediment of Umgeni River, KwaZulu-Natal, South Africa. Environ. Sci. Pollut. Res. 22, 10298–10308. https://doi.org/10.1007/s11356-015-4217-0.

Molnar, E., Maasz, G., Pirger, Z., 2020. Environmental risk assessment of pharmaceuticals at a seasonal holiday destination in the largest freshwater shallow lake in Central Europe. Environ. Sci. Pollut. Res. https://doi.org/10.1007/s11356-020-09747-4.

Moreno-gonzález, R., Rodriguez-mozaz, S., Gros, M., Barceló, D., León, V.M., 2015. Seasonal distribution of pharmaceuticals in marine water and sedi- ment from a mediterranean coastal lagoon (SE Spain). Environ. Res. 138, 326–344. https://doi.org/10.1016/j.envres.2015.02.016.

Murdoch, A., Mantyka-Pringle, C., Sharma, S., 2020. The interactive effects of climate change and land use on boreal stream fish communities. Sci. Total Environ. 700, 134518. https://doi.org/10.1016/j.scitotenv.2019.134518.

Napieralski, J., 2020. Changes in surface water distribution in America' s boomburbs. City Environ. Interact. 3, 100024. https://doi.org/10.1016/j.cacint.2020.100024.

Neller, R.J., 1988. A comparison of channel erosion in small urban and rural catchments, Armidale, New South Wales. Earth Surf. Process. Landforms 13, 1–7. https://doi.org/10.1002/esp.3290130102.

Osorio, V., Marcé, R., Pérez, S., Ginebreda, A., Cortina, J.L., Barceló, D., 2012. Occurrence and modeling of pharmaceuticals on a sewage-impacted Mediterranean river and their dynamics under different hydrological conditions. Sci. Total Environ. 440, 3–13. https://doi.org/10.1016/j.scitotenv.2012.08.040.

Paíga, P., Correia, M., Fernandes, M.J., Silva, A., Carvalho, M., Vieira, J., Jorge, S., Silva, J.G., Freire, C., Delerue-Matos, C., 2019. Assessment of 83 pharmaceuticals in WWTP influent and effluent samples by UHPLC-MS/MS: hourly variation. Sci. Total Environ. 648, 582–600. https://doi.org/10.1016/j.scitotenv.2018.08.129.

Patel, M., Kumar, R., Kishor, K., Mlsna, T., Pittman, C.U., Mohan, D., 2019. Pharmaceuticals of emerging concern in aquatic systems: chemistry, occurrence, effects, and removal methods. Chem. Rev. 119, 3510–3673. https://doi.org/10.1021/acs.chemrev.8b00299.

Patrolecco, L., Ademollo, N., Capri, S., Pagnotta, R., Polesello, S., 2010. Chemosphere occurrence of priority hazardous PAHs in water, suspended particulate matter, sediment and common eels (Anguilla anguilla) in the urban stretch of the river Tiber (Italy). Chemosphere 81, 1386–1392. https://doi.org/10.1016/j.chemosphere.2010.09.027.

Peng, Q., Song, J., Li, X., Yuan, H., Liu, M., Duan, L., Zuo, J., 2020. Pharmaceutically active compounds (PhACs) in surface sediments of the Jiaozhou Bay, North China. Environ. Pollut. 266, 115245. https://doi.org/10.1016/j.envpol.2020.115245.

Pizzuto, J.E., Hession, W.C., McBride, M., 2000. Comparing gravel-bed rivers in paired urban and rural catchments of southeastern Pennsylvania. Geology 28, 79–82. https://doi.org/10.1130/0091-7613(2000)028<0079:CGRIPU>2.0.CO;2.

Proia, L., Von Schiller, D., Sànchez-Melsió, A., Sabater, S., Borrego, C.M., Rodríguez-Mozaz, S., Balcázar, J.L., 2016. Occurrence and persistence of antibiotic resistance genes in river biofilms after wastewater inputs in small rivers. Environ. Pollut. 210, 121–128. https://doi.org/10.1016/j.envpol.2015.11.035.

Radke, M., Maier, M.P., 2014. ScienceDirect lessons learned from water/sediment-testing of pharmaceuticals. Water Res. 55, 63–73. https://doi.org/10.1016/j.watres.2014.02.012.

RBMPH, 2015. River Basin Management Plan, Hungary. http://www.vizugy.hu/index.php?module=vizstrat&programelemid=149. (Accessed 27 July 2021).

Rosi-Marshall, E.J., Royer, T.V., 2012. Pharmaceutical compounds and ecosystem function: an emerging research challenge for aquatic ecologists. Ecosystems 15, 867–880. https://doi.org/10.1007/s10021-012-9553-z.

Russell, K.L., Vietz, G.J., Fletcher, T.D., 2018. Urban catchment runoff increases bedload sediment yield and particle size in stream channels. Anthropocene 23, 53–66. https://doi.org/10.1016/j.ancene.2018.09.001.

Salerno, F., Viviano, G., Tartari, G., 2018. Urbanization and climate change impacts on surface water quality: enhancing the resilience by reducing impervious surfaces. Water Res. 144, 491–502. https://doi.org/10.1016/j.watres.2018.07.058.

da Silva, B.F., Jelic, A., López-Serna, R., Mozeto, A.A., Petrovic, M., Barceló, D., 2011. Occurrence and distribution of pharmaceuticals in surface water, suspended solids and sediments of the Ebro river basin, Spain. Chemosphere 85, 1331–1339. https://doi.org/10.1016/J.CHEMOSPHERE.2011.07.051.

Song, Y., Jiang, C., Liang, Z., Wang, B., Jiang, Y., Yin, Y., Zhu, H., 2020. Casimicrobium huifangae gen. nov., sp. nov., a ubiquitous "most-wanted" core bacterial taxon from municipal wastewater treatment plants. Appl. Environ. Microbiol. 86.

Soós, G., Ignits, G., 2003. Suburbanization and its consequences in the Budapest metropolitan area. Third EuroConference the European City in Transition the City and the Region. Bauhaus-Universität Weimar, Weimar, pp. 1–20.

Sousa, J.C.G., Ribeiro, A.R., Barbosa, M.O., Ribeiro, C., Tiritan, M.E., Pereira, M.F.R., Silva, A.M.T., 2019. Monitoring of the 17 EU watch list contaminants of emerging concern in the ave and the Sousa Rivers. Sci. Total Environ. 649, 1083–1095. https://doi.org/10.1016/j.scitotenv.2018.08.309.

Staszny, A., Dobosy, P., Maasz, G., Szalai, Z., Jakab, G., Pirger, Z., Szeberenyi, J., Molnar, E., 2021. Effects of pharmaceutically active compounds (PhACs) on fish body and scale shape in natural waters, pp. 1–24 https://doi.org/10.7717/peerj.10642.

Strahler, A.N., 1957. Quantitative analysis of watershed geomorphology. Eos Trans. AGU 38 (6), 913–920. https://doi.org/10.1029/TR038i006p00913.

Szöcs, E., Brinke, M., Karaoglan, B., Schäfer, R.B., 2017. Large scale risks from agricultural pesticides in small streams. Environ. Sci. Technol. 51, 7378–7385. https://doi.org/10.1021/acs.est.7b00933.

Tamura, I., Yasuda, Y., Yoneda, S., Nakada, N., Kumar, V., Kameda, Y., Kimura, K., Tatarazako, N., Yamamoto, H., Ichiro, Kagota K., 2017. Contribution of pharmaceuticals and personal care products (PPCPs) to whole toxicity of water samples collected in effluent-dominated urban streams. Ecotoxicol. Environ. Saf. 144, 338–350. https://doi.org/10.1016/j.ecoenv.2017.06.032.

Tang, J., Sun, J., Wang, W., Yang, L., Xu, Y., 2021. Pharmaceuticals in two watersheds in eastern China and their ecological risks. Environ. Pollut. 277, 116773. https://doi.org/10.1016/j.envpol.2021.116773.

Tsenkova, S., 2008. Managing change: the comeback of post-socialist cities. Urban Res. Pract. 1, 291–310. https://doi.org/10.1080/17535060802476525.

Varga, M., Dobor, J., Helenkár, A., Jurecska, L., Yao, J., Záray, G., 2010. Investigation of acidic pharmaceuticals in river water and sediment by microwave-assisted extraction and gas chromatography-mass spectrometry. Microchem. J. 95, 353–358. https://doi.org/10.1016/j.microc.2010.02.010.

Vazquez-roig, P., Andreu, V., Blasco, C., Picó, Y., 2012. Risk assessment on the presence of pharmaceuticals in sediments, soils and waters of the Pego – Oliva marshlands (Valencia, eastern Spain). Sci. Total Environ. 440, 24–32. https://doi.org/10.1016/j.scitotenv.2012.08.036.

Verbunt, M., Groot Zwaaftink, M., Gurtz, J., 2005. The hydrologic impact of land cover changes and hydropower stations in the alpine Rhine basin. Ecol. Model. 187, 71–84. https://doi.org/10.1016/j.ecolmodel.2005.01.027.

Verlicchi, P., Al Aukidy, M., Zambello, E., 2012. Occurrence of pharmaceutical compounds in urban wastewater: removal, mass load and environmental risk after a secondary treatment-a review. Sci. Total Environ. 429, 123–155. https://doi.org/10.1016/j.scitotenv.2012.04.028.

White, D., Lapworth, D.J., Civil, W., Williams, P., 2019. Tracking changes in the occurrence and source of pharmaceuticals within the river Thames, UK; from source to sea. Environ. Pollut. 249, 257–266. https://doi.org/10.1016/j.envpol.2019.03.015.

Wolff, E., van Vliet, M.T.H., 2021. Impact of the 2018 drought on pharmaceutical concentrations and general water quality of the Rhine and Meuse rivers. Sci. Total Environ. 778, 146182. https://doi.org/10.1016/j.scitotenv.2021.146182.

Yang, Y.Y., Toor, G.S., Williams, C.F., 2015. Pharmaceuticals and organochlorine pesticides in sediments of an urban river in Florida, USA. J. Soils Sediments 15, 993–1004. https://doi.org/10.1007/s11368-015-1077-7.

Yuan, S., Jiang, X., Xia, X., Zhang, H., Zheng, S., 2013. Detection, occurrence and fate of 22 psychiatric pharmaceuticals in psychiatric hospital and municipal wastewater treatment plants in Beijing, China. Chemosphere 90, 2520–2525. https://doi.org/10.1016/j.chemosphere.2012.10.089.

Yuan, X., Hu, J., Li, S., Yu, M., 2020. Occurrence, fate, and mass balance of selected pharmaceutical and personal care products (PPCPs) in an urbanized river. Environ. Pollut. 266, 115340. https://doi.org/10.1016/j.envpol.2020.115340.

Zipperer, W.C., Foresman, T.W., Walker, S.P., Daniel, C.T., 2012. Ecological consequences of fragmentation and deforestation in an urban landscape: a case study. Urban Ecosyst. 15, 533–544. https://doi.org/10.1007/s11252-012-0238-3.