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Spa tourism as a source of pharmaceutically active compounds in surface waters: a multi-evidence assessment of occurrence and environmental risk

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ABSTRACT

Tourism-related activities are increasingly recognized as sources of pharmaceutically active compounds (PhACs) in aquatic environments; however, the contribution of spa tourism and associated pathways remains poorly quantified. This study investigated the occurrence, spatiotemporal variability, and environmental risk of caffeine (CAF), carbamazepine (CBZ), and diclofenac (DCF) in the Zala River catchment (Hungary), which is strongly influenced by spa and medical tourism. A multi-evidence approach was applied, combining multi-year monitoring data (2018, 2024, and 2025), questionnaire-based information on pharmaceutical usage, and a multi-parametric mass-balance model. The results revealed pronounced spatial variability linked to spa-impacted river sections, with DCF consistently dominating ecological risk based on both PNEC- and EQS-based assessments. DCF concentrations frequently exceeded risk thresholds and showed significant correlations with the number of medical treatments at selected sites. Questionnaire data indicated that approximately 30% of visitors used DCF-containing medications, supporting the interpretation of bathing-related release pathways. Mass-balance modelling further indicated that observed DCF concentrations in thermal waters can be reasonably explained by direct inputs from bathers, particularly via topical application. Overall, the findings suggest that spa tourism can act as a plausible and locally relevant contributor to pharmaceutical contamination in surface waters, although its role should be interpreted alongside other sources such as municipal wastewater and healthcare facilities. The integration of monitoring data, behavioural information, and mechanistic modelling provides a transferable framework for identifying and characterizing tourism-related sources and pathways in aquatic environments.

1. Introduction

Over recent decades, the occurrence of pharmaceutically active compounds (PhACs) in aquatic environments has become a growing environmental concern due to their continuous input, persistence, and potential adverse effects on aquatic organisms. Among these compounds, caffeine (CAF), carbamazepine (CBZ), and diclofenac (DCF) are the most frequently detected PhACs in surface waters worldwide (Reyes et al., 2021; Xiang et al., 2021; Hernández-Tenorio et al., 2022; Martin et al., 2025).

CAF is widely consumed in beverages and pharmaceutical products, resulting in its ubiquitous presence in wastewater-impacted surface waters (Barone and Roberts, 1996; Nehlig, 2018). The average global per capita intake is approximately 70 mg day^{-1}, corresponding to an annual consumption exceeding 200,000 tons (Li et al., 2020; Nehlig, 2018; Raj et al., 2021). Environmental inputs of CAF originate primarily from human excretion, the disposal of unconsumed caffeinated beverages, and improper medication disposal (Hillebrand et al., 2012). Following human metabolism, only 1–5% of ingested CAF is excreted unchanged in urine (Nehlig, 2018; Glade, 2010; Raj et al., 2021). Although CAF is partly removed during conventional wastewater treatment, reported removal efficiencies vary widely (64–100%), and its frequent detection in surface waters has led to its widespread use as an anthropogenic tracer of wastewater influence (Luo et al., 2014; Raj et al., 2021).

CBZ is a widely prescribed anticonvulsant used since the 1960s for

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the treatment of epilepsy, bipolar disorder, and neuropathic pain (Tolou-Ghamari et al., 2013). Typical therapeutic doses range from 450 to 800 mg day^{-1} (Grzesk et al., 2021), with up to 10% of the administered dose excreted unchanged (Kasprzyk-Hordern et al., 2008; Luo et al., 2014; Hai et al., 2018). Global annual consumption exceeds 1200 tons (Garcia-Espinoza et al., 2018; Oldenkamp et al., 2019). Due to its high persistence and limited removal in conventional activated sludge wastewater treatment plants (removal efficiency <10%), CBZ is frequently discharged into aquatic environments and is commonly applied as a conservative marker of wastewater derived contamination (Guo et al., 2020; Liu et al., 2022).

DCF is one of the most intensively monitored PhACs in the European Union due to its widespread use and well-documented ecotoxicological effects. It is a non-steroidal anti-inflammatory drug administered both orally and topically for human and veterinary purposes (Lonappan et al., 2016). The maximum recommended daily dose is 150 mg, and global annual consumption is estimated at 1400–1500 tons (Acuna et al., 2015; Lonappan et al., 2016; Drugs.com, 2025). While only approximately 1% of orally administered DCF is excreted unchanged, topical application represents a potentially important release pathway, as a substantial fraction of the applied dose may be washed directly into wastewater during bathing and handwashing (Davies and Anderson, 1997; Bielfeldt et al., 2022). Removal efficiencies in conventional wastewater treatment processes are highly variable (30–70%), allowing DCF to persist at measurable concentrations in surface waters (Lonappan et al., 2016). Key physicochemical properties, usage characteristics, and environmental relevance of CAF, CBZ, and DCF are summarized in **Supplementary Table S1**. In line with the objectives of the Water Framework Directive, an Environmental Quality Standard (EQS) of 40 ng L^{-1} has been proposed for DCF in surface waters, although alternative probabilistic approaches suggest higher threshold values (Leverett et al., 2021; SCHEER, 2022).

Together, these compounds represent complementary indicators of different environmental behaviours, source types, and risk profiles relevant to wastewater- and spa-influenced aquatic systems.

Lake Balaton, the largest shallow lake in Central Europe, and its main tributary, the Zala River, have been extensively studied with respect to the occurrence of PhACs and other emerging contaminants (Avar et al., 2016a,b; Maasz et al., 2019, 2021; Molnár et al., 2021a; Prikler et al., 2024; Svigruha et al., 2023; Tóth et al., 2022). The catchment area of the Zala River hosts several major thermal spa facilities, providing a unique opportunity to assess the influence of spa tourism on pharmaceutical contamination in surface water. Despite this, however, only a limited number of studies have explicitly addressed PhAC contamination associated with spa-related activities and their environmental implications (Jakab et al., 2020). Previous monitoring in the River Zala detected 66 out of 134 targeted pharmaceuticals between 2017 and 2018, highlighting the relevance of the region for further investigation (Maasz et al., 2019).

While increasing attention has been devoted to advanced water and wastewater treatment technologies for pharmaceutical removal (Neha et al., 2021; Tormo-Budowski et al., 2021; Lung et al., 2024; Yu et al., 2025), source-oriented studies remain essential for identifying dominant sources and pathways and for designing effective mitigation strategies.

The objectives of the present study were therefore to (i) investigate the spatial and temporal occurrence of CAF, CBZ, and DCF in surface waters influenced by spa and wellness tourism, and (ii) assess the associated environmental risks. Therefore, we applied a multi-evidence approach combining multi-year monitoring, questionnaire data, and screening-level mass-balance modelling to support source attribution in spa-impacted catchments.

We hypothesized that PhAC concentrations in the study area may be influenced by spa-related activities, particularly in the case of DCF, which is commonly used to treat inflammatory and rheumatic conditions associated with spa therapies. To support this hypothesis, a questionnaire survey was conducted within a citizen science framework. In addition to riverine monitoring, thermal pool waters and natural thermal lakes were analyzed to improve understanding of spa-related contribution pathways. Although wastewater treatment plant effluents were not directly sampled, the comparative analysis of surface and thermal waters provides valuable insight into the role of spa tourism in pharmaceutical contamination and related environmental risks.

2. Materials and methods

2.1. Study area

The 138-km-long Zala River, located in western Hungary, is the primary surface water contributor to Lake Balaton, supplying nearly 50% of its total inflow and playing a key role in regional agriculture, fishpond management, and water protection (Britannica, 2019; Farkas et al., 2020; Maasz et al., 2019; Western Transdanubian Water Directorate, 2020).

The Zala River catchment, largely located within Zala County, represents one of Hungary's most important spa and wellness tourism regions (Fig. 1). Between 2018 and 2023 (excluding the COVID-19 period), the area received an average of approximately 3.6 million visitors annually, with daily visitor numbers reaching up to 64,000. Several settlements within the catchment host large thermal spas, wellness centers, and medical bathing facilities, resulting in pronounced population fluctuations and increased wastewater and bathing water discharges (Hungarian Central Statistical Office, 2025).

Municipal wastewater loads within the study area amount to approximately 11.5 million m^3 per year and are supplemented by an estimated 2.2 million m^3 of water discharged from bathing and spa facilities (Western Transdanubian Water Directorate, 2020). All treated wastewater generated within the catchment is ultimately released into the Zala River, either directly via wastewater treatment plant (WWTP) effluents or indirectly through tributary streams (**Supplementary Table S2**).

The initial sampling network (sites 1-7) was established in 2018 within the framework of a broader pharmaceutical monitoring program. These sites primarily covered the main channel of the Zala River and one major tributary (Kiskomarom Channel; site 7*), allowing for the assessment of spatial patterns in PhAC concentration.

Based on the concentration levels and distribution patterns observed in 2018, sampling activities were extended in 2024 and 2025 to include additional locations situated in closer proximity to major spa facilities, thermal water outflows, and spa-affected tributaries. This extended sampling network included the outflow of Lake Hévíz (site 11*), the world's largest natural thermal lake. Lake Hévíz is characterized by a biologically active peat bed and a continuous spring discharge of approximately 435 L s^{-1}, resulting in complete water renewal every ~3 days. Due to geothermal heating, lake water temperatures remain above 22°C in winter and typically reach 35–38°C during summer (Hévíz Spa and Saint Andrew Hospital for Rheumatic Diseases, 2025). Additional sampling locations included the Bányavölgyi Creek (site 12*), which receives waters originating from the Zalakaros area and may be influenced by spa-related and municipal discharges, as well as sites 8, 9, and 10. These latter sites enabled the investigation of river sections potentially affected by effluents associated with the Kehidakustány thermal spa. The inclusion of these locations allowed for a more targeted, source-proximal assessment of pharmaceutical residue loads in surface water potentially influenced by spa and medical tourism activities.

2.2. Data collection

Concentration data from the surface water of the Zala River and its tributaries were obtained during three sampling periods. The first dataset originates from 2018 and was collected as part of our previous pharmaceutical monitoring program. Portions of these data have

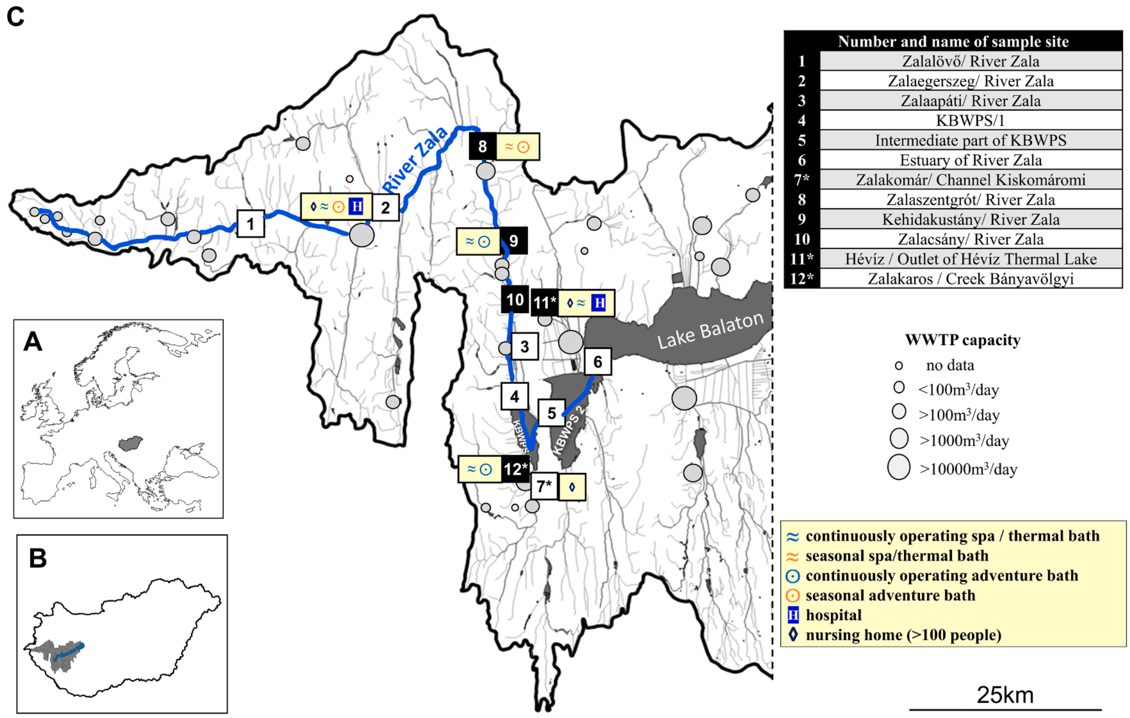

Fig. 1. Map (A) shows the location of Hungary within Europe. Map (B) presents the study area in Hungary. Map (C) shows the sampling sites along the Zala River and within its catchment. Numbers marked with an asterisk indicate sites where sampling was conducted not from the Zala River, but from an inflow. Numbers with a white background indicate sampling sites from 2018, whereas numbers with a black background indicate new sampling sites sampled in October 2024 and 2025 compared to the previous campaign. The map also shows the locations of WWTPs, spas/thermal and adventure baths, hospitals, larger elderly care homes (>100 residents), and the GPS coordinates of the sampling sites. The geographic coordinates of the sampling sites are provided in the Supplementary Information. KBWPS: Kis-Balaton Water Protection System.

already been published (Maasz et al., 2019), while the previously unpublished measurements are presented in this study (**Supplementary Table S3**). Both published and unpublished 2018 data were used for environmental risk assessment (ERA). The second dataset was collected in 2024, and the third in 2025; both represent entirely new, previously unpublished measurements and reflect an expanded sampling design compared to 2018.

The 2018 dataset primarily serves as a baseline for spatiotemporal analysis based on repeated sampling, whereas the 2024 and 2025 campaigns were designed to provide a more targeted, source-proximal assessment focusing on locations in closer proximity to spa facilities and other potential sources.

Accordingly, the different datasets are interpreted within their respective analytical contexts, and direct interannual comparisons are treated with caution.

2.3. *Sample collection, preparation, and analytical measurements*

Fig. 1 illustrates the location of all sampling sites together with major spas, adventure baths, hospitals, nursing homes (>100 people) and WWTPs.

Surface waters of the Zala River were sampled at six riverine sites and one inflow (Kiskomáromi Channel) on four occasions in 2018. For the analysis of three PhACs, 2 L grab water samples were collected in amber borosilicate glass bottles with Teflon-lined caps, acidified immediately with 2 ml HPLC-grade formic acid, stored at 4°C, and transported to the laboratory within 4 h. In the laboratory, 1 L aliquots were spiked with isotopically labelled internal standard (carbamazepine-d10), filtered through glass fiber filters, and extracted using automated solid-phase extraction (AutoTrace 280, Thermo Fisher Scientific) with Strata X-CW cartridges (Phenomenex). Extracts were evaporated under nitrogen, reconstituted in 500 μL acetonitrile, and analyzed by supercritical fluid chromatography coupled to tandem mass spectrometry (UPC^2–MS/MS; Waters Xevo TQ-S) using a BEH analytical column (3.0 × 100 mm, 1.7 μm). Sample preparation, extraction, and analytical procedures followed previously published methods (Maasz et al., 2019 and 2021; Kondor et al., 2020; Jakab et al., 2020).

Based on the 2018 results, the sampling design was refined, and additional campaigns were conducted once in October 2024 and 2025. Sampling was performed in autumn to minimize photodegradation effects. Sample collection and preparation procedures were identical to those applied in 2018; however, the chromatographic separation was performed on a Thermo Vanquish UHPLC system (Thermo Fisher Scientific) equipped with a Kinetex C18 reversed-phase column (1.7 μm, 3 mm × 100 mm; Phenomenex). Gradient elution employed water/formic acid (99.9/0.1, v/v; solvent A) and water/formic acid/methanol (9.9/0.1/90, v/v/v; solvent B) at a flow rate of 250 μL min^{-1}. The gradient program included the following steps: from 0 to 5.0 min, the composition was 50% B; from 5.0 to 8.0 min, it increased from 50.0 to 90.0% B; from 8.0 to 15.0 min, it increased from 90.0 to 100.0% B and remained at 100% B until 17.0 min; then, from 17.0 to 20.0 min, the composition decreased from 100.0 to 50.0% B, followed by a 5-min equilibration of the column.

Mass spectrometric detection was performed using an Orbitrap Exploris 120 instrument (Thermo Fisher Scientific) operated in positive ionization mode using parallel reaction monitoring for data acquisition. The conditions of the heated electrospray ionization source were as follows: the capillary temperature was set to 200°C, the S-Lens RF parameter was set to 80, the spray voltage was 3.5 kV, the sheath gas flow rate was 35 (absolute units), and the auxiliary gas flow rate was 5 (absolute units). A resolution of 60,000 was applied to the orbitrap cell, and the isolation window was set to two Daltons. The collision energy was 20 eV. Quantification was based on the most intense precursor-to-fragment ion transitions for CAF (195.0876 → 138.0655±0.001 m/z), CBZ (237.1017 → 194.0955±0.001 m/z), and DCF (294.0091 → 250.0183±0.001 m/z). Data processing was performed using

Chromeleon™ Chromatography Data System software (v7.3.2). Analytical quality assurance and quality control (QA/QC) procedures included the evaluation of recovery, precision, matrix effects, and method sensitivity. Recoveries were determined at three concentration levels (100, 1000, and 5000 ng L^{-1}) and ranged between 95.9 and 104.5% for the investigated compounds. Relative standard deviations (RSD%) were below 12% for all investigated compounds. Limits of detection (LOD) and limits of quantification (LOQ) ranged between 2.4-11.2 ng L^{-1} and 7.3-39.4 ng L^{-1}, respectively. Matrix effects were evaluated for the major investigated water matrices and compensated by matrix-matched calibration together with isotopically labelled internal standard correction. Procedural and solvent blanks did not show detectable contamination by the investigated target compounds. Detailed validation parameters are summarized in **Supplementary Table S4 and S5.**

2.4. ERA

Environmental risk was characterized using risk quotients (RQ), defined as the ratio of the measured environmental concentration (MEC) to the predicted no-effect concentration (PNEC). PNEC values were derived from available ecotoxicological data, including acute EC_{50} and LC_{50} values, chronic no-observed-effect concentrations (NOECs), or hazardous concentrations affecting 5% of species (HC_5) for algae, cladocerans, and fish. Assessment factors (AFs) ranging from 5 to 1000 were applied according to data availability and quality, following established risk assessment frameworks (Molnar et al., 2021a, b). Calculated RQ values were used as screening-level indicators of environmental risk. In the present study, RQs were classified as follows: <0.01, negligible risk; 0.01-0.1, low risk; 0.1-1, medium risk; and >1, high risk.

In addition to the PNEC-based approach, measured concentrations were compared with available EQS to provide a complementary, regulatory-oriented screening. Among the investigated compounds, an official EQS under the EU Water Framework Directive is currently available only for DCF. Accordingly, an EQS-based risk quotient (RQ_EQS) was calculated as the ratio of the measured concentration to the proposed annual average EQS value of 40 ng L^{-1}.

To account for uncertainties in EQS derivation and to assess sensitivity to alternative threshold assumptions, an additional alternative EQS value of 126 ng L^{-1}, derived from a probabilistic species sensitivity distribution (SSD) approach (Leverett et al., 2021) was also considered. RQ_EQS values based on both thresholds were interpreted as indicative screening-level indicators.

Due to the limited number of samples and the lack of continuous long-term monitoring data, RQ_EQS calculations were primarily performed for individual samples rather than annual averages, and were used to support, but not replace, the PNEC-based ERA. For the 2018 dataset, where four sampling events were available at selected sites, approximate annual average concentrations for DCF were additionally calculated to allow complementary EQS-based interpretation.

It should be emphasized that the calculated RQs are based on single measurements and represent screening-level indicators rather than formal regulatory compliance assessments. Furthermore, potential mixture effects and interactions between compounds were not considered and may influence actual environmental risk levels.

2.5. Questionnaire survey

To support the interpretation of potential spa-related pharmaceutical inputs, a questionnaire-based survey was conducted among visitors at selected thermal spa facilities within the study area, including Kehidakustány and Hévíz, corresponding to sampling sites 10 and 11. Implemented as part of a citizen science approach, the survey aimed to collect information on the consumption of selected PhACs (CAF, CBZ, DCF) and behavioural patterns relevant to potential environmental release pathways.

Participants were recruited voluntarily on-site during spa visits, without financial incentives. In total, 407 individuals completed the survey (see Supplementary Section A for the full dataset and questionnaire). The survey covered (i) purpose of visit (medical vs recreational), (ii) use of selected PhACs, and (iii) mode of diclofenac application (oral vs topical).

Although the number of respondents was relatively high and included multiple spa locations, the sampling strategy was site-specific and non-random; therefore, the dataset is not fully representative of the broader population of spa users. The findings should thus be regarded as indicative rather than statistically representative.

Potential sources of uncertainty include self-reporting and recall bias, as well as possible under- or over-reporting of pharmaceutical use. In addition, dosage frequency and exact quantities were not assessed, introducing further uncertainty when linking behavioural data to environmental concentrations. The survey was conducted anonymously, no personal identifying information was collected, and participants were informed about the study objectives prior to participation.

3. Results & discussion

3.1. Measured concentrations and their distribution

3.1.1. Concentrations in an international context

The concentration ranges observed in this study are generally consistent with global occurrence patterns reported for CAF, CBZ, and

Table 1
The concentrations of the investigated PhACs occurring in river waters of different countries in the last 10 years.

Country	River	CAF	CBZ	DCF	Reference
		Concentration in river water [ng/L]			
Spain	**River Turia**	n.d.	n.d.	49	(Carmona et al., 2014)
UK	**River Thames**	118-735	21-209	-	(Nakada et al., 2017)
Brazil	**River Piraí**	11-213	5-14	9-29	(de Sousa et al., 2014)
Brazil	**River Jundiaí**	994–19330	6-660	37–329	(de Sousa et al., 2014)
Lebanon	**River Beirut**	1994-10234	n.d.	n.d.	(Mokh et al., 2017)
India	**River Ganga**	-	n.d.-26	12-2987	(Prasad et al., 2024)
China	**Yangtze River**	12-57	n.d.	n.d.	(Asghar et al., 2018)
	Jilin Songhua River	Max: 26	n.d.	Max: 20	(He et al., 2018)
	Beiyun River	33- 9785	10-189	8-170	(Dai et al., 2015)
	Jiulong River	8-3060	1-4	1-11	(Sun et al., 2016)
Korea	**Yeongsan River**	Median: 280 Max: 1428	Median: 519 Max: 1763	n.d.	(Park et al., 2018)
Hungary	**River Danube**	10-3400	26-498	2-115	(Kondor et al., 2020)
Hungary	**River Zala**	57-139	70-805	221	(Maasz et al., 2019)
Hungary	**River Zala**	112-4635	44-397	9-2530	This study (Samples from 2018)
		69-137	79-903	4-768	This study (Samples from 2024)
		65-408	81-784	51-731	This study (Samples from 2025)

DCF in surface waters, which typically span from ng L^{-1} to μg L^{-1} levels worldwide (Xiang et al., 2021; Hernández-Tenorio et al., 2022). Table 1 compares concentrations of the three investigated PhACs detected in river waters over the past decade with those measured in the present study. The concentration ranges of CAF (65-4635 ng L^{-1}) and CBZ (44-903 ng L^{-1}) measured in the Zala River fall well within internationally reported values. In contrast, the maximum DCF concentration detected in this study (2530 ng L^{-1}) exceeds most previously reported for European rivers and many Asian river systems by approximately one order of magnitude. Comparable concentrations have previously been reported only in highly impacted rivers, such as the River Ganga in India. To date, very few studies have explicitly addressed pharmaceutical contamination associated with spa activities. Jakab et al. (2020) reported maximum concentrations of 2061 ng L^{-1} for CAF, 189 ng L^{-1} for CBZ, and 58 ng L^{-1} for DCF in used thermal waters from six spas in Budapest, highlighting that spa-related waters may represent relevant, but understudied, sources of pharmaceutical contamination.

The elevated DCF concentrations observed in the present study are consistent with the socio-medical characteristics of the Zala catchment, where thermal spas are primarily used for the treatment of rheumatic and chronic musculoskeletal conditions. In addition, the Zala River flows through the city of Zalaegerszeg, which hosts a major hospital and urban wastewater sources, where high DCF consumption is likewise expected. Consequently, the observed DCF concentrations most likely reflect the cumulative influence of spa tourism and urban medical infrastructure, rather than a single dominant source.

3.1.2. Spatiotemporal distribution in 2018

Fig. 2 illustrates spatiotemporal changes of CAF, CBZ, and DCF concentrations along the Zala River in 2018, together with tourism-related indicators (average monthly guest nights (Hungarian Central Statistical Office, 2025) and number of medical treatments (National Health Insurance Fund Administration of Hungary, 2025)), reflecting spa and medical tourism activity in the catchment (Zala County). For CAF (Fig. 2**A**), concentrations were generally higher in June and October (0-4635 ng L^{-1} and 585-4346 ng L^{-1}, respectively) than in August (0-1557 ng L^{-1}), despite peak tourist activity during summer period. This pattern suggests that CAF concentrations were not directly driven by visitor numbers. Given the known susceptibility of CAF to rapid photodegradation, the relatively low concentration observed in August may be explained by intense and prolonged UV radiation during this period, which likely enhanced CAF degradation in surface waters (Liu et al., 2022). Seasonal temperature effects on microbial community composition and activity as well as WWTP performance may have contributed to this variability (Domanska et al., 2023; Johnston et al., 2019; Kang et al., 2020).

Spatially, CAF concentrations showed marked variability. Higher concentrations were detected at sites 1 and 3 (0-4346 ng L^{-1} and 0-4635 ng L^{-1}, respectively) compared to site 2 (0-585 ng L^{-1}), likely reflecting differences in local WWTP performance and temporary overloading. The comparatively low CAF levels at site 2 may be related to the applications of UV disinfection at the Zalaegerszeg WWTP. Downstream increases at site 3 during all sampling campaigns suggest additional inputs from popular thermal spas and recreational bathing facilities located between sites 2 and 3 (combined with limited removal efficiencies of local treatment systems), suggesting that this river section may be sensitive to tourism-related pressures in combination with other anthropogenic inputs.

CBZ displayed a distinct temporal pattern (Fig. 2**B**), with the highest concentrations in April (146-397 ng L^{-1}), intermediate levels in August and October (78-201 ng L^{-1} and 0-217 ng L^{-1}, respectively), and the lowest concentrations in June (0-158 ng L^{-1}). At most sampling occasions, peak concentrations occurred at site 2, except in August, when the maximum shifted downstream to site 3. No consistent correlation was found between CBZ concentrations and tourism indicators. However, the downstream shift of peak concentration in August may reflect increased spa-related inputs temporarily exceeding urban wastewater contribution. Elevated CBZ levels at site 2 are consistent with the presence of a hospital and a large nursing home in the vicinity, known point sources of pharmaceutical loads (Kosma et al., 2020). The application of UV disinfection at the WWTP serving this area may further contribute to CBZ attenuation, as UV radiation has been shown to facilitate CBZ degradation (Liu et al., 2022).

The measured data suggest increased CBZ concentrations in April, which may tentatively be linked to seasonal variability in CBZ consumption. Previous studies have reported higher incidence of certain neurological and inflammatory conditions during colder and darker periods, potentially leading to increased pharmaceutical use in late winter and early spring (Meesters and Gordijn, 2016; Wu et al., 2021). However, national and county-level pharmaceutical sales data did not indicate a pronounced seasonal decrease in CBZ consumption during summer months, suggesting that this explanation should be treated with caution (**Supplementary Figures S1-2**).

Downstream of site 3, CBZ concentrations continuously decreased at sites 4–6, indicating effective attenuation within the Kis-Balaton Water Protection System (KBWPS), likely driven by extended water residence time, shallow water depths, enhanced UV exposure, and high microbial activity (Aulló-Maestro et al., 2017; Maasz et al., 2019).

DCF exhibited the most pronounced spatiotemporal variability among the investigated compounds (Fig. 2**C**), with consistently the highest concentrations recorded in October. Concentrations were generally highest at site 2, reflecting combined inputs from hospitals, nursing homes, and major spa facilities. In August, however, peak concentrations occurred at site 7*, which receives inflow from a channel draining one of the most intensively used spa tourism centers in the study area. Additional contributions from a nearby large nursing home (>100 residents) cannot be excluded. Strong positive correlations were observed between DCF concentrations and the number of medical

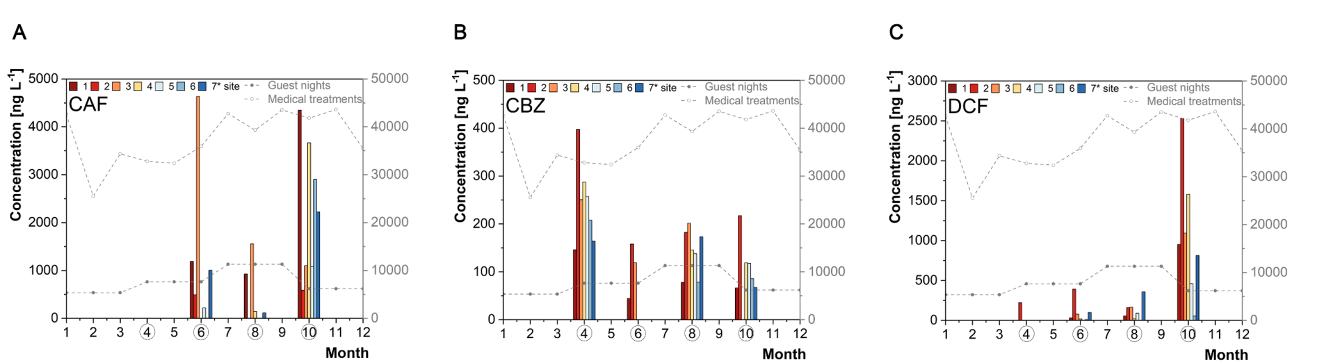

Fig. 2. Temporal changes in the concentrations of CAF (A), CBZ (B), and DCF (C) (primary y-axis) at sampling sites 1-7, together with the number of guest nights and medical treatments in the pilot area (secondary y-axis) throughout 2018. Circled months indicate the sampling periods. Asterisks denote sites where sampling was conducted from an inflow rather than from the Zala River.

treatments at sites 3 and 7* (Pearson correlation coefficient > 0.8; n = 4; Supplementary Figure S3). However, given the limited number of observations, these correlations should be interpreted with caution and considered indicative rather than statistically robust. Nevertheless, they support the hypothesis that health-oriented spa tourism represents a plausible contributor to DCF loads in the study area, alongside other potential sources such as healthcare facilities and municipal wastewater.

To better disentangle spa-related inputs from other healthcare sources, an additional sampling site (site 12*) was introduced in 2024 and 2025 closer to the spa outflow and less influenced by institutional healthcare facilities. Similar to CBZ, DCF concentrations declined markedly downstream of site 4, further highlighting the mitigating role of the KBWPS.

Overall, the observed spatiotemporal patterns reflect the combined influence of urban wastewater inputs, medical infrastructure, and spa-related tourism on PhAC contamination in the Zala River. The consistently elevated DCF levels at sites affected by spa activities, together with strong correlations with medical tourism indicators, provide a robust basis for targeted assessment of spa-related pharmaceutical contributions and their downstream environmental implications.

3.1.3. Spatial distribution in 2024 and 2025

The single sampling campaigns conducted in October 2024 and 2025 enabled a comparison of the spatial distribution of the investigated PhACs along the main course of the Zala River and in selected tributaries potentially influenced by spa-related activities. Concentrations measured along the river course are shown in Fig. 3**A** and 3**C**, while tributary data are presented in Fig. 3**B** and 3**D**.

For CAF, the highest concentrations along the main river course in 2024 were detected at sampling site 9 (137 ng L^{-1}), located downstream of a major thermal spa facility, suggesting a local potential influence of spa-related and associated tourism activities. This pattern persisted in 2025, when the maximum riverine CAF concentration (408 ng L^{-1}) was again observed at the same site. The highest CAF concentration during the 2024 campaign (356 ng L^{-1}) occurred at sampling site 12, a tributary receiving waters influenced by both spa operations and municipal discharges. In contrast, CAF concentrations measured at the outflow of the natural thermal lake (site 11*) remained consistently low (<71 ng L^{-1}), indicating a limited contribution from open-system thermal waters largely unaffected by direct municipal inputs.

CBZ exhibited a highly consistent spatial pattern in both years, with maximum concentration repeatedly observed at sampling site 2, located in an urban setting. Concentrations reached 903 ng L^{-1} in 2024 and 784 ng L^{-1} in 2025, reflecting persistent urban and healthcare-related sources of contamination. The distribution closely matched the pattern observed in 2018, confirming that CBZ loads in the catchment are primarily associated with long-term municipal inputs rather than short-term or seasonal tourism-related activities.

DCF showed greater spatial variability patterns between the two years. In 2024, elevated concentrations (336-768 ng L^{-1}) were detected along the river section encompassing sites 8, 9, 10, and 3, where a large thermal spa is located in close proximity to site 9, suggesting a local spa-

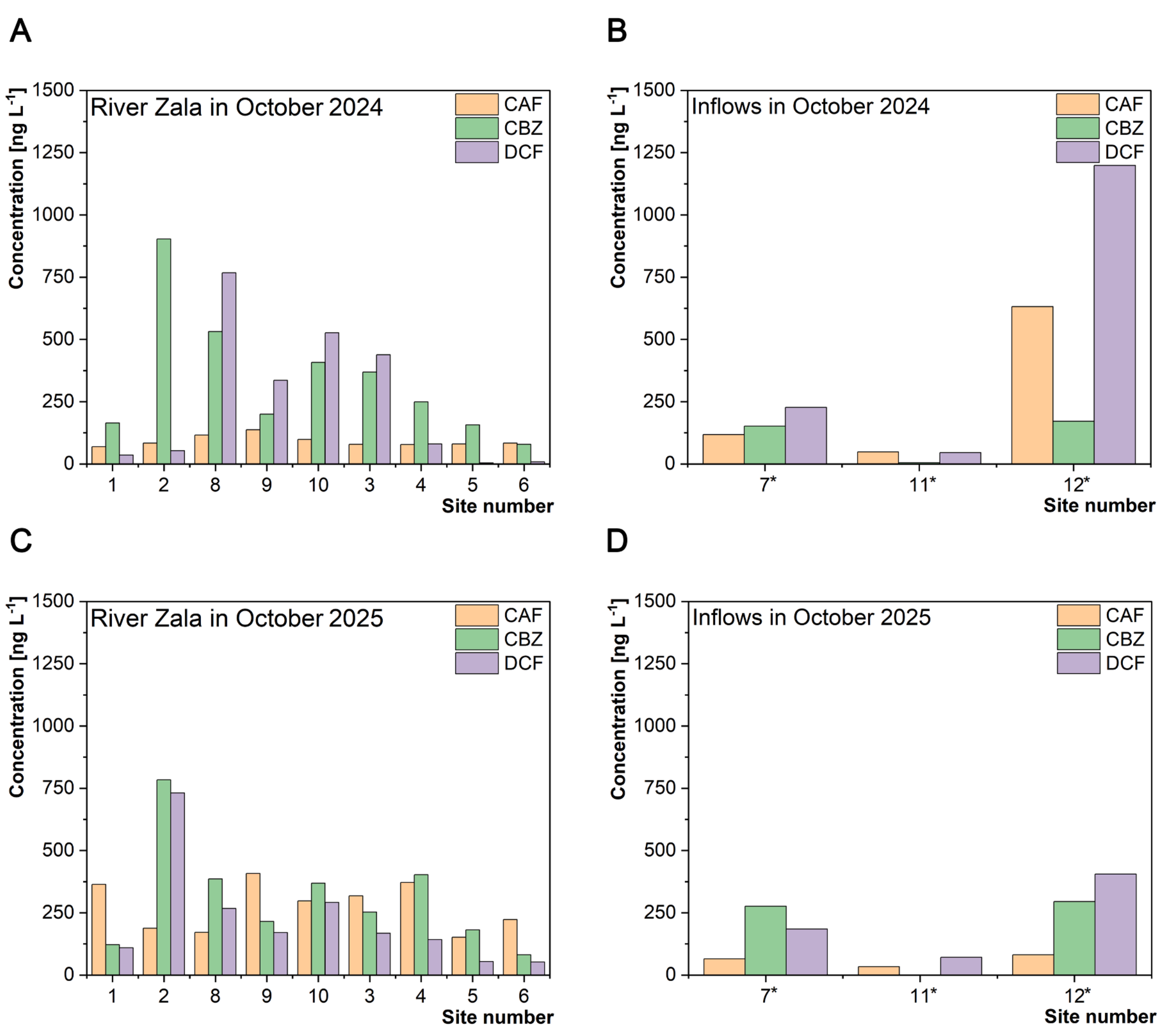

Fig. 3. Spatial distribution of concentration of the investigated PhACs in River Zala (A and C) and its inflows (B and D).

related hotspot. In 2025, however, the highest DCF concentration (731 ng L^{-1}) was recorded at site 2, mirroring the spatial pattern of CBZ and indicating a stronger dominance of urban and municipal sources during this sampling period. Across the entire 2024 campaign, the maximum DCF concentration (1199 ng L^{-1}) was measured at sampling site 12, further supporting the role of localized health-oriented tourism activities in shaping DCF loads in specific parts of the catchment.

Overall, the spatial patterns observed in 2024 and 2025 corroborate the conclusions drawn from the 2018 dataset. While CBZ is consistently associated with persistent urban and municipal sources, DCF, and to a lesser extent CAF, exhibit localized enrichment in river sections and tributaries influenced by spa tourism. In contrast, consistently low concentrations observed at the outflow of the natural thermal lake (site 11*) for all investigated compounds further indicate that open-system thermal lakes, when largely decoupled from municipal wastewater inputs, contribute minimally to pharmaceutical loads in surface waters.

3.2. ERA

The results of the ERA based on freshwater PNEC values for the three investigated PhACs are summarized in Table 2. RQ values were calculated for all available concentration data from 2018, 2024, and 2025, allowing for both spatial and temporal evaluation of potential environmental risks. The ERA results enable comparison of the relative risk profiles of the investigated compounds and the identification of spatial and temporal risk patterns across the study area.

3.2.1. PNEC-based ERA

For CAF, RQ values exceeded the threshold of 1 only during the 2018 monitoring period, indicating an episodic rather than persistent ecological risk. Elevated risk levels were observed on four occasions: at site 3 in June, and at sites 1, 4, and 6 in October. The highest RQ_CAF value (1.998) was recorded at site 3 in June 2018. In contrast, CAF-related risk remained consistently low during the 2024 and 2025 campaigns, with all RQ values below unity.

CBZ posed the lowest ecological risk among the investigated compounds. RQ_CBZ values remained below 1 across all sampling sites and years, reflecting its relatively high PNEC. The maximum RQ_CBZ value was 0.040 at site 2 in April 2018, while the highest value during the later sampling period reached 0.090 at the same site in October 2024. Overall, these results indicate a consistently low environmental risk associated with CBZ throughout the study period.

In contrast, DCF exhibited pronounced ecological risk across most sampling sites and campaigns. RQ_DCF values exceeded unity in approximately 79% of all samples, frequently indicating high risk. The highest RQ_DCF value (238.679) was observed at site 2 in October 2018, highlighting this location as a persistent hotspot of ecological concern. Elevated RQ_DCF values were also recorded at several other sites influenced by urban wastewater and spa-related inputs, including sites 3, 7*, 10, and 12*. These findings identify DCF as the primary potential risk driver among the investigated compounds within the study area.

3.2.2. EQS-based assessment of DCF

Given the frequent exceedance of PNEC-based risk thresholds by DCF, the ERA was extended using EQS as additional screening benchmarks. Both the deterministic EQS of 40 ng L^{-1} proposed under the EU Water Framework Directive (SCHEER, 2022) and the alternative probabilistic threshold of 126 ng L^{-1} derived using a species sensitivity distribution approach (Leverett et al., 2021) were applied. The results are summarized in Table 3.

For the 2018 monitoring period, annual average DCF concentrations were calculated for the main course of the Zala River (sites 1–6), where four sampling campaigns were available. Site-specific annual mean concentrations ranged from 16 ng L^{-1} at site 6 to 825 ng L^{-1} at site 2. Elevated annual average concentrations were observed at sites 1-5 (138-825 ng L^{-1}), exceeding both EQS thresholds, indicating widespread

Table 2
ERA of the three investigated PhACs based on freshwater PNEC values (CAF: 2320.0 ng/L; CBZ: 10,000.0 ng/L; DCF: 10.6 ng/L; Molnár et al., 2021a) and measured concentrations in 2018, 2024, and 2025. Grey shading indicates high risk (RQ > 1). Asterisks denote samples collected from an inflow rather than directly from the River Zala.

	RQ					
Sample time	April 2018	June	August	October	October 2024	October 2025
Sample site 1						
CAF	0.000	0.513	0.399	1.873	0.030	0.157
CBZ	0.015	0.004	0.008	0.007	0.016	0.012
DCF	0.000	3.019	5.283	89.811	3.302	10.268
Sample site 2						
CAF	0.000	0.211	0.000	0.252	0.036	0.081
CBZ	0.040	0.016	0.018	0.022	0.090	0.078
DCF	20.849	36.887	14.906	238.679	5.000	68.960
Sample site 3						
CAF	0.000	1.998	0.671	0.475	0.034	0.137
CBZ	0.025	0.012	0.020	0.000	0.037	0.025
DCF	0.000	7.358	15.472	103.208	41.321	15.842
Sample site 4						
CAF	0.000	0.000	0.063	1.580	0.034	0.016
CBZ	0.029	0.000	0.015	0.012	0.025	0.040
DCF	0.000	1.604	1.887	148.962	7.547	13.385
Sample site 5						
CAF	0.000	0.094	0.000	0.467	0.034	0.066
CBZ	0.026	0.000	0.014	0.012	0.016	0.018
DCF	0.000	0.000	8.396	43.491	0.377	5.093
Sample site 6						
CAF	0.000	0.000	0.000	1.251	0.036	0.096
CBZ	0.021	0.000	0.008	0.009	0.008	0.008
DCF	0.000	0.943	0.000	5.094	0.755	4.916
Sample site 7*						
CAF	0.000	0.433	0.049	0.959	0.051	0.028
CBZ	0.016	0.000	0.017	0.007	0.015	0.028
DCF	0.000	9.340	33.679	76.509	21.370	17.455
Sample site 8						
CAF	n.d.	n.d.	n.d.	n.d.	0.050	0.074
CBZ	n.d.	n.d.	n.d.	n.d.	0.053	0.039
DCF	n.d.	n.d.	n.d.	n.d.	72.453	25.183
Sample site 9						
CAF	n.d.	n.d.	n.d.	n.d.	0.059	0.176
CBZ	n.d.	n.d.	n.d.	n.d.	0.020	0.022
DCF	n.d.	n.d.	n.d.	n.d.	31.698	16.082
Sample site 10						
CAF	n.d.	n.d.	n.d.	n.d.	0.042	0.129
CBZ	n.d.	n.d.	n.d.	n.d.	0.041	0.037
DCF	n.d.	n.d.	n.d.	n.d.	49.717	27.552
Sample site 11*						
CAF	n.d.	n.d.	n.d.	n.d.	0.021	0.015
CBZ	n.d.	n.d.	n.d.	n.d.	0.001	0.000
DCF	n.d.	n.d.	n.d.	n.d.	4.340	6.664
Sample site 12*						
CAF	n.d.	n.d.	n.d.	n.d.	0.153	0.035
CBZ	n.d.	n.d.	n.d.	n.d.	0.017	0.030
DCF	n.d.	n.d.	n.d.	n.d.	113.113	38.234

regulatory concern.

Analysis of individual sampling events confirmed frequent EQS exceedances across the study area. Sampling site 2 consistently exhibited high RQ_EQS_DCF values during the 2018, 2024, and 2025 campaigns, reinforcing its role as a persistent DCF hotspot. Additional high-risk locations included sampling sites 3 and 7*, as well as newly introduced near major spa facilities (sites 8-9-10-12*), where RQ_EQS_DCF values frequently exceeded unity. In contrast, site 11*, representing the outflow of a natural thermal lake, consistently showed low RQ values, indicating a comparatively minor contribution to overall ecological risk.

Despite the limited temporal resolution, the annual averages for 2018 indicate a substantial and spatially extensive DCF risk in the Zala River. Lower risks at downstream sites 5 and 6 highlight the mitigating effects of hydrological retention and attenuation processes within the KBWPS, suggesting reduced risk propagation toward Lake Balaton.

Table 3
ERA of DCF based on concentration data in this study and different EQS thresholds. Grey shading indicates high risk (RQ_EQS_DCF > 1). An asterisk denotes sites where sampling was conducted from an inflow rather than from the Zala River.

Site number	RQ_EQS_DCF											
	EQS=40 ng/L (SCHEER, 2022)						EQS=126 ng/L (Leverett et al., 2021)					
	April 2018	June	August	October	October 2024	October 2025	April 2018	June	August	October	October 2024	October 2025
1	0.000	0.800	1.400	23.800	0.875	2.721	0.000	0.254	0.444	7.556	0.278	0.864
2	5.525	9.775	3.950	63.250	1.325	18.274	1.754	3.103	1.254	20.079	0.421	5.801
3	0.000	1.950	4.100	27.350	10.950	4.198	0.000	0.619	1.302	8.683	3.476	1.333
4	0.000	0.425	0.500	39.475	2.000	3.547	0.000	0.135	0.159	12.532	0.635	1.126
5	0.000	0.000	2.225	11.525	0.100	1.350	0.000	0.000	0.706	3.659	0.032	0.428
6	0.000	0.250	0.000	1.350	0.200	1.303	0.000	0.079	0.000	0.429	0.063	0.414
7*	0.000	2.475	8.925	20.275	5.663	4.625	0.000	0.786	2.833	6.437	1.798	1.468
8	n.d.	n.d.	n.d.	n.d.	19.200	6.673	n.d.	n.d.	n.d.	n.d.	6.095	2.119
9	n.d.	n.d.	n.d.	n.d.	8.400	4.262	n.d.	n.d.	n.d.	n.d.	2.667	1.353
10	n.d.	n.d.	n.d.	n.d.	13.175	7.301	n.d.	n.d.	n.d.	n.d.	4.183	2.318
11*	n.d.	n.d.	n.d.	n.d.	1.150	1.766	n.d.	n.d.	n.d.	n.d.	0.365	0.561
12*	n.d.	n.d.	n.d.	n.d.	29.975	10.132	n.d.	n.d.	n.d.	n.d.	9.516	3.217

Overall, the ERA highlights clear differences in risk profiles among the compounds investigated, with DCF consistently exhibiting the highest RQ values, while CAF and CBZ contribute to a lesser extent under the studied conditions.

3.2.3. *Implications for ecological risk in spa-impacted surface waters*

Overall, DCF emerged as the dominant contributor to ecological risk, particularly at sites exposed to combined urban and spa-related pressures. Elevated DCF-related risks were repeatedly observed at locations influenced by medical infrastructure, urban wastewater inputs and spa tourism, whereas substantially lower ecological risks were detected at downstream river sections and at the outflows of natural thermal waters. These results suggest that surface waters affected by overlapping urban and spa-related inputs represent priority targets for targeted monitoring and risk management strategies.

While RQ values provide useful insight into potential ecological risks, they should be interpreted as screening-level indicators rather than measures of regulatory compliance. The use of single-compound RQ values does not account for potential mixture effects, which may lead to additive or synergistic impacts in aquatic environments. Furthermore, uncertainties associated with limited sampling frequency and spatial coverage should be considered when interpreting these results.

3.3. *Relationship between spa tourism and PhAC pollution*

Three spa facilities were considered in this study: Lake Hévíz (site 11*, Hévíz Spa and Saint Andrew Hospital for Rheumatic Diseases, 2025), a natural thermal lake; the built spa complex of Kehidakustány (site 9, Kehida Thermal Spa and Adventure Bath, 2025); and Zalakaros (site 12*, Zalakaros Spa, 2025). Although the original study design included all three sites for questionnaire surveys (**Supplementary Section A**) and water sampling, the spa facility in Zalakaros declined to participate. Consequently, questionnaire surveys were conducted only at Lake Hévíz and Kehidakustány in October 2025 (n = 407), and internal bathing water samples (lake water and pool water) were collected exclusively at these two locations.

Questionnaire results indicated that most visitors consumed CAF-containing beverages (~80%), CBZ use was negligible (<1%), and approximately one-third (~30%) of respondents reported DCF use. Both oral and topical applications were common, with topical use accounting for a substantial fraction of DCF consumption at both sites (**Supplementary Table S6-7**). The inclusion of questionnaire data from multiple spa locations within the Zala River catchment (Hévíz and Kehidakustány) provides additional local support for the observed patterns of pharmaceutical use among spa visitors. However, the questionnaire results should be interpreted cautiously as region-specific and indicative rather than broadly representative.

Measured PhAC concentrations in bathing waters differed markedly between hydrological system types. In the outdoor thermal pool at Kehidakustány, concentrations reached 682 ng L^{-1} for CAF and 185 ng L^{-1} for DCF, whereas substantially lower levels were observed in the Hévíz thermal lake (79 ng L^{-1} CAF and 70 ng L^{-1} DCF). These differences reflect the contrasting hydrological characteristics of natural thermal lakes and built spa pools. Continuous water renewal and a much larger effective water volume per visitor in Lake Hévíz result in significantly lower PhAC accumulation compared to closed or semi-closed pool systems. CBZ was not detected in bathing waters at either site, consistent with questionnaire data indicating negligible CBZ use and suggesting that bathing-related inputs are not a relevant CBZ source.

Hydrological conditions provide a mechanistic explanation for these patterns. On the sampling day, Lake Hévíz hosted 1025 visitors (average daily attendance in October approximately 820) and has a water volume of 127,950 m^3, with continuous springs discharge of approximately 435 L s^{-1}, resulting in rapid water renewal and short hydraulic residence time. In contrast, the Kehidakustány spa complex has a total pool water volume of 1846 m^3; the sampled outdoor thermal pool had a volume of 72 m^3 and a renewal rate of approximately 140 m^3 day^{-1}, depending on operational conditions and visitor load (with 624 visitors on the sampling day). These differences in water volume per visitor and renewal dynamics explain the markedly higher PhAC concentrations observed in built spa pools.

Among the investigated PhACs, DCF showed the strongest association with bathing activity, suggesting a potential link to spa-related inputs, and concentrations approached reported ecotoxicological thresholds; it was therefore selected for detailed mass-balance modelling. To estimate the contribution of bathers to DCF contamination, a mass-balance model was developed for Lake Hévíz, assuming quasi–steady-state conditions due to relatively stable daily visitor numbers and hydrological characteristics. Under this assumption, the total mass of DCF in the lake and its daily mass loss by dilution are given by:

$$M_{\text{tot}} = C \cdot V \cdot 10^{-6} \text{ and } M_{\text{out}} = C \cdot (k_h \cdot V) \cdot 10^{-6}$$

where:

- M_{tot} is the total DCF mass in the lake [g],
- M_{out} is the daily DCF mass lost by dilution [g day^{-1}],
- C is the measured DCF concentration [ng L^{-1}],
- V is the lake volume [m^3],
- k_h is the water exchange coefficient [day^{-1}]

- 10^{-6} was used as a conversion factor to ensure dimensional consistency.

For $C \approx 70$ ng L^{-1}, the daily DCF input to maintain steady-state conditions is approximately 2.6 g day^{-1}.

Daily DCF input was partitioned into topical and oral pathways:

Topical contribution [g day^{-1}]:

$$M_{\text{topical,water}} = N_{\text{top}} \cdot K \cdot f_{\text{DCF}} \cdot (1-L) \cdot (1-D)$$

Oral contribution [g day^{-1}]:

$$M_{\text{oral,water}} = N_{\text{oral}} \cdot M_{\text{oral}} \cdot f_{\text{oral}} \cdot F_{\text{urine}}$$

Total input [g day^{-1}] and resulting quasi–steady-state concentration [ng L^{-1}]:

$$M_{\text{total}} = M_{\text{topical,water}} + M_{\text{oral,water}}, \quad C_{\text{water}} = \frac{M_{\text{total}}}{k_h \cdot V} \cdot 10^6$$

The mass-balance model distinguishes between topical and oral input pathways and assumes quasi-steady-state conditions driven by continuous water renewal in Lake Hévíz. Model parameters were derived from questionnaire data, literature values, and site-specific hydrological and operational data provided by the facility, and are summarized in Table 4.

A three-level scenario analysis (low, medium, high) was applied to account for uncertainties in key behavioural and exposure parameters, including topical application rate, removal during washing and clothing, and urination behaviour.

Table 4
Model parameters, their assumed values, and corresponding sources. Parameters were derived from questionnaire data, literature values, and site-specific hydrological characteristics. For Lake Hévíz, an average of approximately 820 daily visitors was assumed, of which 29.1% (~240 users day^{-1}) reported diclofenac use, evenly distributed between topical and oral pathways (~120 users each). Parameter ranges reflect variability in user behaviour and application characteristics considered in the scenario analysis.

Symbol	Description	Value / Range	Source / justification
N_{top}	Number of topical DCF users	120 persons day^{-1}	questionnaire and facility-provided site-specific operational data
K	Amount of cream applied per person per occasion	2–4 g	based on experimental application dose and clinical usage data; (Bielfeldt et al., 2022; Davies and Anderson, 1997; Drugs.com, 2025)
f_{DCF}	DCF content in cream	0.015 (1.5 %)	mid-range value based on reported formulation concentrations (Davies and Anderson, 1997; Bielfeldt et al., 2022; Drugs.com, 2025)
L	Fraction of cream washed off hands (→WWTP)	0.4–0.6	literature-supported wash-off process + model assumption (Bielfeldt et al., 2022)
D	Fraction of cream removed from body by clothing	0.2–0.6	literature-supported pathway (clothing transfer) + model assumption (Bielfeldt et al., 2022)
N_{oral}	Number of oral DCF users	120 persons day^{-1}	questionnaire and facility-provided site-specific operational data
M_{oral}	Oral DCF dose per person per day	0.05 g person^{-1}	typical therapeutic dose (Drugs.com, 2025)
f_{oral}	Fraction of unchanged DCF excreted in urine	0.02	literature (Davies and Anderson, 1997)
F_{urine}	Fraction of bathers urinating in the lake	0.2–0.6	behavioural assumption
k_{deg}	DCF degradation rate in water (day^{-1})	0–0.1 (neglected)	literature (Poirier-Larabie et al., 2016)
V	Lake water volume	127,950 m^3	facility-provided site-specific operational data
k_h	Water exchange coefficient	0.294 day^{-1}	facility-provided site-specific operational data

The model is based on several simplifying assumptions, including (i) seasonal quasi–steady-state conditions, (ii) negligible degradation relative to hydrological dilution, and (iii) single daily topical application per user. Injection-based diclofenac use was not included due to its negligible occurrence (<1%) in the questionnaire data, and processes such as sorption or transformation of DCF were not explicitly considered, meaning that the model represents a simplified approximation of system behaviour.

Under these assumptions, scenario analysis suggests that topical application may represent an important pathway of DCF input, while oral contribution appears to be smaller. Predicted quasi–steady-state concentrations (16-94 ng L^{-1}) were in good agreement with the measured value (~70 ng L^{-1}), supporting the plausibility of the proposed input pathways and the role of continuous water renewal in limiting PhAC accumulation in the natural lake **(Supplementary Section B, Table S8**).

In artificial, multi-pool spa complexes, mass-balance assessment is more uncertain due to discontinuous water renewal and heterogeneous visitor distribution. Under such conditions, the proposed framework should be regarded as a screening-level rather than predictive tool.

Although CAF was not selected for detailed modelling due to its higher degradability and lower ecotoxicological relevance compared to DCF, a simplified assessment assuming oral intake and urinary excretion alone yielded predicted steady-state concentrations of 22-108 ng L^{-1}, consistent with measured values. This indicates that CAF concentrations in Lake Hévíz can be plausibly explained by visitor-related inputs without invoking additional external sources.

Overall, Lake Hévíz represents a favorable reference system for evaluating bathing-related PhAC inputs due to its continuous water renewal and well-constrained hydrological conditions. The applied mass-balance framework provides a transferable, screening-level approach for assessing spa-related pharmaceutical contributions in other bathing waters, provided that key hydrological and visitor-related parameters are available.

Despite the insights gained, several limitations of this study should be acknowledged. First, WWTP effluents were not directly sampled, which limits the ability to quantitatively distinguish between spa-related and municipal sources. Second, the 2024 and 2025 datasets are based on single sampling campaigns, restricting temporal resolution and limiting the assessment of seasonal variability. Third, multiple contamination sources co-occur within the catchment, including urban wastewater, healthcare facilities, and spa-related inputs, which complicates source attribution. Finally, uncertainties associated with questionnaire-based data and model assumptions should be considered, as these approaches rely on self-reported information and simplified representations of complex environmental processes. Despite these limitations, the multi-evidence approach applied in this study provides consistent and complementary insights into pharmaceutical occurrence and potential source contributions in spa-influenced aquatic systems.

3.4. Supporting physico-chemical parameters

In addition to PhAC concentrations, selected physico-chemical parameters were measured during the 2024 and 2025 sampling campaigns, including temperature, pH, electrical conductivity, total dissolved solids (TDS), and free chlorine (**Supplementary Table S9**). Water temperatures were significantly higher at sampling sites 11* and 12*, located near the most frequently visited bathing facilities, compared to the other sites. At site 12*, electrical conductivity and TDS values were approximately three times higher than elsewhere, indicating a strong influence of mineralized waters and anthropogenic inputs. Free chlorine was detected at all sites except sites 1 and 11*, although concentrations remained low (ppb range; <212 ppb). Elevated free chlorine levels at site 12* suggest the influence of local water treatment practices, such as disinfection or chlorination, in the vicinity of the sampling location.

Overall, these observations indicate that different types of spa facilities, including natural thermal lakes and artificial spa complexes, can measurably modify local water chemistry. Such alterations represent additional, non-pharmaceutical pressures on receiving waters and highlight the need to consider spa-related activities as a multifaceted source of aquatic environmental impact.

4. Conclusion

This study suggests that spa- and medical tourism-related activities may represent a relevant and locally significant contributor to PhACs in surface waters. Among the investigated substances, DCF consistently emerged as the primary driver of ecological risk, showing clear spatial associations with bathing facilities and elevated RQs under both PNEC- and EQS-based assessment frameworks. In contrast, CBZ was predominantly linked to persistent municipal sources, while CAF exhibited episodic and seasonally modulated risk patterns.

Overall, the results are consistent with the hypothesis that spa-related activities may contribute to PhAC inputs in the study area, with DCF showing the strongest and most consistent association with bathing-related indicators. PhAC residues were repeatedly detected in surface waters receiving spa- and wastewater-influenced discharges, indicating that releases from thermal baths, pools, and associated urban infrastructure may affect downstream aquatic ecosystems. The comparison between built, semi-closed spa systems and a natural, continuously renewed thermal lake provided key insights into the role of hydrological conditions. Despite high visitor numbers, the natural lake exhibited substantially lower PhAC concentrations and reduced ecological risk, highlighting the mitigating effect of large volumes and continuous water exchange.

The applied mass-balance approach further suggests that direct bathing-related inputs, particularly topical DCF use, may contribute to PhAC loads in spa environments. Together, these findings underline the need for targeted environmental monitoring in spa-dominated regions, especially at locations receiving concentrated discharges from bathing facilities. Risk assessment and management strategies in such regions should explicitly account for bathing-related pharmaceutical contributions alongside conventional municipal sources.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT (GPT-5) to assist with language editing, text formulation, and the creation of the graphical abstract. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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CRediT authorship contribution statement

Eva Molnar: Writing – original draft, Visualization, Methodology, Investigation, Data curation, Conceptualization. **Zoltán Németh:** Writing – review & editing, Methodology, Investigation, Data curation. **István Fodor:** Writing – original draft, Investigation, Conceptualization. **Réka Svigruha:** Writing – review & editing, Investigation. **Anna Szántó:** Writing – review & editing, Investigation. **Gabriella Laura Tóth:** Writing – review & editing, Investigation, Conceptualization. **Zsolt Pirger:** Writing – review & editing, Funding acquisition, Conceptualization.

Declaration of competing interest

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

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.hazadv.2026.101408.

Data availability

All relevant data is contained in the manuscript and the associated supplementary materials.

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