Occurrence of pharmaceutical residues, personal care products, lifestyle chemicals, illicit drugs and metabolites in wastewater and receiving surface waters of Krakow agglomeration in South Poland

Katarzyna Styszko, Kathryn Proctor, Erika Castrignanò, Barbara Kasprzyk-Hordern

PII: S0048-9697(20)37891-8

DOI: https://doi.org/10.1016/j.scitotenv.2020.144360

Reference: STOTEN 144360

To appear in: *Science of the Total Environment*

Received date: 17 September 2020

Revised date: 12 November 2020

Accepted date: 2 December 2020

Please cite this article as: K. Styszko, K. Proctor, E. Castrignanò, et al., Occurrence of pharmaceutical residues, personal care products, lifestyle chemicals, illicit drugs and metabolites in wastewater and receiving surface waters of Krakow agglomeration in South Poland, *Science of the Total Environment* (2020), https://doi.org/10.1016/j.scitotenv.2020.144360

Occurrence of pharmaceutical residues, personal care products, lifestyle chemicals, illicit drugs and metabolites in wastewater and receiving surface waters of Krakow agglomeration in South Poland

Katarzyna Styszko[1]*, Kathryn Proctor[2], Erika Castrignanò[23], Barbara Kasprzyk-Hordern[2]*

[1] AGH University of Science and Technology, Faculty of Energy and Fuels, Department of Coal Chemistry and Environmental Sciences, al. Mickiewicza 30, 30-059 Kraków

[2] University of Bath, Department of Chemistry, Bath BA2 7AY, United Kingdom

[3] Department of Analytical, Environmental & Forensic Sciences, School of Population Health & Environmental Sciences, King's College London, London SE1 9NH

*corresponding authors: K. Styszko, styszko@agh.edu.pl, B. Kasprzyk-Hordern, bkh20@bath.ac.uk

Occurrence of pharmaceutical residues, personal care products, lifestyle chemicals, illicit drugs and metabolites in wastewater and receiving surface waters of Krakow agglomeration in South Poland

Abstract

This is the first study of broad range of chemical classes CECs conducted in the upper Wisla river catchment including the biggest WWTPs in this region and surface waters. The list of compounds is extensive and the paper provides, for the first time, better understanding of environmental burden from PCPCs in Poland. Cumulative contribution of hypertension pharmaceuticals, nonsteroidal anti-inflammatory drugs (NSAIDs) and lifestyle chemicals was 85% and 95% in wastewater influent, and 75% in wastewater effluent at both WWTPs. Significant removal efficiencies, exceeding 90%, were found for parabens, UV filters, NSAIDs, steroid estrogens, plasticizers, antibacterials/antibiotics, stimulants and metabolites and lifestyle chemicals. The comparison of the average mass loads of CECs between the influent and effluent, has shown that 27% and 29% of all detected CECs were removed by less than 50%. An increase of concentrations of CECs in the effluent was observed for 18% and 20% of all detected CECs in Kujawy and Plaszow WWTPs, respectively. Negative mass balances of fexofenadine, venlafaxine, o-desmethyltramadol, ketamine and temazepam were noted within WWTPs, which are a result of dissolution of persistent contaminants accumulated in aggregates and/or back-transformation or de-conjugation of metabolites into parent compounds. 44 CECs were detected in surface waters located upstream and downstream of the WWTPs. The concentrations of compounds were largely dependent on the dilution factor of WWTP discharge. The risk quotation (RQ) values for compounds present in surface waters were calculated in relation to their potential for bioaccumulation. Among compounds with high potential for bioaccumulation, with log $K_{OW} \geq 4.5$, diclofenac, atorvastatin and triclosan were found to be of high risk. Many CECs with high, moderate or even low environmental impact have shown high potential for bioaccumulation and should be considered as priority at the same risk level. Moreover, possible synergistic action is still of concern.

Keywords: wastewater, removal rates, risk assessment, river, emerging contaminants

Occurrence of pharmaceutical residues, personal care products, lifestyle chemicals, illicit drugs and metabolites in wastewater and receiving surface waters of Krakow agglomeration in South Poland

1. Introduction

The presence of chemicals of emerging concern (CECs) in wastewaters and surface waters is well acknowledged and is known to pose a potential threat to the ecology of receiving environment (Daughton, 2005; Taylor and Senac, 2014; Gavrilescu et al., 2015; Naidu et al., 2016; Gogoi et al., 2018). Pharmaceutically active compounds, including antibiotics, are an important and diverse group of CECs due to their high and increasing use by aging populations around the world, biological activity and potential ecotoxicological effects (Hernando et al., 2006; Verlicchi et al., 2012a; Jiang et al., 2013; Li, 2014; Richardson and Ternes, 2014; de Jesus Gaffney et al., 2015; Sui et al., 2015; Yang et al., 2017).

CECs enter water systems from various sources, such as sewage, industry and agriculture. Previous work indicated that the effluent from wastewater treatment plants (WWTPs) was one of the major pathways for CECs' discharge into the aquatic environment. CECs are usually present at low concentrations in the environment (they range from pg L^{-1} to µg L^{-1}), but their levels can potentially cause undesired physiological effects in wildlife and humans (Hernando et al., 2011; Stuart et al., 2012; Pal et al., 2014; Zenker et al., 2014). This is more concerning considering that they do not appear individually, but as a complex mixture (Vasquez et al., 2014). Pharmaceuticals and other chemical classes of CECs are present in surface water, sea water and even groundwater, though the highest concentrations are found in crude wastewater (Lapworth et al., 2012; Loos et al., 2013; Luo et al., 2014; Geissen et al., 2015).

During wastewater treatment, CECs may be adsorbed on the suspended solids, biodegraded or chemically degraded and subsequently removed from the aquatic phase (Drewes, 2007; Zhang et al., 2008; De Gusseme et al., 2009; Miege et al., 2009; Onesios et al., 2009; Stasinakis, 2012; Samaras et al., 2013; Guerra et al., 2014; Archer et al., 2017). The removal efficiencies of CECs depend on

chemical properties of individual CECs, operational conditions and type of treatment technology used as well as microbial community composition (Petrović et al., 2003; Suárez et al., 2008; Suarez et al., 2010; Verlicchi et al., 2010; Reyes-Contreras et al., 2011; Jelić et al., 2012; Verlicchi et al., 2012b; Arlos et al., 2015; Ahmed et al., 2017; Kołecka et al., 2019). Temperature and season have been shown to have an effect also. This is also true for wastewater flows and population, as the size of the population can affect the flow rate and hydraulic retention time of the wastewater treatment works.

The main aim of the paper is to present an occurrence and fate of broad range of chemical classes (UV filters, parabens, plasticizer, steroid estrogens, antibacterials/antibiotics, hypertension drugs, non-steroidal anti-inflammatory drugs (NSAIDs), lipid regulators, anti-histamines, anti-depressants, analgesics, drug precursors, stimulants, hallucinogens, lifestyle chemicals, anesthetics, benzodiazepines, phosphodiestearase type 5 inhibitors and selected metabolites) in two main Krakow Wastewater Treatment Plants (WWTPs) and in the receiving rivers. CECs were selected based on their specific chemical character, existing evidence of their harm to living organisms or potential toxicity and ubiquitous presence in the environment worldwide. This paper presents, for the first time, the fate of 68 chemicals of emerging concern (CECs) in the influent and effluent of wastewater treatment plants (WWTPs) from Krakow and in the receiving surface waters. This is the first study of broad range of chemical classes CECs conducted in the upper Wisla river catchment including the biggest WWTPs in this region and surface waters. The list of compounds is extensive and the paper provides, for the first time, better understanding of environmental burden from CECs in Poland. It provides significant information to contribute to resolving the knowledge gap for this region and will be essential for the decision makers in considering new priority pollutants for the Water Framework Directive.

2. Materials and methods

2.1 Materials

A total of 68 CECs (pharmaceutical residues, endocrine disruptors, biomarkers, illicit drugs and related metabolites) were selected for analysis and quantification in wastewater and surface water samples collected in Krakow agglomeration in Poland. The molecular formulas, physical and chemical

properties of the compounds are summarized in Table S1. The highest purity (>97%) standards and internal standards were used in stock and working solutions stored at -20 ^{o} C. Organic solvents, methanol, acetonitrile and chemicals were HPLC grade and purchased from Sigma Aldrich, UK. Ultrapure water used in the experiments was obtained from PURELAB UHQ-PS Unit (Elga, UK). The deactivated glassware was used in the analysis to prevent the adsorption of polar compounds to the hydroxyl groups on the glass surface.

2.2 Sampling sites and sample collection

Wastewater and river water, up and downstream of two major WWTPs were collected in February 2017 (Table S2). The study was conducted in a section of the Drwina and Wisla Rivers in Krakow agglomeration (South Poland) affected by the discharge of a WWTP effluent. Water samples were collected at four sites: two sites upstream and two sites downstream of the local WWTPs discharging wastewater effluent to Drwina and Wisla Rivers, respectively (Fig.1). Drwina is a small river (5.5 km) which is a discharge channel for Plaszow WWTP. It connects with the Serafa River, right tributary of the Wisla river. The locations selected on Drwina were approximately 0.5 km upstream and 1.5 km downstream of effluent discharge point for Plaszow WWTP. The distance between the estuary of Serafa and the discharge channel of Kujawy WWTP to the Wisła River is 850 m. The locations of sample collection at the Wisla River were located before (about 3.5 km) and after (1.5 km) discharge of effluent from Kujawy WWTP.

The wastewater samples were collected from two WWTPs – located in Krakow, that is Plaszow WWTP and Kujawy WWTP. Wastewater from Plaszow WWTP in Krakow is of the greatest importance due to the significant emission route of CECs to the environment resulting from the character of the catchment area (population density, standard of living, large number of medical care facilities etc.). This plant is the biggest in the city and the third largest in the country, which treats > 70% of Krakow wastewater originating from >480,000 of inhabitants from the central parts of the city. Plaszow WWTP has average capacity of 165,000 m^3 day^{-1}. Treated wastewater effluent is discharged to Drwina River. Kujawy WWTP is the second plant by size in Krakow and it is located in east part of the city. It treats around 52,000 m^3 of wastewater per day from 250,000 of inhabitants. Wastewater

effluent from Kujawy WWTP is discharged directly to Wisla through a discharge canal. Both WWTPs use traditional processes to treat wastewater, including activated sludge technology. The WWTPs investigated consist of the following stages: screening of solids, preliminary clarification, conventional activated sludge system (nitrification, denitrification), phosphate removal and final clarification. Average hydraulic and solid retention time is on average 24 h and 12 h at both WWTPs, respectively.

The samples from the rivers and WWTPs were taken for four and six consecutive days, respectively. Time-proportional 24 hour-composite (every 15 min) wastewater influent and effluent samples were collected, whereas river waters were taken as grab samples. Activated sludge was collected for two days at both WWTPs as grab samples. All samples of surface water, wastewater and activated sludge were collected in the morning. Upon collection, all samples were cooled in the refrigerator at about 4^0C followed by transport to the laboratory and immediate processing with SPE. Prior to extraction activated sludge samples were centrifuged. The solid phase was then frozen and freeze dried, whilst the liquid phase was extracted according to the procedure described below.

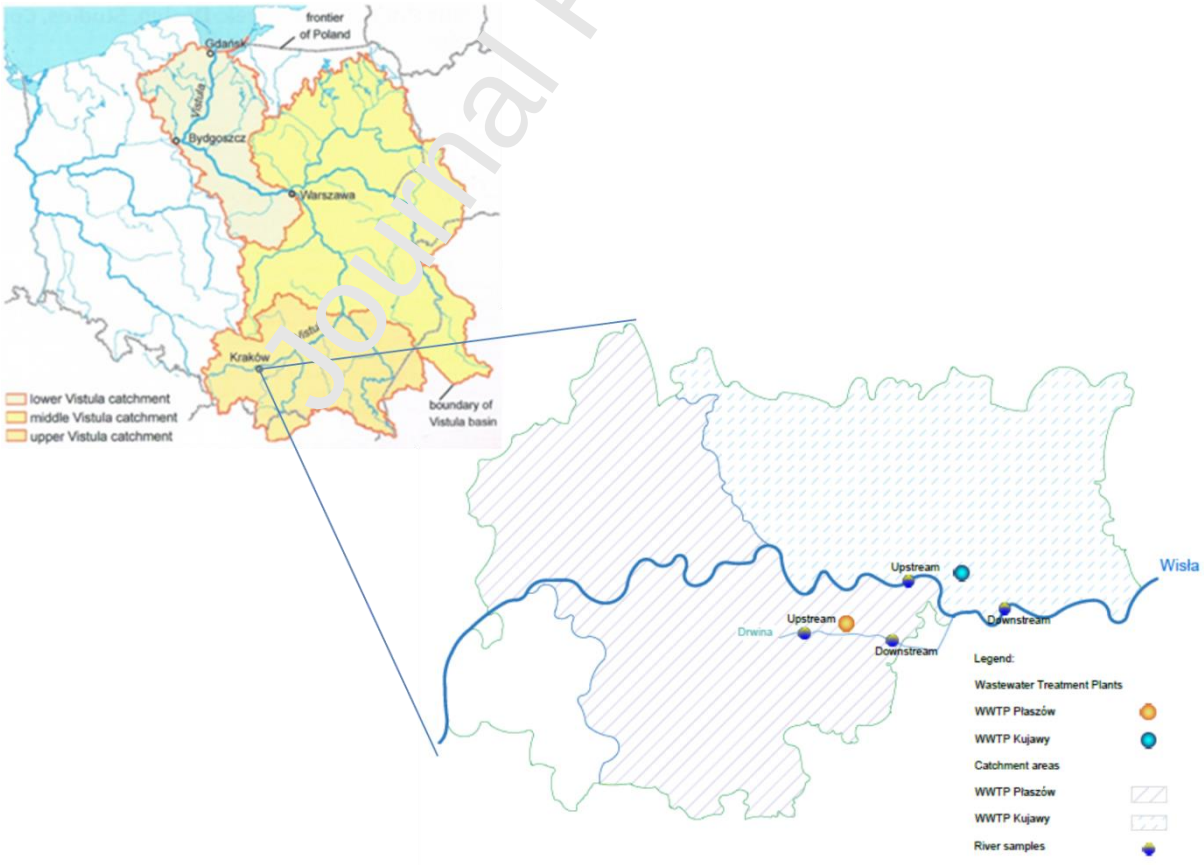


Fig. 1. Sampling sites along the Drwina and Wisla Rivers and locations of wastewater treatment plants in Krakow agglomeration (WWTP Plaszow, WWTP Kujawy, upstream and downstream of the WWTP Plaszow, upstream and downstream of the WWTP Kujawy)

2.3 Solid phase extraction for aqueous phase

Samples were analysed using a method described elsewhere (Petrie et al., 2016). Briefly, solid phase extraction (SPE) was used for the extraction of CECs from the aqueous phase. SPE was performed using a 12-fold vacuum extraction manifold (J.T. Baker, Philipsburg, USA). Extraction volumes were 100 mL for WWTP influent, effluent and surface waters. Each 100 mL sample was spiked with 10 µL (10 µg/mL) of all internal standards. The samples were filtered with 45 mm glass fiber filter, 0.7 µm purchased from Macherey-Nagel. The Oasis HLB 3cc (60 mg/3 mL) SPE cartridges (Waters) were preconditioned sequentially with 2 mL of methanol and 2 mL of deionized water. The samples were passed through the cartridges. The cartridges were then washed with 3 mL of water (except surface water samples), followed by drying. All SPE cartridges were transported on ice within 24h. The analytes were then eluted with 4 mL of methanol. The extracts were evaporated to dryness under the stream of nitrogen using TurboVap evaporator (Caliper, UK 400C, <5psi). Dry residues were finally reconstituted in 500 µL 1mM NH_4OAc and filtered through Teflon syringe 0.2 µm filters. The supernatants were successively transferred into 2 mL autosampler vials for analysis by UPLC-MS/MS.

2.4 Microwave assisted extraction for solid phase

Dried activated sludge samples were transported to the University of Bath on ice within 24h. Details of the microwave assisted extraction (MAE) procedure are described elsewhere (Petrie et al., 2016). Briefly, 500 mg of homogenized freeze-dried activated sludge spiked with 50 ng of internal standards was mixed with 25 ml of methanol:water (50:50 and pH=2) and extracted at 110 ^{o}C for 40 min using a 800 W MARS 6 microwave (CEM, UK). Afterwards, samples were filtered (0.7 µm) and diluted by water (pH=2) to <5% of methanol and extracted using Oasis MCX cartridges. Extracts were dried, reconstituted in mobile phase (80:20 water:methanol) and analysed by UPLC-MS/MS.

2.5 LC-MS/MS analysis

Analyses were carried out at the University of Bath with the usage of Waters Acquity UPLC system (Waters) coupled to a Xevo TQD Triple Quadrupole Mass Spectrometer (Waters, Manchester, UK), equipped with an electrospray ionisation source and a fully validated method by Petrie et al. (Petrie et al., 2016).

The determination of acidic compounds as NSAIDs, antihistamines, lipid regulator, hypertension, antibiotic, antibacterial, steroid estrogens, UV filters, parabens and plasticizer was performed in negative ionization mode with a capillary voltage of 3.20 kV. The basic compounds were analysed in positive mode with capillary voltage of 3.00 kV. The source temperature was 150^{o}C and the desolvation temperature was 400^{o}C, for both methods. The cone gas flow was 100 L h^{-1} and the desolvation gas flow was 550 L h^{-1}. Nitrogen was used as the nebulising and desolvation gas, and argon as the collision gas.

The separation of acidic analytes was performed on a reversed-phase BEH C18 column (150 × 1.0mm, 1.7 µm particle size) (Waters, Manchester, UK) with a 0.2 µm, 2.1 mm in-line column filter maintained at 25 ^{o}C. The mobile phase flow rate was 0.04 mL min^{-1} and an injection volume of 15 µL was used. The mobile phases were composed of a mixture of 80:20 water: methanol containing 1mM NH_4F (A) and 5:95 water: methanol with 1mM NH_4F (B). The basic analytes were separated on the CHIRALPAK CBH HPLC column with 1 mM ammonium acetate/methanol 85:15 (v/v) as mobile phase at 0.1 mL min^{-1} under isocratic conditions (Castrignanò et al., 2016). The injection volume was 20 µL.

The concentrations of target compounds were calculated by using the peak area ratios of the main product ion (quantifier) of the analytes and their assigned surrogate/internal standards to the corresponding ratios in the standard solutions and corrected by recovery percentages. Method validation parameters for water and wastewater samples for tested compounds are presented in Table S3 in the supplementary material. Calibration curves were obtained from standards spiked in mobile phase at concentrations from 0.01 to 1000 ng mL^{-1}.

2.6 Calculations

The cumulative mass loads (g/day) of the target analytes in the effluents of the WWTP Plaszow and WWTP Kujawy during the sampling period were determined using the following equation:

$$L = \frac{C \times Q}{1000000}$$

where C refers to the concentration (in ng L^{-1}) of the analytes detected at the effluent wastewater samples, Q refers to the mean flow rate of the plant ($m^3 day^{-1}$) during each sampling day (found in Table S2). 1000000 is the conversion factor.

Removal efficiencies for each WWTP were calculated by comparison of the load of each compound found in the influent and in the effluent wastewater using the following formula:

$$\%Removal\ Efficiency = \frac{100 \times \left(L_{influent} - L_{effluent}\right)}{L_{influent}}$$

Removal efficiencies obtained are a combination of degradation, transformations and/or formation of products. Negative removal rates can occur due to desorption of the compounds from the solid phase and/or conversion of conjugated metabolites back to the parent compound (Verlicchi et al., 2012b).

The environmental risk assessment (ERA) of detected CECs was estimated for wastewater effluent and upstream and downstream of WWTPs discharge points. The estimation of risk quotation (RQ) was obtained using ratio of the measured environmental concentrations (MEC) of the detected CECs to the predicted no effect concentrations (PNEC):

$$RQ = \frac{MEC}{PNEC}$$

The evaluation was based on the guidelines from the European Medicine Agency (EMA), (European Medicines Agency, 2018), taking into account the lowest PNEC for CECs obtained in tests of cyanobacteria, invertebrates, algae and fish, available in the literature (Carlsson et al., 2006; Bergmann et al., 2011; Archer et al., 2017; Han and Lee, 2017; Zhou et al., 2019). In the first step of environmental risk assessment of medicinal products for human use, according to the EMA Guideline, drugs mobility between aquatic environment and solid phase (bioaccumulation) is evaluated. This

potential to bioaccumulation is based on the value of octanol/water partition coefficient (Log K_{OW}> 4.5). For the ionisable organic compounds log D_{OW} should be considered at pH covering an environmentally relevant pH-range (values ranging from pH 5 to 9). For neutral substance $D_{OW} = K_{OW}$. Besides, the predicted or measured concentration of target compound in the environment should be considered. If the concentration is equal or over 10 ng L^{-1}, next step of the evaluation including environmental fate and impact of drug is needed (Bouissou-Schurtz et al., 2014). In the second step impact and fate of drug in the environment is assessed. In this step risk quotation and other relevant factors like physicochemical properties, toxicology, potential to bioaccumulation (Log K_{OW}>3), degradability are considered. The environmental risk is classified as follows: RQ < 0.01 is insignificant, < 0.1 low risk, 0.1≤ RQ ≥ 1 medium risk and RQ > 1 high risk (Hernando et al., 2006; Chen and Ying, 2015).

3. Results and discussion

3.1 PPCPs and lifestyle chemicals in wastewater

A total of 68 CECs were detected in wastewater influent, and 66 CECs in effluent samples, which represents 18 classes of PPCPs, lifestyle chemicals, illicit drugs and related metabolites (Fig. 2, Table S4 and S5). Corresponding mass loads for the detected compounds and contributions of different chemical classes in loads of influent and effluent are shown in Fig. 3 and 4. Average concentrations of compounds were from a few ng L^{-1} to over 200 µg L^{-1}. The highest concentrations of CECs from three classes - lifestyle chemicals, NSAIDs and hypertension were detected in the influents of both WWTPs (see Fig. 4). Their total-grouped concentrations in the influents of Plaszow WWTP ranged from 179.6 to 300.2 µg L^{-1} of lifestyle chemicals, 42.8 to 235.8 µg $L^{-1}$of NSAIDs and 16.3 to 92.3 µg L^{-1} of hypertension. The total-grouped concentrations of these classes in the influent of Kujawy WWTP ranged from 234.9 to 663.6 µg L^{-1} of lifestyle chemicals, 33.0 to 151.8 µg $L^{-1}$of NSAIDs and 9.1 to 92.7 µg $L^{-1}$of hypertension pharmaceuticals.

Among lifestyle chemicals, caffeine and its main metabolite 1,7-dimethylxantine showed the highest concentrations, with the average values 61.1 ± 19.2 µg $L^{-1}$and 132.7 ± 21.5 µg L^{-1} in the influent of Plaszow WWTP and 60.3± 21.0 µg L^{-1} and 115.2 ± 22.2 µg L^{-1} in the influent of Kujawy WWTP.

These levels are in good agreement with the results by others (Baker and Kasprzyk-Hordern, 2013; Luo et al., 2014; Archer et al., 2017). Moreover, the Kujawy WWTP showed extremely high concentrations of nicotine in daily composite influent samples, ranging from 107 to 424 μg L^{-1} (average 224.9 ± 118.2 μg L^{-1}). Such high concentrations could be explained by the presence of a tobacco company located in the WWTP catchment. This is confirmed by much lower concentration of nicotine in Plaszow WWTP accounting for 25.0 ± 5.8 μg L^{-1} and similar concentrations of cotinine (metabolite of nicotine) at both WWTPs. Concentrations of cotinine were 1.0 ± 0.15 μg $L^{-1}$and 1.4 ± 0.29 μg L^{-1} in Plaszow and Kujawy WWTPs, which is comparable to concentrations reported by others: 4.9 – 11.9 μg L^{-1} and 3.3 – 4.9 μg L^{-1} (Archer et al., 2017), 0.2 – 89.6 μg L^{-1} and 0.5 – 27.7 μg L^{-1} (Ekpeghere et al., 2018), 0.08 – 9.1 μg L^{-1} and 0.04 – 0.06 μg L^{-1} (Baker and Kasprzyk-Hordern, 2013), 1.2 – 104 μg L^{-1} and 1.2 – 42.3 μg L^{-1} (Huerta-Fontela et al., 2008), 4.8 – 8.5 μg L^{-1} and 1.8 – 2.4 μg L^{-1} (Castrignanò et al., 2016) for nicotine and cotinine respectively.

Among NSAIDs, the highest concentrations in raw sewage were related to naproxen (average 94.2 ± 63.4 μg L^{-1} and 48.4 ± 26.5 μg L^{-1}), following diclofenac (average 13.3 ± 9.4 μg L^{-1} and 16.9 ± 13.4 μg L^{-1}) in both Plaszow and Kujawy WWTPs, respectively. The average concentrations of ketoprofen and ibuprofen were 10.7 ± 7.3 μg L^{-1} and 8.1 ± 0.8 μg L^{-1} and 5.2 ± 3.2 μg L^{-1} and 9.5 ± 1.5 μg L^{-1}, in Plaszow and Kujawy WWTPs, respectively. These levels are in agreement with the range of concentrations reported by others (Verlicchi et al., 2012b; Luo et al., 2014). However, the concentration levels of anti-inflammatory drugs determined in this study are higher than those reported in the UK (Kasprzyk-Hordern et al., 2009b). Indeed, the level of pharmaceuticals' consumption in Poland is one of the highest in Europe (Sagan et al., 2011). Additionally, an increasing trend is observed in annual usage of over-the-counter (OTC) pharmaceuticals, especially antitussive, analgesics and anti-inflammatory drugs. The OECD health expenditure statistics show that Polish households spent almost 4 times more in 2020 when compared to 2015 on OTC medicines than on prescribed medicines, and that expenditure on OTC medicines has been growing more rapidly than in other European countries (Sowada et al., 2019).

The high contribution of the hypertension pharmaceuticals was connected with valsartan, with average concentrations at 50.9 ± 31.9 μg L^{-1} and 36.5 ± 29.5 μg L^{-1}, in the influents of Plaszow and Kujawy

WWTPs. The average levels of irbesartan were 1.6 ± 1.1 µg L^{-1} and 0.04 ± 0.05 µg L^{-1}. The high concentration of valsartan and its frequent detection in wastewater and environmental samples has been widely reported (Kasprzyk-Hordern et al., 2009b; Nödler et al., 2016; Archer et al., 2017; Čelić et al., 2019; Papageorgiou et al., 2019)

Considering other chemical classes, concentrations ranging from >1 µg L^{-1} up to 16 µg L^{-1} were observed for parabens, except butylparaben, only for 4-benzophenone, triclosan and bisphenol A. In the review by Verlicchi (Verlicchi et al., 2012b), the reported range of variability for triclosan was 0.22 – 7 µg L^{-1}, which is in line with the results of this research. The concentrations obtained for parabens, UV filters in this study are in agreement with the results reported by (Kasprzyk-Hordern et al., 2009b). Whereas, concentrations of triclosan and bisphenol A were lower in the work of (Kasprzyk-Hordern et al., 2009b).

The antibiotic, sulfasalazine, was determined at the average concentrations of 957 ± 825 ng L^{-1} and 359 ± 315 ng L^{-1}. These results are in agreement with the literature data (Kasprzyk-Hordern et al., 2009b; Verlicchi et al., 2012b; Archer et al., 2017; Szymańska et al., 2019). The values of concentrations observed in this study were higher than the results reported for Slovakia WWTPs (Birošová et al., 2014). Mean concentrations of fexofenadine were 891 ± 677 ng L^{-1} and 400 ± 392 ng L^{-1}. Similar concentrations for fexofenadine were observed by Archer et al. (Archer et al., 2017). The concentrations of fexofenadine recorded in Finland were on average 100 ng L^{-1} (Kosonen and Kronberg, 2009).

Among analgesics and their metabolites, O-desmethyltramadol was dominant, at the average concentrations of 238 ± 34 ng L^{-1} and 357 ± 70 ng L^{-1}. The mean concentrations of O-desmethyltramadol in influent samples in Germany were 331 and 345 ng L^{-1} (Rúa-Gómez and Püttmann, 2012b). The concentrations observed in South Africa ranged from 214 to 1283 ng L^{-1}(Archer et al., 2017).

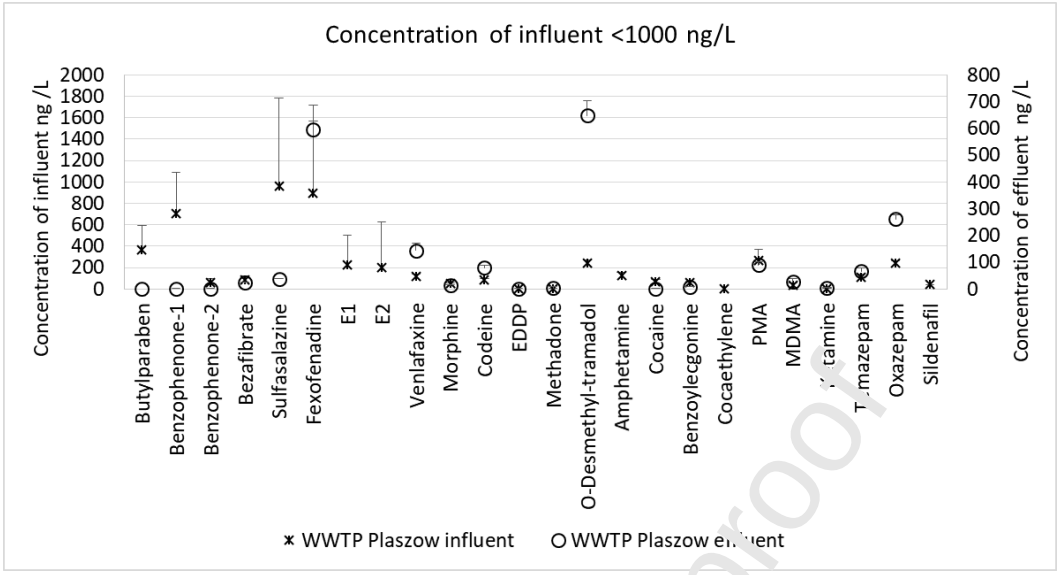
Relatively high concentrations were observed for benzodiazepines, oxazepam and temazepam, at the mean concentrations of 245 ± 14 ng L^{-1} and 111 ± 24 ng L^{-1} in the influents of Plaszow WWTP, 225 ± 7 ng L^{-1} and 102 ± 39 ng L^{-1} in Kujawy WWTP. In comparison to other authors, the mean concentrations determined in this study were higher than those reported by Baker et al.(Baker and

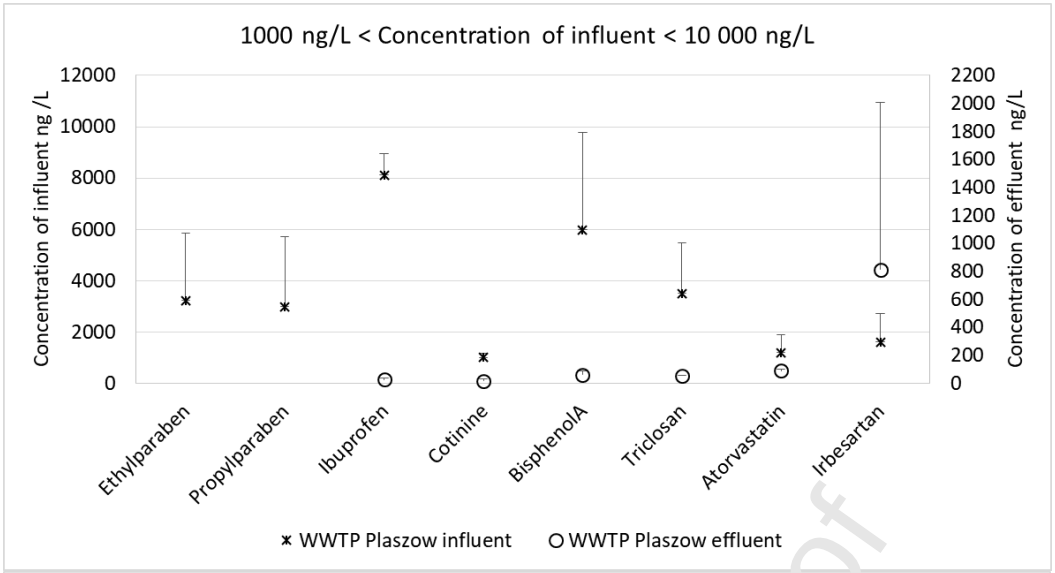
Kasprzyk-Hordern, 2013) and denoted 6.2 – 155.1 ng L^{-1} for oxazepam and 16.8 – 254.7 ng L^{-1} for temazepam.

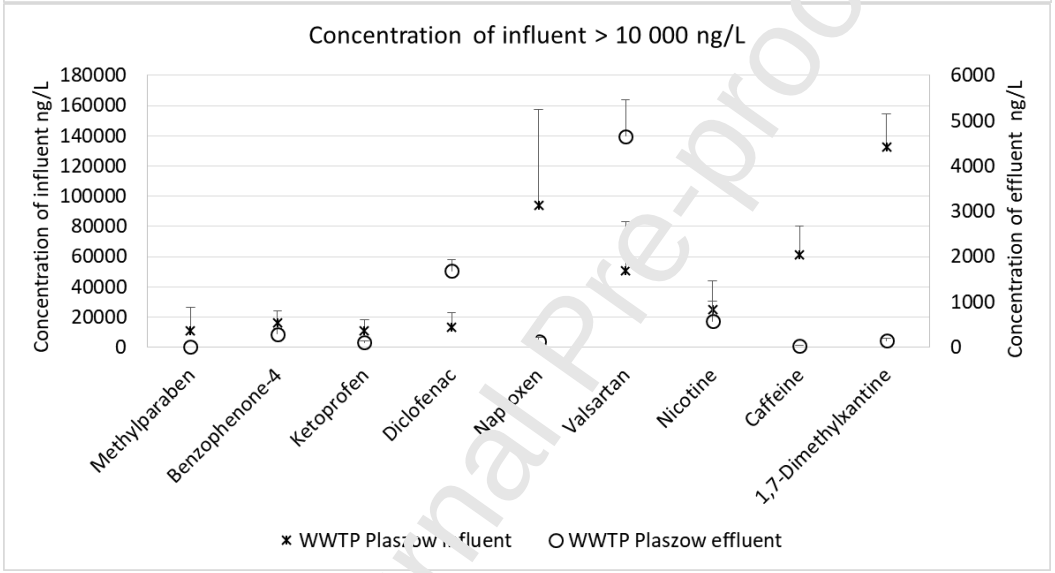
The average concentrations of cocaine and its main metabolite benzoylecgonine were 70 ± 16 ng L^{-1} and 58 ± 17 ng L^{-1} in the influents of Plaszow WWTP, 84 ± 53 ng L^{-1} and 70 ± 12 ng L^{-1} in Kujawy WWTP. These levels are lower than those observed in other works (Postigo et al., 2010; Baker and Kasprzyk-Hordern, 2013; Castrignanò et al., 2016; Archer et al., 2017).

Amphetamine-like stimulants were present in influents of Plaszow and Kujawy WWTPs at mean concentrations 125 ± 28 ng L^{-1} and 209 ± 38 ng L^{-1} for amphetamine, 39 ± 18 ng L^{-1} and 38 ± 26 ng L^{-1} for MDMA and 263 ± 109 ng L^{-1} and 287 ± 82 ng L^{-1} for PMA, respectively. The levels of concentrations of above illicit drugs (except PMA) are lower than those reported by other authors (Castiglioni et al., 2006; Baker and Kasprzyk-Hordern, 2013; Andres-Costa et al., 2014; Castrignanò et al., 2016; Archer et al., 2017; Castrignanò et al., 2018). Even though PMA is a minor metabolite of PMMA, as reported by Lin et al. (Lin et al., 2007), most PMMA is excreted unchanged in the urine. PMMA was not detected in the tested WWTPs. The toxicity of PMMA and PMA, was reported to be substantially higher than with ecstasy and amphetamines, as documented by more than 90 fatal and many severe poisonings attributed to the ingestion of PMMA/PMA in Canada, USA, Australia and Europe (Vevelstad et al., 2012; Jang et al., 2016).

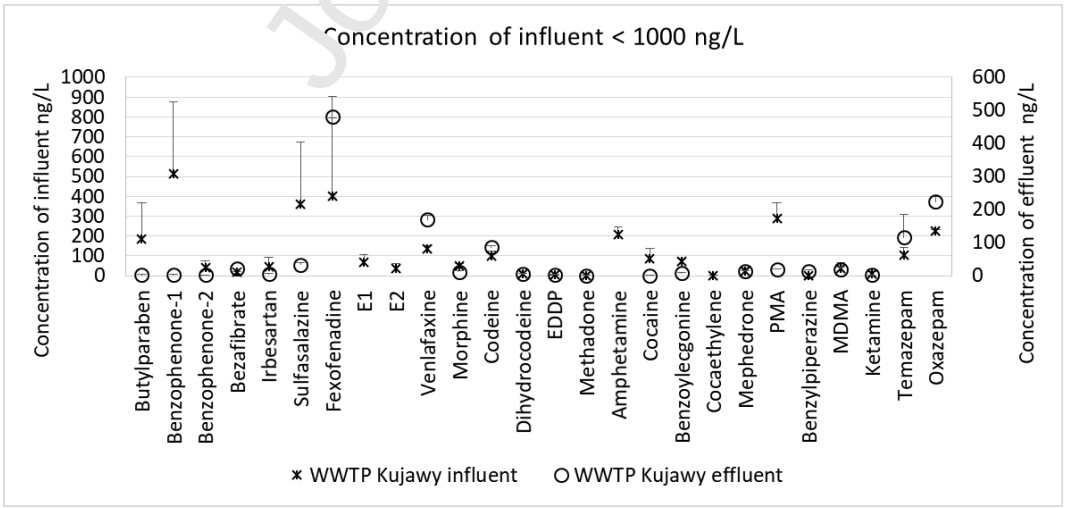
Plaszow WWTP







Kujawy WWTP



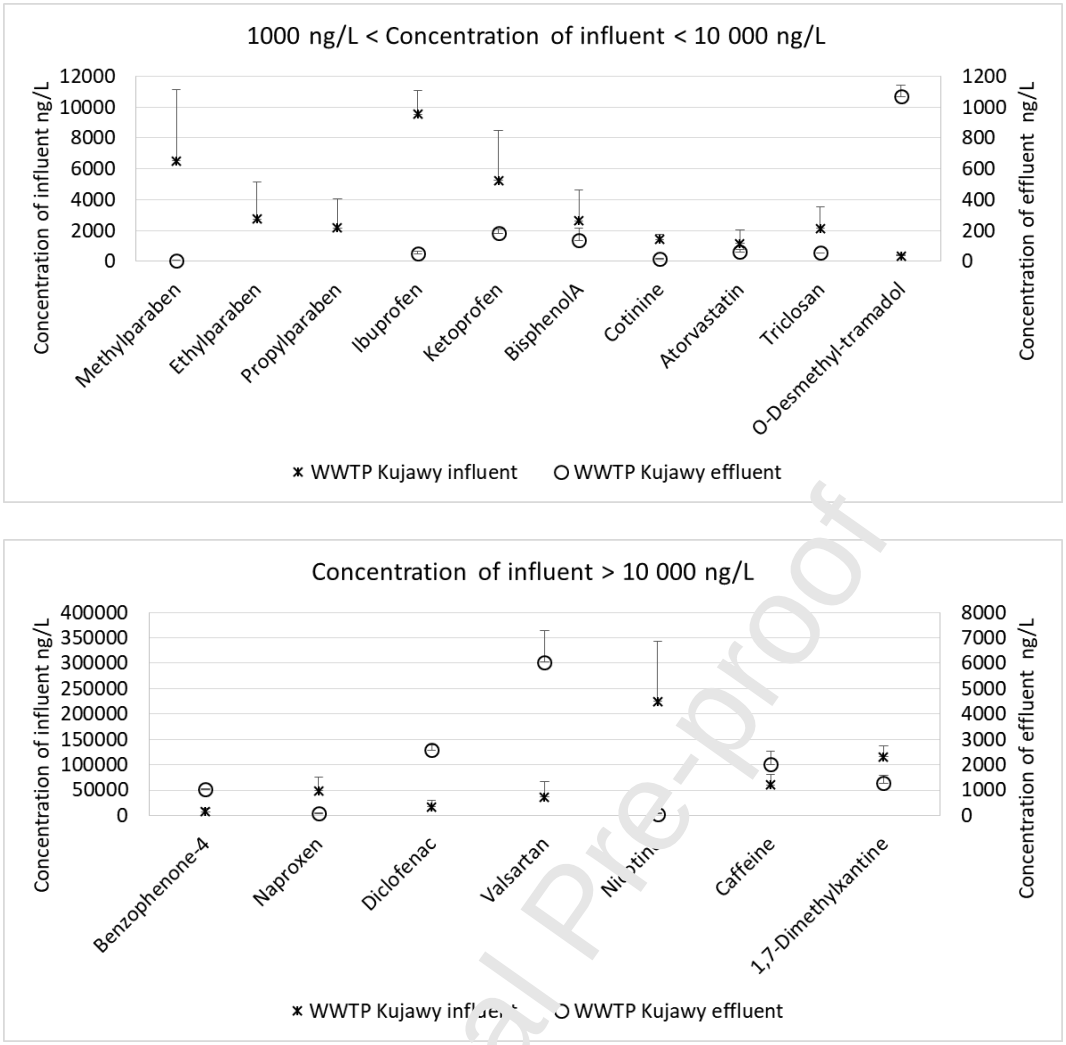


Fig. 2. Average concentration of CECs in the influent and effluent samples collected from WWTPs. Average values for 6 days. Standard deviations indicate variation between sampling days.

Variations of loads of target analytes in the influents and effluents are presented in Fig. 3 and Table S6.The total loads found in the survey denoted 57493 ± 22219g day^{-1} and 1361 ± 172 g day^{-1} and 28402 ± 4957 g day^{-1} and 712 ± 233g day^{-1} for influents to effluents in the Plaszow and Kujawy WWTPs, respectively.

The average contribution of the classes of CECs to the total loads of target compounds, calculated for influents of Plaszow WWTP ranged from <0.01% (average 0.3 ± 0.09 g day^{-1}) for anesthetic (ketamine), 0.01% (average 5.0 ± 2.3 g day^{-1}) for hallucinogen (MDMA), 11% for hypertension (average 6752 ± 4187 g day^{-1}), 26% NSAIDs (average 16319 ± 10766 g day^{-1}) to 53% lifestyle chemicals and metabolites (average 28066 ± 5297 g day^{-1}) (see Fig. 4 and Table S7).

Chemical contribution in the influents of Kujawy WWTP has the same pattern but values for three main groups varied significantly, 7% for hypertension (average 1986 ± 1860 g day^{-1}), 15% for NSAIDs (average 4255 ± 2732 g day^{-1}) and 73% for lifestyle chemicals and metabolites (average 20658 ± 6097 g day^{-1}), which is connected with high concentrations of nicotine (average 11488 ± 5851 g day^{-1}).

Cumulative contribution of these groups was 89% (average 51138 ± 18911 g day^{-1}) and 95% (average 26901 ± 4701 g day^{-1}) in the influents, while in the effluents it was about 75% (average 1039 ± 168 g day^{-1} and 545 ± 203 g day^{-1}) at both Plaszow and Kujawy WWTPs.

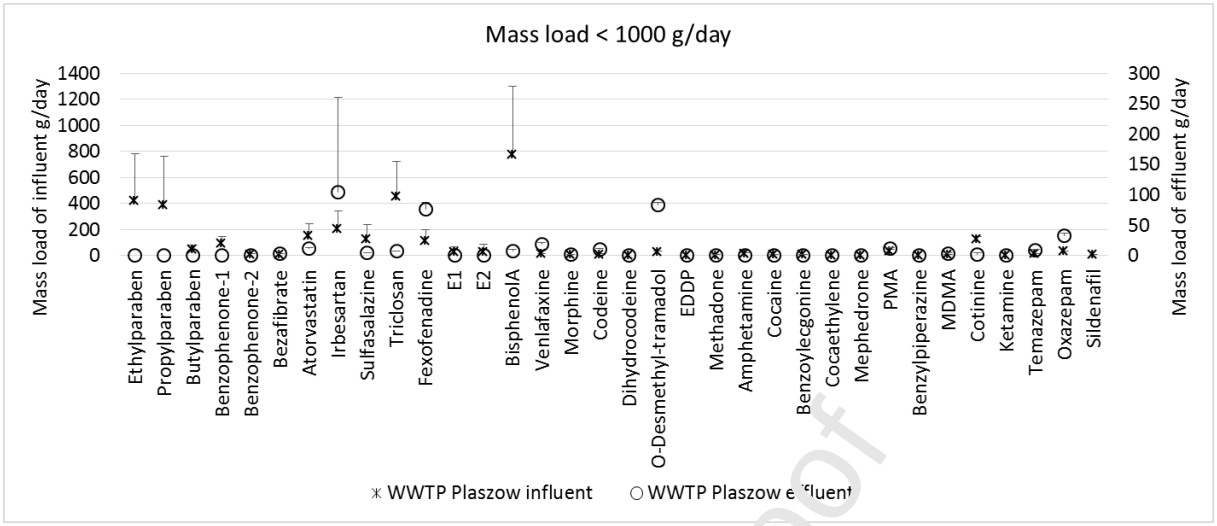
Poor removal of some compounds or even increasing concentrations in the effluents (see Paragraph 3.2) influenced the profile contribution of chemical classes in the effluents (Fig. 4).

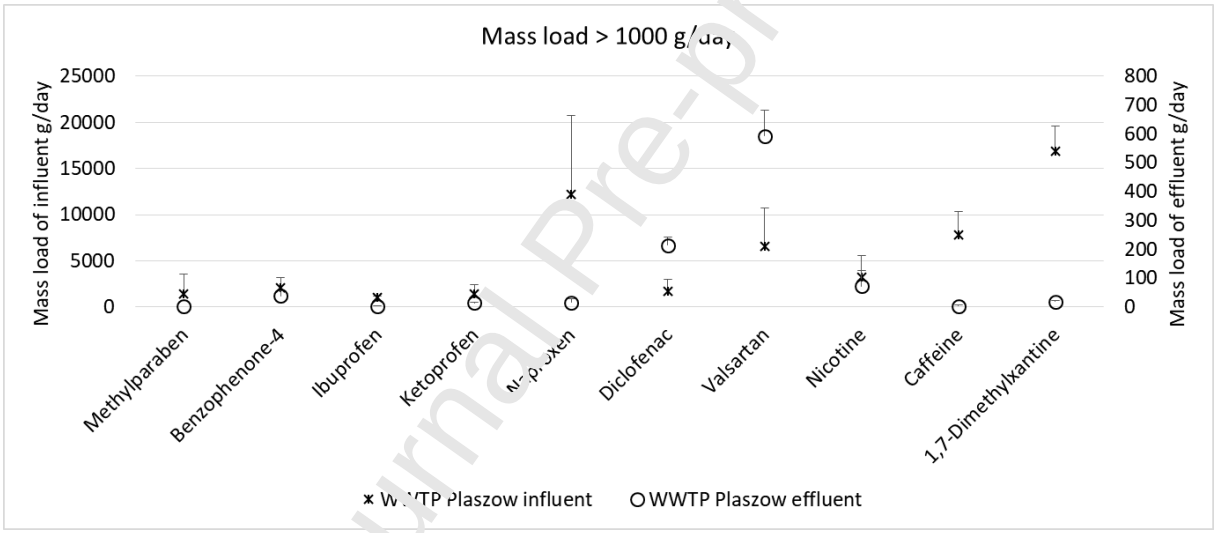
The key CEC contribution in the effluents was related to hypertension with contribution of 51% (average 696 ± 128 g day^{-1}) and 31% (average 252 ± 137 g day^{-1}) at Plaszow and Kujawy WWTPs. Valsartan with average loads of 592 ± 89 g day^{-1} and 203 ± 65 g day^{-1} was the main contributor to hypertension pharmaceuticals in Plaszow and Kujawy WWTPs, respectively.

The contribution of NSAIDs and lifestyle chemicals and metabolites decreased to 18% (average 247 ± 33 g day^{-1}) and 7% (average 96 ± 113 g day^{-1}) in the effluents of Plaszow WWTP. The contribution of lifestyle chemicals also decreased to 28% (average 172 ± 36 g day^{-1}) in Kujawy WWTP, while the contribution of NSAIDs was 15% (average 120 ± 60 g day^{-1}). The highest loads in the group of NSAIDs were noted for diclofenac (average 214 ± 28 g day^{-1} and 129 ± 12 g day^{-1}).

It is noteworthy that nicotine (average 72 ± 107 g day^{-1}) and 1,7-dimethylxantine (average 18 ± 6 g day^{-1}) accounted for the main part of lifestyle chemicals in effluent of Plaszow WWTP. While caffeine (average 103 ± 23 g day^{-1}) and its metabolite 1,7-dimethylxantine (average 65 ± 14 g day^{-1}) were the most prevalent in the effluent of Kujawy WWTP.

Plaszow WWTP





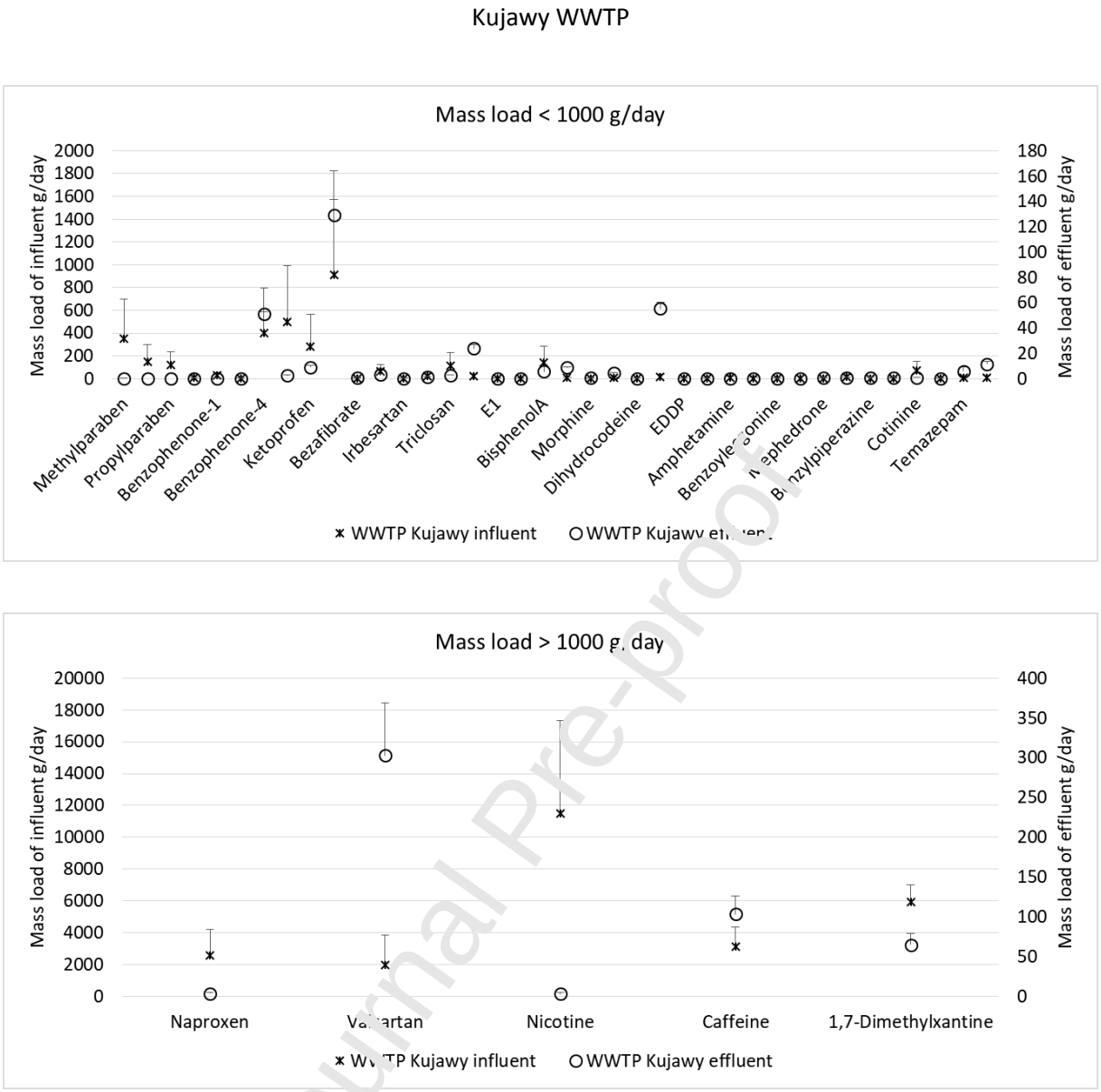
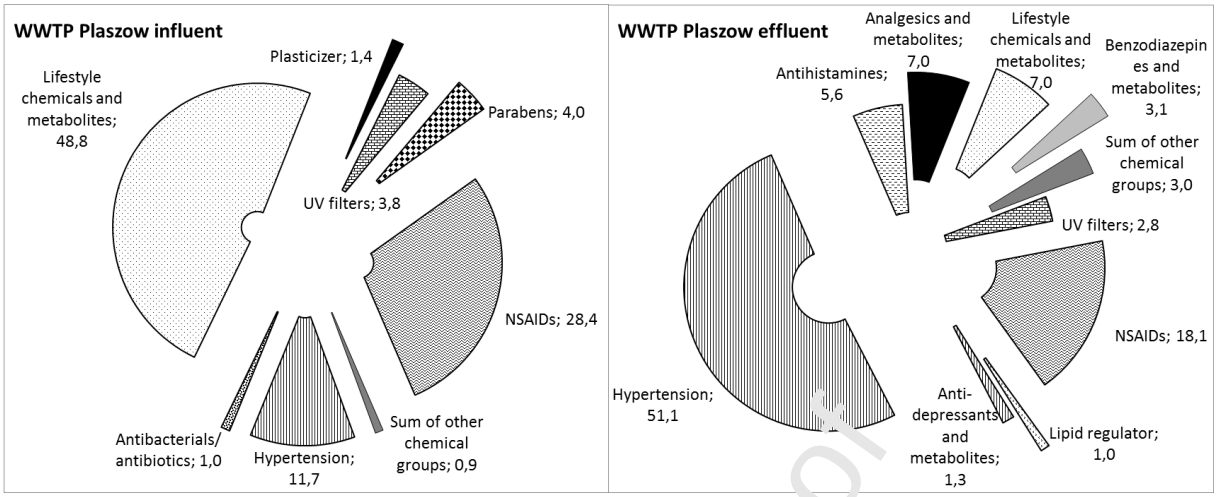


Fig. 3. Average mass loads (g day^{-1}) of detected compounds in influents and effluents of Plaszow and Kujawy WWTPs. Average values for 6 days. Standard deviations indicate variation between sampling days.

Plaszow WWTP



Kujawy WWTP

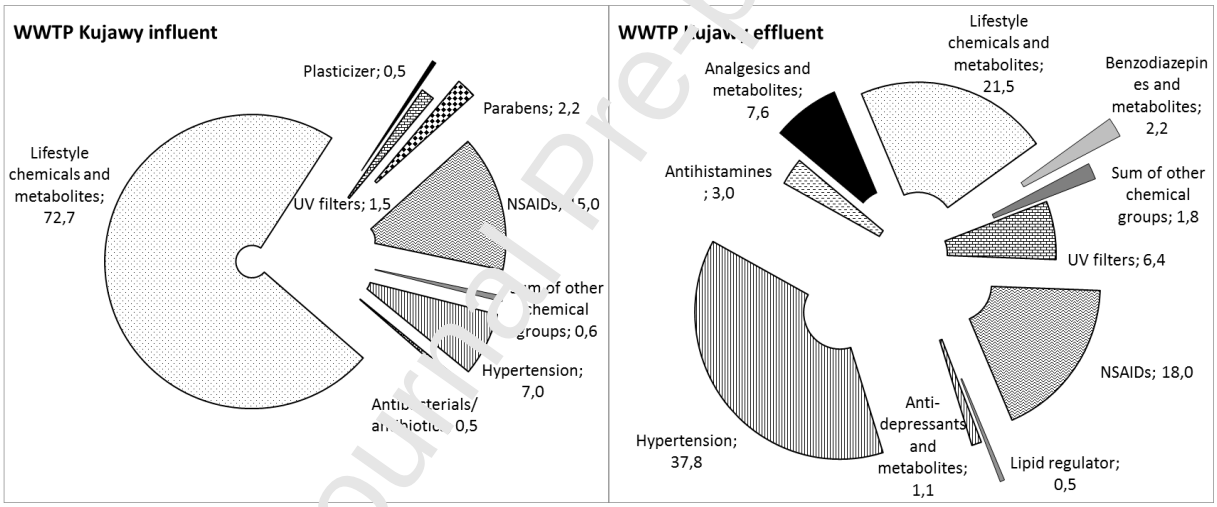


Fig. 4. Contribution of chemical classes in loads expressed in weight %. (**Parabens** – methylparaben, ethylparaben, propylparaben, butylparaben; **UV filters** – benzophenone-1, benzophenone-2, benzophenone-4, **NSAIDs** – ibuprofen, ketoprofen, naproxen, diclofenac; **Lipid regulator** – bezafibrate, atorvastatin; **Hypertension** – irbesartan, valsartan; **Antibacterials/antibiotics** – sulfasalazine, triclosan; **Antihistamines** – fexofenadine; **Steroid estrogens** – E1, E2; **Plasticizer** – bisphenol A; **Anti-depressants and metabolites** – venlafaxine; **Analgesics and metabolites** – morphine, codeine, dihydrocodeine, O-desmethyl-tramadol, EDDP, methadone; **Stimulants and metabolites** – amphetamine, cocaine, benzoylecgonine, cocaethylene, mephedrone. PMA, benzylpiperazine; **Hallucinogens and metabolites** – MDMA; **Lifestyle chemicals and metabolites** –

nicotine, caffeine, cotinine, 1,7-dimethylxantine; **Anesthetic and metabolites** – ketamine; **Benzodiazepines and metabolites** – temazepam, oxazepam; **Phosphodiestearase Type 5 Inhibitor** – sildenafil).

Significant increase in percentage contribution was observed for analgesics and their metabolites, from 0.10% (average 49 ± 5.6 g day^{-1} and 27 ± 4.8 g day^{-1}) to near 10% (average 95 ± 4.5 g day^{-1} and 61 ± 4.9 g day^{-1}). In this group, the highest load was noted for O-desmethyltramadol, (average 82 ± 4.7 g day^{-1} and 55 g ± 4.8 day^{-1}).

The loads of benzodiazepines (average 45.7 ±3.4g day^{-1} and 16.9 ± 2.0 g day^{-1}) and antihistamines (average 114 ± 87 g day^{-1} and 20.4 ± 19.7 g day^{-1}) accounted for 0.0[illegible]% and 0.06%, 0.19% and 0.07% in the influents of Plaszow and Kujawy WWTPs, respectively. Their contributions in the effluents of Plaszow and Kujawy WWTPs were 3.0% (average 41.7 ± 4.3 g day^{-1}) and 2.4% (average 17.7 ± 4.1 g day^{-1}) for benzodiazepines and 5.6% (average 75.8 ± 11 g, day^{-1}), 2.5% (average 20 ± 10 g day^{-1}) for antihistamines. In the case of benzodiazapines, the highest load was observed for oxazepam (average 33 ± 3.1g day^{-1} and 12 ± 1.9 g day^{-1}).

A few percent share of UV filters in the mass load of effluents of Plaszow and Kujawy WWTPs related to benzophenone-4 (average 38 ± 17 g day^{-1} and 51 ± 1.6 g day^{-1}).

In summary, the highest contributions in the discharged effluents were registered for hypertension, NSAIDs, lifestyle chemicals, followed by analgesics, benzodiazepines, antihistamines and UV filters.

3.2 Removal of CECs and lifestyle chemicals during wastewater treatment

Removal efficiencies of the detected compounds varied significantly in the WWTPs sampled in the current study (see Fig. 5 and Table S8). High removal efficiencies, over 90% were found for parabens, UV filters, NSAIDs (ibuprofen, ketoprofen, naproxen), steroid estrogens, plasticizers, antibacterials/antibiotics, stimulants and metabolites (amphetamine, cocaine and cocaethylene) and lifestyle chemicals. The comparison of the average mass loads of CECs between the influent and effluent, has shown that 27% and 29% of all detected CECs were removed by less than 50%, in Kujawy WWTP and Plaszow WWTP, respectively. An increase of concentrations of CECs in the effluent was observed for 18% and 20% of all detected CECs in Kujawy and Plaszow WWTPs, respectively.

Both WWTPs were found to remove personal care products like parabens, UV filters except 4-benzophenone in Kujawy WWTP, antibacterial (triclosan) and plasticizer (bisphenolA) with a very high efficiency exceeding 95%. High removal efficiencies for these compounds,, except benzophenone-4 were reported elsewhere (Kasprzyk-Hordern et al., 2009b; Molins-Delgado et al., 2016; Kapelewska et al., 2018; Mao et al., 2020).

NSAIDs are the most frequently studied CEC group in the environment. Ibuprofen was reported in published literature to be almost completely removed from wastewater in conventional WWTPs. This is in contrast to diclofenac, which removal was only moderate (Clara et al., 2005; Nakada et al., 2006; Kasprzyk-Hordern et al., 2009b; Luo et al., 2014; Afonso-Olivares et al., 2017). The same efficiency of removal was also observed in this study (>99% for ibuprofen and average 69% and 78% for diclofenac). High removal efficiencies noted for ketoprofen (over 95%) and naproxen (over 99%) in this study, are also in agreement with published results (Lindqvist et al., 2005; Kasprzyk-Hordern et al., 2009b; Luo et al., 2014; Afonso-Olivares et al., 2017).

The natural steroid estrogens, 17b-estradiol (E2) and estrone (E1), and synthetic17a-ethinylestradiol (EE2) have been found to be the most potent estrogenic substances in the effluents (Desbrow et al., 1998; Xu et al., 2012). Estrogens were effectively removed in both WWTPs. which is consistent with previous reports (Gabet-Giraud et al., 2010; Verlicchi et al., 2012b; Verlicchi et al., 2013; Ogunlaja and Parker, 2015). According to Suarez et al. (Suarez et al., 2010) natural estrogens (E1 and E2) belong to highly biodegradable compounds under aerobic and anoxic conditions.

Plaszow WWTP gave removal efficiency of sulfasalazine in the range 91-98% while in Kujawy WWTP removal ranged from 73 to 93%. In contrast to this studies low removal efficiency was reported in other works: -79% by Kasprzyk-Hordern et al. (Kasprzyk-Hordern et al., 2009b) and -50% by Verlicchi et al. (Verlicchi et al., 2012b). Weak removal of sulfasalazine was also observed by Suarez et al. (Suarez et al., 2010) and Birošová et al. (Birošová et al., 2014).

The high removal efficiencies of amphetamine (100 %), cocaine (over 97%) and its metabolite benzoylecgonine (87% and 91%), observed in this study were also reported elsewhere (Castiglioni et al., 2006; Kasprzyk-Hordern et al., 2009b; Baker and Kasprzyk-Hordern, 2013; Evgenidou et al.,

2015). The concentrations of MDMA in the effluents of Plaszow WWTP are consistent with the results obtained for this WWTP reported in other work (Styszko et al., 2016).

Bezafibrate has only modest to good removal efficiency at Plaszow with 75% removal but at Kujawy it has -3% removal. Similar results are reported elsewhere(Lindqvist et al., 2005; Kasprzyk-Hordern et al., 2009b; Verlicchi et al., 2012b; Verlicchi et al., 2013).

The removal rates of hypertensions, valsartan and irbesartan varied between compounds and WWTPs. Average removal efficiencies varied from 65 ± 37% for valsartan in Kujawy WWTP to 92 ± 6% in Plaszow WWTP. Mean removal for irbesartan was 72 ± 22% and 7[illegible] ± 20%, which is consistent with previous reports (Kasprzyk-Hordern et al., 2009b; Papageorgiou et al., 2019). Poor removal of irbesartan with average values of <20% was reported by Botero Coy et al. (Botero-Coy et al., 2018).

Caffeine, nicotine and metabolites 1,7-dimethylxanthine and cotinine were effectively removed, with an average of >95% of each compounds, which agrees with published results (Huerta-Fontela et al., 2008; Baker and Kasprzyk-Hordern, 2013; Sun et al., 2014).

The significant values of negative mass balances were observed for fexofenadine (ca. 70%), venlafaxine (19-28%), o-desmethyltramadol (ca. 200%), ketamine (45% only in Plaszow WWTP), temazepam (37-47%). The increase in final effluent concentrations of the compounds likely results from dissolution of persistent contaminants accumulated in aggregates and/or back-transformation or de-conjugation of metabolites into parental compounds (Verlicchi et al., 2012a). This was also reported elsewhere (Verlicchi et al., 2012a; Petrie et al., 2015; Petrie et al., 2016; Archer et al., 2017).

The increase of concentrations of fexofenadine in the effluent could results from metabolism of terfenadine (Nath et al., 2018). The elimination of fexofenadine reported for WWTPs in Finland was low (18%) with occasional higher concentrations in the effluent (Kosonen and Kronberg, 2009).

The higher concentrations of venlafaxine recorded in effluent also could suggest transformation of major active metabolite, desvenlafaxine into parental compound. The cleavage of venlafaxine from its phase two glucuronide metabolite could be the source of parental compound in the effluent. Another explanation is its release to water phase from sewage sludge. It is related to 2, 3 times higher concentrations of venlafaxine observed in sewage sludge than in the water phase (see next Paragraph

3.3). Partial removal of venlafaxine was observed in the work of Rúa-Gómez and Püttmann (Rúa-Gómez and Püttmann, 2012b) and 20-40% removal by Botero-Coy (Botero-Coy et al., 2018).

The highest negative mass balance, with about 3 times higher loads in the effluent than in the influent, was observed for O-desmethyltramadol. Tramadol is rapidly transformed in the liver to two primary metabolites O-desmethyltramadol and N-desmethyltramadol (Ardakani and Rouini, 2007). Only 10-30% of the parental tramadol is excreted in sewage (Ardakani and Rouini, 2007). The present study has shown low potential of sorption of tramadol and its metabolite O-desmethyltramadol to sewage sludge (Paragraph 3.3), although octanol-water partitioning coefficient for tramadol is 3.01 and 2.45 for O-desmethyltramadol. Low sorption potential of this metabolite could indicate that its release from particulate matter is not significant and could suggest that chemical degradation or biodegradation of tramadol lead to higher loads of O-desmethyltramadol in the effluent. Similar effect of negative mass balance of O-desmethyltramadol, above 50%, was observed by Archer et al. (Archer et al., 2017). Partial removal of O-desmethyltramadol, at the level of 36% was reported in (Rúa-Gómez and Püttmann, 2012b).

Assessment of removal efficiencies of EDDP, methadone and ketamine is not conclusive due to very low concentrations of compounds, from 2 ng L^{-1} to 5 ng L^{-1}, in influent and effluents. However, higher levels of EDDP in effluents than in influents were observed by Boleda et al. (Boleda et al., 2009). Negative removal values of ketamine observed in Plaszow WWTP, corroborate results reported in the literature (Huerta-Fontela et al., 2008; Baker and Kasprzyk-Hordern, 2013; Andres-Costa et al., 2014). In contrast, increased concentration of ketamine were observed in Kujawy WWTP. This is also in contrast to the study of Postigo et al. (Postigo et al., 2010).

Limited removal was also observed for benzodiazepines. Temazepam and oxazepam showed for some samples, an increase of concentration in effluents, which is related to predominant excretion in the form of conjugates followed by cleavage to unchanged drugs during treatment (Fitzgerald, 2009; Baker and Kasprzyk-Hordern, 2013).

Removal of codeine was low, at the level of few percent. Removal of codeine below 50% was reported in other studies (Boleda et al., 2009; Kasprzyk-Hordern et al., 2009c, a; Baker and Kasprzyk-Hordern, 2013).

MDMA was removed at about 35% at both WWTPs. Poor removal of MDMA was also reported in the literature (Huerta-Fontela et al., 2008; Baker and Kasprzyk-Hordern, 2013).

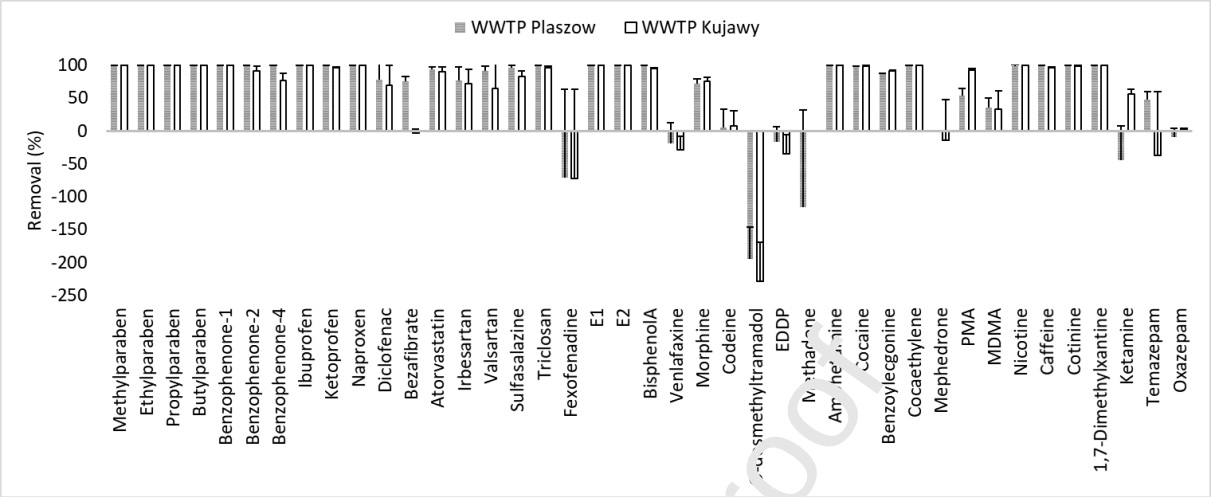


Fig. 5. The average removal efficiencies (%) of the detected compounds at the Kujawy and Plaszow WWTPs. Average values for 6 days. Standard deviations indicate variation between sampling days.

3.3 Partitioning coefficient

During wastewater treatment, APIs can be removed by sorption as well as biodegradation. The degree of partitioning between sludge and aqueous phases in different stages of the treatment process is often used as a key indicator of their environmental fate and in risk assessment for the subsequent disposal of sludge to land (Berthod et al., 2014; Berthod et al., 2017). Many K_d values have been published for various pharmaceuticals and different sludge types (Ternes et al., 2004; Díaz-Cruz et al., 2009; Wick et al., 2009; Jelic et al., 2011; Hyland et al., 2012; Jelic et al., 2012; Stasinakis, 2012; Verlicchi et al., 2012b; Petrie et al., 2015; Semblante et al., 2015).

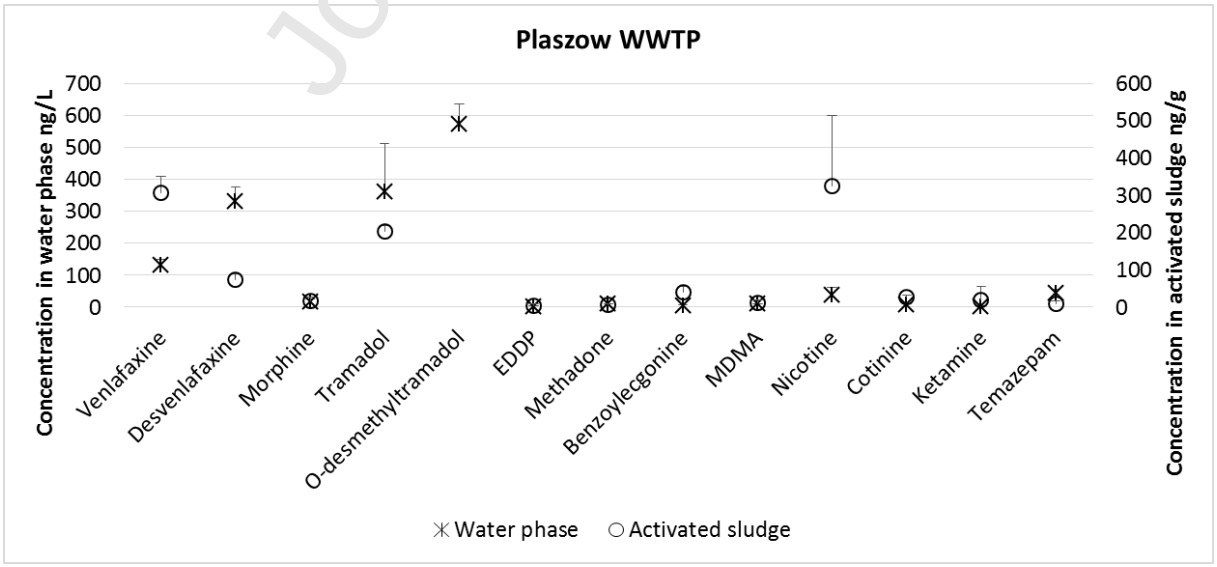
Sorption of target anti-depressants, drugs of abuse, lifestyle chemicals and their metabolites to suspended activated sludge was tested in this study. While data on illicit drugs in wastewater is widely accessible, information on their concentrations in sludge is scarce.

Mean concentrations of target analytes determined in wastewater and sorbed on activated sludge were presented in Fig. 6. Values of average concentrations in solid and water phase (of activated sludge) determined for target compounds were presented in Table S9. Several compounds including norephedrine, amphetamine, methamphetamine, and cocaine were found only in solid phase (activated

sludge) above MQL. While codeine was absent in sewage sludge. The sorption coefficients were not calculated for these compounds.

The sorption potential of hydrophobic compounds was estimated according to their octanol/water partition coefficient (K_{OW}). This approach assumed low sorption potential of compounds with log K_{OW} <2.5, medium (2.5 < log K_{OW}>4.0) and high sorption potential with K_{OW}>4.0 (Rogers, 1996). Further research has shown that removal efficiencies of organic pollutants during activated sludge treatment were co-related with their pH-dependent distribution coefficients, consider both the dissociation constants (pK_a) and the pH of wastewater (Carballa et al., 2008; Rosal et al., 2010). Sorption is defined as negligible for substances with log K_d values less than 2, but it is important when the log K_d value is greater than 4 (Deegan et al., 2011).

Nicotine (4.15) had the highest log K_d values in Plaszow and Kujawy WWTPs, respectively (see Fig. 7). Among other compounds, higher mean log K_d value were calculated for benzoylecgonine (3.89 and 3.93) which is in contrast to their low value of log D_{ow}. These discrepancies were also observed for nicotine and cotinine. Considering the log D_{ow} values of venlafaxine (1.3), tramadol (0.7), MDMA (-1.4) and ketamine (3.2), one could expect low or medium sorption potential of these analytes. Given that the log K_d values of these compounds (see Fig. 7) obtained in this study were close or above of 3 suggest their significant sorption capacity to sludge. Log K_d of venlafaxine, desvenlafaxine determined in this study are in agreement with values reported in literature (Lajeunesse et al., 2012).



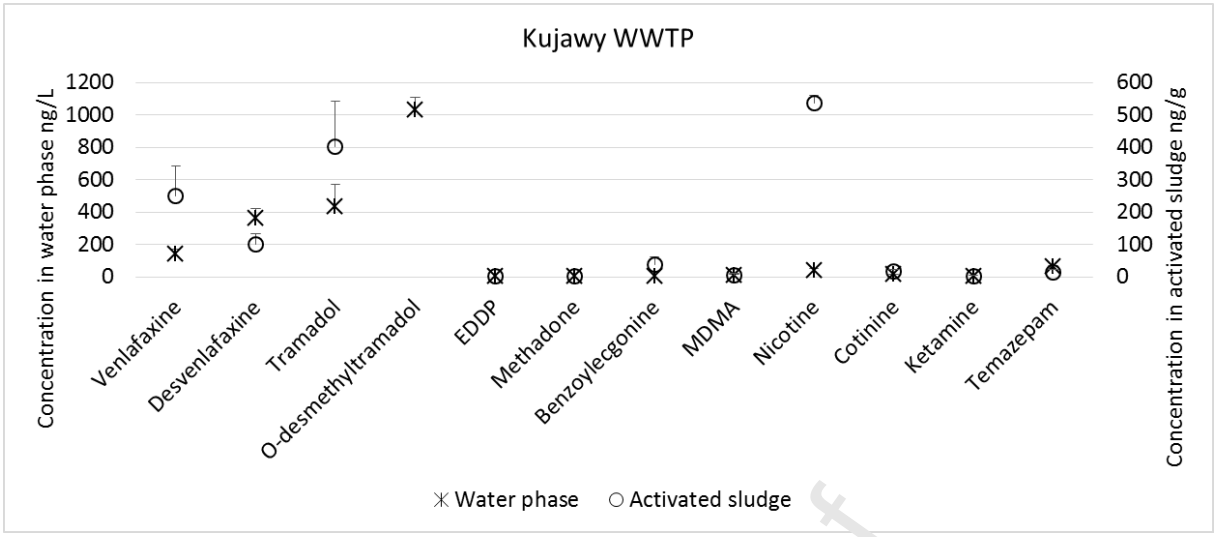


Fig. 6. Average concentrations of analytes in wastewater phase (ng/L) and activated sludge (ng/g). Standard deviations indicate variation between sampling days.

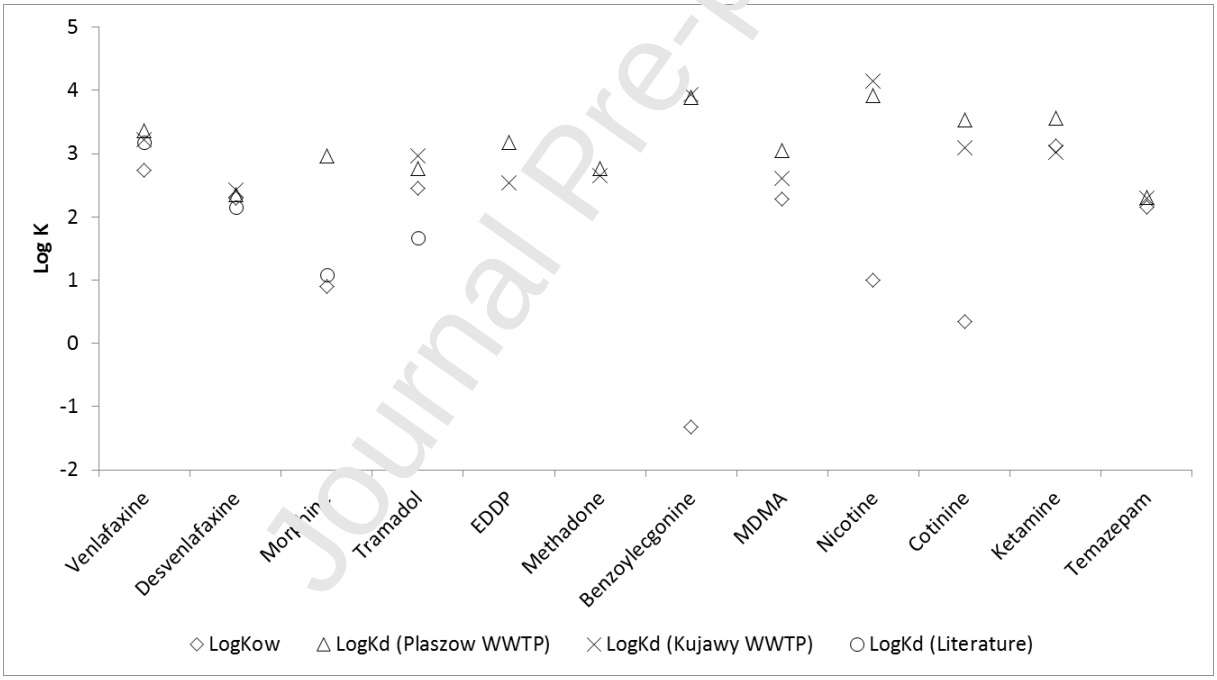


Fig. 7. Octanol/water partitioning coefficients (log K_{OW}) and average partitioning coefficients (log K_d) for compounds determined in wastewater and activated sludge in Plaszow and Kujawy WWTPs obtained in this study and in other works.

Low sorption observed for temazepam is in agreement with the results by Baker and Kasprzyk-Hordern (Baker and Kasprzyk-Hordern, 2013). In contrast to this study, the sorption for several compounds including morphine, cocaine, benzoylecgonine, MDMA, tramadol and amphetamine was

negligible according to other works (Baker et al., 2012; Baker and Kasprzyk-Hordern, 2013). In relation to absolute concentration values of cocaine in sludge, under 10 ng/g (see Fig. 6), negligible sorption could be considered. Similar concentrations of cocaine in suspended particulate matter were reported by Baker et al. (Baker et al., 2012). Mean concentrations in sludge of 5 WWTPs in Slovak Republic for venlafaxine and O-desmethylvenlafaxine (~100 ng/g), caffeine (~ 70 ng/g), tramadol (~ 60 ng/g), codeine (~ 20 ng/g), oxazepam (~10 ng/g), mephedrone (~5 ng/g) were reported by Ivanova et al. (Ivanová et al., 2018). Relatively low sorption affinity of methamphetamine and MDMA to sewage sludge, with mean concentration in sludge at 18 ng/g and 3 ng/g were reported elsewhere (Ivanová et al., 2018). Amphetamine, benzoylecgonine, cocaine were found below LOQ (Ivanová et al., 2018). On the other hand, similar results to those presented in this study were reported by Mastroianni et al. (Mastroianni et al., 2013). This requires further work to fully understand discrepancies in reported data including potential variabilities in the composition of wastewater and activated sludge.

3.4 Environmental concentrations

44 ECs were detected in surface waters located upstream and downstream of the WWTPs (see Table S10 and S11). Mean concentrations of compounds are presented in Fig. 8.

The higher average levels of nicotine, caffeine, 1,7-dimethylxantine and micropollutants like parabens and bisphenolA, in the upstream from the Plaszow WWTP (Drwina upstream) indicate direct discharge and /or illegal dumping of sewage and other waste products into the Drwina river. In this sampling point about 89% of CECs belonged to lifestyle chemicals, among them caffeine and 1,7-dimethylxantine were in the highest concentrations ranging from 20566 to 57374 ng L^{-1}. NSAIDs constituted 5% with the highest average concentration of ibuprofen (2909 ± 869ng L^{-1}). Hypertension accounted for 2.5% with the mean concentration of valsartan at 2172 ± 381ng L^{-1}.

The results obtained for Drwina clearly demonstrate an increase in concentrations of ketoprofen, diclofenac, atorvastatin, irbesartan, valsartan, sulfasalazine, fexofenadine, venlafaxine, desvenlafaxine, codeine, dihydrocodeine, tramadol, O-desmethyltramadol, EEDP, methadone, MDMA, ketamine, norketamine, temazepam and oxazepam downstream of the WWTP discharge point. The increase in

average concentrations between upstream and downstream river water sampling points were from 5% to 92%. The highest differences were observed for ketoprofen (92%), irbesartan (91%) and norketamine (79%). Benzophenone-2, estrogen E1, methadone, EDDP and ketamine were found only in the Drwina river. EDDP was detected only in Drwina downstream from the discharge point.

The average concentration levels of many compounds observed for the Drwina river were higher than for the Wisla river. No data exists for the flow rate downstream of Drwina river, however based on visual observations, the river is very small (length of 5.5 km) and consequently dilution of Plaszow WWTP effluent will be small. The high concentrations seen downstream from Plaszow WWTP can therefore be attributed to high contribution of wastewater to the river. The ratios of the average concentration of a compound in the effluent of Plaszow WWTP to its concentration downstream of Drwina river were lower or equal to 1 for 27 out of 34 compounds (see Fig S1). It means low dilution or/and no dilution of contaminants in Drwina river.

The highest mean concentrations in downstream Drwina river were measured for valsartan (2391 ± 109 ng L^{-1}), irbesartan (1709 ± 323 ng L^{-1}) diclofenac (1304 ± 55 ng L^{-1}), whereas the lowest mean concentrations were observed for benzophenone-2, ethyl- and propylparabens, EDDP, cocaine, just above 1 ng L^{-1}. The mean contribution of chemical groups changed drastically downstream of Plaszow WWTP effluent discharge with hypertension (valsartan and irbesartan) accounting for 42%, NSAIDs for 18%, analgesics/metabolites for 11%, lifestyle chemicals and metabolites for 9% and anti-depressants and metabolites accounting for 5% (see Fig. 9).

Out of the 44 compounds detected in surface water, 37 compounds were determined in the Wisla river. Fig. 8 clearly demonstrates the similar levels of concentrations of target compounds before and after both WWTPs discharge, Wisla – upstream and downstream, hence proves that dilution factor is significantly larger. Mean flow rate of Wisla river in Krakow is 98 m^3/s. The increase in concentrations of benzophenone-4, ketoprofen, diclofenac, atorvastatin, irbesartan, valsartan, fexofenadine, venlafaxine, desvenlafaxine, codeine, tramadol, O-desmethyltramadol, benzoylecgonine and temazepam was observed for Wisla downstream. The differences of concentrations between upstream and downstream of Kujawy WWTP ranged from 3% to 39%. The largest differences at Wisla downstream were observed for venlafaxine (39%), temazepam (25%), valsartan (24%),

desvenlafaxine (24%), diclofenac (22%) and codeine (21%). In Wisla, ketoprofen and irbesartan were detected only in the downstream location. As a result, the contribution of chemical classes both upstream and downstream of WWTP in the Wisla river was at comparable levels. The highest contributions were observed for lifestyle chemicals and their metabolites (52 % and 41%), for hypertension (8% and 16%), for benzodiazepines and metabolites (17% and 13%), for NSAIDs (8% and 11%) and for analgesics and metabolites (5% and 7%) at upstream and downstream, respectively (see Fig. 9).

The highest mean concentrations in downstream Wisla river were observed for 1,7-dimethylxantine (734 ± 100ng L^{-1}), caffeine (362 ± 32 ng L^{-1}), valsartan (345 ± 27 ng L^{-1}), oxazepam (334 ± 84ng L^{-1}) and the lowest mean concentrations were measured for benzophenone-1, ethyl- and propylparabens, dihydrocodeine, cocaine and MDMA, ranged from 0.5 to 1.6 ng L^{-1}.

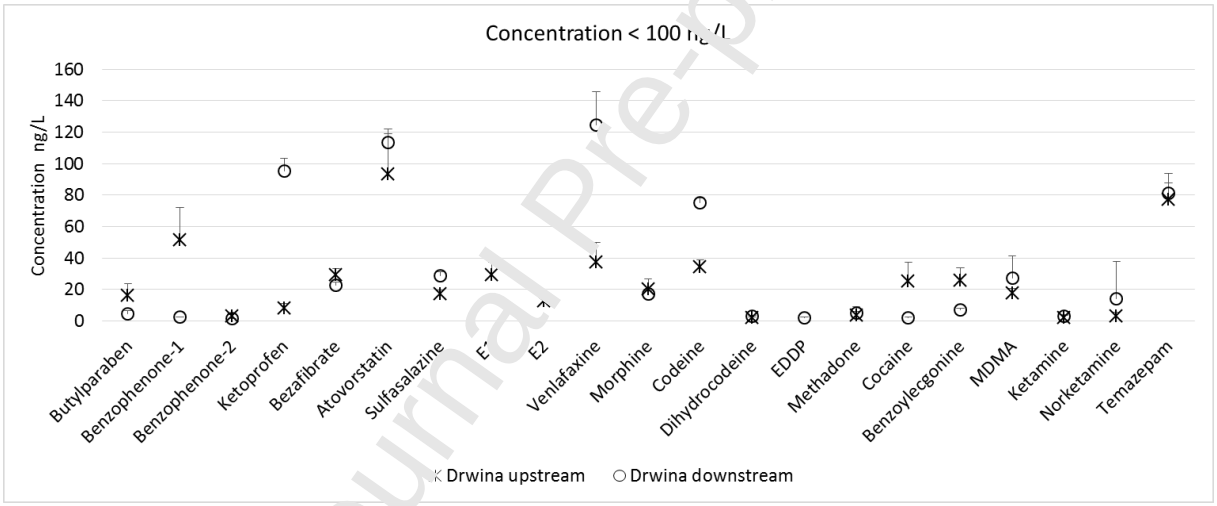
However, similar concentrations of monitored compounds observed upstream and downstream sampling points at the Wisla river show that water quality in the upper section of the river is low. Additionally, as Wisla is a large river, the impact of wastewater effluent will be minimized by high dilution factors.

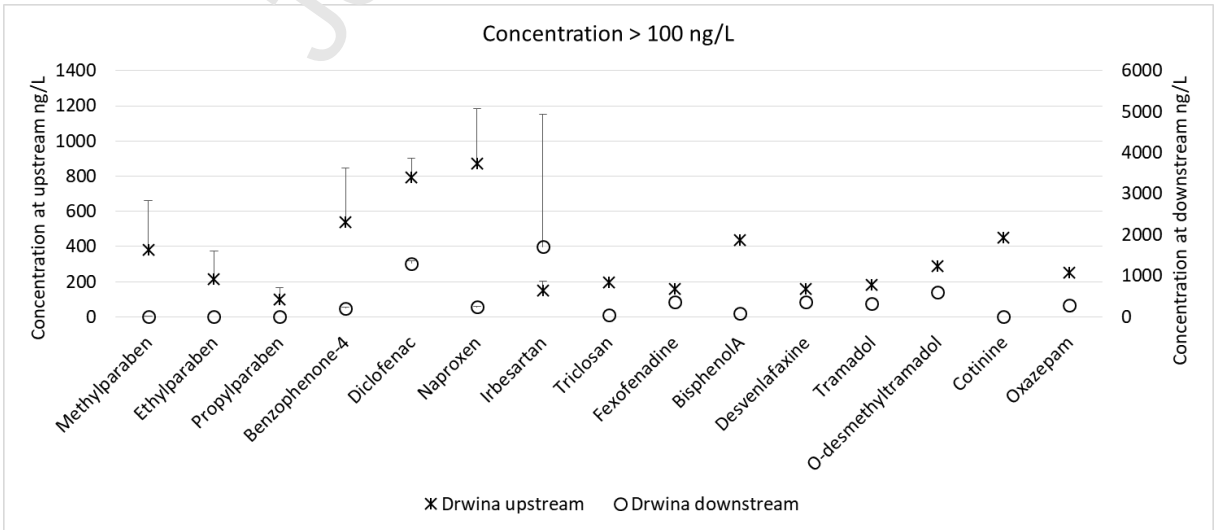
Interestingly, in the case of ketoprofen and irbesartan their loads downstream of Wisla and Drwina rivers are directly associated with the discharged effluent wastewater from tested WWTPs.

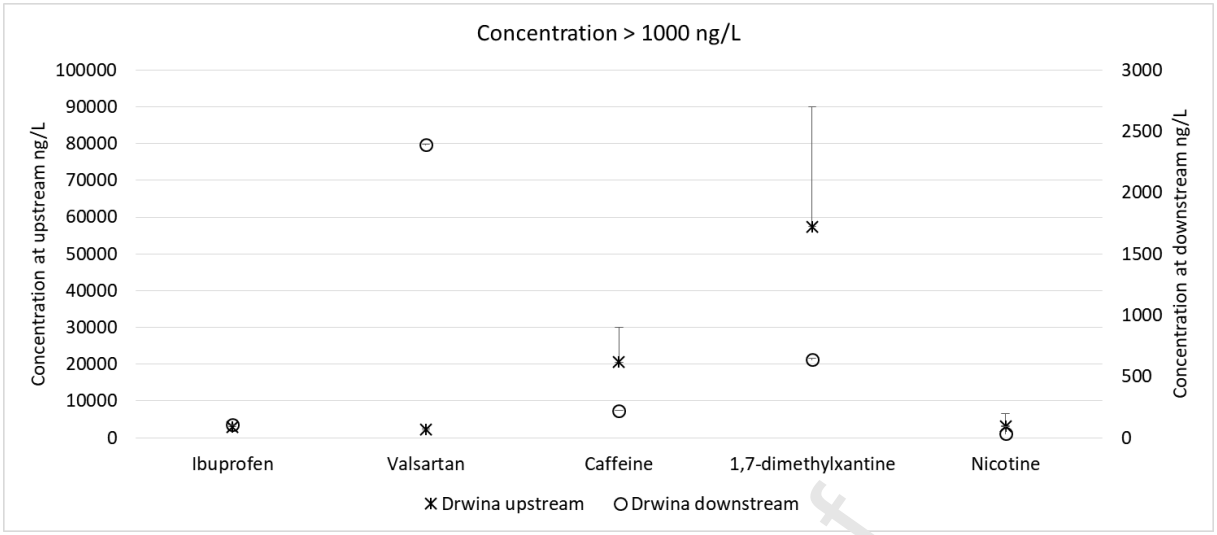
The mean concentrations of valsartan and oxazepam observed in this study, in rivers, were much higher in comparison to those noted in the UK (Petrie et al., 2015). In contrast, the mean concentrations of caffeine in both rivers are comparable to the range reported in UK (Petrie et al., 2015). The mean concentrations of many compounds (ibuprofen, diclofenac, naproxen, ketoprofen, bezafibrate, venlafaxine, tramadol, codeine, dihydrocodeine, morphine, methadone, EDDP, temazepam, ketamine, norketamine, MDMA, cocaine, benzoylecgonine, nicotine, triclosan, bisphenol A, UV filters and parabens) in the Wisla River were consistent with those observed in UK (Petrie et al., 2015). The average values of concentrations of venlafaxine, desvenlafaxine, tramadol and O-desmethyltramadol measured in the Wisla river were quite similar to those observed in German rivers (Rúa-Gómez and Püttmann, 2012a), while the concentrations detected in Drwina river were higher. It

should be noted that, Wisla and examined German rivers were of the similar size, while Drwina river is a small tributary.

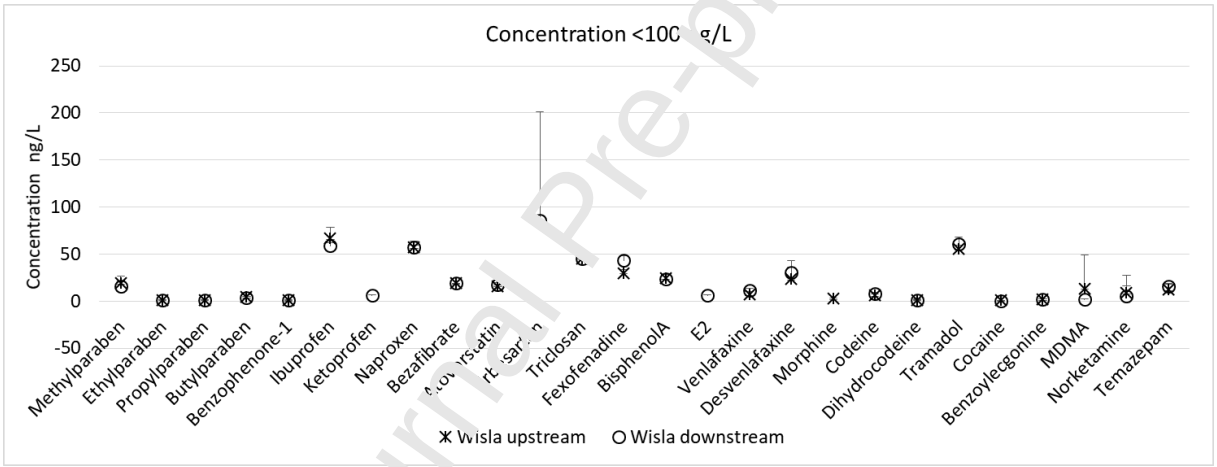
Drwina river







Wisla river



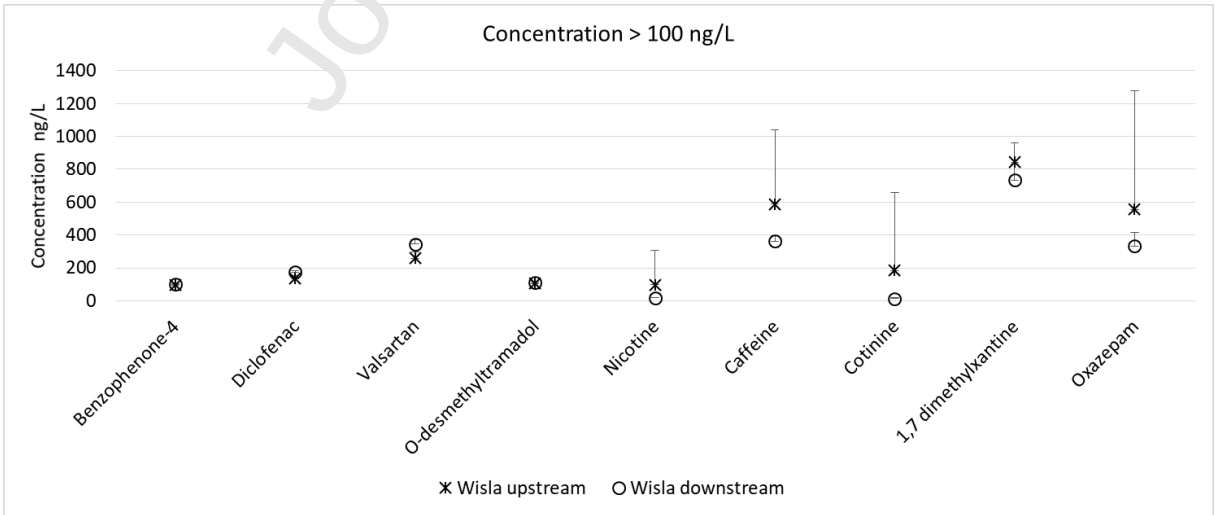


Fig. 8. Mean concentrations of the detected compounds at sampling points located upstream and downstream of the WWTPs. Standard deviation indicate variation between sampling days for the compounds.

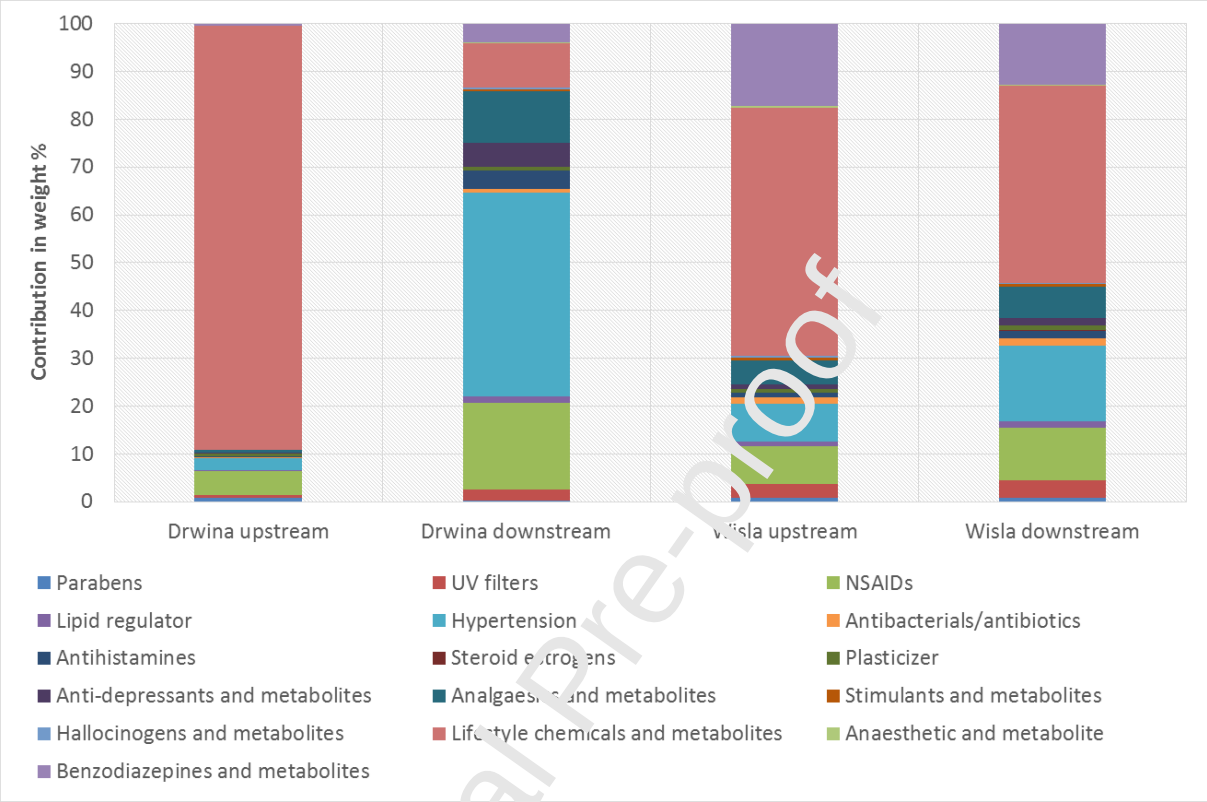


Fig. 9. Contribution of chemical classes in concentrations expressed in weight % at upstream and downstream of WWTPs discharge points. (**Parabens** – methylparaben, ethylparaben, propylparaben, butylparaben; **UV filters** – benzophenone-1, benzophenone-2, benzophenone-4, **NSAIDs** – ibuprofen, ketoprofen, naproxen, diclofenac; **Lipid regulator** – bezafibrate, atorvastatin; **Hypertension** – irbesartan, valsartan; **Antibacterials/antibiotics** – sulfasalazine, triclosan; **Antihistamines** – fexofenadine; **Steroid estrogens** – E1, E2; **Plasticizer** – bisphenol A; **Anti-depressants and metabolites** – venlafaxine, desvenlafaxine; **Analgesics and metabolites** – morphine, codeine, dihydrocodeine, tramadol, O-desmethyl-tramadol, EDDP, methadone; **Stimulants and metabolites** –cocaine, benzoylecgonine, cocaethylene; **Hallucinogens and metabolites** – MDMA; **Lifestyle chemicals and metabolites** – nicotine, caffeine, cotinine, 1,7-dimethylxantine; **Benzodiazepines and metabolites** – temazepam, oxazepam.

3.5 Environmental risk assessment

Compounds detected in investigated effluent of WWTPs and surface waters are continuously emitted into the aquatic environment causing potential risks to biota. The presence of a mixture of active substances and their metabolites from various chemical classes prompts consideration of a potential risk assessment.

According to the guideline (see Paragraph 2.5), the evaluation of drugs mobility between aquatic environment and solid phase (bioaccumulation) is based on the value of octanol/water partition coefficient (Log K_{OW}> 4.5). The evaluation including environmental fate and impact of drug is needed if the concentration is equal or over 10 ng L^{-1}. In the next step, impact and fate of drug in the environment is assessed on the base of risk quotation and such relevant factors like physicochemical properties, toxicology, potential to bioaccumulation (Log K_{OW}> 3).

Considering the environmental impact, special attention was paid in this paper to compounds with high bioaccumulation potential, characterized by Log K_{OW} values equal or greater than 4.5, including diclofenac (4.5), triclosan (4.8), atorvastatin (6.4) and irbesartan (5.3). The values of Log D_{OW} at pH 7.5 are 0.7 and 1.9 for diclofenac and atorvastatin. While, the values of Log D_{OW} of triclosan and irbesartan are 4.8 and 4.9. The concentrations of all these target compounds and many others were above 10 ng L^{-1}. Therefore, the impact of CECs on the environment was estimated. The environmental risk assessment method (ERA) based on lowest PNECs data reported in the literature was used (Zhou et al., 2019) (see Table S12).

The comparison of the average and maximum concentrations of the investigated compounds in surface waters with PNECs reported in the literature, revealed that environmental risk is unlikely to occur for 9 out of 43 (Table S12) detected compounds in surface water. The RQ values were below 0.01 for parabens (except Drwina upstream), UV filters except benzophenone-4, sulfasalazine, fexofenadine, morphine, dihydrocodeine, cocaine and benzoylecgonine.

In upstream and downstream of Wisla river, low or medium risk was observed for naproxen (0.02). bezafibrate (0.08), valsartan (0.07, 0.09), bisphenol A (0.02), codeine (0.11, 0.14), tramadol (0.06), MDMA (0.07, 0.01), cotinine (0.18, 0.01), temazepam (0.01) and oxazepam (0.33, 0.20). As expected, the worst impact on aquatic environment was found in Drwina river, due to its small size and collection of wastewater from the biggest WWTP in this region.

The low or medium risk at upstream of wastewater discharge point at Drwina river were noted for all parabens (0.01 - 0.33), ketoprofen (0.01) naproxen (0.26.), bezafibrate (0.13), valsartan (0.56), bisphenol A (0.44), codeine (0.57), tramadol (0.19), methadone (0.02), cocaine (0.01), MDMA (0.09), cotinine (0.45), temazepam (0.03) and oxazepam (0.15). This is similar to what was found downstream, which also showed low or medium risk, with RQs ranged from 0.01 to 0.69, was found for propylparaben, ketoprofen, naproxen, bezafibrate, irbesartan, valsartan, bisphenol, tramadol, EDDP, methadone, MDMA, cotinine, oxazepam and temazepam,

RQ values exceeding 1.0 were obtained for 11 CECs of interest detected in the surface waters, showing these compounds are of high environmental risk. These CECs included benzophenone-4 (1.2 – 44), ibuprofen (5.8 – 291), diclofenac (136 – 1304), atorvastatin (62 – 437), triclosan (1.0-4.4), venlafaxine (1.2-20.4), nicotine (1.3-229), and 1,7-dimethylxantine (10-4098). In rivers high environmental risk was also observed for E1 (upstream of Drwina, 1.47), E2 (upstream of Drwina, 7.97 and downstream of Wisla, 3.70), codeine (only downstream of Drwina, 1.26) and caffeine (1.13-64.27) in all river sampling points except downstream of Drwina (0.69), (see Table S12). The worst scenario obtained for maximum detected concentrations of CECs is in agreement to general scenario (Table S12). This is in agreement with high environmental risk for diclofenac, codeine and nicotine observed by Archer et al (Stuart et al., 2012; Bouissou-Schurtz et al., 2014; Archer et al., 2017; Yadav et al., 2019; Bagnis et al., 2020, Baran et al., 2020). Europe-wide ranking of environmental risk assessment of CECs considering traditional risk quotients and frequency of MECs exceeding PNEC was presented in work of Zhou et al. (Zhou et al., 2019). The top 45 most frequently studied pharmaceuticals in European surface waters out of 477 analyzed compounds showed a potential environmental risk to aquatic ecosystems (with RQ >1) (Zhou et al., 2019). 13 out of 45 CECs reported by Zhou et al. (Zhou et al., 2019), were also detected in our study.

Among compounds with log $K_{OW} \geq 4.5$, diclofenac, atorvastatin and triclosan were found to be of high risk with RQs 1304, 437 and 4.4, respectively. Among compounds with log Kow < 4.5 but with concentrations exceeding 10 ng L^{-1}, caffeine (Log K_{OW} = 0.2, Log D_{OW} = -0.6), 1,7-dimethylxantine (Log K_{OW} = -0.2, Log D_{OW} = 0.2), benzophenone-4 (Log K_{OW} = 0.4, Log D_{OW} = -0.5) and nicotine

(Log K_{OW} = 1.2, Log D_{OW} = -2.3) were also found to pose risk (RQ 64, 4098, 6.7 and 229, respectively).

Other CECs with concentrations exceeding 10 ng $L^{-1}$and with RQs >1 in at least one sampling point, were ibuprofen, E1, E2 and venlafaxine, these also showed high potential to bioaccumulation with Log K_{OW} values of 3.9, 3.1, 4.0 and 3.2, respectively. While, Log D_{OW} of ibuprofen and venlafaxine are lower, 1.2 and 1.3, respectively.

To summarize, many hazardous compounds with high, moderate or even low environmental impact show high potential for bioaccumulation and should be included as priority at the same risk level (Zhou et al., 2019).

Conventional ERA methods do not include potential toxicological impact due to interaction of mixtures of active compounds, metabolites in given ecosystems. The additive toxicological effects of CECs mixtures on different aquatic species can be observed even at concentrations where the individual compounds showed negligible or minor effects (Petrie et al., 2015). The aspect of continuous introduction of CECs into aquatic environment at lower environmentally relevant concentrations is also significant in the context of chronic toxicity (Bagnis et al., 2020). Furthermore, for some CECs, and in particular for metabolites, no lethal or chronic ecotoxicological data across different trophic levels are available in the literature.

The increased expression of mRNA transcripts of the oestrogen receptor-α (ERα) and protein vitellogenin (VTG) in the liver of male fish, that could cause the increase of levels of plasma VTG in the body was reported as the result of exposure to parabens and UV filters (Inui et al., 2003; Barse et al., 2010). However, concentrations of target parabens and UV filters recorded in this study are far below those found as effective in laboratory tests (Inui et al., 2003; Barse et al., 2010). The levels of chronic toxicity reported for diclofenac ranged from 1.5 µg L^{-1}, 1000 µg L^{-1} and 10 000 µg L^{-1} for fish, invertebrates and algae, respectively (Kosma et al., 2014). Maximum concentrations of diclofenac in surface water were above 1300 ng L^{-1}. This indicates high chronic toxicity of diclofenac in fish and no risk in invertebrates and algae. Similar results were reported elsewhere (Kosma et al., 2014; Papageorgiou et al., 2016). Diclofenac levels ay >1000 ng L^{-1} affect VTG production in fish (Hong et al., 2007). Veldhoen et al. observed modulation of the thyroid endocrine system of the American

bullfrog (Rana catesbeiana) exposed to ibuprofen at concentrations ranging from 1500 to 15 000 ng L^{-1} (Veldhoen et al., 2014). In this study, the concentrations of ibuprofen were below 1500 ng L^{-1} (with one exception: upstream in Drwina river with average 2909 µg/L ± 868). Moreover, exposure to ibuprofen, as well to naproxen at concentration of 100 ng L^{-1} causes the decrease in egg fertilization in fish (Nesbitt, 2011). This threshold was exceeded in this study for ibuprofen and naproxen at both upstream and downstream in Drwina river.

Chronic risk of diclofenac as well ibuprofen and E2 for high trophic level organisms (fish) was reported by Liu et al. (Liu et al., 2015). Values of chronic toxicity in different trophic levels reported in literature were 793 µg L^{-1} (fish) (Maruya et al., 2014), 100 000 µg L^{-1} (algae) (Cleuvers, 2004) for naproxen and 3800 µg L^{-1} (fish) (Kosma et al., 2014) for bezafibrate, which exceeds the concentrations determined in this study. NSAIDs (ibuprofen, diclofenac, naproxen) and lipid regulator (bezafibrate) are generally classified as harmful to aquatic organisms (Petrie et al., 2015; Zhou et al., 2019). Chronic toxicity for venlafaxine, affected predator avoidance behavior of fish larvae, reported in literature ranging from 500 to 5000 ng L^{-1} (Painter et al., 2009). The maximum concentrations detected in surface water (170 ng L^{-1}) in this study were much below reported chronic toxicity levels.

4. Conclusions

The analysis of influents and effluents of the two WWTPs of Krakow gives valuable information of pharmaceuticals residues, personal care products, lifestyle chemicals, illicit drugs and metabolites that are used and emitted in the study area. CECs were present at levels exceeding 400 µg L^{-1} and 8 µg L^{-1} in WWTP influent, effluent respectively. Over 70% of total mass loads of tested compounds is lifestyle chemicals and their metabolites in the influent at both WWTPs. While, in the effluent the highest contribution was observed for the hypertension pharmaceuticals. Removal efficiencies of compounds were also evaluated. The removal efficiencies were generally satisfactory (>95%), but some CECs were persistent and even at higher levels of concentrations in effluent (e.g. fexofenadine, venlafaxine, o-desmethyltramadol, ketamine and temazepam). Moreover, surface water samples were analyzed both upstream and downstream of WWTP effluent discharge. The highest average concentrations in Drwina downstream were noted for valsartan, irbesartan and diclofenac, which is

related to the highest contribution from hypertension pharmaceuticals and NSAIDs. In Wisla downstream, the highest contributions were observed for lifestyle chemicals and their metabolites and hypertension pharmaceuticals. The impact of wastewater effluent from the studied WWTPs to the Wisla river is significantly reduced by high dilution factors. Drwina river, collector of effluent of Plaszow WWTP, is very small (length of 5.5 km) and consequently dilution of effluent is low. The high concentrations seen downstream of Drwina river from Plaszow WWTP can therefore be attributed to high contribution of wastewater to the river. However, similar concentrations of CECs observed in upstream and downstream of Wisla, suggests low quality of water in the upper section of the river. The fate of parental compounds and metabolites in WWTPs has significance for their occurrence in surface waters and environmental risk. The RQs obtained from the measured concentrations in surface waters in comparison to PNECs, has shown medium or high risk for many compounds (e.g. diclofenac, atorvastatin, triclosan) which are characterized by high potential for bioaccumulation. However, current environmental impact assessments do not consider coexistence of CECs as complex mixtures and their effects on molecular and cellular levels in organisms. This warrants the need for further ecotoxicological tests to provide comprehensive risk assessment of CECs in the aqueous environment.

Acknowledgement

Part of this work was supported by the COST Action ES1307 "SCORE - Sewage biomarker analysis for community health assessment. This research was partially financed by the AGH UST grant 16.16.210.476 subsidy of the Ministry of Science and Higher Education. The authors thank the support provided by WWTPs staff in the collection of samples.

The support by Natural Environment Research Council (grant NE/N019261/1 and NE/L009579/1) is also acknowledged.

Conflict of interest

The authors declare no conflict of interest.

References

Afonso-Olivares, C., Sosa-Ferrera, Z., Santana-Rodríguez, J.J., 2017. Occurrence and environmental impact of pharmaceutical residues from conventional and natural wastewater treatment plants in Gran Canaria (Spain). Sci. Total Environ. 599-600, 934-943.

Ahmed, M.B., Zhou, J.L., Ngo, H.H., Guo, W., Thomaidis, N.S., Xu, J., 2017. Progress in the biological and chemical treatment technologies for emerging contaminant removal from wastewater: A critical review. J. Hazard. Mater. 323, Part A, 274-298.

Andres-Costa, M.J., Rubio-Lopez, N., Morales Suarez-Varela, M., Pico, Y., 2014. Occurrence and removal of drugs of abuse in Wastewater Treatment Plants of Valencia (Spain). Environ Pollut 194, 152-162.

Archer, E., Petrie, B., Kasprzyk-Hordern, B., Wolfaardt, G.M., 2017. The fate of pharmaceuticals and personal care products (PPCPs), endocrine disrupting contaminants (EDCs), metabolites and illicit drugs in a WWTW and environmental waters. Chemosphere 174, 437-446.

Ardakani, Y.H., Rouini, M.R., 2007. Pharmacokinetics of tramadol and its three main metabolites in healthy male and female volunteers. Biopharm. Drug Dispos. 28, 527-534.

Arlos, M.J., Bragg, L.M., Parker, W.J., Servos, M.R., 2015. Distribution of selected antiandrogens and pharmaceuticals in a highly impacted watershed. Water Res 72, 40-50.

Bagnis, S., Boxall, A., Gachanja, A., Fitzsimons, M., Murigi, M., Sharpe, J., Tappin, A., Wilkinson, J., Comber, S., 2020. Characterization of the Nairobi River catchment impact zone and occurrence of pharmaceuticals: Implications for an impact zone inclusive environmental risk assessment. Sci. Total Environ. 703, 134925.

Baker, D.R., Kasprzyk-Hordern, B., 2013. Spatial and temporal occurrence of pharmaceuticals and illicit drugs in the aqueous environment and during wastewater treatment: New developments. Sci. Total Environ. 454–455, 442-456.

Baker, D.R., Očenášková, V., Kvicalova, M., Kasprzyk-Hordern, B., 2012. Drugs of abuse in wastewater and suspended particulate matter — Further developments in sewage epidemiology. Environ. Int. 48, 28-38.

Baran, W., Madej-Knysak, D., Sobczak, A., Adamek, E., 2020. The influence of waste from electronic cigarettes, conventional cigarettes and heat-not-burn tobacco products on microorganisms. J. Hazard. Mater. 385, 121591.

Barse, A.V., Chakrabarti, T., Ghosh, T.K., Pal, A.K., Kumar, N., Raman, R.P., Jadhao, S.B., 2010. Vitellogenin Induction and Histo-metabolic Changes Following Exposure of Cyprinus carpio to Methyl Paraben. Asian-Australas J Anim Sci 23, 1557-1565.

Bergmann, A., Fohrmann, R., Weber, F.-A., 2011. Zusammenstellung von monitoringdaten zu umweltkonzentrationen von arzneimitteln. Umweltforschungsplan des bundesministeriums für umwelt, naturschutz und reaktorsicherheit. Forschungskennzahl 360 14 013. Umweltbundesamt von Deutschland. http://www.uba.de/uba-info-medien/4188.html.

Berthod, L., Roberts, G., Whitley, D.C., Sharpe, A., Mills, G.A., 2014. A solid-phase extraction method for rapidly determining the adsorption coefficient of pharmaceuticals in sewage sludge. Water Res 67, 292-298.

Berthod, L., Whitley, D.C., Roberts, G., Sharpe, A., Greenwood, R., Mills, G.A., 2017. Quantitative structure-property relationships for predicting sorption of pharmaceuticals to sewage sludge during waste water treatment processes. Sci. Total Environ. 579, 1512-1520.

Birošová, L., Mackuľak, T., Bodík, I., Ryba, J., Škubák, J., Grabic, R., 2014. Pilot study of seasonal occurrence and distribution of antibiotics and drug resistant bacteria in wastewater treatment plants in Slovakia. Sci. Total Environ. 490, 440-444.

Boleda, M.A., Galceran, M.A., Ventura, F., 2009. Monitoring of opiates, cannabinoids and their metabolites in wastewater, surface water and finished water in Catalonia, Spain. Water Res 43, 1126-1136.

Botero-Coy, A.M., Martínez-Pachón, D., Boix, C., Rincón, R.J., Castillo, N., Arias-Marín, L.P., Manrique-Losada, L., Torres-Palma, R., Moncayo-Lasso, A., Hernández, F., 2018. 'An investigation into the occurrence and removal of pharmaceuticals in Colombian wastewater'. Sci. Total Environ. 642, 842-853.

Bouissou-Schurtz, C., Houeto, P., Guerbet, M., Bachelot, M., Casellas, C., Mauclaire, A.-C., Panetier, P., Delval, C., Masset, D., 2014. Ecological risk assessment of the presence of pharmaceutical residues in a French national water survey. Regul. Toxicol. Pharmacol. 69, 296-303.

Carballa, M., Fink, G., Omil, F., Lema, J.M., Ternes, T., 2008. Determination of the solid–water distribution coefficient (Kd) for pharmaceuticals, estrogens and musk fragrances in digested sludge. Water Res. 42, 287-295.

Carlsson, C., Johansson, A.-K., Alvan, G., Bergman, K., Kühler, T., 2006. Are pharmaceuticals potent environmental pollutants?: Part I: Environmental risk assessments of selected active pharmaceutical ingredients. Sci. Total Environ. 364, 67-87.

Castiglioni, S., Zuccato, E., Crisci, E., Chiabrando, C., Fanelli, R., Bagnati, R., 2006. Identification and measurement of illicit drugs and their metabolites in urban wastewater by liquid chromatography-tandem mass spectrometry. Anal. Chem. 78, 8421-8429.

Castrignanò, E., Lubben, A., Kasprzyk-Hordern, B., 2016. Enantiomeric profiling of chiral drug biomarkers in wastewater with the usage of chiral liquid chromatography coupled with tandem mass spectrometry. J. Chromatogr. A 1438, 84-99.

Castrignanò, E., Yang, Z., Bade, R., Baz-Lomba, J.A., Castiglioni, S., Causanilles, A., Covaci, A., Gracia-Lor, E., Hernandez, F., Kinyua, J., McCall, A.-K., van Nuijs, A.L.N., Ort, C., Plósz, B.G., Ramin, P., Rousis, N.I., Ryu, Y., Thomas, K.V., de Voogt, P., Zuccato, E., Kasprzyk-Hordern, B., 2018. Enantiomeric profiling of chiral illicit drugs in a pan-European study. Water Res. 130, 151-160.

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.

Chen, Z.-F., Ying, G.-G., 2015. Occurrence, fate and ecological risk of five typical azole fungicides as therapeutic and personal care products in the environment: A review. Environ. Int. 84, 142-153.

Clara, M., Strenn, B., Gans, O., Martinez, E., Kreuzinger, N., Kroiss, H., 2005. Removal of selected pharmaceuticals, fragrances and endocrine disrupting compounds in a membrane bioreactor and conventional wastewater treatment plants. Water Res. 39, 4797-4807.

Cleuvers, M., 2004. Mixture toxicity of the anti-inflammatory drugs diclofenac, ibuprofen, naproxen, and acetylsalicylic acid. Ecotoxicol Environ Saf 59, 309-315.

Daughton, C.G., 2005. "Emerging" Chemicals as Pollutants in the Environment:a 21st Century Perspective. Renewable Resources Journal 23, 6-23.

De Gusseme, B., Pycke, B., Hennebel, T., Marcoen, A., Vlaeminck, S.E., Noppe, H., Boon, N., Verstraete, W., 2009. Biological removal of 17α-ethinylestradiol by a nitrifier enrichment culture in a membrane bioreactor. Water Res. 43, 2493-2503.

de Jesus Gaffney, V., Almeida, C.M.M., Rodrigues, A., Ferreira, E., Benoliel, M.J.o., Cardoso, V.V., 2015. Occurrence of pharmaceuticals in a water supply system and related human health risk assessment. Water Res. 72, 199-208.

Deegan, A.M., Shaik, B., Nolan, K., Urell, K., Oelgemöller, M., Tobin, J., Morrissey, A., 2011. Treatment options for wastewater effluents from pharmaceutical companies. International Journal of Environmental Science & Technology 8, 649-666.

Desbrow, C., Routledge, E.J., Brighty, G.C., Sumpter, J.P., Waldock, M., 1998. Identification of Estrogenic Chemicals in STW Effluent. 1. Chemical Fractionation and in Vitro Biological Screening. Environ. Sci. Technol. 32, 1549-1558.

Díaz-Cruz, M.S., García-Galán, M.J., Guerra, P., Jelic, A., Postigo, C., Eljarrat, E., Farré, M., López de Alda, M.J., Petrovic, M., Barceló, D., Petrovic, M., Barceló, D., 2009. Analysis of selected emerging contaminants in sewage sludge. TrAC, Trends Anal. Chem. 28, 1263-1275.

Drewes, J.E., 2007. Chapter 4.1 Removal of pharmaceutical residues during wastewater treatment. in: Petrović, M., Barceló, D. (Eds.). Comprehensive Analytical Chemistry. Elsevier, pp. 427-449.

Ekpeghere, K.I., Sim, W.-J., Lee, H.-J., Oh, J.-E., 2018. Occurrence and distribution of carbamazepine, nicotine, estrogenic compounds, and their transformation products in wastewater from various treatment plants and the aquatic environment. Sci. Total Environ. 640-641, 1015-1023.

European Medicines Agency, 2018. https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-environmental-risk-assessment-medicinal-products-human-use-revision-1_en.pdf.

Evgenidou, E.N., Konstantinou, I.K., Lambropoulou, D.A., 2015. Occurrence and removal of transformation products of PPCPs and illicit drugs in wastewaters: A review. Sci. Total Environ. 505, 905-926.

Fitzgerald, R.L., 2009. Disposition of Toxic Drugs and Chemicals in Man, 8th Edition. Randall C. Baselt. Foster City, CA: Biomedical Publications, 2009, 1720 pp, $247.50. ISBN 978-0- 9626523-7-0. Clin. Chem. 55, 2232-2232.

Gabet-Giraud, V., Miège, C., Choubert, J.M., Ruel, S.M., Coquery, M., 2010. Occurrence and removal of estrogens and beta blockers by various processes in wastewater treatment plants. Sci. Total Environ. 408, 4257-4269.

Gavrilescu, M., Demnerová, K., Aamand, J., Agathos, S., Fava, F., 2015. Emerging pollutants in the environment: present and future challenges in biomonitoring, ecological risks and bioremediation. New Biotechnology 32, 147-156.

Geissen, V., Mol, H., Klumpp, E., Umlauf, G., Nadal, M., van der Ploeg, M., van de Zee, S.E.A.T.M., Ritsema, C.J., 2015. Emerging pollutants in the environment: A challenge for water resource management. International Soil and Water Conservation Research 3, 57-65.

Gogoi, A., Mazumder, P., Tyagi, V.K., Tushara Chaminda, G.C., An, A.K., Kumar, M., 2018. Occurrence and fate of emerging contaminants in water environment: A review. Groundwater for Sustainable Development 6, 169-180.

Guerra, P., Kim, M., Shah, A., Alaee, M., Smyth, S.A., 2014. Occurrence and fate of antibiotic, analgesic/anti-inflammatory, and antifungal compounds in five wastewater treatment processes. Sci. Total Environ. 473–474, 235-243.

Han, E.J., Lee, D.S., 2017. Significance of the abolites in the environmental risk assessment of pharmaceuticals consumed by human. Sci Total Environ 592, 600-607.

Hernando, M.D., Mezcua, M., Fern€ndez-Alba, A.R., Barcel€, D., 2006. Environmental risk assessment of pharmaceutical residues in wastewater effluents, surface waters and sediments. Talanta 69, 334-342.

Hernando, M.D., Rodríguez, A., Vaquero, J.J., Fernández-Alba, A.R., García, E., 2011. Environmental Risk Assessment of Emerging Pollutants in Water: Approaches Under Horizontal and Vertical EU Legislation. Crit. Rev. Environ. Sci. Technol. 41, 699-731.

Hong, H.N., Kim, H.N., Park, K.S., Lee, S.-K., Gu, M.B., 2007. Analysis of the effects diclofenac has on Japanese medaka (Oryzias latipes) using real-time PCR. Chemosphere 67, 2115-2121.

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.

Hyland, K.C., Dickenson, E.R.V., Drewes, J.E., Higgins, C.P., 2012. Sorption of ionized and neutral emerging trace organic compounds onto activated sludge from different wastewater treatment configurations. Water Res. 46, 1958-1968.

Inui, M., Adachi, T., Takenaka, S., Inui, H., Nakazawa, M., Ueda, M., Watanabe, H., Mori, C., Iguchi, T., Miyatake, K., 2003. Effect of UV screens and preservatives on vitellogenin and choriogenin production in male medaka (Oryzias latipes). Toxicology 194, 43-50.

Ivanová, L., Mackuľak, T., Grabic, R., Golovko, O., Koba, O., Staňová, A.V., Szabová, P., Grenčíková, A., Bodík, I., 2018. Pharmaceuticals and illicit drugs – A new threat to the application of sewage sludge in agriculture. Sci. Total Environ. 634, 606-615.

Jang, M., Yang, W., Jeong, S., Park, S., Kim, J., 2016. A fatal case of paramethoxyamphetamine poisoning and its detection in hair. Forensic Sci. Int. 266, e27-e31.

Jelic, A., Fatone, F., Di Fabio, S., Petrovic, M., Cecchi, F., Barcelo, D., 2012. Tracing pharmaceuticals in a municipal plant for integrated wastewater and organic solid waste treatment. Sci. Total Environ. 433, 352-361.

Jelic, A., Gros, M., Ginebreda, A., Cespedes-Sánchez, R., Ventura, F., Petrovic, M., Barcelo, D., 2011. Occurrence, partition and removal of pharmaceuticals in sewage water and sludge during wastewater treatment. Water Res. 45, 1165-1176.

Jelić, A., Gros, M., Petrović, M., Ginebreda, A., Barceló, D., 2012. Occurrence and Elimination of Pharmaceuticals During Conventional Wastewater Treatment. in: Guasch, H., Ginebreda, A., Geiszinger, A. (Eds.). Emerging and Priority Pollutants in Rivers: Bringing Science into River Management Plans. Springer Berlin Heidelberg, Berlin, Heidelberg, pp. 1-23.

Jiang, J.-Q., Zhou, Z., Sharma, V.K., 2013. Occurrence, transportation, monitoring and treatment of emerging micro-pollutants in waste water — A review from global views. Microchem. J. 110, 292-300.

Kapelewska, J., Kotowska, U., Karpińska, J., Kowalczuk, D., Arciszewska, A., Świrydo, A., 2018. Occurrence, removal, mass loading and environmental risk assessment of emerging organic contaminants in leachates, groundwaters and wastewaters. Microchem. J. 137, 292-301.

Kasprzyk-Hordern, B., Dinsdale, R.M., Guwy, A.J., 2009a. Illicit drugs and pharmaceuticals in the environment--forensic applications of environmental data. Part 1: Estimation of the usage of drugs in local communities. Environ Pollut 157, 1773-1777.

Kasprzyk-Hordern, B., Dinsdale, R.M., Guwy, A.J., 2009b. The removal of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs during wastewater treatment and its impact on the quality of receiving waters. Water Res. 43, 363-380.

Kasprzyk-Hordern, B., Dinsdale, R.M., Guwy, A.J., 2009c. The removal of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs during wastewater treatment and its impact on the quality of receiving waters. Water Res 43, 363-380.

Kołecka, K., Gajewska, M., Stepnowski, P., Caban, M., 2019. Spatial distribution of pharmaceuticals in conventional wastewater treatment plant with Sludge Treatment Reed Beds technology. Sci. Total Environ. 647, 149-157.

Kosma, C.I., Lambropoulou, D.A., Albanis, T.A., 2014. Investigation of PPCPs in wastewater treatment plants in Greece: Occurrence, removal and environmental risk assessment. Sci. Total Environ. 466-467, 421-438.

Kosonen, J., Kronberg, L., 2009. The occurrence of antihistamines in sewage waters and in recipient rivers. Environ. Sci. Pollut. Res. Int. 16, 555-564.

Lajeunesse, A., Smyth, S.A., Barclay, K., Sauve, S., Gagnon, C., 2012. Distribution of antidepressant residues in wastewater and biosolids following different treatment processes by municipal wastewater treatment plants in Canada. Water Res 46, 5600-5612.

Lapworth, D.J., Baran, N., Stuart, M.E., Ward, R.S., 2012. Emerging organic contaminants in groundwater: A review of sources, fate and occurrence. Environ. Pollut. 163, 287-303.

Li, W.C., 2014. Occurrence, sources, and fate of pharmaceuticals in aquatic environment and soil. Environ. Pollut. 187, 193-201.

Lin, D.L., Liu, H.C., Yin, H.L., 2007. Recent paramethoxymethamphetamine (PMMA) deaths in Taiwan. J. Anal. Toxicol. 31, 109-113.

Lindqvist, N., Tuhkanen, T., Kronberg, L., 2005. Occurrence of acidic pharmaceuticals in raw and treated sewages and in receiving waters. Water Res 39, 2219-2228.

Liu, J., Lu, G., Xie, Z., Zhang, Z., Li, S., Yan, Z., 2015. Occurrence, bioaccumulation and risk assessment of lipophilic pharmaceutically active compounds in the downstream rivers of sewage treatment plants. Sci Total Environ 511, 54-62.

Loos, R., Carvalho, R., Antonio, 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.

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.

Mao, H., Li, H., Li, Y., Li, L., Yin, L., Yang, Z., 2020. Four typical personal care products in a municipal wastewater treatment plant in China: Occurrence, removal efficiency, mass loading and emission. Ecotoxicol. Environ. Saf. 188, 109818.
Maruya, K.A., Schlenk, D., Anderson, P.D., Denslow, N.D., Drewes, J.E., Olivieri, A.W., Scott, G.I., Snyder, S.A., 2014. An Adaptive, Comprehensive Monitoring Strategy for Chemicals of Emerging Concern (CECs) in California's Aquatic Ecosystems. Integr. Environ. Assess. Manag. 10, 69-77.
Mastroianni, N., Postigo, C., de Alda, M.L., Barcelo, D., 2013. Illicit and abused drugs in sewage sludge: Method optimization and occurrence. J. Chromatogr. A 1322, 29-37.
Miege, C., Choubert, J.M., Ribeiro, L., Euscbe, M., Coquery, M., 2009. Fate of pharmaceuticals and personal care products in wastewater treatment plants - Conception of a database and first results. Environ. Pollut. 157, 1721-1726.
Molins-Delgado, D., Díaz-Cruz, M.S., Barceló, D., 2016. Ecological risk assessment associated to the removal of endocrine-disrupting parabens and benzophenone-4 in wastewater treatment. J. Hazard. Mater. 310, 143-151.
Naidu, R., Arias Espana, V.A., Liu, Y., Jit, J., 2016. Emerging contaminants in the environment: Risk-based analysis for better management. Chemosphere 154, 350-357.
Nakada, N., Tanishima, T., Shinohara, H., Kiri, K., Takada, H., 2006. Pharmaceutical chemicals and endocrine disrupters in municipal wastewater in Tokyo and their removal during activated sludge treatment. Water Res 40, 3297-3303.
Nath, T., Gogoi, M., Nath, P., 2018. Biotransformation of Terfenadine to Fexofenadine by Absidia corymbifera ATCC 14058.
Nesbitt, R., 2011. Effects of Chronic Exposure to Ibuprofen and Naproxen on Florida Flagfish (Jordanella Floridae) over One Complete Life-cycle. Master's thesis.

University of Ontario Institute of Technology, Oshawa, Canada.

https://ir.library.dc-uoit.ca/bitstream/10155/176/1/Nesbitt_Richard.pdf. https://ir.library.dc-uoit.ca/bitstream/10155/176/1/Nesbitt_Richard.pdf.
Nödler, K., Tsakiri, M., Aloupi, M., Gatidou, G., Stasinakis, A.S., Licha, T., 2016. Evaluation of polar organic micropollutants as indicators for wastewater-related coastal water quality impairment. Environ. Pollut. 211, 282-290.
Ogunlaja, O.O., Parker, W.J., 2015. Assessment of the removal of estrogenicity in biological nutrient removal wastewater treatment processes. Sci. Total Environ. 514, 202-210.
Onesios, K.M., Yu, J.T., Bouwer, E.J., 2009. Biodegradation and removal of pharmaceuticals and personal care products in treatment systems: a review. Biodegradation 20, 441-466.
Painter, M.M., Buerkley, M.A., Julius, M.L., Vajda, A.M., Norris, D.O., Barber, L.B., Furlong, E.T., Schultz, M.M., Schoenfuss, H.L., 2009. Antidepressants at environmentally relevant concentrations affect predator avoidance behavior of larval fathead minnows (Pimephales promelas). Environ. Toxicol. Chem. 28, 2677-2684.
Pal, A., He, Y., Jekel, M., Reinhard, M., Gin, K.Y.-H., 2014. Emerging contaminants of public health significance as water quality indicator compounds in the urban water cycle. Environ. Int. 71, 46-62.
Papageorgiou, M., Kosma, C., Lambropoulou, D., 2016. Seasonal occurrence, removal, mass loading and environmental risk assessment of 55 pharmaceuticals and personal care products in a municipal wastewater treatment plant in Central Greece. Sci. Total Environ. 543, 547-569.
Papageorgiou, M., Zioris, I., Danis, T., Bikiaris, D., Lambropoulou, D., 2019. Comprehensive investigation of a wide range of pharmaceuticals and personal care products in urban and hospital wastewaters in Greece. Sci. Total Environ. 694, 133565.
Petrie, B., Barden, R., Kasprzyk-Hordern, B., 2015. A review on emerging contaminants in wastewaters and the environment: Current knowledge, understudied areas and recommendations for future monitoring. Water Res. 72, 3-27.

Petrie, B., Youdan, J., Barden, R., Kasprzyk-Hordern, B., 2016. Multi-residue analysis of 90 emerging contaminants in liquid and solid environmental matrices by ultra-high-performance liquid chromatography tandem mass spectrometry. J. Chromatogr. A 1431, 64-78.

Petrović, M., Gonzalez, S., Barceló, D., 2003. Analysis and removal of emerging contaminants in wastewater and drinking water. TrAC, Trends Anal. Chem. 22, 685-696.

Postigo, C., Lopez de Alda, M.J., Barcelo, D., 2010. Drugs of abuse and their metabolites in the Ebro River basin: occurrence in sewage and surface water, sewage treatment plants removal efficiency, and collective drug usage estimation. Environ Int 36, 75-84.

Reyes-Contreras, C., Matamoros, V., Ruiz, I., Soto, M., Bayona, J.M., 2011. Evaluation of PPCPs removal in a combined anaerobic digester-constructed wetland pilot plant treating urban wastewater. Chemosphere 84, 1200-1207.

Richardson, S.D., Ternes, T.A., 2014. Water Analysis: Emerging Contaminants and Current Issues. Anal. Chem. 86, 2813-2848.

Rogers, H.R., 1996. Sources, behaviour and fate of organic contaminants during sewage treatment and in sewage sludges. Sci. Total Environ. 185, 3-26.

Rosal, R., Rodríguez, A., Perdigón-Melón, J.A., Petre, A., García-Calvo, E., Gómez, M.J., Agüera, A., Fernández-Alba, A.R., 2010. Occurrence of emerging pollutants in urban wastewater and their removal through biological treatment followed by ozonation. Water Res. 44, 578-588.

Rúa-Gómez, P.C., Püttmann, W., 2012a. Impact of wastewater treatment plant discharge of lidocaine, tramadol, venlafaxine and their metabolites on the quality of surface waters and groundwater. J. Environ. Monit. 14, 1391-1399.

Rúa-Gómez, P.C., Püttmann, W., 2012b. Occurrence and removal of lidocaine, tramadol, venlafaxine, and their metabolites in German wastewater treatment plants. Environmental Science and Pollution Research 19, 689-699.

Sagan, A., Panteli, D., Borkowski, W., Dmowski, M., Domański, F., Czyżewski, M., Goryński, P., Karpacka, D., Kiersztyn, E., Kowalska, I., Księżak, M., Kuszewski, K., Leśniewska, A., Lipska, I., Maciąg, R., Madowicz, J., Mądra, A., Marek, M., Mokrzycka, A., Poznański, D., Sobczak, A., Sowada, C., Świderek, M., Terka, A., Trzeciak, P., Wiktorzak, K., Włodarczyk, C., Wojtyniak, B., Wrześniewska-Wal, I., Zelwiańska, D., Busse, R., European Observatory on Health, S., Policies, 2011. Poland: health system review. World Health Organization Regional Office for Europe, Copenhagen.

Samaras, V.G., Stasinakis, A.S., Mamais, D., Thomaidis, N.S., Lekkas, T.D., 2013. Fate of selected pharmaceuticals and synthetic endocrine disrupting compounds during wastewater treatment and sludge anaerobic digestion. J. Hazard. Mater. 244–245, 259-267.

Semblante, G.U., Hai, F.I., Huang, X., Ball, A.S., Price, W.E., Nghiem, L.D., 2015. Trace organic contaminants in biosolids: Impact of conventional wastewater and sludge processing technologies and emerging alternatives. J. Hazard. Mater. 300, 1-17.

Sowada, C., Sagan, A., Iwona, K.-B., 2019. Poland Health System Review 2019. 21.

Stasinakis, A.S., 2012. Review on the fate of emerging contaminants during sludge anaerobic digestion. Bioresour. Technol. 121, 432-440.

Stuart, M., Lapworth, D., Crane, E., Hart, A., 2012. Review of risk from potential emerging contaminants in UK groundwater. Sci. Total Environ. 416, 1-21.

Styszko, K., Dudarska, A., Zuba, D., 2016. The Presence of Stimulant Drugs in Wastewater from Krakow (Poland): A Snapshot. Bull Environ Contam Toxicol 97, 310-315.

Suárez, S., Carballa, M., Omil, F., Lema, J.M., 2008. How are pharmaceutical and personal care products (PPCPs) removed from urban wastewaters? Reviews in Environmental Science and Bio/Technology 7, 125-138.

Suarez, S., Lema, J.M., Omil, F., 2010. Removal of Pharmaceutical and Personal Care Products (PPCPs) under nitrifying and denitrifying conditions. Water Res. 44, 3214-3224.

Sui, Q., Cao, X., Lu, S., Zhao, W., Qiu, Z., Yu, G., 2015. Occurrence, sources and fate of pharmaceuticals and personal care products in the groundwater: A review. Emerging Contaminants 1, 14-24.

Sun, Q., Lv, M., Hu, A., Yang, X., Yu, C.-P., 2014. Seasonal variation in the occurrence and removal of pharmaceuticals and personal care products in a wastewater treatment plant in Xiamen, China. J. Hazard. Mater. 277, 69-75.

Szymańska, U., Soltyszewski, I., Kuzemko, J., Wiergowska, G., Woźniak, M., 2019. Presence of antibiotics in the aquatic environment in Europe and their analytical monitoring: Recent trends and perspectives. Microchem. J. 147, 729-740.

Taylor, D., Senac, T., 2014. Human pharmaceutical products in the environment - The "problem" in perspective. Chemosphere 115, 95-99.

Ternes, T.A., Herrmann, N., Bonerz, M., Knacker, T., Siegrist, H., Joss, A., 2004. A rapid method to measure the solid-water distribution coefficient (Kd) for pharmaceuticals and musk fragrances in sewage sludge. Water Res. 38, 4075-4084.

Vasquez, M.I., Lambrianides, A., Schneider, M., K[illegible]mmerer, K., Fatta-Kassinos, D., 2014. Environmental side effects of pharmaceutical cocktails: What we know and what we should know. J. Hazard. Mater. 279, 169-189.

Veldhoen, N., Skirrow, R.C., Brown, L.L., van Aggelen, G., Helbing, C.C., 2014. Effects of acute exposure to the non-steroidal anti-inflammatory drug ibuprofen on the developing North American Bullfrog (Rana catesbeiana) tadpole. Environ Sci Technol 48, 10439-10447.

Verlicchi, P., Al Aukidy, M., Zambello, E., 2012a. 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.

Verlicchi, P., Al Aukidy, M., Zambello, E., 2012b. 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.

Verlicchi, P., Galletti, A., Petrovic, M., Barcel[illegible], D., 2010. Hospital effluents as a source of emerging pollutants: An overview of micropollutants and sustainable treatment options. Journal of Hydrology 389, 416-428.

Verlicchi, P., Zambello, E., Al Aukidy, M., 2013. Chapter 8 - Removal of Pharmaceuticals by Conventional Wastewater Treatment Plants. in: Petrovic, M., Barcelo, D., Pérez, S. (Eds.). Comprehensive Analytical Chemistry. Elsevier, pp. 231-286.

Vevelstad, M., Øiestad, E.L., Middelthon, G., Hasvold, I., Lilleng, P., Delaveris, G.J.M., Eggen, T., Mørland, J., Arnestad, M., 2012. The PMMA epidemic in Norway: Comparison of fatal and non-fatal intoxications. Forensic Sci. Int. 219, 151-157.

Wick, A., Fink, G., Joss, A., Siegrist, H., Ternes, T.A., 2009. Fate of beta blockers and psycho-active drugs in conventional wastewater treatment. Water Res. 43, 1060-1074.

Xu, N., Xu, Y.-F., Xu, S., Li, J. Tao, H.-C., 2012. Removal of estrogens in municipal wastewater treatment plants: A Chinese perspective. Environ. Pollut. 165, 215-224.

Yadav, M.K., Short, M.D., Gerber, C., van den Akker, B., Aryal, R., Saint, C.P., 2019. Occurrence, removal and environmental risk of markers of five drugs of abuse in urban wastewater systems in South Australia. Environ. Sci. Pollut. Res. Int. 26, 33816-33826.

Yang, Y., Ok, Y.S., Kim, K.-H., Kwon, E.E., Tsang, Y.F., 2017. Occurrences and removal of pharmaceuticals and personal care products (PPCPs) in drinking water and water/sewage treatment plants: A review. Sci. Total Environ. 596-597, 303-320.

Zenker, A., Cicero, M.R., Prestinaci, F., Bottoni, P., Carere, M., 2014. Bioaccumulation and biomagnification potential of pharmaceuticals with a focus to the aquatic environment. J. Environ. Manage. 133, 378-387.

Zhang, Y., Geißen, S.-U., Gal, C., 2008. Carbamazepine and diclofenac: Removal in wastewater treatment plants and occurrence in water bodies. Chemosphere 73, 1151-1161.

Zhou, S., Di Paolo, C., Wu, X., Shao, Y., Seiler, T.-B., Hollert, H., 2019. Optimization of screening-level risk assessment and priority selection of emerging pollutants – The case of pharmaceuticals in European surface waters. Environ. Int. 128, 1-10.

CRediT author statement

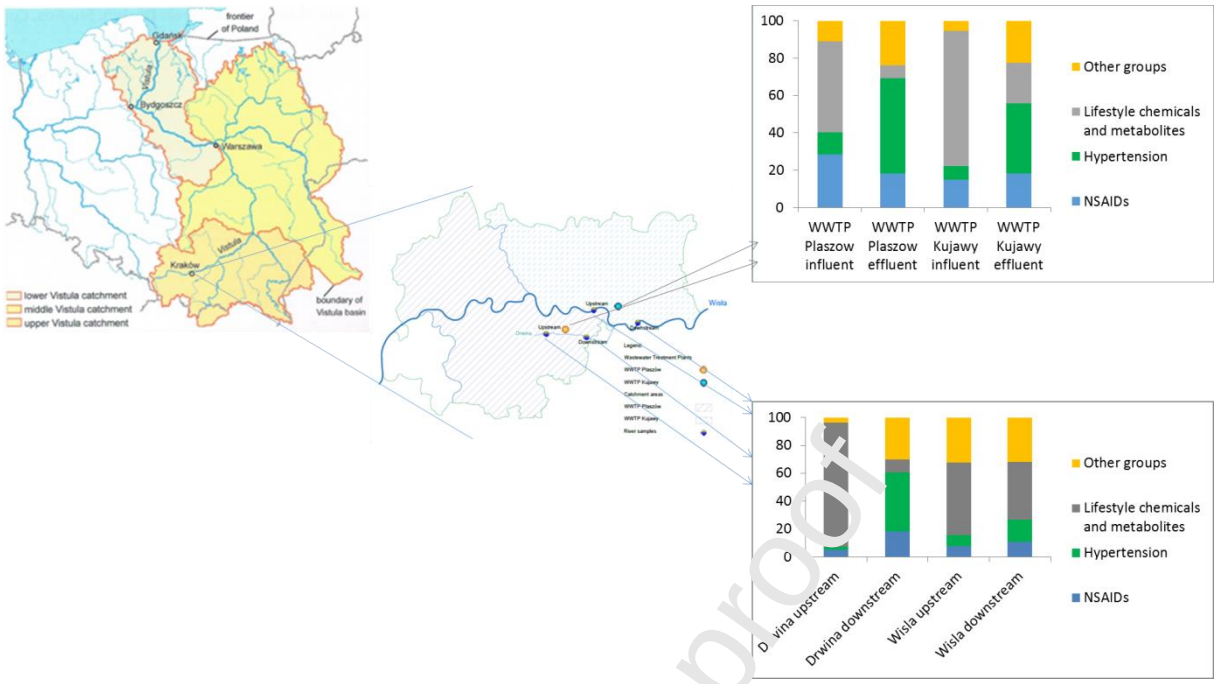
KSt, BK-H: Conceptualization, Methodology, **KSt, EC, KP**: Investigation, Validation, **KSt, BK-H, EC:** Data Curation, **KSt**: Writing – Original Draft, Visualization, **KSt, BK-H, EC, KP:** Writing-Review and Editing

Declaration of interests

☒ 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.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Graphical abstract



Highlights

- Lifestyle marker, hypertension have the highest contributions in WWTPs and waters
- The total mass loads of CECs in influents were reduced at over 95% in WWTPs
- Near 30% of detected CECs were removed by less 50%
- 20% of detected CECs increased concentrations in effluent
- RQ approach, potential to sorption were used for estimation of environmental risk