Examensarbete 30 hp
Mars 2020

Occurrence of organic micropollutants and hormones in Swedish surface water

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Summary

The occurrence and source distribution of organic micropollutants (OMPs) in Swedish surface waters has been studied through a target analysis. A total number of 23 rivers connected to the lakes Vänern, Vättern and Mälaren, 3 Wastewater treatment plants (WWTPs) and 3 Drinking water plants (DWTPs) located in the middle of Sweden was sampled. Compounds such as pharmaceuticals, industrial chemicals, pesticides, personal care products, hormones, PFASs, isoflavones, stimulants and parabens were selected and analysed using solid phase extraction (SPE) and Ultra-performance liquid chromatography tandem mass spectrometry (UPLC-MS/MS).

Of the 121 studied compounds 89 was detected in concentration levels varying between a few ng/L up to 160 µg L^{-1} in wastewater effluent. The detected concentrations of 78 compounds in surface water varied from low ng L^{-1} up to 3.3 µg L^{-1} and 35 OMPs could be found in levels from low ng L^{-1} up to 2.9 µg L^{-1} in the drinking water. The number of detected compounds and concentration levels decreases from wastewater influent to effluent, rivers, lakes and lastly to drinking water.

The concentration levels of OMPs in the surface water samples varied between sampling sites but clear differences between the three different lakes could not be established. Patterns of commonly detected compounds could however be seen in the samples and pharmaceuticals such as antibiotics and antidepressants were most frequently detected. Highest total OMP concentration levels were found in Enköping river (79 µg L^{-1}), Lövsta river (33 µg L^{-1}), Ösan (16 µg L^{-1}) and Lillån (13 µg L^{-1}) which makes these rivers the most polluted ones in this study and can therefore be seen as hot spots.

A risk assessment for drinking water with regard to human health was conducted for two compounds by calculating the Benchmark Quotient (BQ) using drinking water equivalent levels (DWELs). Two compounds, carbamazepine and bezafibrate, was selected based on detection frequency and available toxicity data. While bezafibrate didn't show any indications of risk to human health, carbamazepine had a BQ of 1.47 which indicates a risk to human health when humans are exposed to these concentration levels over a period of a lifetime.

Sammanfattning

Genom att använda en målanalys har förekomsten och källfördelningen av organiska mikroföroreningar i svenska ytvatten studerats. Vattenprover från 23 vattendrag som antingen mynnar ut i eller börjar i någon av sjöarna Vänern, Vättern eller Mälaren, tre avloppsreningsverk och tre dricksvattenverk i mellersta Sverige har samlats in. Ämnen så som läkemedel, industriella kemikalier, pesticider, hudvårdsprodukter, hormoner, PFAS-ämnen, isoflavoner, stimulanter och parabener valdes ut och analyserades med hjälp av fastfasextraktion och vätskekromatografi kopplad till masspektrometer (UPLC-MS/MS).

Av de 121 utvalde ämnens kunde 89 av dessa detekteras i koncentrationer som varierade mellan några få ng L^{-1} upp till 160 µg L^{-1} i utgående avloppsvatten. I ytvattnet kunde 78 av de organiska mikroföroreningarna detekteras i koncentrationer mellan låga ng L^{-1} upp till 3.3 µg L^{-1} medan endast 35 mikroföroreningar kunde detekteras i dricksvattnet. I dricksvattnet varierade koncentrationerna mellan några få ng L^{-1} upp till 2.9 µg L^{-1}. Resultatet visar att antalet detekterade organiska mikroföroreningar och deras respektive koncentrationer tydligt minskar i de olika matriserna från ingående avloppsvatten till utgående, vattendrag, sjöar och slutligen i dricksvattnet.

I ytvattenproverna varierade koncentrationsnivåerna av organiska mikroföroreningar mellan de olika vattendragen men tydliga skillnader mellan de tre olika sjöarna kunde inte säkerställas. Däremot gick det att se trender i vilka ämnen som vanligen detekterades i de olika proverna, särskilt bland läkemedlen då ämnen som är antibiotika-klassade eller hör till gruppen antidepressiva var vanligast förekommande. De högsta totala koncentrationerna av organiska mikroföroreningar kunde hittas i Enköpingsån (79 µg L^{-1}), Lövstaån (33 µg L^{-1}), Ösan (16 µg L^{-1}) samt Lillån (13 µg L^{-1}). Dessa fyra vattendrag är därmed de mest förorenade i denna studie och kan därför ses som särskilt förorenade punktkällor.

En riskanalys med hänsyn till människors hälsa gjordes på dricksvattnet genom att beräkna en referenskvot (BQ) med hjälp av ekvivalenta dricksvatten-nivåer (DWELs). De två ämnena karbamazepin och bezafibrat valdes på grund av deras detektionsfrekvens (FD) och tillgänglighet av toxicitetsdata. Bezafibrat visade ingen potentiell risk medan karbamazepin hade ett BQ-värde på 1,47 vilket indikerar en potentiell risk till människors hälsa om man utsätts för de funna koncentrationerna under hela sin livstid.

Popular science summary

Organic micropollutants (OMPs) is a group of compounds which include compounds such as pharmaceuticals, hormones, PFASs, pesticides, industrial chemicals, etc. They are commonly used in everyday life and many are designed for human and/or veterinary uses and are often persistent to degradation. These properties make the removal process in the WWTPs difficult which leads to a leakage of OMPs into the environment. Microorganisms can degrade OMPs to some extent in both WWTPs and in the environment, or the OMPs can be degraded as a result of sunlight, by sorption onto biomass in the WWTP or sorption into sediments when present in the environment. With microorganisms present, different bi- or transformation products can be formed and might cause negative effects on the aquatic environment. When present in the environment these OMP compounds and their biproducts can cause negative effects on aquatic organisms such as fish, mussels, algae, etc. As an example, painkillers and beta blockers have been shown to have negative physiological effects on mussels in the Baltic Sea.

Water is one of our most valuable resources since it's vital for all living things and also an important part of many human activities such as showering, flushing toilets, etc. In order to have clean water in the environment and in our taps, all wastewater has to be treated in wastewater treatment plants (WWTPs) before released into the environment as wastewater effluent. Other sources for the occurrence of OMPs in surface water is agricultural run-offs, effluents from hospitals or industries. When released into the receiving surface waters such as rivers and lakes, the effluent still contains compounds which are toxic to the aquatic environment. The same surface waters are used for producing drinking water in drinking water treatment plants (DWTPs) before getting to our taps.

OMPs does not occur individually in the environment, but in a mixture of numerous other compounds in different concentrations which all have different effects on the aquatic environment. Individually, these compounds may occur at harmless concentrations whereas the complicated combinations in the mixtures may be harmful. Therefore, it is important to study the occurrence and source distribution of OMPs in environmental waters such as surface waters.

Water samples from 23 different rivers, three WWTPs and three DWTPs were analysed in this study where the main aim was to study the occurrence and source distribution of OMPs in Swedish surface waters. The study was executed in order to assess the current state of the contamination caused by OMPs in rivers connected to either lake Vänern, Vättern or Mälaren.

The sampled waters were analysed, detected compounds could be determined and their respective concentrations was calculated. The results showed a clear decrease in the concentrations and amount of detected OMPs from wastewater influent to drinking water. However, some compounds could still be detected in the drinking water at low concentrations. The reason behind detected OMPs in the drinking water is the amount of detected OMPs in the surface waters.

Results from the river samples showed that various OMPs of different concentrations could be found in all samples proving that more advances treatment techniques are needed in order to reduce the occurrence and concentrations of OMPs in Swedish surface water. Four rivers had the overall highest total OMP concentrations: Enköping river, Lövsta river, Ösan and Lillån making these rivers the most polluted ones in this study. Therefore, these rivers can be seen as

hot spots for OMP contamination. All four rivers are impacted from WWTP effluents which could be the reason for higher concentration levels.

A risk assessment based on the results from the drinking water samples was calculated for two compounds, carbamazepine and bezafibrate. The results indicated a risk to human health caused by carbamazepine. The risk to human health is low due to the period of time for which a human has to be exposed to this high concentration of the compound. The period of time is a lifetime and one should not be afraid of drinking tap water since this value was only found in one DWTP.

Abbreviations

ARF	Average response factor
BAM	Dichlorobenzamide
BQ	Benchmark Quotient
DEET	Dietyltoluamide
DWEL	Drinking water equivalent level
DWTP	Drinking water treatment plant
EQS	Environmental quality standards
FD	Frequency of detection
HPLC	High performance liquid chromatography
IC	Industrial chemical
IS	Internal standard
LC	Liquid chromatography
LOQ	Limit of quantification
ME	Matrix effect
MQ	Milli-Q water
MS	Mass spectrometry
MST	Matrix matching standard
NS	Native standard
NSAID	Non-Steroidal Anti-Inflammatory Drug
OMP	Organic micropollutant
PE	Population equivalent
PFASs	Per- and polyflouroalkyl Substances
PP	Polypropylene
SPE	Solid phase extraction
UPLC-MS/MS	Ultra-high-Pressure Liquid Chromatography tandem Mass Spectrometry
WFD	Water Frame Directive
WWTP	Wastewater treatment plant

Innehåll

1 Introduction

In the modern society, organic micropollutants (OMPs) are used all over the world in large quantities but their potential to reach surface waters and their impact on the aquatic environment has not yet gotten the attention they need. The Water Framework Directive (WFD) came into force in December 2000 and establishes a framework in order to protect inland surface waters, coastal waters, transitional waters and groundwater. Improving the aquatic environment through measurements against priority substances, substances with a significant risk to or via the aquatic environment, is one of the objectives of the WFD (Whalley et al., 2018).

Pharmaceuticals (antidepressants, painkillers, antibiotic, etc.) and hormonal drugs (contraceptive pills, thyroid drugs, etc.) are commonly used for the treatment of different diseases or symptoms in the everyday life of humans or veterinary purposes. Many of these compounds are designed for human and/or animal usage and many of them are very persistent to degradation. The substances reach the Wastewater treatment plants and are thereafter spread into the environment. Take antibiotic substances, they are widely used and when secreted they entail release of substances which increases the risk for development of antibiotic resistant bacteria (Helmfrid et al., 2006).

1.1 Aim of the study

The main aim of this master project is to study the occurrence and source distribution of OMPs in Swedish surface waters by answering the following questions

I. Is there a clear decrease in the concentrations of OMPs from wastewater to drinking water?
II. Is there a clear difference in occurrence and concentrations of OMPs in rivers connected to the lakes Vänern, Vättern and Mälaren and can any hot spots be established??
III. Are there any risks to human health related to OMPs in drinking water from drinking water plants (DWTPs) connected to lake Vänern, Vättern or Mälaren?

1.2 Limitations

Limitations for this project is a target analysis. In this study, a total amount of 121 compounds were analysed and the selection of compounds was done based on the previous study by Rehrl et al. (2020). This limitation was set since the true number of occurring compounds in the water bodies are impossible to know and therefore a nontarget analysis should be performed.

2 Background and Theory

2.1 OMPs in the environment

Water is a very important resource for all living organisms and human activities like industry, agriculture and domestic use. However, humans often take this resource for granted and several organic micropollutants (OMPs) end up in environmental compartments due to reasons like human ignorance and lack of legislation (Barbosa et al., 2016; Whalley et al., 2018). Several studies have shown the occurrence of OMPs in the aquatic environment such as surface water, groundwater and even drinking water at concentrations varying between ng L^{-1} up to µg L^{-1}

(Barbosa et al., 2016; Ericson et al., 2010; Fick et al., 2010; Petrie et al., 2015; Ternes et al., 2015).

It is well known that OMPs have a negative impact on the aquatic environment including aquatic organisms such as fish, mussels, algae, etc. (Ericson et al., 2010; Helmfrid et al., 2006). The known effects are almost exclusively negative for the aquatic environment. It was shown that well known non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and diclofenac and beta blocker propranolol have negative physiological effects on Baltic Sea blue mussels (Ericson et al., 2010). The same study showed that mussels exposed to concentrations of these compounds both individually (diclofenac 100 μgL^{-1}, ibuprofen 1000 and propranolol 5000 μgL^{-1}) and as a mixture (25/75 combination of propranolol and diclofenac in the concentrations 1000 μgL^{-1}) for two weeks, had a lower scope of growth due to less available energy for metabolism. Additionally, the mussels had a lower byssus strength and a lower abundancy of byssus threads, which reduces the mussel' ability to attach to the underlying surface. Psychiatric pharmaceuticals such as anxiolytics and antidepressants have been shown to bioconcentrate in fish tissue such as the brain and liver (McCallum et al., 2017). McCallum et al., (2017) showed that oxazepam increased boldness in European perch while fluoxetine made guppies slower in their respond to threats by reducing the predator response behaviours. However, in the environment, the compounds occur as a complex mixture of different OMPs such as pharmaceuticals, pharmaceutical residues, pesticides, industrial chemicals, hormones, PFASs, etc. and all in varying concentrations of individual compounds in these mixtures which makes it almost impossible to predict the actual effects on the aquatic environment (Barbosa et al., 2016; Wallberg et al., 2016; Whalley et al., 2018). This phenomenon is usually referred to as the cocktail effect, whereby mixtures of compounds that may individually occur at harmless concentrations may affect health and other due to formed complicated combinations (Whalley et al., 2018).

2.2 Wastewater treatment plants

Municipal wastewater treatment plants are designed to treat wastewater derived from households, which basically means they are supposed to treat water with oxygen-consuming substances, easily degraded organic matter (DOM), nitrogen and phosphorus (Helmfrid et al., 2010, 2006). The majority of the WWTPs in Sweden are so called conventional WWTPs and include a combination of mechanical, chemical and biological treatment steps. The first step is the mechanical which separates solid particles like toilet paper, cotton swabs, etc. In the second step, the chemical cleaning, a chemical coagulant is added in order to remove the phosphorus by precipitation. The precipitate forms a sludge which is removed and treated separately while the water continues to the third step which is the biological. Microorganisms removes nitrogen, organic material and remaining phosphorus, often in an so-called activated sludge process (Naturvårdsverket, 2017). Pharmaceutical residues and other organic micropollutants will therefore partially pass the WWTPs and reach the recipient water unchanged and undegraded.

Many OMPs are persistent and most of the pharmaceuticals are designed to endure transport and storing in order to reach its organ of target in the human body without degrading (Wallberg et al., 2016). In order to be secreted most of the pharmaceuticals have a high water solubility,

described as log Kow (or sometimes log Pow or log P) which also affects their ability to bioaccumulate (Wallberg et al., 2016).

The concentrations of different OMPs in the environment depends not only on usage and the WWTPs ability to remove them, but also on the physical-chemical properties of the compounds. Several studies show higher concentrations and amount of detected compounds in the influent wastewater as compared with the effluent, but the effluent water still contains a large number of both parent compounds and metabolites (Helmfrid et al., 2010, 2006; Petrie et al., 2015). Humans often consume the parent compound which then gets excreted from the human body as a number of correlated metabolites but some compounds will pass the body completely intact (Helmfrid et al., 2006; Petrie et al., 2015). Ibuprofen is one example, it gets excreted as a mixture of only 1 % unchanged drug (parent compound) and different metabolites after ingestion (Petrie et al., 2015).

Like the parent compounds, the corresponding metabolites can be very persistent, and, in some cases, they can be transformed back to the active substances (parent compounds). This makes them especially hard to remove during the secondary wastewater treatment which results in their release into the environment (Helmfrid et al., 2006; Petrie et al., 2015; Wallberg et al., 2016).

The removal in the WWTPs can vary between different OMPs from a physically driven process (adsorption) to biologically mediated enzymatic reactions (biodegradation) (Petrie et al., 2015). The physical-chemical properties such as hydrophobicity and water solubility, plays a crucial role in the fate of the compound and determines how and if it will degrade. Sorption onto biomass during the treatment in WWTP or onto the sediments when present in the environment is one option for some compounds (Wallberg et al., 2016). This will however only result in a decrease of the compound in one phase (liquid) and an increase in another (solid). Some antibiotics have a high affinity to solid organic matter which results in their sorption in the WWTP.

Biodegradation is another common possibility for removing OMPs from the aqueous phase of both wastewater and surface waters. However, this process causes the formation of a number of different degradation or transformation products (Petrie et al., 2015; Wallberg et al., 2016). Degradation due to photolysis is also a possibility and this has been proven to be successful for several compounds (Petrie et al., 2015). Nonetheless, as with biological degradation, the removal is not an indication of complete mineralisation and the occurrence of transformation products may be observed. Studies show that even if the parent compound is removed, the result may not be equal to a reduction in toxicity (Petrie et al., 2015; Wallberg et al., 2016)

Fick et al. (2011) performed a national screening in Sweden during 2010 where they included a total of 101 pharmaceuticals and the results showed 92 detected pharmaceuticals in WWTP influent. The found levels ranged from low ngL^{-1} up to 549 μgL^{-1}. However, the removal efficiencies in this study could not be calculated for all compounds since some were only detected in influent and not effluent wastewater. They also showed negative removal rates which indicates an increase in concentrations due to deconjugation of metabolites.

2.3 Surface water

Surface waters include all waters found on the Earth's surface such as rivers and lakes. These water bodies are of outmost importance for all living organisms on Earth and human activities such as agriculture, industrial use and drinking water. OMPs in surface waters originate from sources such as industrial wastewater, agricultural runoff, livestock and agriculture, landfill leakage, domestic and hospital effluents (Barbosa et al., 2016). The concentrations of many OMPs decreases in the WWTPs, as described above, brownification is however a growing problem for the photodegradation in northern Europe and North America. The presence of dissolved organic matter and other particles may negatively affect the degradation kinetics of some compounds in surface waters by clouding the sunlight intensity (Petrie et al., 2015; Vinterstare, 2016).

Implemented regulations on management of industrial effluents has improved the surface water quality in several European countries but an improvement and stricter regulations in other regions of the world are still needed (Barbosa et al., 2016). Although the discharges are being better controlled there's still a lack of proper European Union legislation that obligate surface water quality monitoring of OMPs (Lindim et al., 2016). Screening surveys have however been conducted and Petrie et al. (2015) reported that approx. 70 different pharmaceuticals of variable therapeutic classes have been detected in UK surface waters. According to another screening programme, Fick et al. (2011) found 66 pharmaceuticals in the range from low ngL^{-1} up to 1.8 μgL^{-1} in surface water samples. The detected concentrations were in a comparable range with lower ranges found in a European-wide study (Fick et al., 2011).

A lack in knowledge of disposed wastewater effluent volume and discharge of the river at the sampling point makes the comparison of detected OMP concentrations in wastewater effluent and the recipient surface water difficult. Assumptions can still be made based on the fact that higher effluent concentrations means higher emissions resulting in higher concentration levels in rivers (Lindim et al., 2016). Concentration levels found in the rivers are however much lower than in the effluent due to a higher flow rate which leads to dilution (Barbosa et al., 2016; Sörengård et al., 2019).

2.4 Drinking water treatment plants

Modern treatment processes exist in order to provide lines of defence (or so-called barriers) between waterborne diseases and the consumer. The treatment process train of the Drinking water treatment plant (DWTP) depend on the raw water source (type and contamination) (Gerba, 2009; Svenskt Vatten, n.d.). The raw water sources used for drinking water in Sweden are almost equally divided between surface water and groundwater where approximately 50 % of the groundwater fraction comes from artificial groundwater (Tröger et al., 2018). Artificial groundwater is another expression for infiltrated surface water. An increasing number of OMPs in the water sources obstructs production of drinking water and calls for more advanced treatment. Sand filtration and flocculation are two examples of conventional treatment processes primarily developed and used in order to remove pathogens and nutrients. However, their ability to remove OMPs have been proven insufficient. Modern treatment techniques such as nanofiltration and reverse osmosis membrane treatment have been proven effective in the removal of OMPs while other techniques such as granulated active carbon (GAC) filtration can

only decrease the levels. The effectiveness of GAC generally decreases with time of use and complete removal of OMPs cannot be achieved. The effective treatment techniques can be efficient in small-scale but are impractical in full-scale DWTPs due to high OMP concentrations in the retentate (Tröger et al., 2018). When DWTPs are insufficient in their removal of OMPs human exposure and bioaccumulation of hazardous compounds may increase. In addition to insufficient removal, Swedish DWTPs are required to monitor only a limited number of organic compounds (20 OMPs, besides pesticides) due to Swedish regulations (Tröger et al., 2018).

2.5 Analysis of OMPs

Environmental samples like surface water or wastewater is complex matrices with unknown interferences (Krauss et al., 2010). Liquid chromatography (LC) tandem to mass spectrometry (MS) is one analytical method which is commonly used for analysis of OMPs in such complex matrices

Liquid chromatography means that the dilute is being transported by a liquid through a stationary phase and the mass spectrometry analyses and identifies the mass and structure of a molecule. The two key elements in order for the separation of the sample to work in the LC is having a liquid mobile phase in which the analyte is diluted and a stationary phase represented by the column (Simonsen and Lindegren, 2005). But in order to identify the compound one must also know it's physical-chemical properties and polarity since they determine the retention time (RT) of the compound. Especially the polarity plays an important role in the identification process and in which type of column one chooses since the column affects both the resolution and run time in LC (Simonsen and Lindegren, 2005; Stroobant et al., 2007).

When working with target analysis of non-volatile compounds the triple quadrupole mass spectrometer is a broadly established method, still there is some restrictions for suspect and non-target screening (Krauss et al., 2010; Stroobant et al., 2007). This method uses a principle of a three-step process which involves two stages of mass analysis (MS/MS) via two mass spectrometers. The column separates the target OMPs by electrospray ionization before the analysis in the mass spectrometer where the compound and its fragments can be determined in order to both quantify and qualify the target compound (Krauss et al., 2010). Furthermore, the chromatographical column has to be able to separate the target compounds from endogenous substances with similar retention times in order to avoid false positives identification and also keep the limit of quantification (LOQ) low (Krauss et al., 2010).

3 Materials and Method

3.1 Chemicals and reagents

Ultrapure water was used for the chemical analysis and generated by a Milli-Q (MQ) Advantage Ultrapure Water purification system and then filtered through a 0.22 µm Millipak Express membrane and an LC-Pak polishing unit (Merk Millipore, Billerica, MA). Methanol, acetonitrile, ammonium acetate and ethyl acetate of high analytical grade were obtained from Sigma-Aldrich (Sweden).

All analytical standards that were used for analysis were of high purity grade (>95 %). The native standards (NSs) (n=121) originated from Sigma-Aldrich (Sweden) and the isotopically labelled standards (ISs) (n=26) for the target compounds were acquired from Wellington

Laboratories (Canada), Teknolab AB (Kungsbacka, Sweden), Sigma-Aldrich (Sweden) and Toronto Research Chemicals (Toronto, Canada). Additional and detailed information about the native and internal standards can be found elsewhere (Rostvall et al., 2018).

All samples were filtered through a glass microfibre filter (grade GF/F, Whatman, thickness 0.42 mm, pore size 0.7 µm) purchased from Millipore (Cork, Ireland). Oasis HLB SPE cartridges (200 mg, 6 mL) were used for the solid phase extraction (SPE) and purchased from Waters Oasis, MA, USA.

3.2 Selected compounds

A total amount of 121 compounds were selected for evaluation in this project, including 75 pharmaceuticals, 13 hormones, 13 PFASs, 8 industrial chemicals, 4 personal care products, 3 parabens, 2 stimulants, 2 pesticides and 1 isoflavone. The pharmaceuticals cover a number of therapeutic groups like antibiotics, anticancer, antidepressants, antidiabetics, antidiarrheal, antifungals, antihistamines, antihypertensives, antilipemic agents, antipsychotics, antisecretory agents, beta blockers, diuretics, non-steroidal anti-inflammatory drugs (NSAID) and sedatives. Target compounds were selected based on information in the literature, on their occurrence and ubiquity in aquatic environments and on their human use and consumption. A list of selected compounds can be found in Table A1 in Appendix.

3.3 Study sites and sample collection

The wastewater samples were collected from 3 WWTPs as 24-hour composite samples/grab samples in September 2019 and the surface water samples during one week in October 2019. The sampling bottles were rinsed three times before being filled with the samples. All samples were then stored at -20 °C at the Department for Aquatic Sciences and Assessment at SLU.

Surface water was collected in 1 L PP bottles as grab samples from 23 rivers connected to either Vänern, Vättern or Mälaren. All three lakes are located in the middle of Sweden, FiguresFigure 1Figure 2,Figure 3.. The lakes are the three biggest lakes in Sweden and are major suppliers for drinking water production in the area.

Lake Mälaren is the third largest in Sweden with its surface area of 1 140 km^2 maximum depth of 64 m, water residence time 2.2 years. The drainage basin covers ca 5 % of Sweden's land area and is characterized by 57 % forest area, 20 % agricultural area and 11 % water bodies (Sonesten et al., 2013). Surrounded by cities such as Västerås in the west, Uppsala in the north, Stockholm in the east and Eskilstuna and Södertälje in the south, this area is considered to be one of the fastest economically expanding regions in Sweden. The population increase in Stockholm is also considered to be one of the greatest increases during the next five years in Europe ("Stockholms Handelskammare - Stockholm is fastest growing city in Europe," n.d.). Since the lake is surrounded by a large number of cities it is affected by a number of wastewater discharges and is the main source for drinking water in the Stockholm area (Naturvårdsverket, 2017). The thirteen rivers connected to Mälaren that was chosen and sampled are: Fyris river, Örsunda river, Enköping river, Arboga river, Oxundna river, Kolbäck river, Saga river, Lövsta river, Märsta river, Norrström, Svartån, Hedströmmen and Eskilstuna river. All sampling points around Mälaren, **Fel! Hittar inte referenskälla.**. A complete list of all surface water samples can be found in Table B1 in Appendix B.**Fel! Hittar inte referenskälla.**

Figure 1: Sampling points around Mälaren lake. Miljödata-MVM [2020]. Swedish University of Agricultural Sciences (SLU). National data host lakes and watercourses, and national data host agricultural land, http://miljodata.slu.se/mvm/ [2020-01-07]

Lake Vättern has an area of ca 1 900 km^2 which makes it the second largest lake in Sweden and reaches from Askersund in the north to Jönköping in the south. Maximum depth is 128 m, the water residence time is 58—60 years and it provides around 250 000 pe with drinking water (Christensen et al., 2007). It has a small drainage basin for its size and that's mainly due to its topographic location in comparison with the enclosing land area. The drainage basin covers almost 1 % of Sweden's land area and consists mainly of forest and agricultural areas (Christensen et al., 2007). There are 148 incoming rivers where the biggest one in Huskvarna river and the outlet of the lake is mainly Motala stream (SMHI, n.d.). Four rivers connected to lake Vättern was selected and sampled: Lillån, Munksjön, Huskvarna river and Motala stream. All sampling points around Vättern are shown in Figure 2.

Figure 2: Sampling points around Vättern. Miljödata-MVM [2020]. Swedish University of Agricultural Sciences (SLU). National data host lakes and watercourses, and national data host agricultural land, http://miljodata.slu.se/mvm/ [2020-01-07].

Vänern is the largest lake in Sweden with its area of 5 450 km^2 and the third largest in Europe (SMHI, n.d.). The lake reaches from Karlstad in the north to Trollhättan in the south and surrounded by Gullspång and Götene among others in the east and Säffle and Vänersborg among others in the west. Vänern provides around 800 000 pe with drinking water, has a maximum depth of 106 m, water residence time is 8—9 years and the drainage basin covers 10 % of Sweden's land area (Christensen et al., 2007; SMHI, n.d.). The drainage basin is dominated by forest area with just over 60 % and mostly agricultural area in the south. Five rivers connected to lake Vänern was selected and sampled: Göta river, Tidan, and three different point in Klar river. All sampling points around lake Vänern are shown in Figure 3

Figure 3: Map of lake Vänern with all sampling sites. Miljödata-MVM [2020]. Swedish University of Agricultural Sciences (SLU). National data host lakes and watercourses, and national data host agricultural land, http://miljodata.slu.se/mvm/ [2020-01-07]

3.4 Sample preparation

The sample preparation and analysis was performed on the dissolved aqueous phase with solid phase extraction (SPE) using a validated method described by Rehrl et al. (2020). All water samples (approximately 500 mL aliquot) including blanks (n=3) were extracted by SPE.

In short, all water samples were filtered with pre-baked (550 ˚C for 24 h) glass fibre filters (GFF, 0.45 µm, What-man, GE Healthcare, IL, USA). Aliquots of 500 mL for each sample were transferred to pre-rinsed (methanol) 1 L PP bottles. Every sample was spiked with 20 ng of the ISs mixtures per aliquot of the samples (Sörengård et al., 2019).

For the SPE, 200 mg HLB cartridges (Waters Oasis, MA, USA) were used for all samples. The cartridges were all pre-conditioned with 6 mL methanol followed by 6 mL Milli-Q water by gravity. The samples were then loaded onto the SPE reservoirs and was loaded on the SPE cartridges at a rate of approx. one drop per second. The SPE cartridges were dried and therefore eluted two times with 4 mL methanol into 15 mL PP-tubes (Corning™). A gentle stream of nitrogen gas was then used to evaporate all eluted samples until reaching a volume of 0.5 mL. The extracts were then transferred to 1.5 mL auto-injector glass vials (Eppendorf, Germany) and the walls of the PP-tubes were rinsed thrice with 200 µL methanol before being transferred to the same vials. A volume of 0.5 mL Milli-Q was added to the extracts and the extracts was vortexed for 30 s before analysis (Sörengård et al., 2019).

3.5 Instrumental analysis

The different water samples were analysed by a DIONEX UltiMate 3000 ultra-performance liquid chromatography (UPLC) system (Thermo Scientific, Waltham, MA, USA) coupled to a

triple quadrupole mass spectrometer (MS/MS) (TSQ QUANTIVA, Thermo Fisher Scientific, Waltham, MA, USA). As analytical column an Acquity UPLC BEH-C18 column (50 mm × 2.1 i.d., 1.7 µm, Waters Corporation, Manchester, UK) was used for chromatographic separation of target OMPs. The mobile phase consisted of Milli-Q with 5 mM ammonium acetate and acetonitrile. The flow rate was 0.5 mL min^{-1} and run time was 15 min using switching positive and negative electrospray ionization modes. A 11-point calibration curve from 0.01 to 500 ng mL^{-1} were prepared for the data evaluation. Using TraceFinder™ software (Thermo Fisher Scientific, MA, USA) the instrumental data was evaluated using.

3.6 Quality assurance

In order to test the performance of the method linearity, limit of quantification (LOQs), relative recovery, precision, blanks and matrix effect (ME) was assessed. An eleven-point calibration curve in the concentration range from 0.01 ng/L to 500 ng/L were prepared in order to test the linearity. The linearity of the calibration curves was assessed by calculating the coefficient of determination (R^2). The linearity parameters of each compound can be found in in Table D1 in Appendix D.

LOQ values was calculated as half of the lowest calibration point in the calibration curve where the standard deviation of the average response factor (ARF) was < 30 %. The corresponding peak area to this concentration was then used for calculating LOQ for each individual compound in each sample, see Table D1 in Appendix D.

The absolute recovery describes the efficiency of the sample preparation step by showing the proportion of obtained analyte from the sample during the sample preparation (Kruve et al., 2015). The performance of the extraction method (SPE and UPLC-MS/MS) is done by calculating the absolute recovery by creating so-called fortified samples. Fortified samples were prepared by spiking a known concentration of NS to the samples before SPE extraction, and then correlating it with the detected concentration after extraction and analysis. The fortified samples were spiked with 100 ng of NS and 20 ng of ISs per aliquots of the sample. The average absolute recovery for each analyte can be found in Table D1 in Appendix D.

The repeatability of the study is a way of evaluating the precision of the method and is done by preparing duplicates for every tenth sample. The resulting values enables a comparison of the analysis within a batch of samples and between different batches.

Both the mass and the retention time of a compound is relevant for the detection by the instrument (UPLC-MS/MS). Therefore, using isotopically labelled standards is the optimal approach (European Commission, 2002). That is the ideal case but due to inaccessibility some target compounds in this study could not be matched with the perfectly designed IS, therefore a replacement IS had to be selected. The replacement IS has to have as similar physical-chemical properties, retention time and categorial grouping of the compound as possible in order to achieve acceptable recovery rates for the compounds (European Commission, 2002)

Environmental water samples are not pure water and a mixture of wanted or expected target compounds, the samples also contain unknown compounds which must take into consideration. The exact content of the water is impossible to predict since it's a mixture of various endogenous substances like lipids, proteins, salts, minerals etc. that together or individually can greatly

affect both the extraction and analysis. This is generally referred to as matrix effect and can result in a suppressive or enhancing ion effect. In order to address the matrix effect matrix matching standards (MSTs) were prepared and used. Since the matrix effect is different for every type of sample five different matrices (wastewater influent, wastewater effluent, rivers, lakes, drinking water) were used when comparing all types of samples, and three different matrices (Vänern, Vättern, Mälaren) were used when comparing the surface waters.

MSTs were prepared for each matrix by spiking 20 ng of the ISs and 100 ng of NS per aliquot of sample before analysis.

The ME was calculated by subtracting the peak area/IS ratio determined in non-spiked samples from the peak area/IS ratio in MST samples. Matrix effects were calculated in order to see if there were an ion enhancement or suppression, Table D1 in Appendix D. Negative values means there is an ion suppression while positive values mean there is an ion enhancement.

Each batch of analysis included two blanks containing MQ water and MeOH. This was done in order to eliminate any concerns of contamination and to facilitate memory effects during analysis in the instrument. During the extraction all PP-bottles and SPE reservoirs were rinsed three times with methanol to avoid any contamination. Adapters, stop-cocks from the SPE and needles from the evaporation step were ultrasonicated for 15 mins, twice with methanol or three times with ethanol. Additionally, all analytical work was operated whilst wearing gloves.

3.7 Risk assessment

OMPs doesn't only have negative effects on the aquatic environment, when present in drinking water they can impose a risk on human health (Couto et al., 2019). Many of them have guidelines which describes the highest concentration of which the compound can appear in drinking water, without any negative effects on human health. In order to get a risk assessment of the OMPs the drinking water equivalent levels (DWELs) was calculated with Eq. (1)

$$DWEL = \frac{TDI * M * f}{V} \qquad (1)$$

Where TDI represents the Tolerable Daily Intake (µg/kg bw/day), M is the body weight (60 kg), f represents the drinking water allocation (adopted value 0.2) and V represents the personal drinking water consumption (2 L/day) (Couto et al., 2019). The risk was then assessed by calculating the Benchmark Quotient (BQ) as a ratio between the maximum or mean drinking water concentration and the DWEL value. BQ values of 1 represents a perfect match with the DWEL which makes the water potable. If the BQ ≥ 1 in the drinking water, a potential risk to human health can be observed if exposed to this concentrations over a period of life (Couto et al., 2019).

4 Results

A total number of 121 OMPs have been analysed in five different matrices (wastewater influent, wastewater effluent, rivers, lakes and drinking water).

4.1 Differences between matrices

The difference in occurrence of OMPs in the studied water samples is show in Figure 4. The concentrations in each sample has been summarised for every compound and before plotted in

a boxplot the log10 was used. Negative values represent concentrations in the range between 0-1 ng L^{-1} and the logarithmic values were set to 1 for the summed concentrations equal to zero. It is clear that all three groups of compounds are present in wastewater influent, effluent and rivers. It can be argued that PFAS are stable in the same matrices since the boxplots are similar for these cases (Mazzoni et al., 2019). Both pharmaceuticals and hormones on the other hand decrease in concentrations in the wastewater and rivers, whereas the majority of the compounds were absent in both lakes and drinking water. This may be explained by the dilution effect since the water volume in the river is big and due to a larger distance from the effluent discharges.

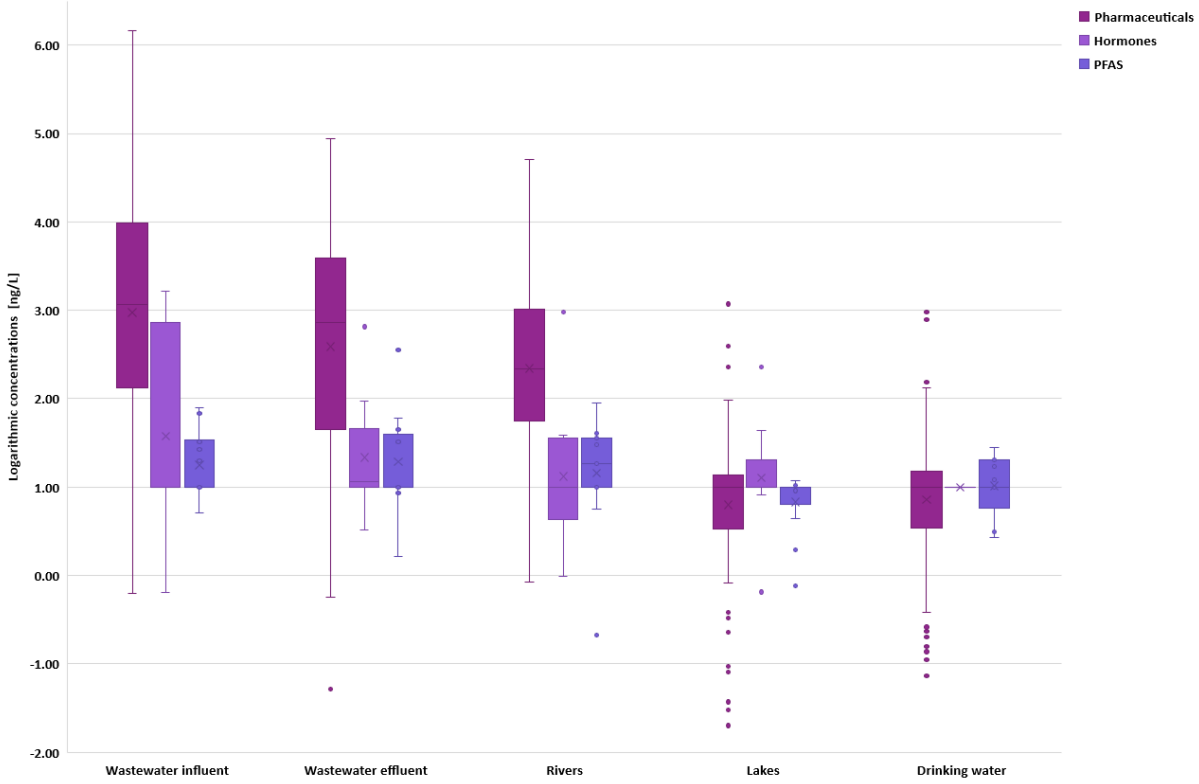

Figure 4: Boxplot of logarithmic concentrations of OMPs (Pharmaceuticals, PFAS and hormones) in different matrices (wastewater influent, wastewater effluent, rivers, lakes and drinking water).

4.2 Frequency of detection

Frequency of detection (FD) was calculated for every compound in order to see how often they were detected in the samples. This was done by dividing the number of positive samples for each compound by the total number of samples. The resulting FD can be seen in figures 5 and 6 for all compounds with a FD > 50 % and all FDs can be found in in Table C1 in Appendix C. The majority of the OMPs (76 of 95) could be found in more than 50 % of the wastewater samples while others couldn't be found due to a decrease during the treatment steps. Pyrimethamine and paroxetine were two compounds that were detected in effluent but not the influent, suggesting that metabolites of these compounds have been transformed back to the parent compound (Helmfrid et al., 2006; Petrie et al., 2015; Wallberg et al., 2016). 4-Chloro-3-methylphenol and ethylparaben were only detected in the influent wastewater which could suggest a successful removal in the WWTPs.

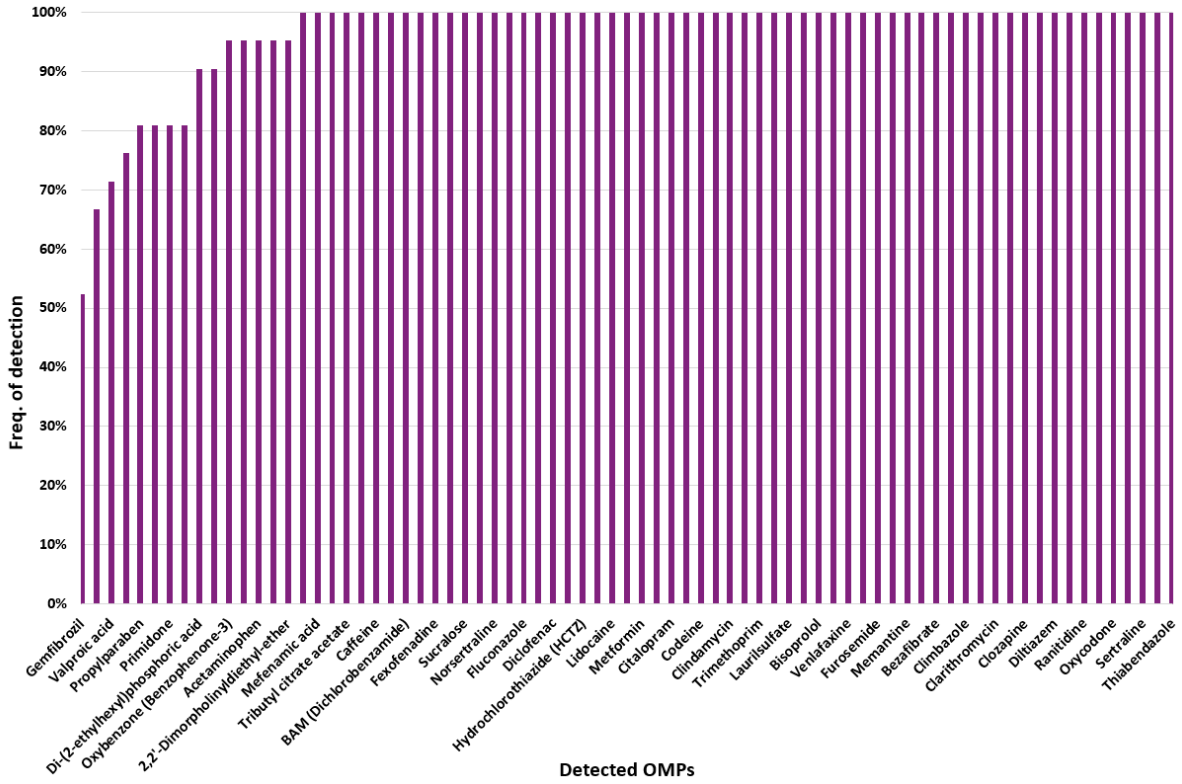

Figure 5: Bar chart of frequency of detection of OMPs in wastewater influent and effluent.

The FDs are generally lower in the river samples and the number of compounds with a frequency of detection greater than 50 % was 69. The lower FDs agrees with previous studies suggesting a lower amount of detected OMPs and concentrations in surface waters. Methylparaben and ifosfamide showed higher FDs in the river samples than wastewater samples (Methylparaben: 87% in surface water, 48 % in wastewater effluent and Ifosfamide: 74 % in surface water, 29 % in wastewater effluent). This could indicate that metabolites transform back the parent compounds, bioaccumulation to sludge in the WWTP or that there might have occurred some error, like contamination, during the sample preparation or analysis (Helmfrid et al., 2010).

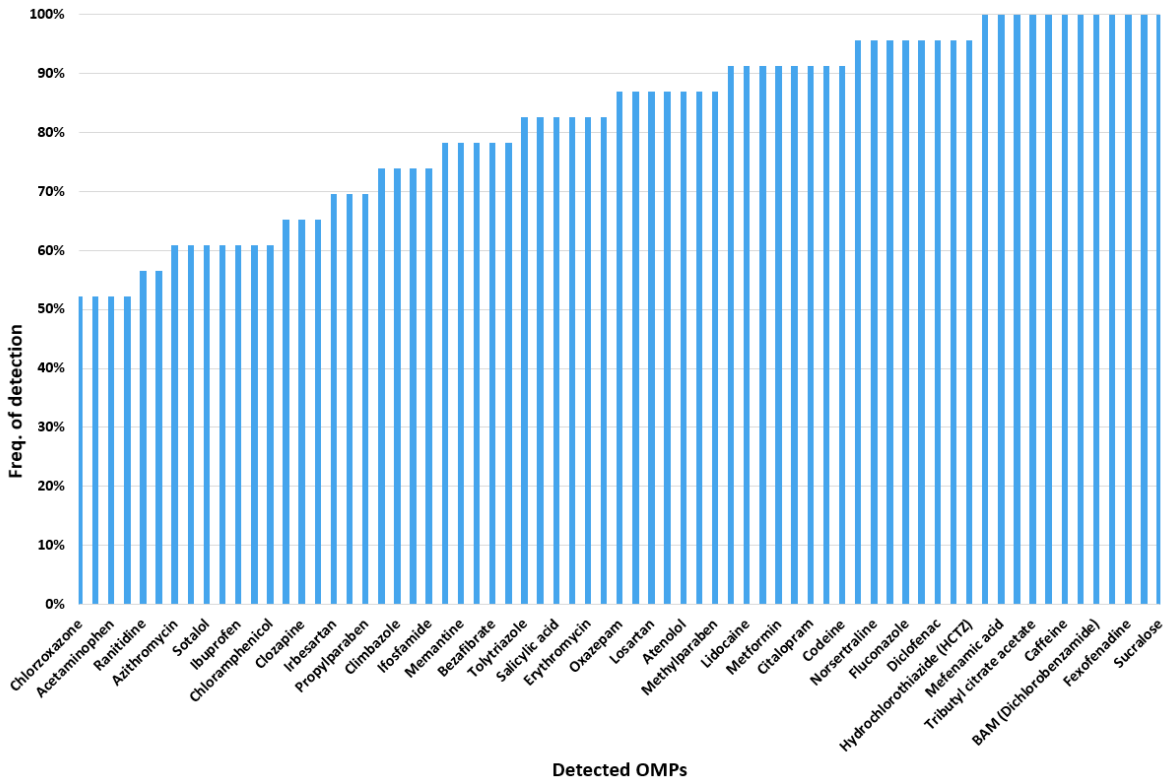

Figure 6: Bar chart of frequency of detection of OMPs in rivers.

The bar chart of the frequency of detection of hormones in figure 7 shows that 10 of the 13 target compounds were detected in the samples. It is clear that 17α-ethynylestradiol has the highest detection frequency while estriol has the lowest. This could be explained by the fact that 17α-ethynylestradiol is an estrogenic compound often used in contraceptive pills. Estriol is a week oestrogen and a minor female sex hormone almost only detectable in pregnant women, which could explain the low FD of this compound (Velicu and Suri, 2009).

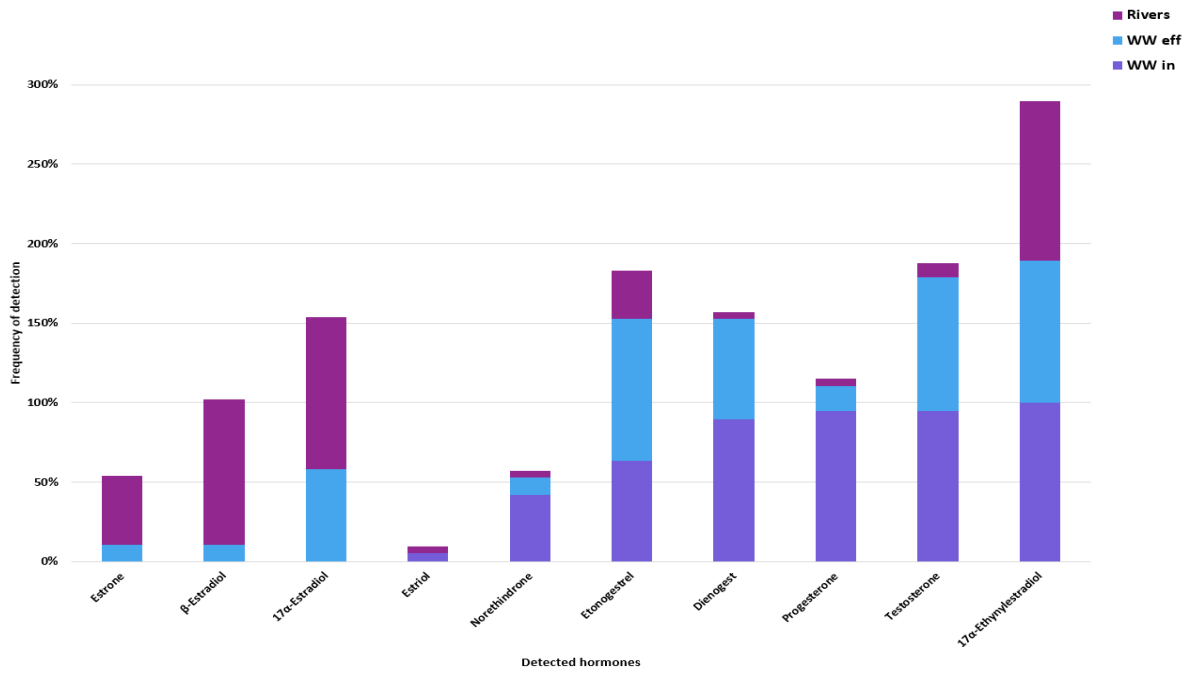

Figure 7: Bar chart of frequency of detection of hormones in wastewater and rivers.

4.3 Distribution of OMPs and hormones in surface water

The distribution of all detected target compounds in all 23 rivers can be seen in figure 8. The target compounds are divided and summed up into seven groups (pharmaceuticals, PFAS, hormones, pesticides, industrial chemicals, stimulants and personal care products) depending on their physical-chemical properties and usage. The river samples are sorted by corresponding lake (Vänern, Vättern, Mälaren) in order to compare the three different lakes to each other. Since both LIII_R3 and LIII_R13 have higher concentrations of OMPs they were placed to the right with a different y-axis.

The majority (14) of the river samples in figure 8 has a total OMP concentration ≤ 2 mg L^{-1} per sample, while the other seven rivers vary in the concentration range of 2 mg L^{-1} up to just below 16 mg L^{-1}. River LII_R4 connected to Vättern has the lowest total concentration with a value of 0.45 mg L^{-1} and LIII_R8 connected to Mälaren is a close second with a total concentration of 0.49 mg L^{-1}

The rivers connected to lake Mälaren has a relatively low total OMP concentrations, but also the two samples with the highest concentrations, as compared to the other to lakes. In sample LIII_R3 the total OMP concentration reaches a value just below 78.8 mg L^{-1} which is really high for a surface water sample. LIII_R13 is with its 33.2 mg L^{-1} the second most contaminated river according to these findings.

Samples connected to Vänern and Vättern are seemingly similar in comparison however, when excluding sample LI_R5 and LII_R1 lake Vättern actually has higher average total concentrations. It can be argued that the surrounding area of the sampling sites has a big impact on the concentrations found in the samples. The total concentration of industrial chemicals is higher in sample LI_R5 which could indicate a number of industries in the area close to the sampling point, or inside the catchment area.

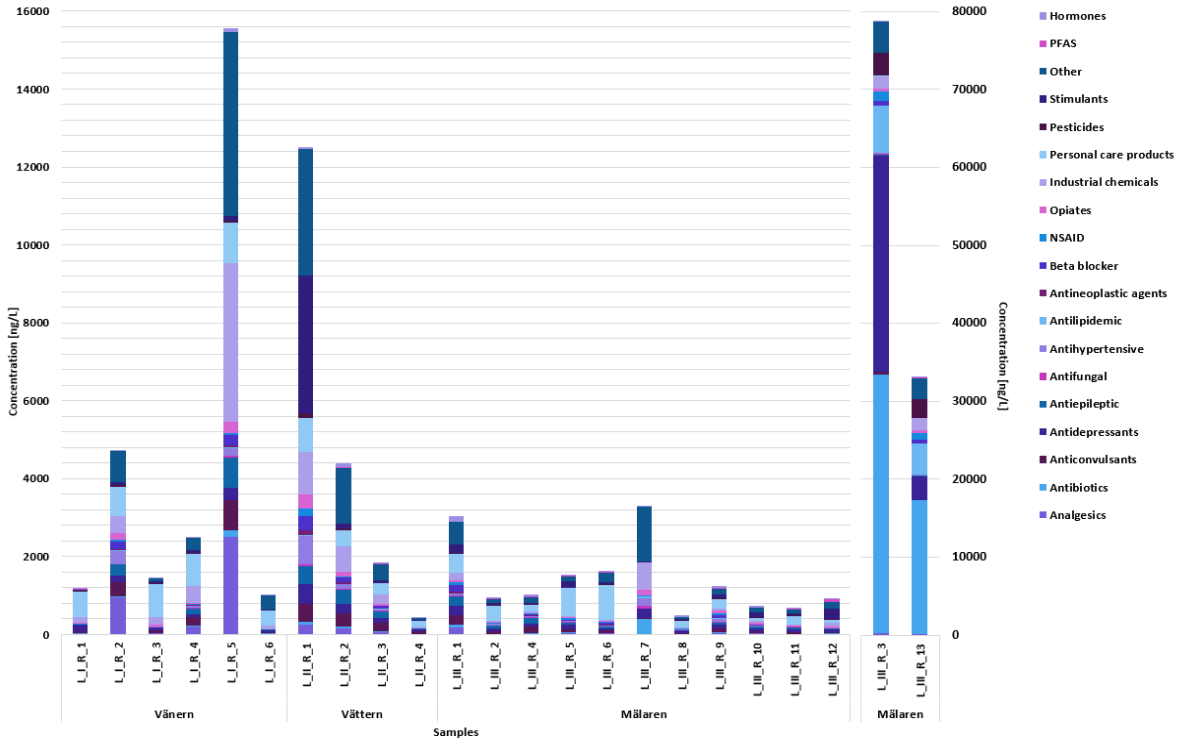

Figure 8: Bar chart of distribution of OMPs (pharmaceuticals, industrial chemicals, personal care products, pesticides, stimulants, PFAS, hormones NSAID, opiates, beta blockers, personal care products, antilipidemic, antihypertensives, analgesics, antibiotics and anticonvulsants) in all sampled rivers.

The total OMP concentration is, as can be seen in Table 1 and figure, highest in the sample LIII_R3 from (79 mg L^{-1}) and lowest in sample LIII_R8 (0.45 mg L^{-1}).

Table 1: Detected concentrations of pharmaceuticals, PFAS, hormones, industrial chemicals, pesticides and stimulants in the 23 different river samples. The total concentrations are in mg L^{-1} whereas the other concentrations are in ng L^{-1}.

Sample	Total OMP [µg L^{-1}]	Pharmaceuticals [ng L^{-1}]	PFAS [ng L^{-1}]	Hormones [ng L^{-1}]	Industrial chemicals [ng L^{-1}]	PPCPs [ng L^{-1}]	Pesticides [ng L^{-1}]	Stimulants [ng L^{-1}]
LI_R1	1.2	310	8.1	13	140	670	8.5	28
LI_R2	4.7	3400	4.6	26	420	760	37	77
LI_R3	1.4	310	4.1	14	210	850	9.9	50
LI_R4	2.5	1100	4.3	27	450	820	11	87
LI_R5	16.0	10 000	6	95	4100	1100	45	130
LI_R6	1.0	510	5.7	13	91	380	9.3	18
LII_R1	13.0	6800	5.8	48	1100	860	140	3500
LII_R2	4.4	3000	7.2	97	660	400	40	140
LII_R3	1.9	1200	13	45	240	280	19	75
LII_R4	0.45	220	3.7	25	27	160	10	9.4
LIII_R1	3.0	2000	8.3	130	190	480	20	230
LIII_R2	0.94	450	5	20	28	390	17	38
LIII_R3	79.0	74 000	38	95	1500	75	3000	7.9
LIII_R4	1.0	690	36	44	46	170	15	27
LIII_R5	1.5	560	11	13	46	710	16	170
LIII_R6	1.6	590	9.7	20	37	900	20	50
LIII_R7	3.3	2600	3	11	690	0.95	9.6	15
LIII_R8	0.49	200	6.2	36	16	180	9.7	44
LIII_R9	1.2	760	12	56	59	230	24	100

Sample	Total OMP [µg L^{-1}]	Pharmaceuticals [ng L^{-1}]	PFAS [ng L^{-1}]	Hormones [ng L^{-1}]	Industrial chemicals [ng L^{-1}]	PPCPs [ng L^{-1}]	Pesticides [ng L^{-1}]	Stimulants [ng L^{-1}]
LIII_R10	0.74	430	13	34	36	86	13	130
LIII_R11	0.68	340	11	23	25	210	11	62
LIII_R12	0.92	380	58	25	120	68	13	270
LIII_R13	33.0	29 000	24	140	1500	32	2400	9.6

The highest concentration of OMPs was found in LI_R5 which is connected to Vänern Lake. The total amount of detected OMPs is 16 mg L^{-1} in river 5 while the other five rivers have varying concentrations in the range between 1.2 mg L^{-1} up to 4.7 mg L^{-1}1.

In order to compare the concentrations of different categories between the three rivers stacked bar charts were prepared in Figures 9, 10 and 11. The category other includes all compounds which do not belong to any of the other 17 categories. It is clear that this category, personal care products, industrial chemicals and anticonvulsants are the dominating categories in rivers connected to Vänern. The total concentrations of OMPs and hormones are generally low with the exception of sample LI_R5 which entails a large amount of industrial chemicals, personal care products and other among other categories. This river is the recipient of WWTP effluent containing hospital waste which could explain higher concentrations of pharmaceuticals and hormones. Sample LI_R6 has the lowest total concentrations which might be explained by the fact that this river was very broad which causes dilution due to the amount of water.

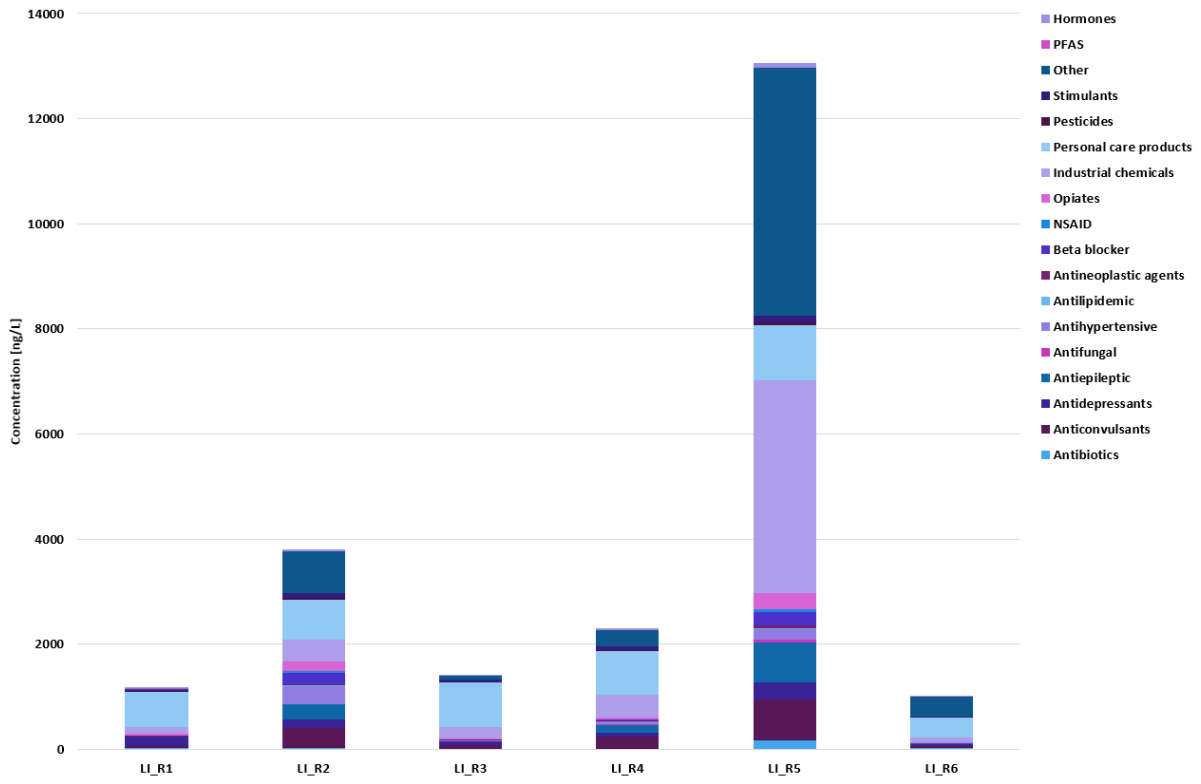

Figure 9: Bar chart of concentrations of target compounds in rivers connected to lake Vänern.

It is harder to see a similar pattern in the rivers connected to Vättern. Stimulants, other, industrial chemicals and personal care products can however be pointed out as the most frequently detected categories in these four rivers. Sample LII_R1 is the most contaminated one

and LII_R4 has the lowest total concentrations. The LII_R1 river is the recipient of WWTP and has a lower water flow then LII_R4 which could be one explanation for the difference. Another reason could be that the sampling point LII_R1 is close to inlet to Vättern while the sampling point for LII_R4 was close to the outlet.

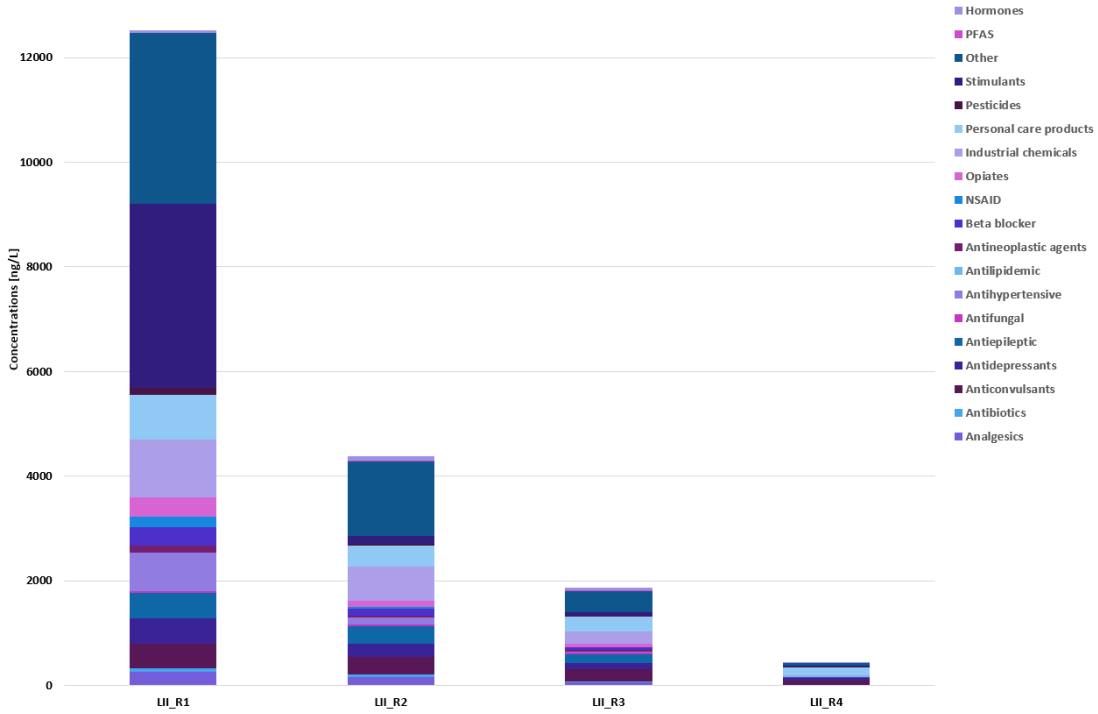

Figure 80: Bar chart of differences in concentration distribution in rivers connected to lake Vättern.

In the 11 rivers to the left in figure 10, the categories other, industrial chemicals and personal care products are the ones that stand out, while the antibiotics, antidepressants and antilipidemic compounds stand out in the two rivers to the left. LIII_R8 has the lowest total concentration of all samples and might be an effect of no bigger cities in the catchment area, the river is the recipient of WWTP effluent but the WWTP is small with 10 500 PE. Differences could be seen when comparing this river sample with LIII_R1 which has higher concentrations and is also a recipient of WWTP effluent for 180 000 PE. However, the amount of PE is not the only reason for differences since sample LIII_R3 was found to be the most polluted river in this study but this river is the recipient of WWTP effluent with 105 000 PE.

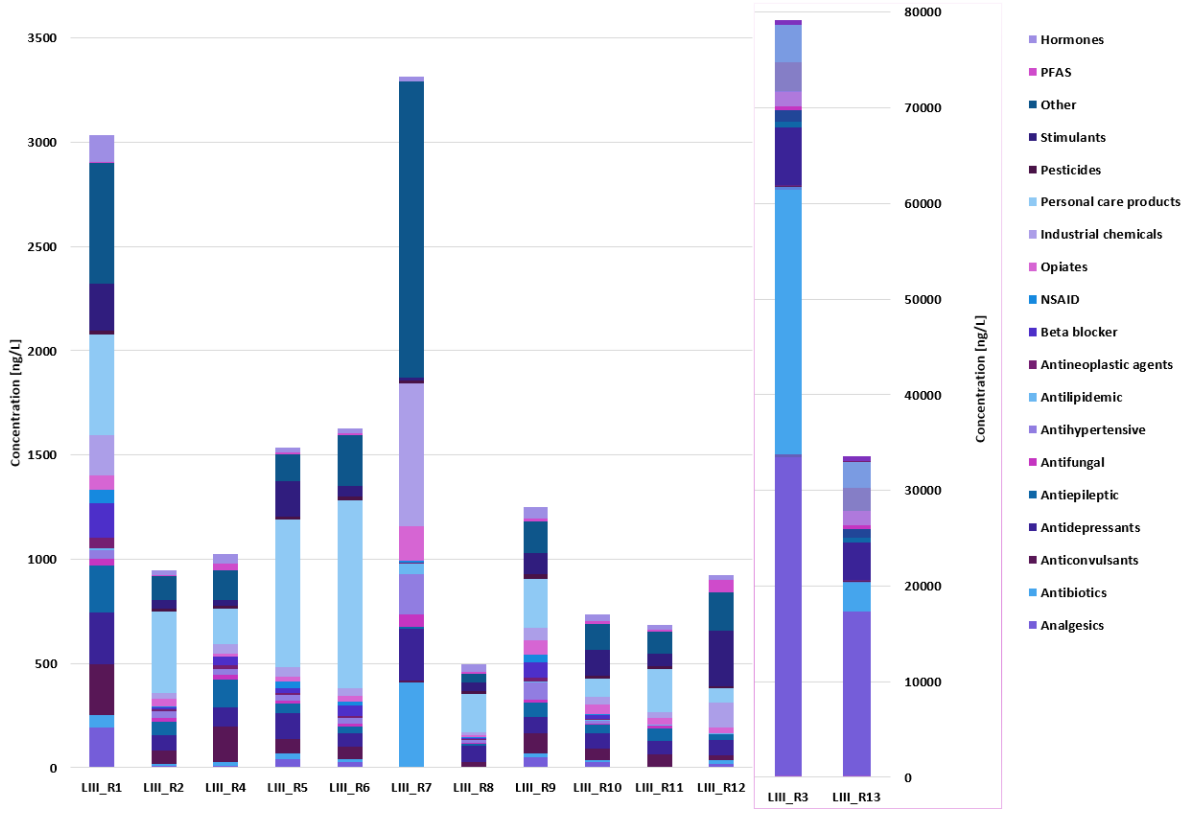

Figure 1: Bar chart of differences in concentration distribution in rivers connected to lake Mälaren.

4.4 DWEL

DWEL was calculated using eq. (1) for two compounds which were detected in the samples from DWTPs. BQs was calculated as a ratio between the maximum or mean concentration of detected compound and the calculated DWEL, resulting in BQ_max where maximum values were used and BQ_mean where mean values were used. Carbamazepine had an FD of 100 % and Erythromycin an FD of 17 % in the three analysed DWTPs. The results can be seen in Table 2. Only Carbamazepine had a BQ ≥ 1 with its BQ_max =1.47 which indicates a potential risk to human health when exposed to these levels for a period of life (Couto et al., 2019).

Table 2: Calculated DWEL-values for five detected compounds. TDI values from Couto et al. (2019).

Compound	TDI	DWEL	BQ_max	BQ_mean
Carbamazepine	0.34	2.04	1.47	0.50
Erythromycin	4.3	25.8	0.54	0.54

5 Discussion

A total of 89 out of the 121 analysed compounds were detected with a FD ≥ 50 % in the wastewater effluent in concentration levels from low ng/L up to 160 µg L^{-1}. In the surface water samples 78 of the 121 target compounds were found at concentrations from low ng L^{-1} up to 3.3 µg L^{-1}. 35 OMPs were detected at levels between low ng L^{-1} up to 2.9 µg L^{-1}. These findings are similar to ones in previous studies (Fick et al., 2011; Loos et al., 2009; Petrie et al., 2015). The concentration levels are however slightly lower than concentrations found in surface waters outside of Sweden (Petrie et al., 2015). This could be a result of differences in consumption rate and differences in legislations or restrictions regarding the handling and discharge of OMPs

(Naturvårdsverket, 2017). The Swedish Environmental Code for example, states that all activities that may inflict harm or inconvenience to the environment, humans or health should be regulated and carried out in best way possible (Naturvårdsverket, 2003). Other reasons for lower concentrations in Swedish surface waters might be explained by consumption differences, a lower population density as compared to other regions in Europe (Loos et al., 2009). Differences in climate conditions negatively effects the biological activity and/or the biodegradation in WWTPs resulting in a lower removal of OMPs (Hey et al., 2012). Thus, the lower concentrations detected in Swedish wastewater effluent may be explained by a colder climate as compared to some of the other countries included in the European wide surveys performed and described by Loos et al. (2009) and Petrie et al. (2015).

The results have shown decreasing of OMPs concentrations from wastewater to drinking water, where the highest concentrations could be found in wastewater and the lowest in drinking water. Even the number of detected compounds in the different matrices decreased when following the water from wastewater to drinking water. It could be explained by the fact that wastewater influent is a complex matrix with loads of different compounds which reduces in both concentrations and amount during the treatment steps. Once the effluent wastewater is discharged into to recipient surface water systems the concentrations will decrease even more due to different degradation pathways (Petrie et al., 2015; Wallberg et al., 2016).

It is difficult to explain the occurrence of some studied compounds at different concentration levels in a particular river compared to another. Low concentrations in the surface waters can also depend on the catchment area, amount of WWTP discharges, the treatment steps at the WWTPs, temperature and pH of the sampled water, water flow rate in the different rivers, etc. (Petrie et al., 2015). This can especially be seen in sample LIII_R3 which is the recipient of WWTP of 105 000 PE, hospital waste and a catchment area which included industries and agricultural land. Higher concentrations of pharmaceuticals such as antibiotics are expected due to the hospital waste, industrial chemicals due to the industries and pesticides such as BAM (2,6-dichlorobenzamide) due to the agricultural run-offs. BAM is a metabolite of the substance Dichlobenil, which usage is banned in the European Union countries but still is frequently found in countries like Sweden, Finland and Denmark (Barbosa et al., 2016; Pukkila and Kontro, 2014; Whalley et al., 2018). Nevertheless, some cases are harder to trace back to the sources, as in the case with sample LI_R5, sampled from river Ösan, where the concentrations of OMPs where much higher as compared to the other rivers connected to Vänern. This river is the recipient of WWTP containing hospital waste which would explain the higher concentrations of both pharmaceuticals and personal care products such as Sulisobenzone and Oxybenzone but not the relatively high concentrations of industrial chemicals such as Tris(2-butoxylethyl) phosphate and Sucralose. Tris(2-butoxylethyl) phosphate is commonly used in plastics, floor finishes, waxes etc. and highly soluble in water (PubChem, n.d.) and the high concentrations may indicate discharges directly into the river.

The sample from river LIII_R3 is by far the most contaminated sample in this study, indicating a hot spot. This sampling site locates in Enköping river and it is close to the WWTP discharge which possibly affects the found concentration levels. High concentrations of antidepressants such as Amitriptyline and Norsertaline and antibiotics such as Chlorampenicol (commonly used for treatment of numerous bacterial infections) were found in this sample. This indicates a higher consumption of these substances and the possible presence of hospital waste in the WWTP effluent or the occurrence of a hospital discharge in the nearby area. A hospital is in

fact located in the nearby area of this sampling point and therefore it's reasonable to assume that hospital waste also reaches the WWTP. Higher concentration levels in this sample is reasonable since the catchment area includes a city with industries, roads and quite many people. The sample site is also close to the wastewater discharge, a small marina and agricultural land area which could affect the mixture of compounds. Industrial chemicals in this study also includes compounds such as Di-(2-ethylhexyl) phosphoric acid which is commonly used in corrosion inhibitors. This could explain why industrial chemicals like this one is found in samples from sites close to marinas.

This study doesn't show a clear difference in concentration levels between the three lakes. A previous study have shown Mälaren lake to be the most polluted (Rehrl et al., 2020) but this cannot be confirmed based on the results of this study. The results suggest that Enköping river has the highest total OMP concentration with 79 µg L^{-1} and Lövsta river are the second most polluted one with 33 µg L^{-1}. These two are connected to lake Mälaren and are more polluted than any of the other Mälaren rivers which has relatively low total OMP concentrations. Ösan (16 µg L^{-1}) and Lillån (13 µg L^{-1}) are the most polluted rivers connected to lake Vänern and Vättern. These results make Enköping river, Lövsta river, Ösan and Lillån hot spots for OMPs in this study. Lillån and Lövsta river were relatively small as compared to Ösan and Enköping rivers suggesting that water flow rate has an impact on the concentration levels. The four rivers are all recipients of WWTP effluents which could be seen as a confirmation of the impact wastewater discharges has on the concentration levels.

Since OMPs could be detected in the surface water it is clear that some compounds are more persistent to the wastewater treatment than others. It is also obvious that the OMPs does not occur separately in the samples, but in a complex mixture of at least 121 different OMPs. Since modern technology are not able to detect and identify all compounds that occur in environmental waters, it is not possible to know for certain, which effects these compounds pose to humans, aquatic organisms or others. Resulting effects and risks on the aquatic environment may be known when compounds are found individually but, as previously told, when found in various mixtures the risks and effects are very complex.

The resulting effects and risks on the aquatic environment may be known for individually occurring compounds (Barbosa et al., 2016; Wallberg et al., 2016; Whalley et al., 2018).. In reality the compounds occur in various mixtures which makes the risks and effects very complex to foresee and calculate. In order to assess these effects extended research on present compounds and toxicity tests has to be made. In fact 95-99 % of all occurring effects comes from these unknown substances (Lundqvist and Oskarsson, 2020) indicating more advanced treatment processes and methods for detection is needed (Wallberg et al., 2016).

The risk assessment for drinking water samples were calculated for only two compounds, Carbamazepine and Bezafibrate. These two compounds were selected based on available toxicity data and their detected concentrations in the analysed drinking water. Only Carbamazepine showed a BQ (1.47) that implies a potential risk to human health when exposed to the compound in this concentration during a lifetime. Sources of error exists since not every human weigh 60 kg and drinks 2 L of drinking water every day, but those assumptions were made in order to calculate the BQ value. In this study, only one compound implied a risk to human health, therefore it can only be seen as an potential indicator of the problems that OMPs causes when present in the environmental waters. Couto et al. (2019) came to similar

conclusions regarding Carbamazepine in drinking water. Carbamazepine is listed as a high priority compound in the Global Water Research Coalition (GWRC) due to its physical-chemical properties that makes it very persistent to treatment among others (KIWA Water Research et al., 2008).

6 Conclusions

This study shows a clear decrease in concentration levels of OMPs in samples from the five different matrices. Highest concentrations of OMPs could be found in wastewater influent and the lowest could be found in the drinking water.

The results show that OMPs occur in different concentration levels and mixtures in Swedish surface water. Clear differences in concentration levels and number of detected compounds could be seen in some samples but not when comparing the three lakes. However, four hot spots could be established in Enköping river, Lövsta river, Ösan and Lillån.

A risk assessment regarding human health issues derived from drinking tap water showed that only carbamazepine poses a threat to human health. Carbamazepine had a BQ of 1.47 indicating that when exposed to these levels for a period of a lifetime, human health may be negatively affected.

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Appendix A – List of compounds

Compounds selected for analysis, their respective category and type are listed in Table A1.

Table A1: List of compounds selected for analysis.

Compound	Category	Type
2,2'-Dimorpholinyldiethyl-ether	Industrial chemical	
3-(4-Methylbenzylidene)camphor	Personal care product	
4-Chloro-2-isopropyl-5-methylphenol	Industrial chemical	
4-Chloro-3-methylphenol	Industrial chemical	
Aceclofenac	Pharmaceutical	NSAID (nonsteroidal anti-inflammatory drug)
Acetaminophen (Paracetamol)	Pharmaceutical	Analgesics (painkiller)
Albuterol (Salbutamol)	Pharmaceutical	Beta blocker
Amitriptyline	Pharmaceutical	Antidepressant
Amoxicillin *	Pharmaceutical	Antibiotic
Atenolol	Pharmaceutical	Beta blocker
Atorvastatin	Pharmaceutical	Antilipidemic Agents
Azithromycin *	Pharmaceutical	Antibiotic
BAM (Dichlorobenzamide)	Pesticide	Metabolite of dichlobenil
Bezafibrate	Pharmaceutical	Antilipemic drug
Bicalutamide	Pharmaceutical	
Bisoprolol	Pharmaceutical	Beta blocker
Caffeine	Stimulant	
Carazolol	Pharmaceutical	
Carbamazepine	Pharmaceutical	Antiepileptic
Cetirizine	Pharmaceutical	Antihistamine
Chloramphenicol	Pharmaceutical	Antibiotic
Chlorzoxazone	Pharmaceutical	
Ciprofloxacin *,**	Pharmaceutical	Antibiotic
Citalopram	Pharmaceutical	Antidepressant
Clarithromycin *	Pharmaceutical	Antibiotic
Climbazole	Pharmaceutical	Antifungal
Clindamycin	Pharmaceutical	Antibiotic
Clozapine	Pharmaceutical	Antipsychotic
Codeine	Pharmaceutical	Opiates, opioids and metabolites
Daidzein	Isoflavone	
DEET (diethyltoluamide)	Pesticide	Insect repellent

Compound	Category	Type
Desvenlafaxine	Pharmaceutical	Antidepressant
Di-(2-ethylhexyl)phosphoric acid	Industrial chemical	
Diazepam	Pharmaceutical	Sedative
Diclofenac *,**	Pharmaceutical	NSAID (nonsteroidal anti-inflammatory drug)
Diltiazem	Pharmaceutical	Antihypertensive
Erytromycin *	Pharmaceutical	Antibiotic
Ethylparaben	Paraben	Antifungal preservative
Fexofenadine	Pharmaceutical	Antihistamine
Fluconazole	Pharmaceutical	Antifungal
Fluoxetine	Pharmaceutical	Antidepressant
FOSA (perfluorooctane sulfonamide)	PFAS	
Furosemide	Pharmaceutical	Diuretics
Gemfibrozil	Pharmaceutical	Antilipidemic Agents
Hydrochlorothiazide	Pharmaceutical	Diuretics
Ibuprofen	Pharmaceutical	NSAID (nonsteroidal anti-inflammatory drug)
Ifosfamide	Pharmaceutical	Anticancer
Irbesartan	Pharmaceutical	Antihypertensive
Lamotrigine	Pharmaceutical	Antiepileptic
Laurilsulfate	Personal care product	
Lidocaine	Pharmaceutical	Anesthetic
Loperamide	Pharmaceutical	
Losartan	Pharmaceutical	Antihypertensive
Meclofenamic acid	Pharmaceutical	NSAID (nonsteroidal anti-inflammatory drug)
Mefenamic Acid	Pharmaceutical	NSAID (nonsteroidal anti-inflammatory drug)
Memantine	Pharmaceutical	
Metformin	Pharmaceutical	Antidiabetic
Methylparaben	Paraben	Antifungal preservative
Metoprolol	Pharmaceutical	Beta blocker
Metronidazole	Pharmaceutical	Antibiotic
Mirtazapine	Pharmaceutical	Antidepressant
Nicotine	Stimulant	
Norsertraline	Pharmaceutical	Antidepressant
Omeprazole	Pharmaceutical	Antisecretory Agent

Compound	Category	Type
Oxazepam	Pharmaceutical	Sedative
Oxybenzone (Benzophenone-3)	Personal care product	UV filter
Oxycodone	Pharmaceutical	Opiates, opioids and metabolites
Panthenol	Pharmaceutical	
Paroxetine	Pharmaceutical	Antidepressant
PFBA (perfluorobutanoic acid)	PFAS	
PFBS (perfluorobutanesulfonic acid)	PFAS	
PFDA (perfluorodecanoic acid)	PFAS	
PFDoDA (perfluorododecanoic acid)	PFAS	
PFHpA (perfluoroheptanoic acid)	PFAS	
PFHxA (perfluorohexanoic acid)	PFAS	
PFHxS (perfluorohexanesulfonic acid)	PFAS	
PFNA (perfluorononanoic acid)	PFAS	
PFOA (perfluorooctanoic acid)	PFAS	
PFOS (perfluorooctanesulfonic acid)	PFAS	
PFPeA (perfluoropentanoic acid)	PFAS	
PFTeDA (perfluorotetradecanoic acid)	PFAS	
PFUnDA (perfluoroundecanoic acid)	PFAS	
Primidone	Pharmaceutical	Antiepileptic
Propranolol	Pharmaceutical	Beta blocker
Propylparaben	Paraben	Antifungal preservative
Pyrimethamine	Pharmaceutical	
Ramipril	Pharmaceutical	
Ranitidine	Pharmaceutical	Antisecretory Agent
Ricinoleic acid	Pharmaceutical	
Roxithromycin	Pharmaceutical	Antibiotic
Salicylic acid	Pharmaceutical	NSAID (nonsteroidal anti-inflammatory drug)
Sertraline	Pharmaceutical	Antidepressant
Simvastatin	Pharmaceutical	Antilipidemic Agents
Sotalol	Pharmaceutical	Beta blocker
Sucralose	Artificial sweetener	
Sulfamethoxazole	Pharmaceutical	Antibiotic
Sulisobenzone	Personal care product	
Tamoxifen	Pharmaceutical	

Compound	Category	Type
Terbutaline	Pharmaceutical	
Thiabendazole	Pharmaceutical	
Tolytriazole	Pharmaceutical	
Tramadol	Pharmaceutical	Analgesics (painkiller)
Tributyl citrate acetate	Industrial chemical	
Triisopropanolamine	Industrial chemical	
Trimethoprim	Pharmaceutical	Antibiotic
Tris(2-butoxylethyl) phosphate	Industrial chemical	
Valproic acid	Pharmaceutical	Antiepileptic
Valsartan	Pharmaceutical	Antihypertensive
Venlafaxine	Pharmaceutical	Antidepressant
17-Alpha-ethinylestradiol (EE2) *, **	Hormone	
17-Beta-estradiol (E2) *, **	Hormone	
estrone (E1)	Hormone	
estradiol *	Hormone	
Etinylestradiol *	Hormone	

***Watch list EU (WFD)**

**** CEC – Contaminants of emerging concern (from WFD)**

Appendix B – Surface water samples

All surface water samples are listed with extraction code, sampling site and extraction code in Table B1.

Table B1: Listed surface water sampling points.

Lake	Extraction code	Sampling site	Reason for sampling
Vänern	LI_R1	Klarälven Almar	
	LI_R2	Klarälven Skoghall, bron vid kemiska fabriken	
	LI_R3	Klarälven Karlstad	Recipient of WWTP
	LI_R4	Tidan, Stadkvarnen i Mariestad	
	LI_R5	Ösan, bron vid Asketorp	Recipient of WWTP containing Skaraborg hospital's wastewater.
	LI_R6	Göta älv Vargön	
Vättern	LII_R1	Lillån Bankeryd, outlet Vättern	Recipient of WWTP Bankeryd. Standard sampling point, part of original study 2006.
	LII_R2	Munksjöns outlet	Most polluted tributary - recipient of: WWTP in Jönköping, impact from an airport and a garbage disposal site.
	LII_R3	Huskvarnaån	Second most polluted tributary. Recipient of WWTP Huskvarna. Part of original study 2006.
	LII_R4	Motala ström	Vättern's effluent, standard sampling point.
Mälaren	LIII_R1	Fyrisån Flottsund	Recipient of WWTPs (172 000 PE and 8 000 PE)
	LIII_R2	Örsundaån	Agricultural run-offs, many unconnected wastewater effluents, recipient of many minor WWTPs.
	LIII_R3	Enköpingsån	Possibly recipient of WWTP.
	LIII_R4	Sagån	Agricultural run-offs, many unconnected wastewater effluents.
	LIII_R5	Svartån Västerås, Turbinbron	Agricultural run-offs, recipient minor WWTP (3 400 PE)
	LIII_R6	Kolbäcksån, Strömsholm	Known to have problems with environmental pollutants. Recipient of two WWTPs (14 000 PE and 7 500 PE)
	LIII_R7	Hedströmmen	Cleanest discharge into Mälaren.
	LIII_R8	Arbogaån Kungsör	Recipient of WWTP (10 500 PE).
	LIII_R9	Eskilstunsån	Recipient of WWTP (105 000 PE).
	LIII_R10	Norrström (outlet)	
	LIII_R11	Oxundnaån	Possibly most polluted river to discharge into Mälaren.
	LIII_R12	Märstaån outlet	Possibly affected by Arlanda airport.
	LIII_R13	Lövstaån	Recipient of WWTP and close to raw water intake for DWTP.

Appendix C – Frequency of detection

The frequencies of detection (FDs) were calculated for all compounds in every matrix and are listed in Table C1.

Table C1: Calculated frequencies of detection for all analysed compounds.

Compound	WW in	WW eff	Rivers	Lakes	DW
17α-Estradiol	0%	58%	96%	100%	0%
17α-Ethynylestradiol	100%	89%	100%	100%	0%
2,2'-Dimorpholinyldiethyl-ether	100%	95%	35%	0%	0%
3-(4-Methylbenzylidene)camphor	100%	0%	0%	0%	0%
4-Chloro-2-isopropyl-5-methylphenol	100%	0%	13%	0%	0%
4-Chloro-3-methylphenol	100%	0%	9%	0%	0%
Aceclofenac	100%	0%	0%	0%	0%
Acetaminophen	100%	95%	52%	0%	0%
Albuterol (Salbutamol)	100%	100%	48%	29%	24%
Amitriptyline	100%	100%	48%	0%	0%
Amoxicillin	100%	0%	0%	0%	0%
Atenolol	100%	100%	87%	33%	6%
Atorvastatin (Lipitor)	100%	95%	61%	5%	0%
Azithromycin	100%	100%	61%	14%	15%
BAM (Dichlorobenzamide)	0%	100%	100%	95%	97%
Bezafibrate	95%	100%	78%	24%	9%
Bicalutamide	62%	100%	100%	100%	79%
Bisoprolol	100%	100%	83%	48%	15%
Caffeine	57%	100%	100%	100%	88%
Carazolol	100%	24%	26%	19%	9%
Carbamazepine	24%	100%	100%	100%	94%
Cetirizine	67%	100%	96%	100%	74%
Chloramphenicol	100%	19%	61%	0%	3%
Chlorzoxazone	100%	100%	52%	0%	9%
Ciprofloxacin	100%	0%	0%	0%	0%
Citalopram	0%	100%	91%	24%	6%
Clarithromycin	100%	100%	70%	10%	0%
Climbazole	100%	100%	74%	0%	0%
Clindamycin	71%	100%	87%	62%	21%
Clozapine	100%	100%	65%	5%	0%
Codeine	100%	100%	91%	10%	9%
Daidzein	100%	81%	43%	19%	18%
DEET	100%	100%	100%	100%	97%
Desvenlafaxine	57%	100%	100%	100%	97%
Di-(2-ethylhexyl)phosphoric acid	100%	90%	57%	5%	3%
Diazepam	100%	95%	52%	14%	9%
Diclofenac	76%	100%	96%	29%	24%
Dienogest	89%	63%	4%	0%	0%
Dihydrotestosterone	0%	0%	0%	0%	0%
Diltiazem	95%	100%	61%	0%	0%
Erythromycin	90%	100%	83%	10%	9%

Compound	WW in	WW eff	Rivers	Lakes	DW
Estriol	5%	0%	4%	0%	0%
Estrone	0%	11%	43%	58%	0%
Ethylparaben	100%	0%	13%	0%	0%
Etonogestrel	63%	89%	30%	0%	0%
Fexofenadine	0%	100%	100%	95%	53%
Fluconazole	76%	100%	96%	95%	97%
Fluoxetine	100%	29%	9%	0%	0%
FOSA	0%	0%	4%	17%	17%
Furosemide	100%	100%	83%	0%	0%
Gemfibrozil	100%	52%	22%	0%	0%
Gestodene	0%	0%	0%	0%	0%
Hydrochlorothiazide (HCTZ)	48%	100%	96%	14%	6%
Ibuprofen	100%	81%	61%	48%	24%
Ifosfamide	95%	29%	74%	38%	18%
Irbesartan	100%	100%	70%	33%	9%
Lamotrigine	100%	100%	91%	100%	91%
Laurilsulfate	100%	100%	87%	100%	97%
Lidocaine	86%	100%	91%	100%	68%
Loperamide	100%	100%	30%	0%	0%
Losartan	10%	100%	87%	43%	26%
Meclofenamic acid	100%	10%	22%	0%	9%
Mefenamic acid	19%	100%	100%	100%	97%
Memantine	100%	100%	78%	24%	6%
Metformin	100%	100%	91%	90%	82%
Methylparaben	100%	48%	87%	0%	0%
Metoprolol	100%	100%	91%	100%	47%
Metronidazole	100%	76%	17%	0%	0%
Mirtazapine	14%	100%	96%	19%	12%
Nicotine	0%	100%	100%	95%	62%
Norethindrone	42%	11%	4%	0%	0%
Norgestrel	0%	0%	0%	0%	0%
Norsertraline	0%	100%	96%	100%	76%
Omeprazole	95%	100%	78%	5%	0%
Oxazepam	100%	100%	87%	90%	41%
Oxybenzone (Benzophenone-3)	100%	95%	78%	81%	85%
Oxycodone	100%	100%	52%	0%	0%
Panthenol	100%	67%	74%	0%	18%
Paroxetine	100%	5%	30%	0%	0%
PFBS	74%	89%	48%	100%	97%
PFDA	0%	0%	0%	0%	0%
PFDoDA	58%	68%	83%	50%	60%
PFHpA	68%	89%	87%	92%	97%
PFHxA	0%	11%	48%	0%	0%
PFHxS	0%	0%	0%	0%	0%
PFNA	58%	68%	96%	67%	40%
PFOA	53%	84%	52%	92%	87%
PFOS_linear	89%	100%	96%	75%	53%

Compound	WW in	WW eff	Rivers	Lakes	DW
PFPeA	100%	100%	96%	100%	100%
PFTeDA	0%	0%	0%	0%	3%
PFUnDA	0%	0%	0%	0%	0%
Primidone	100%	81%	61%	33%	18%
Progesterone	95%	16%	4%	0%	0%
Propranolol	90%	100%	91%	14%	9%
Propylparaben	95%	81%	70%	57%	50%
Pyrimethamine	100%	5%	26%	0%	9%
Ramipril	100%	100%	74%	5%	0%
Ranitidine	100%	100%	57%	5%	3%
Ricinoleic acid	100%	5%	0%	0%	0%
Roxithromycin	100%	38%	13%	0%	0%
Salicylic acid	100%	100%	83%	33%	21%
Sertraline	100%	100%	30%	0%	0%
Simvastatin	100%	0%	39%	0%	0%
Sotalol	67%	100%	61%	0%	0%
Sucralose	0%	100%	100%	57%	62%
Sulfamethoxazole	100%	100%	65%	81%	18%
Sulisobenzone	0%	100%	96%	76%	18%
Tamoxifen	100%	0%	0%	0%	0%
Terbutaline	100%	90%	13%	0%	0%
Testosterone	95%	84%	9%	8%	0%
Thiabendazole	100%	100%	26%	0%	0%
Tolytriazole	95%	100%	83%	90%	74%
Tramadol	14%	100%	78%	90%	35%
Tributyl citrate acetate	0%	100%	100%	100%	97%
Triisopropanolamine	95%	100%	96%	100%	97%
Trimethoprim	100%	100%	87%	38%	15%
Tris(2-butoxylethyl) phosphate	0%	100%	100%	81%	38%
Valproic acid	100%	71%	65%	100%	71%
Valsartan	100%	100%	91%	48%	12%
Venlafaxine	100%	100%	83%	24%	9%
β-Estradiol	0%	11%	91%	100%	0%