Pharmaceutical Residues in Drinking Water

A Case Study on Pharmaceutical Concentration in Rådasjön and Its Impact on Human and Environmental Health

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MASTER'S THESIS ACEX30

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Master's Thesis in the Master's programme Infrastructure and Environmental Engineering

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Examensarbete ACEX30
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Cover page:
Illustrative image of a pharmaceutical in Rådasjön lake, with oral tablets that symbolize the found residue of metformin and gabapentin. Generated by Nano-banana (Gemini)

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Abstract

In recent years, the occurrence of anthropogenic persistent substances, such as pharmaceuticals, in aquatic environments has attracted global attention to find solutions that both mitigate measured concentrations and address the significant challenges they pose to public health and aquatic ecosystems. This study aimed to identify and quantify pharmaceuticals in Lake Rådasjön, western Sweden, which act as a primary drinking water source for Mölndal's inhabitants.

The study identified metformin (MET) and gabapentin (GBP) as the main pharmaceuticals in the lake water using Liquid Chromatography-Mass Spectrometry (LC-MS) analytical method. The analysis showed that only MET was detected at high concentrations in the drinking water treatment plant (DWTP) effluent, while GBP was below the detection limit, indicating that the current treatment methods at Mölndal's DWTP achieved high removal efficiency. MET, on the other hand, remained high, indicating that current treatment processes were insufficient and other advanced processes needed to be adapted.

This thesis was based on a literature review evaluating several treatment methods, followed by laboratory experiments aimed at estimating the removal efficiency of multiple treatment combinations, including ozonation alone, the combination of ozonation and chlorination, and ozonation combined with Granular Activated Carbon (GAC). The results showed that ozonation alone reduced MET concentrations by 52.5%, while the combination of ozonation and chlorination resulted in a similar reduction of 52.9%. The most effective combination to reduce MET concentration, promote human health, and improve the environment was ozonation followed by GAC, which gave a reduction of up to 88.4%.

The calculation of the risk assessment showed that the MET concentration found in DWTP effluent posed no risk to human health. Similarly, the MET concentration in the lake did not pose any risk to fish. However, GBP posed a moderate risk to fish and potentially caused oxidative damage. Finally, further research is necessary to better understand the impacts and risks of GBP and MET and to ensure safe water quality.

Keywords: Metformin, Gabapentin, Rådasjön, Ozonation, GAC, Chlorination, Drinking Water Treatment, Pharmaceutical Residues, Removal Efficiency.

Läkemedelskoncentration i Dricksvatten
En fallstudie om läkemedelskoncentration i Rådasjön och dess inverkan på människors och miljöns hälsa

Examensarbete inom mastersprogrammet infrastrukturer och miljöteknik

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Sammanfattning

Under de senaste åren har förekomsten av antropogena persistenta ämnen, såsom läkemedel, i akvatiska miljöer väckt global uppmärksamhet för att hitta lösningar som både minskar uppmätta koncentrationer och undersöker utmaningar som dessa ämnen utgör för folkhälsan och akvatiska ekosystem. Denna studie syftade till att identifiera och kvantifiera läkemedel i Rådasjön i Västra Sverige, som fungerar som en primär dricksvattenkälla för Mölndals invånare.

Studien identifierade metformin (MET) och gabapentin (GBP) som de mest förkommande läkemedlen i sjövattnet med hjälp av analysmetoden vätskekromatografi-masspektrometri (LC-MS). Analysen visade att endast MET detekterades i höga koncentrationer i dricksvatten (utgående vatten från dricksvattensverk), medan GBP låg under detektionsgränsen, vilket indikerade att de nuvarande reningsmetoderna vid Mölndals vattenverk uppnådde hög avskiljningsgrad. MET, däremot, förblev högt, vilket indikerade att nuvarande reningsprocesser är otillräckliga och att andra avancerade processer behövde tillämpas.

Detta examensarbete baserades på en litteraturgenomgång som utvärderade flera behandlingsmetoder, följt av laboratorieexperiment som syftade till att uppskatta avskiljningsgraden hos flera behandlingskombinationer, inklusive enbart ozonering, kombinationen av ozonering och klorering samt ozonering i kombination med granulärt aktivt kol (GAK). Resultaten visade att ozonering själv minskade MET-koncentrationerna med 52,5 %, medan kombinationen av ozonering och klorering resulterade i en liknande minskning på 52,9 %. Den mest effektiva kombinationen för att minska MET-koncentrationen, främja människors hälsa och förbättra miljön var ozonering följt av GAK, vilket gav en reduktion på 88,4 %.

Beräkningen av riskbedömningen visade att MET-koncentrationerna som uppmättes i dricksvatten inte utgjorde någon risk för människors hälsa. På samma sätt utgjorde inte MET-koncentrationerna i sjön någon risk för fisk. GBP däremot utgjorde en måttlig risk för fisk och kan potentiellt orsaka oxidativ skada. Slutligen krävs ytterligare forskning för att bättre förstå effekterna och riskerna med GBP och MET samt för att säkerställa en säker vattenkvalitet.

Nyckelord: Metformin, Gabapentin, Rådasjön, Ozonering, GAC, Klorering, Dricksvattenrening, Läkemedelsrester, Avskiljningseffektivitet.

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Preface

This thesis has been prepared as part of the Infrastructure and Environmental Engineering master's program at Chalmers University of Technology and comprises 30 credits. The work was carried out between January and June 2026 by Nour Saadeddin and Mohamad Taleb Attar.

The interest in this project emerged during the course Drinking Water Engineering (BOM075) and was further strengthened by the growing attention for ensuring high water quality, reducing contamination in raw water, and mitigating water scarcity by water recycling efforts. Additionally, the study was an extension of our interest in the impacts of pharmaceuticals on human health and the environment.

We would like to begin by thanking our examiner and supervisor, Thomas Pettersson from Chalmers University of Technology, in the division of Water Environment Technology. We owe a special debt of gratitude to Amir Saeid Mohammadi, who supported and supervised us during the experimental part of the project. We want to thank Per Falås for hosting us at Lund University and for providing us with the ozone that was required in the project. We would also like to send our gratitude to Tony Bäckström from Mölndal drinking water treatment plant, who provided us with water samples and funded a part of the ALS analysis.

We would also like to take this opportunity to express our deepest gratitude to our families, whose support and love have been our greatest source of motivation throughout this project and our entire academic journey. We would also like to thank our friends and everyone who has supported us directly or indirectly along the way. We are grateful for all the encouragement and motivation that proved invaluable during this work.

Finally, before diving deep into the thesis, we want to appreciate our cooperation and support throughout the whole thesis. Despite all the delays and barriers that we have faced, we were always patient and worked together as a team. We are convinced that our success would not have been possible without this mutual support.

Gothenburg, June 2026
Nour Saadeddin and Mohamad Taleb Attar

Notations

AOPs	Advanced Oxidation Processes
APIs	Activated Pharmaceutical Ingredients
BBB	Blood-Brain Barrier
BOD	biological oxygen demand
$CaCO_3$	Calcium Carbonate
COD	Chemical oxygen demand
CSO	Combined Sewer Overflow
diMET	Covalent dimer of metformin
DN	Diabetic neuropathy
DRG	Dorsal root ganglion neurons
DWTP	Drinking Water Treatment Plant
GABA	Gamma-Aminobutyric Acid
GAC	Granular Activated Carbon
GBP	Gabapentine
GBP-L	Gabapentin-lactam
GUA	Guanylurea
HAAs	Haloacetic Acid
HOCl	Hypochlorous Acid
HPLC	High-Performance Liquid Chromatography
LC	Liquid Chromatography
LC-MS	Liquid Chromatography-Mass Spectrometry
LOR	Limit of reporting
LPO	Liquid Peroxidation
MBG	Methylbiguanide
MET	Metformin
METOOH	Hydroperoxide of metformin
MgO	Magnesium oxide
MS	Mass Spectrometry
NAFLD	Non-Alcoholic Fatty Liver Disease
NA-GBP	N-acetyl gabapentin
NaOCl	Sodium hypochlorite
NCDC	N-Cyano-N, N-dimethylcarbaminimidic chloride

NDMA	N-Nitrosodimethylamine
OCl^-	Hypochlorite ion
O_3/ H_2O_2	Peroxone Process
PAC	Powdered Activated Carbon
PCA	Protein Carbonyl Activity
PCOS	Polycystic ovary syndrome
PHN	Postherpetic neuralgia
PMAT	Plasma membrane monoamine transporters
PPCPs	Pharmaceuticals and Personal Care Products
RF	Radio Frequency
RSF	Rapid Sand Filtration
SDGs	Sustainable Development Goals
T1D	Type 1-diabetes
T2D	Type 2-diabetes
TCA	Tricyclic antidepressant
THMs	Trihalomethanes
TOC	Total organic carbon
TOF	Time of flight
TPs	Transformative Products
UDMH	1.1-dimethylhydrazine
UV	Ultraviolet
VOC(s)	Volatile Organic Compounds
WWTP	Wastewater Treatment plant
2,4- DAT	2,4-Diamino-1,3,5-Triazine
2,4-AMT	2-Amino-4-Methylamin-1,3,5-Triazine
3,3-CDTA	(3E)-3-(Chloroimino)-N, N-dimethyl-3H-1,2,4-triazol-5-amine

Variables

A	Absorbance
C	Concentration

C_0	Initial Concentration
C_{O3}	Concentration of the ozone stock solution
DF	Driving Force
e	Elektron
eV	Electrovolt
K_H	Henry's constant
l	Cuvette path length
log K_{OC}	Soil-Organic Carbon Partition Coefficient
log K_{OW}	Octanol-water partition coefficient
M	Molar mass
MEC	maximum measured environmental concentration
M/Z	Mass-to-Charge Ratio
PNEC	predicted no effect concentration
RQ	Risk Quotient
T	Contact time
ε	Extinction coefficient

1 Introduction

This section includes a background that defines the problem. The aim, research questions, and limitations will also be discussed.

1.1 Background

In recent years, Sustainable Development Goals (SDGs) have gained worldwide focus to promote the overall welfare of society. SDGs consist of 17 goals that are strongly interconnected with each other (United Nation Development Programme, 2026). Several goals, such as SDGs 3, 6, 14, and 15, can be associated with the scope of this study, specifically SDG 6, which highlights the importance of maintaining clean water and sanitation. With the increased occurrence of pharmaceuticals in the environment, many countries, such as Sweden, Switzerland, the Netherlands, and other international organizations, including the United Nations, have recognized and taken action to reduce the concentration of pharmaceuticals (European Commission, 2019).

The occurrence of pharmaceutical contaminants in aquatic systems has emerged as an important human health and environmental problem, especially in the context of water reuse and reclamation initiatives to mitigate water scarcity and the high reliance on impacted surface water sources for drinking water production. Pharmaceuticals are found at low concentrations in water bodies and are biologically active, which makes them accumulate at the bottom of the water. Additionally, pharmaceuticals are classified as persistent pollutants, can be either hydrophilic or lipophilic, and can be consumed by biota. Conventional water treatment methods have been proven to be inefficient in treating pharmaceuticals, as reported by several studies. Consequently, compounds discharged from the wastewater treatment plant (WWTP) risk being inefficiently treated. As a result, they are continuously transported into receiving water bodies, causing them to persist in the environment despite being resistant to degradation (Zvanaka & Tebogo, 2024; Mohapatra et al., 2025).

Pharmaceuticals in the aquatic environment threaten aquatic ecosystems in different ways. For instance, when pharmaceuticals accumulate in water bodies, their high levels of organic matter can lead to oxygen depletion, which contributes to eutrophication and disturbs photosynthesis. Moreover, antibiotic residues can stimulate the development of resistant bacteria, which affect microbial communities and disrupt the overall function of the ecosystem. Hormonal pharmaceuticals such as progestins and estrogen have shown endocrine and hormonal disruptions in fish populations caused by feminization and impaired reproduction. Also, painkillers such as ibuprofen can have antimicrobial effects against bacteria and pathogenic fungi (Shola et al., 2022).

In addition to their environmental effects on aquatic ecosystems, the occurrence of pharmaceuticals in drinking water sources has also gained huge concern related to the long-term exposure effects on human health. Regardless of their low-level concentration and not being potentially severely harmful, they can still produce long-term problems for public health related to chronic exposure. Therefore, given the limited efficiency of conventional treatment technologies in removing pharmaceuticals, it is crucial to increase attention for further investigation of advanced treatment methods such as ozonation, adsorption, ultraviolet, and advanced

oxidation processes. Additionally, evaluating the efficiency of several combinations of these methods might be beneficial to ensure high drinking water quality and protect both human health and aquatic life (Zvanaka & Tebogo, 2024).

1.2 Aim

This thesis aims to identify and quantify pharmaceuticals present in Lake Rådasjön, located in western Sweden. Furthermore, the study reviews current treatment methods applied at the Mölndal drinking water treatment plant (DWTP), alongside other pharmaceutical treatment methods reported in the scientific literature, to identify the most effective single treatment techniques for removing the targeted pharmaceuticals. Based on the outcomes of this strategic literature review, a laboratory-scale experiment will be conducted to determine whether the combined application of the two preselected treatment methods, ozonation followed by granular activated carbon (GAC) and ozonation followed by chlorination, improves removal efficiency compared to individual treatments or not.

The report will also assess the potential impacts of pharmaceutical residues on human health, the environment, and aquatic biota. Depending on the results obtained, recommendations for future research will be addressed, focusing on the need for implementing these combined treatment methods to efficiently remove pharmaceuticals.

1.3 Research questions

By the end of this study, the following questions will be answered:

- What pharmaceutical compounds are present in Lake Rådasjön, at which concentration levels do they occur, and what potential risks do they pose to human health, the environment, and the aquatic ecosystems?
- Given the treatment methods currently applied at Mölndal drinking water treatment plant, how do they contribute to the removal of pharmaceuticals? Are there any additional approaches that are more efficient reported in scientific literature?
- Does the combination of the most efficient treatment methods conducted from the literature review (ozonation, ozonation combined with GAC, and ozonation combined with chlorination) result in improved removal efficiency compared to only treating pharmaceuticals through single treatment methods?

1.4 Limitations

Several limitations that constrain the scope of the study are presented below:

Due to budget limitations, the treatment efficiency of the WWTP processes will not be examined within the scope of this thesis. As a result, the study focuses only on pharmaceutical occurrence and treatment strategies associated with drinking water treatment without including pharmaceutical discharges from WWTPs.

In addition, owing to financial restrictions, the review and evaluation of single pharmaceutical treatment methods are conducted through strategic literature research rather than laboratory experimentation. Due to that, only two combined treatment

approaches, consisting of two selected treatment methods reported in the literature as the most effective, will be experimentally assessed in the laboratory. Other potential effective combinations will not be further examined. Also, the assessment of the combined treatment methods will be conducted under controlled laboratory conditions, so factors such as the retention time and complex physical, chemical, and biological processes that occur in DWTPs will not be fully considered.

Furthermore, the identification of the pharmaceuticals in field samples is limited to the compounds that can be detected and analyzed in the commercial laboratory. Therefore, pharmaceuticals that cannot be analyzed in the laboratory will not be included in the results. Lastly, due to the lack of appropriate equipment, not all promising efficient pharmaceutical treatment methods could be evaluated in the Chalmers laboratory. Therefore, advanced treatment methods such as membrane filtration, including reverse osmosis (RO), were excluded from laboratory assessment, despite their reported high treatment efficiency for pharmaceuticals.

2 Literature review

This chapter includes a review of the possible contamination sources in the lake and their fate. It also provides a comprehensive review of the removal mechanism underlying the most adopted treatment processes in drinking water treatment plants. Furthermore, it explains how each method functions and the factors that impact removal efficiency. Moreover, this chapter will also highlight additional treatment methods that potentially eliminate or reduce the presence of these pharmaceuticals in water, based on the literature. It will further explain the impact of pharmaceuticals and their by-products on human health, the aquatic ecosystem, and the environment.

2.1 Pharmaceutical pathways and fate

Pharmaceuticals are a sub-category of micropollutants that can be found in the environment and contribute to contamination of drinking and surface water in different ways (see Figure 1). The sources of pharmaceuticals are anthropogenic and mainly come from inefficient treatment processes in wastewater treatment plants, overflow of the combined sewage system (CSO), leakage from old wastewater pipelines, leachate from unsafe disposal of sludge, unsafe disposal of industrial hazardous waste residues, illegal medicine flushing, on-site wastewater treatment, runoff from organic fertilizers from agriculture, and livestock manure (European Commission, 2019; Slósarczyk et al., 2021).

The source of household pharmaceutical residues originates from human metabolism and incomplete digestion of medicines, which are later excreted from the human body and enter the sewer system. The pathway for receiving water depends on whether the residential area is connected to the municipal wastewater system or relies on a septic tank (on-site treatment system). In both cases, pharmaceuticals can enter the raw water sources in different ways (Zheng et al., 2024; Slósarczyk et al., 2021). If the connected system were municipal, then wastewater would be transferred to a wastewater treatment plant, where it would be treated before discharge. However, removal efficiency can differ based on the adapted treatment processes in the plant and the type of pharmaceuticals; most conventional treatment processes (among others, coagulation, flocculation, sedimentation, and filtration) are inefficient in removing pharmaceutical compounds (Slósarczyk et al., 2021).

Pharmaceuticals can also reach the water recipient during extreme weather events through bypassing one or more treatment processes or through combined system overflow. In the same way, overflow or bypasses from industrial wastewater systems that come from pharmacies and pharmaceutical manufacturers can contribute to pharmaceutical discharge during production and waste management processes (Slósarczyk et al., 2021).

Flushing unused medicines down the toilet or disposing them in landfills are both examples of improper pharmaceutical disposal, which can contribute to the presence and spread of pharmaceuticals in nature. The substance can therefore enter the system either through inefficient treatments or through leachate from both biological and chemical degradation in the landfill (Biswas et al., 2021; Slósarczyk et al., 2021). Pharmaceuticals can enter water bodies and aquatic environments via wastewater sludge and composted livestock manure, which are often used as organic fertilizers.

The decomposition and runoff from livestock farming and agriculture can also contribute to the occurrence of pharmaceuticals in surface water (Slósarczyk et al., 2021; Zheng et al., 2024).

Once pharmaceutical compounds reach raw water sources, they can be ingested by humans either by drinking water with high pharmaceutical concentrations or indirectly by accumulation in the aquatic organisms, which then can be transferred to humans through the food chain. Another indirect human exposure to pharmaceuticals is ingestion of water during swimming or water-related activities. However, the rate of degradation and level of concentration of pharmaceuticals in the aquatic environment depend on several factors, such as redox potential, temperature, depth, pH, physicochemical properties of the water, and the presence and activity level of microorganisms (Slósarczyk et al., 2021).

Although pharmaceuticals are anthropogenic in origin, they experience several types of natural processes, such as biodegradation, volatilization, photolysis, hydrolysis, dilution, chemical transformation, sorption, and interaction with organic matter, compounds, and other particles (Slósarczyk et al., 2021).

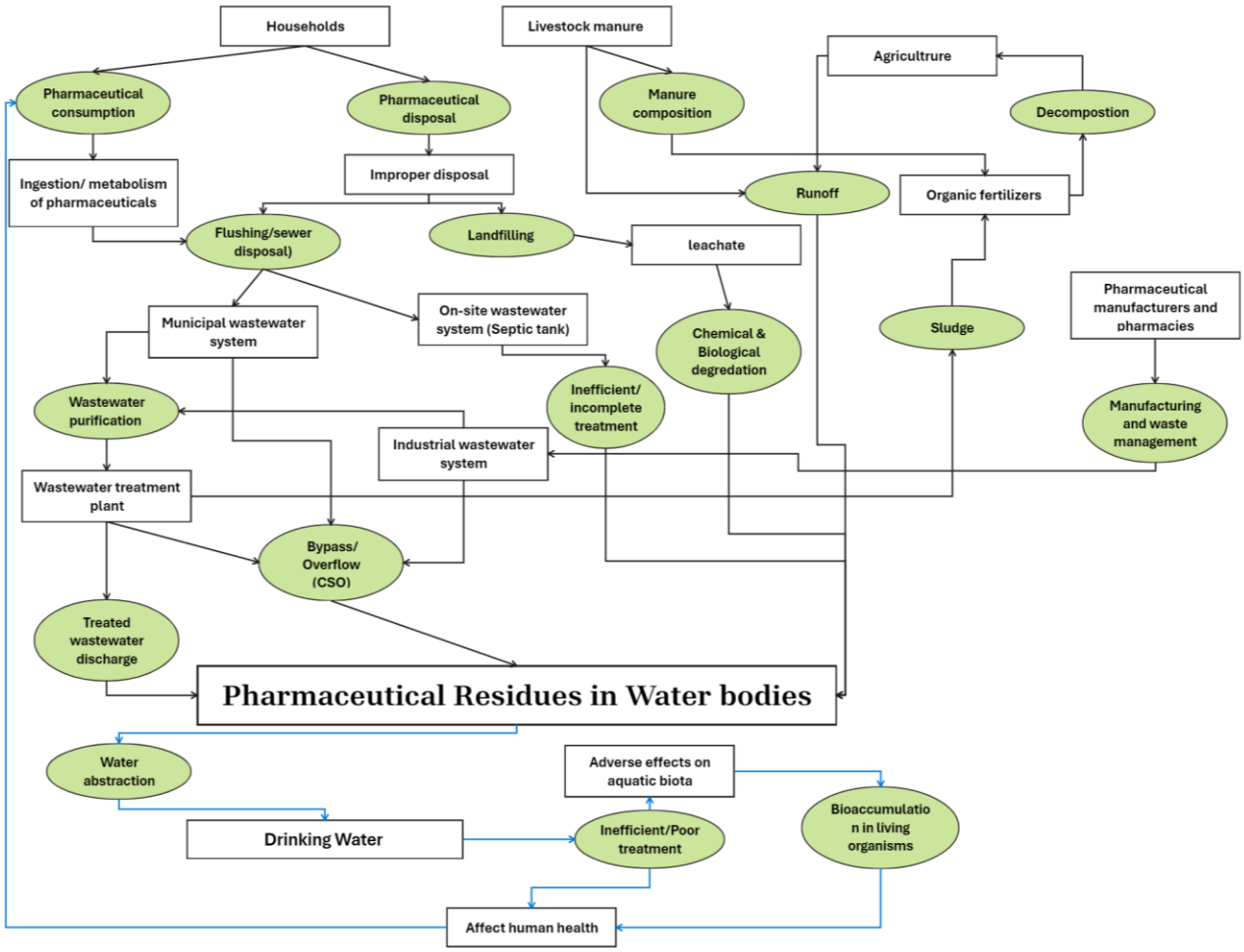

Figure 1: Conceptual diagram describing the possible sources and pathways of pharmaceuticals, their fate in water bodies, and their potential impacts on ecosystems and human health. The blue arrows show the impact of pharmaceuticals on human health, and the black arrows show the pathways (based on European Commission, 2019; Slósarczyk et al.,2021)

2.2 Treatment trains at DWTP

This section provides an overview of the most common treatment processes applied in DWTPs, along with other advanced treatment technologies that potentially can remove pharmaceuticals from drinking water. It will also discuss their working mechanism and their contribution to ensuring safe water quality.

2.2.1 pH adjustment

pH is an important water quality parameter as it indicates whether the water is acidic or alkaline. pH for normal drinking water ranges between 6 and 8.5. However, when water has a pH < 7, then the water is acidic and can result in pipe corrosion, triggering metals to leach, which directly affects human health. Water with a pH > 7 is alkaline and can taste like soda; it can also contribute to corrosion problems. Therefore, it is of great necessity to adjust and control the pH values of drinking water during different treatment processes to ensure high water quality. There are different approaches to adjusting pH, with each having some limitations. These techniques are neutralizing filters and pump systems that are chemically injected with neutralizing solution (Water Systems Council, 2026).

Neutralizing filters are a simple treatment device used to raise pH by adding neutralizing material such as calcium carbonate ($CaCO_3$) for normal pH, and magnesium oxide (MgO) when pH is very low. The pH increase is achieved as these neutralized minerals dissolve in water, leading to increased hardness and alkalinity. As hardness can be a major problem, it is usually treated by ion exchange in a water softener device. This process leads to the removal of salt, which is the main reason for having high hardness values (Water Systems Council, 2026).

A chemical feed pump system operates by mixing soda ash (a compound similar to baking soda) with well water in a tank, resulting in a high pH mixture. A chemical feed pump then injects this mixed system into the piping system in households, which neutralizes the system by reacting with the low pH water. Water quality parameters such as alkalinity, hardness, and sodium content need to be monitored continuously after the installation of the treatment system (Water Systems Council, 2026).

In DWTPs, the treatment system is most efficient when pH varies between 6.8 and 7.5. This pH range contributes to achieving increased effectiveness in the disinfection process and overall high stability of the treatment system. If pH is high, at 8.5, it can weaken the chlorination process as it reduces the hypochlorous acid (HOCl) levels, which means more acid needs to be added to balance the system. At a lower pH of 6, the formation of hypochlorous acid increases, which is considered the most effective chlorination agent. Moreover, different chlorinating agents can affect pH, with pH rising when liquid chlorine is used. Consequently, if no balance in the system is achieved using different acids or buffering agents, the effectiveness of chlorine gas decreases. This is caused by a large amount of chlorine being converted into hypochlorite ion (OCl^-), which is a less effective chlorinating agent than free chlorine. Therefore, pH control is necessary and can be achieved by different methods based on the treatment system's needs (EaiWater, 2026).

2.2.2 Chemical precipitation

Chemical precipitation is a physicochemical water treatment method implemented in drinking water and wastewater treatment plants to remove ionic compounds in water (mainly heavy metals), but also organic molecules, phosphorus, and hardness. The procedure is achieved by adding counter-ions that convert them into insoluble precipitates that can be removed by processes that follow precipitation, such as sedimentation and filtration. Chemical precipitation is affected by different principles that adjust concentrations and other conditions to ensure removal efficiency. Factors such as reaction equilibria, solubility equilibria, ion activity, pH, and reaction kinetics are determined by the precipitation driving force (DF). If DF<1, then no precipitation will occur due to undersaturation; if DF=1, the solution is saturated and precipitation occurs; if DF>1, the solution is oversaturated and precipitation is happening at a very slow rate. Hydroxide precipitation and carbonate precipitation are the main types of chemical precipitation in DWTPs. Hydroxide precipitation is done by raising pH using an alkaline to precipitate heavy metal ions into hydroxide so they can be removed by either filtration or sedimentation, while at carbonate precipitation, metals such as calcium, directly related to water hardness, are removed by direct precipitation using calcium carbonate or by adding carbon dioxide (CO_2) to convert hydroxides into carbonates, which easily form filtered precipitates (Wang et al., 2005).

Regardless of its effectiveness in removing heavy metals from drinking water, chemical precipitation has several limitations that can impact the operation efficiency if not controlled. The sudden change in the increment in temperature rate above 2 °C per hour can lead to instability, causing carryovers to the system, and a temperature imbalance, which can prevent water heating. Additionally, how water flows play a critical role in the system. Rapid flow conditions, such as sudden changes in factors like water volume, can lead to disturbance within the system. As a result, steady-state operation, where the flow rate is relatively constant, is required for the whole system with design limits, aiming to enhance performance and minimize load swings on the equipment. Not only that, but continuous chemical control of the system is also critical to ensure sufficient water quality, especially in surface water bodies, as it can vary due to changes in chemical feed rates (Watertechnologies, 2026).

2.2.3 Coagulation/ flocculation

Coagulation and flocculation are core physicochemical processes in many drinking water treatment plants, mainly applied to remove colloidal particles, suspended solids, turbidity, NOM, bacteria, viruses, parasites, humic materials, and contaminants that cannot be effectively removed by sedimentation or filtration alone. Colloids are small particles that typically range between 0.001-10 μm; they have a large surface area and can be found in water bodies. They are widely distributed and stable because of their electrostatic repulsive forces, which also prevent the particles from aggregating. Aluminum sulfate, ferrous sulfate, and ferric chloride are typical aluminum and iron salts that can be categorized as inorganic chemicals that can be added to water to achieve efficient coagulation (Wang et al., 2005).

These coagulants enhance the destabilization and agglomeration of particulate compounds that are difficult to treat and have a low settling rate. This is done as coagulants undergo dissolution and hydrolysis reactions that form highly charged

metal hydroxides. To achieve the destabilization process, four coagulation mechanisms must be done, which include double-layer compression, adsorption and charge neutralization, particle entrapment to form precipitates, in addition to adsorption and bridging between particles. After the destabilization process, particles get in contact with each other by increasing their collision rate, increasing the attachment potential, and enhancing the aggregation of particles into larger and denser flocs that can then be separated further by sedimentation and/or filtration (Wang et al., 2005).

The efficiency of coagulation and flocculation depends on several factors such as colloid concentration, coagulant dosage, zeta potential, pH value, anions & cations in solution, temperature, alkalinity, mixing conditions, and design conditions of flocculation tanks. One of the most important above-named factors is pH, as it directly controls the solubility of colloidal dispersions and coagulation speciation. Temperature also plays a critical role as coagulation using metallic salts is less effective at low temperatures due to slower velocity, kinetic energy, and decreased chemical reaction rates. As a result of that, alums do not perform well at low temperatures. Therefore, a possible solution could be to use iron-based salts for water with lower temperatures. Another possible method is to add bentonite as a coagulant, as the negatively charged clay particles enhance coagulation via charge neutralization instead of sweep coagulation. To optimize the plant operation, evaluate, and control the coagulation process, the jar test is considered the most efficient method as it controls the selection of several factors such as coagulant types & dosage, optimum operating pH, chemical addition sequence, and optimum energy and mixing time for slow and rapid mixing (Wang et al., 2005).

The ability of coagulation to remove pharmaceuticals from drinking water has been investigated in different studies. According to Vieno & Tuhkanen (2006) pharmaceuticals such as diclofenac, ibuprofen, bezafibrate, carbamazepine, and sulfamethoxazole have shown a low removal efficiency using alum at pH 6 and ferric sulphate at pH 4.5. This shows that coagulation is an ineffective method for pharmaceutical removal, mostly the non-ionizable compounds such as carbamazepine and sulfamethoxazole, which showed a poor removal efficiency with less than 10%. On the other hand, ionizable pharmaceuticals such as diclofenac showed a removal efficiency of 66 % using ferric sulphate as a coagulant in pure water and up to 77 % in water containing dissolved organic matter with high molecular weight. However, several conditions occurring under the coagulation, such as low pH, using iron-based coagulants, and high humic material content, can enhance the removal of ionizable pharmaceuticals. A conclusion that coagulation by itself cannot ensure an efficient pharmaceutical removal. But more likely, it should be treated more as a supportive barrier rather than a main treatment process in drinking water treatment plants.

2.2.4 Rapid sand filtration

Rapid filtration, also known as rapid sand filtration (RSF), is a common method used in drinking and wastewater treatment plants, and it is typically applied either after chemical treatment processes or as a primary filter followed by slow sand filtration (SSF). However, the SSF will not be presented in this section since it is not very efficient in removing most of the pharmaceuticals from drinking water (Nelson et al., 2026). Moreover, SSF tends to have a higher installation cost and a bigger unit size,

around 50-200$m^{2,}$ compared with the RSF, which requires a surface area between 10-100m^2 (The Water Treatments, 2026).

The objective with the RSF treatment method is to reduce suspended solids concentration, remove odor and taste, eliminate Giardia and Cryptosporidium, and reduce turbidity to less than 0.1 and a maximum of 0.3 NTU. RSF is considered the final step in the solid-liquid separation stage of the drinking water treatment processes. The sand grain size typically ranges from 0.4 to 1.5 mm; however, it may vary depending mainly on raw water quality and the treatment method applied prior to it (Ratnayaka et al., 2009).

The treatment method works by having water pass through different layers of the filter, causing contaminants and finer particles to attach to the pores between the sand grains. On the other hand, the treated water accumulates at the bottom of the filter. RSF can treat large amounts of water, as it is described as a rapid treatment process. The main parts of an RSF system are a sand or gravel bed, an underdrain system, and a backwashing mechanism (Water and Wastewater, 2015).

According to Ratnayaka et al. (2009), particle removal in RSF occurs through physical processes such as gravity, hydrodynamic diffusion, and molecular interactions (attraction and repulsion due to Van der Waals forces), as well as physicochemical processes, such as calcium carbonate deposition. Conventional pretreatment methods, such as coagulation and flocculation, need to be implemented to enhance the removal efficiency of small particles in the RSF.

The filter media removes particles within the depth of the filter bed, and as a main design consideration, the filter depth should be 1000 times greater than the effective grain size. Filter installation normally consists of different configurations, and when the number of filtration units is less than five, then they are usually arranged in a single bank; otherwise, they are divided evenly between two banks. RSF consists of different filter materials and includes a minimum of three filter layers. A graded sand bed contains heterogeneous layers of fine to coarse sand with a total depth of 0.7 m, while a homogeneous filter consists of uniform coarse monograde sand with a depth of 0.9 to 1 m (Ratnayaka et al., 2009).

Ratnayaka et al., (2009) describe further that as water passes through the filter media and solids accumulate, pores gradually become clogged, resulting in head losses along the filter depth. Head losses are proportional to flow velocity; therefore, flow control systems become essential to prevent negative head conditions (where head losses get higher than water depth), air binding, crack formation, and mud-balling in the filter bed, all of which deteriorate filtration performance. Water temperature, clog level, and water source, either ground or surface water, are all factors that impact the negative head condition.

Flow control systems include constant-rate filtration, declining-rate filtration, and backwashing. In constant-rate filtration, outlet valves are used to maintain a constant flow rate, and they are opened when the head loss increases. Declining-rate filtration, applied typically in large filtration banks, is based on the idea that the filtration rate decreases with increasing head loss. Backwashing is used to clean the filter after it has

reached its maximum head losses, after a certain operating time, or when filtration performance deteriorates and turbidity increases (Ratnayaka et al., 2009).

Backwashing operates by reversing the flow direction of the water, in which the accumulated particles loosen as the water passes through the filter bed upwards. Under normal operating conditions, backwashing takes place every 1-3 days. Air scouring may also be implemented to enhance the backwashing performance by pumping air into the filter bed to disturb the filter media and release trapped grease and trapped particles. When backwashing is conducted at an adequate velocity, fluidization occurs, meaning that as clean water is pumped from the bottom to create voids between sand grains, the sand will expand, rotate, and rub against each other, leading to the release of contaminants from the filter media. Backwashing efficiency is influenced by water temperature; lower temperatures increase water viscosity, which makes the expansion of the filter bed more difficult and requires a higher backwash velocity. However, insufficient backwashing results in mud-ball formation, nozzle clogging, and sand or gravel particle displacement (Ratnayaka et al., 2009; Water and Wastewater, 2015).

2.2.5 Continuous sand filtration

The DynaSand filter is a sub-category of continuous sand filtration and is marketed under different brand names, such as Suirei (SUIREI, 2026), Parkson in the USA (Parkson, 2026), SuperSand in North America, but the most popular brand is DynaSand (Sulzer, 2026). HUBER sand filter CONTIFLOW® is another example of a continuous sand filter that uses the same principle as the DynaSand filter. The HUBER sand filter is preferable due to its high flexibility and low operation costs (Huber Technology, 2026).

DynaSand filter is usually used to treat influent water, such as drinking water, wastewater, and water from industrial effluent, before it is discharged to water bodies and recipients. The DynaSand filter was developed in the 1970s, and today it has become the most used technique in continuous filtration (Sulzer Nordic water, 2024).

The DynaSand filter has various applications, e.g., reducing suspended solid concentrations, removing nitrogen, phosphorus, as well as BOD and COD to meet environmental standards. It can also be used as a pretreatment to other processes or to treat water bodies containing heavy metals. The DynaSand filter consists of different parts and configurations, and it can be used solely as one single-filter or as several filters installed in the same basin that work in parallel to achieve the required standard and match the capacity (Sulzer Nordic water, 2024).

DynaSand filter comes in different sizes and types, which makes it flexible to fit in several sites with various application requirements. The process has a deep bed with granular filter media and a reverse water flow. The deep filter bed in some of the applications can reduce the requirement of pre-sedimentation or flotation, due to its huge depth that allows the filtration and handling of high levels of suspended solids (Parkson, 2022).

The whole working process of the DynaSand filter can be illustrated through Figure below. The filter works as the raw water enters near the top of the tank via the influent pipe (1) and flows the whole way down through a thin influent annular (2) that is

located between the influent pipe (1) and the airlift housing (14). The raw water reaches the bottom of the sand bed through feed radicals (3) that are open at the bottom. After that, the influent flows upwards to the filter, and all the impurities are seized by the sand. The treated water continues to move up and then exits the filter from the filtrate weir (10) and then through the effluent pipe (5) (Parkson, 2022). The DynaSand filter also has a continuous self-washing mechanism for its filter media. As the sand containing the impurities reaches the filter's top via the airlift system, it directly enters the sandwasher (9), where the impurities and the solid particles that have accumulated on sand grains are removed using a filtered water flow that moves through the sand particles. Following this step, the mix of contaminants and washed water is pushed through the reject compartment (8). From the compartment, the contaminants are carried over the reject weir (11) and finally exit the filter through the reject pipe (12) (Parkson, 2022).

The DynaSand filter has both its own benefits and drawbacks. DynaSand filter has several benefits, for instance, it has continuous backwashing cycles with no shutdowns, which makes it easy to maintain, no pump systems or storage tank, which lowers energy consumption and makes the treatment process more cost-efficient. The continuous sand cleaning reduces filter clogging and reduces the overall pressure drop, which also contributes to lowering energy consumption, as well as reducing machinery wear and maintenance. The wide range of applications can also be considered a significant benefit, especially since it can help remove oil, turbidity, and color at certain flow rates, as well as algae, arsenic, cryptosporidium, and Giardia (Parkson, 2022). Moreover, the ability to handle high concentrations of suspended solids through direct feed without pre-treatment, can be considered a benefit. Additionally, the efficient hydraulic distribution of water on the surface of the filter media helps maximize filtration, reduce dead zones, and provide high-quality effluents (Sulzer Nordic water, 2024).

One of the major drawbacks of the DynaSand filter is the high filtrate turbidity caused by a high filtration rate (flux) or the sand having a short circulation cycle (WEILAN, 2026). This issue can be solved by decreasing the influent flow rate. Another problem is the overflow of sand in the reject water, caused by having too high an airlift airflow or the labyrinthine sandwasher being damaged. A proper solution to this problem is to gradually decrease air pressure. A third issue related to the DynaSand filter is having a low reject water flow due to the high position of the reject weir in the filter. This can be solved by lowering the reject weir to achieve an increased differential head (WEILAN, 2026).

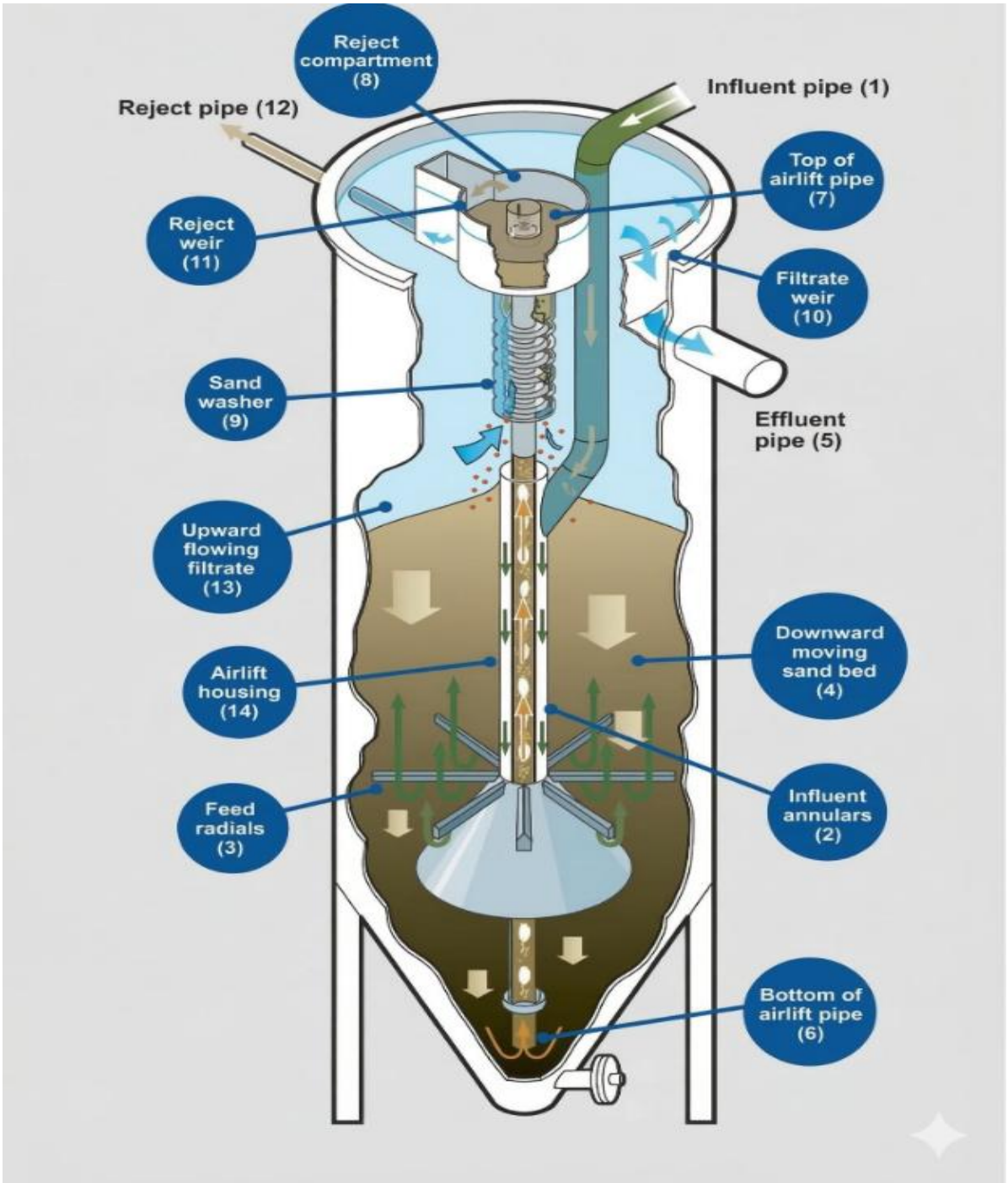

Figure 2: Different components of the Dynasand filter, adapted and remodified with permission by (Parkson, 2022), and processed by AI.

2.2.6 Active carbon

Active carbon can be categorized based on physical form, such as granular active carbon (GAC), powdered active carbon (PAC), extruded activated carbon (EAC), and honeycomb activated carbon, or by the applied raw material (Qizhong, 2024). The carbon source used in GAC and PAC production includes coal, lignite, peat, nutshells, and wood. The applications of different carbon sources depend on the aim; coconut shell, which has micropores, is suitable for the adsorption of small organic compounds and disinfection byproducts; wood carbon with macropores improves the removal efficiency of large organic compounds and improves decolorization. While

coal carbons are most suitable for general organic removal (Water Quality Association, 2013)

This chapter focuses on describing GAC and PAC in detail, since those are the most common adsorption processes.

Granular active carbon

GAC is a porous medium that may consist of micro-, meso-, or macro-pores and is used to absorb dissolved organic compounds, remove byproducts of disinfection, some heavy metals, and pesticides (Water Quality Association, 2013). When it comes to the structure of the GAC, the depth of the media usually ranges from 1-1.2m for filtration and 3m for maximum adsorption; however, the depth depends on the contact time, which typically ranges from 5-30 min. While the flow rate is dependent on the purpose of use, if it is used only as an adsorbing medium, then the velocity of the flow should be 15m/h; otherwise, if it has a dual mission of filtering and adsorbing, then the flow rate should be around 6-7.5 m/h (Ratnayaka et al., 2009).

The adapted indicator for evaluating the ability to adsorb organic compounds is called the iodine number. When the iodine number drops to 60%, the GAC filter needs to be reactivated by incineration to remove organic compounds, and then it can be integrated into the system again. GAC requires maintenance and regular cleaning, typically every 2-3 days for surface water. Cleaning occurs either by backwashing water to remove adhesive pollutants from the filter media or by an air scouring process; however, using regular air scouring leads to the breakdown of the carbon granules. The washing rate for the GAC medium is 5-12 mm/s, and it is influenced by the effective bed size, the applied carbon source, and water temperature. During the backwashing, the carbon bed usually expands between 20 to 30% (Ratnayaka et al., 2009).

GAC has proved to be effective in reducing the concentration of several types of pharmaceuticals and personal care products, including acetaminophen, atrazine, caffeine, carbamazepine, DEET, ibuprofen, and other types of antibiotics. In pilot scaled experiment, GAC has proven to lower the concentration of pharmaceutical and personal care products (PPCP) below the detection limit, but for a certain time. After that, the carbon filter hit its limit, often between 25 and 50 days for PPCP breakthrough. In a full-scale study, the removal efficiency for PPCP exceeded 90% after 7.6 minutes as contact time. Without regular treatment of the GAC filter, the removal efficiency was reduced to 3-63% (Zhang et al., 2016).

Powdered activated carbon (PAC)

Powdered activated carbon is a widely used treatment technology that is similar to GAC. Both PAC and GAC are produced from raw carbon materials, as mentioned earlier, and undergo almost identical processes to activate the carbon source. However, the main difference between these methods lies in surface area and particle size, resulting in diverse properties that influence adsorption capability, stability, costs, and application area (Heycarbons, 2026).

PAC is a fine-graded activated carbon with particle size ranging from 10-100μm and has an enormous surface area that offers high adsorption potentials in the short-term (Newcombe, 2007). This technology is usually applied in water treatment for removing organic components and eliminating both taste and odor. Additionally, it is used in flue industrial gas treatment for removing persistent organic matter, volatile organic compounds (VOCs), and other heavy metals such as mercury. It is also used in the pharmaceutical industry, in the food and beverages industry, and in air purifiers. In the pharmaceutical industry, it is used for removing the organic impurities along with other harmful byproducts that are generated during production. It is also used for decolorization. While in the food industry, it is used to treat the odor, decolorization of some products, and to remove impurities (Puro Carbon, 2024).

PAC can be dosed directly into the water along with the chemical addition, or during settling that takes place before sand filtration, to be then removed in the coagulation process. The method is known for its high adsorption capacity and is primarily used in batch mode, particularly in emergencies when immediate purification is required, such as for algal toxins. However, this method cannot be reused and ends up in the backwashed water (Newcombe, 2007).

The contaminants are removed by molecular diffusion before being adsorbed to the activated carbon. The diffusion process is where contaminated components move from bulk water through the liquid surface film into the pores of the activated carbon, where absorption occurs. The adsorption can occur physically or chemically by the adherence between the activated carbon surface and the contamination compounds in the adsorbate, either by van der Waals forces or by other strong chemical bonds. However, factors such as pH, temperature, size of PAC particle, contact time, mixing condition, adsorbate solubility, and the hydrophobic and electrostatic interaction between activated carbon surface and the adsorbate can affect the adsorption rate, which consequently impacts treatment efficiency (Newcombe, 2007).

Both PAC and GAC have their advantages and disadvantages. The advantages of PAC are that it can be dosed directly into water, it has a lower production cost, but in the long-term, it turns out to generate a higher cost since it needs to be replaced continuously. Fine particles increase the surface area of the filter media and enhance the adsorption capacity for contaminants quicker than GAC. However, since PAC can only be used once, it leads to a higher waste rate, which may raise environmental concerns. Moreover, fine particles can lead to dust formation, which can pose harm to human health (Heycarbons, 2026).

PAC is more suitable for emergency treatment and for rapid adsorption in areas where rapid adsorption is needed, whereas GAC is more suitable for large-scale water treatment and air purification. The GAC requires a fixed-bed reactor, distinct from PAC, which can be added directly to water, as mentioned earlier (Heycarbons, 2026).

2.2.7 UV-radiation

UV radiation, which is also known in some literature as UV-irradiation, is a physical disinfection method used to deactivate bacteria and many viruses without adding chemicals or leaving residual disinfection. UV is also effective in inactivating parasites such as protozoa in water. It is also useful in breaking down the molecules of organic compounds into smaller parts through photo-oxidation, which can reduce the

compounds that cause odor and taste, pesticide concentrations, and the toxicity of algae in the water (Private Water Supplies, 2026). Additionally, it is considered a primary and important disinfection process since both chlorine and ozone are weaker and less effective in inactivating parasites (Persson, 2025).

According to *Disinfection by UV Radiation: Technical Guidance* (2026), microorganism deactivation occurs when UV light passes through the pathogen's cell walls, damages DNA, and disrupts vital cellular functions, leading to cell death and/or limiting its ability to reproduce. The optimal wavelength to have efficient microbial deactivation and DNA damage is 254 nm, although wavelengths between 200 and 300 nm are usually effective against bacteria. Whereas shorter wavelengths of 185 nm are more effective for photo-oxidation of organic compounds. The paper further describes that the effective dose for inactivating protozoa is 6 $mW*s/cm^2$, while viruses require an extremely higher dose of around 100 $mW*s/cm^2$.

UV radiation is generated using low-pressure mercury lamps placed in a stainless-steel reaction chamber with a quartz sleeve in the middle, which allows UV radiation to transmit, cooling and protecting the lamp from fouling. The optimal temperature for the lamp is 40 °C, and it can maintain its efficiency for 10 to 12 months. After that, efficiency deteriorates to approximately 70%. The process needs continuous monitoring and cleaning of both the system sensor and sleeve to avoid fouling (Private Water Supplies, 2026).

The process is sensitive to turbidity, dose, contact time, flow, wavelength, chemical content and quality parameters like hardness and alkalinity. If the water is turbid >1NTU, the suspended particles can act as a shield to protect the microorganisms from interacting with the UV radiation; similarly, if the water contains iron >200 µg/L, manganese >50µg/L, or organic compounds, then the UV transmission to the pathogen's cell becomes low since those compounds will absorb the radiation instead. If the water is hard, a softener might become necessary to avoid the building of limestone that causes fouling. UV has several benefits which make it more likely to use, it is cheap, chemical-free, and provides a low risk of producing by-products. On the other hand, it requires a reliable supply of electricity to operate, very clear water samples, and does not have any lasting residual disinfection to protect the water after exiting the utility (Private Water Supplies, 2026).

2.2.8 Chlorination

Chlorination was first implemented in 1902 in Belgium (Ghernaout, 2017). It is another sub-method within the disinfection category and is considered the final step of the treatment process in many DWTPs to preserve water quality and prevent the reconcentration of pathogens that may occur in water reservoirs or pipelines. According to Olympian water testing (2024), chlorination can be used to target algae and remove taste and odor from the water. However, chlorination agents can be either chlorine gas, sodium hypochlorite, or calcium hypochlorite. Chlorine gas (Cl_2) is the most popular agent, has high decay efficiency, and is more economically beneficial. Sodium hypochlorite is easier to handle and store than Cl_2, but it degrades over time, while calcium hypochlorite is stable, easy to transport, and suitable for emergency scenarios (Olympian Water Testing, 2024). Chlorine dioxide (ClO_2), monochloramine (NH_2Cl), and dichloramine ($NHCl_2$) are other examples of chlorination agents. Both NH_2Cl and $NHCl_2$ are considered sub-categories of chloramine, which are used

primarily as secondary disinfectants (Persson, 2025). However, this section will focus on describing chlorine gas, since it is the most frequently utilized chlorination agent for a large-scale treatment plant (Olympian Water Testing, 2024).

Chlorination is also used to chemically remove microorganisms and deactivate pathogens, including bacteria and viruses, by adding an oxidizing agent such as chlorine gas, which damages microbial cells. Cl_2 reacts with water and passes through hydrolysis to develop HOCL, which is the most effective acid for deactivating the pathogen. However, HOCL can break down into hypochlorite ions (OCl^-) and hydrogen ions (H^+). HOCL is 80 times more effective at inactivating E. coli than OCl^-. To ensure efficient disinfection, the water pH should be between six and seven; in that case, the water will be full of the effective disinfectant acid (HOCL). In contrast, as the pH rises, the water will include more OCl^- (Ghernaout, 2017).

The deactivation mechanism of chlorination involves attacking several spots within the microbial cell. Chlorination agent attacks the cell and damages its wall by making holes that lead to altering the cell's permeability and resulting in leakage of the vital cell's content, then it attacks DNA and RNA, protein, along with other enzymes to damage cell metabolism and prevent it from taking the necessary nutrients, and reduces potassium concentration in the cell. The reaction between HOCL and the iron-sulfur center impacts the cell's ability to respire and to have energy to survive (Ghernaout, 2017).

Disinfectant agent concentration (C), contact time (T), pH, water temperature, and turbidity are factors that influence the deactivation or decay efficiency of chlorination. The CT value is measured in [mg min/L] (see Figure 2 below) and used to estimate the required dose needed to decay or deactivate the pathogen; each pathogen has its own CT value. The higher the temperature, the better the deactivation and the less need for CT. Similarly, at low pH, inactivation becomes more effective, and as pH rises, the acid becomes weaker, and deactivation becomes ineffective. High turbidity levels can act as a barrier for pathogens, hindering them from interacting with the chlorination agent (Ghernaout, 2017). Also, the high concentration of total organic carbon (TOC) can lead to low treatment efficiency since it consumes chlorine first, leaving small doses to react with pharmaceuticals and other pollutants (Zhang et al., 2016).

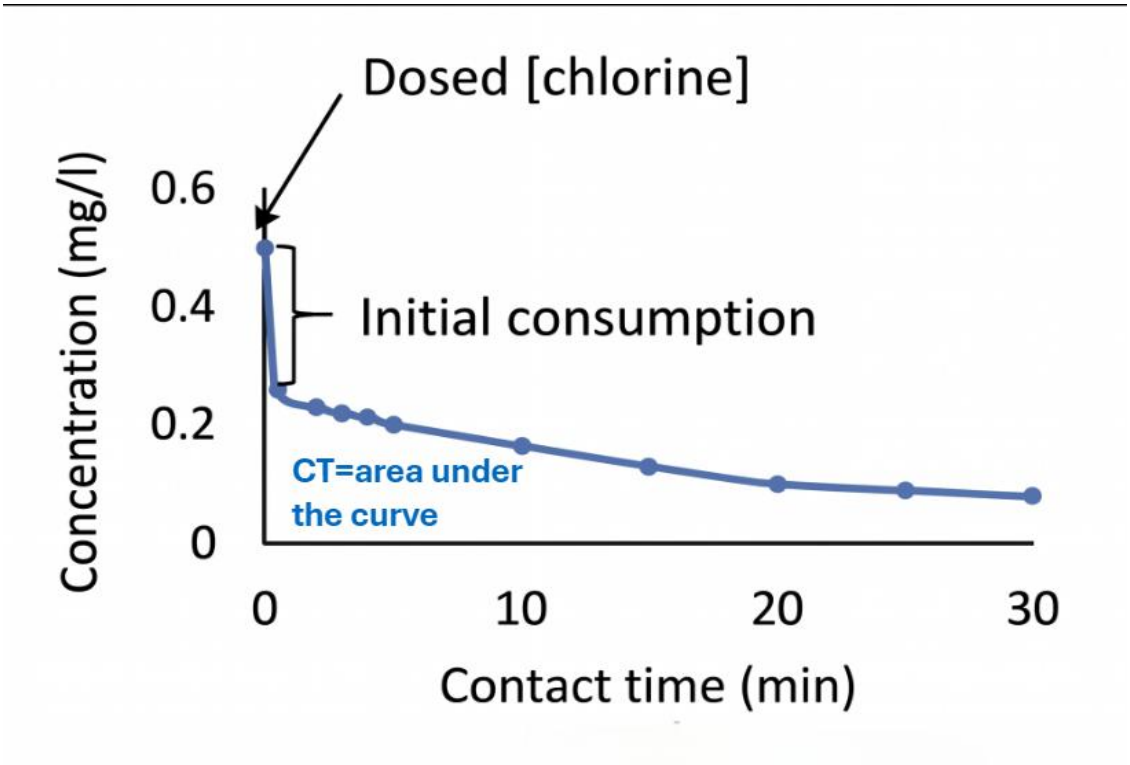

Figure 2: Illustrative Graph of CT (relation between concentration and contact time with chlorine) (Persson, 2025).

Chlorination has been demonstrated in many studies to be effective in reducing both pathogens and other pharmaceuticals. One of the studies shows that the removal of acetaminophen reached 62% when TOC was high, while removal efficiencies exceeded 90% for pharmaceuticals such as sulfamethoxazole, carbamazepine, atenolol, DEET, caffeine, and 17β-estradiol under low TOC conditions (Zhang et al., 2016). Other studies showed that chlorination can widely reduce the concentration of diclofenac, naproxen, and acetaminophen, and have a moderate reduction of ibuprofen with less than 60% (Boledaa et al., 2011). Chlorination can also contribute to Metformin removal, with removal efficiency exceeding 90% (see Chapter 2.3.4 for further information). However, studies agree that chlorination agents have a generally better influence on pharmaceutical removal. Nevertheless, a disadvantage of chlorination is the generation of byproducts such as trihalomethanes (THMs) and haloacetic acid (HAAs), which occur when chlorine reacts with organic matter. These compounds have a negative impact on both human health and the environment (Ghernaout, 2017).

2.2.9 Ozonation

Ozonation has been used in treating drinking water since the 19th century, and in 1997, the US Environmental Protection Agency described ozone as a regulatory in the requirements for surface water treatment in drinking water systems. Ozone (O_3) is a molecule that can either be dissolved in water or coexist with highly purified oxygen. Ozone is one of the most effective disinfectants and is considered a very strong oxidizing agent. Due to its instability, ozone must be produced and implemented onsite. Ozone is produced by electric discharge, where a gas containing oxygen is passed through two electrodes with a high potential difference. Oxygen molecules are

broken down into atoms that are afterwards recombined to form ozone molecules (Wang et al., 2005)

The ozonation process occurs in two different ways: a direct way, where ozone molecules dissolve directly in the water and react with the contaminants, and an indirect way, which involves the formation of hydroxyl radicals through ozone decomposition. Ozone reacts with many organic pollutants and pharmaceuticals because of its high oxidative potential that reaches 2.07 eV, allowing it to break down the molecular structure of the contaminants. Ozonation works best at 7-11 pH levels and requires no chemicals, making it a preferable alternative compared to other drinking water treatment methods such as chlorination. It also generates faster removal rates for many pharmaceuticals. The chemical reaction of producing ozone can be seen in the equation 2.1 below (Wang et al., 2005; Pratiwi o.a., 2025)

$$3O_2 + e^- \leftrightarrow 2O_3 + e^- \qquad 2.1$$

The speed of this reaction increases with increased temperature and happens very fast above 35 ºC. Because of that, the ozone generator needs to be cooled down continuously to reduce the ozone losses (Wang et al., 2005). In comparison with chlorine, ozone does not produce THMs and HAAs, but if bromide ions are present in the analyzed water, other by-products can be generated (Oshiner, 2026). How efficiently ozone can remove pollutants from water relies on several factors, such as pH, ozone flow rate, temperature, dosage rate, and contact time (Pratiwi o.a., 2025).

The advantages of ozonation are that it provides strong oxidizing power with a short reaction time, allowing the pollutants to be killed within a few seconds. Ozonation produces no bad taste or odor and requires no chemicals in the process. It also removes all organic matter content. The process also has some disadvantages, as it has high costs compared with chlorination. Ozone is less soluble in water than chlorine, requiring the installation of special mixing devices (Wang et al., 2005). But overall, as mentioned earlier, ozone technology provides a powerful and chemical-free solution to minimize the pharmaceutical concentrations in both drinking water and wastewater, contributing to protecting the aquatic ecosystem and ensuring safe drinking water that reaches the consumer’s taps.

2.2.10 Advanced oxidation processes (AOPs)

Advanced oxidation processes (AOPs) have recently emerged as highly efficient removal techniques and promise a development in treating pharmaceuticals and their by-products. Additionally, studies related to environmental risks, human health, and ecological impacts of pharmaceuticals on aquatic ecosystems have received attention lately, but the lack of data availability has restricted the research. The fate of pharmaceuticals in the ecosystem is complex and is impacted by multiple factors, which enhances the importance of developing further research methods and testing different treatments to reduce the risk of pharmaceuticals on the environment and human health. As a result, the implementation of AOPs for the removal of pharmaceuticals is an interesting topic to study, which is directly connected to SDG 6, clean water and sanitation (Kanakaraju o.a., 2025).

The concept of AOPs involves the production of strong oxidizing agent radical groups, such as OH radicals, ozone, chlorination, and permanganate. These species

reduce the risk of organic pollutants by breaking them down into smaller and less harmful molecules, which strongly eliminate their side effects. The breakdown is done through four pathways: hydrogen abstraction, radical addition, radical combination, and electron transfer. Besides their capability of forming OH radicals, AOPs in many oxidation applications have a high oxidation potential of 2.8 V, which is the second highest after fluorine, 3.03 V. AOPs are divided into different categories, such as chemical, photochemical, electrochemical, and sonochemical processes. The performance of AOPs can be affected by several factors, for instance, water type, pharmaceutical concentrations, and water complexity. In this section, a different combination of O_3, O_3/UV, O_3/ H_2O_2, and UV/ H_2O_2 will be discussed (Kanakaraju, Sean Goh, & D Glass, 2025; Vašinka et al., 2025).

The UV process by itself can degrade pharmaceuticals and is affected mainly by two factors: the molar absorption coefficient of the treated molecule and the quantum yield (Kanakaraju o.a., 2025). UV photolysis uses ultra-violet light (typically 254 nm) with high-energy UV photons to break down contaminants, while the peroxone process (O_3/ H_2O_2) generates OH radicals from the ozone reaction with hydrogen peroxide. The molar absorption coefficient of ozone is 3300 M^{-1} cm^{-1}, which is much higher at a wavelength of 254 nm compared to the coefficient of H_2O_2, 19.6 M^{-1} cm^{-1}. This indicates that ozone photolysis is more effective than the photolysis of H_2O_2 (Fischbacher o.a., 2018).

An experiment to remove ketoprofen using O_3 and O_3/UV has been conducted in pure water; the results showed that the degradation rate of O_3/UV was 56 times faster compared to O_3 by itself. Additionally, within one hour of treatment, a high mineralization yield of 95% was reported for O_3/UV, compared with only 65% achieved by O_3. Another experiment investigated the oxidation of 40 different pharmaceuticals using O_3, O_3/UV, and O_3/ H_2O_2. In all processes, a more than 90% removal rate was achieved. However, the formation of bromate differed as no bromate was produced after treatment with O_3/ H_2O_2. O_3 alone produced a bromate concentration up to 6 µg/L, while O_3/UV gave slightly lower bromate concentration than O_3 (Fischbacher o.a., 2018).

A study also found that metformin was removed by 37 % using two different combinations of AOPs (O_3/ H_2O_2 and O_3/UV). Additionally, only 20 % degradation was achieved for metformin using UV/ H_2O_2. Changing the dose of H_2O_2 showed a low effect on the degradation yields of metformin, but it limited the bromate formation. This shows that metformin reacts poorly with O_3.To achieve a high removal efficiency reaching 90%, metformin would require a high electrical energy of 0.21-0.39 kWh/m^3 for treatment with O_3/ H_2O_2 and 0.90 – 2.45 kWh/m^3 for all other AOPs combinations (Fischbacher o.a., 2018).

The reaction of bromate formation as a by-product in ozonation processes is pH-dependent, and the reaction rate increases with increased pH to a maximum value of 10.2. If pH is equal to or lower than 7, the reaction becomes very slow, leading to lower efficiency of contaminants degradation and disinfection. Therefore, the pH-dependence of the bromate reaction is of great concern for the efficiency of hydrogen peroxide in controlling bromate formation. N-Nitrosodimethylamine (NDMA) is another human carcinogenic by-product that can be formed during ozonation processes. NDMA concentrations can be influenced by ozone (O_3) dose and bromate

formation; higher ozone doses generally lead to increased bromate formation, which together contribute to a higher risk of forming carcinogenic substances (Fischbacher o.a., 2018).

2.3 Pharmaceutical description

Following the description of the different drinking water treatment methods and how effective they are at removing pollutants, it is necessary to also examine pharmaceuticals by investigating their working mechanisms, chemical properties, remediation, and their associated by-products. This facilitates the evaluation of how effectively some of the previously described techniques can remove both metformin and gabapentin. This section will provide a full-scale description of these two pharmaceuticals

2.3.1 Metformin overview

Diabetes is seen as an epidemic disease worldwide, has huge potential risk to human health, and is ranked as the ninth leading cause of death globally. This disease is related to a metabolic condition in which blood sugar (glucose) is elevated. Diabetes can be divided into three main sorts, including type 1-diabetes (T1D), type 2-diabetes (T2D), and gestational diabetes. Type 1- is where the beta cells, which are responsible for producing insulin, get distracted, whereas type 2- is when the body cannot produce enough insulin or has insulin resistance (Sibiya et al., 2023).

According to the World Health Organization (WHO), there are almost 800 million people diagnosed with diabetes around the world in high, low, and middle-income countries, which is more than four times the ratio compared with 1990 (World Health Organization, 2024). In 2024, Sweden had around 566.6 thousand diagnosed cases of diabetes, and another 161.6 thousand undiagnosed cases (International Diabetes Federation, 2026). Whereas the USA had around 29.1 million people diagnosed with diabetes in 2023, along with another 11 million who are predicted to carry the disease but have not yet been diagnosed (CDC, 2026). However, as the population increases and the adoption of unhealthy lifestyles grows, the risk of getting diabetic diseases will rise as well.

Metformin (MET) is a prescribed oral drug that is widely used worldwide for treating type 2 diabetes. It was first introduced in the 1920s, and many studies have shown a huge range of applications beyond being an antidiabetic drug, such as preventing cardiovascular diseases, controlling inflammation, treating some types of cancers, and chronic diseases, which will be discussed further in Chapter 2.3.3 (Zheng et al., 2024). Briones, Sarmah, & Padhye report in their study that metformin can reduce the incidence of cancer by 30-50%. The study further describes that the active pharmaceutical ingredient of metformin is metformin hydrochloride, which is synthesized by a reaction between dimethylamine hydrochloride and dicyandiamide. However, metformin is sold under different brand names, such as Glumetza, Glucophage, Fortamet, Glucophage XR, and Riomet (Briones et al., 2016). After ingesting the MET, the human body cannot metabolize it, and it is excreted completely from the body, which then can enter the environment through the same pathways as described in Chapter 2.1 and affect both human health and the aquatic ecosystem (Briones et al., 2016; Zheng et al., 2024).

2.3.2 Metformin chemical properties

Metformin has a chemical formula of $C_4H_{11}N_5$, whereas the active pharmaceutical ingredient (APIs), metformin hydrochloride, have a chemical formula of $C_4H_{11}N_5HCl$ (Zheng et al., 2024; Cayman Chemical, 2026). MET is a basic substance with nitrogen functional groups. It has a low soil-organic carbon partition coefficient (log K_{OC}) of around 3.05 and a very low octanol-water partition coefficient (log K_{OW}) of approximately -4.9 and -2.64, as it was reported in other studies by Gao et al. (2025), which signifies that the drug is less absorbed into natural soil, being hydrophilic and therefore has higher aqueous mobility. However, the by-product of metformin, which is Guanylurea (GUA), has a log K_{OW} of -1.22, which indicates lower hydrophobicity in comparison with MET (Gao et al., 2025). Whereas the study conducted by Briones, Sarmah, & Padhye (2016) shows that GUA has a higher ability to be sorbed to soil with high organic carbon compared with metformin. The solubility of 300 g of metformin in a liter of water can occur at 25 ℃, melting between 223-226 ℃, and it is calculated to boil at 268 ℃ (Briones et al., 2016).

Briones, Sarmah, & Padhye (2016) explain further in their study that metformin has a Henry's constant (K_H) value of $7.6*10^{-16}$ atm/m^3/m, which indicates that it is not volatile and does not move to the atmosphere.

2.3.3 Metformin in treating humans

As described earlier, metformin is a drug that is mainly used to treat type 2 diabetes, as it can be orally ingested as tablets or as a soluble solution with a maximum dosage of 2000- 2500 mg/day. After being ingested, metformin reaches the body cells through membrane-bounded proteins called organic cation transporters (OCT1 & OCT3) through plasma membrane monoamine transporters (PMAT), and 90 % of the uptaken dose is eliminated from the body within 24 hours after oral administration. Despite its usage mainly to treat T2D, studies have proven the efficiency of metformin in treating other human diseases, such as polycystic ovary syndrome (PCOS) and non-alcoholic fatty liver disease (NAFLD) (Roberts et al., 2024). Metformin belongs to the biguanide class of medications and acts by reducing hepatic glucose production, decreasing intestinal glucose absorption, and improving insulin sensitivity. MET also aims to increase glucose uptake and make the body use insulin more effectively, resulting in reducing blood sugar instead of increasing insulin levels (Sibiya et al., 2023).

PCOS is a hormonal syndrome that is mainly caused by an ovarian hormonal imbalance. Its consequences involve irregular or absent menstrual periods, increased body hair growth, and difficulties in pregnancy (1177, 2021). Metformin can induce ovulation and reduce the production of androgens, leading to the restoration of the menstrual cycles. Metformin has also been shown to improve insulin sensitivity and promote weight loss. NAFLD is a common disease where fat accumulates in the liver (NHS, 2025). In the case of this syndrome, metformin helps in reducing insulin resistance, reducing body weight, and additionally reduces the metabolic processes, such as accumulated hepatocyte and plasma triglycerides, which contribute to the build-up of fat in human livers (Roberts et al., 2024).

Metformin has also been assessed for its potential role in reducing several types of cancer. This is done by inhibiting and slowing down the cell metabolism processes

related to tumor development and growth, as well as promoting cell cycle. The inhibition of the respiratory chain complex results in increment of produced reactive oxygen species (ROS), which trigger DNA damage, leading to increased apoptosis in damaged cells. As a result of these effects, metformin, as an anti-cancer agent, stimulates the cell death pathways (Roberts et al., 2024).

Metformin, in several studies, has been reported to have antiviral effects. It inhibits and disrupts the cellular pathways associated with DNA replication by inhibiting viral gene repression (Roberts et al., 2024). Additionally, metformin has been shown to reduce proinflammatory cytokines, which are small proteins produced by immune cells that trigger and amplify inflammation (Thermofisher, 2026). By influencing all the above-mentioned processes, metformin creates a toxic replication environment for viruses inside the cells. Taken together, these effects of metformin create huge protection against plenty of viral inflammation. Not only cancer, but different applications of metformin in clinical trials are being tested on animals to treat diseases such as Alzheimer's, Parkinson's, Huntington, and other cardiovascular syndromes (Roberts et al., 2024).

2.3.4 Metformin remediation and its by-products

Metformin does not degrade in the human body, as noted earlier; therefore, it enters the environment primarily through the discharge of inadequately treated wastewater. The concentration can vary between 1 and 3µg/L for MET, and between several µg/L up to 20 µg/L for GUA, depending on the amount of wastewater discharged into rivers and streams (Scheurer et al., 2012). According to Elizalde-Velázquez & Gómez-Oliván (2019), four transformative metabolites of MET can either bypass treatment in WWTP or be formed during treatment processes and then enter surface waters and be uptaken by both plants and/or other aquatic creatures. Those metabolites are 2,4-diamino-1,3,5-triazine (2,4- DAT), guanylurea (GUA), methylbiguanide (MBG), and lastly 2-amino-4-methylamin-1,3,5-triazine (2,4-AMT).

He, Zhang, & Ju (2022), on the other hand, report that there are 32 organic transformative products (TPs) of metformin, and they categorized them based on their pathways and the area of occurrence. The first defined group is biologically produced in wastewater bioreactors, e.g., in aerobic activated sludge, where the main pathway of formation includes metformin demethylation to MBG, which can undergo further deamination and oxidation to produce GUA. It can also form 2,4-DAT and 2,4-AMT as a secondary pathway. The second category occurs both in WWTP and DWTP during AOPs such as UV-photolysis, ozonation, and hydroxyl radical oxidation. This category includes, among others, the covalent dimer of metformin (diMET), hydroperoxide of metformin (METOOH), GUA, MBG, 1.1-dimethylhydrazine (UDMH), and N-nitrosodimethylamine (NDMA). The third category includes TPs such as MBG, GUA, and biuret that occur naturally and slowly in aquatic systems due to microbial degradation (biotic) or photodegradation (abiotic). The last category of TPs occurs as a product of chlorination, where MET reacts instantly with sodium hypochlorite (NaClO), generating (3E)-3-(Chloroimino)-N, N-dimethyl-3H-1,2,4-triazol-5-amine (3,3-CDTA), N-Cyano-N, N-dimethylcarbaminimidic chloride (NCDC), monochlorinated and dechlorinated MET, which are considered extremely toxic and lethal by-products (He et al., 2022).

Factors that affect the occurrence and persistence of MET and its metabolites in both the environment and water bodies include remediation efficiency in WWTPs, water flow rate, dilution frequency in surface water, and the amount of drug consumption (Elizalde-Velázquez & Gómez-Oliván, 2019). The chemical properties of metformin and its TPs, such as log K_{OW} and half-life, can also impact the persistence and the toxicity (He et al., 2022).

There were no comprehensive studies on the removal efficiencies of MET and its TPs for each treatment process in DWTP. According to Scheurer et al., (2012), flocculation, and GAC seem to be inefficient treatments for drinking water compared to ozonation and chlorination, with chlorination being the most effective treatment and flocculation being the worst. Based on an experiment conducted in the laboratory, the detected rate of metformin and guanylurea before and after flocculation was almost the same. On the other hand, a field experiment showed that GAC can remove up to 68% of MET, but it cannot remove any GUA. However, the laboratory experiment showed that GAC had a total breakthrough after 16h, and more than 90% of MET concentration passed through the filter media after 8h of operation. In both ozonation and chlorination steps, the study did not provide any clear information on the concentrations of MET and TPs in both influent and effluent, nor on removal efficiency. Thus, from the degradation graphs presented in the report (see Figure 3), the removal efficiency of MET and GUA could be calculated using the equation 2.2. The removal efficiencies of 1 µg/L MET and GUA with a DOC of 0.9 mg/L by ozonation at an ozone dose of 0.5 g/L O3 after 1 h contact time were calculated to be 50% for MET and 55% for GUA, indicating that GUA has a higher oxidizing potential than MET. From the graphical analysis, it is shown that higher O_3 doses can result in higher removal efficiency. Following the same procedure as in ozonation, the removal efficiency of MET using chlorination after approximately 48h contact time was 100% for chlorine doses of 1mg/L Cl_2 and about 93% for a dose of 0.2mg/L Cl_2 (Scheurer et al., 2012).

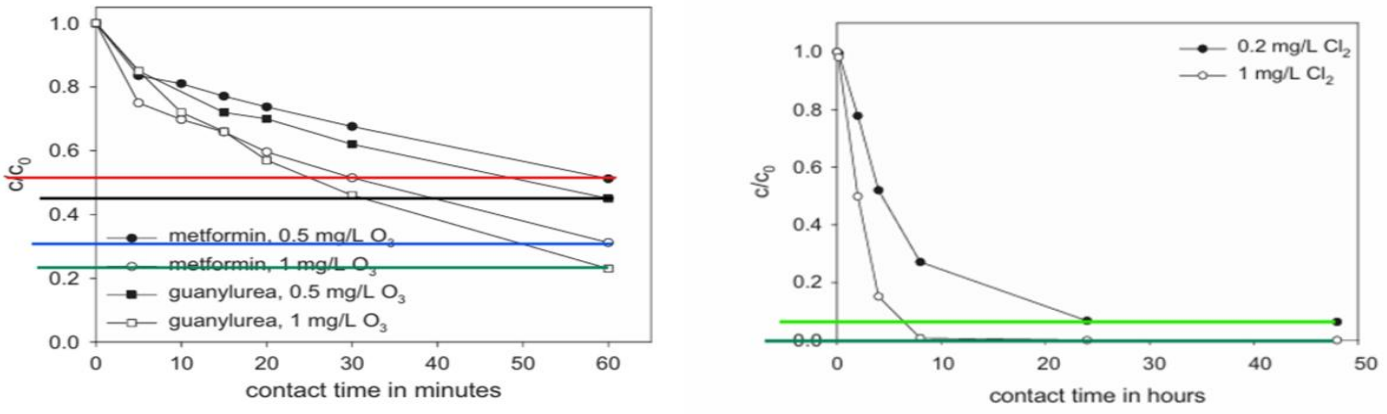

Figure 3: The left graph illustrates the degradation of MET and GUA during ozonation, while the right graph illustrates the removal efficiency of only MET using chlorination from the report (Scheurer et al., 2012). The graph is adapted and remodified with permission from (Scheurer et al., 2012) and the lines represent the reading value of C/C0 that is used to calculate the removal efficiency in equation 2.2

$$Removal\ (\%) = \left(1 - \frac{C}{C_0}\right) * 100\% \qquad 2.2$$

Nevertheless, Elizalde-Velázquez & Gómez-Oliván (2019) reported that the most efficient treatment process in a WWTP was phytoremediation, owing to the low log

K_{ow} values for both GUA and MET. Other methods, such as phytodegradation using $UV_{254,}$ can be applied, but they have low MET removal rates, reaching approximately 24% after 60 minutes. Another study reported that the concentration of metformin following UV-treatment was higher than influent, which can be explained by the fact that some by-products return to the original MET form (Elizalde-Velázquez & Gómez-Oliván, 2019; Briones et al., 2016). Ozonation, on the other hand, has shown a high removal rate of metformin and guanylurea in spiked tap water. The elimination was estimated at 70 and 80%, respectively, for each medicine, after 1h contact time (Briones et al., 2016).

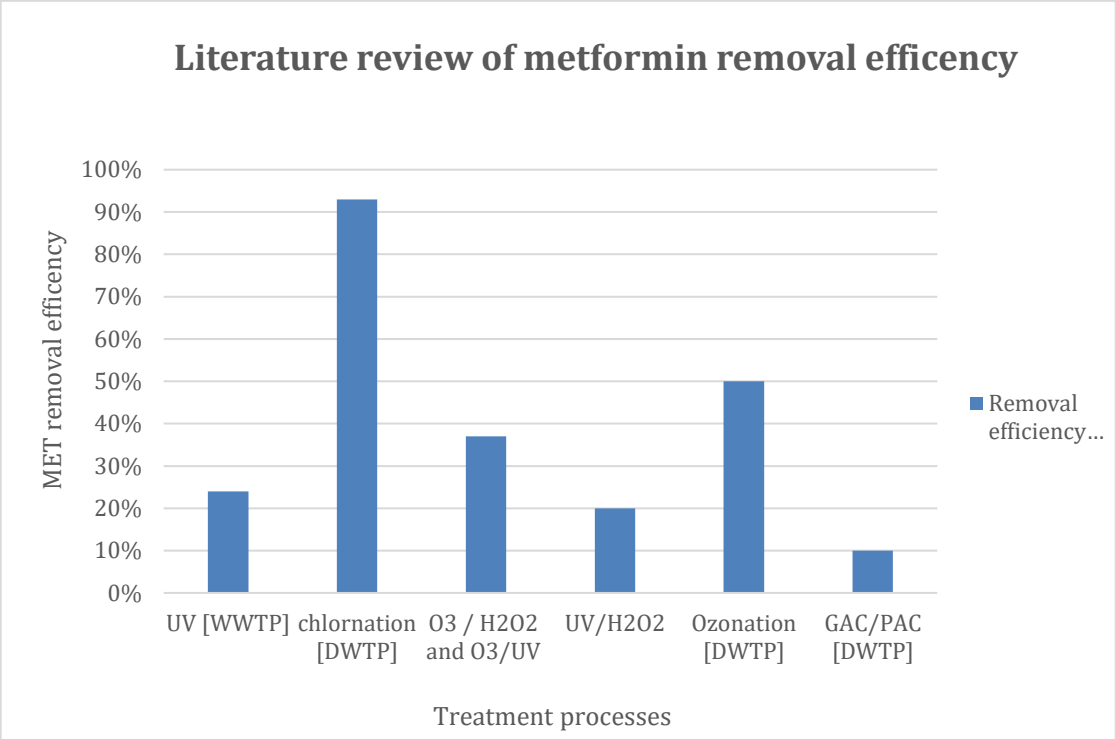

Figure 4: A comprehensive summary of MET removal efficiency at the different treatment trains

Regarding the environmental impact, out of the low net reproductive rate, low population increasing rate, and life expectancy for retrofitter, the GUA tends to be more toxic than MET (Gao et al., 2025). Guanylurea can reduce the growth of T.obliquus. It is also considered a persistent and hard biodegradable substance that can occur at higher concentrations at the wastewater outlet compared with the original substance (metformin). The chronic and acute impact of GUA is still undetermined, but the reaction between GUA and disinfection can lead to cancerogenic substances that end up in water bodies (Briones et al., 2016). GUA and MET were shown to have the potential to bioaccumulate and reach humans through the food chain (Elizalde-Velázquez & Gómez-Oliván, 2019). Moreover, it has been reported that GUA causes oxidative stress, neurotoxic effects, alterations in gene expression, proteins, and metabolism in exposed fish (Danio rerio), as well as changes in some physical characteristics such as weight and length in fish (Japanese medaka) (He et al., 2022).

TPs such as 3,3-CDTA and NCDC pose a significant harm to mammals, reduce algae's photosynthesis and limit their growth, and cause acute toxicity in mice. Other MET byproducts, like NDMA and UDMH, pose significant risks to human health and other biota since they contribute to gene damage, cause cancer, and lead to

developmental defects. On the other hand, NCDC, GUA, and MBG do not have a significant impact on human health (He et al., 2022).

2.3.5 Gabapentin overview

Gabapentin (GBP) is an oral medication that was first developed in 1977, and it is mainly used for treating neuropathic pain and focal seizures. There are other treatment applications, such as bipolar, sleep, and attention deficit disorders, along with complex regional pain syndrome, restless legs syndrome, alcohol withdrawal syndrome, chronic back pain, headaches, and acute postoperative pain. However, these last-mentioned applications are off-label, meaning that they are not officially approved. Gabapentin, also known as 1-aminomethyl cyclohexaneacetic acid, is derived from the structural analog of GABA (gamma-aminobutyric acid), which is a neurotransmitter; however, GBP is proven not to bind to the GABA transmitter or react with it, neither with proteins nor the main liver enzyme system, e.g., cytochrome p450 system, that is responsible for metabolism (Baranowska & Szeleszczuk, 2024). Gabapentin is sold under different brand names, such as Gabapentinoid, and is widely used in high-income countries, while the low-mid income countries show a consumption rate that is more than six times lower. GBP is not metabolized in the human body (liver), and approximately 80% of its formulation is extracted without degradation or change during the extraction process. It can also be used for treating anxiety and pain in pets (Hesová et al., 2025).

GBP underlies the anticonvulsant and analgesic category with an annual prescription of around 18 million, where 84%-95% of this prescription is off-label (Ahmed et al., 2019). This medicine is appropriate for consumption for both adults and children over 12 years, and the daily intake of GBP can vary between 300mg/day and 4200mg/day, divided into a maximum of three tablets per day (Baranowska & Szeleszczuk, 2024). The daily dosage intake depends on the diseases or syndromes that are aimed to treat with Gabapentin; depending on the dose, GBP can show several side effects such as tiredness, calmness, dizziness, weight gain, edema, depression, and suicidal thoughts that can appear directly or in the long-term use (Baranowska & Szeleszczuk, 2024; Kaye et al., 2025).

2.3.6 Gabapentin chemical properties

The chemical formula of Gabapentin is $C_9H_{17}NO_2$, and it is inspired by the amino acid in the GABA transmitter. The PKa values for GBP are 3.68 and 10.79, and the overall charge for GBP is neutral. Nevertheless, GBP is a zwitterion, meaning that it includes both positive and negative charges, which allows it to react under different pH conditions (Baranowska & Szeleszczuk, 2024).

GBP has a short half-life between 5-7 hours, which means higher and more frequent doses are needed in certain cases. Therefore, it is often prescribed in high doses divided into several intakes, and any changes in dosing should be scheduled according to restricted recommendations. GPB is also highly soluble in water, and the volume of distribution is 0.8 L/kg (Kaye et al., 2025). According to Pubchem (2026), the water solubility of GPB is estimated to be 4.49 g/L at 25°C, and it has a log K_{OW} of -1.10. GBP is also lipophilic, which allows it to pass through the blood-brain barrier (BBB) to impact the pain transmitters in the nervous system, but not strong enough to be fat-

soluble (Kaye et al., 2025). According to Echemi (2026), gabapentin also has a low Henry's constant (K_H) of $9.32*10^{-12}$ atm/m^3/m.

2.3.7 Gabapentin in treating humans

Gabapentin is a medical pharmaceutical that is mainly used to treat diseases such as epilepsy, partial seizures, and mixed seizure disorders. Gabapentin has also been proven to have treatment efficiency because of its safety and not interfering with liver enzymes, for treating different sorts of neuropathic pain like postherpetic neuralgia (PHN) and diabetic neuropathy (DN). Gabapentin minimizes pain by directly affecting both the central nervous system, including spinal and supraspinal networks, and peripheral neurons such as dorsal root ganglion neurons (DRG). The medicine suppresses the signals from the injured nerves by decreasing sub-threshold membrane potential oscillations (Kukkar et al., 2013).

Several studies have shown that patients with diabetes suffer from pain and therefore need pain control pharmaceuticals. Usually, tricyclic antidepressant drugs (TCAs) are first in line for pain reduction, with gabapentin as an alternative. However, because of TCAs side effects, gabapentin has evolved to be the main medicine for elderly patients with DN. Clinical tests have been done for 8 weeks, showing reduced pain and enhanced life quality for patients, and a 12-week study showed further improvement. In recent years, gabapentin has also proved to be a favorable therapy for people with PHN who have experienced bad side effects from other treatments. For reducing pain associated with PHN and sleep interference, clinical studies showed that gabapentin can be as effective as nortriptyline with a daily dosage of 1200-2400 mg/day (Kukkar et al., 2013).

Additionally, gabapentin was shown to treat pain in patients suffering from cancer, trigeminal neuralgia, multiple sclerosis, complex regional pain syndromes, headache syndromes, spinal injuries, HIV neuropathy, erythromelalgia, and postpoliomyelitis pain (Rose & Kam, 2002). Despite its benefits, gabapentin has also shown several side effects following its usage by patients with renal disfunctions. This is mainly because gabapentin is not metabolized in the liver, but instead it is directly excreted through the kidneys. Effects such as dizziness, somnolence, ataxia, peripheral edema, and confusion have been reported. Furthermore, cholestasis where dark urine, jaundice, pale stool, and fatigue with severe hepatotoxicity, is also described. Other studies have also shown that sexual disfunction, which involves loss of libido and anorgasmia, has also been reported as a side effect of gabapentin (Kukkar et al., 2013).

2.3.8 Gabapentin remediation and its by-products

Gabapentin is not only popular as a widely persistent pharmaceutical in aquatic environments but also as a precursor to several TPs. Gabapentin-lactam (GBP-L) is the main transformation product of gabapentin, and it is more persistent compared to GBP. As a result, it is highly concentrated in surface water, but its effects on the aquatic ecosystem have not been studied much. GBP is not metabolized by the human body but is mainly excreted in the urine. Therefore, it can be found in WWTPs at high concentrations varying from 13.2 µg/L to 37.4 µg/L. Furthermore, factors such as high consumption, inefficient removal in WWTPs, and low metabolic rate lead to GBP occurrence in surface water with concentrations of 2 µg/L. GBP-L has been detected

in German water with varied concentrations of 0.07 μg/L in portable water, 0.7 μg/L in surface water, and 1.5 μg/L in groundwater (He et al., 2021).

GBP-L has the chemical formula $C_9H_{15}NO$ and is formed mainly through the intramolecular cyclization of carboxylic acid and amino groups (amidation), which builds a γ -lactam. The formation of GBP-L is classified as a biologically mediated process that takes place under aerobic conditions. GBP-L accounted for approximately 18% of the initial GBP concentrations, and its occurrence at high concentrations of 1.5 μg/L in groundwater can be associated with its presence in WWTP effluents. Not only that, but anaerobic conditions during bank or soil filtration and short retention times may also affect and raise the concentration of GBP-L in water sources (Henning et al., 2018). A study that investigated the toxicity of GBP-L with a concentration of 0.01 μg/L up to 100 μg/L on zebra embryo showed multiple severe effects, such as elevated heartbeats, reduced body length, and impaired signals in body systems such as nervous, antioxidant, and immune systems. The results from this study declared that GBP-L is much more toxic than its origin GBP, and even if it is presented at low concentrations, it can still lead to serious effects on aquatic organisms (He et al., 2021).

Other transformation products besides GBP-L are N-acetyl gabapentin (NA-GBP) and carboxycyclohexane acetic acid, which were also identified in different water sources at concentrations up to 260 ng/L (Henning et al., 2021). The overall findings of the TPs illustrate the necessity to include these compounds in future studies by assessing their risk and monitoring their impacts on the environment, especially in the context of drinking water treatment.

The efficiency of gabapentin removal from water sources is based on the treatment method applied, such as adsorption, ozonation, UV, and advanced oxidation processes. A study was conducted to investigate the potential for removing the detected concentration of 40 ng/L gabapentin using ozonation (O_3) in Lake Constance in Germany. The results showed that ozone dose and contact time were the main factors that affected the removal efficiency. A total of 11-36 % of gabapentin was effectively removed after 1 min at a dose of 0.68 to 0.9 mg O_3/L. An increased dose of 0.9 mg O_3/L and a reaction time of 20 min resulted in a total of 88% removal. Lastly, almost 100 % removal efficiency was achieved after 45 min with a dose of 0.9 mg O_3/L. Regarding toxicity, the obtained results showed no toxicity effect or by-product formation (Gowwami o.a., 2019).

GAC has been studied for removing gabapentin in drinking water, and it was shown that gabapentin is biodegradable under aerobic conditions. The results of the conducted pilot-scale study showed only 30% removal of the influent gabapentin after two months of operation. After the operation period (14 months) was over, gabapentin removal efficiency reached 40% after 30 min contact time. When lowering the contact time to 15 min, the removal efficiency decreased to 20%. However, a comparable experiment using unaerated water showed almost 95% breakthrough, meaning that only 5% were removed. This ensures the necessity of dissolved oxygen to achieve an effective adsorption and biodegradation of pharmaceuticals (Sperlich et al., 2017). To summarize the findings from the paper, GAC alone was proven to be inadequate for the removal of gabapentin, meaning that it should either be combined with other

treatment methods or should be replaced with other treatment techniques to achieve meaningful removal efficiencies in drinking water systems.

In both drinking water and wastewater treatments, there are no previous specific studies that focus on the removal of gabapentin through AOPs, and very limited information is provided about UV light treatment. A newer study, which examined the removal of gabapentin using O_3/UV in wastewater, showed that removal efficiency depends mainly on the applied ozone dose. As 5.4 g O_3/m^3 was dosed, 28.8% of gabapentin was removed. A maximum removal rate of 69.7 % was achieved at a dose of 16.7 g O_3/m^3. When UV irradiation was applied, the degradation of gabapentin was affected by both the dose and wavelength. At a wavelength of 254 nm, 11-21 % of gabapentin was removed during a non-recirculation wastewater system. Higher UV doses could give a bigger potential for gabapentin removal, as high doses enhance the production of hydroxyl radicals from hydrogen peroxide and unconsumed ozone. A full treatment series of (O_3/UV → UV → GAC) resulted in a removal efficiency of gabapentin reaching 99% (Vašinka et al., 2025).

2.4 Comparison of metformin and gabapentin chemical properties

In the table below, a comparison of the most relevant chemical properties of both metformin and gabapentin is presented. The chemical properties differ significantly between the pharmaceuticals. These differences are important when selecting which treatment methods should be adapted to remove both pharmaceuticals.

Table 1: Comparison of the chemical properties of the found pharmaceuticals in Rådasjön lake

Chemical properties	**Metformin (MET)**	**Gabapentin (GBP)**
Chemical formula	$C_4H_{11}N_5$	$C_9H_{17}NO_2$
Molecular structure	Small structure with more nitrogen atoms compared with GBP	Bigger structure, containing a cyclohexane ring, an amine, and a carboxylic acid group
Solubility in water at 25℃ $\left[\frac{g}{L}\right]$	High around 300	Low around 4.49
Log K_{ow}	Very low, varies between -4.9 and -2.64	Higher than MET, estimated to be around -1.10
Hydrophilicity	Very high, due to low log Kow	Lower than MET, due to a higher log Kow
Mobility in water	Very high mobility in water and aquatic systems, due to very low Log Kow and high hydrophilicity	Slightly lower mobility than MET, due to higher log Kow and lower hydrophilicity
Volatility & Henry's constant $\left[\frac{\frac{atm}{m^3}}{m}\right]$	$7.6 * 10^{-16}$, which means that it's extremely low to no volatility	$9.32 * 10^{-12}$, which indicates low-non-volatility
Main by-product	Guanylurea (GUA) is the most popular TPs	Gabapentin-lactam (GBP-L)

Persistence	It is very hard to remove, since it is extremely hydrophobic and has high mobility in water. It is not metabolized by the body and is excreted unchanged continuously in water.	Slightly easier to remove, due to its moderate mobility and hydrophilicity

2.5 Impact of pharmaceuticals on humans and the environment

Pharmaceuticals in general have various effects on human health, aquatic biota, and the environment. The impact arises not only from consuming contaminated water with pharmaceutical residues (waterborne exposure) but also from consuming contaminated food (foodborne exposure) through the food chain. The impact can be quantified by structural approaches such as Quantitative Chemical Risk Assessment (QCRA), where simulators are applied to measure human health risk and create sensitive analysis based on different scenarios (Andersson & Svärd, 2021). The impact can also be estimated through experiments where different species are exposed to different pharmaceuticals. The presented impacts in this section were mainly based on a literature review of previous studies related to pharmaceuticals as pollutants and their drawbacks on humans and the environment.

In general, pharmaceutical residues often occur at low concentrations in water bodies; therefore, they often do not pose huge and direct lethal effects on humans or aquatic flora and fauna. Depending on concentration, mixture effects, transformation products of metabolites, and exposure rate of pharmaceutical residues, they may tend to cause acute and chronic toxicity. Pharmaceuticals often interact with each other, with other substances, or with other chemicals in the environment, which can lead to greater toxicity compared to having every pharmaceutical alone. Overall, the existence of pharmaceuticals such as diclofenac, anti-inflammatory medicine, psychiatric drugs, antidepressants, or even synthetic hormone pills in freshwater can result in endocrine disturbance, behavioral change, and extinction of some species. The reproductive ability of fish is affected by synthetic hormones. It influences male fish’s hormones, resulting in sterility. On the other hand, changes in fish behavior are influenced by antidepressant residue, making them bolder, which can expose them to a higher risk of predation. All those medications can result in species endangerment in the long term (OECD, 2019).

According to OECD (2019), pharmaceuticals in drinking water do not pose any risk for human health due to their low concentration, which is much lower than therapeutic doses that may pose harm. However, the spread of antibiotics in water bodies results in the development of antibiotic resistance, which contributes to the annual mortality of 700 thousand people around the world. The paper points out that long-term exposure to low concentrations of different pharmaceutical mixtures that include endocrine-disrupting chemicals and hormonal substances may cause a higher risk to mainly pregnant women and infants. It may cause prostate and breast cancer, develop heart diseases and asthma, and lead to neurological problems such as Alzheimer's, Parkinson’s, and ADHD. It can also lead to early puberty, diabetes, impact the immune system, and cause infertility and reproductive problems (OECD, 2019).

When it comes to the effects on aquatic biota, exposure to MET in fish contributes to hormonal changes, which lead to mutagenesis and intersex, affecting their ability to reproduce. This occurs when insulin interferes with steroidogenesis. Additionally, it can accumulate in the fish, affecting their physiology, energy balance in their cells, swimming and feeding patterns, as well as producing vitellogenin (protein for producing eggs) in the bodies of male fish. MET's exposure results in destruction of the hematopoietic center, which reduces red blood cell production and increases white blood cell production, thereby causing oxidative stress and cell damage. MET destroys both the protein inside the cell and the cell walls by elevating the lipid peroxidation (LPO) and protein carbonyl activity (PCA), along with disrupting and weakening the immune system enzymes, and damaging DNA. Moreover, metformin in water can influence antibiotic resistance by increasing the growth of antibiotic-resistant bacteria (Sibiya et al., 2023).

According to a study examining the ecotoxicology of MET and GUA on aquatic biota, both contribute to slowing the growth of algae and aquatic plants, reducing their density, and affecting photosynthetic processes even at low concentrations of 1 mg/L of GUA or MET. It also affects aquatic species, such as freshwater rotifers and fish. The impacts above influence several factors, but the main effects are linked to reproductive capacity, which affects the population growth rate rather than directly affecting the survival rate. Fish such as zebrafish and Japanese medaka exposed to MET and GUA may have higher rates of egg inactivation than healthy fish. It can also trigger neurotoxicity, influence critical metabolic processes, foster endocrine disruption, and develop oxidative stress that may last for two generations (Gao et al., 2025).

Log K_{ow} is inversely correlated with hydrophilicity and positively correlated with lipophilicity (Drupal, 2026). Since the log K_{ow} is low, as mentioned in Chapter 2.3.2 the bioaccumulation in some species of aquatic environment may not occur. However, it can contribute to deteriorated food quality by reducing the nutrient values in algae due to limited nutrient synthesis, which may result in food restriction for the rotifer (Gao et al., 2025).

However, the risks to human health from long-term exposure to MET and GUA remain unclear and have not yet been fully studied; although it is reasonable to assume that they may contribute to endocrine disruption and antimicrobial resistance, as they do in fish. According to Briones et al., (2016), the recommendation of the U.S. Food and Drug Administration for the daily doses of MET is 2550 mg for adults, and clinical value for toxicity occur at a dose ≥600mg/kg/day, while the German Federal Environment Agency had determined the maximum safe long-life exposure for non-genotoxic substance in drinking water to a value ≤3 μg/L, therefore there is no huge potential health risk for ingesting it through drinking water. However, by-products that occur due to MET oxidation during disinfectant treatment can build NDMA, which poses a potential risk to human health. MET also shows its ability to be absorbed by plant roots and alter the development. For instance, the growth rate of carrots can be negatively impacted, MET can accumulate in oily seeds, while GUA was mainly taken up by grains, beans, and in small potatoes and their peels (Briones et al., 2016).

On the other hand, Gabapentin is another pharmaceutical that was found in the analyzed water samples, and it causes sublethal impact on the aquatic environment, which means that it affects their ability to reproduce and grow. Even at low concentrations of 0.1 μg/L, aquatic biota get significant internal oxidant damage. Same as metformin, gabapentin can cause oxidative stress in fish such as Zebrafish, but it can also disturb heart development, causing increased heart rate and changes in blood flow. GBP can further impact vascular development, disturb both the metabolic system and energy, alter antioxidant response, and modify the expression of immune and neurodevelopmental genes for several aquatic species. GBP can further impact human health and the environment due to its by-products that occur when gabapentin reacts with advanced treatment methods such as ozonation or chlorination, some of which are GBP-nitrile and GBP-lactam (Hesová et al., 2025).

When it comes to the main impacts on human health, GBP has adverse side effects that have been mentioned in the chapters 2.3.5 and 2.3.8. According to Hesová, Svobodová, & Lakdawala (2025), the side effects mostly impact the central nervous system and appear during the first 2-3 weeks of administration. The side effects are considered to be moderate to mild, some of which are weight gain, hyperactivity, behavioral changes, mood swings, tension, dizziness, and fatigue. In summary, gabapentin does not generally cause lethal harm to aquatic biota due to its low trace concentration in the surface water, but it affects their survival rate (Hesová et al., 2025).

3 Material & Method

This chapter presents the methods that were used in this thesis. The method consists of four parts, including a section describing the case study of Rådasjön, a strategic literature search, sample preparation, and a description of LCMS analysis and framework.

After gathering information through literature research and identifying the most concentrated pharmaceuticals in the water samples analyzed at a commercial laboratory, a set of up to four of the most effective single treatment methods will be selected to generate two combined configurations, each including two treatment methods. The combined configurations will be further analyzed and compared based on their removal efficiency.

3.1 Study area description

Rådasjön is a lake on the west coast of Sweden, mainly located between the municipalities of Mölndal and Härryda. The importance of the lake lies in its role as the main drinking water source for 60 000 consumers in Mölndal. It also serves as a reserve water source for an additional 500 000 consumers in the city of Gothenburg in the event of a water shortage or an accident affecting the water source in Göta Älv (Ekaterina et al., 2012).

Rådasjön covers an area of 2 km² with an average depth of 3-15 m and an alkalinity of ≤1 [mekv/l]. The raw water intake from the lake is at a depth of 15 m for Mölndal and around 8 m for Gothenburg (VISS, 2026). According to Ekaterina et al.,(2012) Rådasjön has a catchment area of 14.9 km^2, and the inflow to the lake ranges between 1 and 20 m^3/s mainly through River Mölndalsån. The study further reports that the lake is affected by contamination from emergency sewer system overflows, inefficient on-site wastewater systems located upstream of the water intake, and fecal contamination from animals such as horses and grazing cattle in the surrounding area (see Figure 5) (Ekaterina et al., 2012)

Inefficient wastewater treatment is considered the main pathway for pharmaceuticals, including active pharmaceutical ingredients and personal care products, into the lake. Additional sources include personal care products, such as sunblock, soaps, and toothpaste, that may come from swimming areas (see points 4 & 6 in Figure 5), sewer overflows, and bypasses that occur during extreme weather (Zvanaka & Tebogo, 2024).

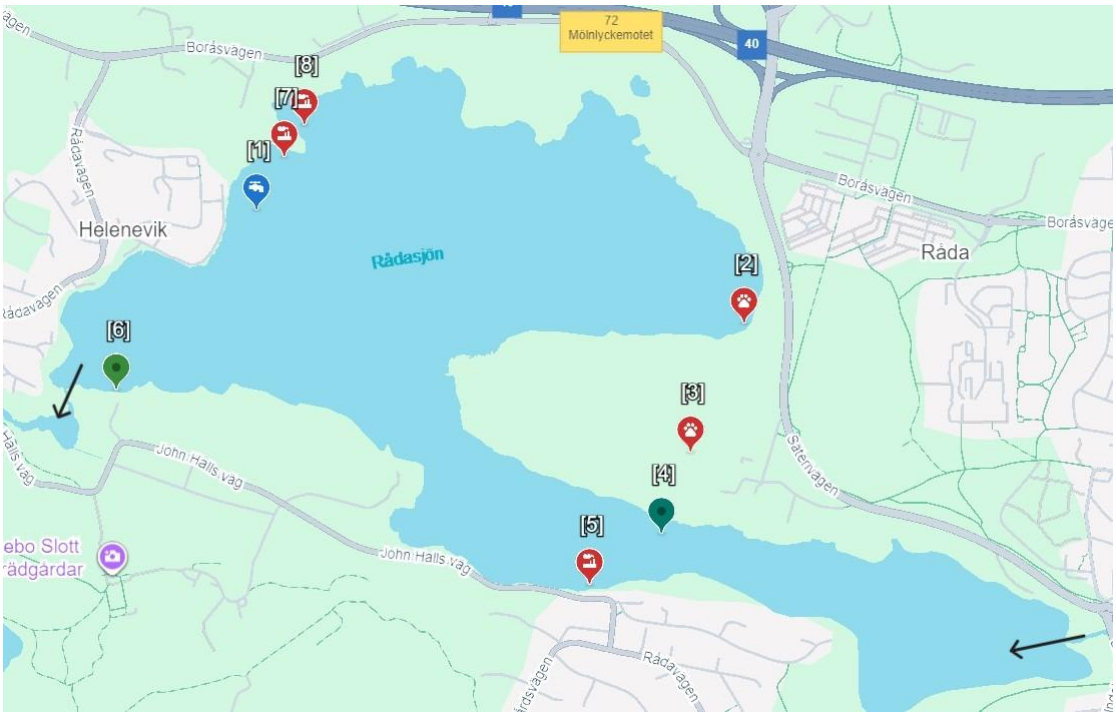

Figure 5: Potential contamination sources in Rådasjön where [1] represents the raw water intake, [2] cattle grazing area, [3] horse riding club, [4]&[6]swimming area, [5] emergency sewer overflow, and [7]&[8] on-site sewer system. The black arrows indicate the inflow and outflow of Rådasjön through River Mölndalsån (based on information from Google Maps and (Ekaterina et al., 2012; Mohamadi, 2026)).

The water entering the drinking water treatment plant in Mölndal is sourced from Rådasjön (see Figure 5) and undergoes eight treatment steps to ensure the safety of tap water. The treatment system consists of pH adjustment, chemical precipitation, coagulation, and flocculation, along with direct rapid sand filtration using a DynaSand filter to capture small particles. This process is designed to remove, among other substances, suspended particles, phosphorus, and nitrogen by capturing them in the sand filter bed and then discharging them through the filter weir. The utility uses PAX (XL 100), an efficient coagulant that promotes the aggregation of the suspended particles. GAC is used to remove taste and odor, and the adsorption carbon source used in the utility is coconut shells with a flow rate of around 15 L/s per one GAC filter. UV-radiation is implemented to inactivate microorganisms. Chlorination, which is the last step in the treatment process, is used to ensure water quality before it reaches consumer's taps (Oskarssona et al., 2020; Mölndals Stad, 2026; Bäckström, 2026). The chlorinating agent used in Mölndal DWTP is sodium hypochlorite. The added concentration is high, estimated to be approximately 150 g_{NaOCl}/L (15%). When it comes to the used dose of sodium hypochlorite, it varies between 360 and 600 mg/m^3, depending on raw water quality (Bäckström, 2026).

Moreover, according to the literature review, most of the conventional treatment processes applied at Mölndal utility appeared to be inefficient in removing pharmaceuticals, in contrast to the advanced treatment methods that showed a better removal efficiency (see Chapter 2.2). Therefore, some supplementary treatment methods, such as Reverse Osmosis, advanced oxidation processes, or even ozonation, might need to be adapted to the utility to improve water quality regarding pharmaceuticals.

In this study, only the process combination of ozonation, GAC, and chlorination will be examined further, since they tend to be the most effective in removing metformin from the water according to the literature review (see Figure 4).

3.2 Description of the LC-MS working mechanism

LC-MS stands for liquid chromatography-mass spectrometry. It is a combination of two techniques used to analyze and detect the type and complex structure of drugs, pharmaceuticals, and other chemicals, alongside their development and toxicity levels. LC and MS are two methods that are connected through a defined boundary. LC operates at atmospheric pressure, unlike MS, which runs under vacuum. As the column eluent flows into the boundary, the solvent is evaporated by applying heat, leading to the analyte molecules being vaporized and ionized (Baluguri o.a., 2011). In the scope of this study, the analyzed mixture will consist of water samples from the DWTP inlet and outlet at Mölndal, and the analyses will be conducted using chemical methods to detect the probable presence of specific pharmaceuticals and determine their concentrations.

Liquid chromatography (LC) includes many related techniques, one of which is high-performance liquid chromatography (HPLC), in which analytes in a dissolved or liquid mixture are separated (Tadikonda et al., 2024). LC can separate compounds with different molecular weights. The separation process is based on the interaction between the analyte in the mobile phase solvent and the stationary-phase particles. The liquid samples are injected into a flowing solvent identified as the mobile phase. The injection can occur manually or automatically with different volumes ranging typically between 1 μm and 100 μm. The injected samples are then pumped through a stainless-steel column, where components are separated before being chemically analyzed to detect the presence of components and their concentrations in the detectors and in the mass-spectrometry (MS) step (Tadikonda et al., 2024; Kailasam, 2024).

The columns are typically designed to have a length varying between 50 and 300 mm, and they are generally packed with silica particles that are combined with carbon chains to ensure a stable stationary phase (Tadikonda et al., 2024; Kailasam, 2024). As the analytes pass through the column, the interaction between the two phases contributes to separation; the weaker the interaction, the shorter the retention time and the faster the analytes will leave the column, and the emerging velocity decreases gradually with higher interaction. When the mobile phase passes out of the column to the detector, it starts to sense and categorize the separated compounds based on their physical and chemical properties, then translates them into peaks with different heights and widths to represent their concentration in the analyzed sample (Kailasam, 2024). The utilized detectors can be, for instance, UV, conductivity, electrochemical, or refractive index detectors (Tadikonda et al., 2024).

Mass spectrometry (MS) is an analytical method mainly used to measure the mass-to-charge ratio (m/z) of the ionized molecules that are related to the studied analyte. MS enables the determination of molecular mass, elemental content, and provides a detailed explanation of the analytes structure. After the ionization process, the ions are separated into the mass analyzer based on their m/z ratio. The mass analyzer measures

the reaction time, rate, and speed of the objects. There are two central types of mass analyzers, which are the quadrupole mass analyzer and the time-of-flight analyzer. The most widely used mass filter in MS is the quadrupole mass analyzer, which consists of four parallel rods placed between two plains and located between an ion source and a detector. The combination of radio frequency (RF) voltages and direct current (DC) can contribute to creating a potential electric field that helps stabilize the ions based on their m/z ratios to easily pass into the detector, while ions with unstable mass and energy are filtered out into the rods (Tadikonda et al., 2024).

A time-of-flight analyzer (TOF) works without any magnetic field; it works by separating the ions based on the required duration they take to arrive at the detector. As the ions are removed from the ionization source, they become exposed to an accelerating voltage in which the lighter ions reach the detectors faster than the heavier ones. TOF allows a rapid scanning of wide m/z ratios, making it easy and effective to identify the ions. Other examples of MS instruments are the Ion Trap mass analyzer and the Fourier Transfer Ion Cyclotron Resonance (Tadikonda et al., 2024).

Using liquid chromatography (LC) itself cannot separate the components. The same things apply to MS; it is less efficient at identifying compounds and determining their characteristics, especially since a combination of overlapping spectra from several components is typically generated from the analyzed mixture. However, when both methods are interconnected, LC-MS becomes more efficient at detecting and, in some cases, eliminating certain chemicals from the analyzed mixture based on their detected mass (Tadikonda et al., 2024).

3.3 Strategic literature research

Strategic literature research was conducted aiming to systematically identify, review, and evaluate scientific resources related to the occurrence of pharmaceutical concentrations in drinking water. It also aimed to investigate the pharmaceuticals found in the analyzed water samples taken from Lake Rådasjön and assess both their treatment mechanism and removal efficiency.

The literature research was limited to only reviewing journal articles, scientific papers, reports, and organizational webpages related to the aim of the thesis. Google Scholar, Scopus, and the Google search engine were used as primary research engines to find relevant sources. To obtain appropriate results and ensure wider coverage of relevant studies, a list of keywords and concepts was applied, such as: *pharmaceuticals, drinking water, pharmaceuticals and personal care products (PPCPs), removal efficiency, conventional treatment methods, advanced treatment methods, ozonation, chlorination, GAC, PAC, UV, and environmental impact.*

The selection and inclusion of literature were determined based on specific criteria, whether they address the presence and removal mechanisms of pharmaceuticals in drinking water, or report and evaluate conventional or advanced treatment methods of pharmaceuticals in contaminated water. The strategic literature research is also restricted to publications accessibility and language limitation, as the used sources were published in English and were accessible as full-text articles. In some cases, relevant articles and studies could not be fully examined because the accessibility to

the full-text articles was unavailable, despite assessing their reliability through their abstracts. This limitation may have affected the comprehensiveness of strategic literature research. The selected literature was reviewed in detail to evaluate the current treatment methods of pharmaceuticals based on their removal efficiency and applicability in DWTPs; also, the found pharmaceuticals were reviewed regarding their chemical properties, ability to treat humans, and formation of by-products.

3.4 Description of the preparation and sampling process

In this chapter, a description of the preparation and sampling processes will be presented.

The water samples were acquired from the drinking water treatment plant in Mölndal, where the facility filled the water in 5L containers. Two samples were collected from the facility, mainly to identify the presence of pharmaceuticals in the lake. The first sample was taken from the influent, and the other from the effluent, after the treatment processes, right before discharging it to consumers. To slow down both biological activity and chemical reactions that may contribute to undesired degradation of the pharmaceuticals, the samples were stored in a fridge immediately after they reached the lab. Before dispatching both the collected samples and spiked samples to the commercial laboratory for additional analysis using LC-MS technology, the water samples needed to be filtered with a 0.2 μm filter to remove suspended particles and microorganisms. This step is considered a main part of the analysis procedure, ensuring that only the dissolved fraction of pharmaceuticals is analyzed and that suspended particles do not clog the columns during LC-MS analysis (Mohamadi, 2026). Before sending the samples to the commercial laboratory, all water samples were properly mixed to ensure sufficient distribution of the added agents such as the ozone, sodium hypochlorite and the GAC

Three different water samples were prepared and mixed to create the base sample (see Table 2), which will then be injected with GAC and a chlorinating agent according to the chapters 3.4.2 and 3.4.3. After that, it will be sent for further analysis, and the results will be used to assess the removal efficiency of the different combinations.

Table 2: Description of the water samples used in this study

Sample	Sample name	Sample description
Sample1	Raw water	Raw water collected from the influent of the Mölndal drinking water treatment plant, representing untreated water.
Sample 2	Raw water spiked with metformin	Raw water spiked with the active substance metformin by diluting a stock solution to achieve the targeted concentration of the pharmaceutical.

Sample 3	Ozonated metformin-spiked raw water	A part of sample 2 after ozonation, where ozone was added to the metformin-spiked raw water to investigate the removal efficiency using ozone treatment

The ozonated metformin-spiked raw water sample was then used as a base for the combined treatment processes, resulting in two additional combined-treatment samples, ozone with GAC, and ozone with chlorination (see Figure 6).

To ensure the reliability of the upcoming results, another raw water sample was taken from the facility (sample 1), one day before spiking (sample 2) with ozone. The reason for collecting a new water sample was mainly to ensure that organic matter levels did not change during the storage time of the sample. Sample 2 was prepared by adding 10 mg of active substance of metformin to a glass bottle to reach a total volume of 100 mL. This step was taken to prepare a stock solution with a concentration of 100 mg metformin/L. The dilution was done using the equation 3.1, by removing 100 µL from 1L raw water and replacing it with 100 µL of the stock solution to obtain a final concentration of 10 µg/L metformin. Sample 2 was considered the initial water sample that would be further analyzed and spiked with ozone.

$$C_{final} = C_{stock} * \frac{V_{added}}{V_{total}}$$

$$C_{final} = 100\left[\frac{mg_{MET}}{L}\right] * \frac{0.0001[L]}{1\,[L]} \qquad 3.1$$

$$C_{final} = 0.01\left[\frac{mg}{L}\right] = 10\left[\frac{\mu g}{L}\right]$$

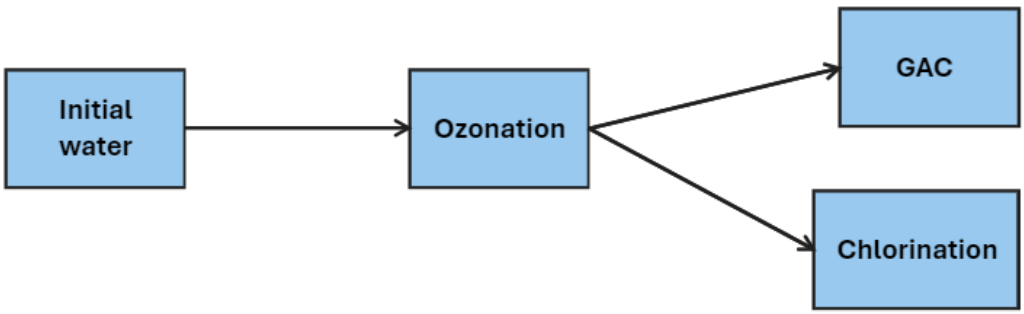

Figure 6: The applied combination of treatment trains sent to ALS for analysis

3.4.1 Sample preparation for Ozonation

The raw water sample taken from the facility (sample 1) was used to measure both the TOC and DOC. The water was filtered with a 0.45 µm syringe filter to measure DOC concentration, while TOC was measured without any filtration.

The ozone treatment took place in the laboratory of Lund University, and the metformin-spiked water sample (sample 2) was transported in cooling boxes to avoid the occurrence of any possible undesired reaction. The concentration of the ozone stock solution (C_{O3}) was calculated to be 52.17 mg/L. The calculation of the concentration was based on measuring absorbance (A) at a wavelength of 260 nm in a spectrophotometer, having an extinction coefficient (ε) of 3200 1/M*cm, a cuvette path length (l) of 0.5 cm, and a molar mass (M) of 48 g O_3/mol (see equation 3.2).

$$C_{O3} = \frac{A}{\varepsilon * l} * M = 52.17\ mg/L \qquad 3.2$$

Following equation 3.3, a 1000 mL of sample 2 was spiked with approximately 84 mL of the ozone stock volume, reaching a total volume of 1084 mL in total. The volume was determined based on the ozone dose per DOC (0.3 mg O_3/DOC) and the DOC content of sample 1, which was measured to be around 14.32 mg DOC/L.

$$V_{stock} = \frac{\left(Ozone\ dose * measured\ DOC\ * V_{sample}\right)}{concetration\ of\ Ozone\ stock\ solution} = 82.3\ mL \qquad 3.3$$

For a detailed calculation of the ozonation sampling process, see Appendix 1

3.4.2 Sample preparation for Chlorination

A total volume of 0.5 L from sample 3 was measured, and based on previous studies, a target free chlorine concentration of 0.2 mg Cl_2/ L was selected. These values correspond to a required chlorine mass of 0.1 mg Cl_2.

The main chlorination source used was sodium hypochlorite (NaOCl), where each unit weight generated 8% chlorine gas. The required mass of NaOCl was calculated to be 1.25 mg for 1 µg metformin. However, since this experiment was based on 10 µg metformin, a total mass (X_{NaOCL}) of 12.5 mg NaOCl was needed. The density of NaOCl (D_{NaOCL}) was 1.24 g/ml, which, according to the equation 3.4, provided a volume (V_{NaOC}) of approximately 10 µL NaOCl, which was then added to sample 3.

$$V_{NaOCl} = \frac{X_{NaOCl}}{D_{NaOCl}} = 10\ [\mu L\ NaOCl] \qquad 3.4$$

For a detailed calculation of the chlorination sampling process, see Appendix 2

3.4.3 Sample preparation for GAC

A 0.5 g of old GAC was added to 100 mL of sample 3. The bottle was tightly sealed and then covered with aluminum foil to avoid light exposure. Following the previous

step, the bottle was then placed on a shaker for 24 hours at a speed of 100 rpm. This step was mainly to ensure a proper distribution and mixing of GAC within the water, also to allow sufficient contact time of the used GAC, as it was initially dry.

4 Results and Discussion

This section provides results obtained from two laboratory analyses and discusses the conducted results, the factors that may have influenced them, alongside their impact on the environment, human health, and aquatic ecosystem.

The first laboratory aimed to identify the presence and determine the concentration of pharmaceutical residues in water samples collected from both the raw water in Lake Rådasjön and the purified drinking water. The second laboratory evaluated the removal efficiency of metformin after applying the different treatment configurations.

4.1 Results from the first laboratory work

The result obtained from the LC-MS analysis conducted by ALS Scandinavia AB showed that only two pharmaceutical compounds out of 100 analyzed compounds, MET and GBP, were found in the influent water (raw water). while only GBP was found in the effluent (purified water)

The results of the influent sample showed that most of the pharmaceuticals were not detected, although they were below the limit of reporting (LOR). The detection limit of the analyzed pharmaceuticals varied between 10 and 500 ng/L, which indicates that concentrations below this span could not be measured with the applied method. However, even though most of the analyzed pharmaceuticals showed very low concentrations below the detection limit in both water samples. In the influent water sample, Figure 7 shows that only gabapentin and metformin were identified and measured at a concentration of 12 ± 4 ng/L and 26 ± 10 ng/L, respectively.

Additionally, the results showed that gabapentin decreased from 12 ng/L in the influent water to below the LOR in the effluent water, which indicates that it has been treated sufficiently. At the same time, metformin decreased only from 26 ng/L in the influent sample to 21 ng/L in the effluent sample, representing about 20 % removal. The other pharmaceuticals, as mentioned above, were below detection limits. Therefore, those pharmaceuticals have not been included in the environmental evaluation and were eliminated from the scope of this project.

The result confirmed the literature, see Chapters 2.3.1 and2.3.2, that metformin cannot be digested and metabolized by the human body, and is very hydrophilic. Therefore, concentration levels of metformin remained high even after treatment (effluent). This indicates that the treatment processes used in Mölndal drinking water treatment plant are not sufficient for removing metformin, and other advanced treatment processes, such as reverse osmosis, ozonation, and advanced oxidation processes (AOP), including ultraviolet radiation UV/H_2O_2 or electrochemical AOP, are required to be implemented to achieve higher removal efficiency. As mentioned in the chapter 2.3.6 gabapentin (GBP) is a zwitterion that interacts differently with water at different pH levels. This facilitates GBP adsorption onto GAC filter media via van der Waals interactions (Water Quality Association, 2013).

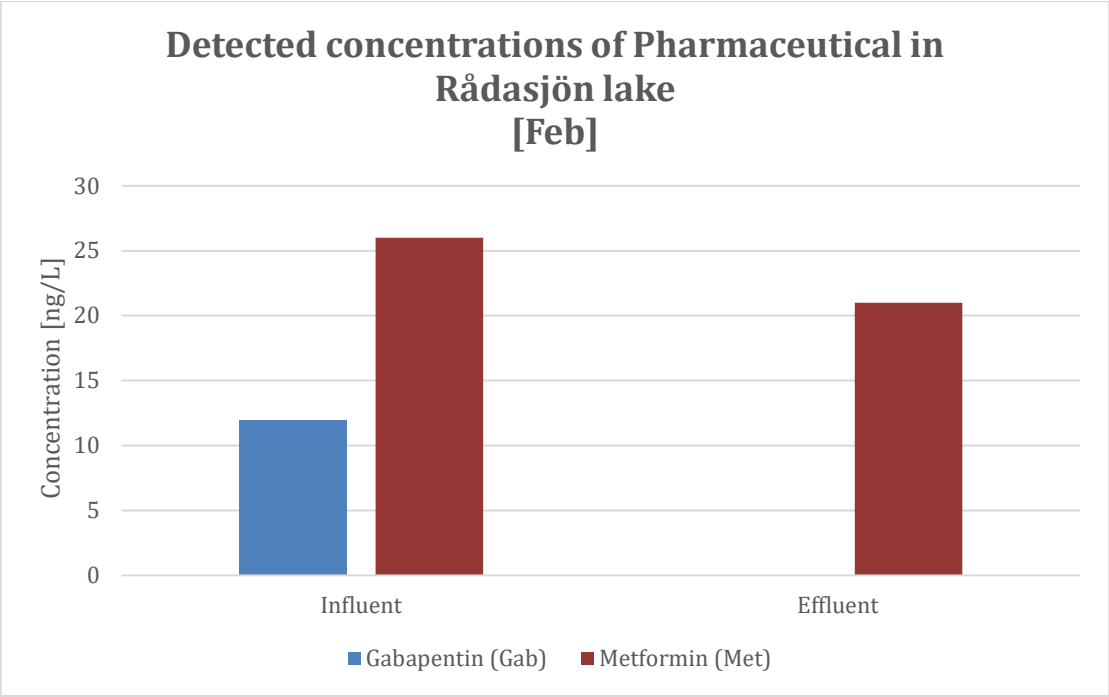

Figure 7: Detected pharmaceutical concentration during the first sampling occasion in Rådasjön lake

Another factor that may have influenced the results is the process of shipping and storage of samples before LC-MS analysis. At Chalmers laboratory, the samples were filtered and prepared for transport to the commercial laboratory (ALS in Stockholm), which requires approximately 5 hours for direct transportation. However, storage temperature and conditions during shipping were neither controlled nor monitored. Also, the samples were delivered to the ALS two days after the collection and filtration. This delay, together with uncertainties in storage and delivery, may have contributed to further biological degradation or chemical transformation of pharmaceuticals presented in the transported water samples. As a result, the above factors may have led to deviations in the reported concentration of pharmaceuticals.

At a later period, following the first sampling occasion. Two additional water samples were collected and analyzed during slightly warmer weather, i.e., in April. This analysis was funded by Mölndal Drinking Water Treatment Plant, and the main goal was to test whether the hypothesis that concentrations would decrease during warmer weather was correct or not.

According to the results from the ALS analysis (see Figure 8), the assumed hypothesis was not correct in this case. The concentrations of both metformin and gabapentin increased. Metformin increased from 26 to 30 ng/L in the influent, representing a 15% increase, and from 21 to 30 ng/L in the effluent, demonstrating a 43% increase. Gabapentin, on the other hand, increased in the influent from 12 to 17 ng/L, which stands for a 42% increase over two months.

The hypothesis assumed that during summer periods or warmer weather, when water has a high temperature, both the concentration levels of metformin and gabapentin should decrease. According to Dong et al., (2024), this can be explained by increasing biodegradation rates, meaning that the microorganisms become more active and can degrade the pharmaceuticals faster by breaking them down into simpler substances. Moreover, as temperatures rise, the growth of microbes improves. In contrast, at

colder temperatures, the growth of microbes deteriorates, leading to lower microbial activity and metabolism, which results in a lower degradation rate and higher concentrations in water bodies. Furthermore, Dong et al., (2024) point out that higher temperatures contribute to better bioavailability and less sorption onto colloidal particles in the water (Dong et al., 2024). This is assumed to result in higher concentration levels of pharmaceuticals in water bodies.

However, the deviation in results between the two sampling periods conducted in the middle of February and early April may be explained by the fact that in February, most of the lake was frozen, and it is possible that some pharmaceuticals from the animal manure in the surrounding areas may run off and accumulate on the top of the ice during this sealed period. As temperatures rise, ice melts and reaches the breakup period; consequently, the pharmaceuticals enter the water and increase the concentration (Zhang et al., 2020). This can also be assumed to be the reason behind the increase in MET and GBP.

Another factor that may have affected the results is the impact of dilution. The winter season is characterized by less sunlight, more cloudiness, and heavy precipitation, which increases the water flow (Kot-Wasik et al., 2016). Both low sunlight and cloud cover can also contribute to lower evaporation rates. Therefore, it is hypothesized that all the above-mentioned factors lead to higher dilution and thus lower concentration of the pharmaceuticals in February and vice versa occurs in April.

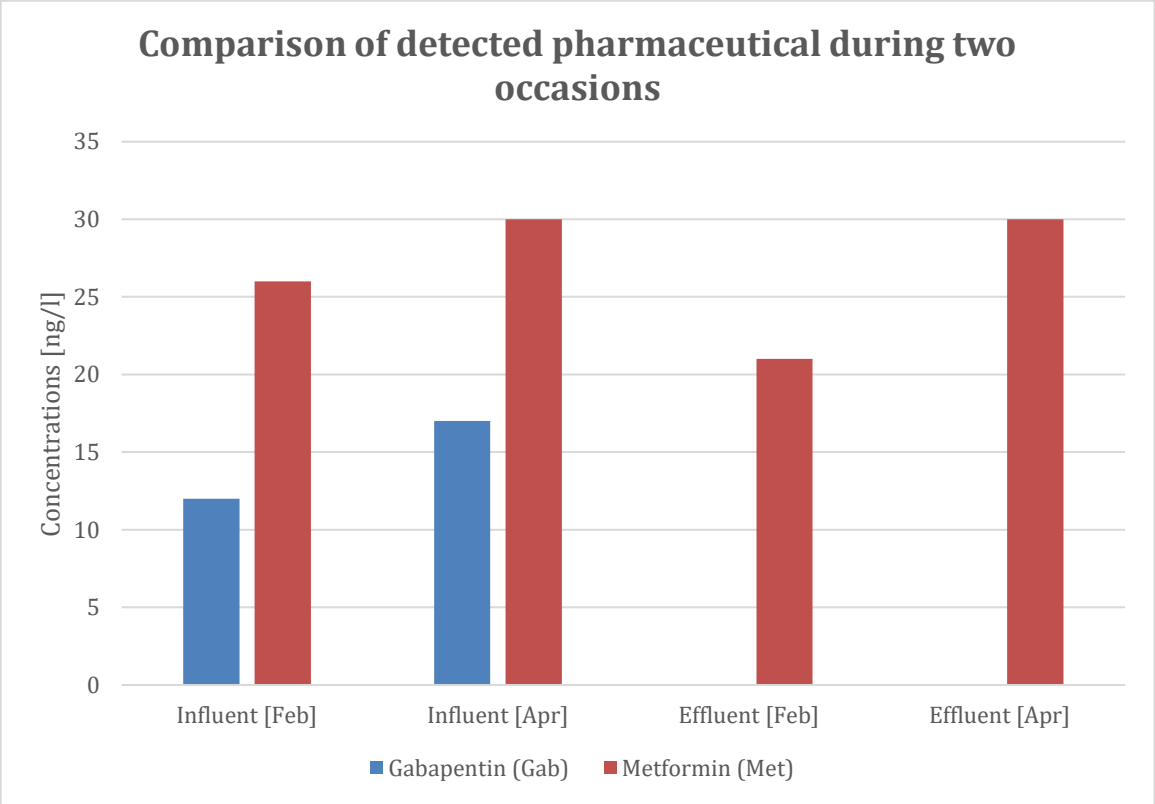

Figure 8: Comparison of the detected concentration of pharmaceuticals following the two sampling occasions

The ecological assessment of Metformin exposure showed extremely low concentrations in the treated drinking water (effluent) compared to the toxicity level associated with human health. The average concentration between the two treated samples (effluent), taken in February and April respectively, was approximately

0.0255 µg/L. On the other hand, the acceptable daily intake of MET is 62 µg/kg × day, which is 3720 µg/day for a 60kg adult (He et al., 2022). Based on calculations, an adult would need to drink around 78 million L of treated water daily to reach the prescribed daily dose of metformin (2000 mg). Additionally, to achieve the potential negative effects on the 60kg adult, around 146 000 L needs to be consumed daily. Therefore, the detected metformin concentrations in the effluent are considered to have no risk to human health under normal consumption. For detailed calculations, see Appendix 3.

To calculate the risk assessment associated with human health and aquatic biota, an approach called Risk Quotient (RQ) was used, and it is calculated as the ratio between the maximum measured environmental concentration (MEC) and the predicted no effect concentration (PNEC), as seen in the equation 4.1 below (Golovko et al., 2020).

$$RQ = \frac{MEC}{PNEC} \qquad 4.1$$

The values obtained from the risk assessment using the RQ method are classified as:

- RQ<0.01 = no risk
- 0.01< RQ<0.1 = low risk
- 0.1< RQ<1= medium risk
- RQ>1= high risk

To calculate the ecological risk of MET on fish specifically (fathead minnow fry), the RQ approach was used. The MEC detected in the influent was 0.03 µg/L, while the PNEC according to Briones et al, (2016) was estimated to be around 40 µg/L. Applying the numbers to the equation 4.1 will give RQ value of 0.00075, which indicates no risk to fish. This also means that fish need to consume at least 1334 times more MET compared with the detected concentration in Lake Rådasjön to cause reproductive and endocrine-disruption effects.

Using the same procedure for Gabapentin, it is shown that fish need to consume around 6 times more GBP compared with the maximum concentration detected in the lake. As mentioned in the chapter 2.5, to cause oxidative damage to aquatic biota, the concentration of GBP in water should be around 0.1 µg/L. When the RQ approach was used, the RQ value was calculated to 0.17, indicating medium risk to fish.

4.2 Results from the second laboratory work

The results from ALS analysis of raw water samples spiked with different treatment agents, such as ozone, sodium hypochlorite, and GAC, showed that the combination of ozonation and chlorination was the least effective compared to the combination of GAC and ozonation, which was the most effective (see Figure 9).

The results showed that the raw water sample, which was initially spiked with 10 µg active substance of metformin, had a final concentration of 12 700 ng/L (12.7 µg), indicating that the raw water included at least 2.7 µg MET/L in addition to the spiked amount. After treatment with ozonation alone, the concentration decreased to 6030 ng/L, which corresponds to 52.5% removal. Similarly, the combination of ozonation and chlorination showed a concentration of 5980 ng/L, equivalent to 52.9% reduction.

The combination of ozonation and GAC resulted in a concentration of 1470 ng/L, showing an 88.4% decrease in metformin concentration.

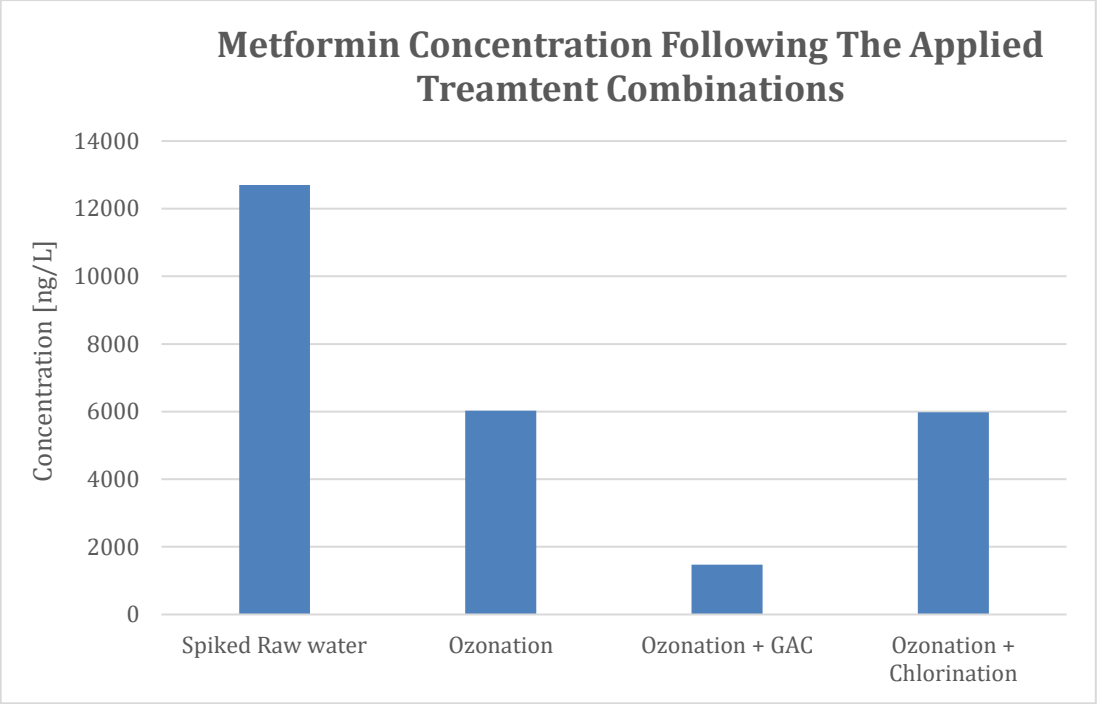

Figure 9: Obtained concentration after the treatment with different methods.

As shown in Figure 10, the laboratory results showed a significant deviation from literature studies, especially for chlorination and GAC. According to the literature, the removal efficiency for chlorination itself was high, around 93%, but the experimental analysis in this project showed that its combination with ozonation contributed to only moderate overall removal efficiency. This result opposes the assumed hypothesis that this combination would be the most effective. However, several factors may have led to the deviation of the results, particularly that ozonation combined with chlorination showed lower removal efficiency of MET compared to chlorination alone that was based on the reported data from the literature.

One of these factors is the influence of pH. As discussed in the Chapter 2.2.1, lower pH enhances the formation of hypochlorous acid (HOCl), which is a more effective chlorinating agent than hypochlorite ion (OCl^-). When pH rises above 8, more chlorine is converted to OCl^-, which reduces the removal efficiency of chlorination. On the other hand, ozonation behaves differently, as described in Chapter 2.2.9. At higher pH values, between 7 and 11, ozone decomposition becomes faster, which leads to the formation of more hydroxyl radicals. Because of their high oxidative potential, they can improve the degradation of some pharmaceuticals.

However, based on findings reported in the literature, a possible explanation and reflection of the obtained results is that the high pH and the rapid reactivity of hydroxyl radicals contributed to the generation of oxidation by-products that may be more resistant to chlorination. Another possible factor is that the added ozone may have partially oxidized MET, especially since it was added before chlorine and can react faster with both organic and inorganic matter (Oshiner, 2026). This reaction may

have led to alterations in the molecular structure of MET and formed new by-products that can be more persistent (Seiwert et al., 2021).

Following ozonation, organic matter, oxidation by-products, and other potential pharmaceuticals existing at low concentrations in the raw water may consume the chlorinating agent and increase the chlorine demand, thereby leaving less active chlorine available to degrade MET. Additionally, ozone may transform natural organic matter (NOM) presented in the raw water into smaller and more reactive compounds by breaking down carbon chains. These compounds can easily react with chlorine, further raising the chlorine demand and minimizing the amount of chlorine available for MET degradation. As a result of the above-mentioned factors, ozonation followed by chlorination may in this case have resulted in lower removal efficiency than chlorination alone.

The chlorinating agent that has been implemented in this experiment was Sodium hypochlorite (NaOCl), and only 8% of its unit weight turns into free chlorine, as mentioned in the chapter 3.4.2. This ratio is theoretical and usually alters depending on the experiment's condition (Mohamadi, 2026). This means that the initial concentration of chlorine that was used in this study may have diverged from the concentration in the literature study, which achieved 93% removal. Therefore, either a higher or lower dose of Sodium hypochlorite may have been required to reach the desired removal efficiency comparable to the literature.

On the other hand, the aged GAC combined with ozonation showed a higher removal rate compared to the literature, where the GAC filter was new. This is mainly because ozonation oxidized MET and other substances in the water and made their by-products more polar than the parent pharmaceutical compound (Seiwert et al., 2021). These more polar compounds may have led to easier adsorption onto GAC which improved the adsorption efficiency. Consequently, the treatment configuration of ozonation and GAC resulted in higher removal efficiency compared to GAC alone that was based on the reported data from the literature.

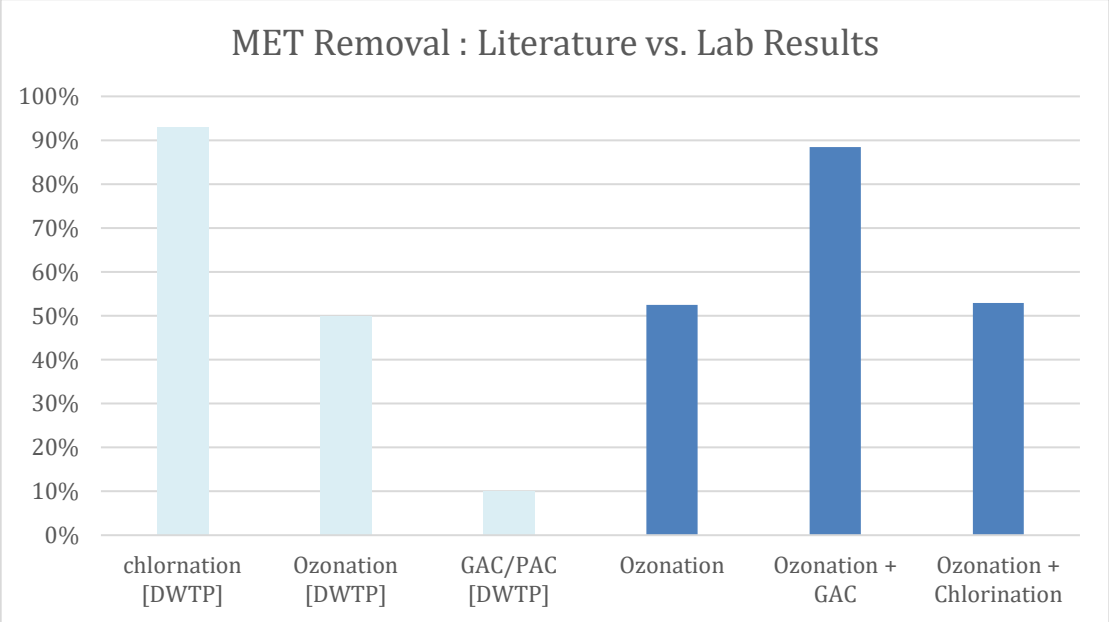

Figure 10: Comparison of MET removal between literature and Lab analysis

5 Conclusion

- The main pharmaceuticals found in Lake Rådasjön, using the LC-MS analytical method, were metformin and gabapentin. Metformin was detected in both influent and effluent water samples, while gabapentin was only observed in the influent water. Samples were collected on two occasions, in mid-February and in early April. The influent concentrations in April were higher for both pharmaceuticals. While MET showed an increased effluent concentration in April, whereas GBP remained under the detection limit.

- In general, MET impacts the aquatic biota by restricting their reproduction rates rather than directly affecting their survival rates. Fish exposed to MET can suffer hormonal and physiological changes, reproductive effects, and develop oxidative stress that causes cell damage. However, long-term exposure to humans has not been fully studied yet. But it is reasonable to assume that they may contribute to endocrine disruption and antimicrobial resistance.

- Gabapentin may cause, for instance, significant internal oxidant damage in aquatic biota, disturbing both vascular and cardiac development, even at low concentrations. GBP can further impact human health and the environment due to the formation of by-products that occur when gabapentin reacts with advanced treatment methods such as ozonation or chlorination.

- The calculation of risk assessment using the Risk Quotient (RQ) method showed that the concentration of MET found in both drinking water and lake water does not pose any harm to human health and the environment. In contrast, GBP showed moderate harm to aquatic biota.

- The current treatment methods at Mölndal DWTP showed high removal efficiency for GBP but a limited effect on MET. This is mainly due to the chemical properties of MET and GBP. Therefore, DWTP needs to adopt new and more advanced treatments to eliminate or reduce the presence of these pharmaceuticals in water. According to the literature, methods such as ozonation, chlorination, and AOP have higher removal potential. However, this study shows that ozonation alone is sufficient, but the most effective method is ozonation followed by GAC.

- The results showed that ozonation alone reduced MET concentrations by 52.5%, whereas the combination of ozonation and chlorination resulted in the least effective combination, which resulted in a similar reduction rate as ozonation by 52.9%. The most effective combination to reduce MET was ozonation followed by GAC, which contributed to 88.4% reduction. This combination showed a better potential for MET reduction compared to using GAC and Ozone individually, according to the literature.

6 Future studies and improvements

- In future studies, it would be beneficial to investigate a wider range of pharmaceuticals beyond those analyzed by the ALS commercial lab. It would also be valuable to furthermore investigate the occurrence, removal efficiency and ecological impacts of transformation by-products such as NDMA, GBP-lactam, and guanylurea which can be formed during ozonation and chlorination processes. Despite these compounds being discussed briefly in the report, their concentration and potential on human health and environment were not assessed within the scope of the thesis.

- Further research could conduct long-term monitoring to evaluate how pharmaceutical concentrations vary during different seasons, weather patterns, and hydrological variations. Additionally, investigating how removal efficiencies may vary with changes in microbial activity and environmental conditions such as temperature occurring between daytime and nighttime, could improve the understanding of pharmaceuticals degradation processes. Future studies could also assess the impact of pharmaceuticals through other quantitative risk assessment approaches, such as QCRA, and develop simulations to evaluate both bioaccumulation and predict how concentrations may increase or decrease based on different scenarios.

- Conducting laboratory experiments where single treatment methods are evaluated on a larger scale, rather than only relying on literature, can elevate the project. It could also be efficient to experimentally test additional advanced treatment methods, such as reverse osmosis (RO), nanofiltration, and AOPs, for removing pharmaceuticals and their by-products, and to compare their removal efficiency with the literature.

- Future research may also study the long-term combined impacts and risks of MET and GBP on human health and the environment. To better understand these impacts, the study should test how the cocktail effects of these pharmaceuticals can pose a greater risk to human health and the environment compared with exposure to each pharmaceutical individually.

- More studies need to test different combinations of multiple treatment techniques beyond those applied in this thesis to identify and evaluate more efficient treatment configurations. Future studies should also investigate the impact of operational parameters such as pH, temperature, treatment agent dosage, and contact time on the removal efficiency of pharmaceuticals.

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8 Appendix

8.1 Appendix 1

OZONATION	
ε	extinction coefficient [1/M*cm]
l	Cuvette path length[cm]
M	Molar mass of ozon [g/mol]
A	Absorbance of wave length from photometry
C	Concentration of ozone
DO3 spec	Ozon dose
Vsample	Water volume
Vstock	Ozon volume added to prepared solution

A	1.739	
ε	3200.000	[1/M*cm]
l	0.500	[cm]
M (mol massa)	47.997	g/mol
C	0.001	mol/L
C_O3 stock	52.167	mg/L

$$C_{O3} = \frac{A}{\varepsilon * l} * M$$

DO3 spec	0.300	mg O3/mg DOC
Doc sample	14.320	mg DOC/L
C _O3 stock	52.167	mg/l
Vsample	1000.000	ml
Vstock	82.351	ml
V total	1082.351	ml

$$V_{stock} = \frac{(Ozone\ dose * measured\ DOC * V_{sample})}{concetration\ of\ Ozone\ stock\ solution} =$$

Appendix 1: Detailed calculation of the ozonation sampling process

8.2 Appendix 2

Chlorintation					
C1	Concentration of Sodium Hypochlorite [mg/L]				
C2	Concentration of Cl2 [mg/L]				
V	Water volume [L]				
m	Chlorine mass [mg]				
X_{NaOCL}	Amount NaOCl needed to be added				
D_{NaOC}	Density of the NaOCl				
V_{NaOC}	NaOCl volume added to the prepared solution				
C2 according to litterature	0.2	[mg Cl2/L]			
V	**0.5**	[L]			
m	**0.1**	[mg Cl2]			
Each 1g of soduiumhyperchlorite can build 8% of chlorine					
Calculating the ratio:					
	Sodium hyprpchlorine		Chlorine		
	1	[mg NaOCl]	0.08	mg [cl2]	
	X_{NaOCL}	[mg NaOCl]	0.1	mg [cl2]	
X_{NaOCL}=					
For 1 µg metformin	1.25	[mg NaOCl]			
For 10µg metformin	12.5	[mg NaOCl]	=	0.0125	[g NaOCl]
D_{NaOC}	1.24	g/mL			
V_{NaOC}	0.01008065	[mL NaOCl]			
	10.08064516	[µl NaOCl]			
$V_{NaOCl} = X_{NaOCl}/D_{NaOCl}$					

Appendix 2: Detailed calculation of the chlorination sampling process

8.3 Appendix 3

METHOD 1: Impact of MET on adults due to exposure to the detected concentration level			
MET toxicity according to US Food and Drug	≥ 600 mg/Kg/day		
Daily doses of MET for Adult	2000 mg	=	2000000 µg
Concentration of MET found in effluent water in Feb	21 ng/L		
Concentration of MET found in effluent water in Apr	30 ng/L		
Avrage concentration	25.5 ng/L	=	0.0255 µg/l
According to the acceptable daily intake of metformin	62 µg/kg·day		
Adult weight	60 kg		
According to the acceptable daily intake for 60 kg adult	3720 µg/day		
water per day to induce any harmful effect	145882.4 L/day		
Amount of water needed to be ingested to match the daily prescribed dose	7.8E+07 L		

Appendix 3: Detailed calculation of the risk assessment of metformin on Human health

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