The fate and occurrence of pharmaceuticals in Cape Town's water network

By

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Abstract

Thousands of pharmaceuticals, pesticides and microplastics are consumed and disposed of directly or indirectly into various water bodies globally. Which are collectively termed "contaminants of emerging concern" or CECs. Contaminants of emerging concerns are defined as micropollutants that are present in the environment that are not regulated and that can pose a risk to the health of both humans and wildlife. The distribution of these CECs in water systems is not isolated to a specific place and is on the rise all over the world. This study aims to investigate the spatial and temporal distribution of pharmaceuticals in the environment regarding the change in concentration along a flow path from potential sources to sink, to assess the occurrence, concentration levels and distribution of pharmaceuticals in various water bodies.

The study focuses on the occurrence of seven pharmaceuticals that are most frequently used and occur in various water bodies around the world based on previous literature, namely acetaminophen, diclofenac, carbamazepine, caffeine, naproxen, rifampicin, and sulfamethoxazole. The research sites include six wastewater treatment plants in Cape Town with receiving rivers and borehole sites nearby and downstream from the wastewater treatment plants. Three landfill sites were chosen as sample sites to investigate their influence as a source for pharmaceuticals in the environment. Liquid chromatography combined with mass spectrometry was the selected method used to analyse the analytes of interest in the collected samples due to its sensitivity to detect analytes of interest in complex matrices, such as wastewater and its low detection limits.

The sampling period was done on four occasions during January 2021, April 2021, July 2021, and September 2021. *In-situ* samples was taken at the WWTPs (influent and effluent) and at the surface water bodies using grab sampling while a submersible pump was used for the groundwater abstraction from boreholes and wells. Laboratory analysis took place at the Division of pharmacology at Stellenbosch University.

The results showed that pharmaceuticals had indeed been distributed from wastewater treatment plants and landfills into receiving water bodies in both surface and groundwater due to the inefficient removal of these compounds. Certain pharmaceuticals were detected at a higher concentration than others, as can be seen in the effluent of one of the sample sites during January 2021, with the following compounds, diclofenac (421 ng/l), sulfamethoxazole (81.4 ng/l), carbamazepine (898.9 ng/l), caffeine (206.7 ng/l), rifampicin (13.2 ng/l), naproxen (147.2

ng/l) and acetaminophen (41.6 ng/l). The reduction of some of these pharmaceuticals, such as caffeine, naproxen, and acetaminophen, was however evident as it passed through the wastewater treatment process.

The efficiencies of wastewater treatment plants were also assessed, to understand the effectiveness of those treatment processes in reducing or removing pharmaceuticals from wastewater. The use of tertiary treatment at WWTP's has shown to be effective in further reducing pharmaceuticals in the effluent, with MBR & UV showing higher removal efficiencies than conventional treatment processes for most compounds, with multiple compounds such as acetaminophen, caffeine and rifampicin showing 100 % removal rates by using MBR and UV combined to treat wastewater.

Persistent compounds however were detected in various samples, for both surface water and groundwater. This was observed with carbamazepine, diclofenac, and sulfamethoxazole, due to their polarity and resistance to biodegradation in the environment. It can be concluded from the results, that the distribution of pharmaceuticals contamination from wastewater discharge points and landfill sites to surface water and groundwater do indeed exist for the 7 pharmaceuticals considered. This study has thus contributed to the global research of emerging contaminants, in understanding how various pharmaceuticals occur throughout the environment and which factors play a role in their reduction or increase in concentrations.

This research therefore recommends the need to improve and upgrade all our Wastewater Treatment Plants with tertiary treatments, to ensure complete or further reduction of emerging contaminants before discharging treated wastewater into the environment. It is also recommended that water quality guidelines and policies in South Africa consider including benchmarks for the concentrations of emerging contaminants in both treated wastewater and potable water, where specialized monitoring must be considered for persistent compounds such as diclofenac and carbamazepine in the environment.

Keywords

Emerging pollutants

Pharmaceuticals

Natural attenuation

Liquid chromatography

Mass spectrometry

Wastewater treatment processes

Surface water monitoring

Groundwater monitoring

Abbreviations and acronyms

ng/l	nanograms per litre
ug/L^{-1}	microgram per litre
WWTP	Wastewater Treatment Plant
MBR	Membrane Bioreactor
UV	Ultra-violet
RE %	Removal efficiency percentage
SPE	Solid phase extraction
LC	Liquid chromatography
MS	Mass spectrometry
GC	Gas chromatography
AOP	Advanced Oxidation Process
CEC' s	Contaminants of Emerging Concerns
SMX	Sulfamethoxazole
LLOQ	Lowest level of quantification
TMG	Table Mountain Group

Declaration

I declare that "The *fate and occurrence of pharmaceuticals in Cape Town's water network"* is my own work, that it has not been submitted for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged by complete references.

Full name: Mikyle Cloete

Date: December 22

Signed: ....

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Contents

List of Figures

List of spatial diagrams of pharmaceuticals in the environment

List of tables

Chapter 1- Introduction

This chapter presents a brief introduction of the occurrence of pharmaceuticals in the environment. The main aim and objectives of the study is also presented below alongside the research problem and thesis statement. The thesis layout is briefly described under this section as well.

Introduction

The quality and availability of water to society is on a downward spiral due to it being vulnerable to various contaminants that are entering the waterways. Thousands of pharmaceuticals, hormones, pesticides, herbicides and microplastics are consumed and disposed of directly or indirectly into various waterbodies or into rubbish bins. Emerging pollutants are defined as micropollutants that are present in the environment, which are unregulated and which can pose a risk to the health of both humans and wildlife (Packer *et al.*, 2003; Sui *et al.*, 2015; Lu *et al.*, 2020)

The dependence on this natural resource by animals and humans reaffirms the need for adequate research on various threats to our water supply and that there are various preventative measures put in place. This will ensure that the quality of the water resource is not only improved but is conserved and effectively managed for future use. This thesis will help understand the fate and occurrence of pharmaceuticals in the environment.

1.1 Background

The first studies concerning the distribution and occurrence pharmaceuticals in the environment began in the 1970's in the United States of America where Scientists reported the presence of various pharmaceuticals including heart medication, pain relievers and contraceptives in its wastewater (Maycock and Watts, 2011). Before the 1970's the phrase "emerging pollutants" in the environment was not as popular as it is today since there was limited knowledge on the distribution and research done on these emerging contaminants in the environment. The occurrence and increase presence of these emerging contaminants, such as pharmaceuticals, in water systems is not isolated to a specific place but is on the rise all over the world (Focazio *et al.*, 2008; Al-Farsi *et al.*, 2018).

Various factors influence the increase in the occurrence of pharmaceuticals in the environment, such as the easy accessibility of pharmaceuticals to the consumer, the lack of awareness among citizens of the consequence of their incorrect disposal of pharmaceuticals, as well as the lack of regulation and maintenance by Government with regard to the way Waste Water Treatment Plants (WWTP's) operate and discharges treated waste water into the environment (Schoeman, Dlamini and Okonkwo, 2017; K'oreje *et al.*, 2018). The increase in the presence of emerging pollutants has led to various global regulatory bodies creating frameworks to help monitor and identify various emerging contaminants in water bodies, these bodies include the United States Environmental Protection Agency, European Union Water framework directive and the World Health Organization.

The occurrence of these pharmaceuticals in rivers and other water bodies is therefore of grave concern as little is known about the long-term exposure of these compounds to humans. A number of studies (Lapworth *et al.*, 2012; Sui *et al.*, 2015; K'oreje *et al.*, 2016; Archer *et al.*, 2017; Al-Farsi *et al.*, 2018) were conducted based on the concentration of various compounds present in various water bodies, whereby certain pharmaceuticals had occurred beyond allowable limits in certain cases. This increase in the presence of pharmaceutical's being discharged into various aquatic bodies, including surface water, has led to morphological changes in certain aquatic species (Gogoi *et al.*, 2018; Zhang *et al.*, 2020). These changes experienced by aquatic species were observed in various studies which included the feminisation of certain fish in British waters due to the estrogenic compounds present in the water as well as the toxicity effects of a mixture of naproxen, sulfamethoxazole and carbamazepine on the development of Australian stripped marsh frogs (Manickum and John, 2014; Melvin *et al.*, 2014).

The fate of these emerging contaminants in the water systems is therefore under constant research to minimise future impacts of these compounds. Observing the fate of emerging pollutants are difficult to understand due to the natural attenuation of the pharmaceuticals through various mediums (Sui *et al.*, 2015; K'oreje *et al.*, 2018). Therefore, to understand the fate and occurrence of these pharmaceuticals one must look at the adsorption and desorption properties of the various compounds which controls their solubility and mobility in both water treatment processes and in surface water (Stuart *et al.*, 2012). For example, the fate and occurrence of carbamazepine is controlled by its poor adsorption characteristics which allows it to be easily entrained in water as it moves through the medium , its chemical characteristics therefore make it resistant to biodegradation (Gogoi *et al.*, 2018).

There is however limited research in South Africa which considers the fate and monitoring of pharmaceuticals in the environment as well as the efficiency of the removal of pharmaceuticals in WWTP's before discharging the treated water into the environment as there is currently no national survey with regard to the distribution of pharmaceuticals in South Africa's water network (Archer, Wolfaardt and Wyk, 2017). South Africa's WWTP's were not designed to remove pharmaceuticals as its focus was to remove suspended solids and to reduce inorganic waste before discharging it into the environment. These treatment plants consist of 3 main treatment stages that involve the primary treatment where the incoming wastewater is pre-treated by screens and grit removal and where solids in the influent are allowed to settle in the settling tanks. The secondary treatment involves activated sludge process whereby biological digestion occurs through aeration, anaerobic and anoxic process which takes place to remove the remaining suspended solids and inorganic compounds in the wastewater. Before waste water is passed to the final disinfection treatment, it is sent to maturation ponds to further treat the waste water before either being dosed with chlorine or passed through UV treatment before discharging it into the environment (Hendricks *et al.*, 2012).

To improve the treated effluent and management of wastewater works in South Africa, the Department of Water and Sanitation created the Green Drop certification programme to ensure that the minimum compliance standards are met, including wastewater quality before discharging the treated wastewater. The Green Drop certification was created to ensure adequate wastewater management and compliance by this sector with regards to laws and regulations in South Africa. However, not all the wastewater treatments plants run optimally due to the breakdown in old infrastructure as well as that it cannot keep up with the incoming wastewater due to the increase in the population size, these issues can thereby increase the risk of environmental degradation if it is not improved, and the infrastructure updated. This is of vital importance especially considering that South Africa is a water scarce country. There are currently no laws in South Africa guiding the concentration limits of pharmaceuticals in treated wastewater. There is, however, the National Water Act (36 of 1998), which governs the quality of the natural resource and conservation there of (Schoeman, Dlamini and Okonkwo, 2017).

The pharmaceuticals of interest in this research were chosen because these compounds are present on the relevant target analytes in South Africa based on prescribed and used medications by its citizens as well as on the priority list of the highest micropollutants occurring in the environment based on previous studies done in the Northern Hemisphere such as in Europe on the EU watchlist of emerging water pollutants as well as in Africa (Packer *et al.*, 2003; C.Osunmakinde, S. Tshabalala, S.Dube, 2013; Paíga *et al.*, 2016; Ebele, Abou-Elwafa Abdallah and Harrad, 2017).

The pharmaceuticals chosen, especially with regard to diclofenac, carbamazepine, sulfamethoxazole and acetaminophen, were also reported in previous studies done in South Africa whereby it was found in final waste water effluent from WWTPs and marine organisms off the coast of Granger Bay ,Cape Town due to sewage outflow (Petrik *et al.*, 2017; Archer *et al.*, 2021).

1.2 Problem Statement

The quality of the water resource is at risk of being contaminated beyond recommended concentration limits, this in turn will affect the availability and management of the water resource in the future, which will further put strain on South Africa's water availability.

With the increase in the distribution of pharmaceuticals in the environment, various research gaps and recommendations were highlighted in various literature ranging from identifying the exact pharmaceuticals and their respective concentrations that pose a risk to human health in various water bodies. As well as the movement of pharmaceuticals from WWTP's through the soils and into groundwater and the fate of these pharmaceuticals as they move through various mediums based on their natural attenuation.

Therefore, the focus of this thesis will be on the fate and distribution of pharmaceuticals through various mediums from source to sink in Cape Town, South Africa, focusing on various water bodies, landfill sites and WWTP's. Special focus will be at waterbodies near WWTP's, as these plants were not designed to filter out certain emerging micropollutants. Even though WWTP's can filter out a wide variety of chemicals, little is known about the remaining parent compounds of the pharmaceuticals present in the 'treated' water.

1.3 Research questions

- How does the concentration of pharmaceuticals change from source, pathways, and receptors?

1.4 Aim and objectives

1.4.1 The Aim of this thesis is therefore:

To investigate the spatial and temporal distribution of pharmaceuticals in the environment regarding the change in concentration along a flow path from potential sources to sink.

1.4.2 To further explain the problem statement, the following key objectives are defined:

1) Assessing the spatial and temporal variation of pharmaceuticals as it moves through various mediums in the environment by sampling at various WWTP's, groundwater wells, rivers, and lagoons to determine the occurrence and distribution of pharmaceuticals.
2) To determine the efficiency of WWTP's with regard to the removal of pharmaceuticals from wastewater in Cape Town.

1.5 Significance of study

Understanding the spatial distribution of pharmaceuticals in the environment is of utmost importance, as an increase in the concentration of these compounds can have a detrimental effect on not only aquatic life but human life as well. This thesis will thus contribute to understanding the fate and distribution of pharmaceuticals in the various water bodies in Cape Town as well as the gaps in previous research regarding the fate and occurrence of these pharmaceutical compounds as it travels from the source to sink such as in alternative drinking supplies. This will thereby help government and various other stakeholders in planning and monitoring treated water as it flows through the environment.

The study is aimed at understanding the spatial and temporal distribution of pharmaceuticals in the environment and determining the efficiency of WWTP's in removing these CEC's. The aim will be achieved by the two objectives set out for the study. The first which is to assess the spatial and temporal variation of pharmaceuticals as it moves through various mediums will be done by sampling at various sites, namely at the influent and effluent of WWTP's, landfill sites and at surrounding waterbodies including rivers, wetlands, and groundwater points. This objective will help to investigate the distribution and concentrations of various pharmaceuticals of interest in different mediums and how far these contaminants are distributed in the environment from source to sink. The second objective, focusing on the efficiency of WWTPS with regards to the removal of pharmaceuticals from wastewater, will provide information on how effective the various WWTP's processes are in removing pharmaceuticals and which pharmaceuticals are more resistant to these treatment processes. The results of this thesis will help understand the fate of these compounds in Cape Town's water network and inform decision makers to implement mitigation strategies. The samples collected through grab sampling will be analysed through solid phase extraction (SPE) coupled with liquid chromatography - mass spectrometry (LC-MS).

1.6 Outline of thesis

Chapter 1: Background

This chapter presents a brief introduction and background of the occurrence of pharmaceuticals in the environment. The main aim and objectives of the study is also presented below alongside the research problem, research framework and thesis statement.

Chapter 2: Literature Review

Reviews current literature based on previous research and gaps pertaining to pharmaceuticals in the environment. Methods used in previous research are also discussed to guide the choice of method to employ in the current study.

Chapter 3: Study area description

A description of the study area is given to understand the landscape such as the geology, climate, and other hydrological characteristics. The study site has a potential to influence the results, therefore various physiographic factors need to be considered.

Chapter 4: Research methodology and design

The methodology used to achieve the aims are discussed in this chapter and why various sites were chosen. A detailed description of the analysis of the samples using SPE and LC/MS is also discussed.

Chapter 5: Results and Discussion

The resulting data obtained from the research conducted is mentioned in this chapter as well as the discussion based on the results. Correlations between several factors controlling the distribution of pharmaceuticals in the environment is also discussed.

Chapter 6: Conclusion and Recommendations

Concluding remarks based on research outcomes and recommendations are given for future studies.

Chapter 2- Literature Review

Under this chapter various literature will be reviewed based on previous research and the fate and occurrence pertaining to pharmaceuticals in the environment. Methods used in previous research are also discussed to guide the choice of method to employ in the current study. The final part of this section will cover the remediation techniques for the treatment of pharmaceuticals in the environment and the gaps identified.

Introduction

Pharmaceuticals are made up of various natural and synthetic compounds that are used to treat various diseases in both humans and animals. These drugs contain various ingredients, including active ingredients which are used to treat diseases or inflammation. Despite this having a significant benefit for the user, the presence of these active ingredients may have a negative effect on various organisms once reaching the environment (Petrik *et al.*, 2017; Lu *et al.*, 2020) .

Identifying and monitoring the temporal and spatial patterns of pharmaceuticals in the environment is therefore of vital importance. The quality of our water resource should thus be closely monitored to prevent contamination by emerging contaminants. This chapter outlines the literature on the history and transport of CEC's in the environment as it relates to the various sources, pathways, and receptors. The methodology used to monitor the concentrations of pharmaceuticals in various waterbodies will also be discussed and in so doing identify the method best suited to achieve the study objectives. The various gaps in previous research will also be reviewed.

2.1 Occurrence of pharmaceuticals in the environment

The increased occurrence of pharmaceuticals in the environment has led to several studies being conducted in order to identify the transport of pharmaceuticals through the environment and the effects of these compounds on human and aquatic life (Deblonde, Cossu-Leguille and Hartemann, 2011; de Santiago-Martín *et al.*, 2020; Lu *et al.*, 2020). According to a number of studies based on pharmaceuticals in the environment (Del Rosario *et al.*, 2014; Gumbi *et al.*, 2017; Fekadu *et al.*, 2019) it was shown that pharmaceuticals do indeed occur in various water bodies (such as surface water and groundwater) at trace levels ranging from 50 ng/l to >100 ng/l. Pharmaceuticals have become persistent pollutants in the environment due to their design of being stable and effective at low doses, as well as their volatile characteristics (Baker and Kasprzyk-Hordern, 2013).

2.1.1 Sources of pharmaceuticals in the environment

To accurately monitor the temporal and spatial patterns of pharmaceuticals in the environment the various sources must first be identified. These sources range from incorrect household disposal to the inefficient removal by WWTP's. Pharmaceuticals enter the environment by various mechanisms but are mostly excreted by humans and animals due to their assimilation in the body being incomplete (Tijani *et al.*, 2016).

2.1.1.1 Wastewater Treatment Plants

The principal contributor of pharmaceuticals to the environment are WWTP's, due to the discharge of treated effluents containing various concentrations of different pharmaceuticals and leakages of untreated sewage through pipes. For example a review by Deblonde, Cossu-Leguille and Hartemann (2011) indicated that at WWTP's in France, beta-blockers and anti-inflammatory drugs such as ibuprofen, are some of the leading micro pollutants present in the environment, due to the removal rates of WWTP's being 30-40%. The reason for this is not only because of the incorrect disposal of it but the inefficiency of WWTP's to completely remove it, as these WWTP's were manufactured during times when the presence of pharmaceuticals in the environment was not of concern. The removal rate of pharmaceuticals by WWTP's are also dependent on the nature of the compound, as it can be transformed into its metabolite during the wastewater treatment process (Osunmakinde, Tshabalala, Dube, 2013).

A similar study was done at WWTP's in Gauteng, South Africa which looked at the presence and concentrations of Efavirenz and Nevirapine (anti-retroviral drugs) and the efficiency of the removal of those pharmaceuticals at various stages at WWTP's. The study indicated that there were low removal rates for those compounds because those compounds had high water solubility and resistant to biodegradation and therefore WWTP's could not eliminate those substances since they were not designed for such (Schoeman, Dlamini and Okonkwo, 2017).

2.1.1.2 Households, hospitals, Agricultural activities, and landfill sites

Another contributing source is households where medication and human excrement are incorrectly disposed of into the environment due to a lack of water and sanitation. This was observed in a Kenyan study where a higher concentration of pharmaceuticals such as paracetamol was observed in rivers and wells situated in informal settlements. This higher concentration was due to the fact that waste products were directly disposed of into the adjacent river, unlike in urban areas where sanitation is up to standard (K'oreje *et al.*, 2016).

Hospitals and agricultural activities are also some of the leading sources with regard to polluting the environment with pharmaceuticals (Zhang *et al.*, 2014; Azuma *et al.*, 2019). This is due to degraded infrastructure such as underground piping that connects these places to WWTP's as well as septic tanks. These sewage leaks thereby have a greater risk of contaminating groundwater or surface water as they are situated directly above or adjacent to these waterbodies.

Certain agricultural activities, such as animal husbandries, increase the risk of distributing pharmaceuticals into various waterbodies. Agricultural farmers administer antibiotics to treat their livestock for various diseases which inadvertently ends up being excreted into the environment. According to Massé, Saady and Gilbert (2014), 70- 90% of the active compound of the antibiotics is excreted into the environment through animal faeces or urine. These active compounds then leach into the vadose zone or open water bodies such as rivers. The use of manure on agricultural fields also plays a contributing factor with regard to the presence of pharmaceuticals in both soil and groundwater, as the medication present in the used manure are able to leach into the aquifers (Zhang *et al.*, 2014).

The distribution of pharmaceuticals into aquifers and rivers are also prevalent at landfill sites where adequate measures are not being taken to prevent contamination of the surrounding environment. This is mainly through the leaching of disposed pharmaceuticals interacting with water (such as rainfall) and the surrounding environment. Several studies have observed the occurrence of CEC's, such as anti-inflammatory, caffeine and antioxidants, in wells placed downgradient of landfills due the transport of these pharmaceuticals in the subsurface or in the groundwater below (Buszka *et al.*, 2009; Vodyanitskii and Yakovlev, 2016).

2.1.2 Common pharmaceuticals in the environment

Certain pharmaceutical products are more common in the environment due to increased use and ease of accessibility. These pharmaceuticals range from anti-biotics, nonsteroidal anti-inflammatory drugs (NSAID's) to various illicit drugs which all have various environmental impacts due to its bioaccumulation. These pharmaceuticals comprise of an active ingredient which enter the environment through both incorrect disposal and via treated wastewater.

2.1.2.1 Analgesics (Pain relivers)

Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the commonly used pharmaceutical groups which form part of the analgesics class. This group of medicines are used to treat symptoms of illnesses such as influenza and to relieve pain and inflammation. The most commonly found NSAIDs worldwide are diclofenac , ibuprofen and naproxen (Packer *et al.*, 2003; Xu *et al.*, 2019; Wojcieszyńska and Guzik, 2020; Zhang *et al.*, 2020).

According to Zhang *et al.*, (2020) diclofenac and ibuprofen are some of the most widely used and prescribed medication due to their efficiency in reducing inflammation and pain. These two medications accounted for 51% and 22% respectively of total NSAID use. Due to the poor adsorption characteristics of these pharmaceuticals and the incapacity of WWTP's to efficiently remove them from wastewaters, they are the most commonly identified compounds in various water bodies (Gogoi *et al.*, 2018; Fekadu *et al.*, 2019; Zhang *et al.*, 2020).

Certain pain-relivers besides NSAID's such as acetaminophen, commonly known as paracetamol, is also found in the environment (Antunes *et al.*, 2013; Paíga and Delerue-Matos, 2016). This pharmaceutical is also used to treat pain and fever and therefore one of the most used pharmaceutical drugs worldwide (Antunes *et al.*, 2013). Its high usage amongst people therefore makes it commonly found in wastewater and consequently into the environment due to its incomplete removal rates by WWTP's (Paíga and Delerue-Matos, 2016).

2.1.2.2 Caffeine

Caffeine is one of the most widely used drugs in the world as it occurs in various domestic products ranging from 360 mg/L in coffees and teas to its use in pharmaceutical products due to its stimulating properties (Sui *et al.*, 2015). This drug is used in pharmaceutical products as it enhances the effect of various analgesic (pain reliever) medications such as those for coughs and headaches and in those that act as a stimulant in cardiac and respiratory medicines (ErgeBu *et al.*, 2003). Caffeine is also used as a marker for pollution in various waterbodies such as in surface water and groundwater, as its presence indicates contamination due to untreated wastewater by domestic use (ErgeBu *et al.*, 2003; Matongo *et al.*, 2015a; Cantwell *et al.*, 2018).

2.1.2.3 Contraceptives (birth control pills) and corticosteroid drugs (hormones)

Contraceptives and Corticosteroids are part of the steroid family which mimic the effects of the hormones in the body thereby altering various functions of it. For example, corticosteroids contain the cortisol hormone which helps reduce inflammation such as with asthma as well as to regulate metabolic processes. Contraceptives on the other hand contain oestrogen and progesterone, which are used to prevent pregnancy. These two pharmaceutical products are therefore common household products due to their efficiency and easy accessibility which makes them prevalent and common in the environment due to the excretion by both humans and animals (Pal *et al.*, 2010; Gogoi *et al.*, 2018). According to Brynhildsen, (2014) and Fleming *et al.*, (2016) contraceptives are one of the most commonly used steroid drugs in the world and it would therefore be useful to monitor them from the influent of WWTP's to various surface water discharge points as well as other waterbodies. According to Adeel *et al.*, (2017) livestock farming is also one of the leading contributors of steroidal oestrogen into the environment. This is due to farmers using it as a growth hormone in both cattle and poultry farming which is then passed through these animals in both their faeces and urine.

2.1.2.4 Antibiotics and anti-retroviral treatment

Certain medications such as antibiotics and anti-retroviral treatment are beginning to be a common occurrence in the environment due to the increase usage to treat various illnesses.

Antibiotics are the group of pharmaceuticals that treats bacterial infections, which when taken destroy and inhibit the growth of bacteria and fungi (Ngqwala and Muchesa, 2020). Sulfamethoxazole, amoxicillin, rifampicin and clavulanic are some of the most frequently used antibiotics worldwide, with antibiotic usage worldwide exceeding 100 000 tons per year, which are used to treat various bacterial infections such as tuberculosis (TB), urinary infections and pneumonia (Orrell *et al.*, 2011; Johnson *et al.*, 2015; Kalyva, 2017; Danner *et al.*, 2019; Folarin *et al.*, 2020). According to a study done by Matongo *et al.*, (2015) at the Msunduzi River, KwaZulu-Natal, South Africa, it was observed that antibiotics occurred at concentrations ranging from <10 ug/L in surface water samples while up to 34.50 ug L^{-1} in wastewater, with a removal efficiency of Waste Water Treatment Plants being at 48.80%.

Antibiotics are not only used for humans but are a frequent medication used in the agricultural industry for the treatment of various illnesses in livestock. The increased use of this pharmaceutical product for livestock makes it more likely to enter the environment directly through the faeces and urine of treated animals as well as from manure containing traces of the antibiotics used as fertiliser (Massé, Saady and Gilbert, 2014; Kivits *et al.*, 2018). This direct exposure puts the soil, surface water and groundwater at risk of being contaminated with antibiotics.

Anti-retroviral treatment is medication that is used to reduce the HIV viral load and prevent further damage to the immune system in infected patients (Orrell *et al.*, 2011; Schoeman, Dlamini and Okonkwo, 2017; Nannou *et al.*, 2020). Efavirenz, nevirapine and tenofovir are some of the commonly used anti-retroviral treatment for patients infected with HIV and AIDS (Fekadu *et al.*, 2019; Nannou *et al.*, 2020). Several studies have indicated that there is an increase in occurrences of these pharmaceuticals in the environment due to the incorrect disposal, especially in low to middle-income countries such as in Kenya and South Africa, as well as the inefficiency of WWTP's removal of the active ingredients (K'oreje *et al.,* 2016; Schoeman, Dlamini and Okonkwo, 2017; Fekadu *et al.*, 2019; Nannou *et al.,* 2020).

These anti-retroviral medications are excreted through both urine and faeces. Due to an increase in availability and access to anti-retroviral treatment it is more likely that they will occur in the environment if they are not properly discarded or removed during WWTP processes (Schoeman, Dlamini and Okonkwo, 2017). According to a report done by the UNAIDS 2019, it is stated that 38 million people were infected with HIV/AIDS worldwide, of which, 7.7 million infections occur in South Africa, with 67% of these people receiving some form of anti-retroviral treatment. The monitoring of these pharmaceuticals in the environment is therefore vital in South Africa because of a high number of patients using TB and HIV medication.

2.1.2.5 Beta-blockers and carbamazepine

Beta-blockers and carbamazepine are chronic medication, used to treat long-lasting illnesses and are therefore in use by many people worldwide. Beta-blockers commonly known as propranolol and atenolol, are some of the most widely used pharmaceutical products. Whilst the fate of these products in the environment are scarce due to a lack of research done on the occurrence and distribution of these pharmaceuticals once it enters the environment (Focazio *et al.*, 2008; Deblonde, Cossu-Leguille and Hartemann, 2011; Maszkowska *et al.*, 2014). This group of pharmaceutical products is used to treat various health-related illnesses such as heart conditions and hypertension by inhibiting the beta-adrenergic receptors thereby lowering the heart rate and lowering blood pressure (Mcbean *et al.*, 2018).

Carbamazepine is another commonly occurring pharmaceutical in the environment due to it being widely prescribed for epilepsy and bipolar disorder (Andreozzi *et al.*, 2002; Santos, Aparicio and Alonso, 2007; K'oreje *et al.*, 2018; Fekadu *et al.*, 2019). It has been found in various effluent from WWTP's due to its low biodegradability as well as the incorrect disposal of expired medication by its users (Andreozzi *et al.*, 2002; Sui *et al.*, 2015). Due to its persistence and mobility in various mediums, carbamazepine is one of the pharmaceuticals at risk of polluting soils surfaces and waterways (Koba *et al.*, 2016).

Pharmaceutical concentrations detected in previous studies are presented below in Table 2.1. The data in Table 2.1 shows that pharmaceuticals are indeed present in different mediums in the environment ranging from surface water to groundwater.

Table 2.1: Pharmaceutical concentrations detected in previous studies

Pharmaceutical	Concentration/ng L^{-1}	Country	Reference
Acetaminophen	4.1–73 (Surface water)	South Korea	Kim *et al.*, 2007
Carbamazepine	282 (Groundwater)	Norway	Eggen *et al.*, 2010
Naproxen	260 (Surface water)	Portugal	Paíga *et al.*, 2016
Caffeine	92 (WWTP effluent)	Jordan	Al-Mashaqbeh *et al.*, 2019
	189 (Groundwater)	Europe	Loos *et al.*, 2010
Diclofenac	2700-5600 (Surface water)	South Africa-Gauteng	Archer *et al.*, 2017
	24 (Groundwater)	Europe	Loos *et al.*, 2010
Sulfamethoxazole	< 10000 (Surface water)	South Africa-Durban	Matongo *et al.*, 2015

2.2 Fate and transport of pharmaceuticals in the environment

Identifying and observing the fate and transport of various pharmaceuticals in the environment is of utmost importance to monitor and regulate their concentrations in the environment. Various research looked at various mediums through which pharmaceuticals are transported into the environment, ranging both surface water and groundwater (Snyder *et al.*, 2003; Nikolaou, Meric and Fatta, 2007; Paíga *et al.*, 2016; Kivits *et al.*, 2018).

2.2.1 Pathways

2.2.1.1 Surface water

Surface water bodies are most at risk of becoming contaminated by pharmaceuticals due to them being directly exposed at the surface (Stuart *et al.*, 2012). There are several types of surface water bodies ranging from rivers to wetlands, which form various ecosystems vital to the survival of various species. The flow of surface water is controlled by several factors ranging from climatic conditions, topography as well as human influence, the latter having a major influence. All these factors can influence the water quantity and quality.

Surface water is also a major source of domestic water supply for various nations such as South Africa and the United States, as it is easily accessible and easily monitored (Stuart *et al.*, 2012). Various rivers and streams are also vital in certain processes such as further treatment of wastewater, whereby the stream power transports and dilutes the effluent until various compounds are reduced in the water system before it is discharged into the environment for use by both humans and other species (K'oreje *et al.*, 2018). It is therefore vital to understand what characteristics of the water bodies govern the flow, to identify if there are any contaminants present in that water body and how far it has been distributed.

Several studies have indicated various pharmaceutical compounds are present in various water bodies, especially near WWTP's and human settlements (Pal *et al.*, 2010; Lapworth *et al.*, 2012; K'oreje *et al.*, 2018). These studies have indicated that pharmaceuticals are distributed from households and WWTP's to the environment through connecting rivers and estuaries as well as surface water and groundwater interaction. This was observed during a review done by Stuart *et al.*, (2012) in the United Kingdom where it was found that pharmaceuticals had entered the groundwater through groundwater-surface water interaction. This occurred when industries and WWTP's discharged treated wastewater into various rivers, which then entered the groundwater by the losing streams, which is where the interaction occurs between the two water bodies.

2.2.1.2 Vadose zone and groundwater

The vadose zone to groundwater is another transport medium of pharmaceuticals, especially when the source is directly above it. There is a link between these two mediums as wastewater travels through the vadose zone and into the groundwater.

The unsaturated zone (vadose zone) is the zone directly above the groundwater table and below the surface, it constitutes both air and pores and thereby providing a pathway for various chemicals to pass through to the aquifer depending on the pore size (Holden and Fierer, 2005). At the water table, the water is at atmospheric pressure (zero gage pressure), whereas fluid pressures in the vadose zone are negative, owing to tension of the soil-surface-water contact. These pore sizes range from fine-grained to course-grained material. Water movement to the aquifer is thereby controlled by, soil texture, soil structure, slope, land-use, heterogenous structures and pore sizes, whereby fine-grained soil has a lower permeability compared to coarse-grained soil, with the latter allowing water to infiltrate faster through the zone into the aquifer. The flow and concentration of pharmaceuticals entering the aquifer from the vadose zone above, if applicable, is therefore controlled by the flow rates and chemical reactions occurring in that zone based on the unsaturated hydraulic conductivity, volumetric water content and matric pressure (Holden and Fierer, 2005).

Once the water moves through the unsaturated zone and into the saturated zone it is known as groundwater and forms an aquifer (Holden and Fierer, 2005). The flow of groundwater and type of aquifer at the site of interest is a vital medium to monitor regarding the fate of pharmaceuticals, as groundwater has various uses and resident times ranging from days to thousands of years. Groundwater can either occur directly below the surface known as a shallow unconfined aquifer or it can occur deep underground where the groundwater is situated between two impermeable layers forming a confined aquifer, due to fractured rocks above and below it. Shallow aquifers such as areas with sandy soils are more likely to be contaminated due to its proximity to the surface and higher hydraulic conductivity compared to confined aquifers and therefore extra precaution should be taken in these areas to prevent or limit contamination (Godfrey, Woessner and Benotti, 2007; Del Rosario *et al.*, 2014).

The link between these two mediums was evident in a study done by Godfrey *et al.*, (2007) done in the United Sates, where it was observed that 3 out of 14 pharmaceuticals studied were found in the coarse grained- shallow unconfined aquifer from an onsite wastewater plant that had either leaked or had been discharged into a 2m thick vadose zone. The study had indicated that various processes that occurred in the vadose zone had reduced certain concentrations of pharmaceuticals by 75% before the wastewater had entered the aquifer.

2.2.1.3 Wastewater Treatment Plants.

WWTP's are both sources and pathways for pharmaceuticals to enter the environment, as they consist of various stages for the treatment of wastewater. Various WWTP's have different treatment processes depending on when they were built, their feasibility and the type of environment in which they are situated. Most WWTP's were designed to remove solids, dissolved organic matter, and excess nutrients from wastewater before discharging it back into the environment (Schoeman, Dlamini and Okonkwo, 2017).

The most widely used treatment-processes in WWTP's are physical, chemical, and biological treatments. Physical treatment is the first stage when influent comes into the WWTP whereby large sediments and objects are removed during the screening process (Gogoi *et al.*, 2018). Aeration is also used during this stage, whereby oxygen is circulated through the wastewater, after which it is then passed through filters to remove various insoluble compounds present.

The biological and chemical treatment processes (secondary treatment) in WWTP's remove suspended solids and inorganics such as nitrates, phosphorus, and ammonia from the wastewater. During the biological treatment, various organic matter is removed or broken down by microorganisms that metabolize the organic matter present in the wastewater through both aerobic and anaerobic processes (Gogoi *et al.*, 2018). An example is the activated sludge process where the wastewater treatment plant uses microbial cultures in the wastewater to biodegrade the organic matter under aerobic conditions such as aeration. This biological process in turn forms biological flocs (groups of useful bacteria) in the settling tank which adsorbs the organic matter from the wastewater forming activated sludge (Chu and Lee, 2004). Certain wastewater treatment plants also have anoxic reactors which further break down nitrogen and phosphorus reducing their concentration levels in the effluent (Yorkor and Momoh, 2019).

During the chemical treatment stage chlorine and oxidizing chemicals are used to further treat the wastewater to ensure that the remaining contaminates in the wastewater such as bacteria and other harmful microbes are destroyed. Certain WWTPS's further treat their wastewater through ozonation, which entails using ozone as the oxidizing agent. This process acts as a biocide in water and alters the functional groups of the organic compounds, further reducing and eliminating certain pharmaceuticals present, such as antibiotics (Gogoi *et al.*, 2018). Ozonation is usually costly and most WWTP's do not apply this process. However, this process was shown to be more effective compared to conventional wastewater treatment in the removal of a wide variety of pharmaceuticals by a study done by Zwiener (2007) in Germany. In the study, compounds with double bonds such as diclofenac, carbamazepine and sulfamethoxazole had higher removal rates with this process.

Although biological and chemical treatments are shown to be effective in reducing pharmaceuticals in the wastewater, certain pharmaceuticals such as anti-retroviral drugs can become transformed into more toxic compounds. This was observed by Schlüter-Vorberg *et al.*, (2015) in Germany, with the anti-retroviral drug acyclovir. Through biological treatment this drug was transformed into carboxy acyclovir, which had a toxic effect on crustaceans in the aquatic environment.

It can further be shown in Figure 2.1, how the various sources and receptors are connected via various pathways. The whole water network from surface water to groundwater is connected and therefore it must be understood to identify the fate and distribution of pharmaceuticals through the environment.

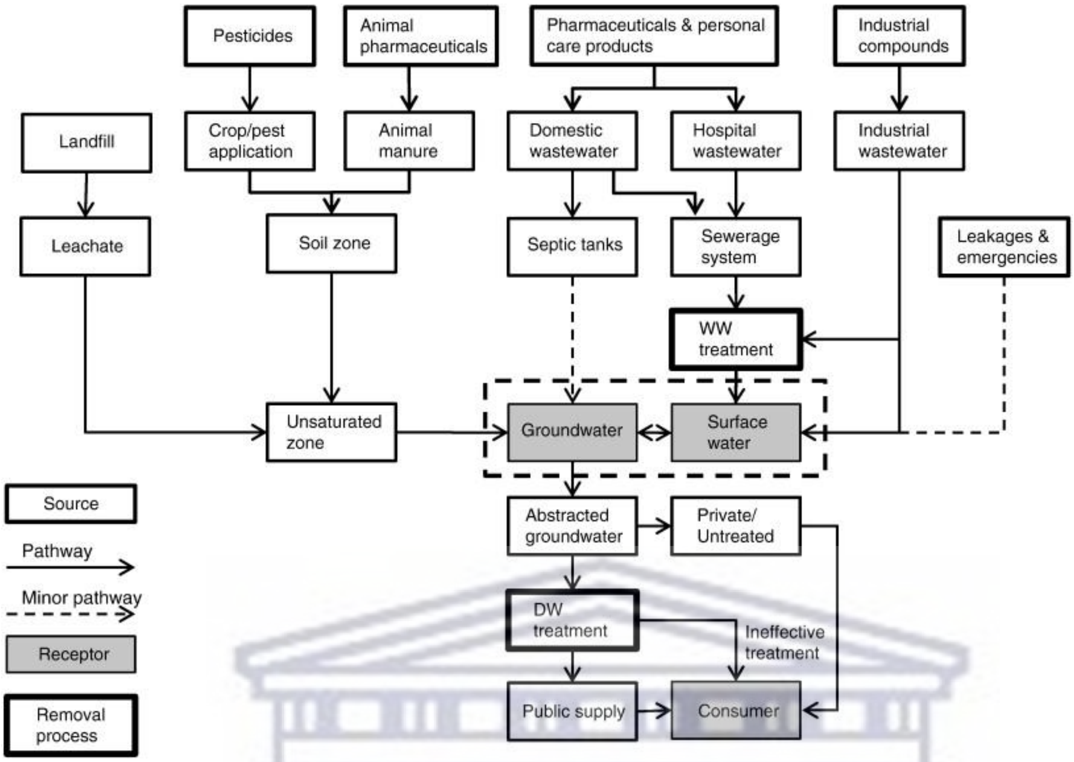


Figure 2.1: Flow chart showing source to sink, adopted from Stuart et al., 2012

2.2.2 Spatial and temporal variation of pharmaceuticals in the environment

The spatial and temporal occurrence of pharmaceuticals can be controlled by various factors such as seasonal variation, physicochemical parameters (pH, hydraulic conductivity, and total dissolved solids) and geological settings (ErgeBu *et al.*, 2003; Tredoux *et al.*, 2009; Sui *et al.*, 2015).

Seasonal variation is one of the key factors to consider when monitoring pharmaceuticals in the environment, as certain climatic conditions, and the specific season (winter, summer, spring, and autumn) can play a role in the increased usage of various pharmaceuticals as well as its increased occurrence in the environment. This observation was observed by Fekadu *et al.*, (2019) in a study that looked at the presence of pharmaceuticals in aquatic environments in both Europe and Africa. In South Africa, it was found that naproxen and ketoprofen (type of NSAID) occurred in a higher concentration in the environment during winter as compared to summer, where little to no concentration of the pharmaceuticals was found in the same location downstream of a WWTP. This was due to the fact that South Africa uses more medication during the winter period, due to the higher occurrence of infectious diseases such as influenza and colds (Gumbi *et al.*, 2017).

Another factor relating to seasonal variation of pharmaceuticals in the environment is the temperature and rainfall rates during various seasons. Increase in temperatures during summer months can degrade certain pharmaceuticals in the surface water when exposed to a higher intensity of solar irradiation (Andreozzi, Marotta and Paxéus, 2003). This was observed by Yarahmadi *et al.*, (2018) who had done research on the seasonal variation of steroidal hormones discharged from the WWTP's into a river located in Quebec, Canada. It was observed that certain steroid pharmaceuticals, such as progesterone, was observed at a higher concentration in the river during the spring season due to the lower temperatures which led to less photodegradation and biodegradation in that season compared to the summer season of 2018. However, the study also noted that although the increase in temperature during the summer months can contribute to the reduction in pharmaceuticals, the reduced flow rates in summer can cause pharmaceuticals to accumulate in the sediments due to less dilution by river flow.

The physicochemical parameters also play a role in the concentration of pharmaceuticals in the environment due to how the pharmaceutical compound reacts in the specific conditions. Certain conditions such as the pH and soil type, through which the pharmaceutical moves can affect the sorption of that compounds when passing through the various mediums. For example, a study done by Zhang *et al.*, (2014) in China, indicated that at a lower pH certain veterinary pharmaceutical, such as sulphonamides (class of antibiotics), were more likely to have a higher sorption capacity compared to a medium with a higher pH due to the ionic strength. This was because of the sulphonamides acting mostly as cations at the lower pH, thereby being attracted to the negatively charged minerals in the underground medium through electrostatic interactions.

The type of geological setting present is important to understand as it controls the distribution and transport of the pharmaceutical through both the vadose zone and groundwater. Certain geological features can reduce the concentration, and some are able to increase the flow of the pharmaceutical into the groundwater (Del Rosario *et al.*, 2014; Tredoux *et al.*, 2009). A study on the direct recharge of treated wastewater and storm water into the aquifer was conducted by Tredoux *et al*., (2009) at the Atlantis Aquifer (Western Cape, South Africa). The study showed how the geological setting can play a role in the reduction of pharmaceuticals present in the direct recharge of treated wastewater. Moreover, the study showed how the treated wastewater was further purified by the subsurface above the aquifer. Certain pharmaceutical concentrations, such as ibuprofen and sulfamethoxazole (antibiotic) were reduced through dilution and adsorption by the geologic material present in the subsurface. Certain geological features such as alluvial and karst aquifers on the other hand are more vulnerable to contamination. This vulnerability is due to both the shallow water table present in alluvial aquifers as well as the conduit flow in karst aquifers, which can transfer contaminants directly from the surface to the aquifer below, thereby increasing the risk of pharmaceuticals in the groundwater (Lapworth *et al.*, 2012).

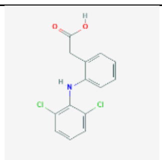
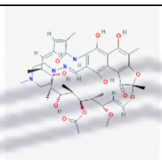
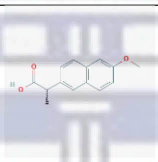
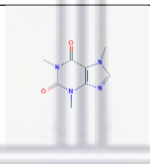
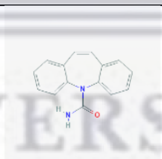
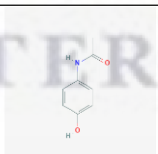
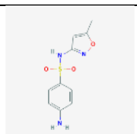
2.2.3 Natural attenuation of pharmaceuticals in the environment

The fate and transport of contaminants in the environment depends on the degree of natural attenuation of the organic compounds through the medium which it moves. The Environmental Protection Agency (EPA) defines natural attenuation as either a physical, chemical, or biological process that reduces the mass, toxicity, and concentration of contaminations in either soil, surface water or groundwater without the influence of humans. Natural attenuation can therefore range from biodegradation, dilution, sorption, and photolysis depending on the pharmaceutical products' polarity, chemical structure, and solubility in water (Pal *et al.*, 2010).

The type of natural attenuation that occurs is based on several factors, including the compound's water partition coefficient (($\log K_{ow}$)-water solubility of the compound) and the pKa of the compound which deals with the hydrogen ion concentration of the compound. These two parameters play a significant role in understanding the distribution of the compounds in the environment, whether they will adsorb or dissociate into the medium (water or soil). It is stated in various publications (Thomas and Foster, 2005; Behera et al., 2011; Ojemaye et al., 2021) that a compound with a high $\log K_{ow}$ would adsorb to the sludge during wastewater treatment process or to sediments once in the environment while a compound with a lower $\log K_{ow}$ would easily be transported in the aqueous medium.

Table 2.2 shows the various logK_{ow} and pKa of selected compounds.

Table 2.2: Log K_{ow} and pKa of selected pharmaceuticals (PubChem contributors)

Pharmaceutical	**Chemical structure**	**Water partition coefficient (Log K_{ow})**	**pKa**
Diclofenac		1.91	4.2
Rifampicin		4.24	1.7
Naproxen		3.18	2.52-4.2
Caffeine		-0.07	10.40
Carbamazepine		2.45	13.9
Acetaminophen		0.46	9.4
Sulfamethoxazole		0.48	7.59

Biodegradation and photodegradation are the two types of natural attenuation which are important in reducing contaminates when discharging treated water into the environment such as in surface water (Packer *et al.*, 2003). Biodegradation involves the breakdown of contaminates by natural biological activity occurring in the river or stream, such as bacteria, fungi or plants that can biodegrade various contaminants. The rate of biodegradation is also dependent on the medium such as surface or groundwater, as different mediums have varying amounts of microbes and oxygen present (Sui *et al.*, 2015). For example, where groundwater, surface water and soils are compared, groundwater has less diverse microorganisms and lower aerobic rates compared to the other mediums thereby leading to variable redox reactions (Lapworth *et al.*, 2012). Biodegradation of pharmaceuticals in groundwater can therefore be degraded incompletely or not at all due to the factors above (Lapworth *et al.*, 2012; Sui *et al.*, 2015).

Photodegradation is another factor controlling the degradation of contaminants, due to the direct sunlight on open water bodies, which alters the chemical composition of the contaminants present in the surface water. The influence of direct photodegradation was observed by Packer *et al.*, (2003) on the Mississippi river in the United States, which looked at the influence of photolysis on diclofenac, ibuprofen, naproxen and clofibric acid in the river. This study showed that both diclofenac and naproxen are photolabile in the river which is directly influenced and changed when exposed to sunlight.

Dilution and sorption are part of the common natural attenuation types that occur regarding the degradation of pharmaceuticals in the environment. Dilution involves the dilution of treated wastewater that enters a river or stream. The rate and efficiency of dilution of the contaminants present depend on the characteristics of the receiving water body such as flow and volume (K'oreje *et al.*, 2016). A higher river flow and greater volume of water, such as a wetland, would reduce certain pharmaceuticals through dilution compared to a smaller stagnant stream.

Sorption of pharmaceuticals in the environment deals with the ability of the contaminant to either be absorbed or adsorbed to soil particles if present in the soil or suspended solids in water bodies. Adsorption of pharmaceuticals is common in the vadose zone whereby various compounds attach to the soil particles or pass through it to the groundwater. This adsorption process depends on the pharmaceutical's sorption characteristics whereas a compound with strong sorption characteristics will less likely leach into the groundwater compared to a compound with low sorption characteristics, which has more mobility in the soil (Sui et al., 2015). This was also shown by Pal *et al.*, (2010), who indicated that pharmaceuticals with a high molecular weight and a high $\log K_{ow}$ (water partition coefficient) of greater than 5 would easily be adsorbed to sediments, which can also then be easily removed by coagulation at WWTPS's and thereby less likely to occur in surface water. It was also shown that pharmaceuticals with lower $\log K_{ow}$ of less than 2.5 would be more likely present in surface water due to its low sorption and higher water solubility such as carbamazepine and atenolol (Pal *et al.*, 2010; Sui *et al.*, 2015).

2.3 Effect of pharmaceuticals on aquatic and human life

The importance of understanding the fate and distribution of pharmaceuticals in the environment is supported by the potential harmful effects of these compounds that can occur not only on aquatic life but on human beings who are in contact with contaminated water. Little is known about the effects of pharmaceuticals at low concentrations (µg/L) in the environment as these are emerging pollutants that were not regulated or monitored before (Gogoi *et al.*, 2018; Zhang *et al.*, 2020). Several studies have indicated the toxicity of various pharmaceuticals on aquatic life that occurred in the environment, namely the presence of diclofenac, antibiotics and ethinylestradiol (Adeel *et al.*, 2017; Gogoi *et al.*, 2018; Zhang *et al.*, 2020). These endocrine disrupting compounds can have adverse effects on both reproductive and morphological functioning of living organisms, as it can impact the normal functioning of various endocrine glands (Tijani *et al.*, 2016; Gogoi *et al.*, 2018).

The effect of pharmaceuticals on living organisms was shown by Zhang *et al.*, 2020 in China, which studied the effects of ibuprofen and diclofenac on Zebra Fish at low concentrations. The study concluded that even though pharmaceuticals occurred at low concentrations, continuous exposure to these endocrine disrupting compounds has led to biochemical and morphological changes in certain organisms such as in Zebra fish (Zhang *et al.*, 2020). Zhang *et al.*, (2020) stated that exposure (56 Hours) to diclofenac and ibuprofen at concentrations between 0.04 and 25.0 µg/L led to certain cardiovascular and muscle mobility issues in Zebra Fish embryos. This was further supported by Schwaiger *et al.*, (2004) who conducted research on the toxic effect of diclofenac on rainbow trout fish in Germany. The study showed the effect of diclofenac, with concentrations ranging from 1 µg/L to 500µg/L over a 28-day period, were found to have altered the function of the kidneys of these fish and had caused damage to the pillar cells, found in the gills of the trout fish.

Ethinylestradiol (EE2) is also one of the contaminants of emerging concerns due to its adverse effect on living organisms once it enters the environment specifically as it relates to reproductive health (Nikolaou, Meric and Fatta, 2007; Pal *et al.*, 2010). This type of oestrogen medication alters various hormonal chemicals in the body, which can be detrimental to other non-target organisms. This was observed in a study by Adeel *et al.*, (2017) in China, which showed how oestrogen altered the physiology of the fish which lead to feminisation of male fish by the reduction in the size of testes as well as other reproductive characteristics.

The effects of steroidal hormones such as oestrogen and testosterone on crops irrigated from treated waste water, containing steroids, was studied by Shargil *et al.*, (2015) in Israel. The study was conducted over a 3-year period and indicated that oestrogen and testosterone concentrations detected in the lettuce exceeded the daily consumption recommendation level set by the Food and Drug Regulation. The presence of these steroids in edible plants is therefore of a concerning nature, as little is known about the long-term effect of these steroids in humans based on consuming food and water containing these pharmaceutical compounds. A similar study by Schapira *et al.*, (2020) also observed involuntary human exposure to carbamazepine when consuming crops irrigated with treated waste water.

The distribution and occurrence of antibiotics and anti-retroviral drugs in the environment is another major concern as it can lead to antibiotic and anti-viral drug resistance amongst microbes and viruses (Jendrzejewska and Karwowska, 2018; Danner *et al.*, 2019; Nannou *et al.*, 2020). The bacteria's resistance to anti-biotics is not only a defence mechanism but an advantage in their adaption in the environment. This adaption to antibiotics is transferred through the bacteria's genetics and mutations, as they reproduce in the natural environment (Jendrzejewska and Karwowska, 2018). The resistance to antibiotics by microbes, especial pathogens, renders the antibiotic ineffective and can be deadly to society, as it will be difficult and costly to treat these resistant pathogens with current medications due to their built up resistance, which could become deadly when patients are gravely ill (Kairigo *et al.*, 2020). It is therefore important to understand the distribution and contamination of these pharmaceuticals in the environment.

2.4 Methods used to analyse pharmaceuticals in the environment

The exact concentration of the various pharmaceutical compounds in a solution, is often difficult to determine with the use of one method, as the concentration fluctuates in various complex matrices from as low as 0.2 ng/l as well as the high polarity of certain pharmaceuticals (Hao, Zhao and Yang, 2007; Al-Odaini *et al.*, 2010; Kumirska *et al.*, 2015). Various literature, therefore, uses a combination of different analytical methods as there is no single method available that can detect and quantify all the pharmaceuticals in the environment (Al-Odaini *et al.*, 2010). The choice of analytical methods is based on several factors ranging from affordability, pharmaceuticals of interest as well as the objectives of the research. These methods can range from a sample preparation method involving, solid phase extraction combined with either, high performance liquid chromatography (HPLC), gas chromatography-mass spectrometry (GC-MS) or liquid chromatography-mass spectrometry (LC-MS) (Iglesias *et al.*, 2012; Gumbi *et al.*, 2017).

2.4.1 Sample preparation

Sample preparation is needed before proceeding with GC-MS or LC-MS to avoid any interference when analysing the sample as well as concentrating the sample if the analyte of interest occurs at low concentrations in the solution. There are several ways to prepare the sample as the clean-up method depends on several factors such as the thermal stability of the analytes of interest as well as the solvent and container used, as this could affect the compounds which could either stick to the container or be absorbed by the solvent.

Solid-phase extraction (SPE) is one of the sample preparation techniques used whereby it involves the separation of the drug analytes, based on its chemical and physical properties from a sample of interest (Sargent, 2013). This process typically involves a syringe which-contains a solid phase stationary sorbent. The sorbent in the SPE cartridge can range from using silica-based sorbents or carbon-18 sorbent depending on if the matrix of the analytes is either polar or non-polar as well as the pore space of the sorbent (Sargent, 2013). The solution of the sample can also be buffered before being passed through the SPE to ensure analytes of interest are maintained and to further separate the analytes in the solution. This procedure involves various steps, namely conditioning, sample loading and elution. The choice of SPE procedure used depends on the sample matrix and the analyte of interest (Sargent, 2013).

Liquid-liquid extraction is another type of method of sample preparation that involves the movement of the target analyte from the original solvent into another solvent (Sargent, 2013). This depends on the compound's solubility between the two immiscible solvents, this is done to make the analyte more soluble in the second solvent. The process is conducted in a separating funnel where it is then further partitioned through a centrifuge process (Sargent, 2013). This step is necessary to accurately separate and quantify the various pharmaceuticals, when injecting the sample into either GC-MS or LC-MS.

2.4.2 Gas chromatography and Mass Spectrometry (GC-MS)

Gas chromatography is used in conjunction with mass spectrometry when wanting to analyse various volatile and non-polar compounds in a solution (Iglesias *et al.*, 2012). During gas chromatography the volatile organic compound is separated into individual components when heated (to elute the volatile compounds) and passed through a column using a gas compound such as helium or nitrogen. The separated components are then passed to the mass spectrometry where this technique can identify the different components based on its mass to charge ratio of the charged particles. This combined method is therefore useful in identifying organic contaminants at trace levels in the solution, ranging from alcohol to non-inflammatory drugs. These two different techniques are therefore coupled together to achieve both quantitative and qualitative analysis of the pharmaceuticals.

To enhance the GC-MS method, certain derivati~~s~~sation methods (conversion of a chemical compound into a compound of similar chemical structure) are used to increase volatility and to enhance the detection of acidic drugs in a solution of interest. The usefulness of derivati~~s~~sation with GC-MS was shown to be useful in a study by Gumbi *et al.*, (2017), with the use of silylation derivatisation, which was shown to be useful in improving the analysis of acidic drugs in the Umgeni River System, Kwa-Zulu Natal, South Africa. Acidic drugs were detected in a range of 0.0200 to 68.14 µg L^{-1} in the system, these drugs included ibuprofen, diclofenac, and naproxen. Although useful, this method has its limitations regarding its application to certain research, due to the low volatility and thermal stability of most drugs occurring in the environment (Iglesias *et al.*, 2012).

2.4.3 High performance Liquid chromatography (HPLC)

High performance liquid chromatography is another separation technique used in the study of pharmaceuticals. The principle of this technique is based on the separation and distribution of the analyte between the mobile phase and the stationary phase, where the mobile phase consists of the elute while the stationary phase consists of the packing material of the column (Petrova and Sauer, 2017). This process involves the solvent being forced under high pressure through the separation column where the individual components of the sample are retained at different rates due to the interaction with the stationary phase leading to different flow rates (Petrova and Sauer, 2017). A chromatogram at the end of the process is then generated by the HPLC software where the identification and quantification of a substance can be obtained, based on the quantity of analyte emerging from the column (Petrova and Sauer, 2017).

2.4.4 *Liquid chromatography and Mass Spectrometry (LC-MS)*

Liquid chromatography combined with mass spectrometry is one of the most useful and commonly used methods, due to it being able to detect analytes of interest in complex matrices, including detecting a wide variety of pharmaceuticals in the environment. This analytical method is mainly used for analysis of polar, non-volatile, and thermolabile pharmaceuticals in a solution (Hao, Zhao and Yang, 2007). The operating principle of combined use of LC-MS technique is firstly based on the LC component, which deals with the separation and distribution of the analyte between the mobile phase and the stationary phase, where the mobile phase consists of the elute while the stationary phase consists of the packing material of the column through which the mobile phase will pass through (Petrova and Sauer, 2017). Once the sample undergoes the liquid chromatography process, it then is analysed by the mass spectrometry where the components are further separated based on the compound's mass to charge ratio (Sargent, 2013).

This combined method can detect pharmaceuticals at low detection limits due to liquid chromatography being able to separate the various polar compounds in a complex mixture while the mass spectrometry has high sensitivity and selection as well as separation capabilities based on the compound's mass to charge ratio (Pitt, 2009; Schoeman, Dlamini and Okonkwo, 2017). Although it is expensive, another advantage of this analytical method is its ability to detect multiple analytes in one analytical run and at a faster pace unlike when using one technique alone (Sargent, 2013).

2.5 Regulations in South Africa applicable to water quality and contaminants

South Africa has various laws in place to ensure the standards of water resources are acceptable for human consumption and to protect and minimize pollution of its natural resources, these include the National Water Act 36 of 1998 and adhering to the South African National Standards (SANS) set out which includes the SANS 241:2015 for drinking water specification. Section 24 of the Constitution deals with the protection of the environment. For effect to be given to this section various laws were implemented such as the Water Service Act 108 of 1997 and the National Water Act 36 of 1998. The main objectives of these Acts are to allow for the right of access to basic water supply and sanitation as well as being a regulatory framework for water services institutions and water services intermediaries. This ensures effective water resource management and conservation while still protecting associated ecosystems. The lack of data on the fate and toxicity of pharmaceuticals in the environment however makes it difficult to regulate (Lapworth *et al.*, 2012; Schoeman, Dlamini and Okonkwo, 2017).

The disposal of waste at landfill sites and WWTP's are controlled by the Department of Water and Sanitation and the Department of Environmental, Forestry's and Fisheries. The Act that guides the disposal of waste is the National Environmental Management; Waste Act, No 59 of

2008. This Act was promulgated to protect health and the environment by providing minimum standards and measures for the prevention of pollution and ecological degradation. It also deals with management of waste activities and the remediation of contaminated land. This Act is vital in ensuring South Africa's water system does not become polluted by emerging contaminates. However, the lack of legislative guidelines, such as concentration limits for emerging contaminants at WWTP's in its discharge of treated wastewater has become an issue (Schoeman, Dlamini and Okonkwo, 2017; Gogoi *et al.*, 2018).

For these laws to be properly adhered to, the education and awareness of South African citizens concerning the effects of emerging contaminants and the incorrect disposal of pharmaceuticals into the environment is needed. These laws can also be effectively implemented by updating infrastructure, implementing different monitoring, and managing techniques at various plants, as various treatments plants are designed differently and therefore cannot apply a one size fits all approach. This will thereby ensure that emerging contaminants are removed or reduced efficiently before entering the environment.

Currently, there are no laws and regulations regarding the concentration limits of pharmaceuticals in various waterbodies or drinking water in South Africa. WWTP's are not mandated to test for these emerging contaminants as they were not designed to reduce or remove contaminants such as pharmaceuticals. The Australian government currently has certain benchmark values (ng/l) when it comes to the occurrence of pharmaceuticals in various water bodies. Table 2.3 below shows these concentration limits for the selected compounds (besides rifampicin) of interest which can be used as a guide to monitor these compounds levels in the environment.

Benchmark values for selected pharmaceuticals are presented below in Table 2.3 based on the Australian guidelines for emerging contaminates in potable water.

Table 2.3: Benchmark values (ng/l) for selected pharmaceuticals according to the Australian guidelines for emerging contaminates in potable water (NWQMS, 2008)

Pharmaceutical	Concentration/ngL^{-1}
Acetaminophen	175000
Carbamazepine	100000
Naproxen	220000
Caffeine	350
Diclofenac	1800
Sulfamethoxazole	3500

2.6 Past research in South Africa with regards to pharmaceuticals in the environment

The overburden and poor maintenance of South Africa's WWTP's is leading to untreated sewage overflowing into receiving waterbodies, which can be detrimental not only to aquatic life but has potential to impact human health. Over half of South Africa's wastewater treatment plants are in poor condition, with 75% of 910 municipal WWTP's reaching less than 50% compliance with minimum effluent standards before discharge during the year 2020 (Daily Mavericks,2021). Myriad studies have therefore been carried out in South Africa to monitor and observe these effects of both raw and treated sewage flowing into the environment.

The Water Research Commission of South Africa conducted a study in 2018 on emerging contaminants in reclaimed water for portable use in order to identify emerging contaminants present, removal capabilities and to provide recommendations (Swartz *et al.*, 2018). It looked at 5 water treatment plants in the Western Cape with various treatment processes ranging from conventional activated sludge treatment to advanced treatment such as reverse osmosis membranes and membrane bioreactors. It concluded that treatment processes were not effectively able to remove CECs such as pharmaceuticals and other emerging contaminants, such as carbamazepine, bisphenol A, sulfamethoxazole and perfluorinated compounds, which had persisted after undergoing various primary and secondary treatment processes with concentrations up to 720 ng/l occurring in the final effluent.

Another study done by Ojemaye and Petrik (2021) looked at the occurrence of emerging contaminates in the marine environment around the False Bay coast, Cape Town, South Africa, from sources such as WWTP's and anthropogenic activities. In addition, the study monitored the distribution of contaminants, such as pharmaceuticals and personal care products, from source to sea outflow and the occurrence of these contaminants in the tissues of aquatic organisms, which included invertebrates and seaweed, which occurred in that area. From the analytes of interest, the study concluded that diclofenac had the highest occurring concentration in many of the matrices, where it was found that marine invertebrates had a concentration range of 67.67-780.26 ng/g dry wt detected while concentration in the seaweed was detected at a range of 101.50-309.11 ng/g dry wt.

2.7 Selected techniques for CEC's remediation

As the global population grows and the use of pharmaceuticals increases, the presence of CECs in the environment also increases. Therefore, certain advanced techniques must be implemented to effectively treat CECs from wastewater effluent.

2.7.1 Advanced Oxidation Process (AOP)

One of the techniques which has shown to be effective in degrading certain CECs, such as organic pollutants, is the Advanced Oxidation Process (AOP). This process is based on photocatalysis and degrades the emerging contaminate by its oxidizing process, which entails generating enough hydroxyl (OH) radicals to attack the compounds' molecular structure (Capodaglio, 2020; Olatunde, Kuvarega and Onwudiwe, 2020). The molecular structure of the pollutant is then changed, which causes the mineralisation of the compound (Munter, 2001). The use of this technique was shown to be effective in the removal of a persistent emerging contaminant, carbamazepine, by Haroune *et al.*, (2014) who investigated the efficiency of the use of photocatalysis (catalysed by Titanium dioxide) as an AOP. This process was shown to be effective in the degradation of the compound and its metabolites within certain environmental parameters.

2.7.2 Advanced Reduction Process (ARP)

Advanced Reduction Process (ARP) is another technique that is being used to degrade contaminates of emerging concern (Olatunde, Kuvarega and Onwudiwe, 2020). This process combines photon sources, such as UV and microwaves, coupled with reductive agents, ferrous iron, sulphide) to generate reactive radicals to reduce emerging pollutants to less toxic products (Capodaglio, 2020; Olatunde, Kuvarega and Onwudiwe, 2020). These reactive radicals include hydrate electrons, hydrogen ions and sulphite radicals, which can produce strong reducing agents. Advanced Reduction Process with the use of sulphite and UV irradiation was shown to be effective in the degradation of diclofenac by a study done by Yu, Cabooter and Dewil (2019) in Belgium. It was observed in the study that the combination sulphite and UV irradiation showed increased effectiveness in the degradation of diclofenac than when compared with direct photolysis due to the interaction with the reductive radicals.

2.7.3 Nanofiltration, the use of Nano zerovalent iron (nZVI) as an adsorbent

Nanofiltration is another viable treatment process that can be used as a tertiary treatment to remove organic or inorganic pollutants from wastewater or aquatic bodies (Phenrat *et al.*,2020).

Its principle is based on a pressure-membrane system that removes certain solutes between 200- 1000 $gmol^{-1}$. This process involves allowing the wastewater to pass through the nano filters containing the active adsorbent, such as Nano zerovalent iron (nZVI), which creates a permeable reactive barrier, which then acts as a reducing agent when pollutants travel through it (Phenrat *et al.*,2020). The oxidation process occurring between the iron and chemical structure of the pollutant alters its structure, thereby transforming it into a less harmful substance or in certain cases immobilising it (Phenrat *et al.*,2020).

2.7.4 Activated carbon

Activated carbon was also shown to be an effective remediation technique for micropollutants such as pharmaceuticals with the use of either Granular Activated Carbon (GAC) or Powdered Activated Carbon (PAC). Granular Activated Carbon is a filtration process whereby wastewater is filtered through either one or multiple bed columns filled with GAC whereas PAC deals with mixing the powered activated carbon into various contact tanks with wastewater which then acts as adsorbent (Kårelid, 2016). Several studies have indicated its efficiency in removing certain pharmaceuticals such as naproxen, diclofenac, and carbamazepine within certain environmental settings (Margot *et al.*, 2013; Altmann *et al.*, 2016; Kårelid, 2016). Therefore, these techniques above in combination with other primary or secondary wastewater treatment processes, would lead to more effective removal of emerging contaminants before the effluent is discharged into the environment.

2.8 Conclusion / Gaps identified in research

Based on the literature reviewed, it can be concluded that there is a limited information about the long-term fate, toxicity, and occurrence of pharmaceuticals in the environment. This is especially evident in developing countries such as South Africa, whereby research is needed to identify the spatial and temporal patterns of pharmaceuticals once they enter the environment. The literature also shows the factors that affect the natural attenuation of various pharmaceuticals in the environment and how their chemical characteristics play a significant role in their distribution.

The major sources contributing to the discharging of pharmaceuticals into the environment have been identified, as WWTP’s, landfill sites, the agricultural sector, and domestic users. These sources need to implement proper effluent management and there is also a need to educate citizens about the future consequences of the presence of pharmaceuticals in the environment. This will not only contribute to improving regulations to guide WWTP’s but also prevent ecological degradation in the near future. The best way to ensure increased removal rates from major sources, such as WWTPs, is implementing tertiary treatments to reduce these compounds before discharging the effluent into the environment. This study will thereby fill the research gap that exists regarding the spatial and temporal patterns of pharmaceuticals in Cape Town's water network, as well as the fate of these compounds from source to sink. Liquid chromatography combined with mass spectrometry (LC-MS) was shown in previous studies to be efficient and effective in detecting a wide variety of pharmaceuticals in the environment and therefore will be applied in this study.

Chapter 3- Study Area

Introduction

This section will cover the study area of the research study which includes various WWTP's, landfill sites and various surface water and groundwater points in Cape Town, South Africa. This section will also cover the description of the study area focusing on the climate, geology, and other physiographic factors to understand certain parameters of the study area.

3.1 Regional Setting: Cape Town

3.1.1 Location

Cape Town is the provincial capital of the Western Cape and is home to approximately 4,4 million people (COGTA,2020). It is located on the slopes of Table Mountain and adjacent to the table bay coast, with an area spanning over 2461 square kilometres. The mainland-uses in Cape Town vary from agricultural activities, urban areas, and industrial activities (COGTA,2020).

Figure 3.1: Study Site- City of Cape Town

3.1.2 Climate

The climatic condition of Cape Town varies due to its position in the Cape Peninsula and the adjacent coast. It has a Mediterranean climate, with summer being warm and dry while experiencing cold wet winters. The average rainfall for Cape Town is 475 mm per year whereby the highest rainfall occurs during the months of June to August (Tredoux *et al.*, 2009 and Maswanganye E, 2018). This variation in climate is due to the South Atlantic high-pressure system during the summer and the mid-latitude cyclones during the winter months that being the increased rainfall (Tadross *et al.*, 2012). Cape Town has an average minimum temperature of 13 °C and an average max temperature of 23 °C (SAWS, 2018).

Figure 3.2: Mean annual precipitation for Western Cape, South Africa (Adopted from: Maswanganye, 2018)

3.1.3 Geology

Cape Town is located on three rock formations known as the Malmesbury Group, Table Mountain Group and Cape Granite, as can be seen in Figure 3.3 below. The oldest of these three and which forms the basement in the Western Cape, is the Malmesbury Group which consists of low-grade metamorphic rocks such as phyllitic shale, quartz, silt and sandstone (Adelana, Yongxin and Vrbka, 2010). The Malmesbury Group is intruded by the harder Cape Granite made of quartz and feldspar. The Table Mountain Group (TMG) which was deposited on top of the eroded Malmesbury group, consists of alternating sedimentary layers of sandstone, shales, and some layers of glacial origin such as boulders and pebbles from the Pakhuis Formation (Rodgers, 2018).

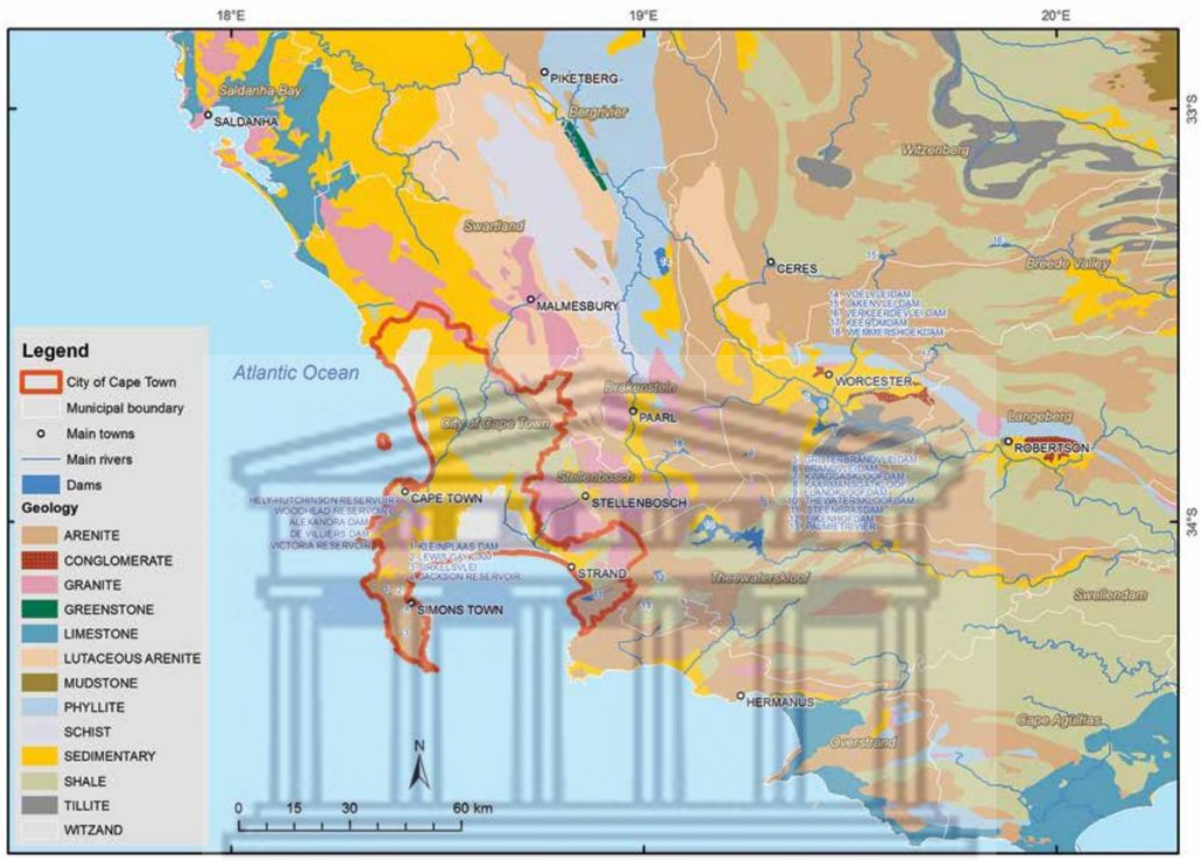


Figure 3.3 The geology of the City of Cape Town, Western Cape (Adopted from:WRC,2016 Report Number: SP 95/16)

3.1.4 Hydrogeology of the area

The weathering and deposition of the shale and quartzite of the Malmesbury and Table Mountain Group contributed to the various aquifers present in Cape Town (Adelana, Yongxin and Vrbka, 2010). These aquifers consist of both the confined TMG Aquifer and the unconfined Cape Flats Aquifer (CFA) which is underlain by the Sandveld and Malmesbury group and spans over an area of 400 km^2 (Adelana, Yongxin and Vrbka, 2010).

It can be seen in the Figure 3.4 below that the Cape Flats Aquifer (CFA) spans over a large area in Cape Town, from the Southern to the Northern part of Cape Town. At certain areas the CFA is closer to the surface such as in the Philippi area which makes it more susceptible to pollution from industrial, urbanisation and land uses for waste disposal and agricultural uses (Adelana, Yongxin and Vrbka, 2010; Ruben Aza-Gnandji *et al.*, 2013). The Cape Flats Aquifer is also a primary water supply for the horticultural activity in the Philippi area as well as one of the recharge zones for the cape flats aquifer.

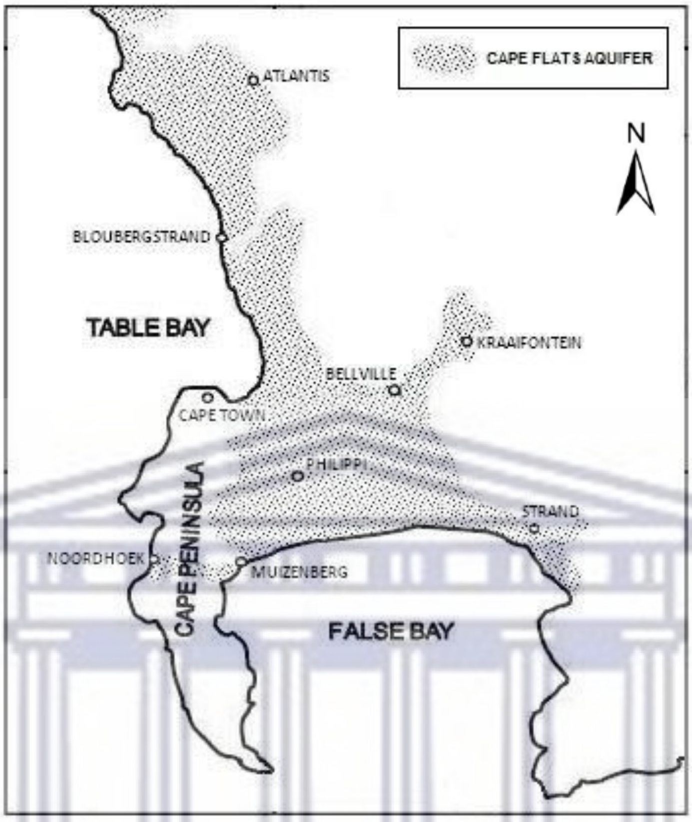


Figure 3.4: Location of the Cape Flats Aquifer, Cape Town (Adelana, Yongxin and Vrbka, 2010)

3.1.4 Surface water – Groundwater Interaction

Various surface waterbodies occur in Cape Town, namely Salt river, Eerste river, Kuilsriver, Diepriver and Zeekoevlei wetland, with other wetlands occurring throughout. These rivers are also connected to tributaries that feed into it, such as the Liesbeek , Lourens and Sout tributries (Adelana, Yongxin and Vrbka, 2010). These rivers feed into the sea at two places, whereby the rivers in the South, such as Eerste river , drains towards False Bay and the rivers in the North such as Diepriver drains into Table Bay (Adelana, Yongxin and Vrbka, 2010).

Certain rivers and wetlands in Cape Town are perennial due to the surface water bodies interacting with various aquifers below them, with some acting as recharge zones during the dry summer period. This interaction is prevalent with the relationship between Zeekoevlei river and the Cape Flats Aquifer beneath it, whereby the aquifer is the sole water contributor during dry summer months (Parsons and Harding, 2002). The interaction between these two water bodies is dependent on the geology present, such as the hydraulic conductivity of the two mediums as well as the soil between the two mediums. The rate and flow of recharge and discharge of the groundwater to surface water or vice versa are also controlled by the hydraulic conductivity and surrounding environment. Although the interconnection is beneficial, the interaction between groundwater and surface water puts both waterbodies at risk of pollution.

3.1.5 Sites of interest

The following sites were chosen, based on the treatment processes used at the WWTP's , proximity to the site and the local understanding of the location, which makes it easy to understand the flow path from source to sink.

Athlone Waste Water Treatment Plant

Athlone WWTP's is situated on the Cape Flats east of the City of Cape Town and was commissioned in 1923. It has a capacity of 105 Ml/day and services surrounding areas including Athlone, Pinelands, Langa, Thornton and Epping. The plant type is activated sludge systems which involves biological processes, chlorination, and maturation ponds as treatments. Once sewage passes screening and grit removal it undergoes primary sedimentation, aerobic and anaerobic digestion. The sludge is then dried and sent away for agricultural purposes or discarded as waste. The treated water after biological treatment is then treated with chlorine as a disinfectant before either sending it straight into the Black River or into the maturation ponds for further treatment. The effluent is diluted by the Black River and Salt River before it reaches the sea. A portion of treated effluent are sent to surrounding golf courses for irrigation.

Belville Waste Water Treatment Plant

Belville WWTP's is one of the advanced treatment plants in Cape Town built in the 1950's but upgraded in 2014 with the countries' largest membrane bioreactor (MBR) infrastructure. This plant receives waste water from surrounding areas that include Belville, Eersteriver , Kuilsriver , Parrow and Stikland. It has a capacity of 70 Ml/day and consists of a conventional treatment plant with primary and secondary treatment which includes screening and aeration and secondary treatment involving biological treatment (anaerobic, anoxic and aerobic) and disinfection by chlorination and ultraviolet (UV). Its upgraded treatment is another section of the plant beside the activated sludge process that directs raw sewage through a biological reactor (anaerobic and anoxic) and then through a 6-membrane train bioreactor (MBR) which further filters the wastewater further through the small pore membranes. This process involves ultrafiltration of the waste water through the bioreactors membranes which improves effluent quality before discharge. Thereafter it is sent through UV channels for disinfection and then to maturation ponds while the sludge is dewatered. The treated effluent is then pumped into the Kuilsriver where it connects with Eersteriver and then exits at Macassar beach. The treated effluent is also used by universities and some industries for other irrigation purposes

Cape Flats Waste Water Treatment Plant

The Cape Flats WWTP is situated adjacent to the False Bay Nature Reserve, which was commissioned in 1960 with a capacity of 200 Ml/day. The surrounding areas to which it services are Tokai, Muizenberg, Constantia, Ottery, and Philippi. Its plant type is activated sludge with its major treatment method being primary and secondary settling. Its primary settling tanks involves biological nutrient removal which includes a gravitational setting tank, aeration and anaerobic digestors. Part of its secondary treatment involves sending the sewerage liquid to maturation ponds whereby chlorine chips are added for disinfection. The treated effluent is then discharged into the Zeekoevlei canal where it flows into Sonwabi beach.

Mitchells Plain Waste Water Treatment Plant

Mitchells Plain Wastewater Treatment Plant is situated southwest of the city of Cape Town, with a capacity of 45 Ml/day. Its services both Mitchells Plain and the adjacent Strandfontein area. This treatment plant has both primary and secondary treatment, with the plant type being Activated Sludge. The influent undergoes grit removal, which is screened, and debris removed from the liquid line before going through the secondary treatment. The secondary treatment involves biological breakdown through aerobic, anaerobic, and anoxic processes which occur in 4 tanks before being sent for chlorine dosing and then into the maturation ponds. The final effluent is passed through underground pipes to Mnandi beach.

Potsdam Waste Water Treatment Plant

Potsdam WWTP was commissioned in 1957 and has a capacity of 47 Ml/day. It is situated in Milnerton and receives wastewater from surrounding areas such as Milnerton, Dunoon, Bloubergstrand, and Montague Gardens. It has multiple fine screens and grit removal processes during its primary treatment to remove any solid wastes such as rags and other debris. It has two main phases for its secondary treatment the first phase being the 3 stage UCT biological reactor, which includes anaerobic, anoxic, and aerobic zone, while the second phase is the 5 stage phoredox reactor (phosphate reduction), which further removes phosphate and nitrogen from municipal wastewater. After these two secondary treatment processes chlorination and

UV disinfection are done before discharging into the Diep River or to the Refinery nearby. The dewatering of the sludge occurs on the drying beds and is sent to landfill sites.

Atlantis Waste Water Treatment Plant (Wesfleur)

Wesfleur Wastewater Treatment Plant was built in 1978 and receives wastewater from the Atlantis community. The plant is separated into two sections that deal with domestic influent and industrial influent separately due to the nature of the raw sewage. Its domestic influent, which has a capacity of 8 Ml/d, is firstly screened and undergoes grit removal before being sent to its secondary treatments. This involves an anaerobic, anoxic and aeration zone to break down biological nutrients in the sewerage. The effluent is then sent to the secondary settling tanks before being dosed with chlorine and sent to the maturation ponds. The industrial influent, which has a capacity of 6 Ml/d, undergoes both primary and secondary treatment as well but there is no anaerobic process involved due to the influent having less nutrients, such as phosphorus, in the sewage. The final effluent is then discharged either for industrial use or into Pond 6, which is a reed bed (further natural treatment process), through which the treated effluent flows.

Groundwater in Atlantis is used as an alternative drinking supply through the managed aquifer recharge process taking place in this area. Treated wastewater and storm water is injected back into the Witsand Aquifers through recharge basins. After abstraction of the groundwater, it is sent to a water treatment plant, which consists of softening and chlorination treatment processes, before discharging the water into its potable water network.

The process of the managed aquifer recharge occurring in Atlantis is depicted below in Figure 3.5.

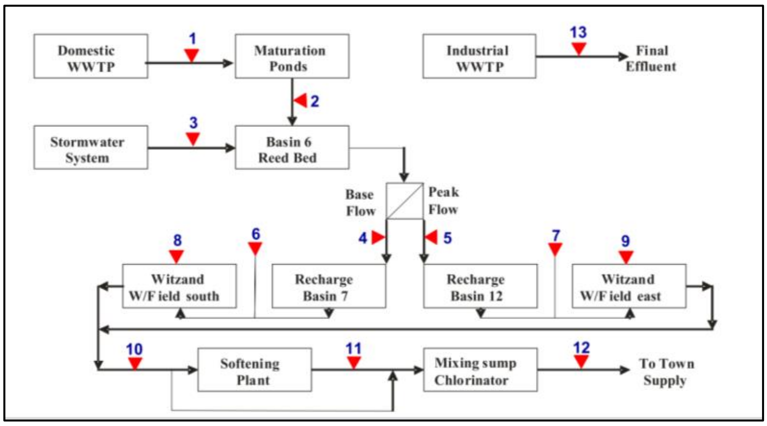


Figure 3.5: Atlantis MAR system (Adopted from: Tredoux et al., 2009)

Chapter 4- Methodology

Introduction

This chapter will cover the research design and methodology that will be used to achieve the objectives and meet the aim of the study. To assess the spatial and temporal variation of pharmaceuticals in the environment various sampling techniques will be followed by sample analysis. Sampling techniques and calculations used in this study were used by previous studies, which carried out similar research based on the fate of pharmaceuticals in the environment (Baker and Kasprzyk-Hordern, 2013b; Mhuka, Dube and Nindi, 2020) .

4.1 Research Design

A qualitative approach was taken in this study to understand and investigate what was happening in the environment regarding the spatiotemporal pattern of pharmaceuticals in the environment from the source to sink. Samples were collected at 21 sites throughout Cape Town which included WWTPs, rivers, canals, landfill sites and various groundwater points, this was done for all 4 seasons (Summer, Autumn, Winter, and Spring). Rainfall data was obtained from the South African Weather Services, to understand the monthly rainfall occurring in Cape Town for the period of the study, which could play a role in the flow of rivers and with the recharge of aquifers. Peer-reviewed journals articles were also used to guide the analytical approach, to select the most appropriate method to analyse the samples once collected. Quarterly sampling at the various selected sites was used to achieve the first objective, which included taking GPS coordinates, physiochemical parameters, and the necessary samples at the site for analysis. Concentrations of analytes of interest were obtained with the use of SPE coupled with liquid chromatography-mass spectrometry. Calculations involving the influent and effluent concentrations of pharmaceuticals were used to achieve the second objective, which was used to determine the efficiency of various WWTP's processes and to see the removal efficiency of the various compounds of interest.

4.2 Selection of sample sites and data collection

The sample sites used in the research study is depicted below in Figure 4.1

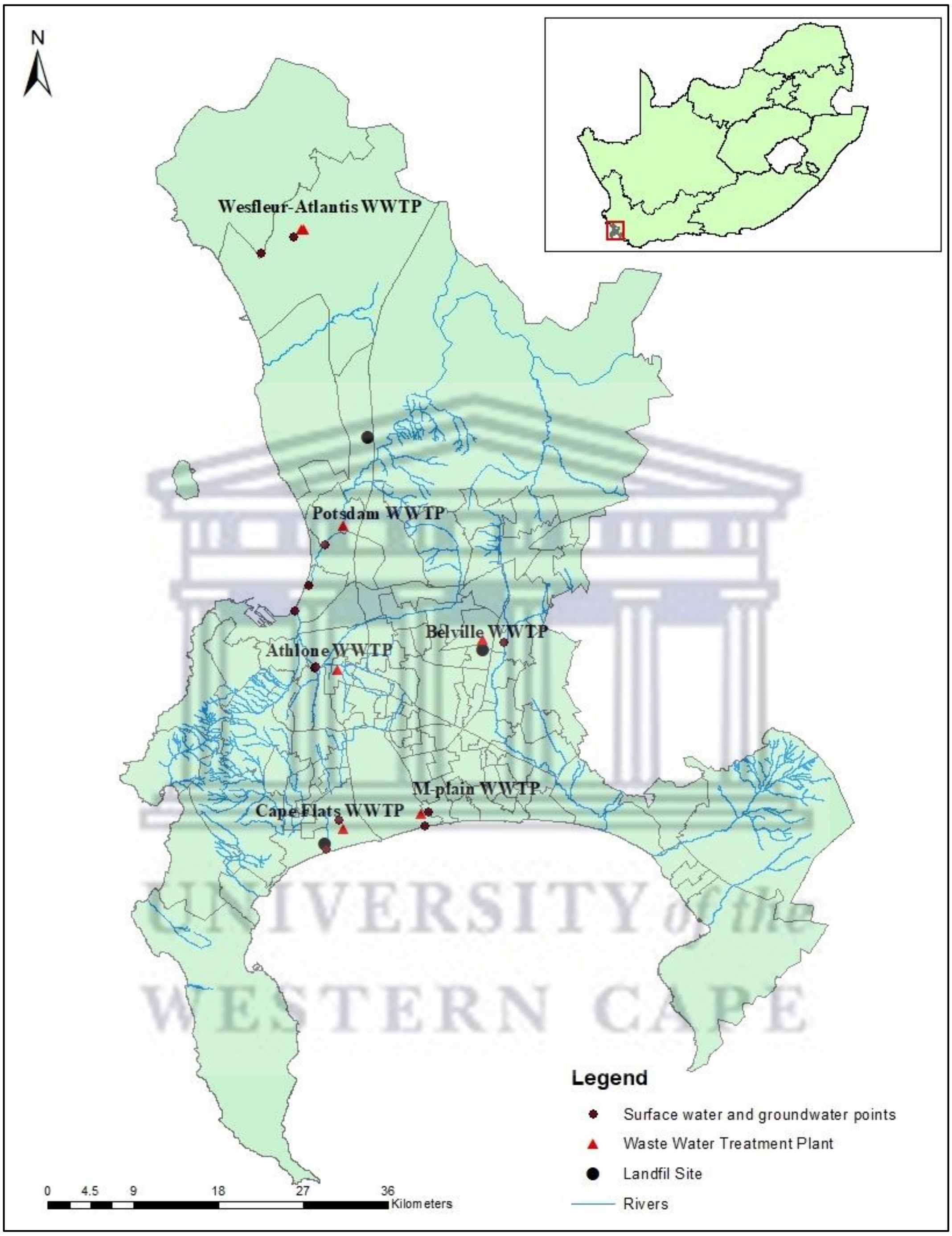


Figure 4.1: Sample site and data collection points in Cape Town, Western Cape

Wastewater treatment plants

WWTP's in Cape Town have various stages in treating wastewater entering the plant from influents to the effluents that are discharged into rivers or into the sea. These processes range from primary to secondary treatment, which includes screening, activated sludge treatment and chlorination. Certain WWTPs sampled at have tertiary treatment processes, firstly such as Ultraviolet, which is used as a disinfectant process before discharging it to the environment. This treatment involves passing treated effluent through UV channels to further reduce faecal coliform and inactivate certain microbes present after primary and secondary treatment. Membrane Bioreactors is another tertiary treatment present at certain WWTPs in Cape Town. This type of treatment involves ultrafiltration of wastewater once it passes through the membrane pores, where further separation of solids from effluent occurs.

Samples were taken at the influent, after screening to get the initial concentration of the pharmaceuticals coming into the WWTP before being treated and then another sample at the effluent of the WWTP's to see the variation in concentration before the treated water was discharged into the environment. Samples were taken using a bailer at various WWTP's namely, Athlone WWTP, Belville WWTP, Potsdam WWTP, Mitchells Plain WWTP, Cape Flats WWTP and Wesfleur (Atlantis) WWTP. The majority of the WWTPs sampled at, discharge their effluent into receiving nearby rivers, except for Mitchells plain (discharges into sea) and Atlantis (discharges into Pond 6).

Surface water points

To analyse the spatial distribution and variation of the pharmaceuticals in the environment in Cape Town, various waterbodies around the WWTP's were sampled at, to observe the distribution from source to sink.

The wastewater treatment plants and effluent exit sample points in this study are presented in Table 4.1

Table 4.1: Wastewater treatment plants and effluent exit sample points

Wastewater Treatment Plant	Effluent discharge point - river/canal	River/canal outflow to sea
Athlone	Black river	Salt river
Belville	Kuilsriver	Macassar beach
Mitchells plain	N/A	Mnandi beach
Cape Flats	Zeekoevlei	Sonwabi beach
Potsdam	Diepriver	Lagoon beach
Wesfleur -Atlantis	N/A	Pond 6-Reed bed

Sampling at the various surface waterbodies was done downstream of the wastewater treatment plant (~2 km) to observe the effects of the surface water on the pharmaceutical concentration after being discharged into it. Samples were taken at the centre of the river flow, which was done to avoid sediments from the riverbank and at a depth of 10 -20 cm below the water surface, to prevent particles which might have interacted with sunlight and could affect the chemistry and concentration of the sample. Furthermore, floating material may influence the sample integrity and yet they are not necessarily a part of the water composition.

Groundwater points

Groundwater was sampled at wellpoints, boreholes near WWTP's and landfill sites to identify if any pharmaceutical leached into these mediums from the wastewater plant or landfill sites. A submersible pump was used at various boreholes to abstract groundwater samples for analysis. Before sampling, the boreholes were purged for 10 – 25 min (depending on the depth of the borehole) to remove any stagnant water. This was done to get an accurate representative sample of the borehole.

In Table 4.2 the sample site where the groundwater was taken and the Wastewater treatment plant near by that is situated above the groundwater body is presented below.

Table 4.2: Groundwater sample point

Wastewater treatment plant	Groundwater point
Athlone	Rondebosch Golf Club
Belville	Belville South Landfill site
Mitchelle plain	Wavecreast Primary School
Cape Flats	Coastal Park Landfill site
Potsdam	Residential borehole near Potsdam
Atlantis	Witsand water treatment plant

4.2.1 Pre and post sampling

All samples were stored in 500ml polyethylene terephthalate bottles with PTFE lids, the ideal sampling bottles are amber glass bottles with a PTFE lined lid, however due to supplier delays and Covid-19 restrictions, polyethylene bottles were used instead to not delay sampling and research timeframe. The bottles were labelled with the site name and date as well as a logbook was used to take notes of the site characteristics of that day, such as weather and river flow.

Before sampling, the bottles and tops were rinsed 3 times with the site water to get rid of contamination from the bottle. The in-situ parameters that were taken at all the sites consisted of pH, electric conductivity, and temperature using the Hach HQ40D portable multimeter probes. These factors affect the presence and chemistry of target pharmaceuticals. After sampling the samples were stored in a cooler box between ice packs for transportation to the laboratory to preserve sample quality and stored at 4^{o} C in the fridge at the University of the Western Cape. Samples were taken to Stellenbosch University for SPE and LC/MS analysis, within one week after collection.

4.3 Sample preparation and quantification

Solid Phase Extraction (SPE) was used to separate the various compounds in the samples, before LC-MS analysis was done. This step prevents impurities from affecting the ionisation process. However, before proceeding with SPE, the samples were first filtered to remove any debris. All samples were analysed at the Division of Clinical Pharmacology at Stellenbosch University.

4.3.1 Sample Preparation and Solid Phase Extraction

All 32 samples were first filtered by taking an aliquot of the sample using a 5ml syringe and pushing it through an attached nylon syringe filter with a 0.22 μl pore size. The filtered aliquot was then transferred into a 5 ml glass test tube with a cap. Before transferring the filtered sample containing the analyte into the Sep-Pak Vac 1cc (100 mg) tc18 cartridges (Waters, Johannesburg, SA), the cartridges were first conditioned and equilibrated to activate the sorbent. This was done by conditioning the sorbent with 1 ml of methanol and then equilibrating it with 1 ml of deionized ultra-pure water (Synergy, Millipore) using a Pasteur pipette, this process allows the sorbent to retain the analyte during the SPE procedure. The samples were then loaded into the cartridges using a P1000 μl pipette with a new pipette tip for every sample. The loading of the cartridge was repeated three times to ensure enough analyte was trapped by the sorbent. After the loading procedure, the tc18 cartridges were washed with deionized ultra-pure water, to remove any other unwanted interference still present in the sorbent. The elution process was the last step of the SPE procedure to remove the analytes from the sorbent. This was done using 1 ml methanol, whereby the analytes were then transferred into glass tubes. The eluates were then evaporated to dryness using a rotary evaporator in a MiVAC Duo concentrator for 40 minutes at 45 ^{o}C. The analyte was then reconstituted with a mobile phase (1:1 methanol and deionized water) and transferred into vials for the LC-MS analysis.

4.3.2 Liquid Chromatography coupled with Mass Spectrometry

The LC-MS method was developed on a Shimadzu Triple Quadrupole LCMS-8040 using LC-20ADXR binary pumps, a SIL-20ACXR autosampler, a CTO-20A column oven and LabSolutions software (Shimadzu Corporation, Kyoto, Japan). Chromatographic separation on the LC-MS was achieved using an Agilent Poroshell 120 EC-C18 column (3.0 x 100mm, 2.7 µm: Agilent Technologies Inc., California, United States)

The procedure before analysis using the LC-MS, was to first create 7 standard reference materials for each pharmaceutical of interest to set up calibration curves with known analyte concentrations. The pharmaceutical standards were purchased from Sigma Aldrich (South Africa). The standards were diluted with an appropriate volume of solvent. This was done by weighing 1 mg of each standard reference material and transferring it into vials and then mixed with methanol. The vials were then sonicated for 1 min and then vortexed for 30 seconds to ensure adequate mixing of the solution. All calibration curves for the analytes of interest had a regression square of 0.99 indicating good calibration curves (Attached in appendix). The calibration range was 0.32-1000 ng/ml. Blank samples were injected after the highest standard concentration to establish carry-over in relation to the lowest level of quantification (LLOQ).

Positive and negative electrospray ionisation methods were used to detect the analytes of interest, with naproxen and diclofenac being detected in the negative ion mode while acetaminophen, rifampicin, carbamazepine, sulfamethoxazole, and caffeine were detected in the positive ion mode, due to the pharmaceuticals' chemical properties. The negative-ionisation method involved a Mobile phase A which was a solution of 10 mM ammonium acetate in water and Mobile phase B which was acetonitrile. The gradient program started with 60 to 95 % B over 3 min; 95 % up to 3.5 min; 95 to 60 % up to 4 min; equilibrate at 60 % until 7 min. The flow rate was 0.5 ml/min. The column used was InfinityLab Poroshell 120 EC-C18 (3.0 x 100 mm, 2.7 µm: Agilent Technologies Inc., California, United States) with the column temperature being kept at 30 ^{o}C.

The positive ionisation method involved a Mobile phase A, made up of 2 mM Ammonium formate with 0.1 % formic acid in H_2O: ACN 95:5 (v/v) with Mobile phase B made up of 2 mM Ammonium formate with 0.1 % formic acid in ACN: H_2O 95:5 (v/v). The gradient program started with 10 to 95 % B over 5 min; 95 % up to 5.5 min; 95 to 10 % up to 6min;

equilibrate at 10 % until 9 min. The flow rate was 0.45 ml/min. The column used was InfinityLab Poroshell 120 EC-C18 (3.0 x 100 mm, 2.7 µm) with the column temperature being kept at 30 ^{o}C.

4.3.2.1 Reagents used for pharmaceutical standard

- **Acetominophen (Sigma Aldrich,SA, 99.0 %)**
- **Carbemazepine (Sigma Aldrich,SA, 98.0 %)**
- **Rifampicin (Sigma Aldrich,SA, 97.0 %)**
- **Caffeine (Sigma Aldrich,SA, 99.0 %)**
- **Sulfamethoxazole (Sigma Aldrich,SA, 98.0 %)**
- **Naproxen (Sigma Aldrich,SA, >98 %)**
- **Diclofenac (Sigma Aldrich,SA, 98.4 %)**

4.3.3 Calculation of removal efficiency

The estimated removal efficiency (%) of the WWTP's was based on the detected concentrations of the various pharmaceuticals in the influent and the effluent after treatment.

$$\frac{\mathrm{Cinf}-\mathrm{Ceff}}{\mathrm{Cinf}} \mathrm{x}\ 100$$

Where:

Cinf- Concentration in influent

Ceff- Concentration in effluent

4.4 Study limitations

The limitation of this study was firstly the use of grab samples instead of composite samples (hourly samples) at WWTPs' influent and effluent due to the variations of inflow rates and the lag times before and after treatment. However, the grab sampling provided an estimate due to the number of samples collected. The acidification of samples after collection and the use of buffer solutions before SPE procedures could have improved the detection and stability of certain analytes.

Chapter 5- Results and discussion

Introduction

The aim of this study was to investigate the spatial and temporal distribution of pharmaceuticals in the environment regarding the change in concentration along a flow path from potential sources to sink. In this study, it was found that various pharmaceuticals were present in receiving waterbodies from Wastewater Treatment Plants (WWTP's), landfill sites and other domestic activities in Cape Town, with concentrations changing along the flow path. The removal efficiencies and performance of WWTPS's to remove contaminants were analysed based on the change in concentration from the influent to effluent after various treatment processes occurred. Certain treatment processes showed a higher removal rate of pharmaceuticals, such as when using Membrane Bioreactors compared to the use of other conventional wastewater processes. Sample collection and data analysis were done seasonally to observe and determine the spatiotemporal changes in pharmaceuticals concentrations, based on pharmaceutical usage and flow rates of receiving water bodies during various seasons. The obtained results were compared to previous studies.

5.1 Spatial variation

To establish the occurrence and spatial distribution of pharmaceuticals along the flow path from source to sink various samples were collected along the path from the WWTP's and landfill sites to both receiving waterbodies, ranging from surface and ground water points. Figure 5.1-5.3 illustrates the spatial variation and distribution of pharmaceuticals once they enter the environment. Certain pharmaceuticals do indeed decrease in concentration after being treated by wastewater treatment processes. However, an increase in pharmaceutical concentration is observed in certain receiving waterbodies.

The major contributing source of the pharmaceuticals into the environment based on this study and in agreement with previous studies (Kosma, Lambropoulou and Albanis, 2014; Paíga *et al.*, 2016; Cantwell *et al.*, 2018) are indeed WWTP's where majority of the pharmaceuticals are present in the effluent before being discharged into the environment.

The spatial distribution of pharmaceuticals in Athlone and surrounding areas (Athlone WWTP) is presented in Figure 5.1.

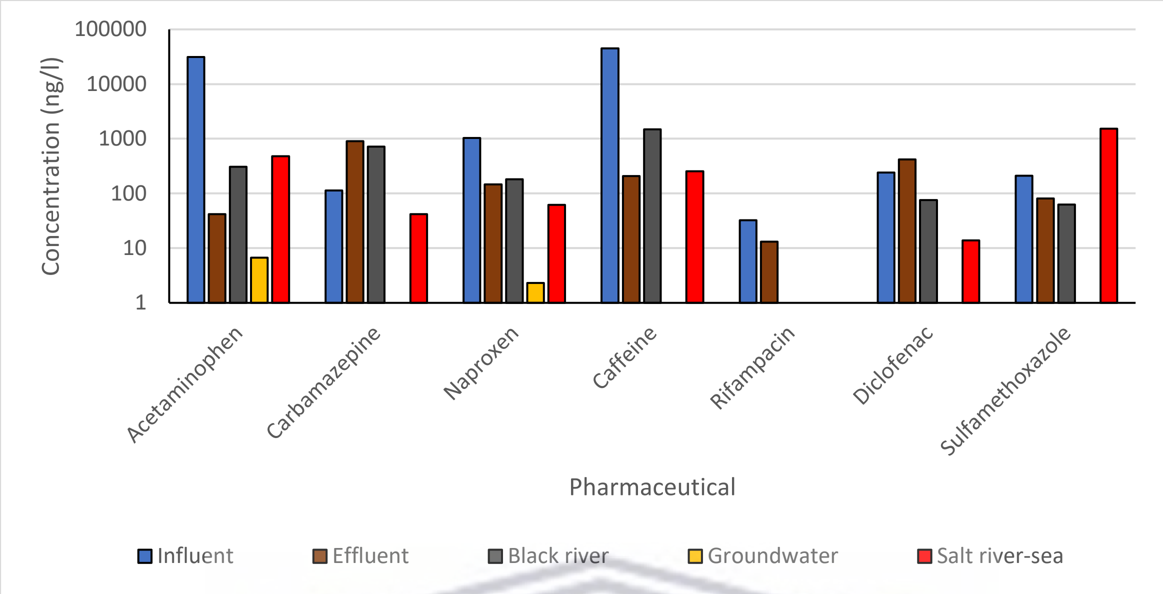


Figure 5.1: Spatial distribution of pharmaceuticals in Athlone and surrounding areas (Athlone WWTP), during summer January- 2021, depicting the concentrations (ng/l) of various pharmaceuticals at each sample point.

In figure 5.1 it can clearly be seen that certain pharmaceuticals are reduced completely, such as rifampicin while others such as acetaminophen, carbamazepine and sulfamethoxazole increased beyond the concentration of the effluent. The average concentration of pharmaceuticals from influent to effluent was 8319.83 ng/l and 390.16 ng/l respectively. The variable concentrations of pharmaceuticals present in the influent, which can be seen in Figure 5.1, are due to several factors ranging from the drug usage, drug availability and drug characteristics.

The presence of acetaminophen, naproxen, and diclofenac at higher concentrations in the influent, can be due to the increased use and easy availability of these drugs for certain illnesses. The pharmaceuticals concentrations found in the influent and effluent can be comparable with other studies, such as by Al-Mashaqbeh et al., (2019) who reported concentrations of caffeine and acetaminophen in the influent ranging from 182500 ng/l and 44700 ng/l respectively while concentrations in the effluent ranging from 92 ng/l and 44ng/l respectively. The compound with the highest concentration in the influent was caffeine. The outcome was expected due to this compound being used in various products, ranging from medicines to certain beverages such as tea and coffee. This could also be seen in Figure 5.2 and Figure 5.3.

In Figure 5.1 an anomaly can be observed with regards to the reduction in the concentration of certain pharmaceuticals along a flow path once they enter the environment from the WWTPs.

There is an increase in the concentration of acetaminophen, naproxen and caffeine in the Black River when comparing it with the effluent. The increase in the concentration of these compounds at this location could be from anthropogenic activities occurring around this area, which could include direct exposure to raw sewage from informal settlements or industrial activities nearby. The joining tributaries connecting with the Black River, such as the Liesbeek river and Elsieskraal rivier, could be another factor, which could be contributing to the occurrence of these compounds, such as acetaminophen, caffeine, and sulfamethoxazole, into the Black River before connecting with the Salt River, thereby increasing these compounds concentrations. The concentrations for certain compounds, such as acetaminophen and sulfamethoxazole detected in this study are at a lower concentration in surface water compared to a study done in KwaZulu-Natal, South Africa by Matongo et al., (2015). This study reported detection of acetaminophen in the Umgeni River at concentrations of < 2000 ng/l and sulfamethoxazole at < 10000 ng/l, it had also observed the influence of tributaries on the Umgeni River.

The spatial distribution of pharmaceuticals in Pelican Park and surrounding areas (Cape Flats WWTP) is presented in Figure 5.2.

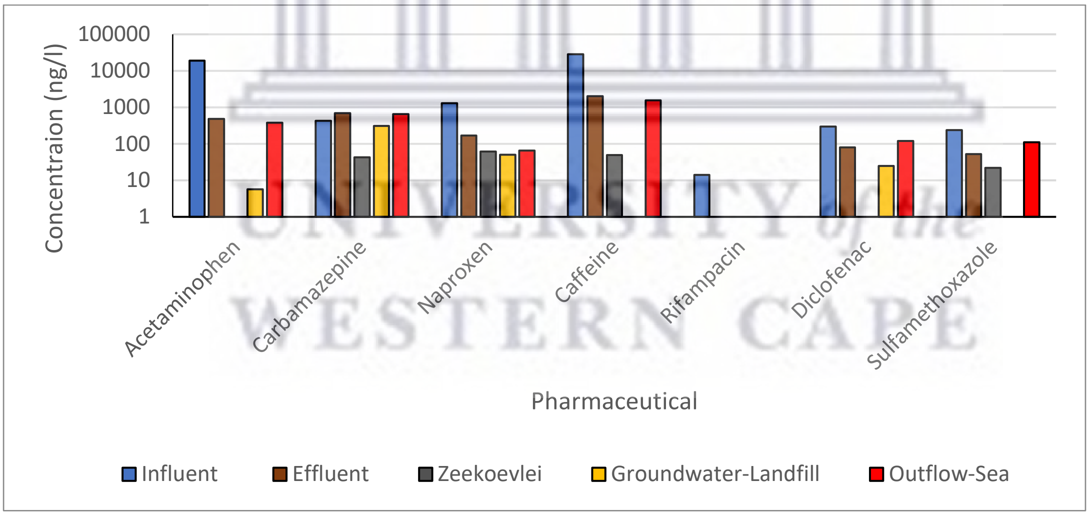


Figure 5.2: Spatial distribution of pharmaceuticals in Pelican Park and surrounding areas (Cape Flats WWTP + Coastal Park Landfill), during summer January- 21, depicting the concentrations (ng/l) of various pharmaceuticals at each sample point.

In Figure 5.2 similar trends can be observed as seen in Figure 5.1. It shows the reduction in certain pharmaceuticals along the flow path once it enters the environment from WWTP's, however some pharmaceuticals are seen to have increased in the surface water (sea) and are also present in the groundwater.

The fate and detection of these pharmaceuticals in the effluent and in receiving waterbodies are also based on the chemical structure and the interaction of these pharmaceuticals in the environment. The pharmaceuticals of interest in this study form part of the non-volatile compounds and therefore the natural attenuation of the compounds is limited to sorption, biological, photodegradation and dilution processes (Pal *et al.*, 2010 and Sui *et al.*, 2015). A reduction in the concentration or complete removal of certain pharmaceuticals, such as with acetaminophen, naproxen, diclofenac, and caffeine, can be seen as it travels through the environment, once the effluent is discharged into the receiving waterbodies, in Figure 5.2 -5.3, this patten can be observed. The reason for the reduction in the concentration of these pharmaceuticals could be the dilution of the compounds taking place once it enters the river or canal or it could be degraded through direct photodegradation occurring over the open surface water bodies, thereby decreasing the compounds' concentration (Packer *et al.*, 2003; Pal *et al.*, 2010; K'oreje *et al.*, 2018).

The water partition coefficient of the compounds also plays a role in the fate and presence of these compounds in the environment, a study by Mompelat et al., (2009) indicated that pharmaceutical compounds with low $\log_{kow}$ <2.5 have low sorption capacity and will therefore be more likely be present in surface water while Pal et al., (2010) reported that compounds with a higher molecular weight and high $\log_{kow}$ of >5 are easily adsorbed to sediments or sludge. This is evident with the presence of the persistent compounds carbamazepine and sulfamethoxazole in receiving water bodies which can be seen in Figure 5.1-5.3 where these compounds are present in the Black River, Salt River, Lagoon Beach and in the Zeekoevlei canal (outflow to sea). These two compounds have a water partition coefficient ranging from $\log_{kow}$ 0.89-2.4 and therefore will easily be transported in the aqueous solution and not be adsorbed to the sludge after the wastewater treatment processes due to their low hydrophobic sorption potential (Mompelat, Bot and Thomas, 2009; Wang *et al.*, 2018). This could also be seen in Figure 5.1 and 5.2 where Carbamazepine is detected at a higher concentration at the effluent than influent due to the accumulation of this compound in the effluent as it was easily transported through the system due to its chemical structure. The pharmaceutical drug Rifampicin on the other hand is effectively degraded in Figure 5.2 and Figure 5.3 as it does not occur in any of the receiving waterbodies which could mean that it adsorbed to the sludge or degraded once it entered the environment.

From the results it can also be noted that pharmaceuticals are not only present in the surface water but is present in groundwater as well, which can be seen in Figure 5.1-5.2. Certain pharmaceuticals such as acetaminophen (≤ 6.7 ng/l), diclofenac (≤ 25 ng/l), naproxen (≤ 50.6 ng/l) and carbamazepine (≤ 308.4) have been detected in the groundwater at the various sites, with higher concentrations and more pharmaceuticals being detected at the groundwater at the Coastal Park landfill site compared to Figure 5.1, where only two pharmaceuticals (acetaminophen and naproxen) less <10 ng/l was found at Ronderbosch Golf Estate borehole. The detection of multiple compounds at the landfill site borehole in Figure 5.2 could be due to the Coastal Park landfill site and Cape Flats WWTP being located on the a shallow unconfined Cape Flats aquifer, which makes it more susceptible to pollution due to its proximity to the surface, whereby polluted water could be able to leach into it at a faster rate (Godfrey, Woessner and Benotti, 2007; Adelana, 2010). A study by Godfrey et al., (2007) in the United States found a similar trend related to the presence of carbamazepine, sulfamethoxazole and caffeine in a shallow unconfined coarse-grained aquifer at levels ranging from 10 to 450 ng/l from infiltrating sewage effluent.

The spatial distribution of pharmaceuticals in Milnerton and surrounding areas (Potsdam WWTP) is presented in Figure 5.3.

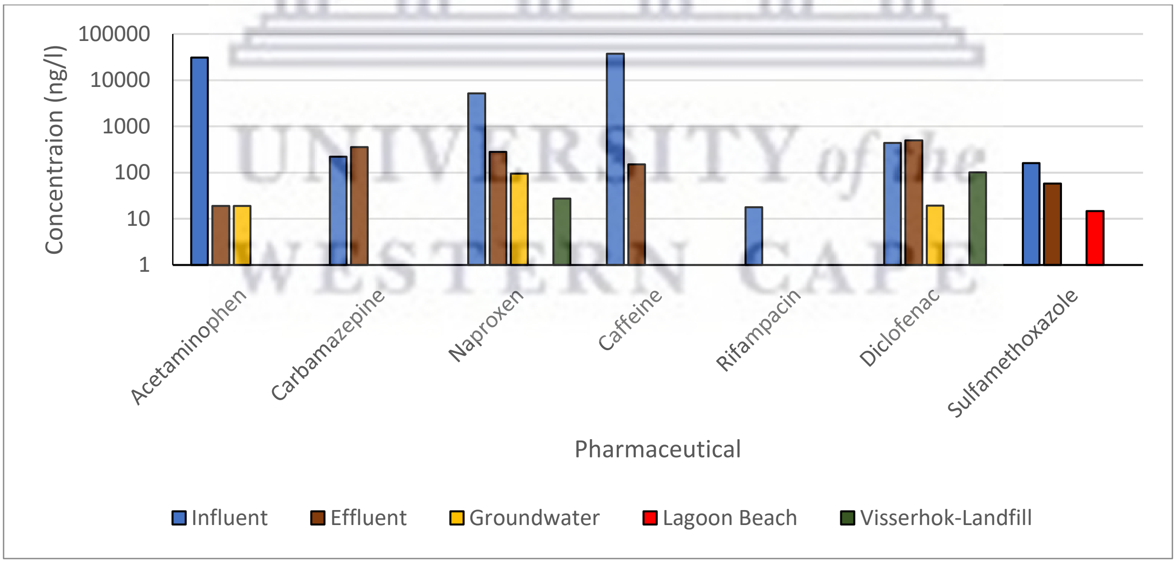


Figure 5.3: Spatial distribution of pharmaceuticals in Milnerton and surrounding areas (Potsdam WWTP), during summer- January 21, depicting the concentrations (ng/l) of various pharmaceuticals at each sample point.

The findings in figure 5.3 agrees with the findings presented in Figures 5.1-5.2 where a reduction is seen with certain pharmaceuticals from source to sink. There is however an increase in carbamazepine and diclofenac in the effluent compared to the influent. The reason for this could be the accumulation of these compounds in the effluent due to it not being broken down by the wastewater processes due to its low sorption capacity and thereby less likely to adsorb to sludge (Mompelat, Bot and Thomas, 2009; Wang *et al.*, 2018). Sampling further downstream of the Potsdam WWTPs at Lagoon beach had shown no detection of diclofenac or carbamazepine, which could be that these compounds have been reduced when traveling through the water system due to biodegradation, photolysis or dilution occurring (Packer *et al.*, 2003).

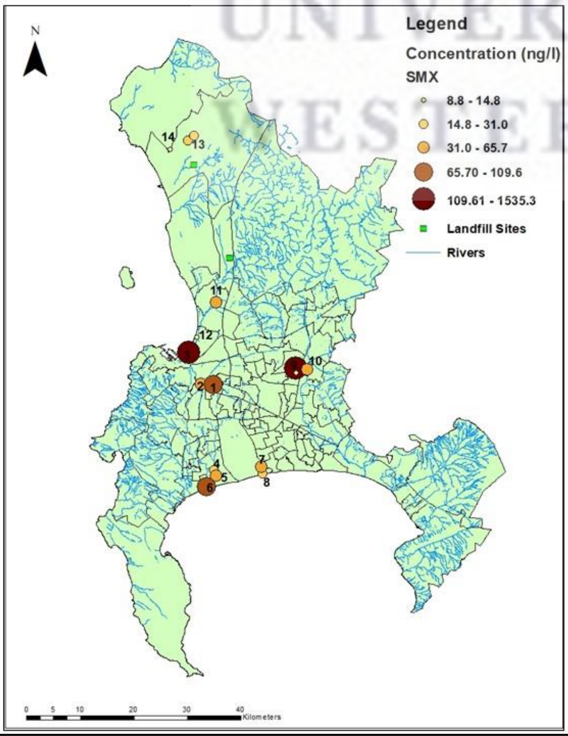
The detection of acetaminophen (19 ng/l) naproxen (95.4 ng/l) and diclofenac (101.1 ng/l) in groundwater and not at Lagoon beach in Figure 5.3 could be due to these compounds being introduced by other sources besides the ground water- surface water interaction. These pharmaceuticals compounds could have been introduced by contaminated surface water or disposed of in their natural form at the landfill site, thereby leaching into the aquifer beneath it. This observation was in agreement with a study by Eggen *et al.*, (2010), who conducted a study on the impact of Municipal leachates on groundwater in Norway. The study concluded that certain pharmaceuticals, such as naproxen and carbamazepine, from landfill sites can leach into the groundwater from leachates containing traces of pharmaceuticals ranging from 0.8 to 282 ng/l.

Looking at all three graphs (Figure 5.1-5.3) the increased presence of the contaminants in the groundwater (Figure 5.1-5.3) indicate that they can pass through the surface and into the subsurface. However, it was observed that the concentrations of these pharmaceuticals are reduced as they travel through the vadose zone to the groundwater from the surface, due to the interaction with geological material and dilution processes that could be occurring once in enters the groundwater (Clara, Strenn and Kreuzinger, 2004; Godfrey, Woessner and Benotti, 2007; Tredoux *et al.*, 2009). A lower concentration of pharmaceuticals can be seen as they pass through the vadose zone, as can be seen in Figure 5.1-5.3 with acetaminophen, naproxen, and diclofenac, when comparing the groundwater with other the surface water bodies, this could be due to the anaerobic degradation or the adsorption to sediments of pharmaceuticals as it flows through the subsurface. The same observation was made in a study by Holm et al., (1995) in Denmark, where certain pharmaceuticals such sulfonamides (group of antibiotics such as sulfamethoxazole) were reduced through anaerobic redox reactions as they infiltrate into the aquifer.

The sorption capacities of pharmaceutical compounds are also affected by the pH of the water body, thereby playing a role in the spatial distribution and occurrence of pharmaceuticals as well. The dissociation of the compound can be contributed to the pH level of the waterbody compared to the pKa (acid strength) of the pharmaceutical compound. When the pH of the waterbody is lower than the pKa, the main form of the compound is an organic form, which then the pH would have little to no influence while when the pH is higher than the pKa, the main form is the conjugate base ionic form due to it becoming deprotonated (removal of proton from an acid), which makes it more soluble in water (Zhang *et al.*, 2014). The reduction in concentration of naproxen (pKa- 4.19) and diclofenac (pKa- 4.15) in groundwater (Figure 5.1-5.3) can be attributed to its pKa being lower than the pH of the sampled groundwater bodies, ranging from pH 5.3-8.11 which makes it deprotonated in this environment and more soluble, thereby becoming dissociated in the groundwater (Quesada *et al.*, 2019; Wojcieszyńska and Guzik, 2020). However, with carbamazepine it has a pKa of 13.94 which is greatest than all the pH at the different sites (appendix A) thereby making it less soluble and being in its organic form throughout the different water bodies, thereby being persistent in the environment.

The spatial variation of certain compounds which occurred at majority of the sites namely diclofenac, carbamazepine and sulfamethoxazole are mapped below to further illustrate the spatial variation from source to sink based on the data gathered during summer, January 2021

The spatial variation of sulfamethoxazole in the environment is depicted below in Diagram 5.1

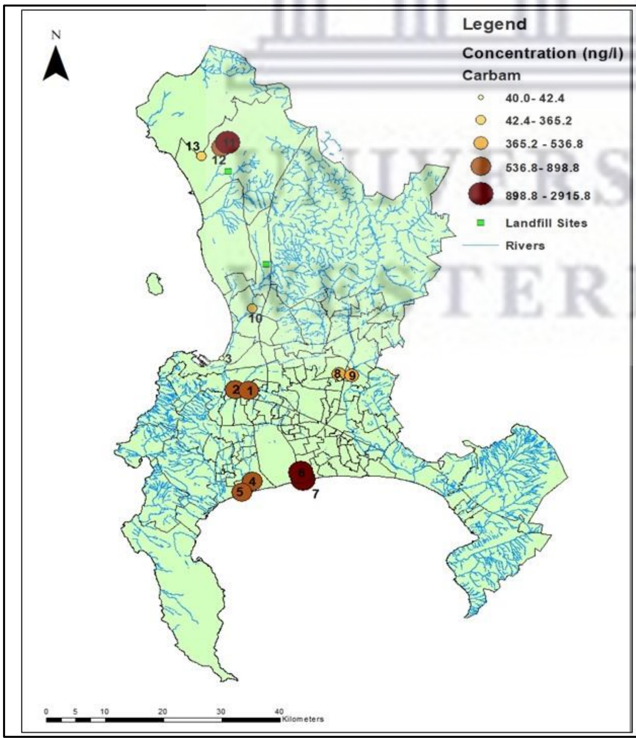


Site number	Location
1	Athlone WWTP
2	Black river
3	Salt river outflow to sea
4	Zeekoevlei
5	Cape Flats WWTP
6	Zeekoevlei canal
7	Mitchells Plain WWTP
8	Mitchells Plain WWTP outflow to sea
9	Belville WWTPP
10	Kuilsriver
11	Potsdam WWTP
12	Lagoon beach
13	Atlantis WWTP
14	Atlantis groundwater point

Diagram 5.1: Spatial variance of sulfamethoxazole (SMX) at various sample sites in the study during January 2021.

A reduction in SMX can be seen from source to sink when looking at sample sites 1-3, 7-8 and 11-12 where Wastewater Treatment Plants were able to reduce the pharmaceutical before discharging it into the receiving surface water body. Further reduction can be seen once it enters the surface water body due to dilution however it can be seen at sample site 3 (Salt River outflow to sea) and 6 (near landfill site) an increase in the concentration of the compound was observed. This patten could be due to anthropogenic activities occurring near the site such as with sample site 3 which occurs in an industrial area while also receiving inflow from storm water and other tributaries as mentioned above. At site 4- Zeekoevlei, SMX can be detected in this lake before it reaches the Zeekoevlei canal, situated after the WWTP, this could indicate that stormwater or tributaries, such as the lotus canal, that drains into the lake could be contributing to the presence of this compound in the water body before combining with the effluent for discharge into the sea.

In diagram 5.2 below the spatial variance of carbamazepine in the environment is depicted below.

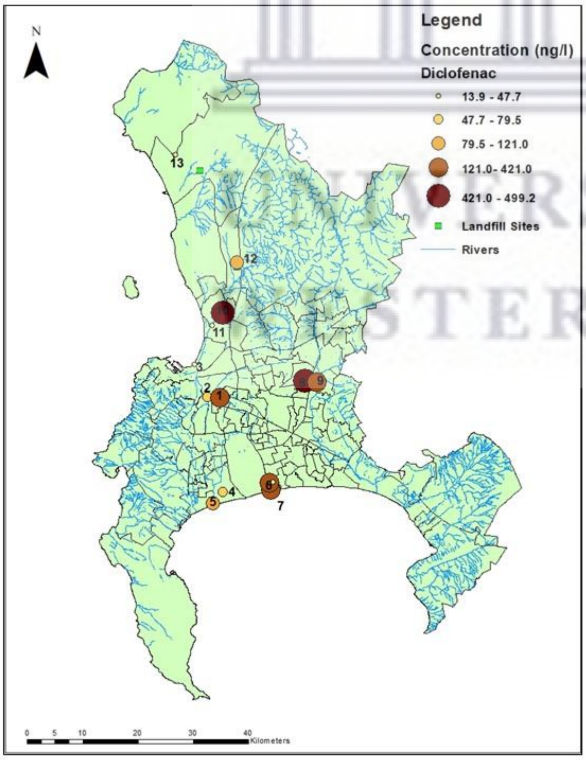


Site number	Location
1	Athlone WWTP
2	Black river
3	Salt river outflow to sea
4	Cape Flats WWTP
5	Zeekoevlei canal
6	Mitchells Plain WWTP
7	Mitchells Plain Outflow to sea
8	Belville WWTP
9	Kuilsriver
10	Potsdam WWTP
11	Atlantis WWTP
12	Pond 6
13	Atlantis groundwater point

Diagram 5.2: Spatial variance of carbamazepine at various sample sites in the study during January 2021.

Carbamazepine was shown to be the most persistent compound throughout the study due to its resistance to degradation at WWTPs. It can be seen in the Figures 5.1-5.3 above and in Diagram 5.2, that there is still a high concentration of carbamazepine at receiving water bodies after WWTPs processes have taken place and being discharged into rivers , this is evident at sample sites such as 1-2, 4-5 and 8-9 with a similar concentrations being seen in Zeekoevlei canal (outflow to sea) and in the Black river , however decrease in concentration is noted further downstream of the black river at sample site 3 where it connects with Salt river which could be caused by dilution and biodegradation once the compound was exposed to natural processes, however its presence at majority of receiving water bodies indicates that it is still stable in the environment. In the Atlantis area, it can be seen at site 11-12 that carbamazepine was reduced as the effluent was discharged to pond 6 however it was detected in the groundwater at sample site 13. This indicates that it can pass through the vadose zone and into groundwater, due to its low water partition coefficient of Log K_{ow} 2.4, thereby being less likely to attach to soil particles when passing through the vadose zone and into the saturated zone (Pal *et al.*, 2010 and Sui *et al.*, 2015).

In diagram 5.3 below the spatial variance of diclofenac in the environment is depicted below.



Site number	Location
1	Athlone WWTP
2	Black river
3	Salt river outflow to sea
4	Cape Flats WWTP
5	Zeekoevlei
6	Mitchells Plain WWTP
7	Mitchells Plain outflow to sea
8	Belville WTTP
9	Kuilsriver
10	Potsdam WWTP
11	Groundwater
12	Visserhok landfill site
13	Atlantis groundwater point

Diagram 5.3: Spatial variance of diclofenac at various sample sites in the study during January 2021.

Diclofenac was shown to be present in majority of sites, as can be seen in Diagram 5.3 due to its chemical characteristics and transformation at WWTPs. At certain sample sites, sites 1-2 and 8-9, an increased reduction is evident once the compound passes through the treatment process and into receiving water bodies, however this is depended on which treatment processes are occurring at the specific plant, as it can be seen at sample site 6-7, diclofenac is not greatly reduced before being discharged into the sea by the outflow point. Diclofenac was also shown to be present at various groundwater points, such as site 11, 12 and site 13. Its presences at Vissershok landfill site (site 12) could be indicating that the compound could directly have leachate into the subsurface, due to the direct disposal of medication containing diclofenac to sites such as landfills. At site 13, even though diclofenac was not detected at the Atlantis WWTPs effluent and at the receiving pond 6 in the study area, it was still found in the groundwater, which could indicate that the groundwater could have been contaminated by other sources such as direct pollution due to either stormwater or through anthropogenic activities occurring in the area.

Based on the spatial results obtained, a pathway indeed exists for the pharmaceuticals chosen from various sources to sink, namely WWTPs and Landfill sites, while other anthropogenic activities could be contributing as a source based on the observed results. Most of the pharmaceuticals of interest was reduced from source to sink, as it is distributed through the environment, with dilution being the greatest contributor to the reduction of pharmaceuticals once it enters the receiving surface water and groundwater bodies.

5.2 Temporal variation

The temporal variation of pharmaceuticals in the environment is based on various factors ranging from weather conditions as well the recharge of both surface and groundwater from rainfall (Jiang *et al.*, 2019; Letsinger *et al.*, 2019). The seasonal use of pharmaceuticals could also play a role in the presence of pharmaceuticals in the environment due to certain illnesses being more prevalent during specific times of the year. The areas used for the temporal variation are the Bellville area with Bellville WWTP discharging its effluent into the Kuilsriver and the Mitchells plain area with Mitchells plain WWTP directly discharging its effluent in the sea. The three landfill sites (Coastal Park, Vissershok and Bellville South) pharmaceutical concentration results were also used under this section to compare the change in concentrations of pharmaceuticals present in the groundwater over the summer and winter period.

The seasonal variation of pharmaceuticals at Belville WWTP, Belville South landfill and Kuilsriver is presented in Figure 5.4 below.

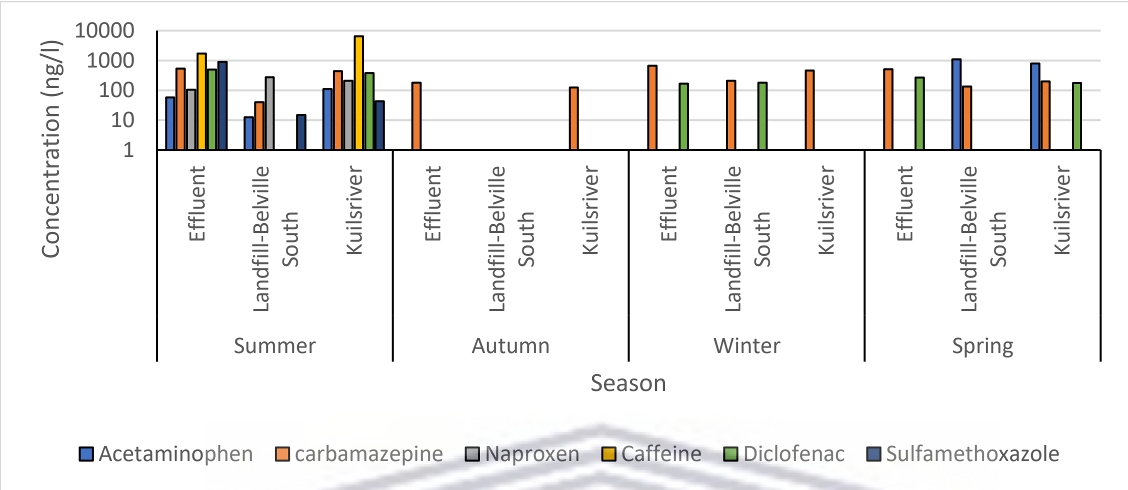


Figure 5.4: Seasonal variation of pharmaceuticals at Belville WWTP, Belville South landfill site and Kuilsriver, during various seasons depicting the concentrations of various pharmaceuticals in each season.

Seasonality plays a key role in the distribution of these contaminants as can be seen in Figure 5.4. Most of the pharmaceuticals were detected in various water bodies during the summer months compared to the other three seasons. This is especially evident in Kuilsriver where all 6 analytes were detected in summer compared to the winter season where less of the analytes were detected. The reason for this observation could be contributed to fact that during summer periods less rainfall had occurred over the Cape Town region compared to the other seasons especially autumn and winter season (Figure 5.5) thereby lower flow rates.

The monthly rainfall for Cape Town is presented in figure 5.5. The wettest months are June to August while January to February are the drier months with less rainfall

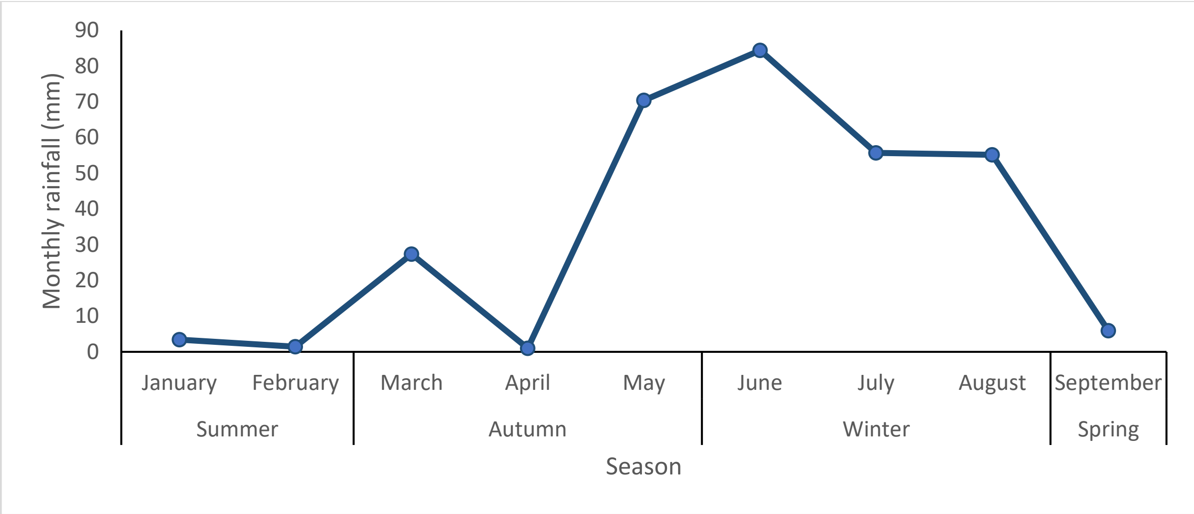


Figure 5.5: Monthly rainfall for the City of Cape Town during sampling period of 2021

The increased rainfalls contributed to increased flow rates of these water bodies, especially concerning the various rivers and canals in this study. The increased flow rates during the autumn, winter and spring period could have thereby contributed to the dilution effect occurring in these water bodies, once effluent had been discharged into it, thereby reducing certain compounds (de Sousa *et al.*, 2014). The higher concentration and detection of pharmaceuticals during lower river flow, was also reported by other studies, such as Pereira et al., (2017) and Baker and Kasprzyk-Hordern (2013), due to less dilution occurring because of the lower flow rates. The flow velocity of a river or canal also plays a role in the aeration occurring in these waterbodies, which contributes to the aerobic biodegradation rates, this could also account for the reduction in the pharmaceutical concentration that is observed in the winter period compared to the summer period (Vitória *et al.*, 2020). The reduction of certain pharmaceuticals in Kuilsriver in summer, can also be contributed to photochemical degradation by ultraviolet radiation occurring over the open water body, whereby the chemical structure of the compounds are altered by the absorption of sunlight (ErgeBu *et al.*, 2003; Jallouli *et al.*, 2016; Ojemaye and Petrik, 2019)

The seasonal variation of pharmaceuticals at Mitchells plain WWTP effluents and outflow at Mnandi Beach is presented in Figure 5.6

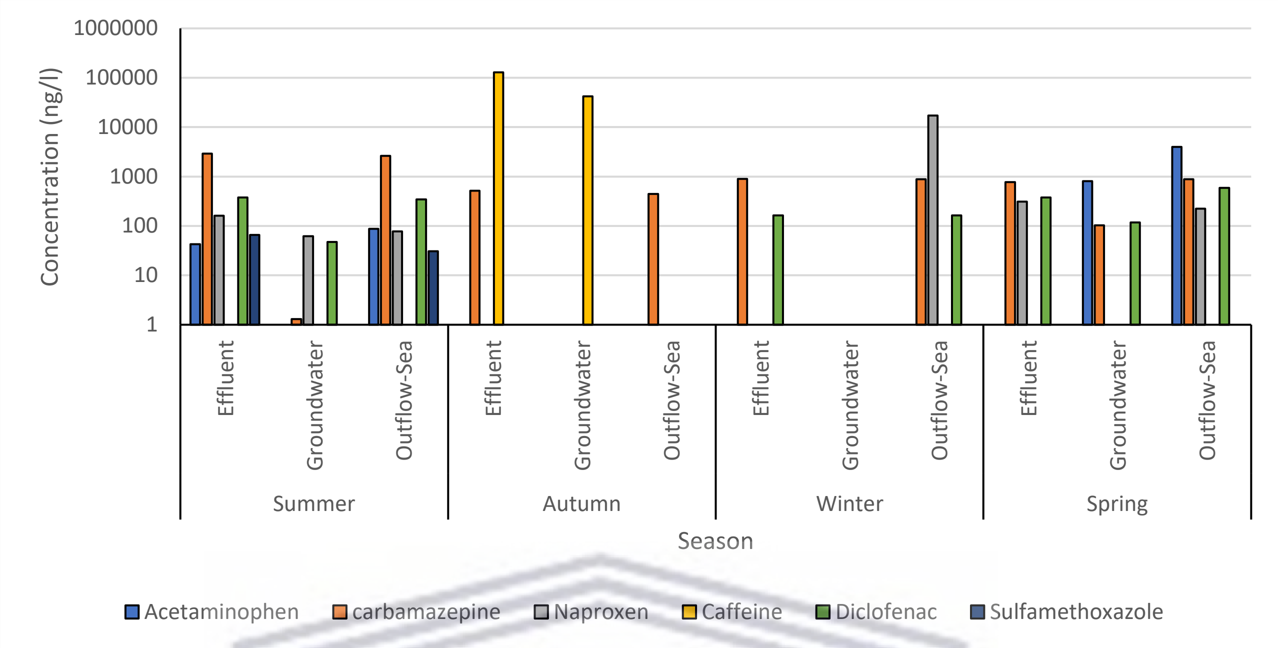


Figure 5.6: Seasonal variation of pharmaceuticals at Mitchells plain WWTP effluents and outflow at Mnandi Beach, during various seasons depicting the concentrations of various pharmaceuticals in each season.

A similar trend is observed in Figure 5.6 as with 5.4 where more pharmaceuticals were detected in Summer than in Winter. Temporal variation is also evident at the groundwater point sampled, as can be seen in Figure 5.6, summer, and spring accounts for when most of the pharmaceuticals were detected in the groundwater when compared with winter. As mentioned, the pharmaceuticals present in the groundwater have low water partition coefficients (-0.07-3.18) which indicates that these compounds will easily migrate and flow into the groundwater from the surface through the hyporheic zone, through either vertical or lateral exchange due to them less likely adsorbing to the soil (Holm *et al.*, 1995; Sui *et al.*, 2015). The increase in the presence and concentration of pharmaceuticals during the summer months could be due to less dilution occurring in the aquifer due to lower recharge rates in the summer months because of a lower rainfall compared to the winter period, as no pharmaceuticals were detected in the winter period at this site. The concentration range of diclofenac, which was 19.2 ng/l- 101.1 ng/l, and carbamazepine, which was <390 ng/l, detected in groundwater are however higher in this study compared to previous studies which found concentration ranges for diclofenac and carbamazepine at levels of 0.28–7.66 ng/l and 390 ng/l respectively in groundwater (Loos *et al.*, 2010; Jiang *et al.*, 2019) however a similar pattern was observed between these studies. In Figure 5.6, caffeine however is only present in Autumn at the Mitchell Plain groundwater point and not in any other season, while also not detected in the outflow of the Mitchells plain WWTP during Autumn, this could indicate point source pollution from anthrophonic activities containing caffeine which could have seeped into the unconfined sandy aquifer.

The Seasonal variation of pharmaceuticals at Athlone WWTP effluents and receiving rivers- Black River and Salt River is present in Figure 5.7

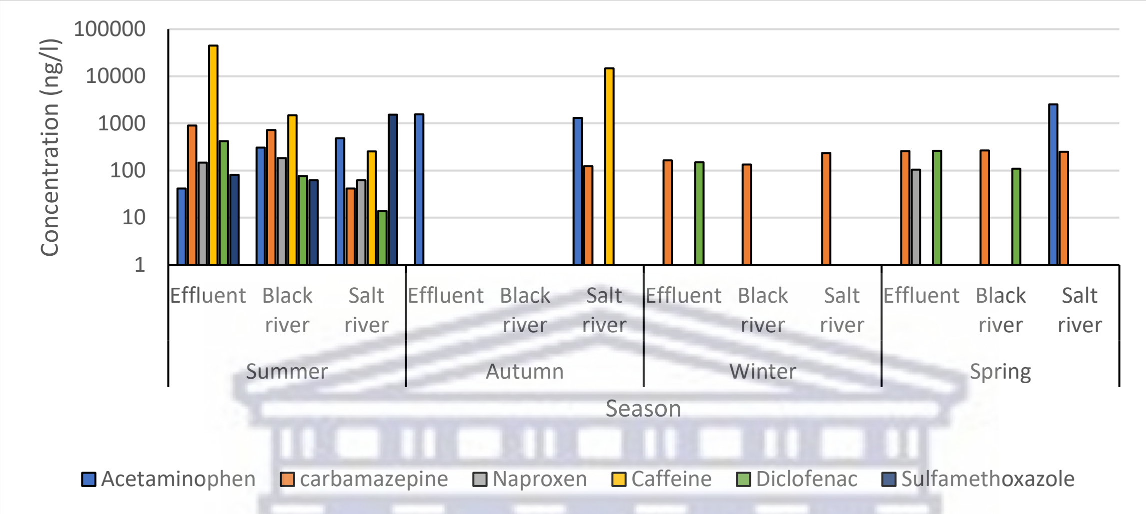


Figure 5.7: Seasonal variation of pharmaceuticals at Athlone WWTP effluents and receiving rivers- Black River and Salt River, during various seasons depicting the concentrations of various pharmaceuticals in each season.

Again, more pharmaceuticals are detected in the Effluent and in the receiving rivers in Summer than during the other seasons besides Autumn. The occurrences and detection of acetaminophen, carbamazepine, and caffeine in Salt River and not in the effluent or Black River (one of its tributaries) during the Autumn period could indicate that there are anthropogenic activities occurring around that river, which could directly be polluting it with those compounds or storm water flowing into it.

Based on the three graphs (Figures 5.4, 5.6 and 5.7) above, the seasonal usage patterns of pharmaceuticals observed by other studies in South Africa (Gumbi *et al.*, 2017; Fekadu *et al.*, 2019) had not been observed in this study, where it was expected that during the winter period there would be a higher concentration rate of antibiotics and pain medication present in the effluent and in various water bodies due to cold and influenza illness prevalent in this season(Archer *et al.*, 2021). In contrast, medications used such as sulfamethoxazole, naproxen and acetaminophen were more frequently detected in summer. However, during the summer period when data was collected in January 2021, South Africa experienced its second wave of infections due the Covid-19 pandemic, which could account for the increased usage of various pharmaceuticals such as antibiotics and pain medications as detected in the effluent at the various WWTPs in Figures 5.4-5.7

5.3 Introduction of pharmaceuticals through MAR

Pharmaceuticals can enter the environment through various sources such as WWTPs, Landfill sites and other anthropogenic activities. Another entry way for emerging contaminants such as pharmaceuticals to the groundwater is through Managed Aquifer Recharge (MAR), whereby treated wastewater is recharged through. As mentioned under the study area relating to this study site, groundwater is used as an alternative drinking supply in Atlantis, Western Cape.

Managed Aquifer Recharge is a useful procedure to ensure adequate recharge of aquifers and when using groundwater as an alternative drinking supply, as is the case in Atlantis, Western Cape. The use of recharge basins, however, provides a pathway for emerging contaminants to pass into the groundwater (Lapworth *et al.*, 2012; Sui *et al.*, 2015). Before treated wastewater and storm water reaches the recharge basin in Atlantis it passes through a reed bed which acts as an extra natural filtration system, this section is known as pond 6.

In Figure 5.8, the presence of pharmaceuticals in various waterbodies before and after treatment in Atlantis area is presented below.

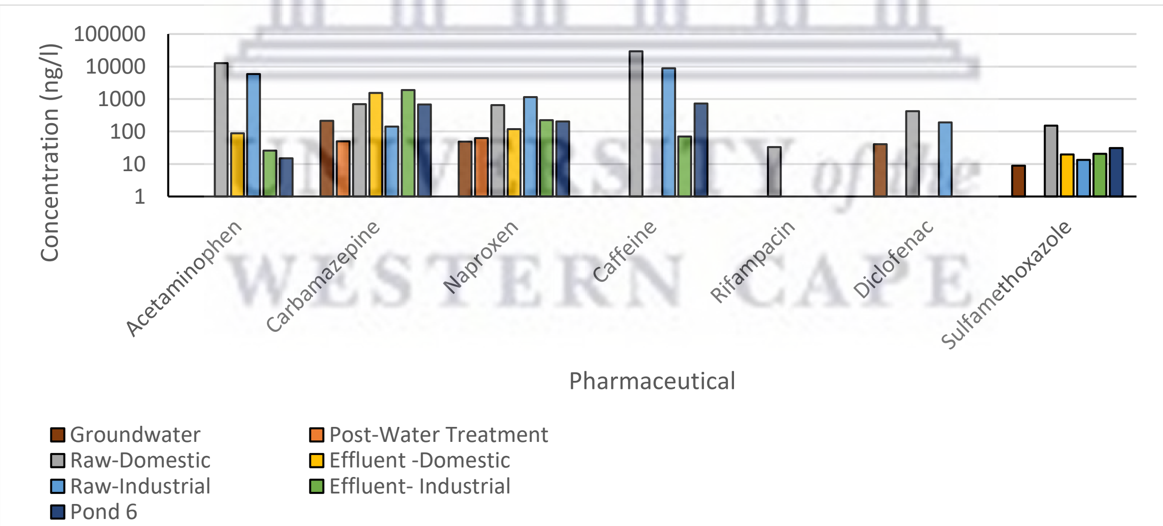


Figure 5.8: Presence of pharmaceuticals in various waterbodies before and after treatment in Atlantis area, during summer January-21, depicting the concentration of pharmaceuticals at various sample sites.

In Figure 5.8, all pharmaceutical compounds were detected in the influent, while most of it (such as acetaminophen, naproxen, and caffeine) was reduced before being discharged into the environment other than rifampicin and diclofenac which were completely removed during wastewater treatment processes. Certain pharmaceuticals were however detected in the groundwater such as carbamazepine, naproxen, and sulfamethoxazole after being either transported through artificial recharge or through point source pollution.

The data in Figure 5.8, show that acetaminophen, carbamazepine, caffeine, and naproxen, were present in the effluent. The pharmaceuticals are however, reduced as they travel through the reed bed (natural filtration system) based on the lower concentrations detected in pond 6. Caffeine and acetaminophen were completely removed and were not detected in the groundwater. Certain pharmaceuticals, however, persist in the groundwater after traveling through the reed bed channels and into the recharge basins. The presence of these compounds can be attributed to the compounds' low water partition coefficient thereby not adsorbing to the sediments in the reed bed as well as in the vadose zone. This is evident with carbamazepine, sulfamethoxazole, and naproxen which have low water coefficients.

The pharmaceutical compounds detected in the groundwater, do show reduced concentrations once entering the groundwater due to either dilution or the interaction with the geological material (Clara, Strenn and Kreuzinger, 2004; Tredoux *et al.*, 2009). The presence of diclofenac in the groundwater and not in pond 6 (Figure 5.8) could indicate that the aquifer was polluted by direct pollution containing this compound either by raw sewage or anthropogenic activities occurring in the area. The detection of carbamazepine and naproxen in drinking water after abstraction and chlorination means that there is need for advanced tertiary treatment when using this groundwater as an alternative drinking water supply.

In Figure 5.9, historical and current data of the presence of carbamazepine and sulfamethoxazole in the Atlantis area is present below to compare previous research in the area.

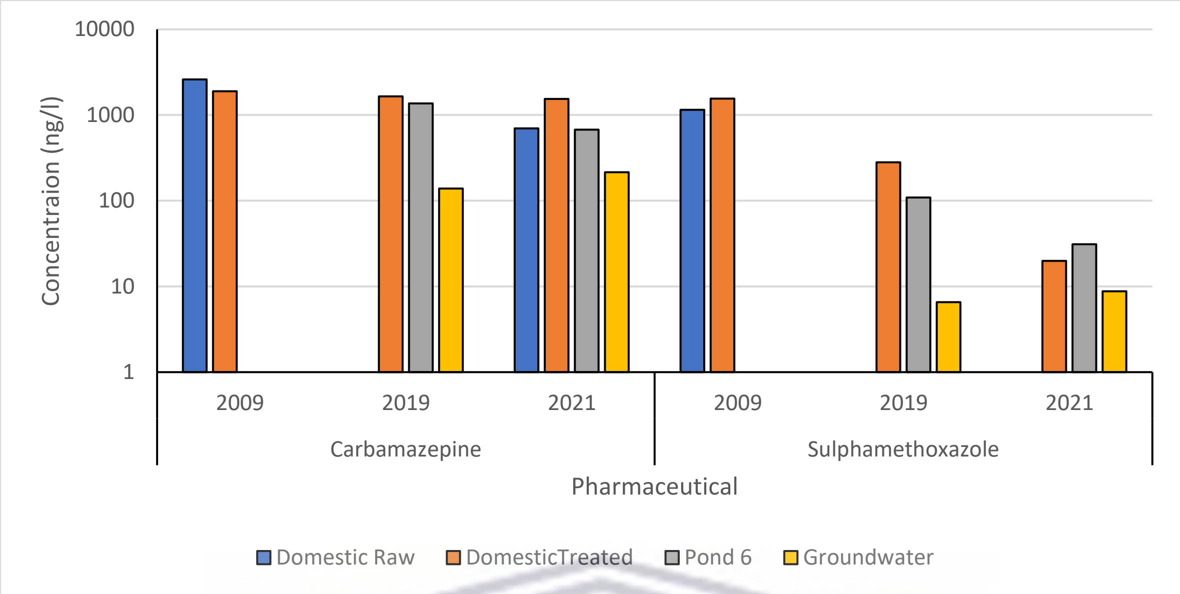


Figure 5.9: Historical and current data of the presence of carbamazepine and sulfamethoxazole in the Atlantis area (Tredoux et al., (2009) and Mzantsi (2019))

In Figure 5.9, current data can be seen to agree with previous data conducted at this study site concerning the occurrence of carbamazepine and sulfamethoxazole in various water bodies. An increase in the presence of these pharmaceuticals can however be seen in the groundwater in 2021 compared to the previous study in 2019.

The detection of carbamazepine and sulfamethoxazole in groundwater at levels of 8 ng/l to 326 ng/l respectively agrees with local studies done by Tredoux *et al.*, (2009) and Mzantsi (2019) which looked at certain emerging contaminants such as pharmaceuticals in both surface water and groundwater through MAR in Atlantis. The data in Figure 5.9 shows that there was a reduction in both compounds in all the studies, as they are distributed through the environment until they reach the groundwater. This observed trend could be due to dilution occurring once the pharmaceuticals compounds mix with storm water and enter the groundwater. The lower concentrations of sulfamethoxazole observed in in the influent (19.9 ng/) 2021, could be attributed to controlled or lower usage rates over the years and improved wastewater treatment processes.

Based on the findings above, even though managed aquifer recharge is beneficial to replenish groundwater, it was shown to be another source of introducing pharmaceuticals to the groundwater system in Atlantis, with the detection of certain pharmaceuticals, such diclofenac and naproxen in the groundwater. The concerning nature of detecting these compounds in the groundwater further indicates the need for advanced water treatment of groundwater, should it be used as an alternative drinking supply to communities. The management of wastewater and agricultural runoff should also be improved to protect both human and environmental health.

5.4 Removal efficiency of Wastewater Treatment Plants

In this section various wastewater treatment processes will be discussed and compared to determine the removal efficiency of various compounds based on the treatment. The removal efficiency rates of pharmaceuticals can be attributed to the type of treatment used at the various WWTP's, the compounds polarity and the amount of inflow the plant receives. All WWTP's in this study uses activated sludge process as their main secondary treatment, while using chlorination as a disinfectant, with some plants using tertiary treatments as a further treatment process (Belville and Potsdam WWTP). It is evident from the estimated removal efficiency figures in Figures 5.10-5.11 below that certain wastewater treatment processes can reduce certain pharmaceuticals before discharging it.

The comparison between a Membrane Bioreactor (MBR) vs Conventional treatment (DO)- Belville WWTP removal efficiencies is presented below in Figure 5.10.

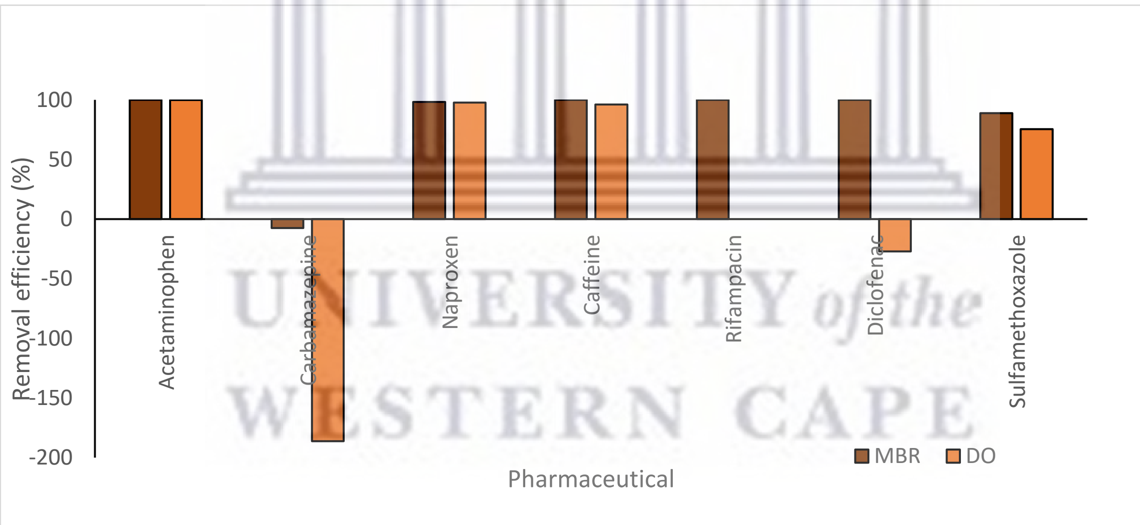


Figure 5.10: The comparison of removal efficiencies of Membrane Bioreactor (MBR) vs Conventional treatment (DO)- Belville WWTP

It can be seen in Figure 5.10, that the use of a membrane bioreactors (MBR) plus ultraviolet (UV) technology is able to reduce contaminants much further than the conventional wastewater treatment processes which does not use MBR treatment during its treatment process at the plant. Certain pharmaceuticals however are not efficiently removed before being discharged into the environment such as with carbamazepine and diclofenac.

The types of treatment used at the WWTP, plays a significant role in the reduction of emerging contaminants, which can be seen in Figure 5.10 with the use of tertiary treatment. The Bellville Wastewater Treatment Plant uses Membrane Bioreactors (MBR) coupled with Ultraviolet as a tertiary treatment process before discharging effluent. The use of this added treatment to its secondary treatment has shown to be effective in the further reduction of pharmaceuticals when comparing it with the conventional treatment (primary and secondary treatment), certain pharmaceuticals such as carbamazepine, diclofenac, and sulfamethoxazole are shown to be greatly reduced with the tertiary treatment, with diclofenac having a 75 % reduction difference with MBR than with the conventional wastewater treatment process. This observation is in agreement with a study by Celiz *et al.,* (2009) which compared MBR and activated sludge systems. This study indicated that the removal efficiency of MBR, regarding diclofenac, increased up to >70 % compared to the lower removal efficiency of just the activated sludge process, while carbamazepine showed a slight increase with the use of MBR but suggested that this should be coupled with use of advanced oxidation processes for better removal rates. The reason for the improved reduction with MBR combined with the conventional treatment is due to the longer solid retention time and higher biomass concentrations, leading to increased biological activity and microbial degradation, coupled with the increased adsorption to the membrane surface and granules in the MBR system (Wang *et al.*, 2018, 2021; Sabri *et al.*, 2020)

Removal efficiencies for most of the compounds of interest are between 70- 99 % (Figure 5.10-5.11) , with caffeine (96 %) and acetaminophen (99 %) being the highest, which is in agreement with other studies findings of the removal efficiencies of > 80% for these compounds (Pal *et al.*, 2010; Wang *et al.*, 2018; Al-Mashaqbeh *et al.*, 2019; Mhuka, Dube and Nindi, 2020). Negative removal efficiencies were observed for certain compounds, whereby the concentrations of the compounds increased from influent to effluent, this was more evident with the use of conventional wastewater treatment processes. These compounds include diclofenac (≥ -27.12 %) and carbamazepine (≥ -186%), with the latter having the lowest removal efficiencies at all WWTPs. The negative removal efficiencies can be due the accumulation of these compounds at the WWTPs due to their resistance to biodegradation, their chemical characteristics and it could be attributed to their transformation into its metabolites after going through the WWTPs processes (Al-Mashaqbeh *et al.*, 2019; Archer et al., 2017; Osunmakinde *et al.*, 2013).

The comparison between a Domestic waste treatment vs industrial waste treatment (no anaerobic treatment) -Wesfleur WWTP (Atlantis) removal efficiencies is present in Figure 5.11 below

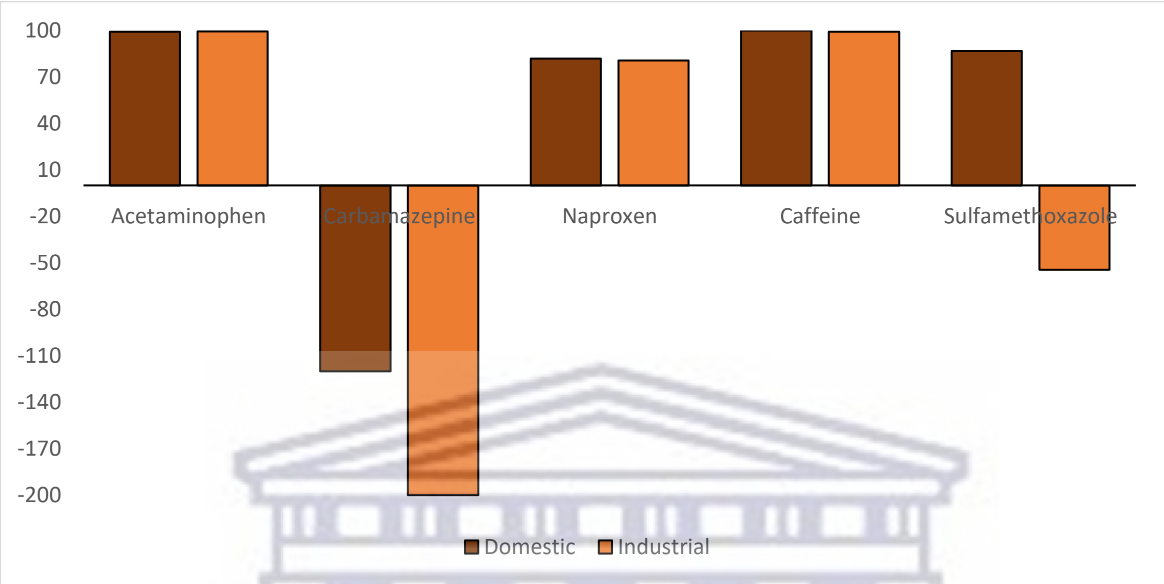


Figure 5.11: The comparison of removal efficiencies of domestic waste treatment vs industrial waste treatment (no anaerobic treatment) -Wesfleur WWTP (Atlantis WWTP)

In the data in Figure 5.11, the use of aerobic treatment during the treatment of domestic wastewater coupled with anoxic and anaerobic treatment is shown to be more effective in reducing certain pharmaceuticals unlike when using aerobic-anoxic treatment without anaerobic for industrial waste, as can be seen in figure 5.11.

The importance of the anaerobic treatment in WWTP's can be seen in the data in Figure 5.11 when comparing the domestic treatment with the industrial treatment processes. The anaerobic process plays a significant role in the breakdown of organic compounds in the wastewater, which contributes to the biodegradation of pollutants. Atlantis WWTP does not use the anaerobic treatment for its industrial wastewater due to the type of influent coming into the plant, which could have a negative effect on the removal of emerging contaminants. According to Manickum and John (2014), secondary biological treatment is the key process behind the degradation of pharmaceuticals at WWTPs, where microbes are used to breakdown compounds through biodegradation.

In Figure 5.11, the removal efficiencies for certain compounds are much higher when using aerobic, anoxic, and anaerobic processes combined (domestic) than just aerobic and anoxic (industrial), as seen with sulfamethoxazole, a negative removal percentage of -54 % was obtained for the industrial treatment compared to the 86 % removal with the domestic treatment processes. There is however a higher removal rate for both domestic and industrial treatment processes with certain compounds such as naproxen (81 %), caffeine (99 %), and acetaminophen (99 %), due to the combination of aerobic and anoxic treatment processes which are used in both domestic and industrial treatment processes. These treatment processes are an important process in the biological treatment and for the reduction of pharmaceuticals, as they contribute to the increased microbial activity and catabolic processes (breakdown of larger molecules into smaller ones) (Manickum and John, 2014; Sui *et al.*, 2015).

The comparison between Potsdam WWTP (phosphate reduction + UV) and Athlone WWTP (conventional WWTP process) removal efficiencies is present in Figure 5.12 below

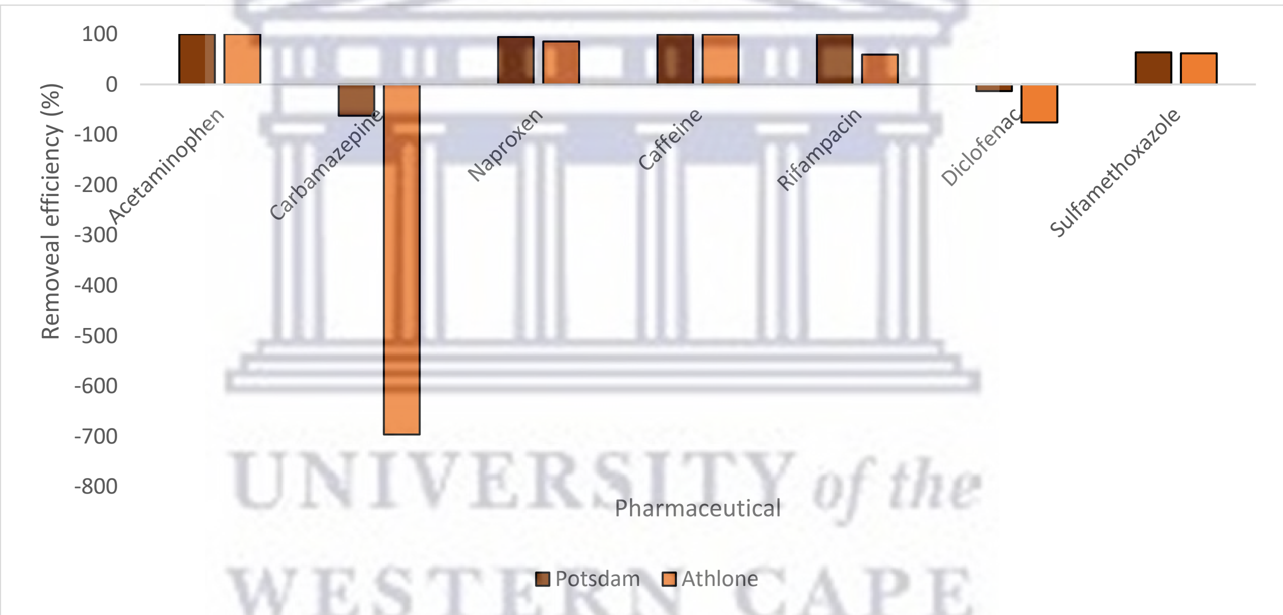


Figure 5.12: The comparison of removal efficiencies of Potsdam WWTP (phosphate reduction + UV) vs Athlone WWTP (conventional WWTP process)

Based on the data in Figure 5.12, the use of conventional wastewater treatment processes combined with phosphate reduction and UV was shown to be effective in further reducing pharmaceuticals at the Potsdam WWTP. Most of the pharmaceuticals had an estimated removal efficiency between 94-99 % while Athlone WWTP which only uses conventional WWTP's processes without UV shows a lower removal efficiency with an estimated efficiency between 59-99%. The data presented in Figure 5.12 has shown similar trends as with Figure 5.11 where diclofenac and carbamazepine had low negative removal efficiencies with the later having the highest negative removal efficiency.

The use of ultraviolet as a tertiary treatment has shown to be an effective treatment in the further reduction of pharmaceuticals and as a disinfectant, with a number of studies agreeing with the improved removal rates with this treatment (Celiz *et al.*, 2009; Wang, Sui and Lu, 2014; Jallouli *et al.*, 2016). Certain pharmaceuticals such as naproxen (94.57 %), diclofenac (- 13.07 %) and rifampicin (100 %) were shown in Figure 5.12 to have a higher removal efficiency at Potsdam WWTP than when compared to the Athlone WWTP, naproxen (85.68 %), diclofenac (- 75.71 %) and rifampicin (59.13%), which only uses primary and secondary treatment. A 10 % to 40 % increase in removal efficiency can be seen for naproxen and rifampicin at Potsdam WWTP, this improved efficiency can be accounted to photolysis, whereby the absorption of the UV rays by these pharmaceuticals alters its chemical structure and thereby causing the reduction or degradation of these compounds (Wang, Sui and Lu, 2014).

The results obtained for the estimated removal efficiencies indicated that majority of the WWTPs sampled at showed high removal rates for certain compounds such as caffeine, acetaminophen, naproxen, and rifampicin, while certain pharmaceuticals such as carbamazepine and diclofenac showed reduced removal rates at certain plants due to their chemical nature and resistances to biodegradation. The use of tertiary treatment at WWTP's has shown to be effective in further reducing pharmaceuticals in the effluent, with MBR & UV showing higher removal efficiencies than conventional treatment processes for most compounds.

5.5 Summary of findings

The results obtained showed the spatial and temporal variation of pharmaceuticals in Cape Town's water network. Major sources were identified, such as WWTP's, landfill sites and other anthropogenic activities, which are important to identify to put the necessary measures in place to further reduce or remove these contaminants from the environment. Most of the pharmaceuticals of interest was reduced from source to sink, as it is distributed through the environment, with dilution being the greatest contributor to the reduction of pharmaceuticals once it enters the receiving surface water and groundwater bodies. A higher concentration of pharmaceuticals was observed during the summer season than the other 3 seasons, which could be accounted to reduced rainfall levels and possibly due to the higher usage of medication during the 2nd covid wave in South Africa.

Managed aquifer recharge was shown to be another source of introducing pharmaceuticals to the groundwater system in Atlantis, with the detection of certain pharmaceuticals in the groundwater. The detection of pharmaceuticals in drinking water (treated groundwater) in Atlantis, such as carbamazepine and naproxen, after MAR and water treatment processes shows that there is need for advanced treatment to remove these contaminants before transferring the water to the potable water network.

Removal efficiencies for most of the compounds of interest was high with caffeine (99 %), rifampicin (80 %), acetaminophen (99 %), and naproxen (< 80 %) showed the highest removal efficiencies of the analytes of interest while diclofenac (-75% to 100%), sulfamethoxazole (-54 % to 82 %) and carbamazepine (< - 700 %) showed lower removal efficiencies in certain cases, with carbamazepine being the most persistent compound at all the study sites due to its resistance to biodegradation. The use of tertiary treatment at WWTP's has shown to be effective in further reducing pharmaceuticals in the effluent, with MBR & UV showing higher removal efficiencies than conventional treatment processes for most compounds with multiple compounds such as acetaminophen, caffeine and rifampicin showing 100 % using MBR and UV combined.

Chapter 6: Conclusion and recommendations

6.1 Conclusion

This study aimed to investigate the spatial and temporal distribution of pharmaceuticals in the environment with regards to the change in concentration along a flow path from potential sources to sink. This was achieved by sampling at the various sampling points identified and by determining the pharmaceuticals removal efficiency of treatment processes used at WWTP's in Cape Town. The main sources of introducing pharmaceuticals in the environment were identified as WWTPs, landfill sites as well anthropogenic activities occurring near rivers or surface water points. A reduction of pharmaceuticals from source to sink was indeed observed for most pharmaceuticals of interest.

Various trends regarding the spatial and temporal variations were observed based on objective one of this research. Certain pharmaceuticals occurred in higher concentrations than others in the influent of WWTPs, depending on its usage in society. These compounds included caffeine, naproxen, and acetaminophen; however, these compounds were reduced through various treatment processes with much lower concentrations detected in the effluent. Carbamazepine, sulfamethoxazole, and diclofenac were shown to be detected in various effluent at higher concentrations than in the influent at certain WWTPs, as well as in various surface and groundwater points. These compounds are therefore known to be persistent and could be used as anthropogenic markers in the environment, due to their resistance to biodegradation. Dilution was shown to be the greatest contributor to the reduction of pharmaceuticals once they enter the environment, based on the reduction in concertation that was observed in various surface water and groundwater bodies.

A seasonal pattern was observed regarding the presence of pharmaceuticals in the environment, whereby a higher rainfall period indicated a greater reduction in the concentration and detection of pharmaceuticals, in this case the winter period compared to other seasons. The change in concentration over the various seasons and areas, indicates that these pharmaceutical compounds are not constantly present in various mediums but fluctuate depending on the nature of the environment and their usage.

The detection of pharmaceuticals in groundwater and in drinking water supply in the Atlantis area, indicates the importance of this study in informing current processes at water treatment plants and future applications of MAR, when using groundwater as an alternative drinking supply. The use of advanced tertiary treatments to remove persistent pharmaceuticals present in groundwater are needed to ensure improved reduction of these contaminants before discharging them for potable water. The concentration ranges detected for the various pharmaceuticals at these sites are however below the benchmark values determined by the Australian government for emerging concerns in potable water. The City of Cape Town could use Atlantis therefore as a case study and the pharmaceuticals detected in this study as a guide for when the city plans to implement the recharge of treated wastewater and storm water into the Cape Flats Aquifer.

The estimation of the WWTPs removal efficiency (%) for the selected pharmaceuticals was shown to be high for all pharmaceuticals (> 80 %) besides for carbamazepine and diclofenac, even though these plants were not designed to remove emerging contaminants. Tertiary treatments such as MBR and UV were shown to have higher removal efficiencies for persistent compounds with improved removal rates, which supports the need to apply these types of treatment processes at all WWTPs in Cape Town not just primary and secondary treatments. The high removal efficiency rates for certain compounds (80 -100 %) in this study however do not account for any transformation or metabolites of the parent compounds present in the effluent after treatment.

This study has contributed to the global research of emerging contaminants, in understanding how various pharmaceuticals occur throughout the environment and which factors play a role in their reduction or increase in concentrations. This study is also one of the first in Cape Town regarding the research in understating the fate of pharmaceuticals along the flow path from WWTPs and landfill sites to receiving water bodies in Cape Town, which provides a base for further studies to compare future results of the occurrence of pharmaceuticals in the environment.

6.2 Recommendations

This research therefore recommends the need to improve and upgrade all our Wastewater Treatment Plants with tertiary treatments, to ensure complete or further reduction of emerging contaminants before discharging treated wastewater. It is also recommended that water quality guidelines and policies in South Africa consider including benchmarks for the concentrations of emerging contaminants in both treated wastewater and potable water, where special monitoring must be considered for persistent compounds such as diclofenac and carbamazepine in the environment.

Routine long-term sampling of both surface water and groundwater is needed for the detection of pharmaceuticals, to monitor any increase in concentrations of persistent compounds beyond benchmark limits suggested by other countries, to ensure aquatic ecosystems and the health of citizens are protected. In the case of monitoring groundwater , borehole depths should also be considered based on geological settings and flow paths which could influence the fate of pharmaceuticals in the environment. Future studies should include transformation or metabolites products of parent's compounds, when doing spatiotemporal studies of pharmaceuticals in the environment, to further understand the fate of these compounds when moving through the environment from source to sink.

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Appendix

Table A1: GPS of location points

Location	Latitude	Longitude
Milnerton Residential Borehole	-33.8561	18.50285
Lagoon Beach	-33.8883	18.48702
Potsdam WWTP	-33.8389	18.519745
Vissershok Landfill	-33.7713	18.542862
Pond 6	-33.6134	18.47274
Water treatment Plant-Witsand	-33.6264	18.44251
Wesfleur WWTP	-33.6068	18.482462
Rondebosch Golf course	-33.9535	18.49239
Black river	-33.9524	18.49436
Athlone WWTP	-33.9541	18.514861
Salt river	-33.9088	18.47368
Belville WWTP	-33.9313	18.65311
Belville South Landfill	-33.9378	18.65442
Kuilsriver	-33.9329	18.67302
Mitchells plain Sea outflow	-34.0776	18.59803
Mitchells plain WWTP	-34.068	18.595253
Wavecreast primary	-34.0669	18.60089
Zeekoevlei	-34.0729	18.51582
Cape flats WWTP	-34.0806	18.52007
Coastal Park Landfill	-34.0904	18.5024
Zeekoevlei canal	-34.0957	18.50411

Table A2: m/z transitions for each pharmaceutical compound

Compound	m/z
Acetominophen	151.85→110.05, 93.05
Carbemazepine	236.9→194.15, 192.95
Rifampicin	823.5→791.4, 179.1
Caffeine	195.1→138.05, 110.05
Sulfamethoxazole	253.85→92.05, 156.0
Naproxen	229.0→170.15, 169.15
Diclofenac	294.0→250.05

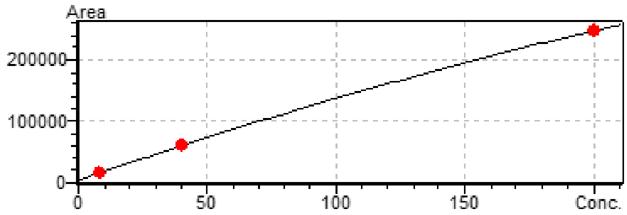
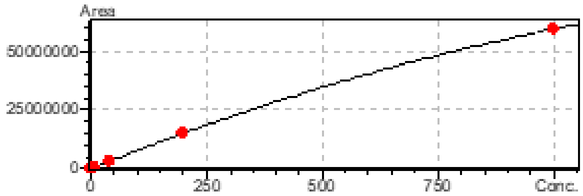
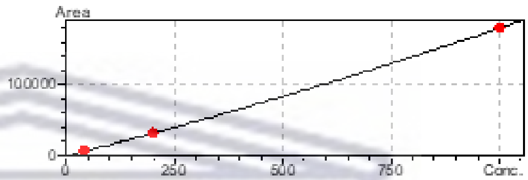
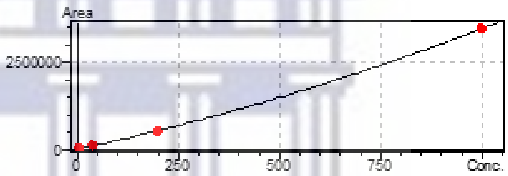
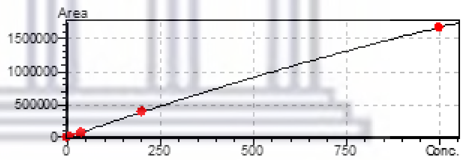
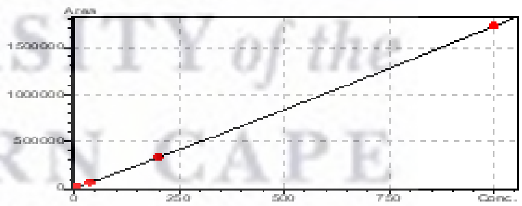
Table A3:Temperature and pH of various samples sites

Site	Sample #	Autumn		Winter		Spring		Summer	
*No data		**pH**	**Temp**	**pH**	**Temp**	**pH**	**Temp**	**pH**	**Temp**
1.Mitchells plain									
Influent	1.1	8.2	22.2	7.86	17.2	8.32	18.3	7.72	*
Effluent	1.2	7.51	18.9	7.41	12.8	7.9	16.4	6.5	*
Groundwater	1.3	6.48	20.3	7.25	18.1	7.79	19.8	6.96	*
Outflow-Sea	1.4	7.4	18.9	7.61	12.8	7.93	16.5	6.67	*
2.Atlantis									
Pre-Water Treatment Groundwater	2.1	7.83	18.7	7.75	15.2	8	18.8	6.62	*
Post-Water Treatment	2.2	8.14	18.5	8.3	15	8.36	15.7	6.78	*
Raw-Domestic-influent	2.3	8.06	21.2	8.55	16.8	8.87	17.3	7.2	*
Post -Domestic-effluent	2.4	8.62	16.5	7.59	12.8	8.19	16.5	7.7	*
Raw-Industrial-influent	2.5	7.63	23	8.29	19.7	8.11	19.7	7.6	*
Post- Industrial-effluent	2.6	8.19	17.7	8.1	13.8	8.14	17.1	6.98	*
Pond 6	2.7	7.7	16.4	7.87	14.8	7.9	17.4	6.59	*
3.Potsdam									
Influent	3.1	7.55	22.2	7.99	16.9	8.47	18.6	7.33	*
Effluent	3.2	7.65	19.5	7.53	14.3	7.88	17.8	6.75	*
GW	3.3	5.71	21.4	5.58	19.8	5.67	19.1	6.32	*
Lagoon Beach	3.4	7.63	18.9	7.56	10.4	8.12	14.4	6.88	*

Visserhoek Landfill	3.5	5.3	21.6	7.04	19.4	7.19	19.7	7.11	*
4.Belville									
MBR-Influent	4.1	7.69	23	7.55	18	7.77	18.5	6.95	*
MBR-Efluent	4.2	7.3	25	7.35	18.8	7.81	18.9	7.04	*
DA-Influent	4.3	7.71	22.6	8.21	18.1	8.58	18.5	7.51	*
DA-Effluent	4.4	7.69	21.1	7.35	16.4	7.88	17.3	7.36	*
Outflow	4.5	7.98	20.8	7.79	15.6	8.02	16.7	7.49	*
Kuilsriver	4.6	7.95	20.7	7.88	13.8	8.25	14.4	7.65	*
Belville South Landfill	4.7	7.46	20.8	7.69	17.8	7.61	17.2	6.83	*
5.Athlone									
Influent	5.1	7.81	22.4	7.49	18.5	7.33	18.8	6.81	*
Effluent	5.2	7.6	23.1	7.03	18.4	7.39	19.7	7.88	*
Black river	5.3	7.77	19.3	7.57	14.4	6.76	18.9	7.87	*
GW-Golf	5.4	6.67	19.6	6.55	18.9	8.11	18.8	6.42	*
Outflow-Sea/Salt river	5.5	7.24	17.6	7.35	13	7.9	17.2	7.51	*
6.Cape Flats									
Influent	6.1	7.68	21	7.56	17.2	7.79	17.9	7.36	*
Effluent	6.2	7.47	19.6	7.44	13.5	7.46	16.9	6.55	*
Zeekoivlei	6.3	8.1	17.3	7.5	13.4	9.94	16.2	9.21	*
Coastal park landfill	6.4	7.68	20.4	7.71	19.2	7.97	19.2	6.53	*
Zeekoevlei canal – outflow to sea	6.5	8.13	17.3	7.92	12.5	7.87	16.6	6.62	*

Table 4:Calibtration curves for pharmaceutical standards

Compound	**Curve**

Acetominophen **$R^2 = 1$**	
Carbemazepine **$R^2 = 0.999$**	
Caffeine **$R^2 = 0.969$**	
Rifampicin **$R^2 = 0.999$**	
Sulfamethoxazole **$R^2 = 0.998$**	
Naproxen **$R^2 = 0.999$**	
Diclofenac **$R^2 = 0.999$**