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Department of Civil Engineering

MASTERS RESEARCH PROJECT

Methods for removing pharmaceuticals from human urine

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“Do your very best to teach yourself”

~Wise words from a wise person

PLAGIARISM DECLARATION

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Date: ___13 December 2021_____

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Abstract

Background

The concept of sustainability is changing the nature of everyday dialogue across many disciplines. The 2030 Sustainable Development Goals provide a practical way to ensure that the basis of sustainability is covered in all disciplines. One of the ways that sustainability can be achieved is through the reuse of various waste streams, such as wastewater.

Conventional wastewater treatment plants aim to remove the nutrients in wastewater to prevent problems such as eutrophication. However, this removal process requires a substantial amount of energy. This increases the total cost for the operation of conventional wastewater treatment plants and contributes to greenhouse gas emissions, depending on the source of energy.

Nonetheless, some wastewater streams (such as domestic wastewater) have valuable nutrients (nitrogen (N), phosphorus (P) and potassium (K)) which are essential for plant growth). Although urine accounts for 1% of the total volume of domestic wastewater, urine carries most of these key nutrients. For example, urine has 80% N, 70% P and 50% K. Consequently, the source separation and collection of urine provides an opportunity for the recycling of these nutrients for use as fertilizers.

Among the many constituents of urine are micropollutants such as pharmaceuticals. Pharmaceuticals pose a challenge for the reuse of urine because fertilizers are required to be free of pharmaceuticals. Therefore, the aim of this work was to find a method for pharmaceutical removal from fresh human urine, while conserving urea.

Methodology

Four pharmaceutical removal methods were investigated namely: a high pH environment (>12), granular activated carbon, hydrogen peroxide and hydrodynamic cavitation. The pharmaceuticals investigated for this work were grouped into two categories: over the counter (OTC) common pharmaceuticals and the antiretrovirals (ARVs). The OTCs are used to

treat a variety of common ailments such as pain, fever, allergies, inflammation, and heart problems in South Africa. The ARVs are used to treat and prevent the human immunodeficiency virus (HIV). Each pharmaceutical removal process had a specific methodology. The methodologies (including the experimental design parameters) were developed based on the literature review of the respective removal methods. Furthermore, the hypothesis for the four removal methods were informed by the results found in literature. The hypotheses were phrased in the following way: the pharmaceuticals can degrade in human urine because the stabilization of human urine using calcium hydroxide increases the pH (>12), resulting in hydroxide ions that degrade the pharmaceutical molecules while conserving urea; granular activated carbon adsorbs the pharmaceuticals and urea in human urine; the addition of hydrogen peroxide to human urine with a high pH (>12) forms hydroxyl radicals which degrade the pharmaceutical molecules, along with the excess hydroxide ions from the high pH, while conserving urea; and the hydrodynamic cavitation system generates high energy cavitation bubbles which result in the oxidation of the pharmaceutical molecules while conserving urea.

In addition, the conservation of urea during the pharmaceutical removal process for each method was considered. It is known that fresh urine should be stabilized to prevent the enzymatic breakdown of urea into ammonia gas. The stabilization of urine can be achieved by acidification or alkalinization. In this work, urine was stabilized using calcium hydroxide (pH >12.5 at 25°C) and citric acid (pH 2 at 25°C) to keep the urea in solution and thus the investigated pharmaceutical removal methods had to ensure that the degradation of urea did not occur. Hence, the percentage urea degradation for each pharmaceutical removal method was also determined.

Pharmaceutical analysis method development

Three high performance liquid chromatography (HPLC) methods were used for this work. The first method was for the analysis of over the counter (OTC) common pharmaceuticals**,** the second for the analysis of antiretrovirals (ARVs) and the third method was for the analysis of a combination of specific OTCs and ARVs. Reverse phase HPLC was used for the three methods and the gradient elution technique was applied for the analysis of the pharmaceuticals. All

three methods used acetonitrile as the organic solvent. However, the HPLC method to analyze OTCs and the HPLC method to analyze both the OTCs and the ARVs used a phosphate as an aqueous buffer, while the method to test for the ARVs used a phosphate buffer with the addition of hexanesulfonic acid as an ion pairing reagent. The calibration curves for each pharmaceutical were not developed since the degradation of the pharmaceuticals was expressed as a percentage loss. Nonetheless, the HPLC chromatograms for the individual pharmaceuticals and the mixture of the pharmaceuticals were generated as a reference for the analysis of the pharmaceutical degradation due to the pharmaceutical removal methods.

Description and performance of the pharmaceutical removal methods

The current work was a comparative study of the pharmaceutical removal methods. All pharmaceutical removal methods were tested in duplicate for the comparative study. Therefore, the standard deviation was not calculated, however, the performance of the pharmaceutical degradation shown in each sample was analyzed in comparison to the other samples.

The use of calcium hydroxide as a urine-stabilizing agent was considered as the high pH pharmaceutical removal method. Fresh urine was spiked with pharmaceuticals and then stabilized with calcium hydroxide for at least 75 days. The calcium hydroxide dosage was kept at the recommended calcium hydroxide dosage of 10 g L^{-1} of fresh urine, to accommodate for urine with different compositions, since urine composition is influenced by factors such as diet. The range of degradation for the over the counter (OTC) common pharmaceuticals due to the high pH was 8 - 44%, with paracetamol and chlorphenamine maleate experiencing the lowest and highest degradation, respectively. Contrary, the range of degradation for the antiretrovirals (ARVs) due to the high pH was 0 - 100%. Abacavir sulfate and nevirapine experienced no degradation, while stavudine, lamivudine, zidovudine and tenofovir experienced complete degradation. The difference in the degradation of the pharmaceuticals was attributed to the difference in the functional groups of the pharmaceuticals. The complete degradation may be attributed to hydrolysis rather than oxidation, including tenofovir which undergoes hydrolysis in basic conditions due to a P – O moiety in its molecular structure. Furthermore, pharmaceuticals with similar functional groups (such as stavudine,

lamivudine and zidovudine) showed a similar degradation pattern. In addition, the high pH only resulted in a 4% loss of urea.

For the granular activated carbon (GAC) removal method, a GAC column was prepared, through which stabilized urine – spiked with pharmaceuticals – was passed. The adsorption from the GAC removed all the pharmaceuticals by more than 94.7%. However, the GAC also removed 83.4% of the urea present in the stabilized-spiked urine solution. The adsorption of both the pharmaceuticals and the urea was caused by microporous structure of the GAC which provides internal surface area on which the pharmaceutical and urea molecules can attach.

Hydrogen peroxide was used as an oxidizing agent to degrade the spiked pharmaceuticals in stabilized urine. The range of degradation for the OTCs, resulting from the addition of hydrogen peroxide to urine with a high pH (>12), was 0 - 64.7%. Diclofenac and chlorpheniramine maleate did not degrade, while salicylic acid experienced the most degradation (64.7%). On the other hand, the ARVs had a range of degradation of 17.2 - 73.4%. Stavudine experienced the least degradation (17.2%) while lamivudine experienced the most degradation (73.4%). The hydroxyl radicals from the addition of hydrogen peroxide and the excess hydroxide ions from the high pH degraded the pharmaceuticals at varying degrees due to the difference in the functional groups of the pharmaceuticals. Additionally, only 12.6% of the urea was degraded by this pharmaceutical removal method.

The hydroxyl radicals generated from the hydrodynamic cavitation (HC) system were used to oxidize the pharmaceutical molecules in the spiked-synthetic urine solution at a low pH (pH 2) and a high pH (pH 12.4). Both the OTCs and the ARVs were analyzed together (due to the high-volume requirement of the experiments) unlike the other degradation methods. The HC system operated at a high pH achieved the highest degradation of 16.6% for chlorphenamine maleate, while paracetamol, zidovudine, lamivudine and stavudine experienced less than 5% degradation. The HC system operated at a low pH reached a degradation range of 10.4 - 49.2%, with paracetamol and zidovudine experiencing the lowest and highest degradation, respectively. The amount of urea which was lost due to the HC system was 6.8%. Thereafter, the HC system was optimized at pH 2, given that the HC system conserved more than 90% of the urea and that it could be readily optimized. The range of degradation improved between 54.5 and 87.6%, with paracetamol and zidovudine again experiencing the

highest and lowest degradation, respectively. The difference in the degradation of the pharmaceuticals was attributed to the difference in the oxidation of the functional groups of the pharmaceuticals.

Conclusion and applicability

The optimized hydrodynamic cavitation (HC) system performed the best out of the four pharmaceutical degradation methods. The optimized HC system had an average pharmaceutical degradation of 74.5%, and resulted in a urea loss of only 5%. The approximate energy required to treat 1 m^3 of treated urine using the optimized HC system under the optimized condition was calculated to be 1.84 kWh m^{-3}. The optimization of the HC system showed potential for the effective removal of pharmaceuticals in urine. Further optimization of the HC system will be beneficial for use as a designated pharmaceutical removal method for the overall urine treatment process.

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List of Abbreviations

Abbreviation	Description
OTCs	Over the counter (OTC) common pharmaceuticals
ARVs	Antiretrovirals
GAC	Granular activated carbon
HC	Hydrodynamic cavitation
HPLC	High performance liquid chromatography
UV	Ultraviolet
SAT	Specific ammonia transfer
TOC	Total oxygen carbon
OH	Hydroxide ion
$Ca(OH)_2$	Calcium hydroxide
H_2O_2	Hydrogen peroxide
MgO	Magnesium oxide
TiO_2	Titanium dioxide
$CO(NH_2)_2$	Urea
PSD	Particle size distribution
API	Active pharmaceutical ingredient
HIV	human immunodeficiency virus

List of Symbols

Symbol	Description
N	Nitrogen
P	Phosphorus
K	Potassium
R_s	Baseline resolution
E	Total energy of the system
E_K	Kinetic energy
E_P	Potential energy
U	Internal energy
Q	System heat
W_s	System work
H_D	Pumping head
H_L	Head loss
Re	Reynolds number
$\tilde{V}$	Volumetric flow rate
V	Volume
P	Pressure
H	Enthalpy
D	Diameter
π	Pi
$\propto$	Kinetic energy correlation factor
v	Velocity
z	Elevation
ρ	Density
μ	Viscosity
ε	Absolute roughness
ϵ	Relative roughness
f	Darcy friction factor

1 Introduction

1.1 The proposed research project

The purpose of the research project was to investigate pharmaceutical removal methods for human urine that also minimized the loss of urea. Four pharmaceutical removal methods were explored: high pH, adsorption onto granular activated carbon, oxidation using hydrogen peroxide and oxidation by hydroxyl radicals generated through hydrodynamic cavitation. Eleven pharmaceuticals were chosen for this study – five over the counter common pharmaceuticals (paracetamol, salicylic acid, diclofenac, clopidogrel and chlorpheniramine maleate) and six antiretrovirals (zidovudine, lamivudine, tenofovir, stavudine, abacavir sulfate and nevirapine).

1.2 Background

1.2.1 Urine as a resource

The recognition of wastewater as a valuable resource has increased over the past few years. Some wastewater streams contain nitrogen, phosphorus, and potassium, which can be reused to produce fertilizer. Although urine accounts for 1% of the total domestic wastewater volume, it contains approximately 80% of the nitrogen that is essential for fertilizer production (Spångberg et al., 2014; Qian, 2016). Urine should therefore be separated at source for reuse as a fertilizer (Behrendt et al., 2002).

1.2.2 Source separation of urine

The source separation of urine is a technique used to collect urine and faeces separately (Behrendt et al., 2002). Source separation provides numerous opportunities for the reuse of urine as it enables the recovery of the high nutrient content found in urine. In addition, the source separation of urine enables wastewater treatment plants to operate with less energy and reduced volume requirements (Maurer et al., 2003).

No-mix toilets and waterless urinals are two ways through which urine can be collected separately (Hellstrom et al., 1999). No-mix toilets allow for the collection of the urine from

the front end of the toilet while the faeces are collected from the rear end (Anand and Apul, 2014). Waterless urinals collect urine separately without the use of water (Münch and Dahm, 2009).

There are challenges that come with the source separation of urine. Waterless urinal systems experience pipe blockages due to the precipitation of the collected urine and the lack of regular maintenance can lead to odour problems (Hellstrom et al., 1999; Hashemi et al., 2015). In addition, the urinal systems would require plumbing systems to be retrofitted for existing conventional systems, which would increase the costs for the overall urinal system (Udert et al., 2003a). Another challenge of reusing urine is the high pharmaceutical content. Urine contains approximately 64% of the pharmaceuticals found in municipal wastewater (Lienert et al., 2007). However, the separate collection of urine also allows for better treatment of the pharmaceuticals found in urine (Larsen et al., 2001).

1.2.3 Pharmaceutical removal in urine

The presence of pharmaceuticals in human urine can pose potential human and environmental health problems. There is evidence that the presence of pharmaceuticals in the environment increases the antibiotic resistance of microorganisms and causes behavioural changes, feminization, and immunosuppression in fish (Zelenakova, 2018). As a result, pharmaceutical removal methods must be developed to ensure that fertilizer products produced from source separated urine are safe for human use and the environment (Bischel et al., 2015).

Different methods have been investigated for the removal of pharmaceuticals and some have also looked at urea degradation resulting from the pharmaceutical removal method. High pH, granular activated carbon, hydrogen peroxide and hydrodynamic cavitation were investigated as methods to remove eleven pharmaceuticals. The focus of this work was to degrade pharmaceuticals from urine that has been stabilized (by alkalinization using calcium hydroxide or by acidification using citric acid) to conserve the urea. All pharmaceutical removal methods were investigated for the degradation of pharmaceuticals from alkalized urine. However, the degradation of pharmaceuticals due to the hydrodynamic cavitation system was also investigated for acidified urine to find the optimum pH at which the pharmaceuticals could

degrade. The degradation of urea was also investigated for each pharmaceutical removal method.

1.3 Significance of the research

A pharmaceutical removal method presents opportunities for the development of safe urine-derived fertilizer products. Additionally, the application of pharmaceutical removal from human urine could be extended for use in other types of wastewaters with pharmaceuticals present. The overall risk of harmful water-borne contaminants would be reduced, thus promoting the well-being of people and the environment.

1.4 Problem statement

Human urine is rich in nutrients required for fertilizer production. However, the direct use of urine as a fertilizer is problematic due to the presence of pharmaceuticals (Maurer et al., 2006). There are over 4 000 pharmaceutical products in the market (Wols et al., 2013). Traces of the consumed pharmaceuticals are already found in municipal wastewater, 64% of which are contained in human urine (Lienert et al., 2007). Therefore, the development of a pharmaceutical removal method for human urine is imperative to produce safe urine-derived fertilizers and recycling of wastewater streams.

1.5 Research questions

The aim of the current work was to answer the following research questions:

1. What is the percentage degradation of pharmaceuticals and urea due to a high pH environment (pH>12)?
2. What is the percentage removal of pharmaceuticals and urea due to adsorption on granular activated carbon treatment?
3. What is the percentage degradation of pharmaceuticals and urea due to oxidation with hydrogen peroxide treatment?

4. What is the percentage degradation of pharmaceuticals and urea due to hydroxyl radicals generated by hydrodynamic cavitation treatment at a low pH (pH 2) and a high pH (pH 12.4)?
5. Which treatment method is best for degrading pharmaceuticals while also retaining urea in solution?

1.6 Hypothesis

Pharmaceuticals can be degraded in human urine by high pH, granular activated carbon (GAC), hydrogen peroxide and hydrodynamic cavitation (HC) due to the following reasons: the addition of the calcium hydroxide causes a very alkaline environment which results in the formation of hydroxide ions that disrupt the pharmaceutical molecules while conserving urea; the microporous structure of GAC provides a surface area on which the pharmaceutical molecules and the urea molecules can adsorb; the extra oxygen atom from the hydrogen peroxide, in the presence of excess hydroxide ions from the addition of calcium hydroxide, oxidizes the pharmaceutical molecules, resulting in the degradation of pharmaceuticals while conserving urea; and the HC system generates hydroxyl radicals that oxidize the pharmaceutical molecules while conserving urea.

1.7 Scope and limitations

Pharmaceutical removal method studies are focused on the degradation of contaminants found in wastewater, however there is also literature on the degradation of pharmaceuticals in urine. The current work aims to contribute to the body of work dedicated to conventional pharmaceutical degradation methods for human urine that also conserve urea. Furthermore, the current work intends to explore hydrodynamic cavitation as an unconventional pharmaceutical removal method in human urine.

Although there are over 4000 pharmaceuticals on the market, only eleven pharmaceuticals were investigated for this study. Additionally, of the four pharmaceutical removal methods which were investigated only the hydrodynamic cavitation method, which proved to be efficient in pharmaceutical removal and urea conservation, was optimized. While the

degradation of the selected pharmaceuticals was investigated for each pharmaceutical removal method, the by-products were not determined. Furthermore, the degradation of the pharmaceuticals and the urea conservation were quantified in relative terms rather than absolute terms.

The following assumptions were made for the current work: the over the counter common pharmaceuticals and antiretrovirals were selected based on availability and did not necessarily represent the commonly found pharmaceuticals in wastewater, particularly urine; the interaction among the pharmaceuticals had no effect on the degradation of the individual pharmaceuticals, therefore, the degradation of the pharmaceuticals was exclusively as a result of the respective degradation methods; the difference in the duration of the pharmaceutical removal method experiments did not have an impact on the comparability of the results from the respective degradation methods; and the appearance of additional peaks on the chromatograms (besides the peaks that appeared in all chromatograms showing other components in urine) were an indication of the degradation of the primary pharmaceuticals, since the degradation of the by-products was not investigated.

2 Literature review

2.1 Urban water

Fast growing urban areas call for new emerging solutions for water challenges faced by an urbanizing world. According to Larsen and co-workers (2016) there is an urgency to develop and implement solutions for cities and aquatic ecosystems. These solutions include new concepts for stormwater drainage, distributed wastewater treatment, on-site wastewater treatment, increased water productivity, source separation of human waste as well as institutional and organizational reforms (Larsen et al., 2016). Over the years, various strategies have been implemented for the practical implementation of water-related solutions.

The Sustainable Development Goals (SDGs) outline the practices that need to be implemented across many disciplines, including engineering (Zhang et al., 2016). These practices are designed as a blueprint to provide intervention to achieve the defined SDGs by the year 2030. One of the commitments made by the SDGs is to reduce the lack of access to

clean water and sanitation, which addresses basic water-related challenges in an urbanizing world.

The role played by environmental engineers to implement water-related solutions is described in *The Ten Grandest Challenges of All* (Mihelcic et al., 2016). As such, the discussion in the work presented by Mihelcic and co-workers (2016) encourages new innovations and opportunities in research, education, practice, and service that will improve the well-being of the environment and humans (Mihelcic et al., 2016). Consequently, cities have the challenge to create self-sufficient water solutions that are driven by physical and political deficits, concerns over water quality and an overload on the capacity of the existing water supply infrastructure (Rygaard et al., 2011).

2.1.1 Urban water challenges

The mismanagement of water within cities causes problems for the cities. For example, traditional stormwater drainage systems were designed to quickly discharge water away from urban areas. However, cities experience frequent waterlogging due to an increase of impervious surface caused by the fast growth of the city (Xia et al., 2017).

While modern self-sufficient water solutions are being developed, they still face challenges. For instance, the integration of alternative water sources, such as reclaimed wastewater, can lead to potential water contamination. Additional challenges may include high energy demand requirements and public resistance (Rygaard et al., 2011). Therefore, challenges in urban water management would have to turn into future opportunities (Niemczynowicz, 1999).

2.1.2 Urban water solutions

Urban hydrology plays a pivotal role in the sustainability of human societies. The sustainable management of water is fundamental for sustainable development. The creation of sustainable solutions is driven by creating technologies that are low cost and robust. A way in which a balanced and sustainable system can be developed is through the harvesting, retention, and the reuse of rainwater (Xia et al., 2017). This is essential in building cities that

manage water well as a resource, which is the responsibility of urban hydrologists (Qian, 2016; Xia et al., 2017).

Urban hydrologists should also consider sanitation in water management systems. Two factors are to be considered for developing urban water solutions. Firstly, urban hydrologists should work with sanitation engineers to develop solutions that are safe, cost-effective, and socially acceptable. Secondly, urban hydrologists should develop solutions that can accommodate both water-borne and dry sanitation technologies (Niemczynowicz, 1999).

The nexus between wastewater, nutrients, energy, and water provides opportunities to drive a more sustainable urban water cycle (Volpin et al., 2018). Traditional urban water systems are built on taking water that has been used for off-site treatment without much consideration for reuse. A study review by Rygaard and co-workers (2011) revealed that there was an increase in the self-sufficiency ratios of the use of alternative water sources. As much as 80% of the water that was used came from rainwater collection, seawater desalination and recycled water (Rygaard et al., 2011).

Clean water sources are also constantly depleting; however, wastewater can be a new source of clean water. As a result, sanitation becomes important in developing sustainable water management systems (Niemczynowicz, 1999). Furthermore, wastewater could be used as a valuable resource (Sikosana et al., 2017), as some wastewater streams also contain essential resources which can be used for fertilizer production (Qian, 2016).

2.2 Urine as a resource

The primary objective of conventional wastewater treatment plants is to remove contaminants from domestic, industrial, and agricultural waste. Yet the treated water remains contaminated with heavy metals, micropollutants, and inorganic nitrogen and phosphorus which can cause eutrophication in the environment (Abdel-Raouf et al., 2012).

Conventional wastewater treatment plant processes also contribute to greenhouse gas emissions. It was found that the nitrogen gas emission from the nitrogen removal process accounts for 26% of the greenhouse gas footprint of the total water chain (Kampschreur et al., 2009). Contrary, it was proven that the nutrients that wastewater treatment plants attempt to remove can be reused at a lower energy demand while reducing the wastewater treatment

plant load (Maurer et al., 2003). Most of the nutrients found in domestic wastewater are carried in urine, even though urine accounts for 1% of the total domestic wastewater volume (Spångberg et al., 2014).

Urine has the essential nutrients to produce urine-derived fertilizer (Maurer et al., 2006). The specific nutrients that make urine a valuable fertilizer are nitrogen, phosphorus, and potassium (Qian, 2016). As a result, modern sanitation systems should consider the use of urine as a resource, making a shift from a 'waste' stream to a 'resource' stream (Randall and Naidoo, 2018). It was shown that source separated urine can be used much like mineral fertilizers, organic fertilizers, sewage sludge and compost from source separated solid waste (Jonsson et al., 1997).

The use of urine as a resource was also found to be more energy efficient than the removal of nutrients from conventional wastewater treatment plants. A study by Maurer and co-workers (2003) found that the primary energy consumption for the recovery and reuse of urine was 65 MJ kg^{-1} N, whereas the energy consumption required for a conventional wastewater treatment system to remove nutrients was 153 MJ kg^{-1} N (Maurer et al., 2003).

2.3 Source separation of urine

The separation of urine and faeces at source is an essential step in the production of valuable products derived from urine (Behrendt et al., 2002). The source separation of urine prompts a shift from the centralized treatment of wastewater to the decentralized treatment of wastewater (Boyer and Saetta, 2019).

2.3.1 Benefits of source separated urine

Source separated urine has many benefits. It reduces the load on conventional wastewater treatment plants, allows for better use of the nutrients found in urine and provides an opportunity for the effective removal of micropollutants (Larsen et al., 2001). Furthermore, urine-derived products can be produced at a low cost with easy-to-operate equipment (Behrendt et al., 2002).

A study by Chipako and Randall (2020a) highlighted benefits associated with the use of decentralized systems for urine collection and fertilizer production. The use of such a system within the City of Cape Town could be operated at a lower energy demand and with less greenhouse gas emissions, as compared to a conventional wastewater treatment process. Furthermore, the system could theoretically yield a net present value if the fertilizer were to be sold at a competitive price in the market (Chipako and Randall, 2020a). However, the public perception and acceptance for the reuse of urine remains a challenge (Ishii and Boyer, 2016).

2.3.2 Public perception of urine source separation technologies

The public acceptance of a urine source separation technology is a determining factor in the technology's success or failure. Ishii and Boyer (2016) looked at the student support and perceptions for urine source separation technologies in a university community. The statistical data from the study showed high levels of support for source separation technologies after the survey participants watched a video on the expected benefits (such as water conservation) associated with using source separation technologies (Ishii and Boyer, 2016).

Another social study by Chipako and Randall (2019) was conducted as part of the investigation for the feasibility of fertilizer-producing urinals. The online survey found that 87% of the respondents would use the fertilizer-producing urinals (Chipako and Randall, 2019). However, Ishii and Boyer (2016) discovered that female participants showed less support with concerns over the disposal of urine-soiled toilet paper in the dustbin. In addition, participants were willing to pay little to nothing for using the source separation technology, even though it was shown that the use of a fertilizer-producing urinal could save up to 18 ML of water annually (Ishii and Boyer, 2016; Chipako and Randall, 2019).

Apart from the use of source separation technology, the willingness to consume goods grown from urine-derived fertilizer was considered. Chipako and Randall (2019) reported that 79% of the respondents from a survey would eat food grown from urine-derived fertilizer products (Chipako and Randall, 2019). A recommendation was made by Ishii and Boyer (2016) to increase the public acceptance of source separation technologies. Educating the public about the associated benefits, which include water saving and the reduced nutrient discharge to the

environment, are ways in which the public acceptance of source separation technologies can be achieved (Ishii and Boyer, 2016).

2.3.3 Challenges of source separated urine

There are other problems that source separation technologies encounter besides public acceptance. These challenges include the collection and storage of urine, recovery of nutrients, elimination of pharmaceuticals, improper maintenance, and the overall economic and environmental impact (Boyer and Saetta, 2019).

The main challenge is the high urease activity in pipes which breaks down the urea in the urine, resulting in a rise in pH. Precipitates occur spontaneously when the pH of urine rises. This is because calcium and magnesium ions, which occur naturally in urine, react with phosphate ions to form solids (Etter et al., 2014). The inorganic salt precipitation of the collected urine then causes blockages in the urine collection system (Hashemi et al., 2015). Urine odour (Hashemi et al., 2015), the need to retrofit the plumbing for existing conventional systems (Udert et al., 2003a) and the ability to handle large urine volumes are additional challenges for source separation technologies (Hellstrom et al., 1999).

2.3.4 Technologies for source separated urine

The collection of source separated urine dates to ancient times. Hashemi and Han (2017) described how ancient Koreans practiced the separation of urine and faeces which enabled the reuse of the waste matter. The study also described how the ancient Persians used acetic acid and sodium bicarbonate to control odour resulting from collected urine (Hashemi and Han, 2017).

Today, the conventional urine source separation technologies which are commonly used are no-mix toilets and waterless urinals. A no-mix toilet requires 50% of the water used by a conventional flushing toilet, thus reducing the cost of water and energy significantly (Jonsson et al., 1997). Waterless urinals, as the name suggests, do not require water. The urinals can be connected to a urine storage tank which collects pure, undiluted urine (Münch and Dahm,

2009). Figure 1 shows a no-mix toilet (Anand and Apul, 2014) and a waterless urinal (Münch and Dahm, 2009).

Figure 1: (A) No-mix toilet (Anand and Apul, 2014); (B) Waterless urinal (Münch and Dahm, 2009).

A simple urine collection system was developed by Lind and co-workers (2001). The study showed that by freezing urine at a temperature of -14˚C, the volume of the urine can be reduced to 25% of the original volume. Therefore, collected urine can be easily managed through storage and transportation (Lind et al., 2001).

Senecal and Vinnerås (2017) developed a dehydrating urine-diverting toilet that could collect, contain, treat, and reduce the urine volume. A static ash bed was preferred over a bed dose system, because of a simpler application and the retention of more nitrogen. There was no liquid disposal from the collection system, unlike the freezing method developed by Lind and co-workers (2001) which discards 75% of the liquid component of urine. As a result, the cost of storage, transportation and fertilizer application was significantly reduced. A schematic of the urine-diverting toilet is shown in Figure 2 (Senecal and Vinnerås, 2017).

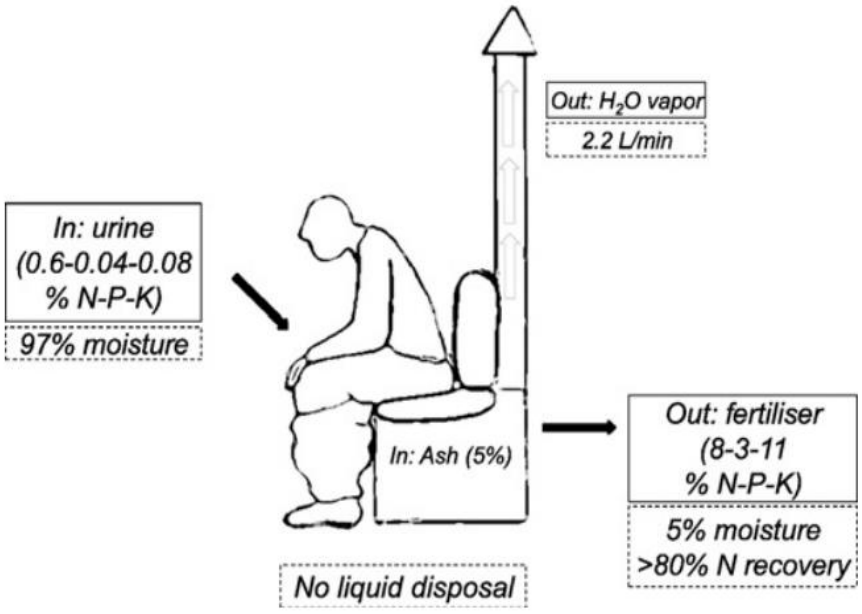


Figure 2: Urine-diverting dry toilet (Senecal and Vinnerås, 2017).

A novel fertilizer-producing urinal made from a plastic funnel and a collection tank was developed by Flanagan and Randall (2018). The system (shown in Figure 3) was designed to collect urine and produce fertilizer on-site with minimal energy required. However, the fertilizer-producing urinal did not consider the on-site volume reduction of urine (Flanagan and Randall, 2018).

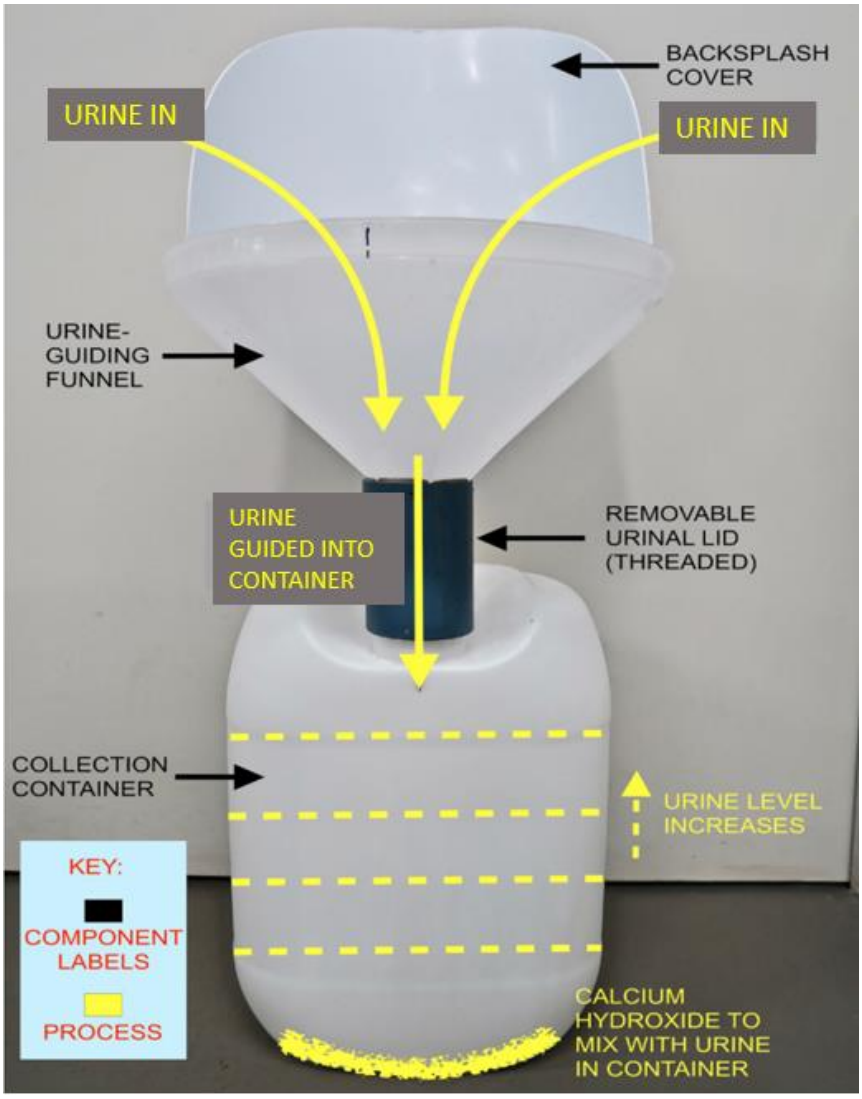


Figure 3: Fertilizer-producing urinal (Flanagan and Randall, 2018).

As such, a decentralized urine collection system was proposed by Chipako and Randall (2020a) for the collection of urine from malls in the City of Cape Town using the fertilizer-producing urinals developed by Flanagan and Randall (2018). The combined process of alkaline stabilization and volume reduction (shown in Figure 4) had the potential to produce 78 m^3 of liquid fertilizer and 4420 kg of solid calcium phosphate per week (Chipako and Randall, 2020a).

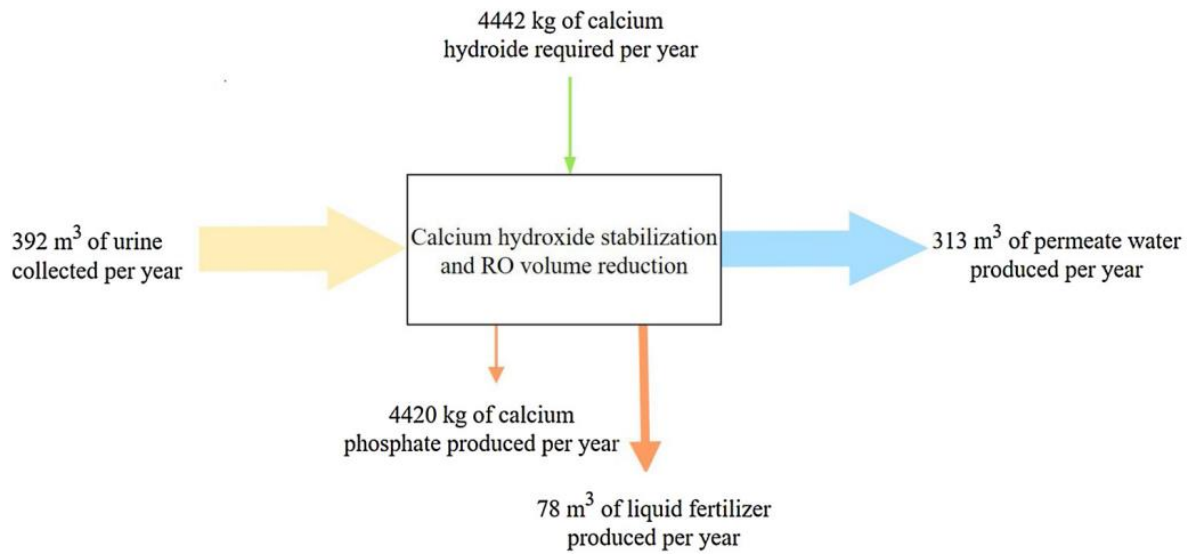


Figure 4: Mass balance for the recovery of resources from a urine recovery system (Chipako and Randall, 2020a).

Chipako and Randall (2019) stated that the use of the on-site fertilizer-producing urinal, developed by Flanagan and Randall (2018), has the potential to complete the nutrient recovery loop by reusing urine and producing fertilizer products. In fact, the use of the fertilizer-producing urinals across the University of Cape Town has the potential to produce twice the required amount of fertilizer required for the university's sports fields (Chipako and Randall, 2019).

There is a concern over the health risk associated with the handling of source separated urine though. However, Höglund and co-workers (2002) mentioned that the risk of viral infection from the handling of source separated urine is low. As a result, the use of source separated urine in the agricultural sector as a fertilizer source was recommended (Höglund et al., 2002). Furthermore, the hydrolysis of urea should be considered for the collection and storage of urine using source separation technologies.

2.4 Urea hydrolysis

The high concentration of urease produced by urease-producing bacteria in the urine collection system results in the hydrolysis of urea (Ray et al., 2018). It is known that 85% of nitrogen in fresh urine is in the form of urea ($CO(NH_2)_2$) (Krajewska, 2009). However, fresh

urine undergoes hydrolysis caused by the urease enzyme that breaks down the urea into ammonium and bicarbonate ions (Alexander, 1977). When urine is hydrolyzed the pH increases to a pH range of 8.9 - 9.3 from an initial fresh urine pH range of 6.71 - 6.78 (Liu et al., 2008).

The hydrolysis of urea poses challenges for the storage, transportation, and the application of urine since urea hydrolysis causes mineral scaling in bathroom fixtures, piping and storage tanks (Ray et al., 2018). Therefore, the prevention of urea hydrolysis is necessary to avoid these challenges (Rodhe and Johansson, 1996).

It is important to understand the mechanism of urea hydrolysis to better extract nutrients from urine. Fresh urine takes three to seven days to completely hydrolyze and the rate of urea hydrolysis increases with an increase in storage temperature (Hellstrom et al., 1999; Liu et al., 2008). The hydrolysis of urine results in the chemical reaction shown in Equation 1 (Chipako and Randall, 2020b). This is enzymatic hydrolysis, which is induced by the enzyme urease, however, chemical hydrolysis can also occur when urine is exposed to elevated temperatures (above 50˚C) or a rapid increase in pH (Randall et al., 2016).

$$NH_2(CO)NH_2 + 2H_2O \rightarrow NH_3 + {NH_4}^+ + {HCO_3}^- \quad (1)$$

In the first step of the hydrolysis the urea reacts with water to form ammonia, ammonium, and bicarbonate ions. The pH of about 9.3, to which fresh urine rises due to hydrolysis, is also the buffer pH which indicates whether ammonia or ammonium is formed (Leyva-Ramos et al., 2004). The interaction between ammonia and ammonium in urine is explained in Equation 2.

$${NH_4}^+ \leftrightarrow NH_3 + H^+ \quad (2)$$

Furthermore, the relationship between ammonia and ammonium is influenced by the composition of the urine (Leyva-Ramos et al., 2004). As a result, the stabilization of urine is essential in the prevention of urea hydrolysis.

2.5 Stabilization of urine

Hellstrom and co-workers (1999) showed that there is a relationship between the pH of human urine and the rate of urea decomposition. The behaviour of urine at different pH environments was used to understand the stabilization of urine (Hellstrom et al., 1999).

The investigation by Chipako and Randall (2020b) considered the correlation between the pH of the urine and the most efficient technology that needs to be applied for nutrient recovery. The study provided insight for the use of fresh urine that has been stabilized compared to hydrolyzed urine. A distinction was made between fresh, hydrolyzed, and stabilized urine – each characterized by different pH values. The high nitrogen content (from urea) in fresh urine when compared to hydrolyzed urine, meant fresh urine had a higher nutrient recovery potential than hydrolyzed urine. As such, fresh urine could be stabilized to conserve urea. Therefore, the use of stabilized urine was preferred over hydrolyzed urine due to its higher urea content (Chipako and Randall, 2020b).

2.5.1 Acidification

Acidic compounds that are added to urine may reduce urea hydrolysis and the volatilization of ammonia (Aguilar, 2011). The acidification of the urine inhibits the formation of ammonia gas, thus reducing the loss of nitrogen in fresh human urine (Tun et al., 2016). For example, Hellstrom and co-workers (1999) showed that a one-time dosage of 60 meq sulphuric/acetic acid L^{-1} of undiluted urine was shown to inhibit the decomposition of urea for more than 100 days in stored urine. The urine had an average initial pH of 6.15 which decreased after acidification. The added acid also killed the pathogens present in the urine (Hellstrom et al., 1999).

There are several acids that can be used to stabilize urine. Different acids were investigated by Ray and co-workers (2018) for the inhibition of hydrolysis in fresh urine. The initial pH of the fresh and synthetic urine was within the range of pH 6 - 6.5. Glacial acetic acid, citric acid and vinegar were effective urea hydrolysis inhibitors dosed at concentrations within the range of 3.2×10^1 to 1.6×10^2 meq L^{-1}. Furthermore, citric acid was the most effective inhibitor (Ray et al., 2018). Although sulphuric acid and hydrochloric acid are stronger acids compared to

citric acid, it is much safer to use citric acid especially to produce urine-based fertilizers used for consumable goods.

Aguilar (2011) showed that there are alternative acid sources (such as olive oil mill wastewaters (OOMW) and water bubbled with carbon dioxide (CO_2)) that can be used to prevent the hydrolysis of urea for a storage period of more than six months. A dosage higher than 10% of OOMW stabilized urine with an initial pH of 5.7. The stabilized urine was compatible for fertilizer production (Aguilar, 2011).

Literature showed that the acidification of urine can prevent urea hydrolysis, even though the amount of urea that was conserved was not explicitly quantified. Furthermore, considerations for the application of an acid for the stabilization of urine is important. Ray and co-workers (2018) proposed an application method for acid inhibitors used in no-water urinals. The acid inhibitors would have to be released starting in the morning, with periodic dosing throughout the day, depending on the usage of the urinal (Ray et al., 2018). Alternatively, a one-time dosage of sulphuric/acetic acid and OOMW, shown in the study by Hellstrom and co-workers (1999) and Aguilar (2011), acidified urine samples for more than 100 days and six months respectively (Hellstrom et al., 1999; Aguilar, 2011).

2.5.2 Alkalinization

Alkalinizing human urine also inhibits the enzyme urease that causes urine hydrolysis (Liu et al., 2008). There are different alkalinization agents which can be used such as wood ash, calcium hydroxide ($Ca(OH)_2$) and magnesium oxide (MgO) (Randall et al., 2016; Senecal and Vinnerås, 2017; Simha et al., 2021).

Senecal and Vinnerås (2017) used wood ash as an alkaline ash-based dehydration bed for collected urine. Fresh urine was used for the study. The initial pH of the urine was not specified, however the pH of urine increased to more than 10.5, thus preventing the hydrolysis of urea. A static ash bed was most effective at a loading rate of 20 L kg^{-1} of ash, which achieved an effective urea retention range of 64 - 89.9% (Senecal and Vinnerås, 2017).

The use of $Ca(OH)_2$ has proven to be useful for the stabilization of urine. Dutta and Vinnerås (2016) developed a drying technique which used $Ca(OH)_2$ to inhibit the hydrolysis of urine. The initial pH of the urine was 6.1 and increased (pH > 10) after $Ca(OH)_2$ was dosed. Only 74% of the nitrogen was retained at 35˚C. The loss of 26% of nitrogen was attributed to a reduced evaporation rate, flooding of urine over drying agent and blockages in airflow (Dutta and Vinnerås, 2016).

Another study by Randall and co-workers (2016) showed that $Ca(OH)_2$ can effectively stabilize human urine. A dosage of 10 g $Ca(OH)_2$ L^{-1} of fresh urine was recommended to stabilize fresh urine. It was discovered that a temperature below 40 °C is optimal for the stabilization of fresh urine using $Ca(OH)_2$ (Randall et al., 2016). Furthermore, Randall and co-workers (2016) developed a provisional design chart for the stabilization of urine using $Ca(OH)_2$ (shown in Figure 5). The line 1 – 2 – 3 – 4 represents the saturation pH curve for $Ca(OH)_2$. Negligible urea loss is observed within the green region along point (2) and point (3). Although the rate of chemical urea loss is slow at a temperature below 14˚C, the excessively high pH (>13) increases the rate of urea loss. The rectangular region is an area where there is excessive enzymatic urea hydrolysis when the pH is below 11. An increase in the temperature below a pH of 11 causes a transition to occur from enzymatic to chemical urea hydrolysis. When the temperature is above 55˚C the enzymatic urea hydrolysis is inactivated and only the chemical urea hydrolysis occurs (Randall et al., 2016).

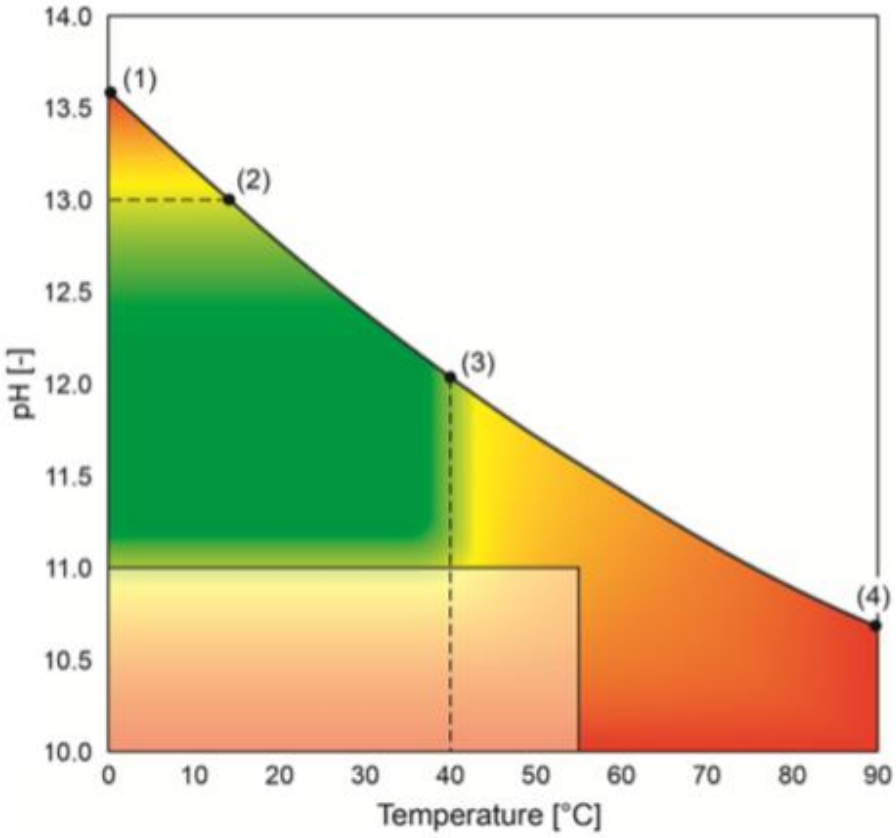


Figure 5: Design chart for the ideal operating conditions with respect to pH and temperature for the stabilization of urine with $Ca(OH)_2$ (Randall et al., 2016).

Recently, Simha and co-workers (2021) showed that the use of MgO as an alkaline agent is effective as a hydrolysis inhibitor for collected source separated fresh urine. Less than 2 g L^{-1} of MgO is required to increase the pH of the urine from a pH < 7 to a pH ± 10. The local collection and treatment of source separated urine using alkaline dehydration has a potential to recover 99% of nitrogen and 100% of potassium and phosphorus (Simha et al., 2021; Vasiljev et al., 2022).

The consensus from literature is that the alkalinization of urine occurs when the pH is greater than 10. The retention of urea varies among the methods, with the least urea retention (64%) recorded by Senecal and Vinnerås (2017) and the most retention of urea (99%) achieved by Vasiljev and co-workers (2021). Although $Ca(OH)_2$ is a much stronger base than MgO, less than 20% of the $Ca(OH)_2$ used to stabilize fresh urine is required for MgO to stabilize the same amount of fresh urine (Randall et al., 2016; Simha et al., 2021). This is because the recommended $Ca(OH)_2$ dose by Randall and co-workers (2016) was an overestimate to

account for urine with different compositions. Alkalinization is also preferred over acidification as a method for urea inhibition due to safety reasons and the ease of application (Chipako and Randall, 2020b).

2.6 Nutrient recovery from source separated urine

The use of source separated urine can be seen as a sustainable solution for resource recovery because it addresses the issues of sanitation, hygiene, water, and food security in a closed-loop nutrient cycle (Ganesapillai et al., 2016). However, technologies for closed-loop sanitation are still underdeveloped, therefore, further research is required (Simha and Ganesapillai, 2017).

According to Simha and Ganesapillai (2017) there are two main factors that influence the development of nutrient recovery systems. The first is the integrated treatment of post-urine diversion for the creation of value and risk minimization. The second is to address the issue of micropollutants such as pharmaceuticals and pathogens (Simha and Ganesapillai, 2017). In addition, the energy required to operate such a system should be considered.

The energy required for nutrient recovery from urine is comparable to and at times much less than the energy required for nutrient removal at a conventional wastewater treatment plant (Maurer et al., 2003). An example is the application of steam stripping and evaporation for the recovery of nutrients from source separated urine which led to high energy savings (Tettenborn et al., 2007).

The energy demand for a nutrient recovery technology is dependent on the complexity of the urine treatment process. Harder and co-workers (2019) investigated the pathways and the treatments of urine. Two strategies were identified for the treatment of urine and yellow water. The first strategy involved the inhibition of urea hydrolysis, the separation of water from urine, and the separation and elimination of micropollutants. The second strategy required the volume reduction of urine which would then enable selective nutrient extraction (Harder et al., 2019). It can be said that the volume reduction of urine is recommended for any nutrient recovery technology since the first strategy mentioned by Harder and co-workers (2019) also requires the separation of water from urine.

2.6.1 Volume reduction methods

The volume reduction of urine offers a sustainable way to manage the reuse of urine (Lind et al., 2001). Although urine only accounts for 1% of the total domestic wastewater volume (Spångberg et al., 2014), volume reduction methods still need to be considered for source separated urine. This is because a potential limitation with urine-derived fertilizer is the low nutrient concentration. As a result, there would be high-cost implications for the transportation of the collected urine due to the high volume required for urine reuse as a fertilizer (Pahore et al., 2010). However, volume reduction increases the concentration of the urine-derived fertilizer, making it comparable with commercial fertilizers (Senecal and Vinnerås, 2017).

Literature concerning volume reduction methods point to drying methods (such as evaporation), reverse osmosis and freezing methods (Hellstrom et al.,1999; Maurer et al., 2003). These methods often precede nutrient recovery methods discussed in section 2.6.2. Each of the methods are applied differently, however, all the methods attempt to achieve efficient volume reduction, while conserving the nutrients in the urine.

2.6.2 Nutrient recovery technologies

The nutrient content of source separated urine determines the quality of the urine-derived fertilizer. Hence, volume reduction offers an opportunity for the value creation of source separated urine by concentrating the urine. Therefore, the aim of a nutrient recovery technology is to produce urine-derived fertilizers, with maximum nutrient recovery at a low cost (Behrendt et al., 2002). Despite the development of nutrient recovery technologies over the years, some studies investigated the applicability of the direct use of urine as a fertilizer.

Heinonen-Tanski and co-workers (2007) directly used source separated urine as a fertilizer to grow cucumbers. The grown cucumbers were found to have the same quality as cucumbers grown from commercial mineral fertilizer (Heinonen-Tanski et al., 2007). Another study by Aguilar (2011) used stabilized urine directly as a fertilizer, but the effects of the fertilizer on crop production and pollution were not investigated (Aguilar, 2011). As such, the direct use of urine as a fertilizer is a concern due to the presence of pharmaceuticals (Maurer et al., 2006). Therefore, nutrient recovery technologies offer advanced methods for the better

extraction of nutrients from urine, while considering the elimination of micropollutants present in source separated urine.

2.6.2.1 Evaporation technologies

Evaporation occurs between the wet surface and the atmosphere when the local loss of latent heat is in equilibrium with the net supply of heat from radiation, convection, or conduction (Monteith, 1981). Evaporation is useful for volume reduction, while retaining the essential nutrients for fertilizer production by concentrating the solution (Antonini et al., 2012).

There are many ways to achieve evaporation. Pahore and co-workers (2010) used vertical gauze sheets to facilitate the evaporation of water from source separated urine. The objective of the study was to reduce the volume of 10 L of urine per day under the following conditions: 30 - 40˚C temperature and 20 - 40% humidity. The concentration of nitrogen, phosphorus and potassium in the fresh urine was 7 - 9, 0.2 - 0.21 and 0.9 - 1.1 g L^{-1} respectively. The nutrients were concentrated in 20% of the initial volume at optimal dry conditions (Pahore et al., 2010).

Another study assessed the evaporation performance of a photoreactor to produce urine-derived fertilizer. The method produced 360 g of solid fertilizer from 50 L of undiluted urine. The nutrient content in the fertilizer was comparable to that found in commercial mineral fertilizer, however micropollutants in the fertilizers were not investigated (Antonini et al., 2012).

Drying beds can be used as a dehydration technique to retain essential nutrients from urine. Dutta and Vinnerås (2016) used ash and calcium hydroxide as a drying bed media for fresh urine to produce urine-derived fertilizer. The optimal temperature condition of 35˚C, achieved 74% nitrogen recovery (Dutta and Vinnerås, 2016).

Senecal and Vinnerås (2017) also investigated the efficiency of drying beds. Fresh urine was added to the wood ash drying bed and evaporated at 35˚C and 65˚C, reducing the volume of the urine by up to 95%. The urine concentrate could be used as a urine-derived fertilizer product. The nutrient content of the concentrated urine was 7.8% nitrogen, 2.5% phosphorus and 10.9% potassium by weight, which was comparable to commercial fertilizers (Senecal and Vinnerås, 2017).

Another study by Vasiljev and co-workers (2022) explored the addition of magnesium-doped alkaline substrates to fresh human urine, after which it was dried at 38˚C. Complete nutrient recovery was achieved at pH > 10. A solid fertilizer product was produced with 10 - 11% nitrogen, 1 - 2% phosphorus and 2 - 3% potassium (Vasiljev et al., 2022).

Most of the urine-derived fertilizers manufactured through evaporation are comparable to commercial fertilizers. Although a higher evaporation temperature is favourable for faster evaporation, the decomposition of urea at a temperature greater than 40˚C remains a limiting factor (Randall et al., 2016). Literature has shown that a temperature range of 35 – 40˚C is optimal to produce commercial fertilizers through evaporation, which is favourable for urea conservation (Dutta and Vinnerås, 2016; Senecal and Vinnerås, 2017; Vasiljev et al., 2022).

2.6.2.2 Reverse osmosis and membrane processes technologies

Reverse osmosis is a membrane process driven by pressure. It is the most used technology in desalination plants (Wenten and Khoiruddin, 2016). Reverse osmosis can be applied to recover nitrogen from urine. This is achieved when membrane separation is used to get low nitrogen rejection and a high rejection for salts and other contaminants (Ray et al., 2020).

In a study by Thorneby and co-workers (1999), reverse osmosis reduced the volume of animal wastewater by 75 - 80% and the liquid fraction of slurry by up to 60%. Tubular polyamide membranes (AFC99) were used for the reverse osmosis process. The amount of ammonia retained was 93 - 97%, depending on the feed, and more than 98% of chemical oxygen demand and phosphorus was retained (Thorneby et al., 1999).

Ek and co-workers (2006) showed that the volume of source separated urine and rejected water from the digestion of sludge in sewage treatment plants could be reduced by at least 90% using reverse osmosis, while recovering 80 - 90% of the nitrogen. Two types of membranes were used: PCI AFC99 tube membranes and Filmtec SW30-HR spiral membranes. It was discovered that reverse osmosis was more economical than evaporation, which required double the cost of reverse osmosis and three times the energy needed by reverse osmosis (Ek et al., 2006).

More recently, Courtney and Randall (2022) showed that urine stabilized with calcium hydroxide would require pre-treatment to prevent membrane scaling as a result of excess calcium. Three pre-treatments were proposed: air bubbling, sodium bicarbonate addition and ammonium bicarbonate addition. The air bubbling pre-treatment was the most efficient for recovering nutrients and did not require additional chemicals. It was also shown that the recovery of nutrients from urine stabilized with citric acid was higher. However, organic fouling during the operation of the reverse osmosis process reduced the permeate flux significantly. Therefore, air bubbling pre-treatment for urine stabilized with calcium hydroxide was preferred (Courtney and Randall, 2022).

As an alternative to reverse osmosis, forward osmosis can be used to recover nitrogen and phosphorus from human urine, to be made into viable fertilizer products. Forward osmosis membranes with an active polyamide active layer were used in a study by Volpin and co-workers (2018). The process yielded a 60% concentration of the urine with a 40% and 50% recovery of phosphorus and nitrogen, respectively. Although the treatment process was categorized as low cost and robust, it was less efficient in the retention of nitrogen (Volpin et al., 2018).

There are other alternative membrane processes. Tun and co-workers (2016) showed that the application of direct contact membrane distillation for source separated urine was feasible to produce nitrogen-based fertilizer. Flat sheet commercial membranes with 0.45 µm pore sizes were used for the membrane distillation. The membrane distillation system was most effective for acidified and filtered source separated human urine. The specific ammonia transfer (SAT) was used as a measure of the ammonia retention capacity of the system. A SAT of 6.91 x 10^{-5} g-N/g-H_2O was attained, which is low meaning that most of the ammonia was retained in the urea (Tun et al., 2016).

Another study by Nagy and co-workers (2019) used hydrophobic gas separation membranes to recover nitrogen from wastewater and human urine. A maximum ammonia recovery of 85% was achieved at the following conditions: 60 membrane surface area/reactor volume ratio, 35˚C feed temperature with 350 L m^{-2} h^{-1} acid and an 8 h hydraulic retention time. It was recommended that the optimization of the hydrophobic gas separation system can become a competitive alternative nutrient recovery method (Nagy et al., 2019).

At least 80% of nitrogen can be retained by reverse osmosis (Ek et al., 2006), which is higher than the 50% of nitrogen recovered by forward osmosis (Volpin et al., 2018). Alternative membrane processes have also shown potential in the retention of nitrogen. The hydrophobic gas separation system was effective in retaining 85% of ammonia, which is within the range of nitrogen retention by reverse osmosis (Ek et al., 2006; Nagy et al., 2019). However, the hydrophobic gas separation system may only be limited to hydrolyzed urine as it retained nitrogen in the form of ammonia and not urea.

2.6.2.3 Freeze technologies

The freeze-thaw method concentrates the nutrients in the urine by freezing the urine and reducing the volume (Lind et al., 2001). An alternative freeze method is eutectic freeze crystallization (EFC). EFC cools a solution down to its lowest melting temperature known as the eutectic point (Randall and Nathoo, 2015).

Randall and Nathoo (2018) showed that the recovery of salts from stored urine was feasible under EFC conditions. The addition of acids to stored urine could produce more salts at higher temperatures, thus increasing the economic benefit of the process (Randall and Nathoo, 2018).

In addition to urine, Randall and Nathoo (2015) highlighted the potential use of EFC for the treatment and concentration of complex wastewaters. However, the use of the technology in the industry is still lacking for reasons such as excessive costs, complex mechanics, and a limited operation capacity (Rahman et al., 2007; Williams et al., 2013). Despite the challenges, a hybrid process that combines reverse osmosis as a pre-treatment for EFC was suggested as an alternative resource recovery method. This is because the combined process would not experience the problem of scaling and the addition of chemicals (Randall and Nathoo, 2015).

Lind and co-workers (2001) investigated freezing urine at -14 ˚C. The study allowed for 80% of the nutrients to be concentrated in 25% of the original volume. This method showed to be effective in the recovery of nutrients in source separated urine (Lind et al., 2001). It was noted that the effectiveness of the freezing method is comparable to that of reverse osmosis only in terms of concentration, but not in terms of energy (Lind et al., 2001; Ek et al., 2006).

2.6.2.4 Precipitation technologies

There are different forms of precipitates that can form, such as struvite, calcite, and hydroxyapatite (Udert et al., 2003b). The type of precipitate that forms is influenced by several factors including pH, temperature, the length of the pipe in a urine collection system and the type of flushing water (Udert et al., 2003b; Udert, Larsen et al., 2003a; Ronteltap et al., 2010).

Pradhan and co-workers (2017) used a combined nitrogen and phosphorus precipitation technique to recover nitrogen and phosphorus from human urine. The urine had an initial pH of 9.3, confirming that the urine was hydrolyzed (Chipako and Randall, 2020b). Calcium hydroxide was added to human urine to increase the pH that resulted in the production of ammonium gas and a calcium-phosphorus compound. The ammonium gas was stripped and passed through sulphuric acid producing ammonium sulfate and hydrogen triammonium disulfate. At the end of the process 85 – 99% of the nitrogen and 99% of the phosphorus was recovered (Pradhan et al., 2017).

Precipitation is also useful as a secondary resource recovery method. A stripping method was applied to recover nutrients from a column overflow, following the adsorption of urea from hydrolyzed human urine (pH between 9.1 - 10.2) using microwave activated carbon prepared from coconut shells. More than 90% of struvite was recovered after the column overflow was dephosphatized using magnesium oxide (Ganesapillai et al., 2016).

There are several types of struvite that can be formed through precipitation. Two forms of struvite were investigated by Wilsenach and co-workers (2007), namely magnesium ammonium phosphate and potassium magnesium phosphate (struvite-K), which were produced from synthetic urine. The synthetic urine solution was adjusted to a pH of 9.4 using urease. The compaction of the struvite was inefficient; however, the crystals maintained their orthorhombic structure. The average influent phosphate which was removed was 95%, for both ammonium and potassium struvite. The study recommended struvite precipitation as a downstream biological-N removal process rather than a resource recovery process (Wilsenach et al., 2007).

The precipitation technologies which have been reviewed have shown that the precipitation method is applicable for hydrolyzed urine with a pH of approximately 9.3 (Liu et al., 2008).

However, the pH of the hydrolyzed urine used by Ganesapillai and co-workers (2016) reached a pH of 10.2. This is because the addition of magnesium or calcium to urine results in the formation of phosphate-based precipitates, and an increase in pH (Barbosa et al., 2016). Therefore, precipitates can form at a high pH while conserving urea since the urine would be stabilized by alkalinization. However, when precipitates are formed within a pH range of 7 - 9.3, the urine is often only hydrolyzed, thus the urea is not conserved.

2.6.2.5 Hybrid technologies

Hybrid technologies maximize the advantages of the individual technologies to enhance the efficiency of the overall hybrid technology or to mitigate the disadvantages of the individual hybrid systems.

An example of a hybrid technology is anion exchange resin (which uses ferric oxide) for the recovery of phosphorus. O'Neal and Boyer (2013) treated different waste streams (undiluted fresh urine, diluted fresh urine with tap water, greywater, mixture of urine and greywater, anaerobic digester supernatant, and secondary wastewater effluent) with the technology. The study discovered that source separated fresh urine had the highest potential for phosphorus recovery. The amount of phosphorus recovered was 868 mg P^{-1} d^{-1}, compared to 590 mg P^{-1} d^{-1} recovered from hydrolyzed urine (O'Neal and Boyer, 2013). This suggests that the use of source separated fresh urine is more beneficial than hydrolyzed urine for resource recovery.

Another study by Chipako and Randall (2020b) investigated the combined use of urine alkalinization and volume reduction as an efficient urine treatment process. Calcium hydroxide and reverse osmosis were used for alkalinization and volume reduction, respectively. The hybrid system is like the first strategy recommended by Harder and co-workers (2019) for nutrient recovery from urine. The theoretical yield of the liquid fertilizer had an NPK ratio of 3.3 : 0 : 0.8. In addition, the recovered calcium phosphate was 11 g L^{-1} of treated urine (Chipako and Randall, 2020b). This proves that the use of hybrid nutrient recovery systems is beneficial, even though they may have higher cost implications.

Boyer and Saetta (2019) identified some nutrient recovery technologies for stabilized urine. Membrane distillation, eutectic freeze concentration and solar evaporation were identified

as some of the nutrient recovery and volume reduction technologies for urine. The technologies could offer more benefits than conventional systems, however there are still research gaps (Boyer and Saetta, 2019). Therefore, the combined use of the technologies (once fully developed) for nutrient recovery and volume reduction can be beneficial for urine diversion systems. Nonetheless, resource recovery processes need to consider the removal of micropollutants such as pharmaceuticals to ensure that safe fertilizer products are produced (Simha and Ganesapillai, 2017).

2.7 Pharmaceuticals in the environment

Pharmaceuticals are used for biological activity and often remain unchanged when excreted (Kummerer, 2010). They are designed to stimulate a response in the human or animal body with a specific target (Zuccato et al., 2006). Over the years, the demand for pharmaceutical products (for domestic and hospital use) has increased (Li, 2014). In the past, little was known about the exposure of pharmaceuticals in the environment, however, there is some evidence of the effects of pharmaceuticals in the environment (Halling-Sorensen et al., 1998; Kummerer, 2010). Therefore, the cumulative effects of the pharmaceuticals in the environment need to be investigated, even though pharmaceuticals are administered at a low dosage (Zuccato et al., 2006).

2.7.1 The occurrence of pharmaceuticals in the environment

Some of the pharmaceuticals that are released in the environment are degraded through natural processes. Nature uses biotransformation, photolysis, and sorption to reduce pharmaceuticals present in the urine. Yet, there are other pharmaceuticals which are not biodegradable (Li, 2014).

Significant amounts of pharmaceuticals have been found in wastewater treatment plants (Halling-Sorensen et al., 1998). The wastewater treatment process is a crucial step in the control of pharmaceutical contamination, but wastewater treatment processes do not effectively remove most of the water-borne pharmaceuticals (Zuccato et al., 2006).

It was discovered that wastewater treatment plants remove pollutants at an efficiency below 10%. This leads to a considerable number of contaminants passing through the wastewater treatment plants into the environment (Calisto and Esteves, 2009). As a result, the presence of pharmaceuticals in the environment can have an ecotoxicological effect. For instance, pharmaceuticals in the aquatic environment cause a disruption to the endocrine system of aquatic life (Sumpter, 1998).

Pharmaceuticals found in the environment are in the order of ηg - μg L^{-1}. Furthermore, there is evidence of the bioaccumulation of pharmaceuticals in the environment. Even though the concentration levels are below the toxic level, the chronic level should be determined to assess the long-term effects of the presence of pharmaceuticals in the environment (Calisto and Esteves, 2009). Pharmaceuticals in the environment such as antibiotics, contribute to bacterial resistance and the transfer of the pharmaceutical molecules to humans through the food-chain biomagnification (Zuccato et al., 2006).

The pollution resulting from the presence of pharmaceuticals in the environment is different in each country due to the preferred treatment options and market availability. A national scale case study was conducted by Zuccato and co-workers (2006) to investigate the extent of the environmental contamination of pharmaceuticals in Italy. The findings from the study suggested that pharmaceuticals are widespread contaminants that enter the environment through various points (Zuccato et al., 2006).

Despite the unknown risks of the presence of pharmaceuticals in the environment, such as antibiotics, the proper use and disposal of the pharmaceuticals is necessary to reduce the risk posed to people and the environment (Kümmerer, 2004).

2.7.2 The fate of pharmaceuticals in the environment

Recently, the emergence of pharmaceuticals in the environment has become a global concern. Data concerning the effects of pharmaceuticals present in the environment has been scattered, lacking a systematic approach in its findings (Zuccato et al., 2006). Strategies have been proposed for the management and reduction of pharmaceuticals in the environment.

The persistence and fate of pharmaceuticals present in the environment is a key factor to consider in conducting an ecological risk assessment process. The frequent entry of pharmaceuticals into the environment, through the discharge of wastewater, should be considered for an ecological risk assessment (Ankley et al., 2007).

An environmental load system was developed to quantify the number of pharmaceuticals present in the environment. It is an indicator which determines the extent of the pharmaceutical contamination in the environment. The environmental load is calculated by multiplying the rate of metabolism (in humans or animals) with the sales figures (Zuccato et al., 2006).

A risk management strategy was recommended to limit the presence of pharmaceuticals in the environment. The strategy is to set up regulations and standards for emerging organic contaminants to effectively manage, control and restrict the entry points of pharmaceuticals into the environment. In addition, controlling and restricting the source of the pharmaceuticals would be effective in reducing the presence of pharmaceuticals in the environment (Li, 2014).

2.8 Pharmaceutical removal methods

Various methods have been developed for the removal of pharmaceuticals. Benefits associated with the better removal of pharmaceuticals in wastewater include improvements in the endocrine system (Ahmed et al., 2016).

Furthermore, it is known that the removal of pharmaceuticals from source separated urine is energy efficient. The energy required for the removal of pharmaceuticals in source separated urine is comparable to the energy required in a conventional wastewater treatment plant to remove pharmaceuticals (Tettenborn et al., 2007).

Farmers have expressed concerns over the direct use of untreated source separated urine as a fertilizer. The pharmaceuticals in the untreated urine can be transmitted to the grown vegetation, posing a threat to human health (Udert and Wächter, 2012). Therefore, pharmaceutical removal methods are vital for the safe use of urine-derived fertilizers.

2.8.1 Biological removal methods

Biodegradation occurs when microorganisms (such as bacteria and fungi) break down organic substances into simpler chemical substances. This results in the partial or complete mineralization of the organic substance (Garcia-Rodríguez et al., 2014).

Ahmed and co-workers (2016) investigated the efficiency of some biological removal methods. The study suggested that the integrated use of activated sludge processes with ozonation/membrane bioreactors improves the removal efficiency of emerging contaminants. The pesticides were removed more efficiently when microalgae were applied with biological activated carbon. The hybrid system, which included biological activated carbon, was most effective in the removal of endocrine disrupting compounds and personal care products. Another hybrid ozonation-ultrasound system removed almost 100% of many pharmaceuticals (Ahmed et al., 2016). An observation was made that biological removal methods are most effective when used as a combined system.

2.8.2 Membrane separation methods

Membrane technologies are used to purify wastewater, thus removing contaminants from the wastewater stream. Membrane technologies are defined by the membrane pore size. The most used membrane technologies are microfiltration (0.01 - 0 µm), reverse osmosis (up to 100 Da), nanofiltration (100 - 500 Da) and ultrafiltration (500 - 100,000 Da) (Nicolaisen, 2002).

Membrane technologies can be applied to treat wastewater influent. Hartig and co-workers (2001) used microfiltration and subsequent ultrafiltration to treat municipal waste which was spiked with sulphonamides in the order of µg L^{-1}. The elimination rate of low molecular weight micropollutants was improved when the waste stream was treated further with powered activated carbon (Hartig et al., 2001).

Contrary, Pronk and co-workers (2006) investigated the pharmaceutical removal from source separated urine using nanofiltration. The study found that the NF270 membrane by Dow-Filmtec was most effective, removing over 92% of pharmaceuticals and estrogenic compounds from salts. Moreover, electrodialysis membranes were also recommended for the removal of pharmaceuticals (Pronk et al., 2006).

Although the pharmaceuticals are said to be removed from the waste stream by the membrane technology, they are separated from the waste stream rather than removed. The objective of membrane technology is to produce pure water downstream. However, the brine solution from treated source separated urine would be the fertilizer product. It was shown that a nanofiltration membrane rejects over 90% of pharmaceuticals in fresh urine (Pronk et al., 2006). This suggests that the fertilizer product (which is upstream) would still have pharmaceuticals.

2.8.3 Chemical oxidation methods

Chemical oxidation happens when an oxidant (such as chlorine, chlorine dioxide, ozone or OH radicals) reacts with the pharmaceuticals, thereby degrading the pharmaceutical molecules (Prousek, 1996). Oxidative methods and photolysis are often used as a combined method to degrade pharmaceuticals. In addition, the knowledge of the photostability of pharmaceuticals assists in understanding the degradation of the pharmaceuticals due to oxidation and photolysis (Ahmad et al., 2016).

Three alternative chemical oxidation processes were considered for the removal of micropollutants: ozonation, ozonation with postelectrodialysis and electrodialysis with postozonation. Ozonation on its own was less effective than the two latter removal processes. The latter removal processes achieved the same level of nutrient and micropollutant extraction as a conventional wastewater treatment plant (Dodd et al., 2008). This proves that the combined oxidative treatment of waste is more applicable for the removal of pharmaceuticals.

A study by Wols and co-workers (2013) used a UV/H_2O_2 process to degrade 40 pharmaceuticals found in source water. Most of the pharmaceuticals were well degraded, but the degradation rates of the pharmaceuticals varied significantly. However, a 90% degradation was observed for most of the pharmaceuticals in natural water at a UV dose between 500 (MP) and 1000 (LP) mJ cm^{-2}, and 10 mg L^{-1} hydrogen peroxide (Wols et al., 2013).

Another study by Ahmed and co-workers (2016) investigated the following chemical oxidation removal methods: ozonation/H_2O_2, UV photolysis/H_2O_2 and photo-Fenton processes. The oxidation processes removed almost 100% of the pharmaceuticals, pesticides, and beta

blockers. The most effective processes for the removal of contaminants of emerging concern was the ozonation/H_2O_2 removal process (Ahmed et al., 2016).

Literature suggests that the combined use of oxidation methods is more efficient in the removal of pharmaceuticals. Thus, the right combination of oxidation methods yields a high degradation of pharmaceuticals. It seems the most common oxidation method which is used is the UV/H_2O_2 process, but Ahmed and co-workers (2016) showed that the ozonation/H_2O_2 is more effective in the removal of pharmaceuticals. Although oxidative methods are effective, the cost implications and the complex application of the removal methods may be a hindrance for use in a simple urine treatment process.

2.8.4 High and low pH methods

The pH is an important parameter to consider for the degradation of pharmaceuticals. It has an impact on the degradation rate of the pharmaceuticals, however, the degradation of the pharmaceuticals due to a change in pH is dependent on the molecular structure of the pharmaceuticals (Yin et al., 2017).

Yin and co-workers (2017) investigated the degradation of five pharmaceuticals (atenolol, metoprolol, propranolol, fluoxetine, and venlafaxine) to evaluate the pharmaceutical degradation variability within a pH range of 2 - 12. The degradation of propranolol and venlafaxine increased with an increase in pH while atenolol, metoprolol and fluoxetine experienced the highest degradation at a pH of 7, 2 and 12, respectively. The half-lives of the pharmaceuticals varied significantly which were as follows: 5.7 - 28.5 d for propranolol, 29.6 - 78.2 d for metoprolol, 56.3 - 81.4 d for atenolol, 46.6 - 183.2 d for fluoxetine and 68.8 - 145.4 d for venlafaxine (Yin et al., 2017). It is inferred that the pharmaceuticals were deprotonated at varying degrees due to the difference in the acid and basic functional groups (such as carboxylic acid, hydroxyl groups and amines) which are present in the structure of the pharmaceuticals (Hapeshi et al., 2010).

On the other hand, Mohammed-Ali (2012) found that tetracycline was less stable in an alkaline solution than an acidic solution. The absorbance of tetracycline was measured, and a linear degradation (with a positive slope) was observed over five days, thus, the degradation

of tetracycline progressed over time. The degradation of tetracycline in high pH occurred when tetracycline opened its ring to form isotetracycline (Mohammed-Ali, 2012).

Another study by Agrahari and co-workers (2015) found that tenofovir was less stable in strong acidic and alkaline environments. The approximate shelf-life, half-life and time required for a 90% degradation of tenofovir was 3.84, 25.3, and 84 h under acidic conditions, and 58.3, 385, and 1280 h under alkaline conditions. The degradation of tenofovir was more favourable in a strong acidic environment, since further hydrolysis in strong acidic conditions occurs due to non-chromophoric low molecular weight compounds that alter the bonds of the degradation products (Agrahari et al., 2015).

The change of pH influences other micropollutants apart from pharmaceuticals. The calcium oxide (CaO) treatment of *A. suum* eggs (which pose an infective hazard) was investigated for sewage sludge. A concentration of 10% (w/w) CaO (85%) was added to the sewage sludge. The high pH (>12) destroyed the embryonate ability of the *A. suum* eggs (Eriksen et al., (1996).

Literature has shown that adjusting the pH of a solution (to become either basic or acidic) influences the degradation of the pharmaceuticals. Yin and co-workers (2017) showed that the degradation of each pharmaceutical under different pH conditions is varied. As such, Table 1 provides a summary of the degradation behaviour due to a change in pH of the pharmaceuticals investigated for this work.

Table 1: The degradation of pharmaceuticals due to a change in pH.

Pharmaceutical	Degradation of the pharmaceutical due to a change in pH
Paracetamol	Yang and co-workers (2008) discovered that the degradation of paracetamol (in aqueous solution) by TiO_2 photocatalysis increased slowly between pH 3.5 and 9.5. However, the degradation rate decreased at a pH between 9.5 and 11.0 (Yang et al., 2008).
Salicylic acid	Rao and co-workers (2009) used a ZnO catalyst to degrade salicylic acid. The study found that the degradation of salicylic acid was most effective at a neutral pH (Rao et al., 2009).
Diclofenac	Bagal and Gogate (2013) used a combined process of hydrodynamic cavitation and heterogeneous photocatalysis to degrade diclofenac sodium. The optimal degradation pH was pH 4 (Bagal and Gogate, 2013).
Clopidogrel	The study by Raijada and co-workers (2010) suggested that alkaline microenvironments need to be avoided for clopidogrel bisulphate since it causes the drug to change to an oily free base i.e., causes degradation (Raijada et al., 2010).
Chlorpheniramine maleate	Lv and co-workers (2015) showed that increasing the pH of the chlorpheniramine increased the degradation of the drug. A higher degradation rate was observed between pH 8 to 9 which might be due to the release of more OH radicals (Lv et al., 2015).
Zidovudine	A study by Dunge and co-workers (2004) investigated the degradation behaviour of zidovudine under various conditions. Zidovudine hydrolyzed more in an acidic environment than an alkali environment (Dunge et al., 2004).
Lamivudine	Wang and co-workers (2019) investigated the degradation of lamivudine using bicarbonate enhancing electrochemical degradation. The study showed that the initial pH did not have an effect in the degradation of lamivudine due to the bicarbonate enhancing electrochemical degradation (Wang et al., 2019).
Tenofovir	According to Golla and co-workers (2016) the degradation of tenofovir alafenamide fumarate (TAF) and tenofovir disoproxil fumarate (TDF) increased with an increase in pH. TDF was more unstable than TAF at pH 5, 6.8 and 10 (Golla et al., 2016).
Nevirapine	Bhembe and co-workers (2020) investigated the photocatalytic degradation of nevirapine. The study showed that nevirapine showed a higher degradation efficiency in an acidic environment than an alkaline environment (Bhembe et al., 2020)
Stavudine	A study by Dunge and co-workers (2004) investigated the degradation behaviour of stavudine under various conditions. Stavudine hydrolyzed more in an acidic environment than an alkali environment (Dunge et al., 2004).
Abacavir sulfate	A study by Ramesh and co-workers (2020) revealed that when abacavir sulfate was subjected to alkaline hydrolysis, the pharmaceutical was not degraded (Ramesh et al., 2020).

2.8.5 Granular activated carbon methods

Granular activated carbon (GAC) is an adsorptive method that is used for the removal of micropollutants such as pharmaceuticals. GAC is an appealing pharmaceutical removal method for the following reasons: it requires a low energy, it can be used in batch or continuous-flow reactors, the reactors can be arranged in multiple ways and the used GAC filter beds can be reused and reactivated (Crittenden et al., 1999).

The granular size of the GAC is an important consideration for the adsorption of micropollutants. Köpping and co-workers (2020) investigated the removal of 11 pharmaceuticals from nitrified and distilled urine using GAC. Two columns of GAC (one with coarse GAC and the other with fine GAC) were used for the experiments. The removal efficiency of the two GAC columns was the same because the internal surface area of the fine and coarse GAC were similar. It was deduced that the dominating adsorption occurs in the internal surface area of the GAC. However, the amount of GAC which would be required to treat the same volume of urine would be different due to the difference in the intraparticle diffusion path. Nevertheless, most of the nutrients in the nitrified urine were retained, while effectively removing the pharmaceuticals (Köpping et al., 2020).

It was discovered that the adsorption efficiency of GAC varies for each micropollutant. A study by Yang and co-workers (2011) investigated the removal of pharmaceutically active compounds and personal care products found in wastewater. Various methods were selected for the treatment of the wastewater, including GAC, which removed 88% and 77% of carbamazepine and erythromycin on average, respectively. Yet, primidone, DEET and caffeine were not adsorbed by the GAC. The difference in the adsorption of the compounds was attributed to the physical-chemical properties of the compounds. Furthermore, GAC tends to adsorb hydrophobic compounds (Yang et al., 2011).

GAC can be combined with a filtration process. Li and co-workers (2018) investigated lab-scale GAC sandwich slow sand filters with varying GAC depths. A sand filter with 20 cm GAC achieved 98.2% pharmaceutical removal. The results from the study suggested that the GAC sandwich slow sand filters were an effective treatment process for the removal of pharmaceuticals and personal care products from wastewater (Li et al., 2018).

The type of sorbent is also a crucial factor for the absorbance of micropollutants. Rostvall and co-workers (2018) studied the removal efficiency of five different sorbents (sand, lignite, Xylit, granular activated carbon (GAC) and GAC + Polonite®) for the removal of 83 selected micropollutants (including pharmaceuticals). GAC and GAC + Polonite® were the most effective sorbents with an average removal of 97%. It was 57% more efficient than a common sand filtration bed system. The internal surface of the GAC contributed the most in the high removal efficiency of the micropollutants (Rostvall et al., 2018). The macro- and mesopores of the GAC allowed the micropollutants to reach the micropores where most of the sorption happens (Kose, 2010; Priya and Radha, 2017).

Furthermore, the regeneration and reactivation ability of saturated GAC is important for the reuse of GAC, thus reducing GAC waste. Many ways are offered for the regeneration of GAC which are thermal volatilization, chemical extraction, and bio-regeneration. Alternatively, ultrasound applied at 20 kHz can be used to regenerate GAC (Lim and Okada, 2005).

2.8.6 Hydrogen peroxide methods

Oxidation is a mechanism through which the degradation of pharmaceuticals can happen in liquid or solid form. Hydrogen peroxide is a specific oxidant that can selectively oxidize sulphides to sulfoxides. Hydrogen peroxide is reduced to form hydroxyl radicals, which makes it highly oxidizing (Hovorka and Schoneich, 2001).

Some pharmaceuticals have shown not to degrade when exposed to hydrogen peroxide. For example, zidovudine was stable when exposed to hydrogen peroxide. Since zidovudine is unable to form epoxides, thus, it cannot be oxidized by hydrogen peroxide (Dunge et al., 2004). Instead, hydrogen peroxide is often combined with ultraviolet (UV). Less than 5% of paracetamol was degraded when only hydrogen peroxide was used. However, paracetamol was completely degraded when hydrogen peroxide was applied with UV. The UV increased the formation of hydroxyl radicals which degraded paracetamol (Bavasso et al., 2020). A similar pattern was observed for the degradation of salicylic acid. The degradation rate of salicylic acid increased as the amount of hydrogen peroxide used was increased, while UV was applied simultaneously (Adan et al., 2006).

The type of hydrogen peroxide influences the degradation of pharmaceuticals. The degradation of nevirapine was investigated for two different hydrogen peroxide concentrations. Hydrogen peroxide 6% (w/v) and hydrogen peroxide 50% (w/v) yielded a degradation of 4.93% and 21.97% respectively. From the results it can be deduced that a stronger hydrogen peroxide allows for more hydroxyl radicals to be formed, thus resulting in more degradation (Kaul et al., 2004).

Literature was reviewed for the degradation of each pharmaceutical chosen for this work due to hydrogen peroxide (shown in Table 2). The findings from literature were as follows: two hours was the most common retention time range; the 30% v/v was the most common type of hydrogen peroxide used; and for some studies, electrogenerated hydrogen peroxide was preferred over liquid hydrogen peroxide. However, a dose of 1 mL of liquid hydrogen peroxide per 10 mL of solution was used by Agrawal and co-workers (2003).

Table 2: The degradation of pharmaceuticals due to hydrogen peroxide.

Pharmaceutical	Degradation of the pharmaceutical due to hydrogen peroxide
Paracetamol	Bavasso and co-workers (2020) showed that the combination of UV and electrogenerated hydrogen peroxide formed oxidizing species that resulted in the total degradation of paracetamol. The use of hydrogen peroxide alone yielded a degradation of less than 5% (Bavasso et al., 2020).
Salicylic acid	A study by Adan and co-workers (2006) showed that the degradation rate of salicylic acid increased with increasing the amount of hydrogen peroxide that was added when combined with UV (Adan et al., 2006).
Diclofenac	Hofmann and co-workers (2007) showed that diclofenac can be degraded using heterogeneous catalytic oxidation with hydrogen peroxide (Hofmann et al., 2007).
Clopidogrel	An investigation by Agrawal and co-workers (2003) found that the degradation of clopidogrel bisulphate due to hydrogen peroxide was 18.63% after an hour of treatment (Agrawal et al., 2003).
Chlorpheniramine maleate	A study by Moyano and co-workers (2005) found that hydrogen peroxide degrades chlorpheniramine maleate by 3% after 30 minutes of treatment (Moyano et al., 2005).
Zidovudine	Dunge and co-workers (2004) showed that zidovudine was stable when exposed to hydrogen peroxide (Dunge et al., 2004).
Lamivudine	A study by Feliciano and co-workers (2020) discovered that a 95% degradation of lamivudine could be achieved by adding 250 mg L^{-1} of hydrogen peroxide (Feliciano et al., 2020).
Tenofovir	A stability indicating study by Bhirud and Hiremath (2013) showed that tenofovir disoproxil fumarate degraded by 4.79% after 8 hours of exposure to hydrogen peroxide (Bhirud and Hiremath, 2013).
Nevirapine	A stability indicating study by Kaul and co-workers (2004) investigated the degradation of nevirapine at two different concentrations of hydrogen peroxide. The degradation of hydrogen peroxide 6% (w/v) and hydrogen peroxide 50% (w/v) were 4.93% and 21.97% respectively (Kaul et al., 2004).
Stavudine	A study by Dunge and co-workers (2004) showed that stavudine degraded when exposed to hydrogen peroxide (Dunge et al., 2004).
Abacavir sulfate	Rao and co-workers (2011) found that the 3% hydrogen peroxide was ineffective in degrading abacavir sulphate even after 7 days (Rao et al., 2011).

2.8.7 Hydrodynamic cavitation methods

Hydrodynamic cavitation (HC) is an energy and cost-effective technology used to treat effluents. It is a physical process which requires minimal chemical addition (Dular et al., 2015). Cavitation bubbles are created which grow from their original size, causing high velocities, high pressures, and elevated temperatures. This results in noises and damage to material i.e., causing degradation (Brennen, 1995). The turbulent collapse of the cavitation bubbles results in the creation of hydroxyl radicals, which then degrade micropollutants such as pharmaceuticals (Thanekar and Gogate, 2018).

Dular and co-workers (2015) found that HC was more applicable than acoustic cavitation in terms of easiness to scale, robustness, continuous operation, and removal efficiency (Dular et al., 2015). Additionally, a thorough literature study by Mancuso and co-workers (2020) showed that HC is an effective mechanical process for use in wastewater treatment plants to treat effluents with organic, toxic, and bio-refractory contaminants. However, the technology is new and would require process optimization (Mancuso et al., 2020).

Literature shows that the degradation of pharmaceuticals due to HC is enhanced when used as a combined process. Bagal and Gogate (2013) used HC to remove diclofenac sodium. A slit venturi with a throat diameter of 1.91 mm was the cavitation device. A maximum degradation of 95% (with a 76% reduction in TOC) was observed when HC was combined with UV/TiO_2/H_2O_2. The degradation of diclofenac sodium increased due to the increased production of hydroxyl radicals which degrade the pharmaceutical. The primary degradation mechanism of diclofenac was hydroxylation, since diclofenac sodium has a non-volatile nature (Bagal and Gogate, 2013).

Another study by Wang and co-workers (2017) investigated the degradation of tetracycline using HC. A venturi tube with a throat diameter of 2 mm was used as the cavitation device. The process was combined with TiO_2 (P25) photocatalytic. A synergistic effect was observed for the combined process. The combined process was more effective than the individual process. A removal efficiency greater than 90% was achieved by the combined process after 90 minutes (Wang et al., 2017). Tetracycline is a compound with high solubility and low vapour pressure, thus, the degradation of tetracycline due to only HC was from oxidation due to the hydroxyl radicals (Suslick et al., 1997). The addition of a catalyst provided surface area

on which photoactivity could occur, thereby increasing the degradation of tetracycline (Chen and Smirniotis, 2002). Nevertheless, it is known that there are factors that influence the degradation efficiency of the HC system which are the inlet pressure, cavitation device and temperature.

The inlet pressure is a key factor for a HC system which influences the cavitation intensity. Each solution has a specific optimum inlet pressure at which it can be treated (Rajoriya et al., 2016). Mishra and Gogate (2010) found the optimum inlet pressure (486.4 kPa) to treat Rhodamine B dye. When the pressure was increased to 587.7 kPa, the degradation of the Rhodamine B dye decreased significantly (Mishra and Gogate, 2010). A similar pattern was observed in a study by Gogate and Bhosale (2013). The study found that the optimum inlet pressure to treat orange acid II dye with a HC system was 490.3 kPa. However, when the inlet pressure was increased to 686.5 kPa the extent of degradation decreased by 26.9% (Gogate and Bhosale, 2013).

The operating temperature of a HC system influences the degradation of micropollutants in wastewater (Rajoriya et al., 2016). Some of the researchers have reached a consensus that the maximum cavitation aggressiveness happens at a temperature of 50˚C (Šarc et al., 2017). It was shown by Wang and co-workers (2009) that the maximum degradation of Rhodamine B occurred at a temperature of 50˚C (Wang et al., 2009). Another study by Wu and co-workers (2014) discovered that the degradation of chitosan increased from 54% to 89% when the temperature was adjusted from 30˚C to 70˚C (Wu et al., 2014). Although previous studies suggest that the maximum cavitation occurs at a temperature of 50˚C, it was important to consider that urea undergoes chemical hydrolysis at a temperature greater than 40˚C (Randall et al., 2016).

The type of cavitation device affects the degradation of micropollutants in wastewater. Jain and co-workers (2014) investigated the optimal geometrical and operational parameters of slit and circular venturis. The highest cavitational yield for a slit venturi was achieved at an inlet pressure of 810.6 kPa, 1:1 slit height to length ratio and a divergent angle of 5.5˚. The slit venturi had a slit of 2 mm and a depth of 3.14 mm. Contrary, the highest cavitational yield for a circular venturi was achieved at an inlet pressure of 505.6 kPa, 1:1 slit height to length ratio and a divergent angle of 6.5˚. The throat of the circular venturi had a 2 mm diameter. It was also found that a higher divergent angle resulted in a decrease of the cavitational

intensity (Jain et al., 2014). Randhavane (2019) showed that an orifice plate with seventeen 1.5 mm orifices performed better than an orifice plate with a single 2 mm orifice (Randhavane, 2019). It was also shown that for orifices under the same flow condition, an orifice with a greater number of holes and a small hole diameter had a better removal efficiency (Sivakumar and Pandit, 2002). Furthermore, Saharan and co-workers (2013) suggested that a circular venturi performs better than an orifice.

The solution pH is an important parameter which influences the degradation of micropollutants (Madhu et al., 2015). The optimization of the solution pH assists in achieving maximum degradation in the shortest time. However, the optimum pH of each waste solution is different (Rajoriya et al., 2016). For instance, the maximum degradation of acid red 88 dye was at pH 2, while the maximum degradation of malachite green was achieved at pH 11 (Saharan et al., 2012; Madhu et al., 2015). Another study by Ghaly and co-workers (2014) looked at the degradation of orange IV dye at pH 2 and pH 10. The study found that the optimum degradation for orange IV dye was at pH 2, while the degradation at pH 10 only achieved 12.4% of the degradation at pH 2 (Ghaly et al., 2014).

Literature suggests that the HC system is most efficient when combined with a chemical oxidation process. The use of a venturi with a small throat diameter (≤ 2mm) was effective in the removal of pharmaceuticals. However, the application of an orifice with a similar diameter was reviewed through literature. Additionally, little is known about the degradation of pharmaceuticals in urine due to a HC system, therefore, the factors that influence the degradation of pharmaceuticals would need to be considered.

2.9 Pharmaceutical analysis methods

2.9.1 High performance liquid chromatography

Chromatography is a separation technique used to identify components in a mixture. The components in the mixture are separated when they dissolve in a solvent or when they are adsorbed onto a surface. Methods of chromatography have a stationary phase (static part) and a mobile phase (moving part) (Faust, 1997). According to Faust (1997), the stationary phase of HPLC has smaller particles, as a result, high pressure is applied to the solvent to overcome the increase in capillary action which causes difficulty for the column to drain. The

stationary phase is usually made of uniform porous silica particles with a diameter of 10^{-6} m and surface pore diameter of 10^{-8} - 10^{-9} m. A non-volatile liquid is used to bond the silica particles by covalent bonds. The stationary phase particles are packed inside the HPLC column and are held in position by glass fibre columns with an inert alkyl silane molecule coat. The HPLC columns are 10 - 30 cm long, with a 4 mm internal diameter. The reproducibility of the HPLC is maintained by keeping a constant flow rate. Twin cylinder reciprocating pumps are usually used which can produce up to 10 MPa. Therefore, the instrumentation of the HPLC is made of stainless steel to withstand the high pressure. The flow rate in the HPLC is slow (0.5 - 5 mL min^{-1}) which requires quick and precise sample injections; and the sample volumes are small (5 – 10 mm^3). As a result the samples are too small to be extracted, rather, the solutes are analyzed while they leave the column. The components are analyzed in a micro cell using ultraviolet radiation. The retention time for the solute is then established for the analysis of the components in the solute for a column operated at certain conditions (Faust, 1997).

2.9.2 Ultraviolet spectroscopy

According to Clark and co-workers (1993) ultraviolet (UV) spectroscopy measures the absorbance of a solution (which is directly proportional to the concentration of the solution) as a function of wavelength. Different compounds have specific wavelengths at which they can be detected by the UV spectroscopy (Clark et al., 1993). Therefore, each pharmaceutical has a specific wavelength at which it can be analyzed.

2.10 Motivation for the current study

There is substantial work done in the development of pharmaceutical removal methods, particularly for the following removal methods: high pH, granular activated carbon (GAC), hydrogen peroxide and hydrodynamic cavitation (HC). However, the degradation of pharmaceuticals from stabilized urine was not explicitly defined through literature for the pharmaceutical removal methods. The high pH (>12) was chosen because of the inherent use of calcium hydroxide as a urine stabilizing agent (Randall et al., 2016). Additionally, granular activated carbon (GAC) showed potential for the treatment of nitrified urine (Köpping et al., 2020). However, the removal of pharmaceuticals from urine stabilized with calcium hydroxide

was not considered. The combined use of hydrogen peroxide and ultraviolet could achieve a 90% degradation for most pharmaceuticals (Wols et al., 2013). Nevertheless, the sole use of hydrogen peroxide was investigated for the current work, since it has not been investigated for urine stabilized with calcium hydroxide i.e., a high pH environment. Furthermore, HC is a new pharmaceutical removal method which has not been optimized for the degradation of pharmaceuticals in stabilized urine. Therefore, the aim of the current work was to remove eleven pharmaceuticals (from stabilized urine) with minimal urea loss using high pH, GAC, hydrogen peroxide and HC.

3 Methodology

The aim of this work was to investigate four pharmaceutical removal methods (high pH, granular activated carbon, hydrogen peroxide and hydrodynamic cavitation) as well as the loss of urea due to the respective pharmaceutical removal methods. The pharmaceutical analysis methods are described in section 3.1, while the secondary pharmaceutical analysis method used for the current work is given in section 3.2. Furthermore, the urine analysis method and the analysis for pH is described in section 3.3 and section 3.4, respectively. The pharmaceutical removal methods are outlined in section 3.5, including section 3.5.5 which provides details for the optimized hydrodynamic cavitation system. A summary of all the experiments is given in section 3.6. Finally, the research method challenges are outlined in section 3.7.

3.1 HPLC analysis methods

Three high performance liquid chromatography (HPLC) methods were used for this work: analysis method for over the counter (OTC) common pharmaceuticals, analysis method for antiretrovirals (ARVs) and analysis method for both OTCs and ARVs. Further description of the methods is given in section 3.1.1 to section 3.1.3. Eleven pharmaceuticals were investigated (five OTCs and six ARVs) for this work.

The pharmaceutical structures for the OTCs used for the current work are shown in Figure 6. These OTCs are used in South Africa to treat several pain and muscular inflammations. Acetaminophen (commonly known as paracetamol) is an analgesic drug commonly used for fever and pain management. Paracetamol is commonly found in other OTCs such as Panado, Panadol etc. Paracetamol is an aminophenol derivative and thus contains hydroxyl, amide, and phenol (ring) functional groups in its structure.

Salicylic acid is a beta-hydroxy acid and a precursor and metabolite of acetyl-salicylic acid (more commonly known as aspirin). Aspirin is used to treat pain and fever, whereas salicylic acid is well known in treating acne. Salicylic acid and paracetamol have similar structures as both are substituted phenolic compounds. Salicylic has a carboxylic acid substituent and paracetamol has an amide substituent (side chain).

Diclofenac (a common OTC sold under the brand name: Voltaren, Cataflam) is used to treat inflammation and pain associated with joint, muscle and bone problems. It is usually found as capsules and tablets although it is also available as gels and patches. It has only one carboxylic acid (like salicylic acid) consisting of phenylacetic acid with a dichlorophenylamino group substituent.

Clopidogrel is an antiplatelet agent used to prevent blood clots. It is a thienopyridine class of drug. The sulphur ring and the nitrogen ring are grouped together, with methyl ester and chlorophenyl substituents.

Chlorpheniramine maleate (Rinex, Flusim) is an antihistamine used to treat symptoms associated with upper respiratory allergies. Chlorpheniramine maleate is a salt with maleic acid. It belongs to the amine class of compounds with a phenyl and pyridine (ring with nitrogen) substituents.

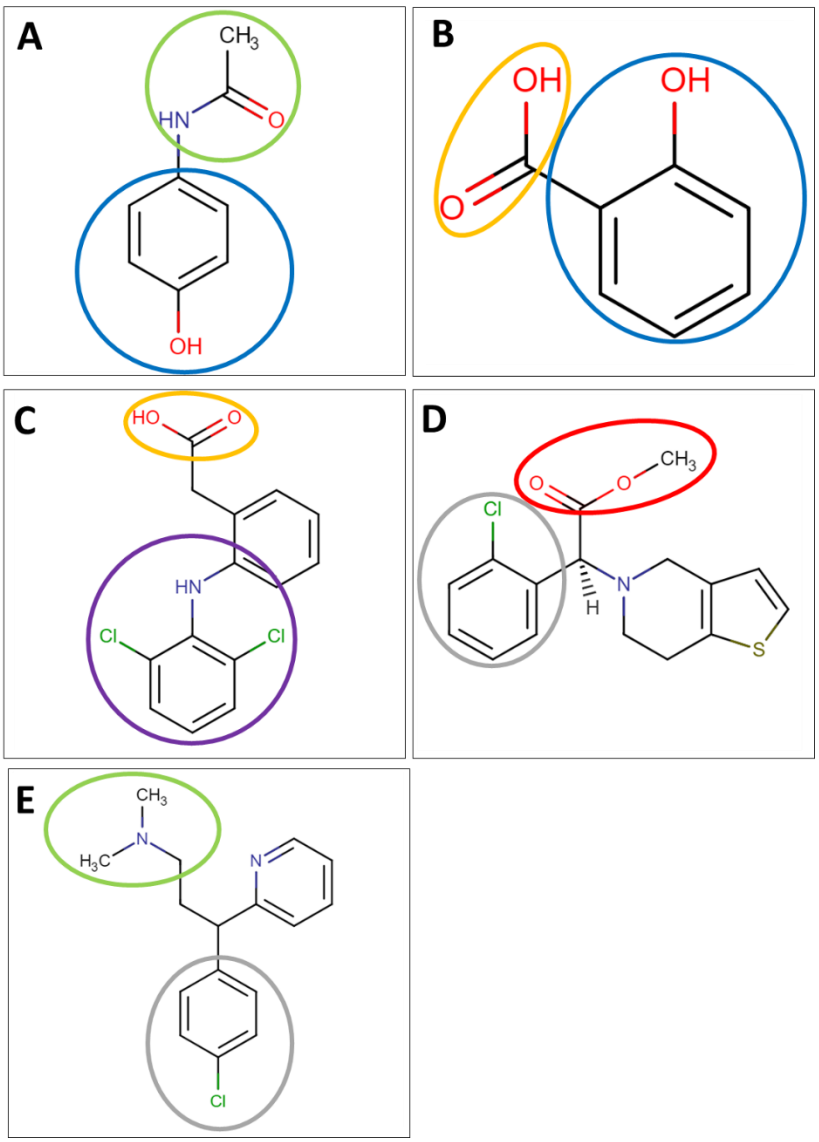


Figure 6: OTCs pharmaceutical structures: (A) paracetamol; (B) salicylic acid; (C) diclofenac; (D) clopidogrel; and (E) chlorpheniramine maleate. The functional groups are as follows: carboxylic acid (yellow); amine (green); phenol (blue); and methyl ester (green).

The pharmaceutical structures for the ARVs used for this work are shown in Figure 7. The human immunodeficiency virus (HIV) is a problem for South Africa, as a result, many people are taking ARVs. Subsequently, excessive amounts of ARVs are found in the South African wastewaters (including urine).

Tenofovir is a nucleotide analogue used to treat HIV infections. It is an effective antiretroviral therapy which has lower toxicity when compared to stavudine. Tenofovir is a diester analogue of adenosine monophosphate. It has a phosphate group bound to the nitrogenous base.

Zidovudine is a dideoxynucleoside used to treat HIV infections based on thymine. It is a nucleotide reverse transcriptase inhibitor which acts against HIV Virus Type 1. Zidovudine has hydroxyl and azido groups and a thymine ring.

Lamivudine is a reverse transcriptase used to treat HIV and hepatitis B. Like zidovudine, lamivudine acts against HIV Virus Type 1. Lamivudine is a zalcitabine analog with a sulphur atom in the pentose ring. It is based on a cytosine backbone.

Stavudine is a dideoxynucleoside used to treat HIV infections. Stavudine is also used against HIV Virus Type 1. It has similar functional groups as zidovudine; however, it has an uracil (RNA base) backbone instead of a thymine (DNA) base. Stavudine also contains an azide group. Because stavudine, lamivudine and zidovudine are based on DNA and RNA structures, they are similar in structure and are expected to behave in an analogous way when undergoing chemical treatment.

Nevirapine is a non-nucleoside reverse transcriptase inhibitor used to manage HIV. It is also used to treat HIV Type 1; however, it is a non-nucleoside reverse transcriptase which explains the difference in the functional groups when compared to stavudine, lamivudine and zidovudine. Abacavir sulfate is an antiviral nucleoside reverse transcriptase inhibitor used to treat HIV Type 1. Although abacavir sulfate is a nucleoside reverse transcriptase inhibitor, both nevirapine and abacavir sulfate have conjugated double bonds and nitrogen in their pharmaceutical structures.

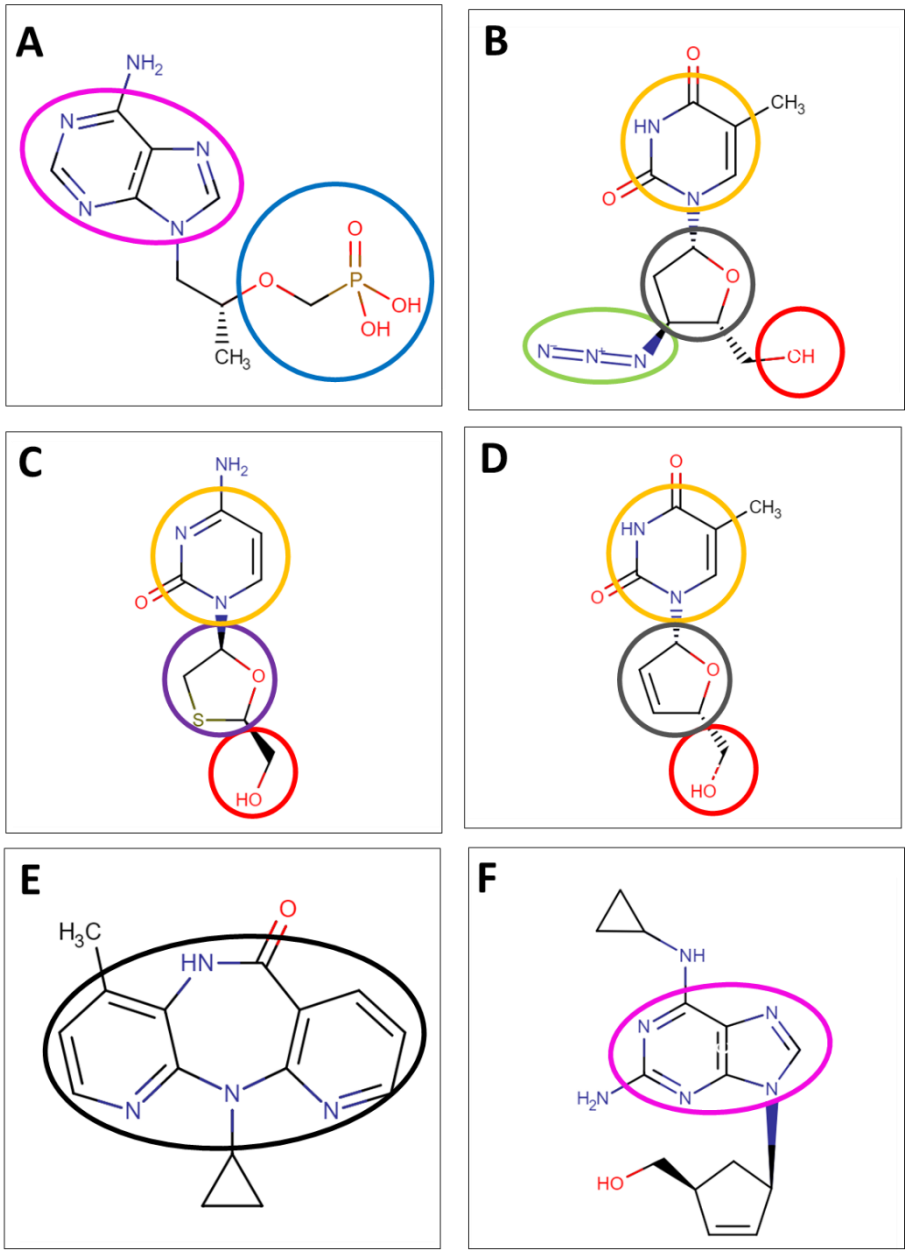


Figure 7: Pharmaceutical structures for ARVs: (A) tenofovir; (B) zidovudine; (C) lamivudine; (D) stavudine; (E) nevirapine; and (F) abacavir sulfate. The functional groups are as follows: phosphate (blue); azide (green); alcohol (red); oxathiolane ring (purple); furan ring (grey); purine (pink); thiamine ring for B and D (yellow); and cytosine ring for C (yellow).

The HPLC instrument used for the three HPLC methods was an Agilent 1220 LC system (Agilent Technology Inc., Urdorf, Switzerland) equipped with Agilent Poroshell 120 C18 column (4.6 cm x 50 mm x 2.7 µm), which was connected to a diode array spectrophotometric detector (Agilent Technology Inc., Urdorf, Switzerland).

3.1.1 HPLC analysis method for OTCs

Chromatographic separations were performed at 35°C using 15 mM phosphate buffer pH 3.25 (solvent A) and acetonitrile (solvent B) as the mobile phase with gradient elution at a flow rate of 1 mL min^{-1}. The gradient elute program is shown in Table 3**.** Detection of all the components was carried out at 254 nm and 230 nm with adequate sensitivity.

Table 3: Gradient elution programme for the OTCs analysis method.

Time (min)	%A	%B
0	90	10
3	80	20
16	45	55
17	35	65
26	10	90
27	80	20
30	80	20

3.1.2 HPLC analysis method for ARVs

The diode array spectrophotometric detector was operating at wavelengths of 210 nm, 254 nm, and 280 nm. The chromatographic separations were performed at a flow rate of 0.8 mL min^{-1}. The mobile phase was made of 0.05 M NaH_2PO_4 containing 0.005 M hexanesulfonic acid at pH 3.0 (solvent A) and acetonitrile (solvent B). The gradient elution program is described in Table 4.

Table 4: Gradient elution programme for the ARVs analysis method.

Time (min)	%A	%B
0	100	0
9	90	10
20	50	50
25	50	50

3.1.3 HPLC analysis method for both OTCs and ARVs

The chromatographic separations were performed at a flow rate of 0.8 mL min^{-1} and the injection volume was 5 µL. The mobile phase was made of 0.0015 M phosphate buffer at pH 3.25 (solvent A) and acetonitrile (solvent B). The gradient elution program is described in Table 5.

Table 5: Gradient elution programme for the combined OTCs and ARVs analysis method.

Time (min)	%A	%B
0	100	0
5	80	5
10	35	20
20	35	65
22	100	0
23	100	0

3.2 UV spectroscopy

For the current work, the UV spectroscopy was used to analyze the degradation of paracetamol. Paracetamol was chosen as an indicator pharmaceutical to determine the optimal pressure under which the hydrodynamic cavitation system could be operated. The maximum UV spectroscopy wavelength for paracetamol is 243 nm, which is within the UV light wavelength range of 220 - 280 nm (Saeed, 2017; Mcmillan et al., 2008). An alternative method could have been to test for the UV absorbance at 254 nm which was proven as a reliable surrogate parameter to test for micropollutants in wastewater (Altmann et al., 2016). However, the work by Altmann and co-workers (2016) analyzed pharmaceutical removal using activated carbon, therefore, the use of paracetamol as an indicator pharmaceutical was applied for this work.

A quartz cuvette was used to analyze the samples due to the low wavelength range at which paracetamol can be analyzed. The analysis of the samples using the UV spectroscopy was quick and much cheaper when compared to the HPLC method (Köpping et al., 2020).

Therefore, UV spectroscopy was used to determine the degradation of paracetamol, over a short space of time, to find the optimal pressure under which the hydrodynamic cavitation system could be operated.

3.3 Analysis of urine

Urine is composed of various compounds namely: urea, ammonium, phosphorus, chlorine, sulphate, sodium, potassium, calcium, and magnesium (Randall et al., 2016). The urine compounds which were of interest for this work were urea and ammonium. An automated photometric analyzer (Gallery Discrete Analyzer, Thermo Fisher Scientific, Massachusetts, United States) was used to measure the urea and the ammonium of the analyzed urine.

The photometric analyzer had an upper limit of 600 mg L^{-1} and 12.5 mg L^{-1} for urea and ammonium, respectively. Each 1 mL sample of the analyzed urine was diluted in a 25 mL volumetric flask. The samples were diluted using deionized water. The diluted sample was filtered through a 0.22 µm pore size syringe filter, then analyzed using the Gallery Discrete Analyzer. The analysis of the urea and ammonium was done for the urine samples before and after they were treated with the respective degradation methods. Samples were only taken before and after the experiments, not throughout. Therefore, the degradation measurements were calculated in relative terms, with reference to the initial value.

3.4 Analysis of pH

A pH probe (ACCSEN pH 8, Lasec, Cape Town, South Africa) was used to measure the pH of the urine solution for the first three degradation methods i.e. high pH, granular activated carbon, and hydrogen peroxide. Another pH probe (HI5221, Hanna, Johannesburg, South Africa), fitted with a temperature probe, was used for hydrodynamic cavitation degradation method since the degradation method generated heat. Both pH probes were calibrated each morning of the experiment at pH 4, pH 7 and pH 10 with a buffer solution (Hanna, Johannesburg, South Africa) at each pH value.

3.5 Pharmaceutical removal methods

Four pharmaceutical removal methods were investigated namely: high pH, granular activated carbon, hydrogen peroxide and hydrodynamic cavitation. The removal of eleven pharmaceuticals was investigated: five over the counter (OTC) common pharmaceuticals (paracetamol, salicylic acid, diclofenac, clopidogrel and chlorpheniramine maleate) and six antiretrovirals (zidovudine, lamivudine, tenofovir, stavudine, abacavir sulfate and nevirapine). The description of each pharmaceutical is given in Annexure A1. Each pharmaceutical removal method was designed to test for the hypothesis created for the specific pharmaceutical removal method. All the pharmaceutical removal methods were tested in duplicate. Two samples for each experimental condition were run. Therefore, the standard deviation was not calculated, however, the degradation results from each sample were compared to the other samples.

3.5.1 High pH removal method

3.5.1.1 High pH experimental procedure

Despite the varied degradation patterns of the pharmaceuticals seen in literature, the degradation of the pharmaceuticals due to a high pH was investigated for this work. The stabilization of urine is the first step for the proposed urine treatment process suggested by Chipako and Randall (2020b). The discussion in section 2.5.2 highlighted the preferred use of alkalinization over acidification due to safety reasons (Chipako and Randall, 2020b). However, citric acid is not a safety hazard since it is the main organic acid found in citric fruits (Grewal and Kalra, 1995). Nevertheless, the novel use of calcium hydroxide (as suggested by Randall and co-workers (2016) for the alkalinization of urine) was applied for this work. The recommended dosage of 10 g L^{-1} was used to stabilize urine. The dosage was an overestimate, to account for different urine compositions since the urine composition is influenced by factors such as diet (Randall et al., 2016; Maurer et al., 2006).

Fresh urine was used for the high pH degradation method. The urine was from one subject and it was clear of all the pharmaceuticals. The pH of the urine was measured to verify that it was below pH 7 (Chipako and Randall, 2020b). The urine was not fully characterized, only the

urea and ammonium were measured (shown in Annexure A3.1) as they were the subjects of interest for this work.

Fresh urine samples of 3 mL were spiked with pharmaceuticals. The spiked concentration of each pharmaceutical is given in Annexure A2.1. The over the counter (OTC) common pharmaceuticals and the antiretrovirals (ARVs) were analyzed separately, therefore, the OTCs samples and the ARVs samples were prepared individually. Four samples were prepared – two samples for the OTCs and two samples for the ARVs. Each sample was stabilized with calcium hydroxide (Kimix Chemicals, Cape Town, South Africa) at a concentration of 10 mg mL^{-1}, thus increasing the pH (>12) (Randall et al., 2016).

A stability study, to determine the percentage degradation of the pharmaceuticals, was conducted over a period of at least 75 days. The 3 mL samples were prepared at room temperature, and they were kept at room temperature for the duration of the experiment. To prepare the samples for analysis, 1 mL of the before and after samples were filtered through a 0.22 µm pore size syringe filter. The HPLC was used to analyze the degradation of pharmaceuticals. The OTCs were analyzed using the method described in section 3.1.1 and the ARVs were analyzed using the method described in section 3.1.2.

3.5.1.2 Urea and ammonium analysis for high pH experiments

A control experiment was conducted for fresh and stabilized urine to determine the effect of the high pH on the urea and the ammonium. Fresh urine samples of 5 mL were stabilized with calcium hydroxide at a concentration of 10 mg mL^{-1}. The concentration of the urea and the ammonium before and after the experiment were analyzed using the Gallery Discrete Analyzer (described in section 3.3) to determine the percentage degradation.

3.5.2 Granular activated carbon removal method

3.5.2.1 Granular activated carbon experimental procedure

The adsorptive characteristic of granular activated carbon (GAC) aids in the removal of pharmaceuticals from solutions. GAC produced from coconut shells was pre-washed with deionized water to remove excess GAC dust. To prevent the dilution of the sample solution,

the GAC was air dried two days before the experiment commenced. A Perspex cylinder, with a cross sectional area of 39.6 cm^2 and an inner diameter of 7.1 cm, was lined with a 40-gsm membrane which acted as a filter. The GAC was packed inside the Perspex cylinder to a height of 10 cm. The over the counter (OTC) common pharmaceuticals and the antiretrovirals (ARVs) were analyzed separately, therefore, the OTCs sample solutions and the ARVs sample solutions were prepared individually.

The experimental approach for this work was like that of Köpping and co-workers (2020). Two types of GAC particle sizes were tested. A sieve analysis (Star Screen test sieves, Nigel, South Africa) showed that the majority of the GAC particle sizes were within the range of 0.60 mm and 2.36 mm (see section 4.2). The two GAC sizes were classified as follows: 0.60 – 1.80 mm and > 1.80 mm. Therefore, four GAC columns were prepared for the degradation of the pharmaceuticals: one 0.60 – 1.80 mm and one > 1.80 mm GAC column size to test for the OTCs, and one 0.60 – 1.80 mm and one > 1.80 mm GAC column size to test for the ARVs.

Urine was collected from one subject for a day and kept at 4˚C to prevent urea hydrolysis. The urine was clear of all pharmaceuticals. The pH of the urine was measured before each experiment to ensure it was below pH 7 (Chipako and Randall, 2020b). Fresh urine samples, with a volume of 200 mL, were spiked with pharmaceuticals. The spiked concentration of each pharmaceutical is given in Annexure A2.2. The urine was then stabilized with calcium hydroxide (Kimix Chemicals, Cape Town, South Africa) at a concentration of 10 mg mL^{-1} of urine. The composition of the urine is shown in Annexure A3.2.

The GAC experimental setup is shown in Figure 8. The experiment was conducted at room temperature. The spiked urine solution was then pumped into the GAC column with a MasterFlex Easy-Load pump (Vernon Hills, United States) at a rate of 0.96 L hr^{-1}. To prepare the samples for analysis, 2 mL of the before and after samples were filtered through a 0.22 µm pore size syringe filter. The percentage pharmaceutical degradation was analyzed using the HPLC methods described in section 3.1.1 for the OTCs and section 3.1.2 for the ARVs.

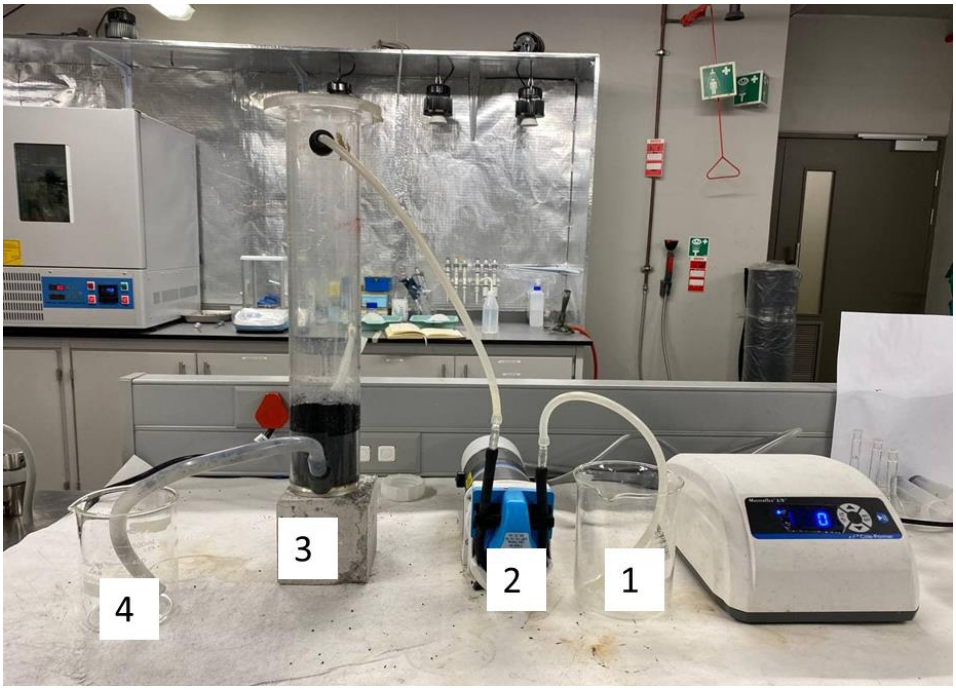


Figure 8: Granular activated carbon experimental setup: (1) untreated solution beaker; (2) peristaltic pump; (3) GAC column; (4) treated urine solution beaker.

3.5.2.2 Granular activated carbon urea and ammonium analysis

A control experiment was conducted to determine the degradation of urea and ammonium due to the GAC removal method. A similar experimental procedure described in section 3.5.2.1 was followed, except for the spiked pharmaceuticals. The concentration of the urea and ammonium before and after the experiment were analyzed using the Gallery Discrete Analyzer (described in section 3.3) to determine the percentage degradation.

3.5.3 Hydrogen peroxide removal method

3.5.3.1 Hydrogen peroxide experimental procedure

Hydrogen peroxide is often used as an oxidant for chemical oxidation pharmaceutical removal methods. The sole use of hydrogen peroxide as an oxidant has proven inefficient through literature (as discussed in section 2.8.6). However, hydrogen peroxide dosed into urine stabilized with calcium hydroxide was considered for this work.

The urine used for the experiments was from one subject and it was clear of all the pharmaceuticals. Fresh urine samples of 15 mL were spiked with the respective

pharmaceuticals. The spiked pharmaceutical concentrations are given in Annexure A2.3. The over the counter (OTC) common pharmaceuticals and the antiretrovirals (ARVs) were analyzed separately, therefore, the OTCs samples and the ARVs samples were prepared individually. Four samples were prepared – two samples for the OTCs and two samples for the ARVs. The spiked urine sample solutions were then stabilized with calcium hydroxide (Kimix Chemicals, Cape Town, South Africa) at a concentration of 10 mg mL^{-1}. The urine composition is given in Annexure A3.3.

The experiment was conducted at room temperature. Hydrogen peroxide 30% v/v (Clicks, Cape Town, South Africa) was dosed into the urine solution at a ratio of 0.1 mL mL^{-1} of urine solution. Literature revealed that the 30% (v/v) hydrogen peroxide was the most used form of hydrogen peroxide (Agrawal et al., 2003; Dunge et al., 2004; Moyano et al., 2005). Some studies used an electrogenerated hydrogen peroxide, however, a dose of 0.1 mL mL^{-1} was used for liquid hydrogen peroxide (Agrawal et al., 2003). The urine sample solutions for this work were dosed with hydrogen peroxide at a concentration of 0.1 mL mL^{-1} for 2 hours. To prepare the samples for analysis, 2 mL of sample, before and after peroxide treatment were filtered through a 0.22 µm pore size syringe filter. The percentage degradation of urine was determined using the HPLC methods developed in section 3.1.1 for the OTCs and section 3.1.2 for the ARVs.

3.5.3.2 Hydrogen peroxide urea and ammonium analysis

A control experiment was conducted to determine the degradation of urea and ammonium due to the hydrogen peroxide pharmaceutical removal method. A similar experimental procedure described in section 3.5.3.1 was followed, except for the spiked pharmaceuticals. The concentration of the urea and the ammonium before and after the experiment were analyzed using the Gallery Discrete Analyzer (described in section 3.3) to determine the percentage degradation.

3.5.4 Hydrodynamic cavitation system

The application of the hydrodynamic cavitation (HC) system for the removal of pharmaceuticals from wastewater is new (Mancuso et al., 2020). There are two mechanisms

through which the degradation of pharmaceuticals occurs in this equipment: thermal decomposition of the pharmaceuticals due to the collapsing cavitation bubbles and the reaction of the hydroxyl radicals with the pharmaceuticals (Rajoriya et al., 2016). The HC system which was used for the current work has a capacity of 80 L, even though 10 L was used for the experimental runs. The HC system was like the one shown in Figure 9, except for a cooling system.

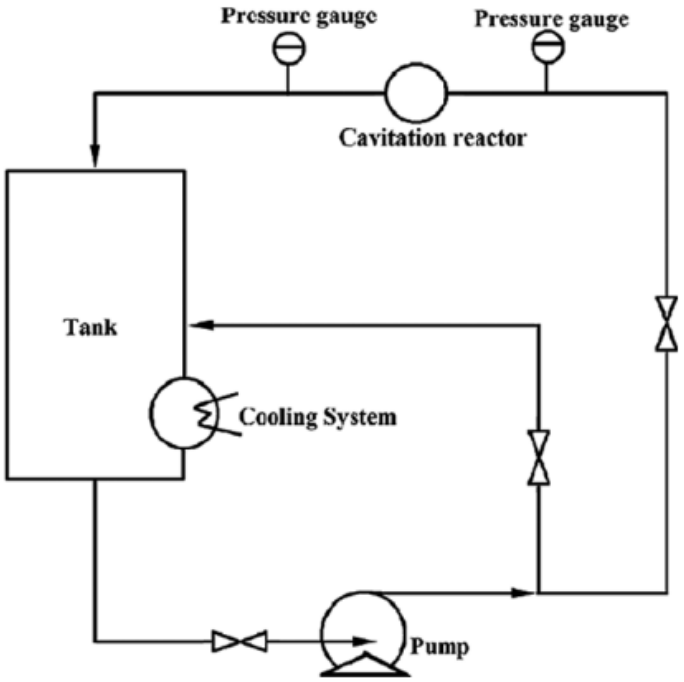


Figure 9: Typical hydrodynamic cavitation experimental system (Yuequn et al., 2016).

It is important to consider the inlet pressure, temperature, cavitation device and pH of a HC system because they all have an influence on the degradation efficiency of the pharmaceuticals (Rajoriya et al., 2016). Saharan and co-workers (2013) suggested that a circular venturi performs better than an orifice. Therefore, a circular venturi was used for the initial HC system. Literature revealed that the optimum inlet pressure is within the range of 480 – 490 kPa, however an initial inlet pressure of 200 kPa was chosen for the current work. This was to check whether the degradation efficiency of the HC system operated at a low inlet pressure was sufficient to degrade the pharmaceuticals, since the operational costs would be less when compared to the HC system operated at a higher inlet pressure. It has been shown that the optimization of the solution pH assists in achieving maximum degradation in the

shortest time. However, the optimum pH of each waste solution is different (Rajoriya et al., 2016). Therefore, two solution pH conditions were considered for this work (pH 2 and pH 12.4) to find the optimal pH at which the HC system could be operated.

3.5.4.1 Hydrodynamic cavitation experimental procedure

The concentration of the spiked pharmaceuticals for the hydrodynamic cavitation (HC) system was lowered due to the high sample volume required for each experiment. The occurrence of pharmaceuticals in the environment does not exceed 1 µg L^{-1} (Halling-Sorensen et al., 1998). Therefore, using lower concentrations for the spiked pharmaceuticals would give a realistic indication of the HC system pharmaceutical removal efficiency. Different concentrations of the pharmaceuticals were used to confirm the acceptable concentration of pharmaceuticals which could be detected by the HPLC method. Paracetamol was used as an indicator pharmaceutical for the experiment to determine a detectable concentration. Table 6 gives a summary of the experimental findings. A minimum concentration of 0.025 mg L^{-1} could be spiked for each pharmaceutical.

Table 6: Results from the experiment to determine a detectable pharmaceutical concentration for the HPLC method.

	Concentration (mg L^{-1})	**Detected (YES/NO)**
Initial	0.100	YES
Dilution 1	0.050	YES
Dilution 2	0.025	YES
Dilution 3	0.013	NO
Dilution 4	0.006	NO

A simple urea-water solution was used instead of fresh urine due to the high-volume demand of the cavitation system. At least 10 L of solution per experimental run was required. Urea (Sigma-Aldrich, Darmstadt, Germany) was added to tap water to make up the simplified urea-water solution. The urea was dosed at a concentration ± 10 g L^{-1}. The OTCs and the ARVs were

spiked in the same solution. The spiked pharmaceutical concentrations are given in Annexure A.2.4.

The cavitation system was investigated at two pH conditions – pH 2 and pH 12.4. Two samples were run per pH condition. Calcium hydroxide (Kimix Chemicals, Cape Town, South Africa) was used to adjust the pH of the urea-water solution to 12.4, while citric acid (Science World, Parow, South Africa) was used to adjust the pH of the urea-water solution to 2. The HC system is shown in Figure 10.

Figure 10: A simple schematic of the University of the Western Cape pilot cavitation system: (pump); (2) cavitation device; (3) solution tank.

Each experiment was run at the following conditions: 200 kPa pressure for 30 minutes. A circular venturi with a 1:1 slit height to length ratio was used as the cavitation device (shown in Figure 11). The circular venturi had the following dimensions: 10 mm throat diameter, 10 mm throat length, 13˚ convergent angle and a divergent angle of 3˚. A pump (Dutchi NL Type 112M2, Frankenthal, German) was used to recycle the solution through the system to create a continuous flow. To prepare the samples for analysis, 2 mL of the before and after samples were filtered through a 0.22 µm pore size syringe filter. The percentage degradation

of the pharmaceuticals was determined for each pH condition with the HPLC method described in section 3.1.3 which analyzed both OTCs and ARVs.

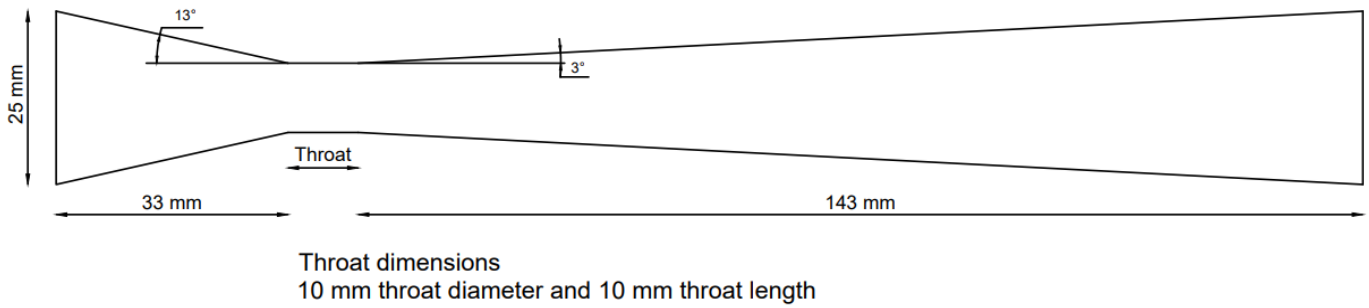


Figure 11: Cross section of a circular venturi cavitation device.

3.5.4.2 Hydrodynamic cavitation urea analysis

A control experiment was not conducted to determine the degradation of urea resulting from the hydrodynamic cavitation degradation method. However, a control experiment was conducted to find the optimum inlet pressure for the optimized cavitation system. The urea degradation for the HC system was determined for the experimental runs described in section 3.5.4.1.

3.5.5 System optimization for hydrodynamic cavitation

3.5.5.1 Optimization of the cavitation device

A change of cavitation device was considered for the optimized hydrodynamic cavitation system. A circular venturi was used as the initial cavitation device. Although it was shown that a circular venturi performs better than an orifice (Saharan et al., 2013), a 3 mm orifice with a plate diameter of 25 mm, was chosen as the cavitation device for the optimized cavitation system.

3.5.5.2 Optimization of the inlet pressure

The inlet pressure was optimized since it influences the degradation efficiency of the hydrodynamic cavitation system (Saharan et al., 2013). A control experiment was conducted to determine the optimum inlet pressure. Three pressures were investigated: 200 kPa, 300 kPa and 400 kPa. Paracetamol was used as an indicator pharmaceutical for the experiments. The experimental approach was like that described in section 3.5.4.1, except for the variation in pressure. The UV spectroscopy, instead of the HPLC, was used to analyze the samples for the degradation of paracetamol. The UV spectroscopy method is described in section 3.2.

3.5.5.3 Optimized hydrodynamic cavitation experimental procedure

The sample solutions for the optimized hydrodynamic cavitation system were prepared using the method described in section 3.5.4.1. The sample solutions were spiked with each pharmaceutical at a minimum concentration of 0.025 mg L^{-1} (given in Annexure A.2.5). A 3 mm orifice was fitted in the cavitation system instead of a venturi. The optimized system parameters are given in Table 7. The temperature and pH were monitored throughout the experimental runs. The before and after samples were prepared for analysis by filtering 2 mL of each sample through a 0.22 µm pore syringe filter. The percentage degradation was analyzed using the HPLC method described in section 3.1.3 for the analysis of both OTCs and ARVs.

Table 7: Optimized experiment parameters.

Parameter	Value	Unit
Orifice size	3	mm
pH	2	
Run	30	min
Pressure	400	kPa
API concentration	0.025	g/l

3.6 Summary of experiments

Table 8 gives a summary of all experiments conducted for the current work.

Table 8: Summary of all the experiments conducted.

Experiment	Equipment and Materials	Run Procedure
High pH	Calcium hydroxide	**Experiment:** Fresh urine samples were spiked with APIs at a concentration of 1 mg mL^{-1} Calcium hydroxide was added at a concentration of 10 mg mL^{-1} of urine The degradation of the pharmaceuticals was determined as a function of time
Granular Activated Carbon (GAC)	Perplex column (7.1 cm inner diameter) Pump GAC Cloth Filter Calcium hydroxide	**GAC preparation:** The GAC was pre-washed with deionized water and air dried. Thereafter, the GAC was packed in a column **Experiment:** (The urine was prepared as described for high pH procedure) The urine was pumped through the GAC column at a rate of 0.96 L hr^{-1} The degradation of the pharmaceuticals was determined after GAC treatment
Hydrogen peroxide	30% v/v hydrogen peroxide Calcium hydroxide	**Experiment:** (The urine was prepared as described for high pH procedure) Hydrogen peroxide was dosed at a concentration of 0.1 ml mL^{-1} and the samples were treated for 2 hours The degradation of the pharmaceuticals was determined after 2 hours of treatment
Hydrodynamic Cavitation	Hydrodynamic cavitation system Citric acid Urea Calcium hydroxide	**Urea-water solution preparation:** The urea was mixed with tap water at a concentration of 10 g L^{-1} **Experiment:** The pharmaceuticals were spiked into the urea-water solution The hydrodynamic cavitation system was set to the following conditions: 200 kPa for 30 minutes using a circular venturi. Furthermore, the samples were running at pH 2 and 12.4 **Optimized cavitation system:** The cavitation system operating conditions: pH 2, 400 kPa for 30 minutes using a 3 mm orifice
Notes All experiments were run in duplicate All experiments used fresh urine, except for the hydrodynamic cavitation experiments which used a simplified urea-water solution All experiments tested for ARVs and OTCs degradation The HPLC was used to determine the degradation of pharmaceuticals for each experiment The Gallery Discrete Analyzer was used to measure the urea and ammonium		

3.7 Research method challenges

The pharmaceutical analysis methods were able to quantify the concentration of each pharmaceutical as the area under the chromatograms, instead of the absolute concentration. This is because the calibration curves for the HPLC were not developed due to a time constraint and a limited stock of pharmaceuticals. Therefore, the degradation of each pharmaceutical was calculated in relative terms rather than absolute terms. This did not have an impact on the overall assessment of the degradation of the pharmaceuticals since the degradation was based on the initial concentration of each pharmaceutical. The pharmaceutical removal methods supported the investigation of all the research questions for this work since the methodology was informed by literature. As a result of the time constraint, only one pharmaceutical removal method was optimized for this work.

4 Results and discussion

4.1 High pH

A comprehensive literature review in section 2.8.4 showed that a high pH environment can degrade some pharmaceuticals. Results from the study by Yin and co-workers (2017) indicated that pharmaceuticals such as fluoxetine experienced the highest degradation in a high pH environment, while other pharmaceuticals were degraded more in acidic and neutral environments (Yin et al., 2017). Furthermore, the analysis from Table 1 indicated that the degradation of the pharmaceuticals (chosen for this work) varies across the pH spectrum.

The addition of calcium hydroxide to human urine caused a high pH (>12) which degraded each of the selected pharmaceuticals for this work at varying degrees (shown in Figure 12). The recommended calcium hydroxide dosage of 10 mg mL^{-1} of fresh urine was an overestimate to account for urine with different compositions, while ensuring there were excess hydroxide ions available for the degradation of the pharmaceuticals (Randall et al., 2016). The exposure of the pharmaceuticals to the high pH environment was for at least 75 days. Since some of the antiretrovirals (ARVs) showed complete degradation after 75 days, the over the counter (OTC) common pharmaceuticals were left for more than 75 days to see

whether complete degradation would occur. Even though the samples were left for a total of 112 days (refer to Annexure B.1.1), the degradation of the NSIADs did not improve over time.

The OTCs showed a degradation range of 8 - 44%, with paracetamol and chlorpheniramine maleate experiencing the lowest and highest degradation, respectively. The range of degradation for the ARVs due to the high pH was 0 - 100%. Abacavir sulfate and nevirapine experienced no degradation, while stavudine, lamivudine, zidovudine and tenofovir experienced complete degradation. The detailed experimental results are provided in Annexure B1. As such, the degradation of the pharmaceuticals investigated for this work due to a high pH (>12) was not the same for all eleven pharmaceuticals. The difference in the degradation of the pharmaceuticals is attributed to the level of deprotonation of the acid and basic functional groups (such as carboxylic acid, hydroxyl groups and amines) which are present in the structure of the pharmaceuticals (Hapeshi et al., 2010). Thus, the degradation of a pharmaceutical due to a change in pH was dependent on the molecular structure of the pharmaceutical (Yin et al., 2017).

Paracetamol recorded the least degradation of 8% for the OTCs. The amide bond in the structure of paracetamol (shown in Figure 6) is more resistant to hydrolysis with a base, than the carboxylic acid group in the structure of salicylic acid and diclofenac. This is because it could form resonant structures which reinforces the stability of paracetamol. Furthermore, Yang and co-workers (2008) mentioned that there is a significant decrease in degradation for paracetamol in a strong alkaline environment. The study revealed that the degradation of paracetamol decreased significantly when the pH was greater than 9.5 (Yang et al., 2008). Calcium hydroxide dissociates into calcium and hydroxide ions in an aqueous solution, which means more hydroxide ions would be available at a higher pH (Copeland and Greenberg, 1960). It can be assumed that the low degradation of paracetamol was also attributed to the absence of a catalyst, despite an increase in the concentration of available hydroxide ions which are formed from the dissociation of calcium hydroxide.

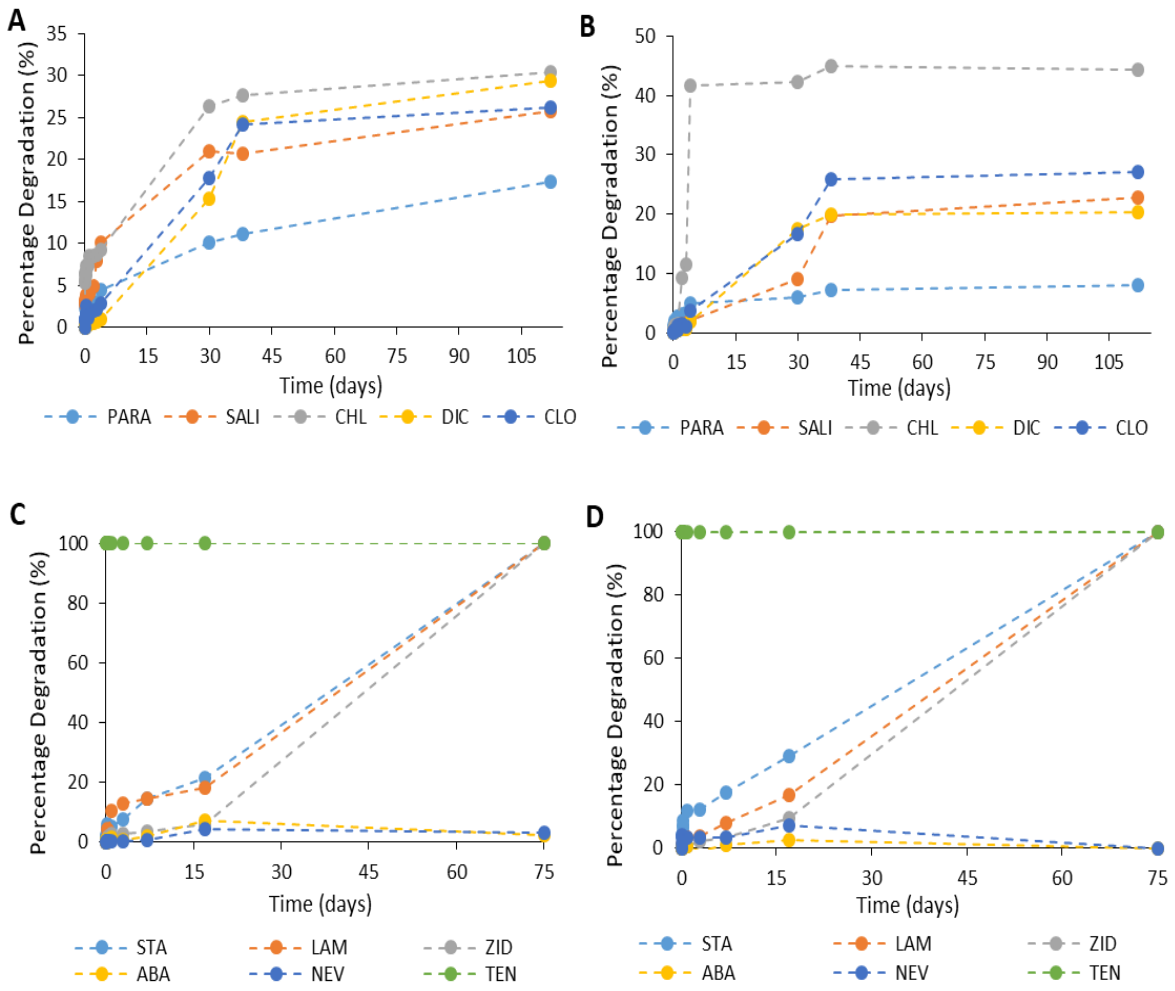


Figure 12: High pH results: OTCs sample 1 (A), OTCs sample 2 (B), ARVs sample 1 (C), ARVs sample 2 (D). The respective abbreviations of the pharmaceuticals labelled under each graph are as follows: paracetamol (PARA), salicylic acid (SALI), chlorpheniramine maleate (CHL), diclofenac (DIC), clopidogrel (CLO), stavudine (STA), lamivudine (LAM), zidovudine (ZID), abacavir sulfate (ABA), nevirapine (NEV) and tenofovir (TEN).

Salicylic acid and diclofenac both have carboxylic acids in their groups (shown in Figure 6). However, salicylic acid is stabilized by the positioning of the carboxylic acid (COOH) group which is close to the phenol group. The carboxyl group is stabilized by resonance, making it resistant to hydrolysis. Contrary, the extra carbon chain between the hydroxyl group and the ring in diclofenac decreases the potential for the ring and the nitrogen to provide resonance, thereby making diclofenac susceptible to hydrolysis. As a result, diclofenac experienced more degradation than salicylic acid. The nitrogen-sulphur ring and the ester in the structure of clopidogrel (refer to Figure 6) are close to each other, resulting in steric hindrance, thereby

providing hydrolysis resistance for clopidogrel. Thus, less degradation was observed for clopidogrel when compared to diclofenac.

The highest degradation for the OTCs was observed from chlorpheniramine maleate (44%). Although the amine group in chlorpheniramine maleate (shown in Figure 6) is resistant to hydrolysis, it is less resistant than the carboxyl, amide and ester group, which is the cause for chlorpheniramine maleate to experience the most degradation. Lv and co-workers (2015) found that there was an increase in the degradation of chlorpheniramine maleate when the pH was elevated from 8 to 9. This was attributed to an increase in the formation of hydroxide ions. However, further analysis showed that the degradation from the hydroxide ions was less effective compared to the degradation from ozonation (Lv et al., 2015). This may explain why less than 50% of chlorpheniramine maleate was degraded, even though the formation of the hydroxide ions increased when the pH increased. Therefore, the difference in the structures of the pharmaceuticals caused each pharmaceutical to react differently with the hydroxide ions. None of the OTCs experienced a degradation of more than 45%, while most of the ARVs were completely degraded after the 75-day period.

Stavudine, zidovudine and lamivudine have similar structures (shown in Figure 7), thus they behave in an analogous way in a high pH environment. Stavudine and zidovudine both have the furan ring, thiamine ring and the alcohol group. Additionally, zidovudine has an azide group in its structure. Dunge and co-workers (2004) found that the hydrolysis of stavudine and zidovudine is enhanced in an acidic condition rather than an alkaline condition. As a result stavudine did not experience immediate degradation in an alkaline condition. Furthermore, the absence of epoxide formation for zidovudine suggests that the degradation of zidovudine is a result of normal hydrolysis (Dunge et al., 2004). Therefore, it was deduced that the degradation of stavudine and zidovudine observed from the current work was caused by hydrolysis. The structure of lamivudine is similar to that of stavudine and zidovudine, however it has a cytosine ring, oxathiolane ring and an alcohol group. Wang and co-workers (2019) mentioned that the degradation of lamivudine is independent from the initial pH of the solution. It was inferred that the degradation of lamivudine was also due to normal hydrolysis.

Further analysis showed that the degradation of tenofovir (an antiretroviral drug) was almost immediate due to the high pH. This was expected since Golla and co-workers (2016) showed that the degradation of tenofovir increased with an increase in pH, thus tenofovir experienced higher instability in basic conditions (Golla et al., 2016). The degradation of tenofovir is attributed to a P – O in its structure (refer to Figure 7), which undergoes hydrolysis in basic conditions (Berger and Wittner, 1966).

Nevirapine and abacavir sulfate have conjugated double bonds (shown in Figure 7) which gives resonance to the pharmaceuticals. Thus, the pharmaceuticals can stabilize, being resistant to hydrolysis. As a result, the pharmaceuticals did not experience degradation due to the high pH. Therefore, the difference in the pharmaceutical structures lead to the difference in the degradation of the pharmaceuticals. Furthermore, the high pH degradation method conserved 96% of the urea (refer to section 4.6). Overall, the results from the current work build on the existing evidence of the pharmaceutical degradation due to high pH.

4.2 Granular activated carbon

The microporous structure of granular activated carbon (GAC) provides surface area on which the pharmaceuticals can attach. GAC has proven to be an efficient pharmaceutical removal method. The discussion in section 2.8.5 showed that at least 77% and up to 98.2% of the pharmaceuticals can be removed by GAC from waste streams (Yang et al., 2011; Li et al., 2018).

The mechanism by which activated carbon removes micropollutants from waste streams is the adhesion of substances in the micropores of the GAC, which provide the internal surface area on which the micropollutants can attach (Mcdougall, 1991). Figure 13 shows the internal structure of GAC. The greater the adsorption surface area, the more the micropollutants can be adsorbed (Mcdougall, 1991). Other surface characteristics of GAC, such as texture and surface physicochemical properties, contribute to the adsorption capacity of GAC (Mcdougall, 1991; Laszló et al., 2001). However, the internal surface area of GAC has a major influence on the adsorption capacity. Therefore, the choice of GAC for the current study was influenced by the internal surface area of the GAC.

Previous studies have shown that GAC from bituminous coal has a high pharmaceutical removal efficiency of 97% (Rostvall et al., 2018). Furthermore, it was shown that the internal surface area of GAC derived from coconut shells was 731 m^2 g^{-1}, which is comparable to the surface area of the GAC derived from bituminous coal (Li et al., 2011; Rostvall et al., 2018). As a result, GAC made from coconut shells was chosen for the current study over bituminous coal because it is a greener and more sustainable technology.

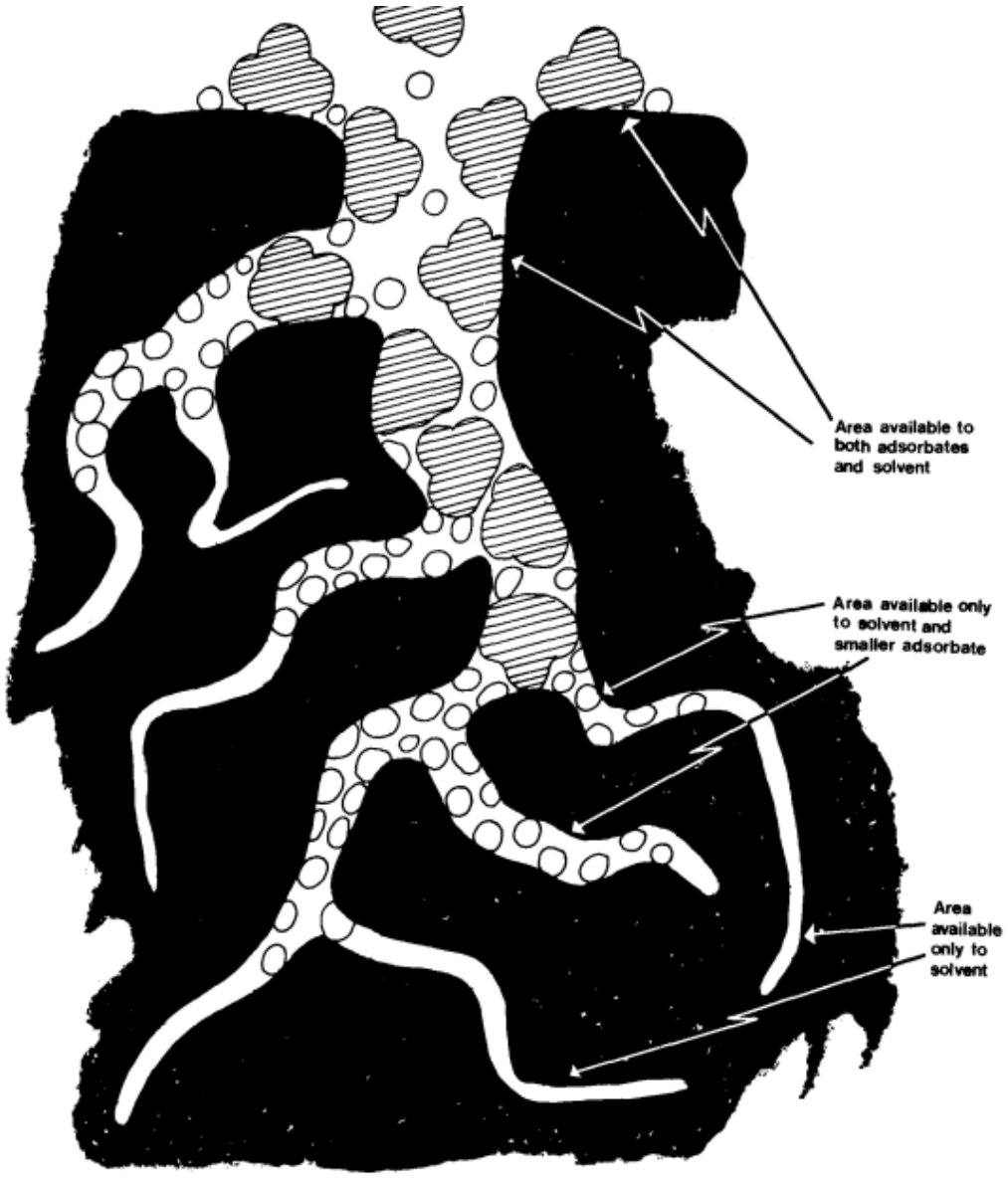


Figure 13: Molecular screening in micropores (Mcdougall, 1991).

The particle size distribution (PSD) of the GAC used for this work is given in Figure 14. Most of the particle sizes lie between 0.60 mm and 1.18 mm. A narrow PSD was caused by particle uniformity. The fraction of the total pore volume that an adsorbate can access is influenced by the PSD (Pelekani and Snoeyink, 1999). Additionally, the particle size has an influence on the packing density of the particles (Sohn and Moreland, 1968). As a result, the amount of GAC required to remove micropollutants (such as pharmaceuticals) from waste streams using coarse and fine GAC would be different. However, the pharmaceutical removal efficiency of the fine and course GAC would be the same due to a similar internal surface area capacity (Köpping et al., 2020). Following the results from the PSD for this work, two GAC particle sizes ranges were chosen namely: 0.60 – 1.18 mm and > 1.18 mm.

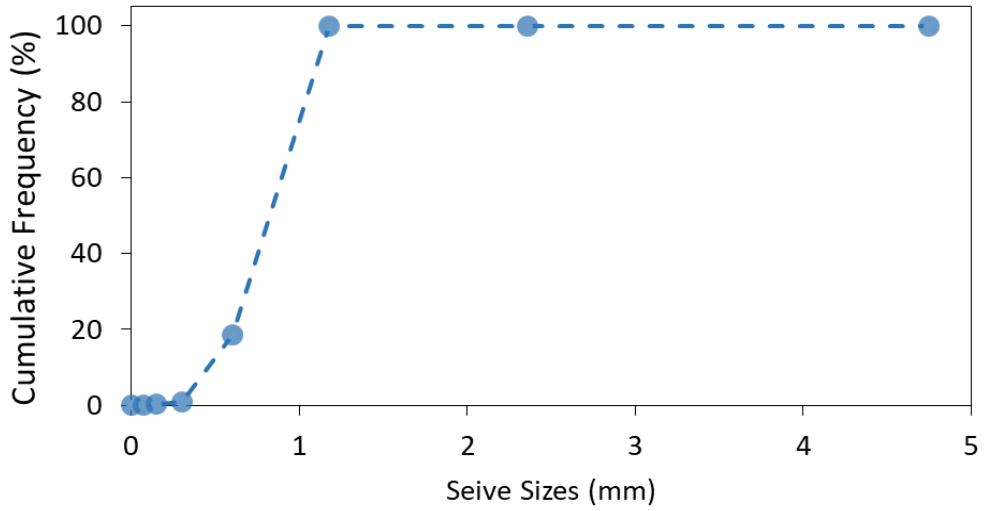


Figure 14: GAC particle size distribution diagram.

The adsorption ability of the GAC, derived from coconut shells, degraded each of the pharmaceuticals investigated for this work. Each pharmaceutical experienced a degradation of more than 94% (shown in Figure 15). The detailed experimental results are given in Annexure B2. This has shown that the microporous structure of the GAC used for this work provided sufficient surface area on which the pharmaceuticals could attach, thus eliminating the pharmaceuticals from the sample solutions. This was true for both the OTCs and ARVs.

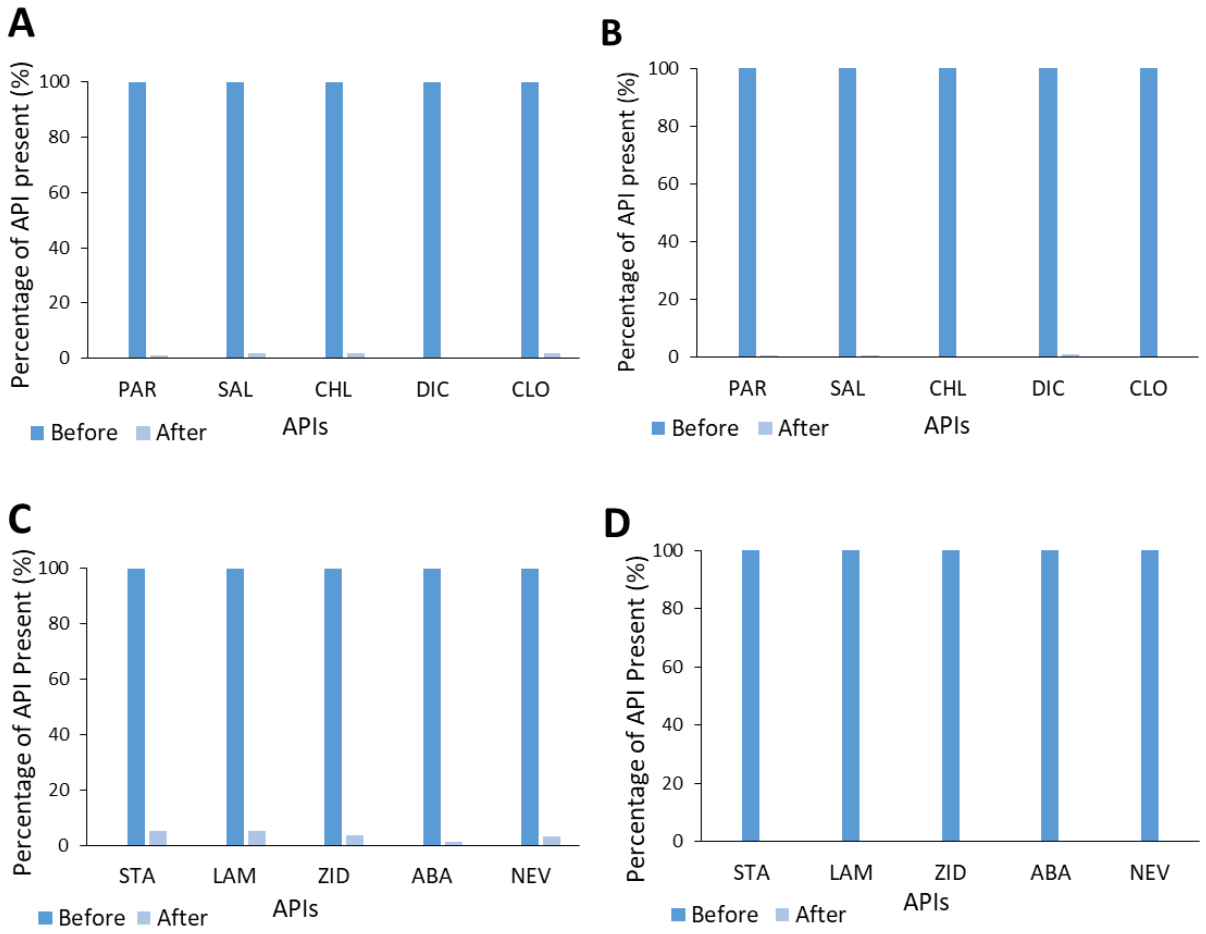


Figure 15: Granular activated carbon results: OTCs sample 1 (A), OTCs sample 2 (B), ARVs sample 1 (C), ARVs sample 2 (D). The respective abbreviations of the pharmaceuticals labelled under each graph are as follows: paracetamol (PARA), salicylic acid (SALI), chlorpheniramine maleate (CHL), diclofenac (DIC), clopidogrel (CLO), stavudine (STA), lamivudine (LAM), zidovudine (ZID), abacavir sulfate (ABA) and nevirapine (NEV).

The peaks of the pharmaceuticals were distinguishable in the chromatograms for sample 1 (A) and sample 2 (B) shown in Figure 16. Furthermore, the overlay of the before and after samples on the chromatograms gives a clear representation of the degradation of the pharmaceuticals. Salicylic acid and paracetamol seemed to peak at the same place for the second sample. A slight shift of the peaks occurred because the experiments were conducted on different days, thus the composition of the urine may have changed slightly. As such, the standard samples were rerun to verify the peak locations of salicylic acid and paracetamol for the second sample.

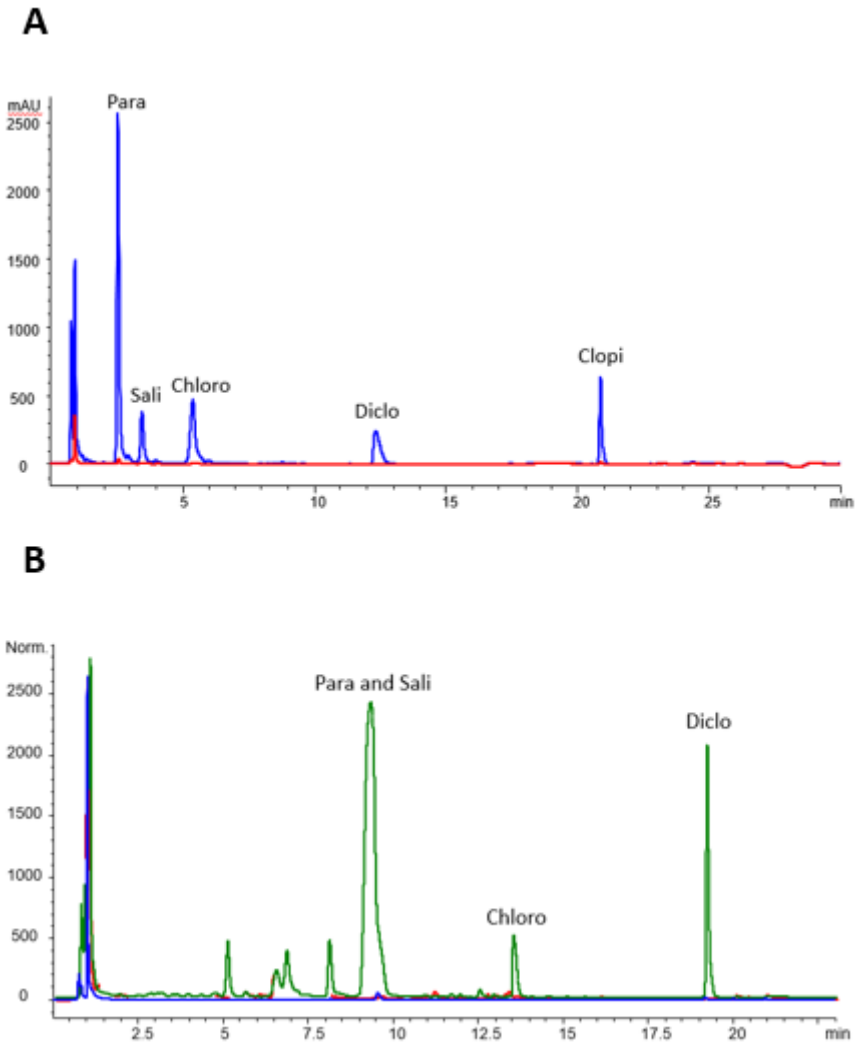


Figure 16: OTCs chromatograms for GAC: (A) sample 1 and (B) sample 2. The blue and the red chromatograms are for the untreated and treated sample respectively for sample 1. The green and blue chromatograms are for the untreated and treated sample respectively for sample 2. The respective abbreviations of the pharmaceuticals represent the following pharmaceuticals: paracetamol (Para), salicylic acid (Sali), chlorpheniramine maleate (Chloro), diclofenac (Diclo), clopidogrel (Clopi).

The individual pharmaceutical peaks for sample 1 (A) and sample 2 (B) are shown in Figure 17. However, a similar trend as for the OTCs sample 2 was observed where the standard samples had to be rerun to verify the peaks of the individual pharmaceutical.

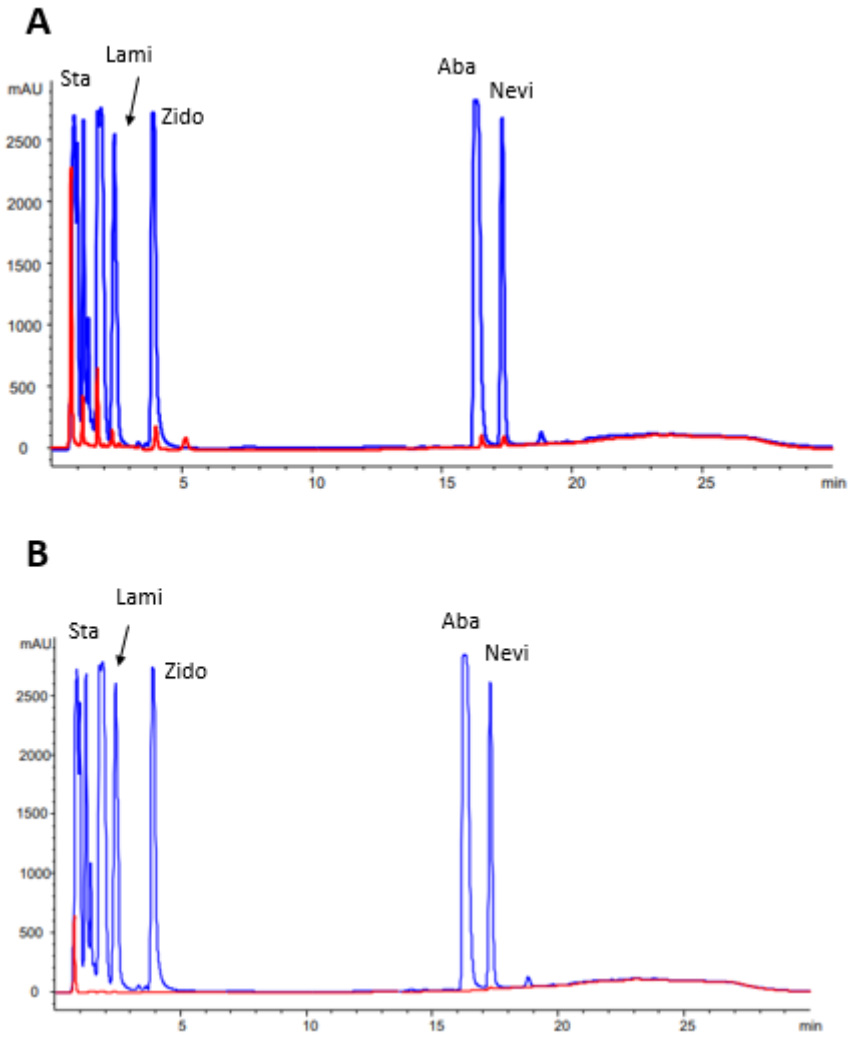


Figure 17: ARVs chromatograms for GAC: (A) sample 1 and (B) sample 2. The blue and the red chromatograms are for the untreated and treated sample, respectively. The respective abbreviations of the pharmaceuticals represent the following pharmaceuticals: stavudine (Sta), lamivudine (Lami), zidovudine (Zido), abacavir sulfate (Aba) and nevirapine (Nevi).

The results showed that GAC is effective in the removal of the pharmaceuticals chosen for this work. This supports the hypothesis that GAC will eliminate the pharmaceuticals from the sample solutions since more than 94% of each pharmaceutical was removed. The results from the current work agree with the findings from the study by Rostvall and co-workers (2018) which stated that the average pharmaceutical removal efficiency of GAC was 97%.

The results suggest that GAC derived from coconut shells is effective in the removal of pharmaceuticals. Furthermore, a nominal GAC surface area of 731 m^2 g^{-1} provides enough micropores on which the pharmaceuticals can attach.

The sample 1 and sample 2 of the OTCs and the ARVs used different GAC particle sizes. The difference in the degradation of the pharmaceuticals by the different GAC grain sizes was minor. Slight improvements in the degradation of the pharmaceuticals were observed when the GAC column was packed with fine GAC instead of coarse GAC. The pharmaceutical removal efficiency of the OTCs improved by 0.8%, while the pharmaceutical removal efficiency of the ARVs improved by 3.9%.

Köpping and co-workers (2020) found that the removal of pharmaceuticals with high adsorption is similar for both fine and coarse GAC. This is because the internal surface area of fine and coarse GAC is similar (Köpping et al., 2020). Therefore, it can be assumed that the OTCs and the ARVs used for this work had high adsorption since more than 94% of each pharmaceutical was removed by the fine and coarse GAC. Furthermore, the difference in the removal efficiency of the OTCs and the ARVs was less than 4%. This was an indication that although the external surface area of course and fine GAC is different, it has no major influence in the degradation of the pharmaceuticals. Therefore, the internal surface area is a contributing factor to the degradation of pharmaceuticals. It was assumed that the slight difference in the degradation efficiency of fine and coarse GAC was caused by the difference in amount of GAC which could be packed in the same column volume. Fine GAC was more densely packed than coarse GAC due to the narrow PSD.

Although the degradation of eleven pharmaceuticals (five OTCs and six ARVs) due to GAC was investigated for this work, only ten (five OTCs and five ARVs) appear in the results. This was expected since the sample solutions were stabilized with calcium hydroxide (pH > 12). It was proven for the high pH degradation method that tenofovir (an antiretroviral drug) degrades almost immediately when the pH of the sample solution is increased (pH > 12) – refer to section 4.1.

Furthermore, a minor shift of the pharmaceutical peaks occurred on the chromatograms since urine collected on different days was used. The difference in the urine composition of the collected urine was caused by factors such as diet (Maurer et al., 2006).

The results from the current work agree with the study by Rostvall and co-workers (2018) which investigated the removal of 83 micropollutants – 7.5 times more than the pharmaceuticals investigated for the current work. Therefore, it can be said that the results of the current work are valid.

Some of the advantages of using GAC include low operation costs, easy installation of the GAC system, minimal maintenance costs and the use of cost-effective adsorption (Chen et al., 2012). This means that a GAC system would be easily scalable. However, adsorbents with fine particles may cause hydraulic issues for the GAC system during operation. It is also difficult to separate some adsorbents from the aqueous phase (Chen et al., 2012). Therefore, a filtration process as post-treatment would be required. Additionally, the adsorption by the GAC is not selective since results from this work showed that both the pharmaceuticals and the urea (refer to section 4.6) were adsorbed. Therefore, GAC also removes urea from the stabilized urine which is contrary to the desired objective of the current work; that urea is conserved during the pharmaceutical removal process. As a result, GAC was not suitable as a pharmaceutical removal method for stabilized urine even though it removed most of the pharmaceuticals.

4.3 Hydrogen peroxide

Hydrogen peroxide is often used as an oxidant for the removal of pharmaceuticals. The sole use of hydrogen peroxide as an oxidant has proven inefficient through literature (as discussed in section 2.8.6). Nevertheless, the combined use of hydrogen peroxide and calcium hydroxide was applied in this work, which resulted in the degradation of some pharmaceuticals. This is because the calcium hydroxide would stabilize the urine (pH>12), thereby conserving urea for nutrient recovery. Furthermore, the dosage of the calcium hydroxide used to stabilize the urine was an overestimate, which resulted in excess hydroxide ions that aided in the degradation of pharmaceuticals. Additionally, the hydroxyl radicals from the hydrogen peroxide oxidize the pharmaceuticals, thereby causing the pharmaceuticals to degrade. Therefore, the combined effect of the oxidation from the hydrogen peroxide and the excess hydroxide ions from the addition of calcium hydroxide degraded the OTCs and ARVs selected for the current work at varying degrees (shown in Figure 18). The range of

degradation for the OTCs resulting from the addition of hydrogen peroxide was 0 - 64.7%. Diclofenac and chlorpheniramine maleate did not experience any degradation, while salicylic acid experienced the highest degradation. The range of degradation for the ARVs was 17.2 - 73.4%, which was better than the range of degradation for the OTCs. Stavudine experienced the least degradation, while lamivudine experienced the highest degradation. The detailed experimental results are given in Annexure B3. This means that the additional oxygen atom from the oxidation of hydrogen peroxide (in the presence of excess hydroxide ions from the addition of calcium hydroxide) oxidized some of the pharmaceuticals such as salicylic acid and lamivudine. However, some pharmaceuticals (diclofenac and chlorpheniramine maleate) were unoxidized by hydrogen peroxide.

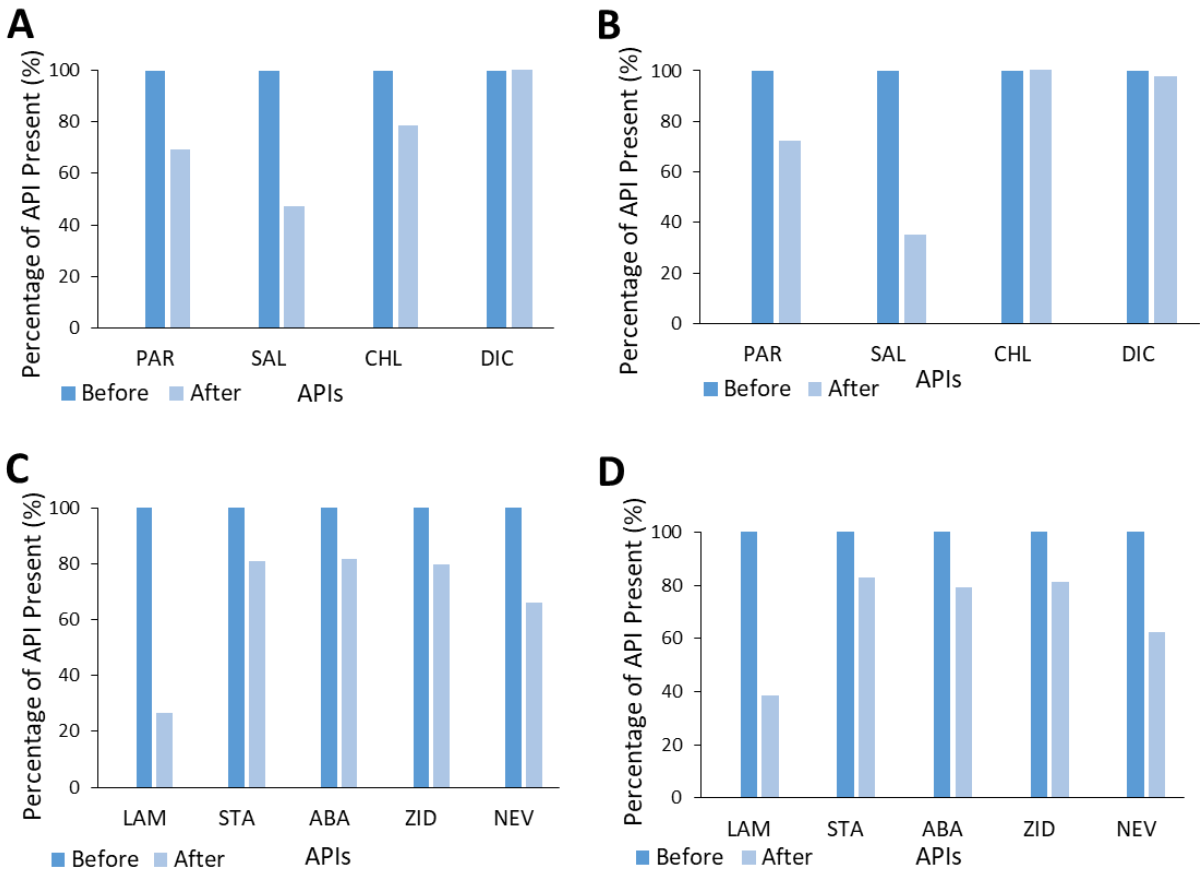


Figure 18: Hydrogen peroxide results: OTCs sample 1 (A), OTCs sample 2 (B), ARVs sample 1 (C), ARVs sample 2 (D). The respective abbreviations of the pharmaceuticals labelled under each graph are as follows: paracetamol (PARA), salicylic acid (SALI), chlorpheniramine maleate (CHL), diclofenac (DIC), stavudine (STA), lamivudine (LAM), zidovudine (ZID), abacavir sulfate (ABA) and nevirapine (NEV).

The chromatograms for the OTCs samples (shown in Figure 19) had defined peaks for each pharmaceutical. However, extra peaks (indicated with asterisks) were observed for the analysis of the treated samples. The peaks were not identified since the focus of the current work was the degradation of the primary pharmaceuticals. Nonetheless, it was assumed that the extra peaks represent by-products that occur because of the pharmaceutical degradation.

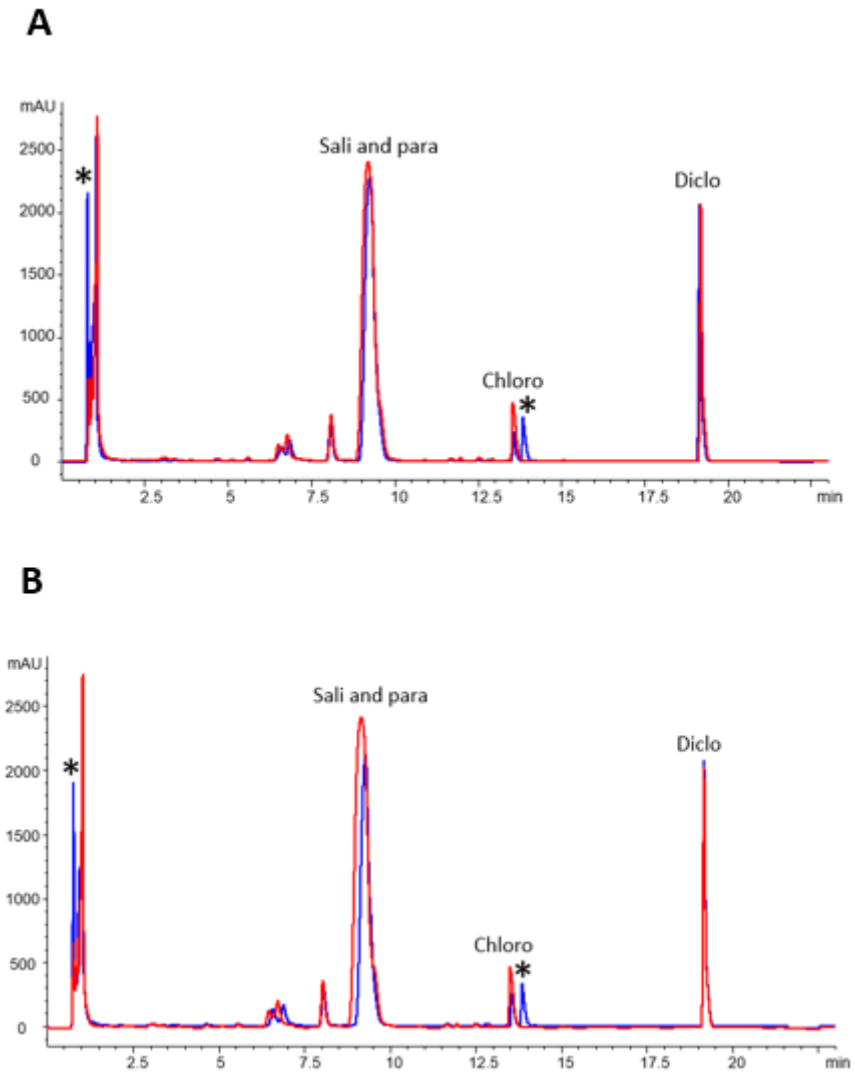


Figure 19: OTCs chromatograms for hydrogen peroxide: (A) sample 1 and (B) sample 2. The red and the blue chromatograms are for the untreated and treated sample, respectively. The respective abbreviations of the pharmaceuticals represent the following pharmaceuticals: paracetamol (Para), salicylic acid (Sali), chlorpheniramine maleate (Chloro), diclofenac (Diclo).

The degradation of the ARVs due to hydrogen peroxide is represented in the chromatograms (shown in Figure 20). The peaks for each pharmaceutical were clearly distinguished. The chromatograms show that some pharmaceuticals were more degraded than others.

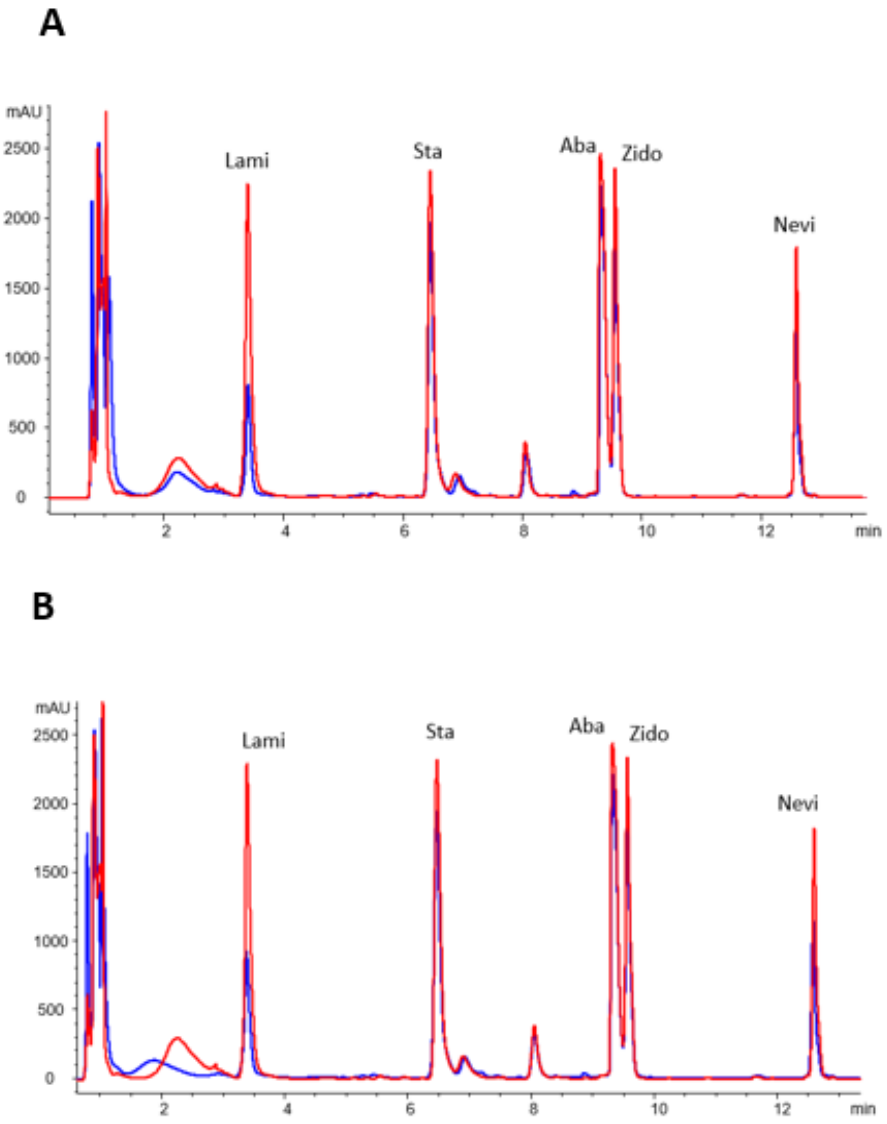


Figure 20: ARVs chromatograms for hydrogen peroxide: (A) sample 1 and (B) sample 2. The red and the blue chromatograms are for the untreated and treated sample, respectively. The respective abbreviations of the pharmaceuticals represent the following pharmaceuticals: stavudine (Sta), lamivudine (Lami), zidovudine (Zido), abacavir sulfate (Aba) and nevirapine (Nevi).

The results suggested that the sole use of the hydrogen peroxide with calcium hydroxide is not suitable for the degradation of pharmaceuticals. This contradicts the hypothesis which is that the combined effect of oxidation due to hydroxyl radicals from the addition of hydrogen peroxide in the presence of excess hydroxide ions from the stabilization of urine using calcium hydroxide, will degrade the pharmaceuticals. Some pharmaceuticals experienced high degradation of up to 73% (lamivudine), while other pharmaceuticals experienced no degradation (diclofenac and chlorpheniramine maleate). The degradation of some pharmaceuticals increased (paracetamol, salicylic acid, abacavir sulphate and nevirapine), while the degradation of other pharmaceuticals decreased (chlorpheniramine maleate, nevirapine, stavudine, lamivudine and zidovudine). Furthermore, the average degradation rate due to the addition of hydrogen peroxide in urine stabilized with calcium hydroxide decreased when compared to the average degradation rate as result of just increasing the pH. It was inferred that oxidation plays a minor role in the degradation of pharmaceuticals. Instead, hydrolysis (as a result of hydroxide ions from an increase in pH) is the major form of degradation.

This result agrees with literature since Feliciano and co-workers (2020) proved that a hydrogen peroxide dosage of 250 mg L^{-1} could degrade 95% of lamivudine. The oxidation of lamivudine may be attributed to the oxathiolane and cytosine ring (shown in Figure 7). Hofmann and co-workers (2007) showed that diclofenac could degrade by heterogeneous catalytic oxidation using hydrogen peroxide (Hofmann et al., 2007). However, a catalyst was not used for the current work, which may have caused diclofenac did not degrade as a result of the phenyl ring which is in its structure (refer to Figure 6). On the other hand, only 3% of chlorpheniramine maleate degraded after 30 minutes of treatment using hydrogen peroxide (Moyano et al., 2005). A similar pattern was observed for the current work since chlorpheniramine maleate did not degrade when hydrogen peroxide was added in the sample solution. The absence of the C = O bond in the structure of chlorpheniramine maleate makes it impossible for hydrogen peroxide to oxidize the pharmaceutical.

Although lamivudine and stavudine have a similar structure, they experienced the highest and lowest degradation for the ARVs, respectively. The extra sulphur on the oxathiolane ring and the NH_2 group on the cytosine ring instead of an OH group for lamivudine (shown on Figure 7) may have caused the degradation of lamivudine to be more when compared to

stavudine. It was noted that Dunge and co-workers (2004) said zidovudine cannot be degraded by hydrogen peroxide because zidovudine cannot form epoxides. Yet, results from the current study showed that zidovudine experienced an average degradation of 19.4%. The degradation of zidovudine (through hydrolysis) was caused by the presence of hydroxide ions from the pH adjustment. Since the structure of zidovudine, lamivudine and stavudine are similar, the degradation of the pharmaceuticals could result from the excess hydroxide ions from the high pH. Nevertheless, the results contribute to a clearer understanding of the degradation of pharmaceuticals due to a one-time dosage of hydrogen peroxide.

There was an expectation that the pharmaceuticals would be oxidized by the hydrogen peroxide, however, literature agrees that the degradation of pharmaceuticals using hydrogen peroxide is more effective when used as a combined chemical oxidation method. The combined use of hydrogen peroxide and ultraviolet (UV) is one such way as proven by Wols and co-workers (2013). A 90% degradation could be achieved for pharmaceuticals in natural water at UV doses between 500 (MP) and 1000 (LP) mJ cm^{-2} and 10 mg L^{-1} hydrogen peroxide (Wols et al., 2013). The investigation of the combined use of hydrogen peroxide and UV was beyond the scope of this work.

The use of the 30% (v/v) hydrogen peroxide and a dosage of 0.1 mL mL^{-1} for a two-hour period was valid for this work since they were based on literature. It is important to recognize that the parameters were based on average values found in literature. The influence of factors such as other forms of hydrogen peroxide, different hydrogen peroxide dosages and the duration of treatment were not investigated for this work. Literature suggests that hydrogen peroxide is most efficient when used as a combined chemical oxidation process. It would be more beneficial to determine the degradation of the combined chemical oxidation treatment process rather than optimize the parameters of the one-time dosage of hydrogen peroxide to degrade pharmaceuticals in urine stabilized with calcium hydroxide.

The pharmaceuticals which were used for the current work were sourced from donations and clopidogrel (an antiplatelet agent) was out of stock. Nonetheless, the results from the current work were conclusive since Agrawal and co-workers (2003) confirmed that the degradation of clopidogrel due to hydrogen peroxide was 18.63% after an hour of treatment. Furthermore, the study by Agrawal and co-workers (2003) used the same type of hydrogen peroxide (30% v/v) as was used for this study (Agrawal et al., 2003).

As expected, tenofovir is not shown in the results of the current work as the sample solutions were stabilized with calcium hydroxide, raising the pH (>12). Tenofovir degraded almost immediately at a high environment (refer to section 4.1). Despite the limited number of pharmaceuticals used for the current work, the results of this work agree with literature and add to the existing knowledge and understanding of the degradation of pharmaceuticals due to a one-time dosage of hydrogen peroxide for urine stabilized with calcium hydroxide. The combined effect of the hydrogen peroxide in a high pH environment was inefficient for the degradation of the pharmaceuticals investigated for this work. Furthermore, the urea conservation of degradation method was 87.4% (refer to section 4.6).

4.4 Hydrodynamic cavitation

The degradation of the pharmaceuticals due to the hydroxyl radicals generated by the hydrodynamic cavitation (HC) system was different at an acidic condition (pH 2) and an alkaline condition (pH 12.4), shown in Figure 21. The degradation range at pH 2 was 10.4 - 49.2%, with paracetamol and zidovudine reporting the lowest and highest degradation, respectively. The degradation range did however drop to 0 - 16.6% at pH 12.4. Chlorphenamine maleate had the highest degradation of 16.6%, while paracetamol, zidovudine, lamivudine and stavudine experienced less than 5% degradation at a high pH. The detailed experimental results are given in Annexure B4.

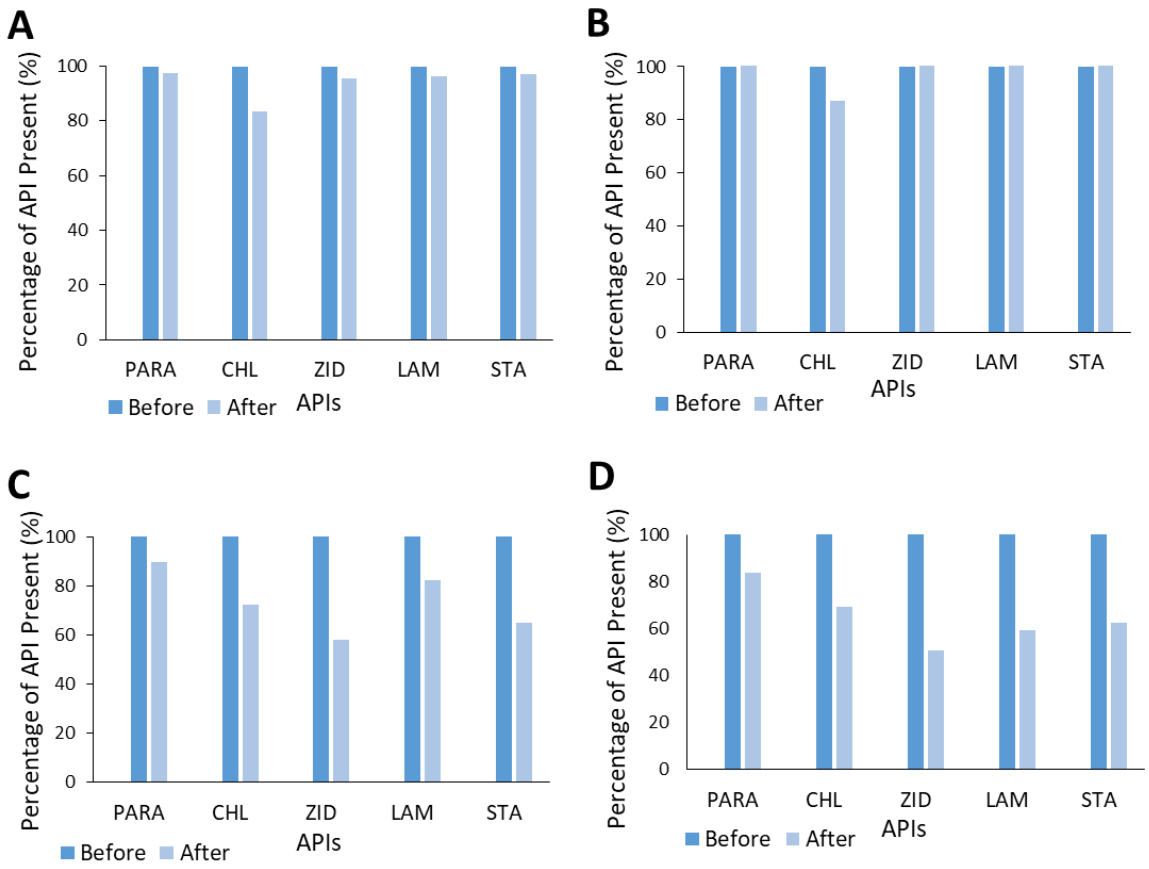


Figure 21: Hydrodynamic cavitation results: Basic sample 1 (A), Basic sample 2 (B), Acidic sample 1 (C), Acidic sample 2 (D). The respective abbreviations of the pharmaceuticals labelled under each graph are as follows: paracetamol (PARA), chlorpheniramine maleate (CHL), stavudine (STA), lamivudine (LAM) and zidovudine (ZID).

The chromatograms (in Figure 22) for the HC system operated at pH 12.4 showed a slight decrease of the peaks representing the pharmaceuticals even though there was a slight increase in the degradation products identified for paracetamol. Therefore, the HC system operated at a high pH was ineffective in the degradation of the pharmaceuticals over a 30-minute period. The y-axis is not shown, since the graph shows the relative comparisons of the samples at three different time intervals. The chromatograms were given to illustrate the degradation of the pharmaceuticals over time, and not to quantify the degradation from the chromatograms.

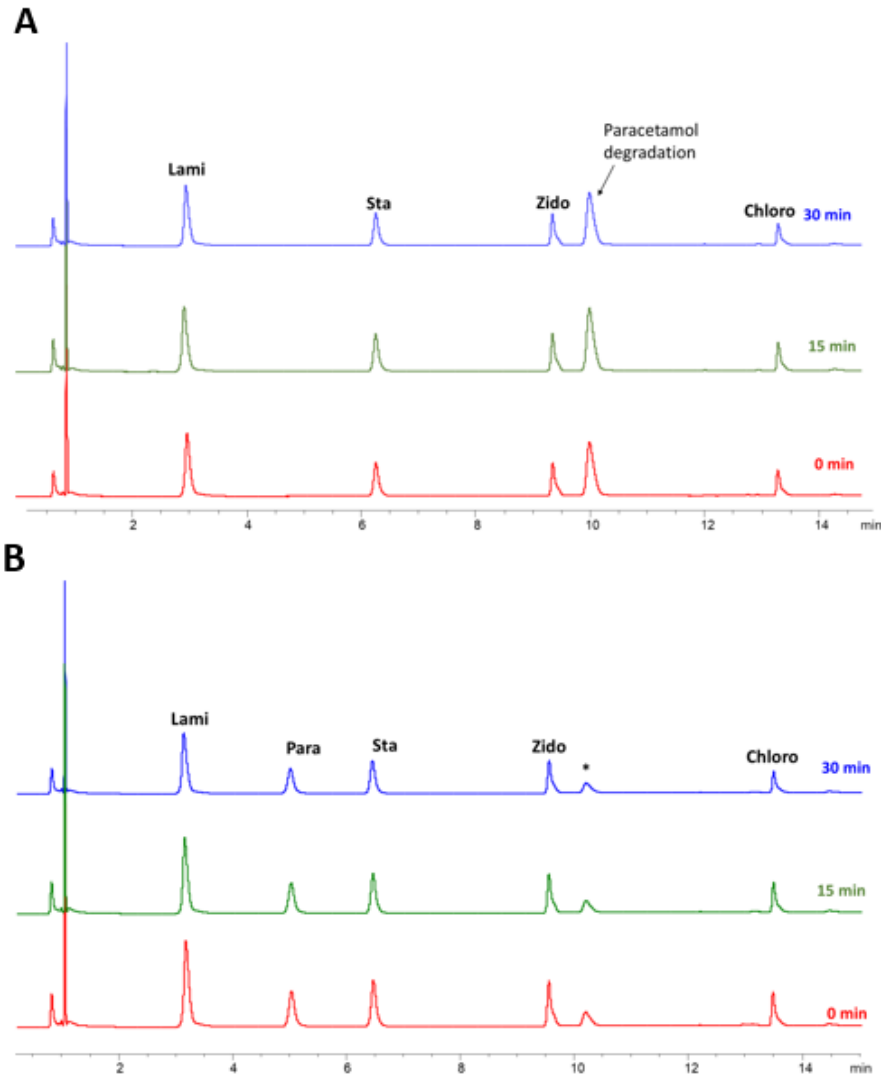


Figure 22: Chromatograms for hydrodynamic cavitation at pH 12.4: sample 1 (A) and sample 2 (B). The colour coded chromatograms correspond to the time during the HC system as follows: 0 minutes (red); 15 minutes (green) and 30 minutes (blue). The respective abbreviations of the pharmaceuticals represent the following pharmaceuticals: paracetamol (Para), chlorpheniramine maleate (Chloro), stavudine (Sta), lamivudine (Lami) and zidovudine (Zido).

Contrary, the chromatograms (shown in Figure 23) represent the degradation of the pharmaceuticals at a low pH (pH 2) over a 30-minute duration. Furthermore, there was an increase in the peaks of the degradation products. Although the degradation products were not identified, the increase in their concentration confirmed that the primary pharmaceuticals were more degraded by the HC system operated at pH 2 when compared to the HC system operated at pH 12.4.

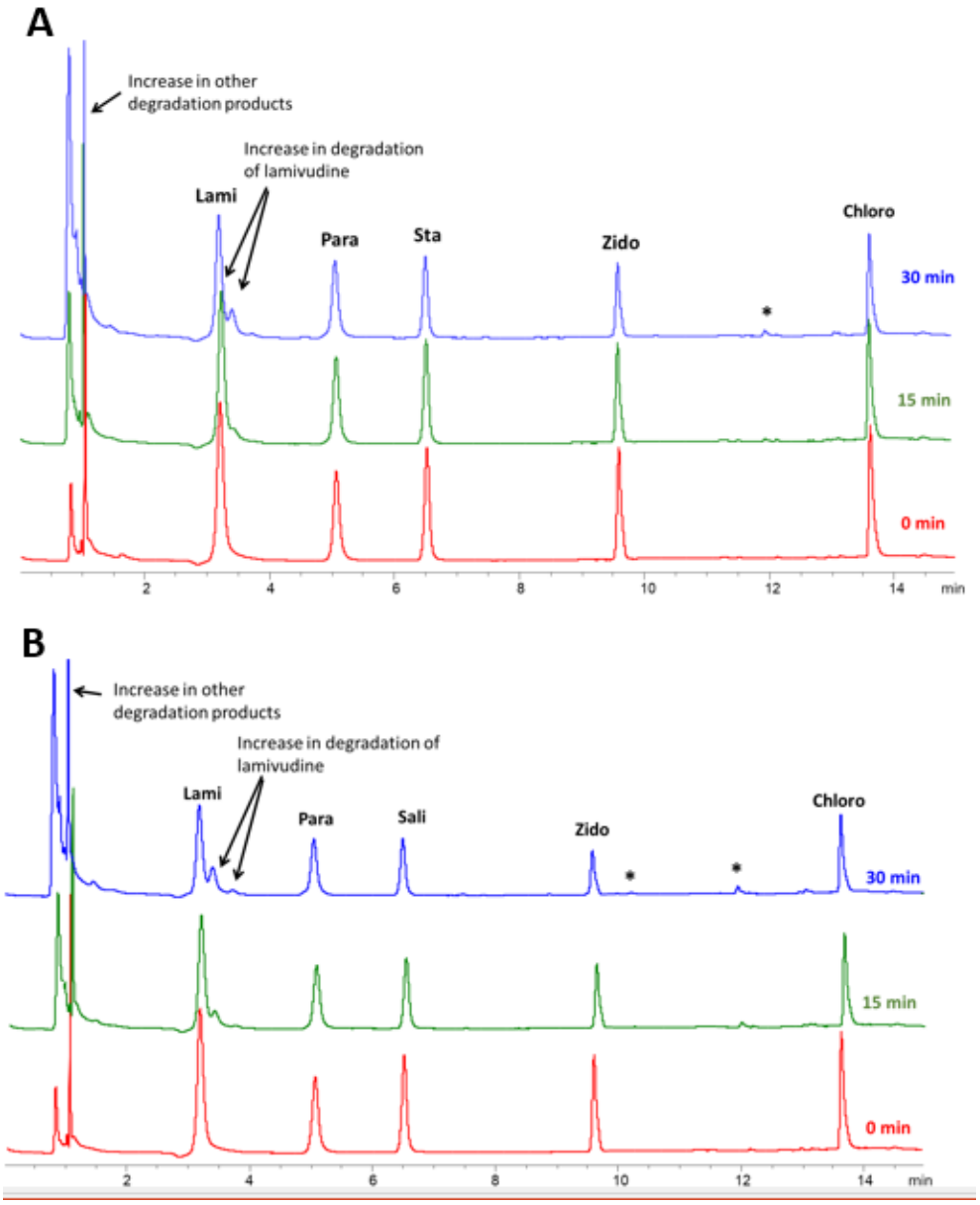


Figure 23: Chromatograms for hydrodynamic cavitation at pH 2: sample 1 (A) and sample 2 (B). The colour coded chromatograms correspond to the time during the HC system as follows: 0 minutes (red); 15 minutes (green) and 30 minutes (blue). The respective abbreviations of the pharmaceuticals represent the following pharmaceuticals: paracetamol (Para), chlorpheniramine maleate (Chloro), stavudine (Sta), lamivudine (Lami) and zidovudine (Zido).

The results from the HC experiments showed potential in the degradation of pharmaceuticals from the hydroxyl radicals generated from the cavitation process. The HC system operated at a low pH (pH 2) resulted in a higher degradation than the system operated at a high pH (12.4). It was postulated that the bonds in the pharmaceutical structures are weaker at a low pH since hydroxyl radicals are produced for both the hydrogen peroxide and the HC system.

However, the HC was less effective at a high pH. Therefore, a low pH was ideal for the oxidation of the pharmaceuticals by the hydroxyl radicals.

The difference in the degradation of the pharmaceuticals at different pH environments is explained by the fact that each solution has an optimum pH at which pharmaceuticals can degrade (Rajoriya et al., 2016). This proves that the degradation of pharmaceuticals improved when the pH was optimized to pH 2. The results from the HC degradation method at a high pH also showed that hydroxyl radicals were ineffective in degrading pharmaceuticals at a high pH. Nevertheless, the results from the optimization of the pH for the HC system suggest that the optimization of the other parameters that influence the degradation of pharmaceuticals using the cavitation system might further improve the degradation efficiency of the cavitation system. Based on the findings from literature, the optimization of inlet pressure, temperature and cavitation devices improve the degradation efficiency of a HC system (Rajoriya et al., 2016).

An inlet pressure of 200 kPa was initially applied for this work, but literature showed that the optimum inlet pressure for the removal of various dyes was within the range of 480 – 490 kPa (Mishra and Gogate, 2010; Gogate and Bhosale, 2013). This explains the low pharmaceutical degradation efficiency at a pressure of 200 kPa. The temperature was not monitored for the initial HC experiments, however there is a consensus from literature that a temperature of 50˚C is optimal for the degradation of micropollutants (Wang et al., 2009; Šarc et al., 2017). In addition, Saharan (2013) found that a circular venturi performs better than an orifice. It can be assumed that the cavitation device did not have an influence on the degradation of the pharmaceuticals since a circular venturi was used for the initial HC experiments.

The HC experiments required larger sample volumes. For this reason, a simplified urea-water solution was used instead of real urine. This compromised the use of all the eleven selected pharmaceuticals for the current work since the pharmaceuticals were acquired through donations. This is because the pharmaceuticals were expensive, therefore, the quantity of the pharmaceuticals which could be used was restricted. As a result, only five pharmaceuticals (two OTCs and three ARVs) were used for the HC experiments. Nonetheless, the results were valid since studies for the degradation of pharmaceuticals are often focused on one specific micropollutant instead of a mixture of micropollutants. Furthermore, the five

pharmaceuticals were representative of the eleven pharmaceuticals (five OTCs and six ARVs) chosen for the current work since two OTCs and three ARVs were used.

The optimization of the HC system was considered for this work since it also conserved more than 90% of urea (refer to section 4.6). Besides being a new pharmaceutical removal technology, it was less invasive than the optimization of the hydrogen peroxide method which would require more equipment and a new setup for the combined hydrogen peroxide/ultraviolet system. Furthermore, the optimization of GAC was not considered because it already had a high pharmaceutical removal efficiency (>94%). Additionally, changing the dosage of calcium hydroxide would not be beneficial since a dosage of 10 g L^{-1} was an overestimate for the stabilization of urine (Randall et al., 2016).

4.5 Optimized hydrodynamic cavitation system

4.5.1 Pharmaceutical degradation

Of the four pharmaceutical removal methods, the hydrodynamic cavitation (HC) system (operated at a pH 2) showed the greatest potential for pharmaceutical degradation (upon optimization) while conserving urea (>90%). Two parameters were optimized: the inlet pressure and the change of the cavitation device. In addition, the temperature of the system was monitored throughout the optimized HC experiments. Therefore, the HC system was optimized at pH 2. Furthermore, the optimum pressure was found to be 400 kPa using a 3 mm orifice. The optimized HC system improved the degradation of the pharmaceuticals (seen in Figure 24). A pharmaceutical degradation range of 54.5 - 87.6% was achieved, with paracetamol and zidovudine experiencing the highest and lowest degradation, respectively. Annexure C2 gives the detailed experimental results.

It can be argued that the pharmaceutical degradation efficiency of the optimized system is not good when compared to that of the granular activated carbon. However, it is important to consider the fact that pharmaceuticals in the environment exist in concentrations in the order of 1 µg L^{-1} or less (Halling-Sorensen et al., 1998). The concentrations used for HC system where 25 000 times more than what is found in the environment. Therefore, the system operated at the optimized HC conditions was efficient in the removal of pharmaceuticals in the waste solutions.

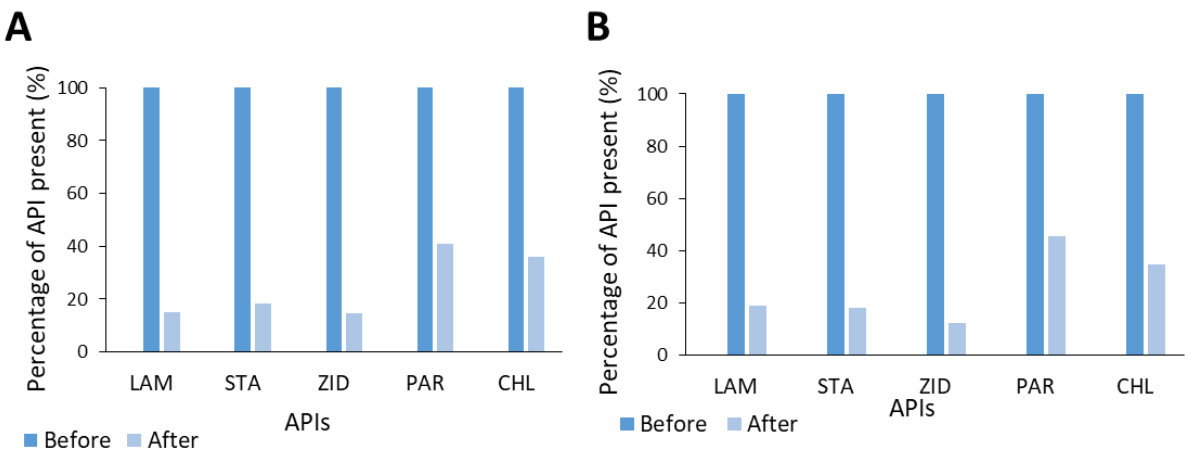


Figure 24: Optimized hydrodynamic cavitation pharmaceutical degradation results: Optimized hydrodynamic cavitation sample 1 (A), Optimized hydrodynamic cavitation sample 2 (B). The respective abbreviations of the pharmaceuticals labelled under each graph are as follows: paracetamol (PARA), chlorpheniramine maleate (CHL), stavudine (STA), lamivudine (LAM) and zidovudine (ZID).

The chromatographs of the samples for the optimized HC system are given in Figure 25. The chromatograms of the samples at three different times (time 0, 15 and 30 minutes) are superimposed to illustrate the extent of degradation due to the optimized HC system. The asterisks indicate the formation of degradation products. Although the degradation products were not identified, they confirmed the degradation of the primary pharmaceuticals.

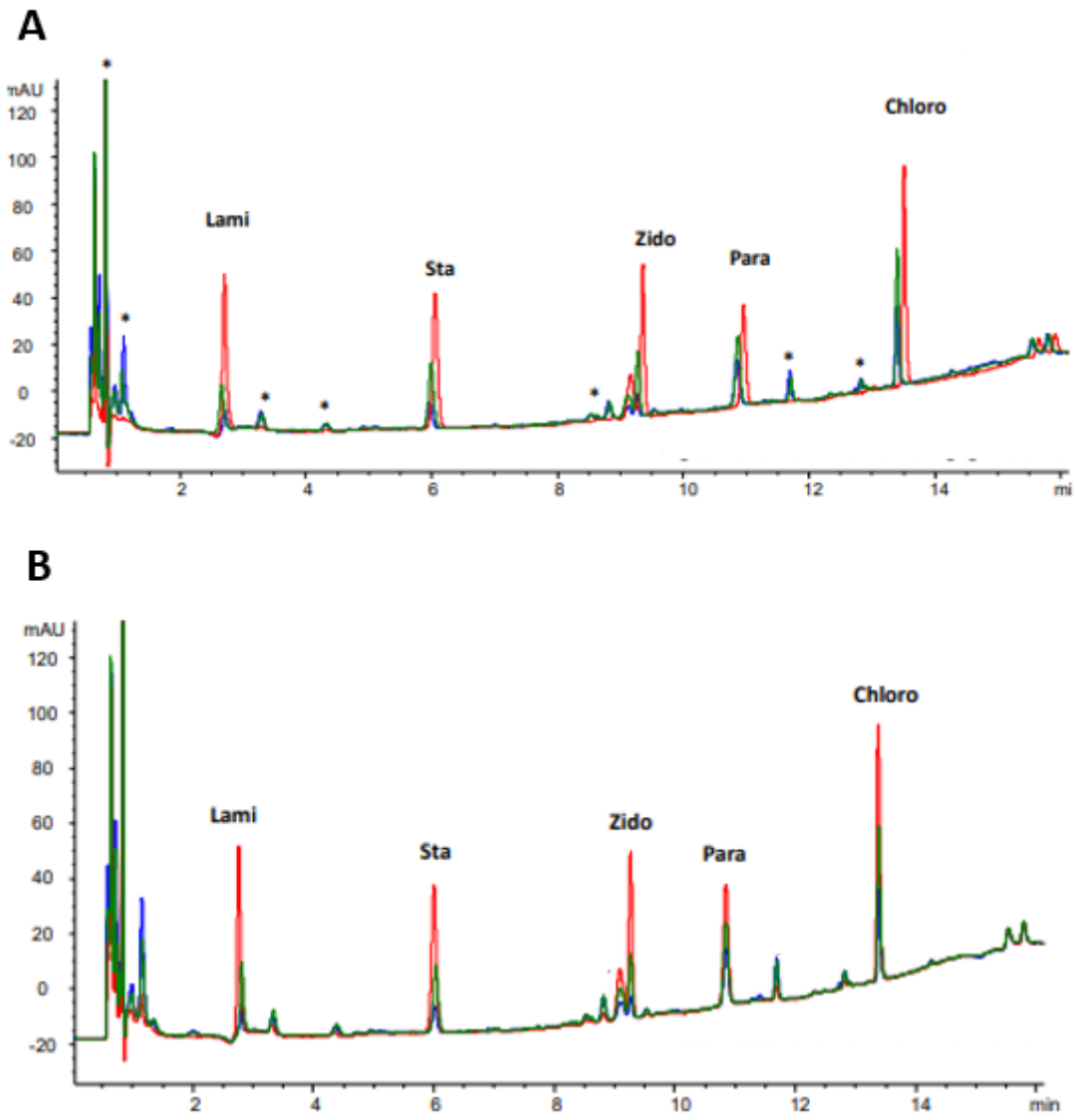


Figure 25: Optimized hydrodynamic cavitation pharmaceutical degradation chromatograms: sample 1 (A), sample 2 (B). The colour coded chromatograms correspond to the time during the HC system as follows: 0 minutes (red); 15 minutes (green) and 30 minutes (blue). The respective abbreviations of the pharmaceuticals represent the following pharmaceuticals: paracetamol (Para), chlorpheniramine maleate (Chloro), stavudine (Sta), lamivudine (Lami) and zidovudine (Zido).

4.5.2 The effect of temperature and pH

The temperature of the optimized HC system increased linearly over time. Figure 26 shows the change of temperature and pH over time for the optimized cavitation system. The R-squared values for sample 1 (A) and sample 2 (B) were 0.95 and 0.98 respectively, which confirm the linearity of temperature over time. The full details are given in Annexure C4.

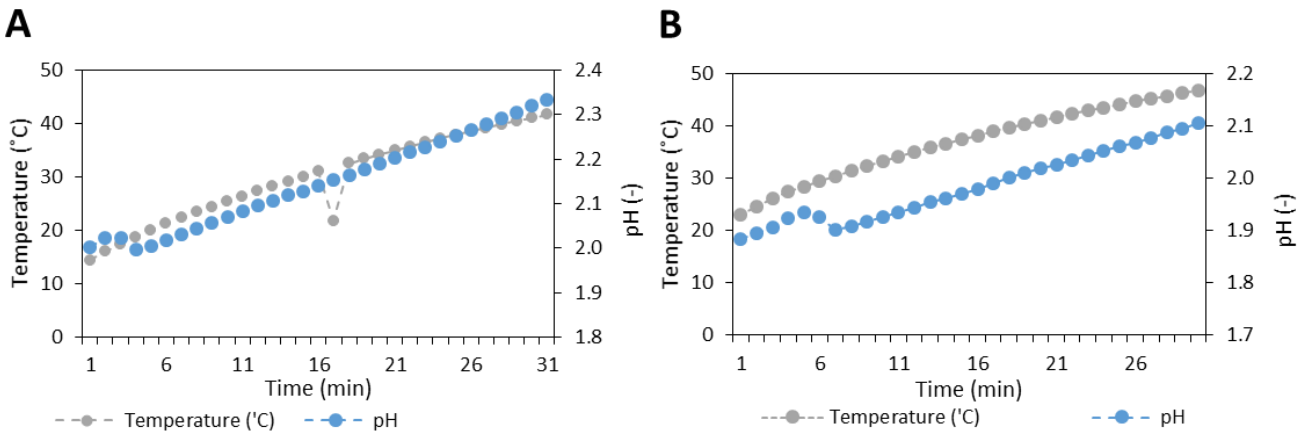


Figure 26: Optimized hydrodynamic cavitation system temperature and pH analysis: Optimized hydrodynamic cavitation sample 1 (A), Optimized hydrodynamic cavitation sample 2 (B).

Furthermore, the pH was consistent throughout the experiments. The sample solutions were adjusted to pH 2 following the results shown in section 4.2.4. This implied that the urine treated using HC would be stabilized by acidification instead of alkalinization. Rather than dosing with calcium hydroxide then adjusting the solution pH to 2, the urine solution will be adjusted to pH 2. Both the urea and the ammonium would be conserved (refer to the discussed in section 2.5.1), since the ammonium ions form at a low pH.

4.5.3 Cavitation device

Although it was said that a circular venturi is more effective than an orifice (Saharan et al., 2013), the cavitation device was changed from a circular venturi to a 3 mm orifice. This was to verify whether the statement made by Saharan and co-workers (2013) was valid for all sample solutions. The results from this work showed that a 3 mm orifice was more effective in the removal of pharmaceuticals than a circular venturi. This may be attributed to the throat diameter of the venturi. It is known that hydroxyl radicals are produced when cavitation bubbles (generated in the throat of the venturi) collapse due to the pressure difference created from a low-pressure zone to a high pressure (Warade et al., 2016). However, a big throat diameter of a venturi limits the pressure drop, which results in less hydroxyl radicals being generated, consequently less pharmaceutical degradation.

4.5.4 Inlet pressure

The optimum inlet pressure of the HC system was found by varying the inlet pressure of the HC system. Since a 3 mm orifice was chosen as the cavitation device for the optimized system, the optimum pressure was determined for a 3 mm orifice. Three pressures were investigated: 200 kPa, 300 kPa and 400 kPa. The results from this work showed that the optimum inlet pressure was 400 kPa (given in Annexure C1). The degradation at of paracetamol at 200 kPa, 300 kPa and 400 kPa was 19.5%, 18.8% and 29.6% respectively. This suggests that the cavitation bubbles formed at 200 kPa and 300 kPa were not big enough, since a significant pressure drop is required to produce and grow the cavitation bubbles (Kuldeep et al., 2014). Therefore, less hydroxyl radicals were produced at 200 kPa and 300 kPa when compared to 400 kPa because they are derived from the collapse of the cavitation bubbles which enables the dissociation of water to form hydroxyl radicals (Saharan et al., 2012).

4.5.5 Effect of temperature

There is a concern over the rise in temperature of the urine sample solution when using the HC system. This is because urea degrades at a temperature of more than 40˚C (Randall et al., 2016). The optimized system reached a maximum temperature of almost 50˚C (shown in Annexure C4). The temperature matches the temperature at which the maximum cavitation aggressiveness occurs (Šarc et al., 2017). This means that at a temperature of 50˚C, the cavitation is most effective in the degradation of micropollutants such as pharmaceuticals.

The urea was analyzed to find out how much of it had degraded. Contrary to what Randall and co-workers (2016) found, more than 95% of the urea in the sample solution treated by the optimized system was conserved. However, the system was run for 30 minutes, and the temperature of the sample solution was above 40˚C for the last 10 minutes. Additionally, the loss of urea is not immediate once the temperature of a solution is above 40˚C.

Since the degradation of the urea was determined in relative terms and not absolute terms, the samples may have both lost urea. The samples were kept at 4 ˚C since it is known that the rate of urea hydrolysis increases with an increase in storage temperature (Hellstrom et al., 1999). This was to make sure that there was no hydrolysis that occurred which would result in the loss of ammonium.

4.5.6 Practical application of the hydrodynamic cavitation system

The optimized hydrodynamic cavitation (HC) system would require 1.84 kW m^{-3} (refer to Annexure F). The energy required is realistic for industry application considering that Yen (2016) used 1.73 kW m^{-3} to decolourize textile water using the UV/H_2O_2 process. The energy from the treatment process by Yen (2016) is comparable to the energy which is required to operate the HC system at the optimized operating conditions used for this work (Yen, 2016).

Furthermore, the HC system would be scalable since it requires a simple reactor design for larger-scale operation capacity (Yuequn et al., 2016). A study by Garuti and co-workers (2018) investigated a full-scale HC pre-treatment process in an agricultural biogas plant. The system was equipped with three digesters (each with a capacity of 1.4 ML) which were installed in series. The findings from the study revealed that the system was efficient and could be operated at a low energy. Furthermore, it was easy to implement the cavitation system (Garuti et al., 2018). With that being said, it would be possible to implement the HC system in a urine treatment plant.

Chipako and Randall (2020a) proposed a decentralized system for the collection of urine (used for fertilizer production) for the City of Cape Town. An estimated amount of urine that could be collected from malls within the City of Cape Town was 392 m^3 yr^{-1}, which translates to approximately 1080 L d^{-1} (Chipako and Randall, 2020a). The findings from the study suggest that the 80 L cavitation system would need to be scaled by a factor of at least 20, which can accommodate for a flow of up to 1600 L d^{-1}.

Chipako and Randall (2020b) made a further recommendation for fresh urine treatment. However, the inclusion of a HC system to degrade the pharmaceuticals found in urine would alter the proposed urine treatment train. Instead of base stabilization with calcium hydroxide, the fresh urine would be stabilized by acidification (pH 2). Citric acid is recommended for use to acidify the urine since citric acid is the main organic acid found in citrus fruits (Grewal and Kalra, 1995). Therefore, traces of citric acid in urine-derived fertilizer will not be harmful for human handling and consumption. The stabilized urine would not be filtered since the solubility of citric acid is higher than that of calcium hydroxide. Furthermore, precipitation does not occur at low pH. The last stage will be an evaporation process to concentrate the urine solution instead of reverse osmosis. This is because acidified urine results in brown

fouling on the reverse osmosis membrane surface which reduces the permeate flux of the reverse osmosis process (Courtney and Randall, 2022). However, the cost and energy required for evaporation is up to three times more than what is required for reverse osmosis (Ek et al., 2006).

4.6 Urea conservation results

The conservation of urea and ammonium varied significantly across the four degradation methods (shown in Figure 27). The detailed degradation results are outlined in Annexure D.

The addition of calcium hydroxide to the urine sample solution caused a high pH (>12), which resulted in a 4% and 18.5% loss of urea and ammonium, respectively. The result was expected since the stabilization of urine with calcium hydroxide at a concentration of 10 g L^{-1} of fresh urine will conserve the urea in the urine. This is because the urease activity (shown to hydrolyze urine in section 2.4) is inhibited by the high pH environment (Randall et al., 2016).

The adsorption ability of granular activated carbon (GAC) removed most of the urea and ammonium in the sample solution since 83.4% of urea and 72.4% of ammonium was lost. Similarly, a study by Safwat and Matta (2018) discovered that the urea removal efficiency of GAC increases with an increase in pH value. The adsorption of the urea is a result of the porous characteristic of GAC (Safwat and Matta, 2018).

The oxidation from the hydrogen peroxide degraded only 12.6% of the urea in the sample solution, however, almost half of the ammonium (50.6%) was degraded. A similar result was reported by Long and co-workers (2019) when 12.8% of urea was degraded by hydrogen peroxide (used with ultraviolet) from swimming pool water. The low degradation of urea was attributed to the weak effect of the hydroxyl radicals created by the UV/H_2O_2 process (Long et al., 2019). Similarly, the results from the current work suggest that the hydroxyl radicals did have a stronger effect on the degradation of ammonium.

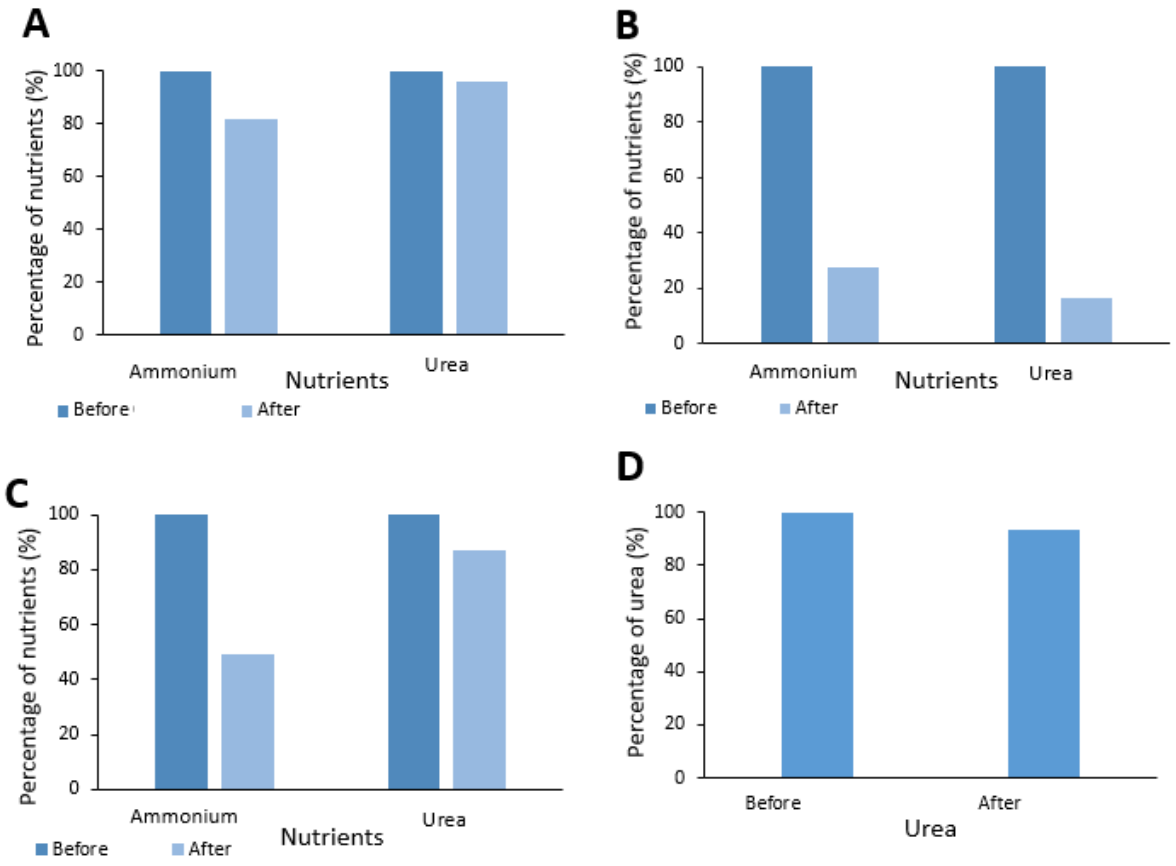


Figure 27: Urea degradation results: high pH (A); granular activated carbon (GAC) (B); hydrogen peroxide (C); and hydrodynamic cavitation (D). Graph D does not have ammonium since a simple urea-water solution (with only water and urea) was used for the experiment due to the high-volume requirement.

The hydrodynamic cavitation (HC) system experienced only 6.8% degradation of urea due to the hydroxyl radicals formed during cavitation. A study by Song and co-workers (2019) discovered that the high activity of the free hydroxyl radicals produced by the HC system had an insignificant effect on the removal of nitrogen (Song et al., 2019). It was inferred that the high activity of the free hydroxyl radicals generated from the HC system had negligible effect on the degradation of urea since more than 93% of the urea was conserved. Table 9 gives a summary of the degradation of urea and ammonium due to each pharmaceutical degradation methods.

Table 9: Summary of the degradation of urea and ammonium due to the four degradation methods.

Degradation method	Urea loss (%)	Ammonium (%)
High pH	4	18.5
Granular activated carbon	83.4	72.4
Hydrogen peroxide	12.6	50.6
Hydrodynamic cavitation	6.8	-

The conservation of urea for a pharmaceutical removal method is imperative for the reuse of stabilized urine. It was expected that the high pH method would have the highest conservation of urea since a high pH (> 12) was shown to stabilize the urea in the urine, thus preventing urea hydrolysis (Randall et al., 2016). Although the HC system and the hydrogen peroxide both generate hydroxyl radicals, there was a 5.8% difference in the degradation of the urea. This may be attributed to the difference in the amount of free hydroxyl radicals.

It was inferred that the urea molecules attached themselves to the microporous structure of the GAC. This statement agrees with the hypothesis made for the GAC degradation method. Contrary, Köpping and co-workers (2020) showed that most of the nutrients were conserved when GAC columns were used to remove eleven pharmaceuticals. However, Köpping and co-workers (2020) used nitrified urine instead of stabilized urine.

The conservation of ammonium is also important but the nitrogen in fresh urine is mainly in the form of urea. Hence, the urea-water solution samples for the HC system only had urea and not ammonium.

Previous studies have shown that nutrient recovery methods, such as reverse osmosis and precipitation technologies, can conserve up to 90% of the nitrogen content in urine (Ek et al., 2006; Wilsenach et al., 2007; Ganesapillai et al., 2016; Pradhan et al., 2017). Based on this finding, a 90% urea conversation was selected as a requirement for the pharmaceutical removal methods which were investigated for the current work. Consequently, only the high pH and the HC degradation methods met the standard for urea conservation for this work.

The urea degradation resulting from the optimized HC system was checked to verify whether it was consistent with the urea degradation observed in the initial HC system experiments. The operation of the optimized HC system resulted in less than 5% urea loss (shown in Annexure C3), which was similar to the urea loss of 6.8% experienced in the initial HC system.

5 Conclusion

The aim of the current work was to investigate methods for pharmaceutical removal from human urine that also minimize the loss of urea. To achieve this, four pharmaceutical removal methods were investigated: high pH, granular activated carbon (GAC), hydrogen peroxide and hydrodynamic cavitation (HC). The degradation of eleven pharmaceuticals were investigated for the current study – five over the counter (OTC) common pharmaceuticals (paracetamol, salicylic acid, diclofenac, clopidogrel and chlorpheniramine maleate) and six antiretrovirals (ARVs) (zidovudine, lamivudine, tenofovir, stavudine, abacavir sulfate and nevirapine). The development of the four pharmaceutical removal methods was the focus of this work and pharmaceutical analysis methods were used to analyze the degradation of the pharmaceuticals due to the respective pharmaceutical degradation methods.

High performance liquid chromatography (HPLC) was the primary analysis method. Three HPLC analysis methods were used for the current work. The first method was for the analysis of OTCs only. The second method was for the analysis of ARVs only. The third method was for the analysis of a mixture of OTCs and ARVs. The concentrations of the pharmaceuticals were quantified as the area underneath the peaks for each individual pharmaceutical on the chromatogram. The calibration curves for each pharmaceutical, from which the absolute concentrations of the pharmaceuticals could be derived, were not developed. Instead, the area underneath the peak of each pharmaceutical on the chromatogram was integrated to find the concentration of the pharmaceuticals. The use of the integrated areas under the chromatogram was valid, since the degradation of the pharmaceuticals was expressed as a percentage loss. In addition, the UV spectroscopy was used to verify the degradation of paracetamol (used as an indicator pharmaceutical) for the optimization of pressure for the HC system.

The high pH treatment method conserved most of the urea (96%), however, it failed to degrade all the pharmaceuticals. Fresh urine was spiked with pharmaceuticals, after which calcium hydroxide was dosed at a concentration of 10 g L^{-1}, which increased the pH of the solution to pH 12.5. The samples were exposed to the high pH environment for at least 75 days which resulted in a degradation range of 8 - 44% for the OTCs and a degradation range of 0 - 100% for the ARVs.

The GAC removal method performed the best (out of the four removal methods) in the removal of the pharmaceuticals (>94.7%), however, it also removed most of the urea (83.4%) in the sample solution. To prepare the sample solution, fresh urine was spiked with pharmaceuticals then stabilized with calcium hydroxide at a dosage of 10 g L^{-1}. GAC derived from coconut shells was added to columns for the removal of pharmaceuticals in the sample solution. Although the GAC removal method was very efficient in the removal of pharmaceuticals, the method should not be used for urine stabilized with calcium hydroxide since more than 80% of the urea is also lost during this treatment process.

The hydrogen peroxide removal method degraded some of the pharmaceuticals, with minimal loss of urea. Fresh urine was spiked with pharmaceuticals then stabilized with calcium hydroxide at a dose of 10 g L^{-1}. The 30% (v/v) hydrogen peroxide was used for this work since it was the most used type of hydrogen peroxide in literature. The removal process achieved a pharmaceutical degradation range of 0 - 64.7% for the OTCs and a pharmaceutical degradation range of 17.2 - 73.4% for the ARVs. Additionally, only 12.6% of the urea was degraded by the treatment of the sample solution using hydrogen peroxide. Therefore, the sole use of hydrogen peroxide (with calcium hydroxide) was inefficient in the degradation of some pharmaceuticals.

The optimized HC system was the only pharmaceutical removal method that degraded more than 70% of the all the pharmaceuticals present in the sample solution while also conserving more than 90% of the urea present in the solution. The pH of the sample solution was adjusted to pH 2, following the results from the initial HC experiments. The optimized system was operated at an inlet pressure of 400 kPa, with a 3 mm orifice cavitation device. Due to the high-volume requirements of the sample solution, a urea-water solution was used which was spiked with pharmaceuticals and urea. Based on the findings from the respective

pharmaceutical removal methods, the optimized HC system was effective in the removal of pharmaceuticals, while also conserving urea.

The results from this work are a valuable contribution to the body of work dedicated to finding suitable pharmaceuticals removal methods for source separated urine that can be reused to produce products such as fertilizers. Although previous studies have looked at the pharmaceutical removal of source separated urine, there is limited knowledge on the removal of pharmaceuticals from stabilized source separated urine. Therefore, the findings from the current work are important in building the knowledge of pharmaceutical removal methods for source separated urine which has been stabilized. In addition, the work on the removal efficiency of the HC system at a low pH (pH 2) is vital and provides a novel method for removing pharmaceuticals from source separated urine.

6 Recommendations

Literature suggests that the combined use of hydrogen peroxide and ultraviolet is effective in the removal of pharmaceuticals. The combined removal treatment process was not investigated for this work, however future studies should also look at the pharmaceutical degradation efficiency of the combined use of hydrogen peroxide and ultraviolet in a high pH environment.

The pressure and cavitation device of the hydrodynamic cavitation (HC) system were optimized. The optimization improved the pharmaceutical degradation efficiency of the system. However, future studies should consider optimizing the cavitation device further. There are other orifice sizes (2 mm, 4 mm, 5 mm, and 6 mm) which can be investigated, including the different configurations of the orifices on a plate where more than one orifice is on a plate. Additionally, the combined use of an orifice and a venturi can be investigated to determine whether there would be an improvement on the pharmaceutical removal efficiency.

The temperature of the sample solutions when using the optimized HC system reached 47˚C, however the effect of the temperature on the degradation of the pharmaceuticals was not investigated in this work. Future studies should look at the influence of temperature on the

degradation of the pharmaceuticals when using a HC system. Alternatively, the temperature of the HC process needs to be controlled, but this would impact the cost of the process.

The degradation of the pharmaceuticals investigated in this study was based on degradation of the primary pharmaceutical compounds. By-products are formed because of breakdown of primary pharmaceutical compounds. Therefore, future studies should also consider what by-products are formed for each degradation method.

References

Abdel-Raouf, N., Al-Homaidan, A.A. and Ibraheem, I.B.B. (2012) 'Microalgae and wastewater treatment', Saudi Journal of Biological Sciences, 19(3), pp. 257–275.

Adan, C., Coronado, J. M., Bellod, R., Soria, J. and Yamaoka, H. (2006) 'Photochemical and photocatalytic degradation of salicylic acid with hydrogen peroxide over TiO_2/SiO_2 fibres', Applied Catalysis A: General, 303, pp. 199–206.

Agrahari, V., Putty, S., Mathes, C., Murowchick, J. B. and Youan, B. C. (2015) 'Evaluation of degradation kinetics and physicochemical stability of tenofovir', Drug Testing and Analysis, 7(3), pp. 207–213.

Agrawal, H., Kaul, N., Paradkar, A. R. and Mahadik, K. R. (2003) 'Stability indicating HPTLC determination of clopidogrel bisulphate as bulk drug and in pharmaceutical dosage form', Talanta, 61, pp. 581–589.

Aguilar, M. J. (2011) 'Fertilizer NPK from human urine and olive oil mill wastewaters', Journal of Water Reuse and Desalination, 1(3), pp. 152–159.

Ahmad, I., Ahmed, S., Anwar, Z., Ali Sherez, M. and Sikorski, M. (2016) 'Photostability and photostabilization of drugs and drug products', International Journal of Photoenergy, 2016(8135608).

Ahmed, M. B., Zhou, J. L., Ngo, H. H., Guo, W., Thomaidis, N. S. and Xu, J. (2016) 'Progress in the biological and chemical treatment technologies for emerging contaminant removal from wastewater: a critical review', Journal of Hazardous Materials, 323, pp. 274–298.

Altmann, J., Massa, L., Sperlich, A., Gnirss, R. and Jekel, M (2016) 'UV 254 absorbance as real-time monitoring and control parameter for micropollutant removal in advanced wastewater treatment with powdered activated carbon', Water Research, 94, pp. 240–245.

Anand, C. K. and Apul, D. S. (2014) 'Composting toilets as a sustainable alternative to urban sanitation – a review', Waste Management, 34(2), pp. 329–343.

Ankley, G. T., Brooks, B. W., Huggett, D. B. and Sumpter, J. (2007) 'Repeating history: pharmaceuticals in the environment', Environmental Science and Technology, 41(24), pp. 8211–8217.

Antonini, S., Nguyen, P. T., Arnold, U., Eichert, T. and Clemens, J. (2012) 'Solar thermal evaporation of human urine for nitrogen and phosphorus recovery in Vietnam', Science of the Total Environment, 414, pp. 592–599.

Bagal, M. V and Gogate, P. R. (2013) 'Degradation of diclofenac sodium using combined processes based on hydrodynamic cavitation and heterogeneous photocatalysis', Ultrasonics Sonochemistry, 21(3), pp. 1035–1043.

Barbosa, S. G., Peixoto, L., Meulman, B., Alves, M. M. and Pereira, M. A. (2016) 'A design of experiments to assess phosphorous removal and crystal properties in struvite precipitation of source separated urine using different Mg sources', Chemical Engineering Journal, 298, pp. 146–153.

Bavasso, I., Poggi, C. and Petrucci, E. (2020) 'Enhanced degradation of paracetamol by combining UV with electrogenerated hydrogen peroxide and ozone', Journal of Water Process Engineering, 34(101102).

Beck, S. and Collins, R. (2008) Moody diagram. Wikimedia. Available at: https://commons.wikimedia.org/wiki/File:Moody_diagram.jpg 08 June 2022.

Behrendt, J., Arevalo, E., Gulyas, H., Niederste-Hollenberg, J., Niemiec, A., Zhou, J. and Otterpohl, R. (2002) 'Production of value-added products from separately collected urine', Water Science and Technology, 46(6–7), pp. 341–346.

Berger, J. E. and Wittner, E. (1966) 'Adsorption of phosphoramidates', Adsorption of Phosphoramidates on Iron, 70(4), pp. 1025–1030.

Bischel, H. N., Ozel, B. D., Strande, L., Mcardell, C. S., Udert, K. M. and Kohn, T. (2015) 'Pathogens and pharmaceuticals in source-separated urine in eThekwini, South Africa', Water Research, 85, pp. 57–65.

Boyer, T. H. and Saetta, D. (2019) 'Opportunities for building-scale urine diversion and challenges for implementation', Accounts of Chemical Research, 52(4), pp. 886–895.

Brennen, C. E. (1995) Cavitation and bubble dynamics. Oxford: Oxford University Press. Available at: https://authors.library.caltech.edu.

Calisto, V. and Esteves, V. I. (2009) 'Psychiatric pharmaceuticals in the environment', Chemosphere, 77(10), pp. 1257–1274.

Chen, Y. C. and Smirniotis, P. (2002) 'Enhancement of photocatalytic degradation of phenol and chlorophenols by ultrasound', Industrial and Engineering Chemistry Research, 41(24), pp. 5958-5965.

Chen, W., Zhang, Z., Li, Qi. and Wang, H. (2012) 'Adsorption of bromate and competition from oxyanions on cationic surfactant-modified granular activated carbon (GAC)', Chemical Engineering Journal, 203, pp. 319–325.

Chipako, T. L. and Randall, D. G. (2019) 'Urinals for water savings and nutrient recovery: a feasibility study', Water SA, 45(2), pp. 266–277.

Chipako, T. L. and Randall, D. G. (2020a) 'Investigating the feasibility and logistics of a decentralized urine treatment and resource recovery system', Journal of Water Process Engineering, 37(101383).

Chipako, T. L. and Randall, D. G. (2020b) 'Urine treatment technologies and the importance of pH', Journal of Environmental Chemical Engineering, 8(1).

Copeland, S. A. and Greenberg, L. E. (1960) 'The thermodynamic functions for the solution of calcium hydroxide in water', Thermodynamic Functions for Calcium Hydroxide in Water, 64(10), pp. 1057–1059.

Courtney, C. and Randall, D. G. (2022) 'Concentrating stabilized urine with reverse osmosis: how does stabilization method and pre-treatment affect nutrient recovery, flux, and scaling?' (Paper currently under review).

Crittenden, J. C., Sanongraj, S., Bulloch, J. L., Hand, D. W., Rogers, T. N., Speth, T. F. and Ulmer, M. (1999) 'Correlation of aqueous-phase adsorption isotherms', Environmental Science and Technology, 33(17), pp. 2926–2933.

Dodd, M. C., Zuleeg, S., Von Gunten, U. and Pronk, W. (2008) 'Ozonation of source-separated urine for resource recovery and waste minimization: process modelling, reaction chemistry, and operational considerations', Environmental Science and Technology, 42(24), pp. 9329–9337.

Dular, M., Griessler- Bulc, T., Gutierrez- Aguirre, I., Heath, E., Kosjek, T., Klemencic, A. K., Oder, M., Petkovsek, M., Racki, N., Ravnikar, M., Sarc, A., Sirok, B., Zupanc, M., Zitnik, M. and Kompare, B. (2015) 'Use of hydrodynamic cavitation in (waste) water treatment', Ultrasonics - Sonochemistry, 29, pp. 577–588.

Dunge, A., Chakraborti, A. K. and Singh, S. (2004) 'Mechanistic explanation to the variable degradation behaviour of stavudine and zidovudine under hydrolytic, oxidative and photolytic conditions', Journal of Pharmaceutical and Biomedical Analysis, 35, pp. 965–970.

Dutta, S. and Vinnerås, B. (2016) 'Fertilizer from dried human urine added to ash and lime – a potential product from eco-sanitation system', Water Science and Technology, 74(6), pp. 1436–1445.

Ek, M., Bergstrom, R., Bjurhem, J. E., Bjorlenius, B. and Hellstrom, D. (2006) 'Concentration of nutrients from urine and reject water from anaerobically digested sludge', Water Science and Technology, 54(11–12), pp. 437–444.

Eriksen, L., Andreasen, P. and Ilsøe, B. (1996) 'Inactivation of *Ascaris suum* eggs during storage in lime treated sewage sludge', Water Research, 30(4), pp. 1026–1029.

Etter, B., Udert, K. M. and Goundan, T. (2014) 'VUNA – Scaling up nutrient recovery from urine', to be submitted for the Tech4Dev conference (EPFL).

Faust, B (1997) 'Modern chemical techniques', The Royal Society of Chemistry (1997).

Feliciano, A. R. S., de Lucena A. L. A., da Rocha Santana, R. M., Zaidan, L. E. M. C., da Silva, P. M., Napoleao, T. H., Duarte, M. M. M. B. and Napoleao, D. C. (2020) 'Advanced oxidation processes employment for the degradation of lamivudine: kinetic assessment, toxicity study and mathematical modeling', Water Quality Research Journal, 55(3), pp. 249–260.

Flanagan, C. P. and Randall, D. G. (2018) 'Development of a novel nutrient recovery urinal for on-site fertilizer production', Journal of Environmental Chemical Engineering, 6(5), pp. 6344–6350.

Ganesapillai, M., Simha, P., Gupta, K. and Jayan, M. (2016) 'Nutrient recovery and recycling from human urine: a circular perspective on sanitation and food security', Procedia Engineering, 148, pp. 346–353.

Garcia-Rodríguez, A., Matamoros, V., Fontas, C. and Salvado, V. (2014) 'The ability of biologically based wastewater treatment systems to remove emerging organic contaminants — a review', Environmental Science and Pollution Research, 21, pp. 11708–11728.

Garuti, M., Langone, M., Fabbri, C. and Piccinini, S. (2018) 'Bioresource technology monitoring of full-scale hydrodynamic cavitation pretreatment in agricultural biogas plant', Bioresource Technology, 247(September 2017), pp. 599–609.

Geankoplis, C. (1994) 'Transport processes and unit operations: 3rd edition', Chemical Engineering Science, 49(9), pp. 1487–1488.

Ghaly, A. E., Ananthashankar, R., Alhattab, M. and Ramakrishnan, V. V. (2014) 'Production, characterization and treatment of textile effluents: a critical review', Chemical Engineering and Process Technology, 5(1), pp. 1–18.

Gogate, P. R. and Bhosale, G. S. (2013) 'Comparison of effectiveness of acoustic and hydrodynamic cavitation in combined treatment schemes for degradation of dye wastewaters', Chemical Engineering and Processing: Process Intensification, 71, pp. 59–69.

Golla, V. M., Kurmi, M., Shaik, K. and Singh, S. (2016) 'Stability behaviour of antiretroviral drugs and their combinations. 4: Characterization of degradation products of tenofovir alafenamide fumarate and comparison of its degradation and stability behaviour with tenofovir disoproxil fumarate', Journal of Pharmaceutical and Biomedical Analysis, 131(May), pp. 146–155.

Grewal, H. S. and Kalra, K. L. (1995) 'Fungal production of critric acid', Biotechnology Advances, 13(2), pp. 209–234.

Halling-Sorensen, B., Nors Nielsen, S., Lanzky, P. F., F., Ingerslev, Holten Liitzhofl, H.C. and Jorgensen, S.E. (1998) 'Occurrence, fate and effects of pharmaceutical substances in the environment – a review', Chemosphere, 3(2), pp. 357–393.

Hapeshi, E., Achilleos, A., Vasquez, M. I., Michael, C., Xekoukoulotakis, N. P., Mantzavinos, D. and Kassinos, D. (2010) 'Drugs degrading photocatalytically: kinetics and mechanisms of ofloxacin and atenolol removal on titania suspensions', Water Research, 44(2010), pp. 1737-1746.

Harder, R., Wielemaker, R., Larsen, T. A., Zeeman, G. and Oberg, G. (2019) 'Recycling nutrients contained in human excreta to agriculture: pathways, processes, and products', Critical Reviews in Environmental Science and Technology, 49(8), pp. 695–743.

Hartig, C., Ernst, M. and Jekel, M. (2001) 'Membrane filtration of two sulphonamides in tertiary effluents and subsequent adsorption on activated carbon', Water Research, 35(16), pp. 3998–4003.

Hashemi, S. and Han, M. (2017) 'Methods for controlling stored urine odor in resource-oriented sanitation', Journal of Water, Sanitation and Hygiene for Development, 7(3), pp. 507–514.

Hashemi, S., Han, M. and Kim, T. (2015) 'Practical Paper Identification of urine scale problems in urinals and the solution using rainwater', Journal of Water, Sanitation and Hygiene for Development, 5(2), pp. 322–329.

Heinonen- Tanski, H., Sjoblom, A., Fabritius, H. and Karinen, P. (2007) 'Pure human urine is a good fertiliser for cucumbers', Bioresource Technology, 98, pp. 214–217.

Hellstrom, D., Johansson, E. and Grennberg, K. (1999) 'Storage of human urine: acidification as a method to inhibit decomposition of urea', Ecological Engineering, 12(3-4), pp. 253–269.

Himmelblau, D. M. and Riggs, J. B. (2012) 'Basic principles and calculations in chemical engineering. 3rd edn. Austin: Pearson Prentice Hall (2012).

Hofmann, J., Freier, U., Wecks, M. and Hohmann, S. (2007) 'Degradation of diclofenac in water by heterogeneous catalytic oxidation with H_2O_2', Applied Catalysis B: Environmental, 70, pp. 447–451.

Höglund, C., Stenström, T. A. and Ashbolt, N. (2002) 'Microbial risk assessment of source-separated urine used in agriculture', Waste Management and Research, 20, pp. 150–161.

Hovorka, S. W. and Schoneich, C. (2001) 'Oxidative degradation of pharmaceuticals: theory, mechanisms and inhibition', Journal of Pharmaceutical Sciences, 90(3), pp. 253–269.

Ishii, S. K. L. and Boyer, T. H. (2016) 'Student support and perceptions of urine source separation in a university community', Water Research, 100, pp. 146–156.

Jain, T., Carpenter, J. and Saharan, V. K. (2014) 'CFD analysis and optimization of circular and slit venturi for cavitational activity', Journal of Material Science and Mechanical Engineering, 1(1), pp. 28–33.

Jonsson, H., Stenstrom, T. A., Svensson, J. and Sundin, A. (1997) 'Source separation urine-nutrient and heavy metal content, water saving and faecal contamination', Water Science and Technology, 35(9), pp. 145–152.

Kampschreur, M. J., Temmink, H., Kleerebezem, R., Jetten, M. S. M. and van Loosdrecht, M. C M. (2009) 'Nitrous oxide emission during wastewater treatment', Water Research, 43(17), pp. 4093–4103.

Kaul, N., Agrawal, H., Paradkar, A. R. and Mahadik, K. R. (2004) 'HPTLC method for determination of nevirapine in pharmaceutical dosage form', Talanta, 62, pp. 843–852.

Köpping , I., Mcardell, C. S., Borowska, E., Bohler, M. A. and Udert, K. M. (2020) 'Removal of pharmaceuticals from nitrified urine by adsorption on granular activated carbon', Water Research X, 9(100057).

Kose, H. (2010) 'The effects of physical factors on the adsorption of synthetic organic compounds by activated carbons and activated fibers', All Theses, 930.

Krajewska, B. (2009) 'Ureases I. Functional, catalytic and kinetic properties: a review', Journal of Molecular Catalysis B: Enzymatic, 59(1–3), pp. 9–21.

Kummerer, K. (2010) 'Pharmaceuticals in the environment', Annual Review of Environment and Resources, 35, pp. 57–75.

Kuldeep, Carpenter, J. and Saharan, V. K. (2014) 'Study of cavity dynamics in a hydrodynamic cavitation reactor', Energy Technology and Ecological Concerns: A Contemporary Approach, pp. 37–43.

Kümmerer, K. (2004) 'Resistance in the environment', Journal of Antimicrobial Chemotherapy, 54(2), pp. 311–320.

Larsen, T. A., Peters, I., Alder, A., Eggen, R., Maurer, M. and Muncke, J. (2001) 'Peer reviewed: re-engineering the toilet for sustainable wastewater management', Urban Planet, 35(9), pp. 192A-197A.

Larsen, T. A., Hoffmann, S., Lüthi, C., Truffer, B. and Maurer, M. (2016) 'Emerging solutions to the water challenges of an urbanizing world', Science, 352(6288), pp. 928–933.

Laszló, K., Josepovits, K. and Tombácz, E. (2001) 'Analysis of active sites on synthetic carbon surfaces by various methods', Analytical Sciences, 17, pp. 1741–1744.

Li, J., Zhou, Q. and Campos, L. C. (2018) 'The application of GAC sandwich slow sand filtration to remove pharmaceutical and personal care products', Science of the Total Environment, 635, pp. 1182–1190.

Li, L., Liu, S. and Liu, J. (2011) 'Surface modification of coconut shell based activated carbon for the improvement of hydrophobic VOC removal', Journal of Hazardous Materials, 192(2), pp. 683–690.

Li, W. C. (2014) 'Occurrence, sources, and fate of pharmaceuticals in aquatic environment and soil', Environmental Pollution, 187, pp. 193–201.

Lienert, J., Escher, B. I. and Burki, T. (2007) 'Reducing micropollutants with source control: substance flow analysis of 212 pharmaceuticals in faeces and urine', Water Science and Technology, 56(87–96).

Lim, J. and Okada, M. (2005) 'Regeneration of granular activated carbon using ultrasound', Ultrasonics Sonochemistry, 12(4), pp. 277–282.

Lind, B., Byden, S. and Ban, Z. (2001) 'Volume reduction and concentration of nutrients in human urine', Ecological Engineering, 16(4), pp. 561–566.

Liu, Z., Zhao, Q., Wang, K., Lee, D., Qiu, W. and Wang, J. (2008) 'Urea hydrolysis and recovery of nitrogen and phosphorous as MAP from stale human urine', Journal of Environmental Sciences, 20(8), pp. 1018–1024.

Long, L., Bu, Y., Chen, B. and Sadiq, R. (2019) 'Removal of urea from swimming pool water by UV/VUV: the roles of additives, mechanisms, influencing factors, and reaction products', Water Research, 161, pp. 89–97.

Lv, J., Wang, L., Song, Y. and Li, Y. (2015) 'N-nitrosodimethylamine formation from ozonation of chlorpheniramine: influencing factors and transformation mechanism', Journal of Hazardous Materials, 299, pp. 584–594.

Madhu, G. M., Thomas, A., Deepak, S., Preetham, H. S. and Rajanandam, K. S. (2015) 'Escalation of degradation of malachite green and Methyl violet using hydrodynamic cavitations using different orifice geometry', International Journal of Environmental Sciences, 5(4), p. 6088.

Mancuso, G., Langone, M. and Andreottola, G. (2020) 'A critical review of the current technologies in wastewater treatment plants by using hydrodynamic cavitation process: principles and applications', Journal of Environmental Health Science and Engineering, 18, pp. 311–333.

Maurer, M., Pronk, W. and Larsen, T. A. (2006) 'Treatment processes for source-separated urine', Water Research, 40(17), pp. 3151–3166.

Maurer, M., Schwegler, P. and Larsen, T. A. (2003) 'Nutrients in urine: Energetic aspects of removal and recovery', Water Science and Technology, 48(1), pp. 37–46.

Mcdougall, G. J. (1991) 'The physical nature and manufacture of activated carbon', Journal of the Southern African Institute of Mining and Metallurgy, 91(4), pp. 109–120.

Mcmillan, T. J., Leatherman, E., Ridley, A., Shorrocks, J., Tobi, S. E. and Whiteside, J. R. (2008) 'Cellular effects of long wavelength UV light (UVA) in mammalian cells', Journal of Pharmacy and Pharmacology, 60(8), pp. 969–976.

Mihelcic, J. R., Naughton, C. C., Verbyla, M. E., Zhang, Q., Schweitzer, R. W., Oakley, S. M., Wells, E. C. and Whiteford, L. M. (2016) 'The Grandest Challenge of All: the role of environmental engineering to achieve sustainability in the world's developing regions', Environmental Engineering Science, 34(1), pp. 16–41.

Mishra, K. P. and Gogate, P. R. (2010) 'Intensification of degradation of Rhodamine B using hydrodynamic cavitation in the presence of additives', Separation and Purification Technology, 75(3), pp. 385–391.

Mohammed-Ali, M. A. J. (2012) 'Stability study of tetracycline drug in acidic and alkaline solutions by colorimetric method', Journal of Chemical and Pharmaceutical Research, 4(2), pp. 1319–1326.

Monteith, J. L. (1981) 'Evaporation and surface temperature', Quarterly Journal of the Royal Meteorological Society, 107(451), pp. 1–27.

Moyano, M. A., Rosasco, M. A., Pizzorno, M. T. and Segall, A. I. (2005) 'Simultaneous determination of chlorpheniramine maleate and dexamethasone in a tablet dosage form by liquid chromatography', Journal of AOAC International, 88(6), pp. 1677–1683.

Münch, E. V and Dahm, P. (2009) 'Waterless urinals: a proposal to save water and recover urine nutrients in Africa', 34th WEDC International Conference, Addis Ababa, Ethiopia, 2009, pp. 1–8.

Nagy, J., Kaljunen, J. and Jozsef, A. (2019) 'Nitrogen recovery from wastewater and human urine with hydrophobic gas separation membrane: experiments and modelling', Chemical Papers, 73(8), pp. 1903–1915.

Nicolaisen, B. (2002) 'Developments in membrane technology for water treatment', Desalination, 153, pp. 355–360.

Niemczynowicz, J. (1999) 'Urban hydrology and water management – present and future challenges', Urban Water, 1(1), pp. 1–14.

O'Neal, J. A. and Boyer, T. H. (2013) 'Phosphate recovery using hybrid anion exchange: applications to source-separated urine and combined wastewater streams', Water Research, 47(14), pp. 5003–5017.

Pahore, M. M., Ito, R. and Funamizu, N. (2010) 'Rational design of an on-site volume reduction system for source-separated urine', Environmental Technology, 31(4), pp. 399–408.

Patel, P. N., Samanthula, G., Shrigod, V., Modh, S. C. and Chaudhari, J. R. (2013) 'RP-HPLC method for determination of several NSAIDs and their combination drugs', Chromatography Research International, 2013(242868).

Pelekani, C. and Snoeyink, V. L. (1999) 'Competitive adsorption in natural water: role of activated carbon pore size', Water Research, 33(5), pp. 1209-1219.

Pradella, M., Dorizzi, R. M., Rigolin, F. and Statland, B. E. (1988) 'Density of Urine: Methods and Clinical Significance', CRC Critical Reviews in Clinical Laboratory Sciences, 26(3), pp. 195–242.

Pradhan, S. K., Mikola, A. and Vahala, R. (2017) 'Nitrogen and phosphorus harvesting from human urine using a stripping, absorption, and precipitation process', Environmental Science and Technology, 51(9), pp. 5165–5171.

Priya, S. S. and Radha, K. K. (2017) 'A review on the adsorption studies of tetracycline onto various types of adsorbents', Chemical Engineering Communications, 204(8), pp. 821-839.

Pronk, W., Palmquist, H., Biebow, M. and Boller, M. (2006) 'Nanofiltration for the separation of pharmaceuticals from nutrients in source-separated urine', Water Research, 40(7), pp. 1405–1412.

Prousek, J. (1996) 'Advanced oxidation process for water treatment', Chemicke Listy, 90, pp. 229–237.

Qian, Y. (2016) 'Sustainable management of water resources', Engineering, 2(1), pp. 23–25.

Rahman, M. S., Ahmed, M. and Chen, X. D. (2007) 'Freezing – melting process and desalination: review of present status and future prospects', Internationanl Journal of Nuclear Desalination, 2(3), pp. 253–264.

Rajoriya, S., Carpenter, J., Saharan, V. K. and Pandit, A. B. (2016) 'Hydrodynamic cavitation: an advanced oxidation process for the degradation of bio-refractory pollutants', Reviews in Chemical Engineering, 32(4).

Randall, D. G., Krähenbühl, M., Köpping, I., Larsen, T. A. and Udert, K. M. (2016) 'A novel approach for stabilizing fresh urine by calcium hydroxide addition', Water Research, 95, pp. 361–369.

Randall, D. G. and Naidoo, V. (2018) 'Urine: The liquid gold of wastewater', Journal of Environmental Chemical Engineering, 6(2), pp. 2627–2635.

Randall, D. G. and Nathoo, J. (2015) 'A succinct review of the treatment of reverse osmosis brines using freeze crystallization', Journal of Water Process Engineering, 8, pp. 186–194.

Randall, D. G. and Nathoo, J. (2018) 'Resource recovery by freezing: a thermodynamic comparison between a reverse osmosis brine, seawater and stored urine', Journal of Water Process Engineering, 26(October), pp. 242–249.

Randhavane, S. B. (2019) 'Comparing geometric parameters of a hydrodynamic cavitation process treating pesticide effluent', Environmental Engineering Research, 24(2), pp. 318–323.

Ray, H., Perreault, F. and Boyer, T. H. (2020) 'Rejection of nitrogen species in real fresh and hydrolyzed human urine by reverse osmosis and nanofiltration', Journal of Environmental Chemical Engineering, 8(4).

Ray, H., Saetta, D. and Boyer, T. H. (2018) 'Characterization of urea hydrolysis in fresh human urine and inhibition by chemical addition', Environmental Science Water Research and Technology. Royal Society of Chemistry, 4, pp. 87–98.

Ronteltap, M., Maurer, M., Hausherr, R. and Gujer, W. (2010) 'Struvite precipitation from urine – Influencing factors on particle size', Water Research, 44(6), pp. 2038–2046.

Rostvall, A., Zhang, W., Dürig, W., Renman, G., Wiberg, K., Ahrens, L. and Gago- Ferrero, P. (2018) 'Removal of pharmaceuticals, perfluoroalkyl substances and other micropollutants from wastewater using lignite, Xylit, sand, granular activated carbon (GAC) and GAC+ Polonite® in column tests – role of physicochemical properties', Water Research, 137, pp. 97–106.

Rygaard, M., Binning, P. J. and Albrechtsen, H. (2011) 'Increasing urban water self-sufficiency: new era, new challenges', Journal of Environmental Management, 92(1), pp. 185–194.

Saeed, A. M. (2017) 'Spectrophotometric determination of paracetamol in some manufactured tablets in Iraqi markets', International Journal of Pharmacy and Pharmaceutical Sciences Review and Research, 42(11), pp. 53–57.

Safwat, S. M. and Matta, M. E. (2018) 'Adsorption of urea onto granular activated alumina: a comparative study with granular activated carbon', Journal of Dispersion Science and Technology, 39(12), pp. 1699–1709.

Saharan, V. K., Pandit, A. B., Selvam, P. K. S. and Anandan, S. (2012) 'Hydrodynamic cavitation as an advanced oxidation technique for the degradation of acid red 88 dye', Industrial and Engineering Chemistry Research, 51(4), pp. 1981–1989.

Saharan, V. K., Rizwani, M. A., Malani, A. A and Pandit, A. B. (2013) 'Effect of geometry of hydrodynamically cavitating device on degradation of orange-G', Ultrasonics Sonochemistry, 20(1), pp. 345–353.

Šarc, A., Stepišnik- Perdih, T., Petkovšek, M. and Dular, M. (2017) 'The issue of cavitation number value in studies of water treatment by hydrodynamic cavitation', Ultrasonics Sonochemistry, 34, pp. 51–59.

Senecal, J. and Vinnerås, B. (2017) 'Urea stabilisation and concentration for urine-diverting dry toilets: urine dehydration in ash', Science of the Total Environment, 586, pp. 650–657.

Sikosana, M. K. L. N., Randall, D. G. and Blottnitz, H. V. (2017) 'A technological and economic exploration of phosphate recovery from centralised sewage treatment in a transitioning economy context', Water SA, 43(2), pp. 343–353.

Simha, P., Friedrich, C., Randall, D. G. and Vinnerås, B. (2021) 'Alkaline dehydration of human urine collected in source-separated sanitation systems using magnesium oxide', Frontiers in Environmental Science, 8(619901), pp. 1–9.

Simha, P. and Ganesapillai, M. (2017) ‘Ecological sanitation and nutrient recovery from human urine: how far have we come? A review,’ Sustainable Environment Research, 27(3), pp. 107–116.

Sivakumar, M. and Pandit, A. B. (2002) ‘Wastewater treatment: a novel energy efficient hydrodynamic cavitational technique’, Ultrasonics - Sonochemistry, 9(3), pp. 123–131.

Snyder, L. R., Kirkland, J. J. and Glajoh, J. L. (1988) ‘Practical HPLC method development’. 2nd edn. New Jersey: John Wiley & Sons, Inc.

Sohn, H. and Moreland, C. (1968) ‘The effect of particle size distribution on packing density’, The Canadian Journal of Chemical Engineering, 46(3), p. 1968.

Song, L., Yang, J., Yu, S., Xu, M., Liang, Y., Pan, X. and Yao, Li (2019) ‘Ultra-high efficient hydrodynamic cavitation enhanced oxidation of nitric oxide with chlorine dioxide’, Chemical Engineering Journal, 373, pp. 767–779.

Spångberg, J., Tidåker, P. and Jönsson, H. (2014) ‘Environment Environmental impact of recycling nutrients in human excreta to agriculture compared with enhanced wastewater treatment’, Science of the Total Environment, 493, pp. 209–219.

Sumpter, J. P. (1998) ‘Xenoendocrine disruptors - environmental impacts’, Toxicology Letters, 102–103, pp. 337–342.

Suslick, K. S., Mdleleni, M. M. and Ries, J.T. (1997) ‘Chemistry induced by hydrodynamic cavitation’, 119(39), pp. 9303-9304.

Tettenborn, F., Behrendt, J. and Otterpohl, R. (2007) ``Resource recovery and removal of pharmaceutical residues Treatment of separate collected urine’. Hamburg, Germany: Institute of Wastewater Management and Water Protection and Hamburg University of Technology.

Thanekar, P. and Gogate, P. (2018) ‘Application of hydrodynamic cavitation reactors for treatment of wastewater containing organic pollutants: intensification using hybrid approaches’, Fluids, 3(98), pp. 1–24.

Thorneby, L., Persson, K. and Tragardh, G. (1999) ‘Treatment of liquid effluents from dairy cattle and pigs using reverse osmosis’, Journal of Agricultural Engineering Research, 73(2), pp. 159–170.

Tun, L. L., Jeong, D., Jeong, S., Cho, K., Lee, S. and Bae, H. (2016) ‘Dewatering of source-separated human urine for nitrogen recovery by membrane distillation’, Journal of Membrane Science, 512, pp. 13–20.

Udert, K. M., Larsen, T. A., Biebow, M. and Gujer, W. (2003a) ‘Urea hydrolysis and precipitation dynamics in a urine-collecting system’, Water Research, 37(11), pp. 2571–2582.

Udert, K. M., Larsen, T. A. and Gujer, W. (2003b) ‘Estimating the precipitation potential in urine-collecting systems’, Water Quality Research Journal, 37(11), pp. 2667–2677.

Udert, K. M. and Wächter, M. (2012) ‘Complete nutrient recovery from source-separated urine by nitrification and distillation’, Water Research, 46(2), pp. 453–464.

Vasiljev, A., Simha, P., Demisse, N., Karlsson, C., Randall, D. G. and Vinnerås, B. (2022) 'Drying fresh human urine in magnesium-doped alkaline substrates: capture of free ammonia, inhibition of enzymatic urea hydrolysis and minimisation of chemical urea hydrolysis', Chemical Engineering Journal, 428(131036).

Volpin, F., Chekli, L., Phuntsho, S., Cho, J., Ghaffour, N., Vrouwenvelder, J. S. and Shon, H. K. (2018) 'Simultaneous phosphorus and nitrogen recovery from source-separated urine: a novel application for fertiliser drawn forward osmosis', Chemosphere, 203, pp. 482–489.

Wang, X., Wang, J., Guo, P., Guo, W. and Wang, C. (2009) 'Degradation of rhodamine B in aqueous solution by using swirling jet-induced cavitation combined with H_2O_2', Journal of Hazardous Materials, 169(1–30), pp. 486–491.

Wang, X., Jia, J. and Wang, Y. (2017) 'Combination of photocatalysis with hydrodynamic cavitation for degradation of tetracycline', Chemical Engineering Journal, 315, pp. 274–282.

Wang, Y., Zhou, C., Chen, J., Fu, Z. and Niu, J. (2019) 'Bicarbonate enhancing electrochemical degradation of antiviral drug lamivudine in aqueous solution', Journal of Electroanalytical Chemistry, 848, p. 113314.

Warade, A. R., Gaikwad, R.W., Sapkal, R.S. and Sapkal, V.S. (2016) 'Review on wastewater treatment by hydrodynamic cavitation', IOSR Journal of Environmental Science, 10, pp. 67–72.

Wenten, I. G. and Khoiruddin, K. (2016) 'Reverse osmosis applications: Prospect and challenges', Desalination, 391, pp. 112–125.

Williams, P. M., Ahmad, M. and Connolly, B. S. (2013) 'Freeze desalination: An assessment of an ice maker machine for desalting brines', Desalination, 308, pp. 219–224.

Wilsenach, J. A., Schuurbiers, C. A. H. and van Loosdrecht, M. C. M. (2007) 'Phosphate and potassium recovery from source separated urine through struvite precipitation', Water Research, 41, pp. 458–466.

Wols, B. A., Hofman-Caris, C. H.M., Harmsen, D. J.H. and Beerendonk, E. F. (2013) 'Degradation of 40 selected pharmaceuticals by UV/H_2O_2', Water Research, 47(15), pp. 5876–5888.

Wu, Y., Huang, Y., Zhou, Y., Ren, X. and Yang, F. (2014) 'Degradation of chitosan by swirling cavitation', Innovative Food Science and Emerging Technology, 23, pp. 188–193.

Xia, J., Zhang, Y., Xiong, L., He, S., Wang, L. and Yu, Z. (2017) 'Opportunities and challenges of the sponge city construction related to urban water issues in China', Science China Earth Sciences, 60(4), pp. 652–658.

Yang, L., Yu, L. E. and Ray, M. B. (2008) 'Degradation of paracetamol in aqueous solutions by TiO_2 photocatalysis', Water Research, 42, pp. 3480–3488.

Yang, X., Flowers, R. C., Weinberg, H. S. and Singer, P. C. (2011) 'Occurrence and removal of pharmaceuticals and personal care products (PPCPs) in an advanced wastewater reclamation plant', Water Research, 45(16), pp. 5218–5228.

Yen, H. Y. (2016) ‘Energy consumption of treating textile wastewater for in factory reuse by H_2O_2/UV process’, Desalination and Water Treatment, 57(23), pp. 10537–10545.

Yin, L., Ma, R., Wang, B., Yuan, H. and Yu, G. (2017) ‘The degradation and persistence of five pharmaceuticals in an artificial climate incubator during a one year period’, RSC Advances, 7(14), pp. 8280–8287.

Yuequn, T., Jun, C., Xiulan, H., Bin, L. and Zhixiong, G.. (2016) ‘Application of hydrodynamic cavitation to wastewater treatment’, Chemical and Engineering Technology, 38(8), pp. 1363–1376.

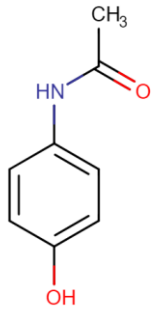
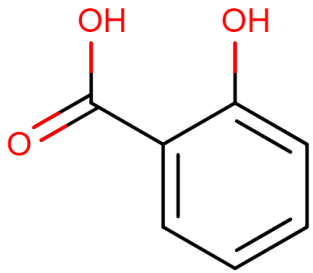
Zelenakova, M. (2018) ‘Water management and the environment: case studies’. 86th edn. Kosiac: Springer International Publishing AG.

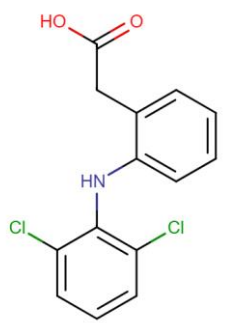
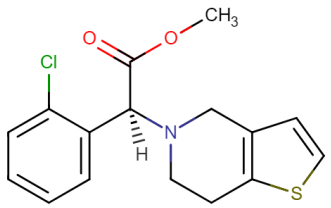
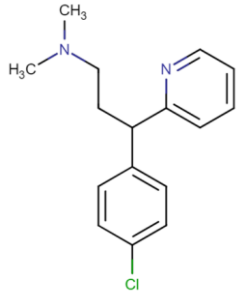
Zhang, Q., Prouty, C., Zimmerman, J. B. and Mihelcic, J. R. (2016) ‘More than target 6.3: a systems approach to rethinking sustainable development goals in a resource-scarce world’, Engineering, 2(4), pp. 481–489.

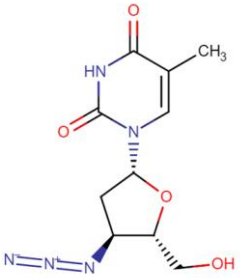
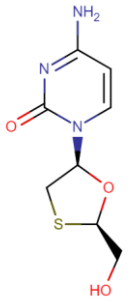
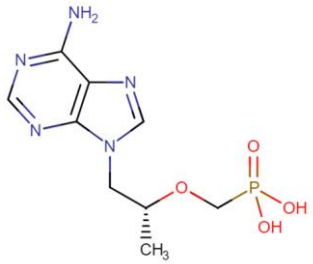
Zuccato, E., Castiglioni, S., Fanelli, R., Reitano, G., Bagnati, R., Chiabrando, C., Pomati, F., Rossetti, C. and Calamari, D. (2006) ‘Pharmaceuticals in the environment in Italy: causes, occurrence, effects and control’, Environmental Science and Pollution Research, 13, pp. 15–21.

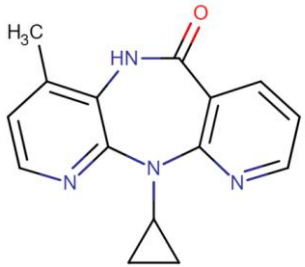
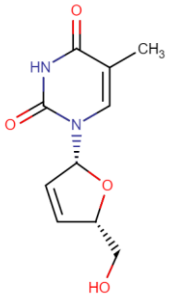
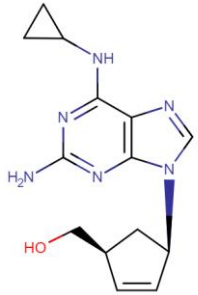
Annexure A: Pharmaceutical analysis methods details

Annexure A1.1: Pharmaceutical profile

API TYPE	API	Molecular formula	API Structure	Water Solubility (mg mL^{-1})	pKa (Strongest Acidic)
OTCs	Paracetamol	C8H9NO2		4.15	9.46
	Salicylic acid	C7H6O3		11.3	2.79

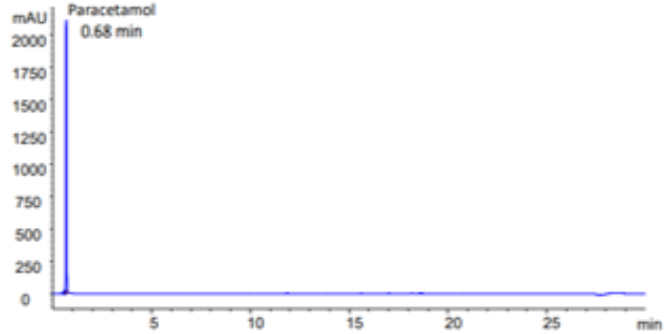
	Diclofenac	C14H11Cl2NO2		0.00447	4.0
	Clopidogrel	C16H16ClNO2S		0.0118	5.14
	Chlorpheniramine maleate	C16H19ClN2		0.0519	9.47

ARVS	Zidovudine	C8H11N3O3S		16.3	9.96
	Lamivudine	C8H11N3O3S		2.76	14.29
	Tenofovir	C9H14N5O4P		1.87	1.35

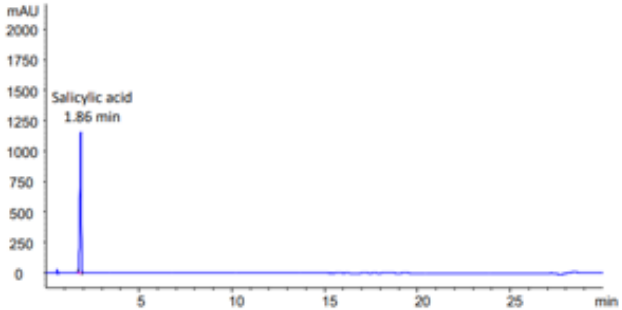
	Nevirapine	C15H14N4O		0.105	5.06
	Stavudine	C10H12N2O4		40.5	9.95
	Abacavir sulfate	C14H18N6O		1.21	15.41

Annexure A1.2: OTCs HPLC method standards

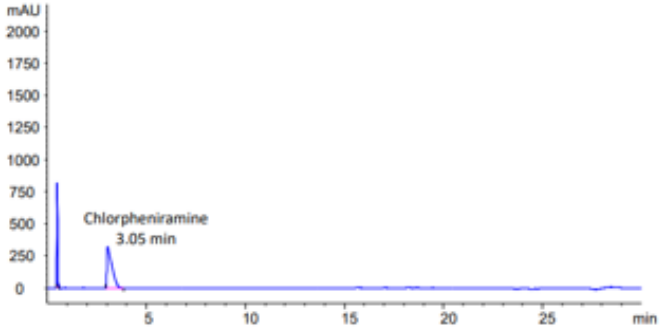
Paracetamol



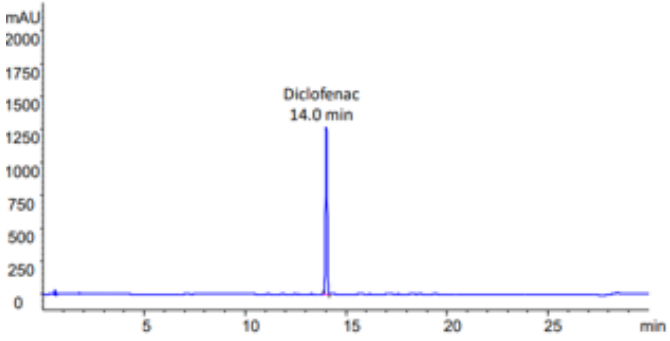
Salicylic acid



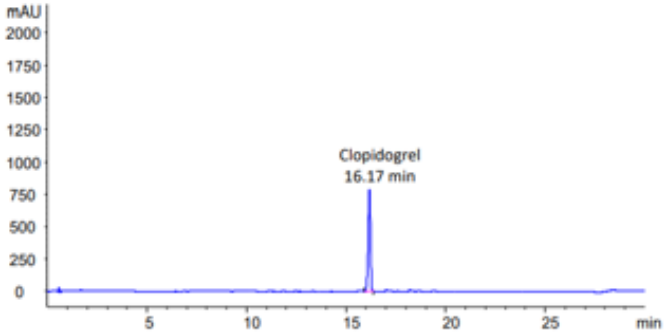
Chlorpheniramine



Diclofenac

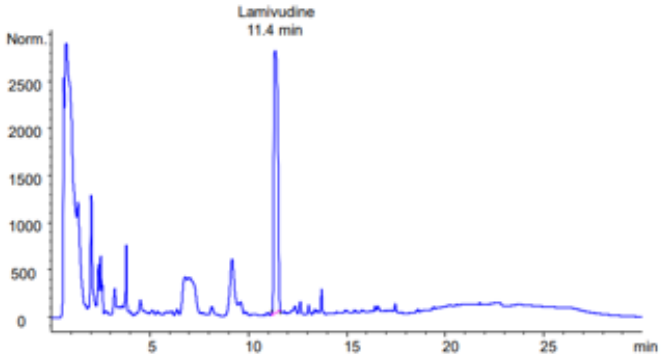


Clopidogrel

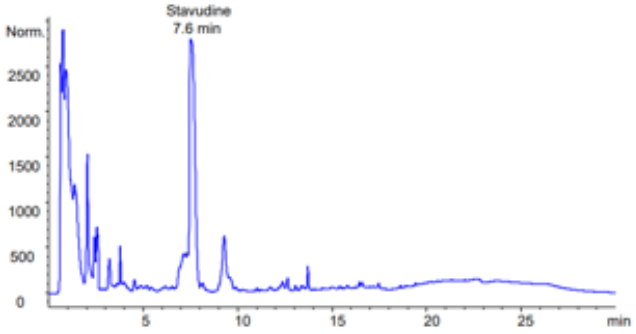


Annexure A1.3: ARVs HPLC method standards

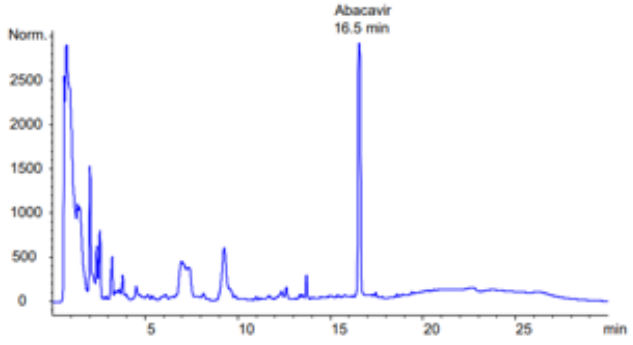
Lamivudine



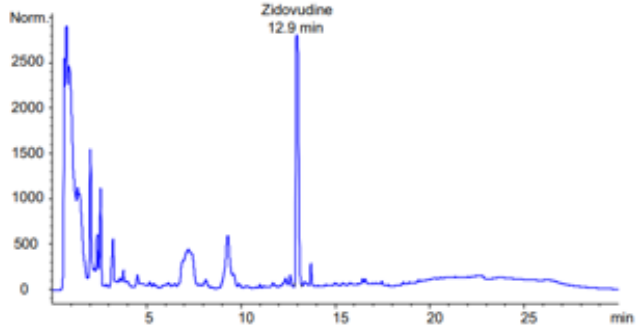
Stavudine



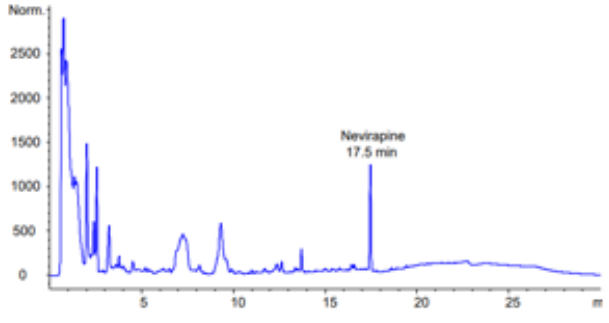
Abacavir sulfate



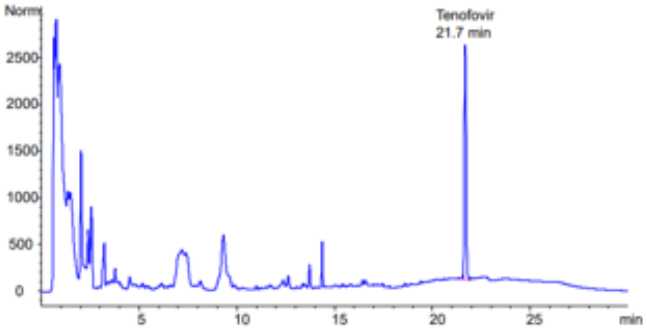
Zidovudine



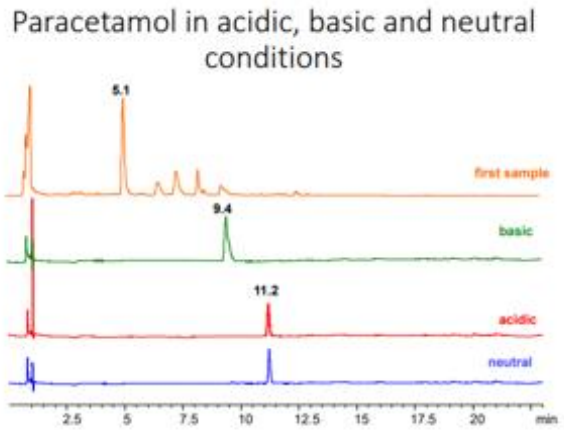
Nevirapine

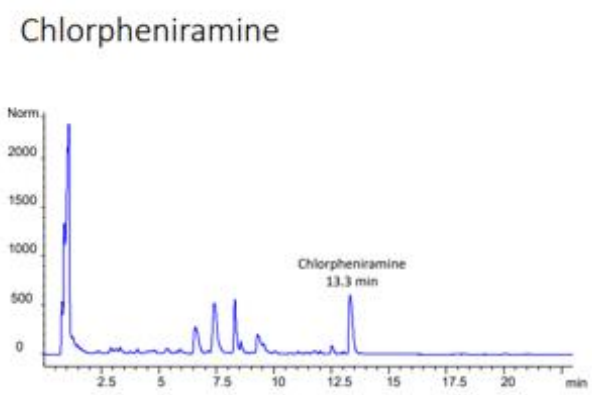


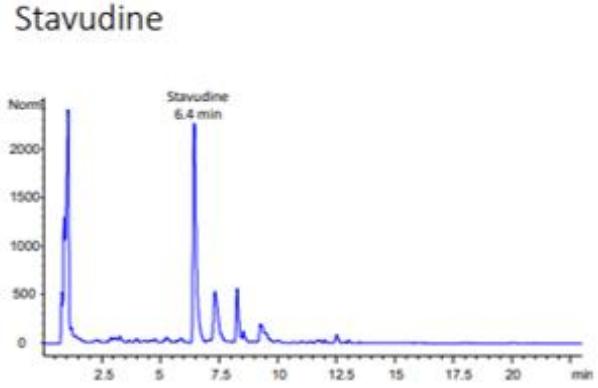
Tenofovir

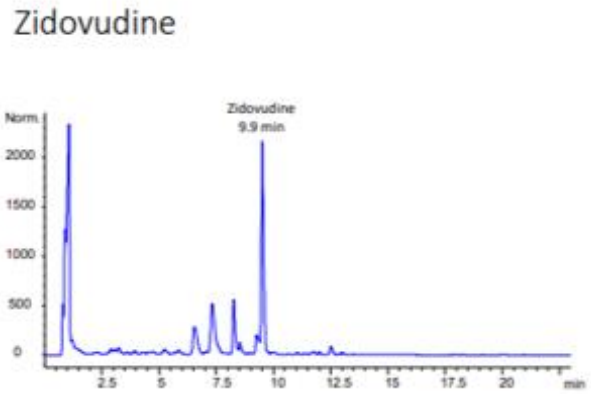


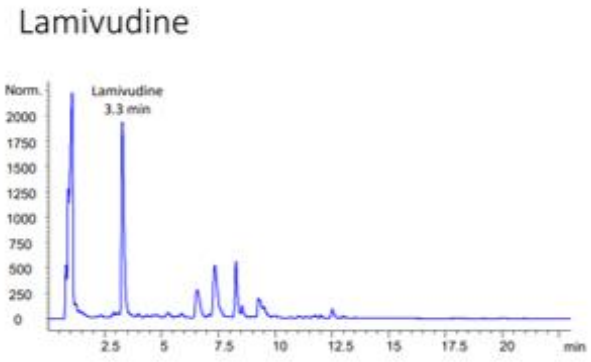
Annexure A1.4: Combined OTCs and ARVs HPLC method standards











Annexure A2: Spiked pharmaceutical concentrations

A2.1 High pH

Over the counter (OTC) common pharmaceuticals					
Sample 1					
		Concentration ($mg\ mL^{-1}$)	**DOSING (mg)**		
			Before	After	Actual
1	Paracetamol	1	3.0	0.0	3.0
2	Salicylic acid	1	3.0	0.0	3.0
3	Clopidogrel	3	15.0	0.0	15.0
4	Chlorpheniramine maleate	3	15.7	0.8	14.9
5	Diclofenac	1	3.2	0.0	3.2
6	$Ca(OH)_2$	10	30.3	0.5	29.8
Sample 2					
		Concentration ($mg\ mL^{-1}$)	**DOSING (mg)**		
			Before	After	Actual
1	Paracetamol	1	3.2	0.0	3.2
2	Salicylic acid	1	3.1	0.0	3.1
3	Clopidogrel	3	15.0	0.0	15.0
4	Chlorpheniramine maleate	3	15.0	0.5	14.5
5	Diclofenac	1	3.0	0.0	3.0
6	$Ca(OH)_2$	10	30.5	0.0	30.5
Antiretrovirals (ARVs)					
Sample 1					
		Concentration ($mg\ mL^{-1}$)	**DOSING (mg)**		
			Before	After	Actual
1	Zidovudine	1	3.4	0.0	3.4
2	Lamivudine	1	3.2	0.0	3.2
3	Tenofovir	1	3.0	0.3	2.7
4	Nevirapine	1	3.0	0.0	3.0
5	Stavudine	1	3.2	0.0	3.2
6	Abacavir sulfate	1	3.3	0.5	2.8
7	$Ca(OH)_2$	10	30.6	0.0	30.6
Sample 2					
		Concentration ($mg\ mL^{-1}$)	**DOSING (mg)**		
			Before	After	Actual
1	Zidovudine	1	3.4	0.0	3.4
2	Lamivudine	1	3.1	0.7	2.4
3	Tenofovir	1	3.4	0.0	3.4
4	Nevirapine	1	3.1	0.0	3.1
5	Stavudine	1	3.4	0.0	3.4
6	Abacavir sulfate	1	3.2	0.4	2.8
7	$Ca(OH)_2$	10	30.8	0.6	30.2
Notes					
Each sample was 3 mL					

A2.2 Granular activated carbon

Over the counter (OTC) common pharmaceuticals					
Sample 1					
		Concentration (mg mL^{-1})	**DOSING (mg)**		
			Before	After	Actual
1	Paracetamol	1	201.4	1.7	199.7
2	Salicylic acid	1	204.7	3.1	201.6
3	Diclofenac	1	207.1	2.5	204.6
4	Clopidogrel	1	200.1	1.7	198.4
5	Chlorpheniramine	1	203.2	0.0	203.2
6	$Ca(OH)_2$	10	2008.0	0.467	2007.0
Sample 2					
		Concentration (mg mL^{-1})	**DOSING (mg)**		
			Before	After	Actual
1	Paracetamol	1	207.2	0.0	207.2
2	Salicylic acid	1	205.3	3.1	202.2
3	Diclofenac	1	201.0	3.3	197.7
4	Clopidogrel	1	205.1	1.0	204.1
5	Chlorpheniramine	1	203.5	0.0	203.5
6	$Ca(OH)_2$	10	2008.0	0.47	2007.0
Antiretrovirals (ARVs)					
Sample 1					
		Concentration (mg mL^{-1})	**DOSING (mg)**		
			Before	After	Actual
1	Zidovudine	1	200.4	0.0	200.4
2	Lamivudine	1	200.7	0.0	200.7
3	Tenofovir	1	201.9	0.8	201.1
4	Nevirapine	1	202.2	1.5	200.7
5	Stavudine	1	200.8	0.0	200.8
6	Abacavir sulfate	1	200.4	1.7	198.7
7	$Ca(OH)_2$	10	2010.5	11.7	1999.8
Sample 2					
		Concentration (mg mL^{-1})	**DOSING (mg)**		
			Before	After	Actual
1	Zidovudine	1	201.9	8.7	193.2
2	Lamivudine	1	203.9	0.8	203.1
3	Tenofovir	1	201.1	1.6	199.5
4	Nevirapine	1	208.3	2.1	206.2
5	Stavudine	1	202.4	0.0	202.4
6	Abacavir sulfate	1	204.6	3.0	201.6
7	$Ca(OH)_2$	10	2005.5	10.3	1995.2
Notes					
Each sample was 200 mL					

A2.3 Hydrogen peroxide

Over the counter (OTC) common pharmaceuticals					
Sample 1					
		Concentration ($mg\ mL^{-1}$)	**DOSING (mg)**		
			Before	After	Actual
1	Paracetamol	1	15.2	0.0	15.2
2	Salicylic acid	1	15.3	0.0	15.3
3	Diclofenac	1	15.4	0.0	15.4
4	Chlorpheniramine maleate	1	15.0	0.0	15.0
5	$Ca(OH)_2$	10	152	0.12	152
Sample 2					
		Concentration ($mg\ mL^{-1}$)	**DOSING (mg)**		
			Before	After	Actual
1	Paracetamol	1	15.4	0.0	15.4
2	Salicylic acid	1	15.7	0.8	14.9
3	Diclofenac	1	15.2	0.9	14.3
4	Chlorpheniramine maleate	1	15.1	0.9	14.2
5	$Ca(OH)_2$	10	151.1	0.1	151.0
Antiretrovirals (ARVs)					
Sample 1					
		Concentration ($mg\ mL^{-1}$)	**DOSING (mg)**		
			Before	After	Actual
1	Zidovudine	1	15.4	0.8	14.6
2	Lamivudine	1	15.9	1.0	14.9
3	Tenofovir	1	15.6	1.4	14.2
4	Nevirapine	1	15.8	1.2	14.6
5	Stavudine	1	15.8	0.0	15.8
6	Abacavir sulfate	1	15.1	0.4	14.7
7	$Ca(OH)_2$	10	150.9	0.9	150.0
Sample 2					
		Concentration ($mg\ mL^{-1}$)	**DOSING (mg)**		
			Before	After	Actual
1	Zidovudine	1	15.9	0.0	15.9
2	Lamivudine	1	15.3	0.7	14.6
3	Tenofovir	1	15.0	1.2	13.8
4	Nevirapine	1	15.6	0.6	15.0
5	Stavudine	1	15.4	0.0	15.4
6	Abacavir sulfate	1	15.1	1.9	13.2
7	$Ca(OH)_2$	10	151.4	1.1	150.3
Notes					
Each sample was 15 mL					

A2.4 Hydrodynamic cavitation system

Low pH (pH 2)					
Sample 1					
		Concentration ($g\ L^{-1}$)	**Dosing (g)**		
			Before	After	Actual
1	Paracetamol	0.03	0.3	0.0	0.3
2	Chlorpheniramine	0.05	0.5	0.0	0.5
3	Zidovudine	0.03	0.3	0.0	0.3
4	Lamivudine	0.03	0.3	0.0	0.3
5	Stavudine	0.03	0.3	0.0	0.3
6	(Lamivudine*)	0.03	0.3	0.0	0.3
7	Urea	10.0	100.6	0.0	100.6
Sample 2					
		Concentration ($g\ L^{-1}$)	**Dosing (g)**		
			Before	After	Actual
1	Paracetamol	0.03	0.3	0.0	0.3
2	Chlorpheniramine	0.05	0.4	0.0	0.4
3	Zidovudine	0.03	0.3	0.0	0.3
4	Lamivudine	0.03	0.3	0.0	0.3
5	Stavudine	0.03	0.3	0.0	0.3
6	(Lamivudine*)	0.03	0.3	0.0	0.3
7	Urea	10.0	100.5	0.1	100.5
Each sample was 10 L Lamivudine* was unknown. However, was later confirmed to be Lamivudine					

High pH (pH 12.4)					
Sample 1					
		Concentration ($g\ L^{-1}$)	**Dosing (g)**		
			Before	After	Actual
1	Paracetamol	0.03	0.3	0.0	0.3
2	Chlorpheniramine	0.05	0.5	0.0	0.5
3	Zidovudine	0.03	0.3	0.0	0.3
4	Lamivudine	0.03	0.3	0.0	0.3
5	Stavudine	0.03	0.3	0.0	0.3
6	(Lamivudine*)	0.03	0.3	0.0	0.3
7	Urea	10.0	99.8	0.1	99.7
Sample 2					
		Concentration ($g\ L^{-1}$)	**Dosing (g)**		
			Before	After	Actual
1	Paracetamol	0.03	0.3	0.0	0.3
2	Chlorpheniramine	0.05	0.5	0.0	0.5
3	Zidovudine	0.03	0.3	0.0	0.3
4	Lamivudine	0.03	0.3	0.0	0.3
5	Stavudine	0.03	0.3	0.0	0.3
6	(Lamivudine*)	0.03	0.3	0.0	0.3
7	Urea	10.0	100.8	1.1	100.7
Each sample was 10 L Lamivudine* was unknown. However, was later confirmed to be Lamivudine					

A2.5 Optimized hydrodynamic cavitation system

Optimized cavitation system (pH 2)					
Sample 1					
		Concentration ($g\ L^{-1}$)	**Dosing (g)**		
			Before	After	Actual
1	Paracetamol	0.025	0.25	0.00	0.25
2	Chlorpheniramine	0.038	0.38	0.00	0.37
3	Zidovudine	0.025	0.25	0.00	0.25
4	Lamivudine	0.025	0.25	0.00	0.25
5	Stavudine	0.025	0.25	0.00	0.25
7	Urea	10.0	100.2	0.01	100.2
Sample 2					
		Concentration ($g\ L^{-1}$)	**Dosing (g)**		
			Before	After	Actual
1	Paracetamol	0.025	0.25	0.00	0.25
2	Chlorpheniramine	0.038	0.38	0.00	0.38
3	Zidovudine	0.025	0.25	0.00	0.25
4	Lamivudine	0.025	0.25	0.00	0.25
5	Stavudine	0.025	0.25	0.00	0.25
7	Urea	10.0	100.1	0.03	100.0
Each sample was 10 L					

Annexure A3: Urea and ammonium characterization

A3.1 High pH

OTCs Sample 1 Untreated Urine		
Nutrient	**Units**	**Actual value**
Ammonium	mgN L^{-1}	293.3
Urea	mgUrea L^{-1}	15145
OTCs Sample 2		
Untreated Urine		
Nutrient	**Units**	**Actual value**
Ammonium	mgN L^{-1}	176.1
Urea	mgUrea L^{-1}	13372

ARVs Sample 1 Untreated Urine		
Nutrient	**Units**	**Actual value**
Ammonium	mgN L^{-1}	331.5
Urea	mgUrea/L	13480
ARVs Sample 2		
Untreated Urine		
Nutrient	**Units**	**Actual value**
Ammonium	mgN L^{-1}	291.8
Urea	mgUrea L^{-1}	11425

A3.2 Granular activated carbon

OTCs Column 1 Untreated Urine		
Nutrient	**Units**	**Actual value**
Ammonium	mgN L^{-1}	139.8
Urea	mgUrea L^{-1}	5845
OTCs Column 2		
Untreated Urine		
Nutrient	**Units**	**Actual value**
Ammonium	mgN L^{-1}	139.8
Urea	mgUrea L^{-1}	5845

ARVs Column 1 Untreated Urine		
Nutrient	**Units**	**Actual value**
Ammonium	mgN L^{-1}	103.5
Urea	mgUrea L^{-1}	3300
ARVs Column 2		
Untreated Urine		
Nutrient	**Units**	**Actual value**
Ammonium	mgN L^{-1}	103.5
Urea	mgUrea L^{-1}	3300

A3.3 Hydrogen peroxide

OTCs Sample 1 Untreated Urine		
Nutrient	**Units**	**Actual value**
Ammonium	mgN L^{-1}	101.3
Urea	mgUrea L^{-1}	4911
OTCs Sample 2		
Untreated Urine		
Nutrient	**Units**	**Actual value**
Ammonium	mgN L^{-1}	101.3
Urea	mgUrea/L	4911

ARVs Sample 1 Untreated Urine		
Nutrient	**Units**	**Actual value**
Ammonium	mgN L^{-1}	101.3
Urea	mgUrea L^{-1}	4911
ARVs Sample 2		
Untreated Urine		
Nutrient	**Units**	**Actual value**
Ammonium	mgN L^{-1}	101.3
Urea	mgUrea/L	4911

A3.4 Hydrodynamic cavitation system

Low pH Sample 1 Untreated Urine		
Nutrient	**Units**	**Actual value**
Urea	mgUrea L^{-1}	9846.2
Low pH Sample 2		
Untreated Urine		
Nutrient	**Units**	**Actual value**
Urea	mgUrea L^{-1}	8514.2

High pH Sample 1 Untreated Urine		
Nutrient	**Units**	**Actual value**
Urea	mgUrea L^{-1}	9434.1
High pH Sample 2		
Untreated Urine		
Nutrient	**Units**	**Actual value**
Urea	mgUrea L^{-1}	8473.6

A3.5 Optimized hydrodynamic cavitation system

Sample 1 Untreated Urine		
Nutrient	**Units**	**Actual value**
Urea	mgUrea L^{-1}	10017
Low pH Sample 2		
Untreated Urine		
Nutrient	**Units**	**Actual value**
Urea	mgUrea L^{-1}	10003
Notes		
The values are nominal, based on the concentration of the urea added to the sample solution		

Annexure A4: Sieve Analysis

Sieve Test - Hand shaken				
Sieve Sizes (mm)	**Mass of the sieve (g)**	**Total mass (g)**	**GAC mass (g)**	**% GAC mass (%)**
4.750	447.7	447.7	0.0	0.0
2.360	409.1	409.2	0.1	0.0
1.180	515.6	790.5	274.9	81.4
0.600	322.6	382.2	59.6	17.7
0.300	281.4	283.5	2.1	0.6
0.150	489.3	489.8	0.5	0.1
0.075	252.5	252.6	0.1	0.0
Pan	494.8	495.1	0.3	0.1
Total			337.6	100.0

Annexure B: Pharmaceutical degradation results

Annexure B1: High pH experiment results

B1.1 High pH OTCs

OTCs Sample 1					
HPLC Data					
Days	**Paracetamol**	**Salicylic acid**	**Chlorphenamine**	**Diclofenac**	**Clopidogrel**
0.00	7757.9	9728.6	893.5	7982.4	1786.4
0.04	7745.2	9456.5	845.6	7968.8	1771.7
0.08	7778.0	9467.5	845.2	7972.6	1769.0
0.13	7588.1	9422.7	841.9	7970.9	1768.3
0.17	7743.8	9437.1	837.5	7967.3	1769.6
0.21	7723.3	9417.4	836.4	7967.5	1771.6
0.25	7754.8	9403.0	832.8	7965.9	1758.3
0.29	7689.0	9373.6	838.6	7961.6	1757.1
0.33	7657.7	9359.0	828.2	7961.2	1741.3
0.96	7678.8	9332.2	827.5	7958.0	1767.4
1.00	7630.4	9338.0	817.5	7954.8	1753.3
2.00	7553.6	9253.3	817.3	7945.4	1752.0
3.00	7527.4	8957.3	816.5	7930.3	1748.2
4.00	7410.6	8754.9	811.5	7905.9	1734.9
30.0	6979.1	7686.6	659.0	6759.8	1470.2
38.0	6897.9	7721.8	647.0	6028.7	1356.1
112	6409.3	7225.8	622.5	5639.5	1319.8
Percentage Degradation					
Days	**Paracetamol**	**Salicylic acid**	**Chlorphenamine**	**Diclofenac**	**Clopidogrel**
0.00	0.0	0.0	0.0	0.0	0.0
0.04	0.2	2.8	5.4	0.2	0.8
0.08	-0.3	2.7	5.4	0.1	1.0
0.13	2.2	3.1	5.8	0.1	1.0
0.17	0.2	3.0	6.3	0.2	0.9
0.21	0.4	3.2	6.4	0.2	0.8
0.25	0.0	3.3	6.8	0.2	1.6
0.29	0.9	3.6	6.1	0.3	1.6
0.33	1.3	3.8	7.3	0.3	2.5
0.96	1.0	4.1	7.4	0.3	1.1
1.00	1.6	4.0	8.5	0.3	1.9
2.00	2.6	4.9	8.5	0.5	1.9
3.00	3.0	7.9	8.6	0.7	2.1
4.00	4.5	10.0	9.2	1.0	2.9
30.0	10.0	21.0	26.2	15.3	17.7

38.0	11.1	20.6	27.6	24.5	24.1
112	17.4	25.7	30.3	29.4	26.1

OTCs Sample 2					
HPLC Data					
Days	**Paracetamol**	**Salicylic acid**	**Chlorphenamine**	**Diclofenac**	**Clopidogrel**
0.00	8334.6	9546.8	367.5	6435.9	1615.2
0.04	8259.0	9523.5	366.0	6433.2	1614.3
0.08	8258.0	9519.0	365.9	6429.9	1612.5
0.13	8235.8	9513.8	365.4	6427.3	1612.6
0.17	8239.0	9492.5	365.0	6424.8	1611.6
0.21	8225.1	9488.1	366.5	6425.9	1611.5
0.25	8189.4	9488.2	366.5	6423.2	1611.1
0.29	8170.3	9479.5	366.1	6419.2	1608.7
0.33	8194.5	9485.5	363.0	6409.6	1607.5
0.96	8118.7	9465.8	363.3	6408.4	1607.7
1.00	8106.0	9451.0	362.5	6404.3	1596.5
2.00	8079.1	9409.2	333.8	6401.1	1592.5
3.00	8052.7	9403.2	325.5	6395.4	1597.7
4.00	7926.4	9345.5	214.1	6318.6	1556.8
30.0	7843.8	8692.0	212.4	5311.3	1345.3
38.0	7732.2	7656.0	202.6	5151.7	1197.3
112	7669.7	7373.1	205.0	5128.8	1177.6
Percentage Degradation					
Days	**Paracetamol**	**Salicylic acid**	**Chlorphenamine**	**Diclofenac**	**Clopidogrel**
0.00	0.0	0.0	0.0	0.0	0.0
0.04	0.9	0.2	0.4	0.0	0.1
0.08	0.9	0.3	0.4	0.1	0.2
0.13	1.2	0.3	0.6	0.1	0.2
0.17	1.1	0.6	0.7	0.2	0.2
0.21	1.3	0.6	0.3	0.2	0.2
0.25	1.7	0.6	0.3	0.2	0.3
0.29	2.0	0.7	0.4	0.3	0.4
0.33	1.7	0.6	1.2	0.4	0.5
0.96	2.6	0.8	1.1	0.4	0.5
1.00	2.7	1.0	1.4	0.5	1.2
2.00	3.1	1.4	9.2	0.5	1.4
3.00	3.4	1.5	11.4	0.6	1.1
4.00	4.9	2.1	41.7	1.8	3.6
30.0	5.9	9.0	42.2	17.5	16.7
38.0	7.2	19.8	44.9	20.0	25.9
112	8.0	22.8	44.2	20.3	27.1

B1.2 High pH ARVs

ARVs Sample 1						
HPLC Data						
Days	**Stavudine**	**Lamivudine**	**Zidovudine**	**Abacavir sulfate**	**Nevirapine**	**Tenofovir**
0.04	23926.3	37267.3	25121.7	20352.1	12131.8	0.0
0.08	23356.9	37267.3	25092.7	20219.2	12315.6	
0.13	23439.6	37073.6	25120.6	20201.3	12112.6	
0.17	22471.0	37105.8	25023.5	20192.3	12102.8	
0.21	22899.8	36901.9	25018.8	20183.1	12107.5	
0.25	22899.8	36656.7	25082.5	20197.9	12082.6	
0.29	22843.5	35619.4	25106.4	20197.0	12087.2	
0.33	22569.0	35754.1	24587.6	20197.0	12087.2	
1.00	22671.5	33354.0	24437.8	20061.2	12087.3	
3.00	22050.2	32401.3	24372.7	20202.8	12083.1	
7.00	20480.4	31834.8	24249.8	19941.2	12061.2	
17.0	18782.7	30486.2	23554.7	18843.8	11610.1	
75.0	0	0	0	19888.0	11741.1	
Percentage Degradation						
Days	**Stavudine**	**Lamivudine**	**Zidovudine**	**Abacavir sulfate**	**Nevirapine**	**Tenofovir**
0.04	0.0	0.0	0.0	0.0	0.0	100.0
0.08	2.4	0.0	0.1	0.7	-1.5	
0.13	2.0	0.5	0.0	0.7	0.2	
0.17	6.1	0.4	0.4	0.8	0.2	
0.21	4.3	1.0	0.4	0.8	0.2	
0.25	4.3	1.6	0.2	0.8	0.4	
0.29	4.5	4.4	0.1	0.8	0.4	
0.33	5.7	4.1	2.1	0.8	0.4	
1.00	5.2	10.5	2.7	1.4	0.4	
3.00	7.8	13.1	3.0	0.7	0.4	
7.00	14.4	14.6	3.5	2.0	0.6	
17.0	21.5	18.2	6.2	7.4	4.3	
75.0	100.0	100.0	100.0	2.3	3.2	

ARVs Sample 2						
HPLC Data						
Days	**Stavudine**	**Lamivudine**	**Zidovudine**	**Abacavir sulfate**	**Nevirapine**	**Tenofovir**
0.04	26139.2	29666.9	24027.2	19585.2	12617.8	0.0
0.08	26195.6	29547.7	24005.1	19579.4	12440.2	
0.13	25080.9	29420.1	24031.6	19513.4	12218.7	
0.17	25845.9	29330.1	23927.5	19505.4	12114.3	
0.21	24236.5	29377.8	23859.1	19494.7	12172.9	
0.25	24361.8	29271.8	23997.1	19490.3	12183.1	
0.29	24795.0	28845.2	23990.8	19486.1	12178.3	
0.33	23906.8	28847.4	23960.1	19484.4	12172.3	
1.00	23036.4	28652.4	23865.0	19435.3	12173.6	
3.00	22988.1	28588.9	23539.8	19743.0	12176.5	
7.00	21512.4	27281.6	23191.0	19368.4	12175.2	
17.0	18496.5	24647.1	21781.3	19052.8	11704.0	
75.0	0	0	0	42420.6	19774.6	
Percentage Degradation						
Days	**Stavudine**	**Lamivudine**	**Zidovudine**	**Abacavir sulfate**	**Nevirapine**	**Tenofovir**
0.04	0.0	0.0	0.0	0.0	0.0	100.0
0.08	-0.2	0.4	0.1	0.0	1.4	
0.13	4.0	0.8	0.0	0.4	3.2	
0.17	1.1	1.1	0.4	0.4	4.0	
0.21	7.3	1.0	0.7	0.5	3.5	
0.25	6.8	1.3	0.1	0.5	3.4	
0.29	5.1	2.8	0.2	0.5	3.5	
0.33	8.5	2.8	0.3	0.5	3.5	
1.00	11.9	3.4	0.7	0.8	3.5	
3.00	12.1	3.6	2.0	-0.8	3.5	
7.00	17.7	8.0	3.5	1.1	3.5	
17.0	29.2	16.9	9.3	2.7	7.2	
75.0	100.0	100.0	100.0	0.0	0.0	

Annexure B2: Granular activated carbon experiment results

B2.1 Granular activated carbon OTCs

OTCs					
Sample 1					
	Paracetamol	**Salicylic acid**	**Chlorphenamine**	**Diclofenac**	**Clopidogrel**
Before	16168.2	3451.9	6660.9	4799.9	3780.8
After	195.7	66.4	119.2	0	63.3
Percentage Degradation					
Before	100	100	100	100	100
After	1.21	1.92	1.79	0.00	1.67
Sample 2					
	Paracetamol	**Salicylic acid**	**Chlorphenamine**	**Diclofenac**	**Clopidogrel**
Before	3343.8	52894.1	3563.4	10390	(TBC)
After	14.8	410.8	8.7	102.5	(TBC)
Percentage Degradation					
Before	100	100	100	100	100
After	0.44	0.78	0.24	0.99	(0)

B2.2 Granular activated carbon ARVs

ARVs					
Sample 1					
	Stavudine	**Lamivudine**	**Zidovudine**	**Abacavir sulfate**	**Nevirapine**
Before	42261.1	25539.5	34957.2	51520.6	25736.3
After	2224.2	1359	1320.5	613.6	865.5
Percentage Degradation					
Before	100	100	100	100	100
After	5.26	5.32	3.78	1.19	3.36
Sample 2					
	Stavudine	**Lamivudine**	**Zidovudine**	**Abacavir sulfate**	**Nevirapine**
Before	46385.8	26298.9	33911.9	52715.5	23865.4
After	0	0	0	0	0
Percentage Degradation					
Before	100	100	100	100	100
After	0.00	0.00	0.00	0.00	0.00

Annexure B3: Hydrogen peroxide experiment results

B3.1 Hydrogen peroxide OTCs

Sample 1				
	Paracetamol	**Salicylic acid**	**Chlorphenamine**	**Diclofenac**
Before	13895.10	12969.70	2941.70	4342.20
After	9628.10	6103.20	2309.70	4342.20
Percentage Degradation				
Before	100	100	100	100
After	69.3	47.1	78.5	100
Sample 2				
	Paracetamol	**Salicylic acid**	**Chlorphenamine**	**Diclofenac**
Before	13544.2	10924.1	1911.2	5790.9
After	9774.5	3858.52	1911.2	5655.2
Percentage Degradation				
Before	100	100	100	100
After	72.17	35.32	100	97.66

B3.2 Hydrogen peroxide pH ARVs

ARVs					
Sample 1					
	Lamivudine	**Stavudine**	**Abacavir Sulfate**	**Zidovudine**	**Nevirapine**
Before	15309.0	16807.6	18878.2	12741.5	8582.9
After	4077.3	13573.6	15450.3	10168.3	5670.3
Percentage Degradation					
Before	100.0	100.0	100.0	100.0	100.0
After	26.6	80.8	81.8	79.8	66.1
Sample 2					
	Lamivudine	**Stavudine**	**Abacavir Sulfate**	**Zidovudine**	**Nevirapine**
Before	15051.7	16857.1	19076.0	12712.8	8730.2
After	5801.3	13956.4	15112.3	10344.5	5441.5
Percentage Degradation					
Before	100.0	100.0	100.0	100.0	100.0
After	38.5	82.8	79.2	81.4	62.3

Annexure B4: Hydrodynamic cavitation experiment results

B4.1 Hydrodynamic cavitation low pH (pH 2)

Acid (2.0)					
Sample 1					
	Paracetamol	**Chlorphenamine**	**Zidovudine**	**Lamivudine**	**Stavudine**
Before	581.3	558.8	468.1	1100.7	566.0
After	521.0	403.6	272.0	907.2	367.7
Percentage Degradation					
Before	100.0	100.0	100.0	100.0	100.0
After	89.6	72.2	58.1	82.4	65.0
Sample 2					
	Paracetamol	**Chlorphenamine**	**Zidovudine**	**Lamivudine**	**Stavudine**
Before	530.5	523.4	424.9	1168.6	526.4
After	444.3	361.8	216.0	694.6	328.1
Percentage Degradation					
Before	100.0	100.0	100.0	100.0	100.0
After	83.8	69.1	50.8	59.4	62.3

B4.2 Hydrodynamic cavitation high pH (pH 12.4)

Basic					
Sample 1					
	Paracetamol	**Chlorphenamine**	**Zidovudine**	**Lamivudine**	**Stavudine**
Before	1358.9	362.2	493.0	1217.9	602.7
After	1326.7	301.9	470.6	1172.0	584.1
Percentage Degradation					
Before	100.0	100.0	100.0	100.0	100.0
After	97.6	83.4	95.5	96.2	96.9
Sample 2					
	Paracetamol	**Chlorphenamine**	**Zidovudine**	**Lamivudine**	**Stavudine**
Before	504.3	332.2	452.0	1117.8	552.2
After	507.7	289.3	453.1	1125.0	557.5
Percentage Degradation					
Before	100.0	100.0	100.0	100.0	100.0
After	100.7	87.1	100.2	100.6	101.0

Annexure C: Optimized hydrodynamic cavitation system

C.1 Optimized inlet pressure

UV Spectroscopy			
Wavelength	230 mm		
API	Paracetamol		
Device	3 mm orifice		
	Pressure(kPa)		
Sample	200	300	400
Before	1.325	1.056	1.096
After	1.067	0.857	0.772
% Degradation	**19.5**	**18.8**	**29.6**

C.2 Optimized pharmaceutical degradation

Optimized System					
Sample 1					
	Lamivudine	**Stavudine**	**Zidovudine**	**Paracetamol**	**Chlorphenamine**
Before	321.5	345.6	259.4	256.8	319.1
After	49	63.2	38.2	104.7	114.5
Percentage Degradation					
Before	100.0	100.0	100.0	100.0	100.0
After	15.2	18.3	14.7	40.8	35.9
Sample 2					
	Lamivudine	**Stavudine**	**Zidovudine**	**Paracetamol**	**Chlorphenamine**
Before	295.2	305	245.9	248.1	333.2
After	56	55.6	30.6	112.8	116.2
Percentage Degradation					
Before	100.0	100.0	100.0	100.0	100.0
After	19.0	18.2	12.4	45.5	34.9

C.3 Optimized urea degradation

Optimized Sample 1				
Nutrient	**Units**	**Dilution Factor**	**Value**	**Actual value**
Before	mgUrea L^{-1}	25	288.4	7211
After	mgUrea L^{-1}	25	278.0	6950

Percentage Degradation	
Before	100.0
After	96.4

Optimized Sample 2				
Nutrient	**Units**	**Dilution Factor**	**Value**	**Actual value**
Before	mgUrea L^{-1}	25	336.4	8410
After	mgUrea L^{-1}	25	331.6	8290

Percentage Degradation	
Before	100.0
After	98.6

C.4 Effect of temperature and pH

Optimized System		
Run no.	1	
Pressure (kPa)	400	
Starting pH	1.938	
Time (min)	**pH**	**Temperature ('C)**
1	2.001	14.4
2	2.023	16
3	2.023	17.4
4	1.997	18.7
5	2.005	20
6	2.018	21.2
7	2.03	22.3
8	2.044	23.4
9	2.057	24.4
10	2.071	25.4
11	2.082	26.4
12	2.096	27.4
13	2.106	28.3
14	2.119	29.2
15	2.128	30.1
16	2.141	31
17	2.153	21.8
18	2.165	32.6
19	2.177	33.4
20	2.19	34.2
21	2.202	35
22	2.215	35.7
23	2.226	36.5
24	2.24	37.2
25	2.253	37.9
26	2.265	38.6
27	2.279	39.2
28	2.292	39.9
29	2.306	40.5
30	2.32	41.1

Optimized System		
Run no.	2	
Pressure (kPa)	400	
Starting pH	2.048	
Time (min)	**pH**	**Temperature ('C)**
1	1.883	23.1
2	1.895	24.7
3	1.907	26.1
4	1.923	27.4
5	1.935	28.5
6	1.926	29.5
7	1.902	30.5
8	1.909	31.5
9	1.918	32.4
10	1.927	33.3
11	1.936	34.2
12	1.943	35
13	1.954	35.9
14	1.962	36.7
15	1.97	37.5
16	1.979	38.2
17	1.99	39
18	2.001	39.7
19	2.011	40.4
20	2.019	41.1
21	2.026	41.7
22	2.034	42.4
23	2.045	43
24	2.053	43.6
25	2.062	44.2
26	2.069	44.8
27	2.078	45.3
28	2.089	45.8
29	2.096	46.4
30	2.106	46.9

Annexure D: Urea results

D.1 High pH urea results

Untreated urine									
Nutrient	**Units**	**Dilution Factor**	**Sample 1**	**Sample 2**	**Sample 3**	**Average value**	**Actual value**	**Standard deviation**	**Error (%)**
Ammonium	mgN L^{-1}	25.0	9.4	9.4	9.3	9.4	234.0	0.1	1.0
Urea	mgUrea L^{-1}	25.0	430.9	424.3	418.0	424.4	10610	6.5	1.5
Treated urine									
Nutrient	**Units**	**Dilution Factor**	**Sample 1**	**Sample 2**	**Sample 3**	**Average value**	**Actual value**	**Standard deviation**	**Error (%)**
Ammonium	mgN L^{-1}	25.0	7.2	8.1	7.7	7.6	190.7	0.4	5.7
Urea	mgUrea L^{-1}	25.0	395.1	420.5	407.0	407.6	10190	12.7	3.1

Average Degradation		
	Ammonium	**Urea**
Before	100.0	100.0
After	81.5	96.0

D.2 Granular activated carbon urea results

	Column Type1					
	Ammonium			Urea		
	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3
Before	126.2	119.8	111.2	6308	6381	6168
After	22.1	53.2	13.2	374.3	1625	590.9
	Percentage of Nutrients Present					
	Ammonium			Urea		
	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3
Before	100.0	100.0	100.0	100.0	100.0	100.0
After	17.5	44.4	11.8	5.9	25.5	9.6

	Column Type 2					
	Ammonium			Urea		
	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3
Before	190.9	197.1	208.2	9654.3	9675	10300
After	96.7	39.8	43.6	4335.2	484.8	919.9
	Percentage of Nutrients Present					
	Ammonium			Urea		
	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3
Before	100.0	100.0	100.0	100.0	100.0	100.0
After	50.6	20.2	20.9	44.9	5.0	8.9

Percentage Degradation				
	Column 1		Column 2	
	Ammonium	Urea	Ammonium	Urea
Before	100.0	100.0	100.0	100.0
After	24.6	13.7	30.6	19.6

Average degradation		
	Ammonium	Urea
Before	100.0	100.0
After	27.6	16.6
Standard Deviation		
	Ammonium	Urea
Before	0.3	4.5
After	0.5	3.3

D.3 Hydrogen peroxide urea results

Untreated urine									
Nutrient	**Units**	**Dilution Factor**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 4**	**Average value**	**Actual value**	**Standard deviation**
Ammonium	mgN L^{-1}	25	4.1	4.1	4.1	4.1	4.1	101.3	0.0
Urea	mgUrea L^{-1}	25	196.5	196.5	196.5	196.5	196.5	4911	0.0
Treated Urine									
Nutrient	**Units**	**Dilution Factor**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 4**	**Average value**	**Actual value**	**Standard deviation**
Ammonium	mgN L^{-1}	25	2.4	1.9	2.0	1.7	2.0	50.1	0.3
Urea	mgUrea L^{-1}	25	179.2	169.6	169.0	169.1	171.7	4293	5.0

Percentage Degradation		
	Ammonium	Urea
Before	100.0	100.0
After	49.4	87.4

D.4 Hydrodynamic cavitation system urea results

Untreated urine									
Nutrient	**Units**	**Dilution Factor**	**Sample 1**	**Sample 2**	**Sample 3**	**Average value**	**Actual value**	**Standard deviation**	**Error (%)**
Urea	mgUrea L^{-1}	25	381.9	391.1	385.2	386.0	9651	4.7	1.2

Treated urine									
Nutrient	**Units**	**Dilution Factor**	**Sample 1**	**Sample 2**	**Sample 3**	**Average value**	**Actual value**	**Standard deviation**	**Error (%)**
Urea	mgUrea L^{-1}	25	330.3	378.7	370.8	359.9	8999	26.0	7.2

Percentage Degradation	
	Urea
Before	100.0
After	93.2

Annexure E: Pharmaceutical analysis methods

High performance liquid chromatography (HPLC) with diode array detection (HPLC-DAD) was the primary pharmaceutical analysis method for the current work. Five over the counter (OTC) common pharmaceuticals (paracetamol, salicylic acid, diclofenac, clopidogrel and chlorpheniramine maleate) and six antiretrovirals (ARVs) (zidovudine, lamivudine, tenofovir, stavudine, and abacavir sulfate) were used in this study. The individual pharmaceutical profiles are given in Annexure A1.

The development of HPLC methods is essential for the accurate analysis of samples. Snyder and co-workers (1988) identified common steps which are followed in the development of an HPLC method. Figure E1 gives an overview of the HPLC method development steps (Snyder et al., 1988).

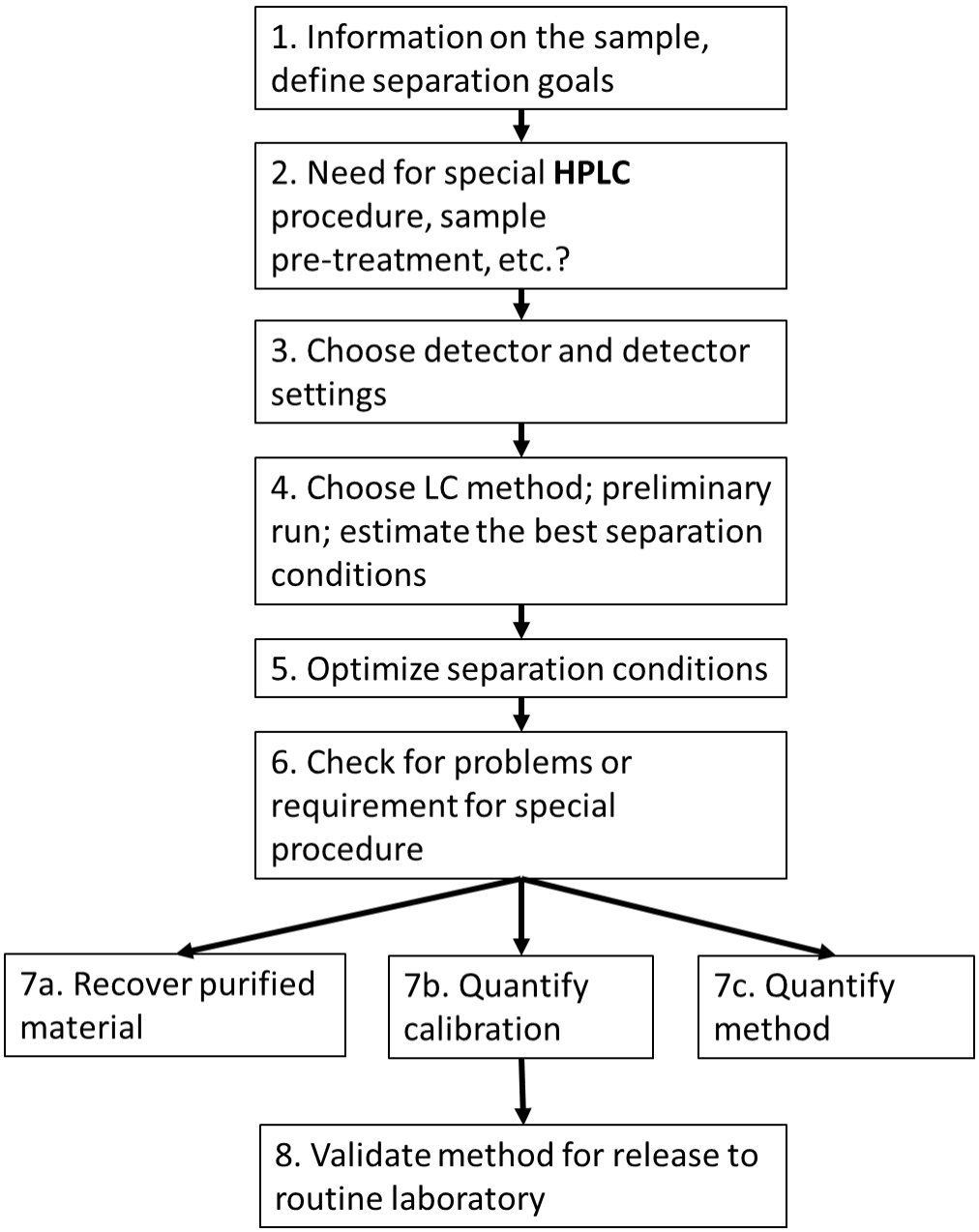


Figure E1: HPLC method development steps (Snyder et al., 1988).

According to Snyder and co-workers (1988) the function of each step in the HPLC method development process helps in developing an efficient analysis method. The details of each step are provided in this section. As such, HPLC methods used for the current work were based on the work by Patel and co-workers (2013). Three methods were developed: a method to test for the over the counter (OTC) common pharmaceuticals, a method to test for the antiretrovirals (ARVs) and a method to test for both the OTCs and the ARVs.

E.1 Sample description

The sample description influences the separation goals which are defined for the HPLC. The factors that are considered for the sample description include the number of compounds present, sample solubility, compound chemical structures (including ultraviolet (UV)), molecular weight, polarity, concentration of compounds and the pK_a values of the compounds (Snyder et al., 1988).

Some of the factors proposed by Snyder and co-workers (1988) for the sample definition were considered for the current work. Eleven pharmaceuticals (paracetamol, salicylic acid, diclofenac, clopidogrel, chlorpheniramine maleate, zidovudine, lamivudine, tenofovir, nevirapine, stavudine and abacavir sulfate) were chosen for the current work. Annexure A1.1 gives a description of each pharmaceutical in terms of the type of pharmaceutical, the molecular formula, chemical structure, water solubility and the pK_a value. Furthermore, a nominal concentration of 1 mg mL^{-1} was used to spike the pharmaceuticals in the urine samples. This concentration was chosen since it was high enough for all pharmaceuticals to be detected using the HPLC. The UV wavelength at which all the OTCs could be detected were 254 nm and 230 nm, while all the ARVs could be detected at wavelengths of 210 nm, 254 nm, and 280 nm. Furthermore, the optimum wavelength at which both the OTCs and the ARVs could be detected was 210 nm. Overall, the main factor which influenced the development of the HPLC methods was the type of pharmaceutical i.e., whether the pharmaceuticals were OTCs or ARVs.

E.2 Separation goals

According to Snyder and co-workers (1988), the definition of the HPLC separation goals is fundamental in the development of a HPLC method. Firstly, the primary goal of the HPLC method should be determined, whether it is for quantitative analysis, to characterize samples, to detect samples, for sample isolation or sample purification. Other factors included the number of sample components which need to be resolved, the level of accuracy for quantitative analysis, sample matrices and the analysis of the samples (Snyder et al., 1988).

For this work, the HPLC methods were used for quantitative analysis. The subjects of the HPLC analyses were the pharmaceuticals chosen for the current study. As a result, each

pharmaceutical was resolved as a sample component during the analysis process. The level of accuracy for the sample analysis was adequate for the integration of the areas (under the chromatogram) to derive the concentration of the pharmaceuticals.

A simple sample matrix was used for the development of the HPLC methods. The samples which were analyzed were as follows: a pure water sample and a urine sample, both of which were used as negative controls, individual pharmaceuticals in water, individual pharmaceuticals in urine, pharmaceutical mixture in water and pharmaceutical mixture in urine (used as positive controls). The samples were run as a reference for the analysis of the samples from the pharmaceutical removal method experiments. The samples which were analyzed for each pharmaceutical removal method were as follows: blank urine sample, spiked-untreated urine sample and the treated urine sample.

E.3 Sample pre-treatment and detection

Snyder and co-workers (1988) mentioned that while other samples are ready for injection, some samples require dilution, buffering, volumetric manipulation, and internal standard. Moreover, solid samples need to be dissolved or extracted, while others may require filtration (Snyder et al., 1988).

The samples which were prepared for the current work did not require dilution, buffering, addition of an internal standard nor other volumetric manipulation. Given that some samples were stabilized with calcium hydroxide, which partially dissolved in the urine solution, the samples were filtered through a 0.22 µm pore size to prevent damage to the HPLC column or equipment.

E.4 Developing the separation

Snyder and co-workers (1988) proposed the use of the sample solution knowledge and the HPLC separation goals to determine the conditions for the initial experimental conditions. Figure E2 illustrates the thought process of the selection of suitable initial conditions for the analysis of samples. The process only shows the possible pathways for an HLPC method (Snyder et al., 1988).

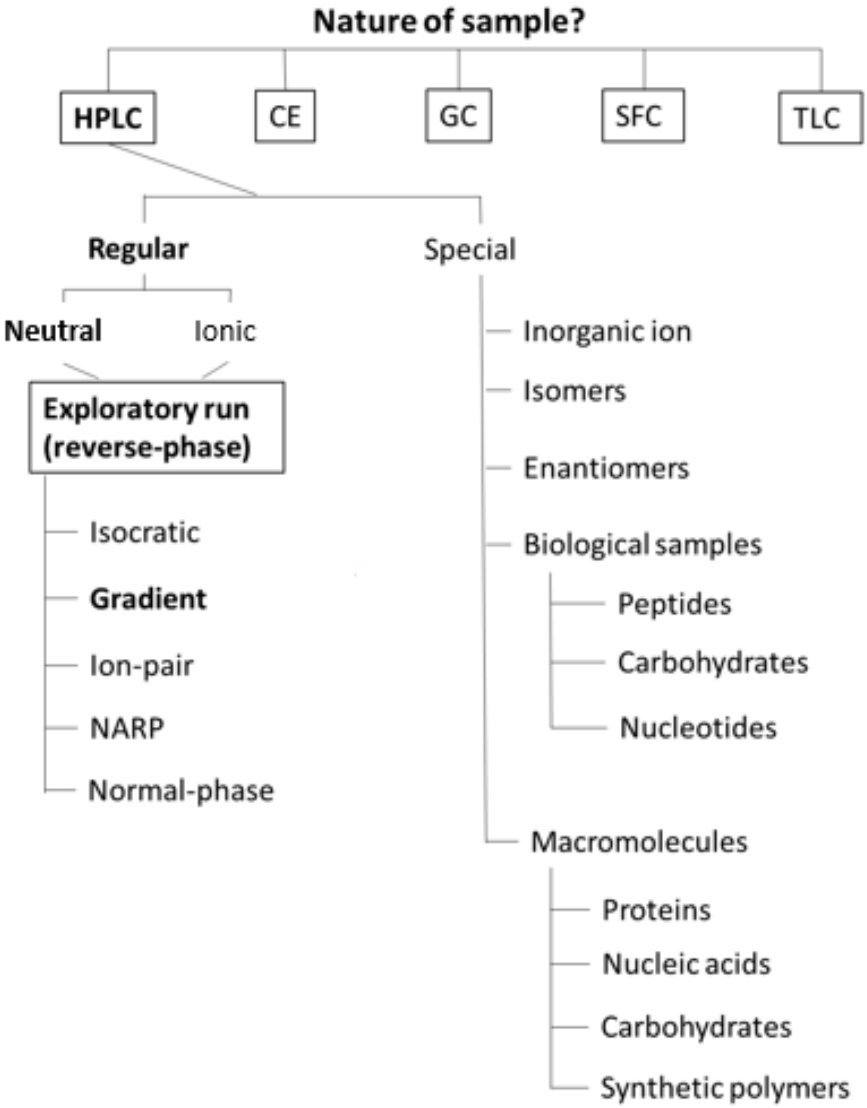


Figure E2: The use of the sample information to determine the initial conditions of an HPLC method (Snyder et al., 1988).

Although the parameters for initial HPLC methods used for the current work were based on the paper by Patel and co-workers (2013), a similar thought process described by Snyder and co-workers (1988) was applied for the HPLC method development. Reverse phase HPLC, which is commonly used, was used for the HPLC methods developed for this work. The current work looked at the acidity and basicity of the pharmaceuticals and their polarity to find the elution order and the required mobile phases.

E.4 Method development

Snyder and co-workers (1988) recommended an isocratic elution with a high percentage of aqueous solvent and a low organic phase for the initial development of the HPLC analysis method, which remains unchanged for the run. However, gradient elution (which is the percentage change of the aqueous and organic phase during the analysis run) yields a better separation of the components. For this reason, gradient elution was applied for the three HPLC methods developed for the current work. Acetonitrile was used as the organic solvent for all three methods. However, the HPLC method to analyze OTCs and the method to analyze both the OTCs and the ARVs used a phosphate as an aqueous buffer, while the method to analyze ARVs used an aqueous phosphate buffer with added hexanesulfonic acid.

The standard chromatograms for each HPLC method were generated. The chromatogram for the initial method separating the OTCs is shown in Figure E3. In a mixture of five pharmaceuticals, only four pharmaceuticals were detected using this method, clopidogrel, was the fifth pharmaceutical but it was not able to be identified. The chromatograms of the individual pharmaceuticals are given in Annexure A1.2, including the chromatogram for clopidogrel which shows that the peak of clopidogrel appears at a time of 16.17 minutes.

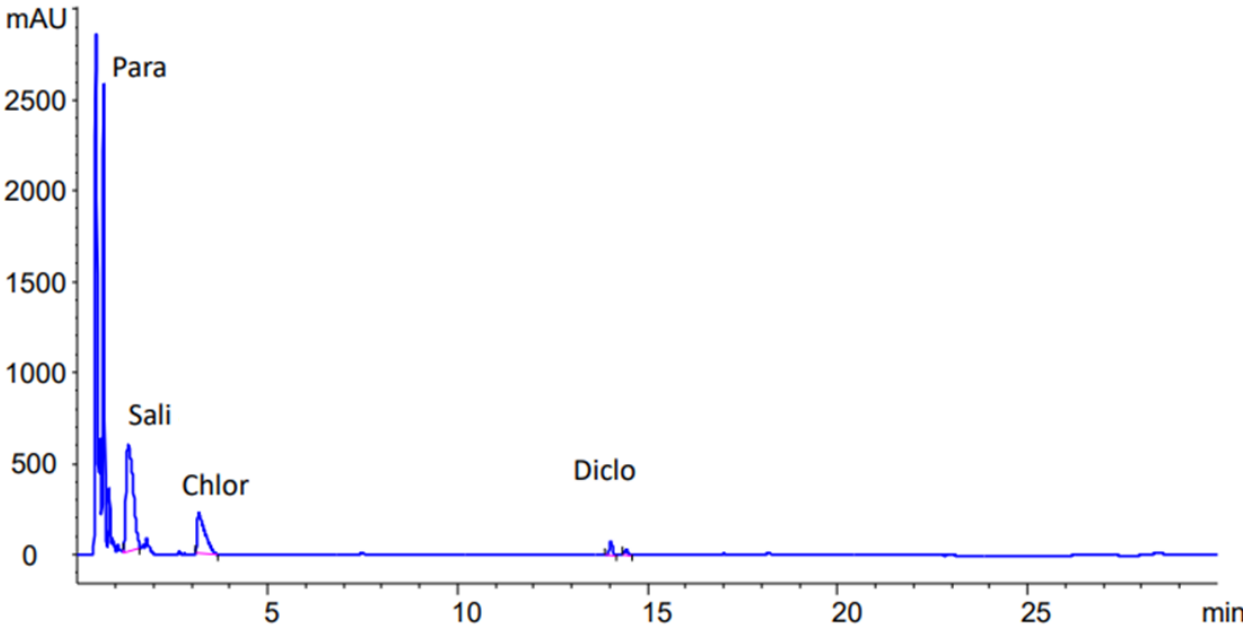


Figure E3: OTCs mixture standard chromatogram. The pharmaceuticals indicated in the chromatogram: paracetamol (Para); salicylic acid (Sali); chlorphenamine maleate (Chor) and diclofenac (Diclo).

The chromatogram for the HPLC method to test for the ARVs is shown in Figure E4. All six pharmaceuticals had clearly defined peaks, however additional peaks were also observed in the chromatogram. The peaks were not considered as a sign of no degradation nor a representative of a pharmaceutical since all the urine sample chromatograms had the same peaks. Rather, the peaks represent other components in the urine since the composition of urine is influenced by factors such as diet (Maurer et al., 2006). The chromatograms for the individual pharmaceuticals are given in Annexure A1.3.

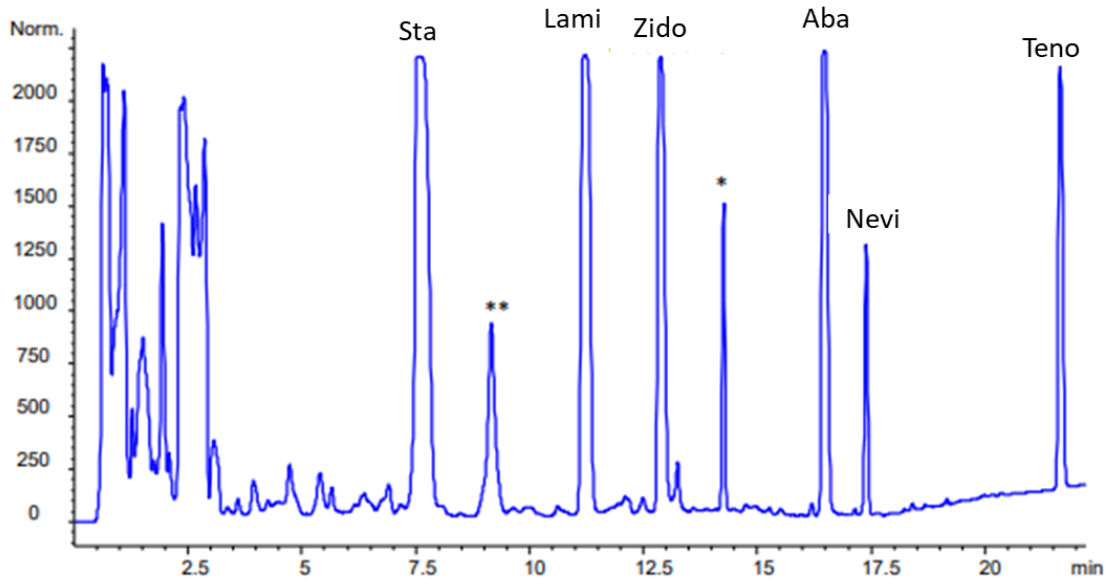


Figure E4: ARVs mixture standard chromatogram. The pharmaceuticals indicated in the chromatogram: stavudine (Sta); lamivudine (Lami); zidovudine (Zido); abacavir sulfate (Aba); nevirapine (Nevi) and tenofovir (Teno).

The chromatogram of the HPLC method to analyze for both OTCs and ARVs showed a small peak for chlorphenamine maleate (shown in Figure E5). This meant that the concentration was low. Therefore, in the spiking experiments, the concentration of chlorpheniramine maleate was increased 1.5 times more than the concentration of the other pharmaceuticals, to ensure that the pharmaceutical would be well-detected by the HPLC method. The additional peaks which appear in the chromatogram represent the other pharmaceuticals which were investigated for the current study, which were not analyzed using this method.

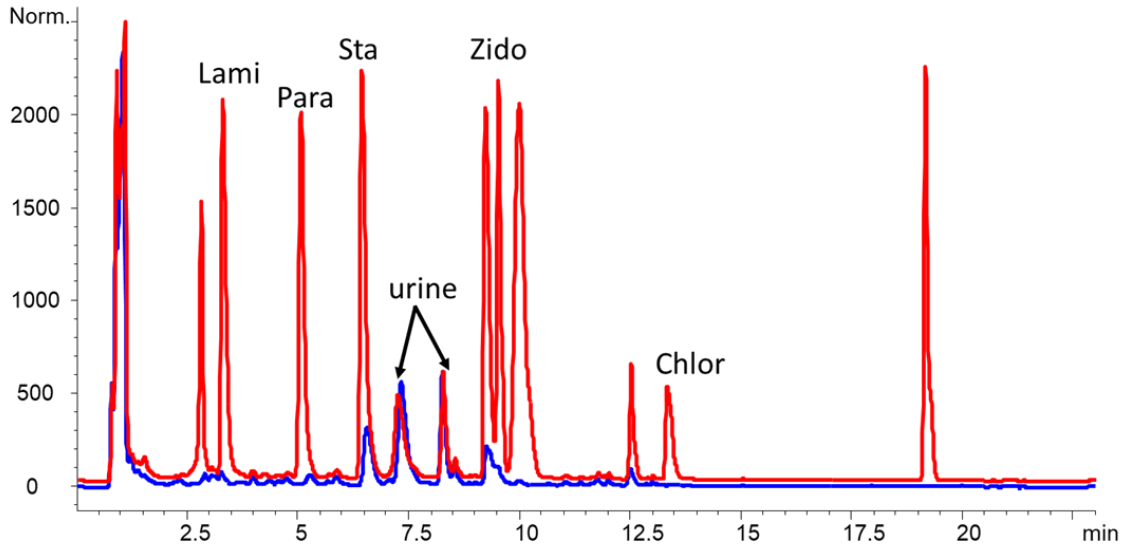


Figure E5: Combined OTCs and ARVs mixture chromatogram. The pharmaceuticals indicated in the chromatogram: paracetamol (Para); chlorphenamine maleate (Chor), lamivudine (Lami), zidovudine (Zido) and stavudine (Sta).

E.5 Improving the separation

According to Snyder and co-workers (1988) the time needed to separate the components of the samples using the HPLC influences the run time of the samples (Snyder et al., 1988). The run time for each sample analysis was 20 minutes. The extra time was used to re-equilibrate the column to the initial conditions for the next sample.

E.6 Repeatable separation

Snyder and co-workers (1988) emphasized the importance of column equilibrium since it is an indication of the repeatability of the experiments. A repeat experiment under the same conditions is required to achieve equilibrium. Failure to equilibrate the column and to reproduce the chromatograms, results in the hindrance of the HPLC method development (Snyder et al., 1988). As such, column equilibrium was maintained for the current work. A minimum passage of 10 column volumes of a new mobile phase was applied, like what was suggested by Snyder and co-workers (1988).

The remaining steps which were suggested by Snyder and co-workers (1988) (quantitation and method validation; problem identification; and method robustness) were not considered for HPLC methods developed for this work. This is because the methods were not developed for publication, rather, they were developed to quantify the percentage degradation of the pharmaceuticals due to the respective pharmaceutical degradation methods.

Annexure F: Optimized system energy requirement

The energy required to operate the optimized hydrodynamic cavitation (HC) system was calculated to find whether the use of the optimized HC system to degrade pharmaceuticals is economical. The principle of energy conservation for the optimized HC energy requirements.

We know from Himmelblau and Riggs (2012) that the equation given for the energy balance equation is as follows:

$$\frac{\Delta E}{\Delta t} = F_{in}E_{in} - F_{out}E_{out} + Q - W$$

$\frac{\Delta E}{\Delta t}$ = Cumulative system energy

$F_{in}E_{in}$ = Transfer of energy into the system

$F_{out}E_{out}$ = Transfer of energy out of the system

Q = Generated system energy

W = Consumed system energy

Furthermore, the total energy of the system was given as a sum of three different forms of energy which are: kinetic energy (E_k), potential energy (E_p) and internal energy (U), see Equation 5. The kinetic energy results from the movement of the sample solution from one point of the system to another, while E_p is due to the relative position of a sample solution within a gravitational field. On the other hand, U represents all the other energy types found within a system including vibrational energy in chemical bonds (Geankoplis, 1994). As such, the total energy of a system is explained by Geankoplis (1994) in the following way:

$$E = E_K + E_P + U$$

Where:

E_K = $\frac{v^2}{2}$, where v is the velocity of the sample solution

E_P = zg, where z is the relative position of the sample solution and g is the acceleration of gravity

U = $U = H - PV$, where H is the enthalpy, P is the pressure and V is the volume

Furthermore, Geankoplis (1994) gave the overall energy balance equation for a steady state system as follows:

$$H_2 - H_1 + \frac{1}{2 \propto} ({v_2}^2 - {v_1}^2) + g(z_2 - z_1) = Q - W_s$$

Where:

Q = System heat

W_s = System work

Energy calculation

The energy balance for the optimized hydrodynamic cavitation (HC) system considered the pump position as the reference point i.e., position 1. The HC system shown in Figure F1 was used for the energy balance calculations. To simplify the energy balance calculation, two tanks are shown in the diagram, however, only one tank is used in the actual HC system since the sample solution is recycled throughout the cavitational process.

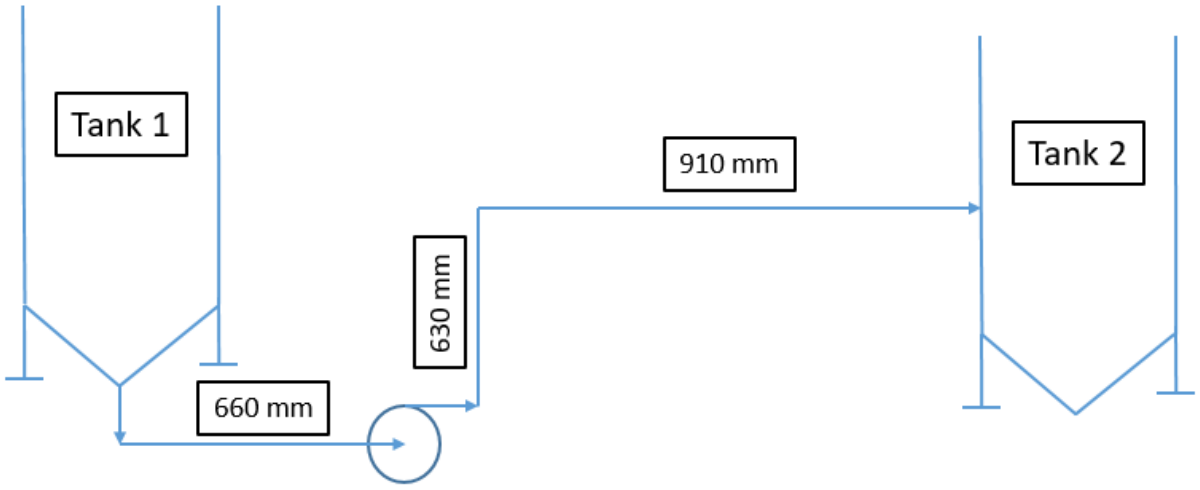


Figure F1: Hydrodynamic cavitation system energy diagram.

The following assumptions were made for the energy balance calculations:

1. Point 1 is the reference elevation, therefore $z_1 = 0$
2. The tank is open to the atmosphere, therefore $P_1 =$ atmospheric pressure
3. There was no phase change or chemical reactions that occurred during the cavitation process
4. The velocity at point 1 is negligible, therefore $v_1 = 0$
5. The sample solution is incompressible; therefore, the density of the fluid remains constant
6. Although a urea-water solution was used, the urine density of 1025 kg/m^3 was used (Pradella et al., 1988)
7. Steady flow in the pipes
8. Surface friction occurred in the pipes
9. Friction loses resulting from contraction, fittings, valves, venturi, and the orifice plate were negligible
10. The viscosity of urine was used even though a urea-water solution was used
11. Stainless steel was used for the pipe material

The input parameters for the energy balance calculations are given in Table F1.

Table F1: Energy balance input parameters.

Parameter description	Value	Unit
Density (ρ)	1025	Kg/m^3
Discharge pressure (P_2)	400 000	Pa
Height (Z_2)	0.63	m
Inner diameter (D)	0.025	m
Total length (L)	2.2	m
Suction pressure (P_1)	101325	Pa
Viscosity (μ)	0.000716	Pa.s
Volumetric flow rate (Ṽ)	0.000120	m^3 s^{-1}

Pump head calculation

Geankoplis (1994) defined the pumping head of a fluid as the distance the fluid can be lifted using the pump. This is defined by Equation 7 as follows:

$$H_D = (Z_2 - Z_1) + \frac{{v_2}^2 - {v_1}^2}{2\alpha g} + \frac{P_2 - P_1}{\rho g} + H_L$$

Where:

$Z_2 - Z_1$ = elevation change (m)

${v_2}^2 - {v_1}^2$ = velocity change (m/s), the velocity before (v_1) and after (v_2) the fluid enters the pump

α = kinetic energy correction factor

g = acceleration of gravity (m s^{-2})

H_L = head loss

ρ = density (kg m^{-3})

$P_2 - P_1$ = pressure change (Pa)

Once the pumping head was calculated, the power of the fluid would be determined after which the energy required to operate the hydrodynamic cavitation (HC) system at the optimized conditions would be quantified. However, to a calculate the pumping head, the area of the pipe, the velocity of the fluid, the Reynold number, friction factor and the head loss were calculated first.

Pipe area

$$A = \frac{\pi d^2}{4} = \frac{\pi(0.025)^2}{4} = 4.91 \times 10^{-4}\, m^2$$

Fluid velocity

$$v = \frac{\tilde{\mathrm{V}}}{A} = \frac{0.000120}{4.91 \times 10^{-4}} = 0.24\, m\, s^{-1}$$

Reynold number

$$Re = \frac{\rho v D}{\mu} = \frac{1025 \times 0.24 \times 0.025}{0.000716} = 8589.39$$

Since the Reynold number exceeds 4100, the flow within the optimized HC system is turbulent (Geankoplis, 1994).

Friction factor

The absolute roughness (ε) of stainless steel is 3 x 10^{-5} m, and the relative roughness is given by $\epsilon = \frac{\varepsilon}{D}$ (Geankoplis, 1994).

$$\epsilon = \frac{\varepsilon}{D} = \frac{3 \times 10^{-5}}{0.025} = 1.2 \times 10^{-3}$$

Using the Moody chart (given in Figure F2), the Darcy friction factor for the optimized HC system was 0.038.

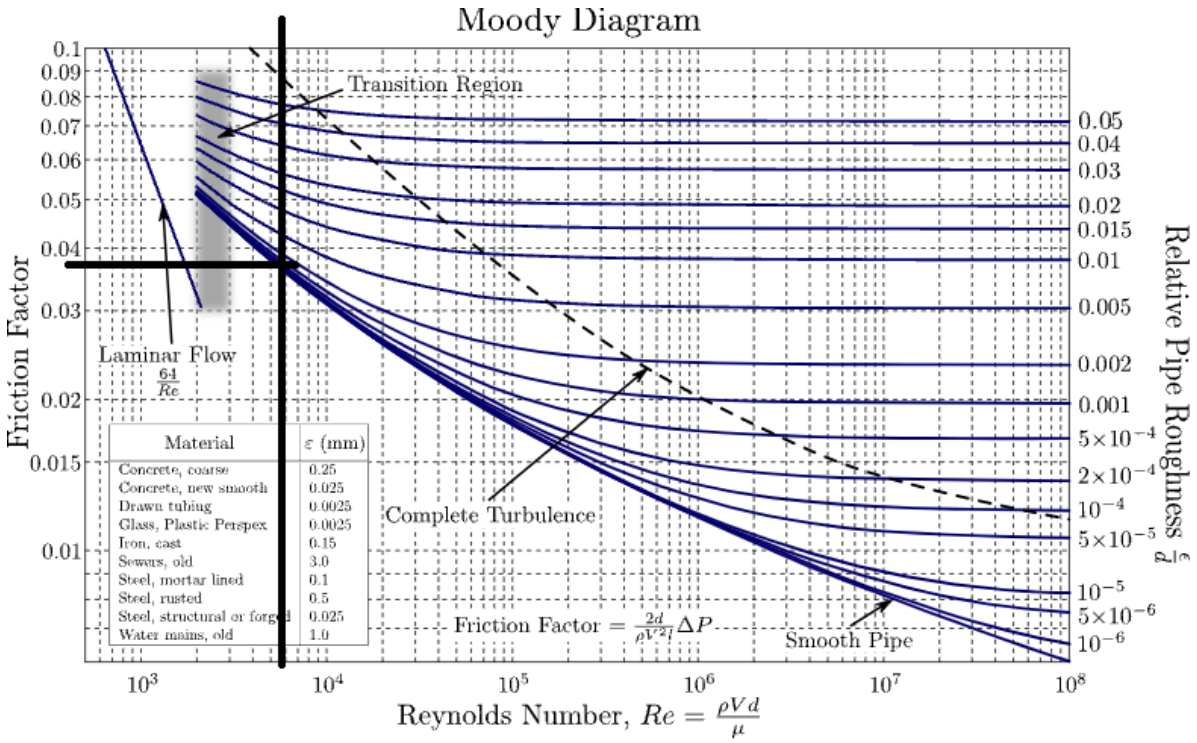


Figure F2: Moody Diagram (Beck and Collins, 2008).

Head loss

$$H_L = f \times \frac{L}{D} \times \frac{v^2}{2g} \text{ (Geankoplis, 1994)}$$

$$H_L = 0.038 \times \frac{2.2}{0.025} \times \frac{0.24^2}{2 \times 9.81} = 0.00982\ m$$

Pumping head

Since we know that the fluid is under turbulent flow, the kinetic energy coefficient (α) is given as 1, therefore:

$$H_D = (Z_2 - Z_1) + \frac{{v_2}^2 - {v_1}^2}{2\alpha g} + \frac{P_2 - P_1}{\rho g} + H_L$$

$$H_D = (0.63 - 0) + \frac{0.24^2 - 0^2}{2 \times 1 \times 9.81} + \frac{400\,000 - 101325}{1025 \times 9.81} + 0.00982 = 30.42\ m$$

Fluid power

$$POWER_{Fluid} = \tilde{V} \times \rho \times H_D \times g$$

$$POWER_{Fluid} = 0.000120 \times 1025 \times 30.42 \times 9.81 = 36.71\ W$$

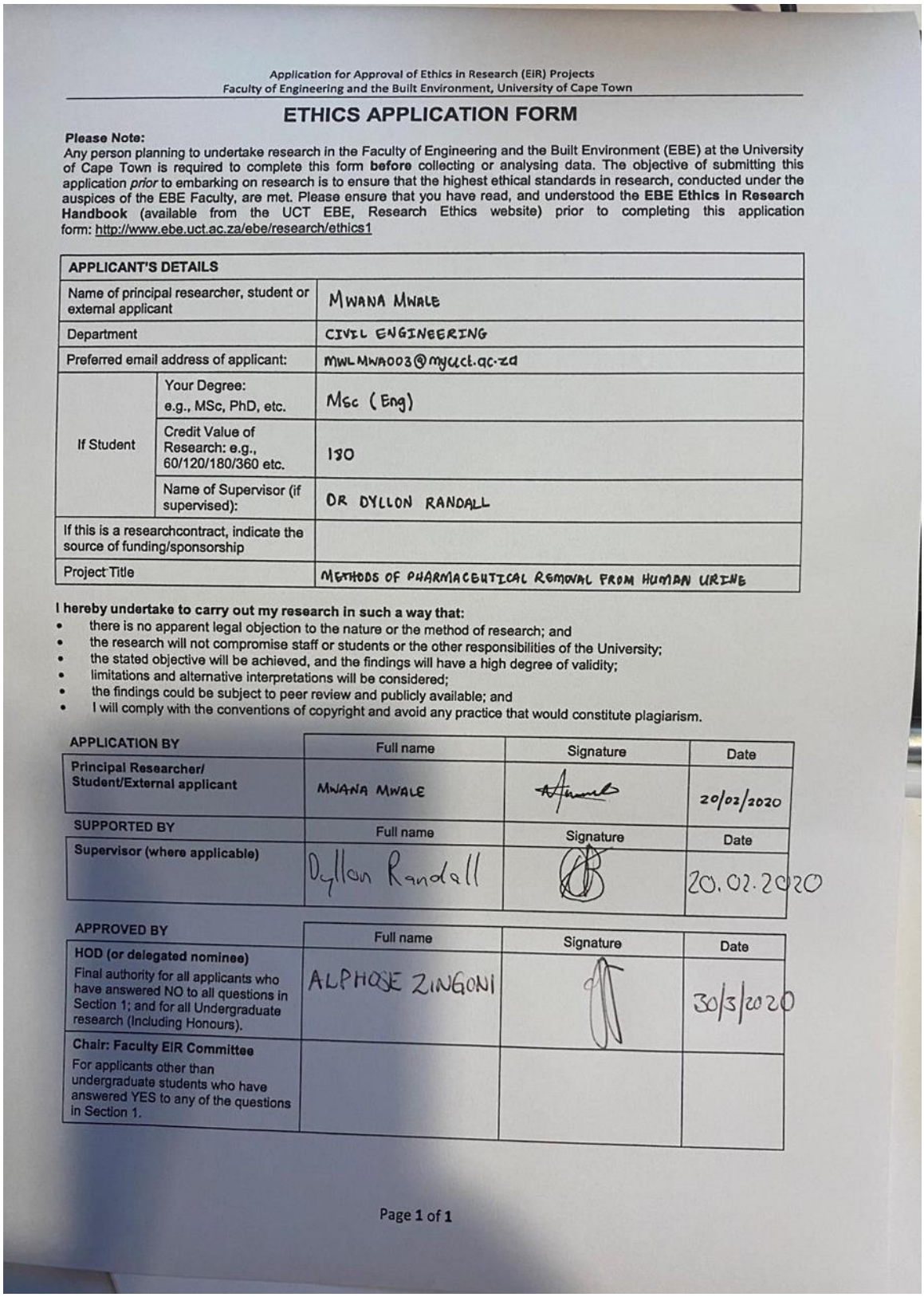
System energy required

The power required to operate the optimized HC system for an average pharmaceutical degradation of 74.5% is 36.71 W. The corresponding energy required to treat the waste solution using the optimized HC system is:

$$36.71\ W \times \frac{1\ kW}{1000\ kW} \times 30 \times \frac{1\ h}{60\ min} \times \frac{1}{10\ L} \times \frac{1000\ L}{m^3} = 1.84\ khW\ m^{-3}$$

Therefore, the optimized HC system would require 1.84 kW m^{-3}. The energy required is realistic for industry application considering that Yen (2016) used 1.73 kW/hr for the decolourize textile water using the UV/H_2O_2 process. The energy from the treatment process by Yen (2016) is comparable to the energy which required to operate the HC system at the operating conditions which were optimized for the current work (Yen, 2016).

Annexure G: Ethics approval



Application for Approval of Ethics in Research (EiR) Projects
Faculty of Engineering and the Built Environment, University of Cape Town

ETHICS APPLICATION FORM

Please Note:
Any person planning to undertake research in the Faculty of Engineering and the Built Environment (EBE) at the University of Cape Town is required to complete this form **before** collecting or analysing data. The objective of submitting this application *prior* to embarking on research is to ensure that the highest ethical standards in research, conducted under the auspices of the EBE Faculty, are met. Please ensure that you have read, and understood the **EBE Ethics in Research Handbook** (available from the UCT EBE, Research Ethics website) prior to completing this application form: http://www.ebe.uct.ac.za/ebe/research/ethics1

APPLICANT'S DETAILS		
Name of principal researcher, student or external applicant		MWANA MWALE
Department		CIVIL ENGINEERING
Preferred email address of applicant:		MWLMWA003@myuct.ac.za
If Student	Your Degree: e.g., MSc, PhD, etc.	MSc (Eng)
	Credit Value of Research: e.g., 60/120/180/360 etc.	180
	Name of Supervisor (if supervised):	DR DYLLON RANDALL
If this is a researchcontract, indicate the source of funding/sponsorship		
Project Title		METHODS OF PHARMACEUTICAL REMOVAL FROM HUMAN URINE

I hereby undertake to carry out my research in such a way that:

- there is no apparent legal objection to the nature or the method of research; and
- the research will not compromise staff or students or the other responsibilities of the University;
- the stated objective will be achieved, and the findings will have a high degree of validity;
- limitations and alternative interpretations will be considered;
- the findings could be subject to peer review and publicly available; and
- I will comply with the conventions of copyright and avoid any practice that would constitute plagiarism.

APPLICATION BY	Full name	Signature	Date
Principal Researcher/ Student/External applicant	MWANA MWALE		20/02/2020
SUPPORTED BY	**Full name**	**Signature**	**Date**
Supervisor (where applicable)	Dyllon Randall		20.02.2020

APPROVED BY	Full name	Signature	Date
HOD (or delegated nominee) Final authority for all applicants who have answered NO to all questions in Section 1; and for all Undergraduate research (Including Honours).	ALPHOSE ZINGONI		30/3/2020
Chair: Faculty EIR Committee For applicants other than undergraduate students who have answered YES to any of the questions in Section 1.			

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