

**UNIVERSITY OF RWANDA  
COLLEGE OF SCIENCE AND TECHNOLOGY  
SCHOOL OF SCIENCE  
DEPARTMENT OF CHEMISTRY**

**DETERMINATION AND REMOVAL OF IBUPROFEN, ACETAMINOPHEN,  
DICLOFENAC, CARBAMAZEPINE AND SULFAMETHOXAZOLE  
RESIDUES IN WASTEWATER.**

**CASE STUDY: CHUK AND MASAKA HOSPITALS**

*A dissertation submitted to the Department of Chemistry, School of Science, College of Science and Technology, University of Rwanda, in partial fulfillment of the requirements for the Degree of Masters of Science in Environmental Chemistry.*

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**Kigali, July 2023**

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I, **Emmanuel NZAYISENGA** hereby declare that, this master dissertation entitled **“DETERMINATION AND REMOVAL OF IBUPROFEN, ACETAMINOPHEN, DICLOFENAC, CARBAMAZEPINE AND SULFAMETHOXAZOLE RESIDUES IN WASTEWATER.”** is my own original work. It is submitted at the University of Rwanda for partial fulfilment for the award of the Degree of Masters in Environmental Chemistry of the University of Rwanda. This dissertation has never been submitted and will not be submitted elsewhere for any other award of a degree or academic certificate.

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## **DEDICATION**

Our Almighty God first of all, for his protection and keeping me being out of illness and my parents.

## **ACKNOWLEDGEMENTS**

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## **LIST OF ABBREVIATIONS AND ACRONYMS**

**ACT:** Acetaminophen

**AOP:** Advanced oxidation process

**CF:** Cystic fibrosis

**CHUK:** University teaching hospital of Kigali

**COX-1:** cyclooxygenase-1

**DCF:** Diclofenac

**EC50:** Half maximal effective concentration

**EOC:** Emerging organic pollutants

**GACs:** Granulated activated carbon

**GI:** Gastro intestine

**HPLC:** High performance liquid chromatography

**IBP:** Ibuprofen

**IUPAC:** International union of pure and applied chemistry

**LOEC:** Lowest observed effect concentration

**NSAID:** Non-steroidal anti-inflammatory drug

**OA:** Osteo-arthritis

**PDA:** Potent Ductus Arteriosus

**PPCPs:** Pharmaceuticals and personal care products

**RA:** Rheumatoid

**UV:** Ultra violet

**WHO:** World health organization

**WWTPs:** Wastewater treatment plants

## **ABSTRACT**

Pharmaceuticals such as non-steroidal anti-inflammatory drugs are prescribed to the patients due to different sickness and are sometimes found in wastewater discharged in the environment. These chemicals reach the environment due to the lack of effective ways of treating wastewater from hospitals. This study focused on the determination of level of diclofenac, ibuprofen, sulfamethoxazole, carbamazepine and acetaminophen residues in wastewater from two hospitals located in Kigali City which are Centre Hospitalier Universitaire de Kigali (CHUK) and Masaka Hospital. High Performance Liquid Chromatography (HPLC) with UV detector was used to conduct this chemical analysis. Results have indicated that no any of these pharmaceuticals were present in the wastewaters taken from these two hospitals in their pure forms. However, HPLC indicated the presence of other no identified chemicals in these wastewaters. An adsorption method was also investigated for the removal of these pharmaceuticals from synthetic wastewater. Adsorbents made from charcoal indicated effectiveness in removing these pharmaceuticals in wastewater. Pharmaceuticals were retained in the pores of the adsorbent then removed with it. In a synthetic wastewater, the level of acetaminophen, diclofenac, carbamazepine, sulfamethoxazole and ibuprofen were reduced as the dosage of the adsorbent and temperature for adsorption process increased.

The advanced technologies for wastewater treatment are recommended for all wastewater coming from hospitals in Rwanda and many more assessment of these non-steroidal anti-inflammatory drugs using a highly sensitive mass spectrometer detector which is mostly not available in most of the laboratories for a safety of environment.

**Keywords: Wastewater, non-steroidal anti-inflammatory drugs, CHUK, Masaka hospital**

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# CHAPTER 1. INTRODUCTION

## 1.1. Background

Ibuprofen, acetaminophen and diclofenac are used as anti-inflammatory, they are also used as analgesic and antipyretic agents in humans. Ibuprofen which was introduced in 1960s is a 2-phenylpropionic acid with relatives to the group of substituted phenylalkanoic acids, this drug was first introduced in England in 1967 later in United states of America in 1974. This has been introduced after the removal of the ibufenac due to hepatotoxicity [1]. Acetaminophen (paracetamol) was first discovered in Germany in 1887, initially this drug was rejected due to its structure related to phenacetin which was considered to be toxic. In 1940s it was reviewed and found safer than other alternative agents [2]. Diclofenac which is (2-(2-(2,6 dichlorophenylamino) phenyl acetic acid is used as a non-steroidal anti-inflammatory drug to relieve pain and they are taken as the oral tablets. It is found on the market with the following commercial names; Diclofenbeta, acoflam, algosenac, almiral, anthraxiton, ana-Flex antinflam, arthrex, arthrifen, arcanafenac, arthotec, diclabeta, dicloabac, diclac, diclodoc, diclomex, diclofenac–ratiopharm, diclowal, difen, dicuno, diklotab, eese, efekton, dolgit–diclo, jutafenac, motifene, monoflam dual, sigafenac, voltaren and rewodina. According to the world health organization for the daily dose of the diclofenac which is 100g less than 1mg is eliminated out from the body in diclofenac pure form, 11 mg are eliminated as the diclofenac conjugates and the remaining part as metabolites of diclofenac and conjugates [3].

Carbamazepine provide effective medication for the grand mal seizures and psychomotor caused by epilepsy, so, it is taken as the best antiepileptic drug for the treatment of wide seizure disorders in adults and children [4]. Carbamazepine which is also known as the anticonvulsant is among the first pharmaceuticals that persists in the environment and it is known to persists in the wastewater effluents and this is due to that conventional wastewater treatment is not effective for the removal of it [5]. When compared to the other pharmaceuticals carbamazepine resist to the biodegradation and the photo degradation [6]. This also results to its persistence in drinking water and surface water, due to these mentioned, the antiepileptic drugs are more concerned in aquatic environment as well as to the aquatic organisms [4].

Sulfamethoxazole is mostly used as an antibiotic for humans and livestock and it is always available as 1g, 500mg tablets and as 500mg/ml suspension which are taken orally, the trade names of this antibiotic are sometimes Radonil, Gantanol, MS-53, Sinomin and Ro 4-2130. [7]. By different studies it has been found in the wastewater treatment plant effluents and the aquatic environment at a level between ng/l up to the mg/l. In all pharmaceuticals the antibiotics contribute around 40% in contaminating freshwater worldwide [8]. Sulfamethoxazole is found in the sulfonamide group, it acts by inhibiting the bacteria from synthesizing dihydrofolic acid and by this the bacteria cannot survive. The detection of Sulfamethoxazole in wastewater treatment effluents indicate that it persists in the aquatic environment. The degradation of this antibiotic in the environment occur by only photolysis and by hydrolysis, so there is slow rate of the photo degradation in river water and estuarine due to the dissolved organic matter PH and salinity [9].

So, as the population increases, the demand in health services also increases and this require much more use of pharmaceutical products. The continuous use of these pharmaceuticals products is associated with some negative effects to the environment as they are released in the environment in their active forms, after being transformed in the environment they undergo biodegradations to give different metabolites and this generates toxicity to the ecosystem, this is a major problem to be concerned especially in developing countries like Rwanda with no advanced ways of treating hospital wastes before being ejected in the environment [10].

Ibuprofen, diclofenac, acetaminophen, carbamazepine and sulfamethoxazole like the other pharmaceutical and personal care products which may be natural or synthetic chemicals are found in the prescribed medicines, these medicines contain the active ingredients with pharmacological effects which are significant to the society. The continuous use of these pharmaceutical products in humans and veterinary medicines, aquaculture and in the agricultural products results in the release of these chemicals in the environment. These enter the environment through different routes including animal excretions, industrial waste where they are manufactured, wastewater effluents, treated sewage sludge and the medical wastes from the health care and veterinary facilities, bio solids, and the landfill leachate [11]. Hospital wastes consists of many different pollutants when compared to the other urban wastes, so, in the treatment facilities hospital wastes are taken as the main sources of pollutants which include the antibiotics, the outdated

pharmaceutical and personal care products (PPCPs) and their treatment are taken more carefully than the others [12].

PPCPs that are found in the hospital waste will reach the surface water and end up by intoxicating the living things that are contained in the water. The following include some of the effects that occur in the living things of the area; The change in the sex ratio, anatomical malfunction, changes in the biochemical cycles etc. The toxicants that are found in the PPCPs include different chemicals grouped according to their use, such as, anticonvulsants, analgesics, antimicrobials, lipid regulators, nonsteroidal anti-inflammatory drugs, antibiotics, and synthetic hormones. The contamination of the environment from the PPCPs comes from the deposition of the outdated medication, excretion of PPCPs metabolites, the untreated veterinary and hospital wastes. PPCPs are known to persist in the environment [13].

By getting the knowledge related to the removal of these pharmaceutical products in the wastes; wastewater, and the sludge wastes will have a positive impact on the natural water and soils, this also will lead to the reuse of water instead of continuous use of fresh water. The removal of these micropollutants can be achieved by the use of different strategies including their adsorption to the activated sludge, advanced oxidation process(AOP) and so on, this uses the combination of oxidants such as photocatalyses, ultrasound oxidation and ozonation, also the adsorbents materials which can be used include activated carbon [14].

This study focuses on the determination of the level of some pharmaceutical products in the hospital wastes from one of the hospitals found in Rwanda and to attempt their removal, the main pharmaceuticals assessed include ibuprofen, acetaminophen, diclofenac carbamazepine and sulfamethoxazole. This is due to that all of these drugs are mainly used in our health services for taking care the patients compared to the others, and also from the literatures stated that they are involved in hospital wastes in high concentrations compared to the others.

## 1.2. Problem statement

The pharmaceuticals products and other personal care products, are taken nowadays as environmental contaminants at their low amount of around ng/l which have health effects to the organisms and environment in general [15]. The PPCPs include veterinary and human pharmaceuticals, cosmetics products, fragrances and plasticizers. These products have attracted attention in the past due to the associated analytical challenges such as low detection limit and the insufficient separation [16]. These products result from the laboratories, diagnosis, and also as the excretions from patients. Therefore, these products are more likely to be present in the hospital wastes. Hospital wastes many times are in the form of wastewaters and are discharged together with the urban wastewater, this create a big problem as these pharmaceutical products cannot be removed by conventional wastewater treatment [17]. The high level of these products in the environment is toxic to aquatic life and nearby ecosystems, they are also toxic to the human beings. These contaminations mainly reach the environments through the pharmaceutical wastewater, domestic waste water and hospital effluents [18]. Acetaminophen is a pharmaceutical product which is toxic in low amount, it is known to cause the protein denaturation, lipids oxidative degradation and is associated with the genetic disorders in the living organisms [19]. Ibuprofen which is ranked as the third drug mostly consumed in the world is also taken as a contaminant to the environment and living organisms, this is due to its metabolites associated after entering wastewater, and also its adverse effects can occur in low amount [20]. Diclofenac is known to cause a negative effect to the marine organisms such as mussels and it also cause the damages in fish eggs and embryo [21]. Carbamazepine according to the study showed that it affect the development and normal growth of embryo and larva in zebra fish and this occur up on exposure to the low amount which is at the level of  $\mu\text{g/l}$  and also it is known to be resistant to photo degradation and biodegradation [4]. Sulfamethoxazole which is an antibiotic mostly prescribed to the patients, by the recent study showed that it harmful to the exposed bacteria like *vibrio fischeri* and the crustaceans such as *daphnia magna* that are present in the aquatic environment [9].

### **1.3. Objectives**

#### **1.3.1 General objective**

The general objective of this study was to assess the levels of pharmaceutical residues in the wastewater discharged from the hospitals and their removal.

#### **1.3.2 Specific objectives**

The specific objectives were the following:

- i. To determine the levels of ibuprofen, acetaminophen, diclofenac, carbamazepine and sulfamethoxazole residues in the hospital wastewater of CHUK, and Masaka hospital.
- ii. To remove these residues from the contaminated wastewater.

### **1.4. Research questions**

To carry out this research it has been asked the following questions which will be answered;

- i. To what level of pharmaceutical such as ibuprofen, acetaminophen, diclofenac, carbamazepine and sulfamethoxazole in the hospital waste from CHUK and Masaka?
- ii. To what extent these pharmaceuticals can be removed?

### **1.5. Significance of the study**

The motivation to conduct this research was due to nowadays the increase in the resources use has been increased and as the resources use increase also the production of wastes that comes after the use of the resources also increases, the wastes produced are of different kinds and contain different toxicity depending on the constituents of the resources consumed, the health sector is among the one that use these products manufactured from the natural resources like pharmaceutical products and these products may be toxic when they are consumed in high dose or in bad manner, these also can be toxic to the aquatic life, living things in the environment, and results in difficult work when they are trying to remove them in case they reach the surface water or the wastewater. CHUK and Masaka hospitals are among the biggest hospitals in our country which are mainly based in Kigali city which is known to give health services to many patients and are recognized to use many pharmaceuticals products when they are providing services and also they are known to give out

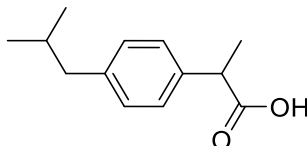
different wastes with high level of the pharmaceutical residues such as outdated medications and the excreta coming from a huge number of patients in the hospitals.

Our study which involves the assessment of the pharmaceutical products in hospital wastes and the removal of them will let us know their level so that specific measures may be taken including the reduction of the wastes, special handling of this hospital wastes including the use of specific ways of treating this wastes, by removing for example and disposing them in a safer manner that cannot have impacts to the environment.

## CHAPTER 2. LITERATURE REVIEW

### 2.1. Ibuprofen

#### 2.1.1. Definition and structures of ibuprofen



Ibuprofen

Ibuprofen abbreviated as IBP is used in many places as non-steroidal anti-inflammatory drug to treat different symptoms of illness [22]. It is prescribed and mostly used, this works by inhibiting cyclooxygenase-1(COX-1) and cyclooxygenase-2. These cyclooxygenases, are the key for the synthesis of prostaglandins, and these prostaglandins are responsible for the production of inflammation, pain and fever. Ibuprofen is in the form of tablets as the other many pharmaceutical products having a potency of 200 up to 800 mg, usually the dose for a patient is from 400 to 800 mg three times in the day, the drug is absorbed orally and directly transformed in the period of 1.8 to 2 h, it takes 24 h for being eliminated from the body, this is done through excretion route of the body where its metabolites are excreted together with the urine. By this drug to the old age people or those with renal impairment does not pose the problems related to elimination. After the degradation of this drug results to the production of the following products; 2,3-dihydroxysuccinic acid, dihydroxyibuprofen, 3-isobutylphenol, ibuprofenol, ibuprofenol acetate, 2-hydroxyibuprofen, 1-hydroxyibuprofen and other aliphatic products [20].

#### 2.1.2. Therapeutic applications

About the therapeutic applications of ibuprofen mainly is used as an analgesic, an antipyretic and an anti-inflammatory agent. For the treatment of mild to moderate pain which is related to headache, migraine dysmenorrhea, postoperative and dental pain, the treatment is done by the use of the racemic ibuprofen and S (+) enantiomers. It is also used for management of osteoarthritis, spondylitis soft tissue disorder and rheumatoid arthritis [23]. The following are the therapeutic applications of ibuprofen [24]:

- PDA (potent ductus arteriosus): This mainly occur in the young children, for healing indomethacin and overcoming this complication. Ibuprofen has shown to provide effectiveness as this indomethacin. Ibuprofen as well as indomethacin occur by closing the ductus arteriosus.
- OA and RA (Osteo-arthritis Rheumatoid): The low toxicity of ibuprofen compared to the other therapeutic drugs is used for the treatment of the disorders produced by rheumatic and musculoskeletal.
- CF (cystic fibrosis): Ibuprofen here is used due to it is effective in the inflammation reduction, it does not also produce the GI effects after use.
- Fever and headache: The tension type headache is treated by ibuprofen, and the combination of the placetamol and ibuprofen is very effective for the fever, this complication is known to be related to malaria. Ibuprofen is known to reduce the temperature compared to placetamol in a period of 4 to 5 h.

Ibuprofen also is commonly used for dental, cancer pain reduction. The treatment of Parkinson and Alzheimer disease.

### **2.1.3. Toxicity and occurrence of ibuprofen in environment**

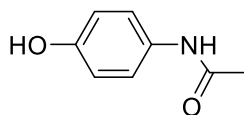
PPCPS are now taken as Emerging Organic Contaminants (EOCs), EOCs are the artificial organic substances which are not naturally present in the environment and these are known to cause high damage to the ecosystem and environment in general. They are introduced in the environment by the industrialization and manmade activities. The toxicity of PPCPS is more dangerous than the other pollutants due to their hazardous toxic metabolites and their bioactive nature. Ibuprofen is ranked as the third most popular and prescribed salable over the counter medicine in the world, and listed by world health organization (WHO) as essential drug in 2010 list. This drug has more toxicity to the environment due to its bioactive nature in the environment and toxic metabolites that results after its use and when it arrives in the environment, and its toxicity continue to increase by now due to population pressure. From the recent study they suggested that for a one dose of ibuprofen 99% form bond with albumin and 15% of the dose is excreted in its pure form.

Some of its metabolites excreted include; Hydroxyibuprofen, carboxyibuprofen and carboxyhydratropic acid. The metabolites of ibuprofen in the sewage and wastewater are the following; 4-ethylphenol, 4-isobutyricbenzaldehyde, 2-[4-(1-hydroxyisobutyl) phenyl] propionic

acid, 1-(4-isobutylphenyl)-1-ethanol, 4- ethyl benzaldehyde and 1-ethyl-4-(1-hydroxy) isobutyl benzene. The ibuprofen causes different kinds of toxicity which are acute or chronic these include the following to some aquatic organisms; The fish spawning, endocrine disruption, its presence caused the induction of antioxidative stress. It also increased the activity of catalase, superoxidase dismutase, phase II glutathione S-transferase and glutathione reductase after its exposure within 7 days. There was observed membrane damage in digestive gland and increased lipid peroxidation level. There is also the aerobic respiration, skeletal development and immune function damage [20].

## 2.2. Acetaminophen

### 2.2.1. Definition and the structure of acetaminophen



Acetaminophen

Acetaminophen is as the other kind of drugs that are found in tablets (350 to 500 mg) form like ibuprofen, it is used as anti-inflammatory, antipyretic and analgesic. It is used as an alternative to aspirin for the patients with the peptic ulcers, coagulation disorder, it means for those people who cannot tolerate aspirin like children. Firstly, the use of acetaminophen in clinical medicine started in 1893. In USA it has been used as prescription product in 1951, so its availability without prescription started in 1955 and now in many countries is available without prescription. Dose for the adult by conventionally is between 500-1000 mg and this can be taken after every 4 h, for the children the dose is between 10-15 mg/kg and no more than five dose should be taken in 24 h, so the prolonged use is not good for the young children. Production of the acetaminophen is done by the process of the acetylation of para-aminophenol with acetic anhydride or acetic acid. This drug is synthesized in different countries such as Argentina, China, India, Brazil, Korea Taiwan, Romania, UK, Turkey, USA, Germany, Japan, Mexico, Poland, Columbia and France [25].

### 2.2.2. Occurrence and toxicity of acetaminophen in environment

#### 2.2. 2.1. Occurrence

Acetaminophen like the other pharmaceuticals arrive in the environment after their consumption in native form and in their metabolites, these forms are excreted and are found in wastewater

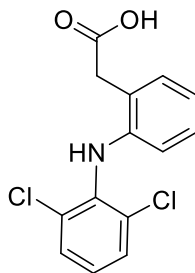
treatment plants (WWTPs) sewer systems and other natural(soils) or aquatic environments (groundwater, surface water, water sediments). In 2006, the investigation of ACT concentration in wastewater in South Korea, United States of America (USA), China, United Kingdom (UK) France, and other countries in the world find that ACT range from 0.1 to 300 mg/l and 100% was found in every sample [19]. In surface water ACT has been detected like in wastewater and sewages, in the following countries; China, South Korea, Singapore, and Taiwan. South Korea the ACT was found and has detected 80% in the samples taken about the concentration, It was present at 33 ng/l than other PPCPs in the river [26]. The contamination of groundwater by ACT has been reported in countries like France and Serbia and their appearance was about 17% and 15% of the groundwater samples taken for being tested [27]. In USA the groundwater tested are those from Tennessee River basin, the range of ACT was varying from 2.1 to 12.3 ng/l and has been detected in ~13% of the groundwater samples taken [25]. California, ACT detection frequency was 0.32% and the concentration was 1.89 mg/l [28]. From the concentrations found in wastewater, and surface water groundwater is less contaminated, this is due to it is filtered by soils as it moved on to the ground [29].

#### **2.2.2.2. Toxicity**

ACT which is toxic to aquatic and human life causes oxidative degradation of lipids, the genetic code damage and the protein denaturation in the cells. Its toxicity vary from low to moderate and can be acute or chronic depending on the exposure conditions [30]. The ACT toxicity has been studied in different organisms like protozoan, bacteria, fish, algae and macrophytes. So the in vitro and freshwater invertebrates presented the lowest effective concentration which is below 50 mg/l [31]. ACT is present in drinking water and is dangerous to the public health. The following are the metabolites that are produced after acetaminophen transformation in the body of living organisms and when it is in the environment; acetaminophen glucuronide, acetaminophen sulfate acetaminophen- glutathione and acetaminophen glucoside. These are formed after glucuronisation, glucosidation, sulfation and the reactions with proteins and nucleic acids [32].

## 2.3. Diclofenac

### 2.3.1. Definition and the structure of diclofenac



Diclofenac

Diclofenac is a white to off white crystalline, odorless and hygroscopic powder which is 2-(2-(2,6-dichlorophenylamino) phenyl) acetic acid according to the IUPAC nomenclature system and the following is its physical, chemical properties and its structural formula [3].

**Table 1. Physical and chemical properties of diclofenac**

Parameters	Values
Water solubility	2.37 mg/l
pH	7.2
pKa	4.15
log K <sub>ow</sub>	4.51
Chemical formula	C <sub>14</sub> H <sub>10</sub> Cl <sub>2</sub> NO <sub>2</sub>

### 2.3.2. Human metabolism of diclofenac

Diclofenac is applied orally or topically in the human body it is completely transformed and the topical gel adsorption is between 6-7% and the remaining part is washed away or attached to the clothes [33]. Metabolites for both topical and oral administration are the same in human urine. The following are 6 different metabolites that are produced and by the study 90% of the total diclofenac administered are in urine and 65% are found in the feces. These are 5-OH-DCF(5-hydroxy-diclofenac), 4'-OH-DCF(4-hydroxy-diclofenac), 3'-OH-DCF (3-hydroxy-diclofenac), 4',5-OH-DCF(4,5-dihydroxy-diclofenac), 4'-OH-3'-OCH<sub>3</sub>-DCF (4-hydroxy-3-methoxy-diclofenac) and 3'-OH-4'-OCH<sub>3</sub>-DCF(3-hydroxy-4-methoxy-diclofenac) as the human metabolites, the two first

are the main metabolites. It has been shown that 4'-OH-DCF has 30% of the antipyretic and anti-inflammatory activity of diclofenac. Less than 1% is known to be excreted unchanged [3].

### **2.3.3. Diclofenac in wastewater, drinking water, effluents and environment**

Diclofenac which is among the most detected pharmaceuticals in the environmental compartments has the following concentrations in different media. In the municipal wastewater it has been found that varies between 0.44 µg/l and 7.1 µg/l, the concentration in hospital wastewater raised to 6.881µg/l and it is found to be 233 µg/l in wastewater coming from the pharmaceutical manufacturing region in south Korea [34]. The value also around this has been detected in the hospitals of Sweden. By the reports, a mass varying from 195 up to 940 is the mean amount consumed to every inhabitant [35].

Due to the lack of complete elimination of the diclofenac in the wastewater treatment plant, many times it is detected in their effluents and the concentrations according to the reports made are as follow; 3.7 µg/l has been detected in wastewater effluents according to the Norway reports. 1200ng/l has been found in the German rivers that receive the effluents. Few amounts which is sometimes under the detection limits are found in the underground water [3].

### **2.3.4. Ecotoxicology effects of diclofenac**

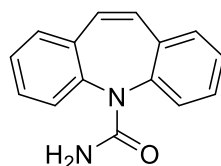
By the study conducted it has been found that the toxicity of diclofenac varies from 1 µg/l up to 80 mg/l depending on the exposed species and the duration of exposure [36]. It can result to the acute toxicity and chronic toxicity but chronic toxicity at the low level (there is lowest observed effect concentration). The studies showed that diclofenac is more toxic to the fish organs such as kidney, liver and gills than the other pharmaceuticals such as carbamazepine. For the zebra mussels that have been exposed to diclofenac resulted to the lipid peroxidation at a concentration of 1 µg/l of diclofenac [37].

**Table 2. Ecotoxicological effects of diclofenac [35].**

Species	Exposure time	End point	LOEC
Polystichum Setiferum	48 hours	Mitochondrial activity	0.3 µg/L
Oncorhynchus mykiss	28 days	Changes in liver ultrastructure, liver glycogen and kidney protein	1 µg/L
Dreissena polymorpha	96 hours	Lipid peroxidation	1 µg/L
Mytilus trossulus	8 days	Byssus strength	1 µg/L

## 2.4. Carbamazepine

### 2.4.1. Definition and structure of carbamazepine



Carbamazepine

Carbamazepine is an anticonvulsant with molar mass of 236.269 g/mol and IUPAC name is 5H-dibenzo[b,f]azepine-5-carboxamide (C<sub>15</sub>H<sub>12</sub>N<sub>2</sub>O), mainly the trade name for carbamazepine is trigtol and it is used for treating epilepsy and neuropathic pain. The following are the main human metabolites of carbamazepine and by the reports more than 30 metabolites have been identified in the human faeces and urine 1/2/3//4-OH-CBZ (O-Glucuronide), EP-CBZ (N-Glucuronide), DiOH-CBZ, Ox-CBZ, 10-OH\_CBZ,9-HMCA [38].

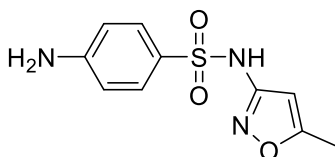
## 2.4.2. Carbamazepine in the environment and its toxicity

Carbamazepine is like the other pharmaceuticals which are toxic in the environment due to mainly their resistance to biodegradation and this carbamazepine is among the pharmaceuticals which are mainly detected. Carbamazepine resulted to the inhibition on the growth of *Streptomyces platensis* when its concentration was over 2.5 mg/l [39].

## 2.5. Sulfamethoxazole

### 2.5.1. Definition and structure of sulfamethoxazole

Sulfamethoxazole with this IUPAC name N-(5-methyl-3-isoxazolyl) sulfanilamide, is always found as white to slightly off-white, it is a crystalline powder which is odorless, about the solubility of sulfamethoxazole, it is slightly soluble in water (0.5 g/l) it is also slightly soluble in chloroform, benzene, isopropanol and diethyl ether and it is soluble in methanol and ethanol. After metabolism sulfamethoxazole provide N-acetyl derivatives and there are always found in the human urine [40]. During the treatment sulfamethoxazole can be used alone or in combination with trimethoprim.



Sulfamethoxazole

### 2.5.2. Sulfamethoxazole toxicity in the environment

Like the other antibiotics and pharmaceuticals in general sulfamethoxazole cause a threats to the environment and the species available. Pharmaceuticals are mainly detected in a very tiny amount but they are dangerous to the environment in their small amount. Sulfamethoxazole which is an antibiotic which is mostly prescribed can enter the environment though different routes like urine faeces and so on, it can get in the environment in its pure form or in its metabolites. After reaching in the environment sulfamethoxazole is known to cause much more effects to the aquatic organisms such as crustaceans, crayfish *Pacifastacus leniusculus*. From the toxicity of sulfamethoxazole certain species have been reduced due to the effects related to this pharmaceutical for example in Europe fresh water crayfish have reduced [9].

### **2.5.3. Uses of sulfamethoxazole**

Sulfamethoxazole started to be used in 1960 as an antibacterial drug for treating different systematic infections in humans and other animals. Mainly it was used for the treatment of meningitis, gonorrhoea, urinary tract and respiratory infections. Nowadays it is used in combination with trimethoprim for the treatment of various infections. This combination also is used for the treatment of urinary tract infections treatment of chloroquine resistant plasmodium falciparum malaria [7].

### **2.6. Pharmaceutical products in hospital wastes**

The occurrence of the pharmaceutical products in hospital waste such as wastewater, solid waste and sediments has been confirmed from the study conducted in five hospitals of Gujrat in Pakistan [18]. From this study, six human pharmaceuticals have been detected after conducting this study by using high performance liquid chromatography-ultraviolet, among the pharmaceuticals detected acetaminophen was in high concentrations by comparing with the other pharmaceuticals and it was detected in all samples taken in five hospitals (maximum of 696 ng/ml). Other pharmaceuticals detected including; diclofenac (186 ng/ml), naproxen (220 ng/ml), ibuprofen (596 ng/ml), amlodipine (303 ng/ml) and rosuvastatin (104 ng/ml). They were chromatographed on C-18 column at 254 nm by using liquid-liquid extraction [18].

## **CHAPTER 3. MATERIALS AND METHODS**

### **3.1. Collection and the pretreatment of samples**

The samples were taken from the waste streams in CHUK and Masaka hospitals directly after conventional wastewater treatment, before these wastewaters enter in the environment. They were collected in the amber bottles in order to protect them from the radiations that could harm the contents of the samples and were immediately transferred to the laboratory in insulated box or cooler together with ice where they were kept in the freezer at 4 °C before extraction. Samples were collected throughout all months of this study and after a composite sample was produced. Also, before samples analysis they were filtered by using a membrane filter of 0.45 µm to remove no dissolved solid matters prior to extraction [41].

### **3.2. Reagents and materials**

Acetaminophen, ibuprofen, diclofenac, carbamazepine and sulfamethoxazole were used as analytical standards purchased from medical supplier in Kigali. Chloroform, formic acid pure deionized water obtained after its purification system by micro filter membrane, acetonitrile and methanol were used as reagents for this study [42]. HPLC Shimadzu with UV detector, auto sampler, a temperature controlled column chamber, a tertiary pumping system, and fraction collector with 125× 4.6 mm column was used for all samples and standards.

### **3.3. Sample extraction**

Sample extraction was achieved by using 20 mL chloroform in three different successive extractions in a separating funnel. 40 mL of wastewater sample and chloroform was shaken for 10 min and then allowed to stand for phase separation. The organic layer was collected and gently evaporated to dryness at 38 °C. The residue was reconstituted in 2 mL of a mixture of acetonitrile and acidified water (pH of 3.0), 85:15 (v/v) and transferred into a 2 mL vial for chromatographic analysis [43].

### **3.4. Method quality assurance**

The mobile phase was injected in the HPLC before to ensure that they are free from acetaminophen, ibuprofen, diclofenac, carbamazepine and sulfamethoxazole analytes of interest.

10  $\mu\text{l}$  of mobile phase was injected and the results have shown that no peaks formed and the mobile phase was free from any analytes of interest.

### **3.5. HPLC analysis**

For the determinations of the pharmaceutical residues, high performance liquid chromatography (HPLC) with UV detection equipped with waters Symmetry C18 column, was used. All the analysis by HPLC were done at room temperature. In the chromatograms, the analytes of interest were identified by comparing the standard solution chromatograms with that of the sample solutions, the retention time of the peaks in both solutions were used to give exactly the concentrations of acetaminophen, ibuprofen, diclofenac, carbamazepine and sulfamethoxazole in the sample solution measured. Target compounds were quantified by using a constructed matrix-matched calibration curves by spiking matrix extracts after the extraction. For the analysis of Diclofenac and ibuprofen, a mixture of acetonitrile and water, 60:40 (v/v), (acidified with formic acid up to pH 3.0), was used as mobile phase and injected at the flow rate of 0.8 mL/min. A volume of 10  $\mu\text{L}$  of the sample was injected in HPLC with UV detector and three minutes of re-equilibration were programmed between successive injections. The analysis of both Diclofenac and Ibuprofen was conducted at the wavelength of 230 nm, while a wavelength of 265 nm was used for Sulfamethoxazole analysis. The mobile phase used for this analysis was a mixture of 30% acetonitrile and 70% ultrapure water containing 0.1% formic acid, the flow rate was 1.0 ml/min and while the injection volume of the sample was 10  $\mu\text{L}$  [44]. Acetaminophen analysis; the same HPLC system as described above and the mobile phase made of the acetonitrile, acidified deionized water (40:60) were used at the flow rate of 1.5 mL/min and the detection of acetaminophen was performed at 243 nm with retention time of 2.2 min at ambient temperature [45]. Carbamazepine analysis; mobile phase used is composed of pure water for HPLC adjusted at pH 4 with hydrochloric acid and methanol at this ratio (30:70, v/v), the injection volume used was 10  $\mu\text{l}$  and a flow rate of 1 mL/min. The wavelength was 226 nm, [46].

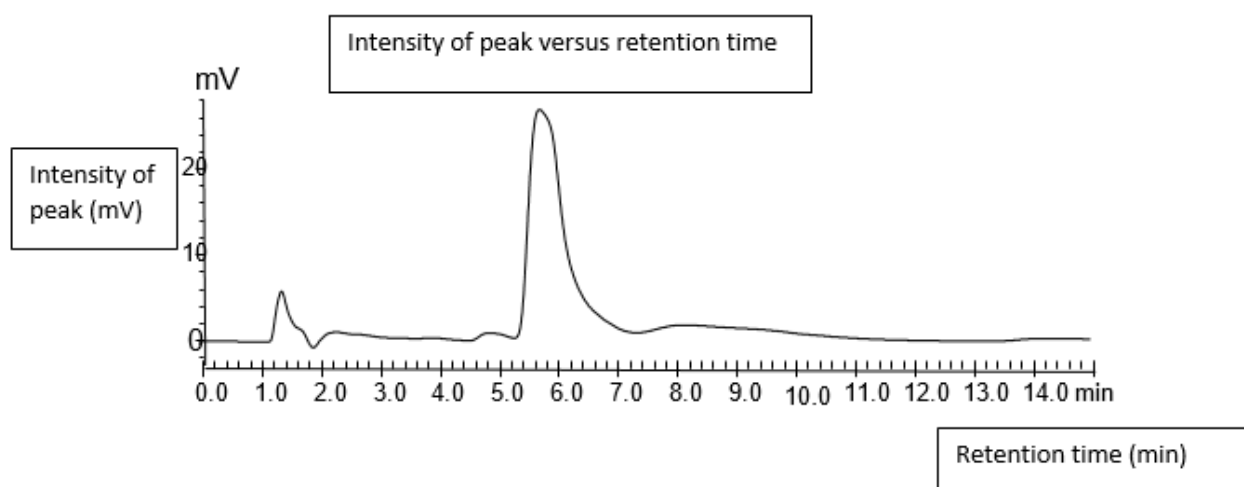
### **3.6. Principles of removing pharmaceuticals in wastewater**

Adsorption provides effective removal of pharmaceuticals from wastewater, this is due to that they get adsorbed to a particular adsorbent. The pores of the adsorbent retain these products. We have used adsorption for the removal of these pharmaceuticals in wastewater sampled from different sites. A granulated activated carbon (GAC) was used as adsorbent. This was prepared from the

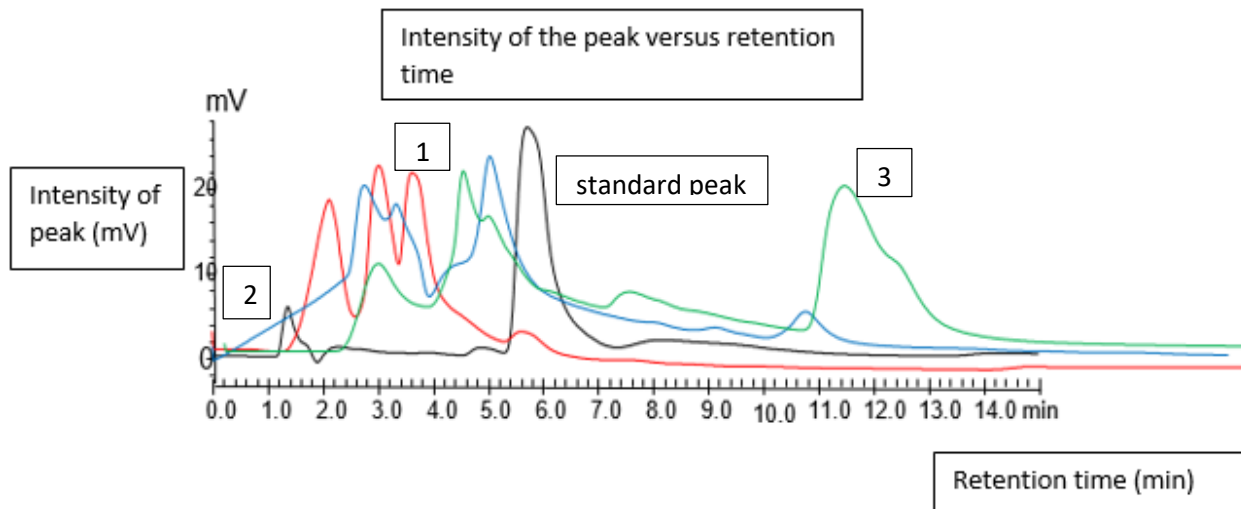
charcoal bought from the market and grounded to a fine powder, after calcium chloride solution was added to enhance the porosity of adsorbent, this were kept in oven for a period of 2 hours to make it dry. So different ranges of mass between 1 g and 3 g adsorbent produced were poured in different containers of synthetic wastewater prepared, each contained 25 ml. This was followed by stirring, also the removal of these pharmaceuticals were performed at different temperature ranges which are 293 K, 298 K, 300 K and 315 K in the same amount of adsorbent, after adsorbent were removed by a membrane syringe filter. The residual concentrations of pharmaceuticals were determined so as to know the removed amount. [47].

## CHAPTER 4. RESULTS AND DISCUSSION

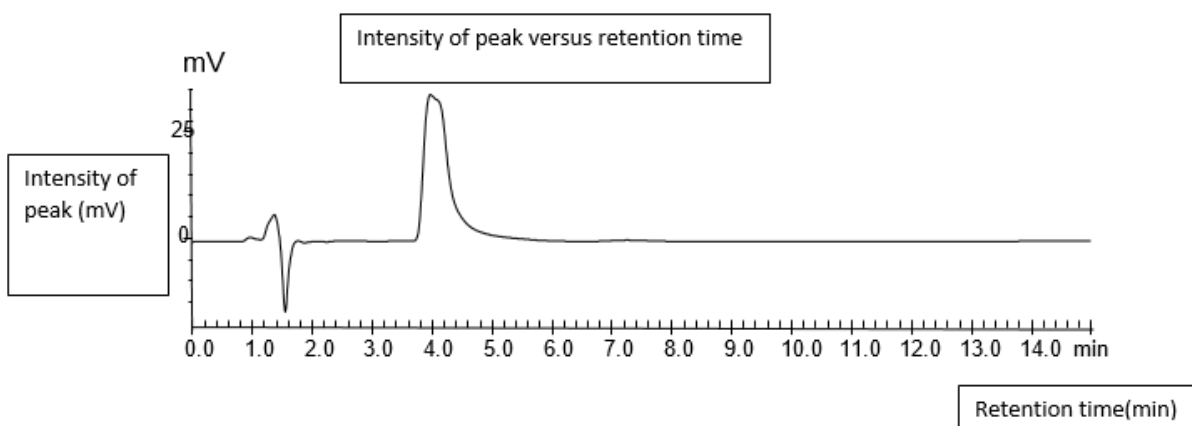
The chromatograms of five standards namely diclofenac, ibuprofen, carbamazepine, sulfamethoxazole and acetaminophen and wastewater samples from CHUK and Masaka hospitals are shown by the figures 1 up to 10, to the figure Y-axis is the intensity of the peak expressed in millivolts (mV) and retention time to the X-axis expressed in minutes. The wavelength of 230 nm was used for the analysis of diclofenac and ibuprofen, 226 nm for carbamazepine, 265 nm for sulfamethoxazole and 243 nm for acetaminophen with UV detection. These wavelengths were fixed in HPLC analysis conditions so as to improve the detection sensitivity. The figures 1, 3, 5, 7, and 9 show the chromatographic separation of five standard solution listed above with the retention times of 5.7, 2.3, 2, 4 and 5.69 min for diclofenac, sulfamethoxazole, acetaminophen, carbamazepine and ibuprofen, respectively.



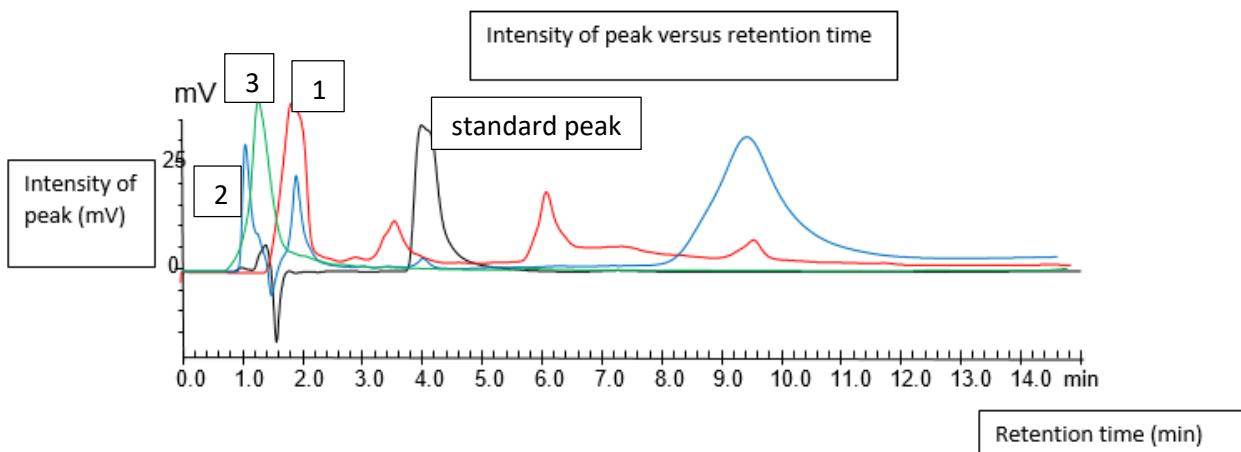
**Figure 1. Chromatogram for diclofenac standard solution (660 ppb)**



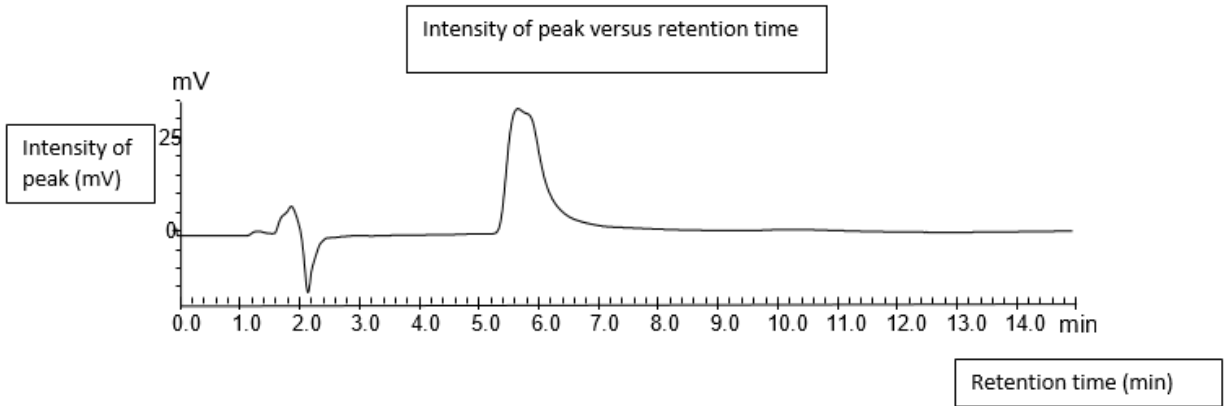
**Figure 2. Chromatograms of wastewater samples analysis for diclofenac a) CHUK (1) b) CHUK (2) C) Masaka (3)**



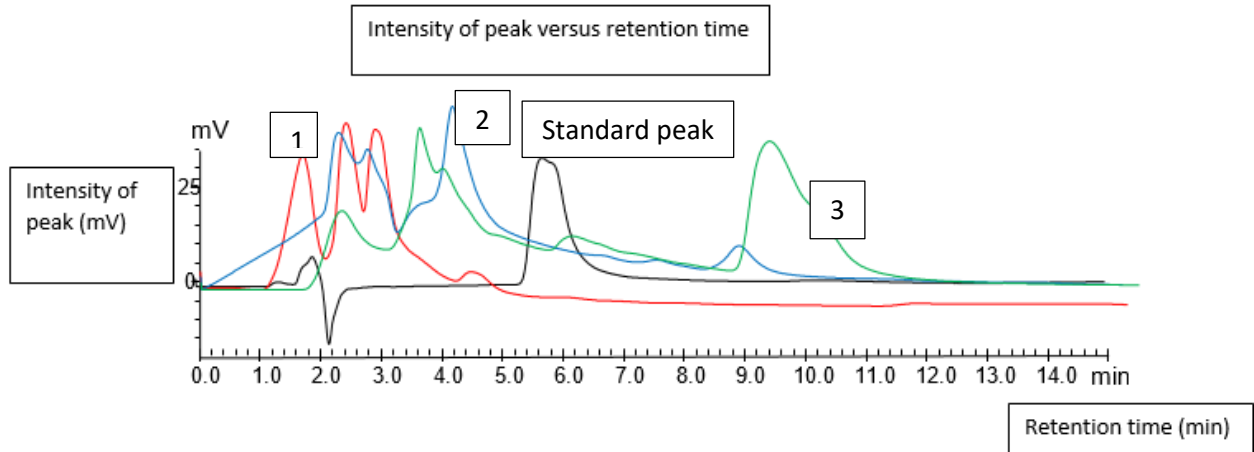
**Figure 3. Chromatogram for carbamazepine standard solution (330 ppb)**



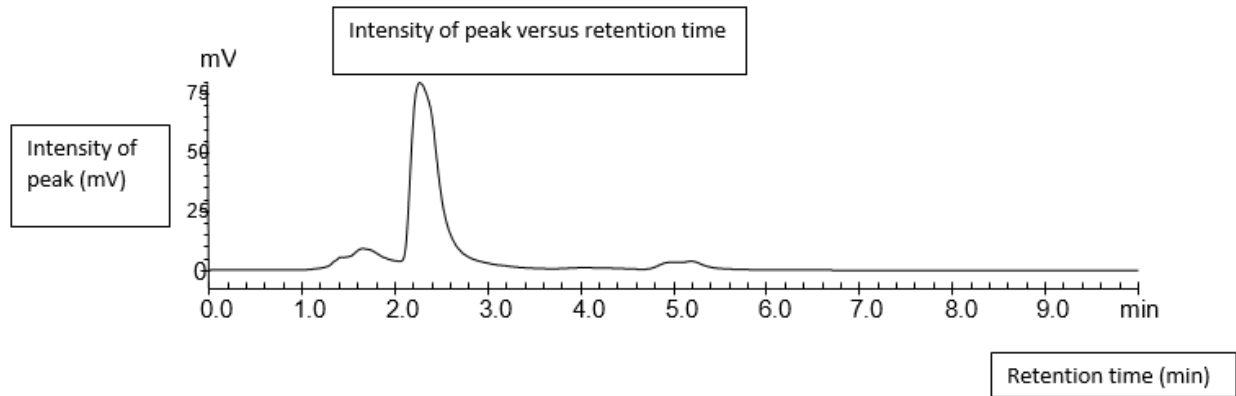
**Figure 4. Chromatograms of wastewater samples analysis for carbamazepine a) CHUK (1) b) CHUK (2) c) Masaka (3)**



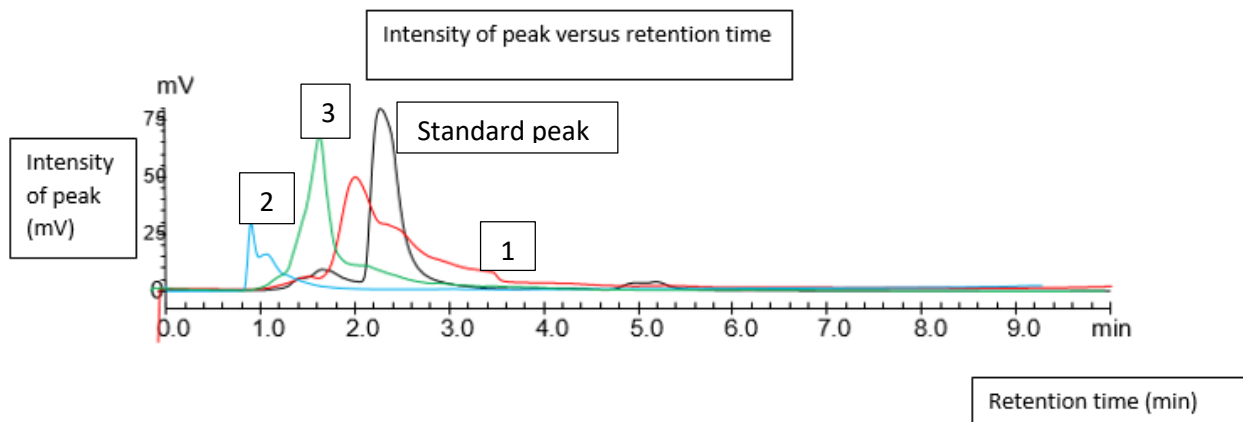
**Figure 5. Chromatogram for ibuprofen standard solution (66 ppb)**



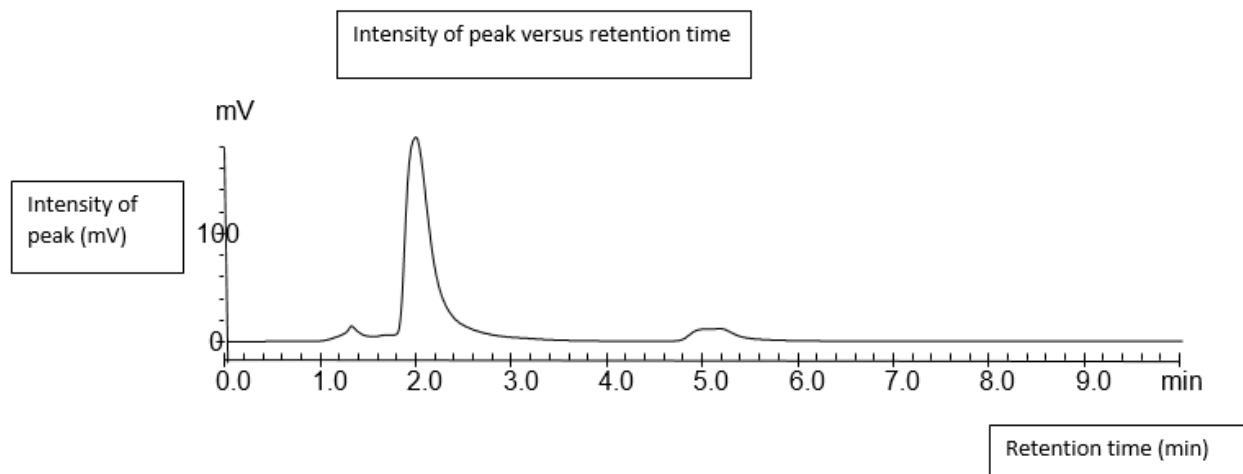
**Figure 6. Chromatograms of wastewater samples analysis for ibuprofen a) CHUK (1) b) CHUK (2) c) Masaka (3)**



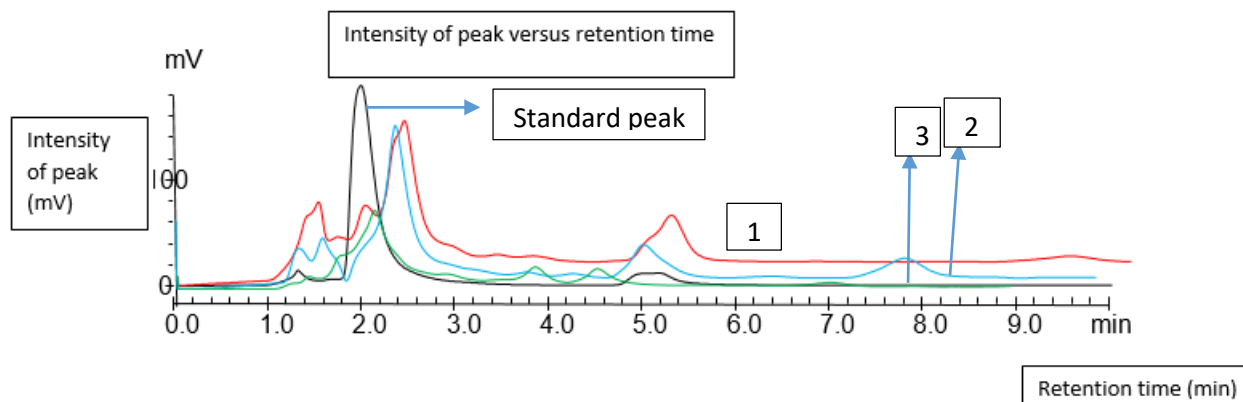
**Figure 7. Chromatogram for sulfamethoxazole standard solution (20 ppm)**



**Figure 8. Chromatograms of wastewater samples analysis for sulfamethoxazole a) CHUK (1) b) CHUK (2) c) Masaka (3)**

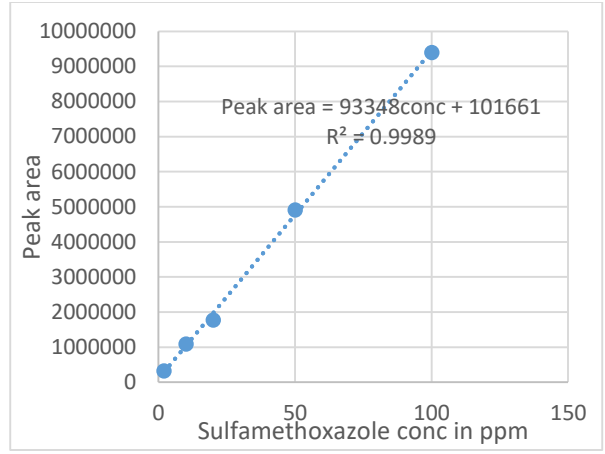
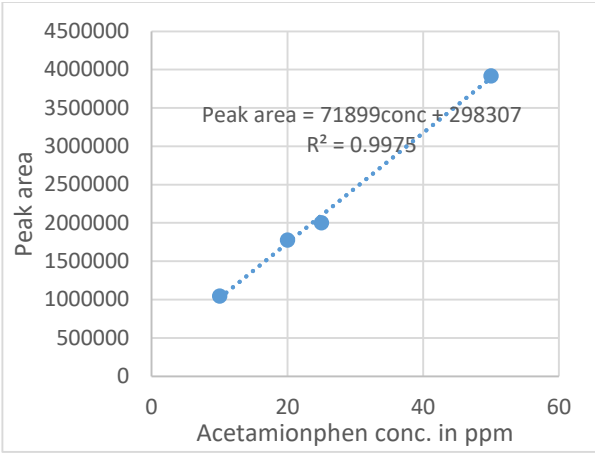


**Figure 9. Chromatogram for acetaminophen standard solution (50 ppm)**

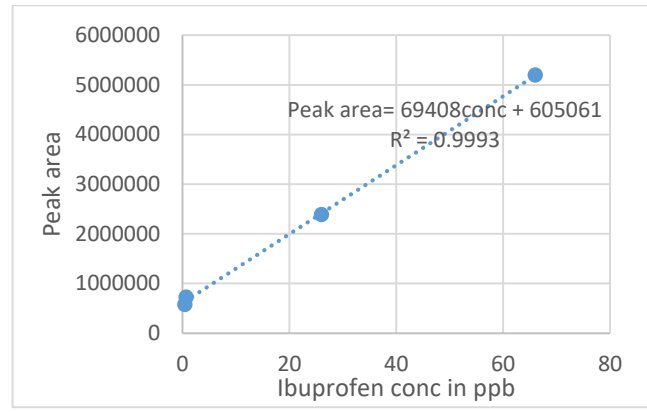
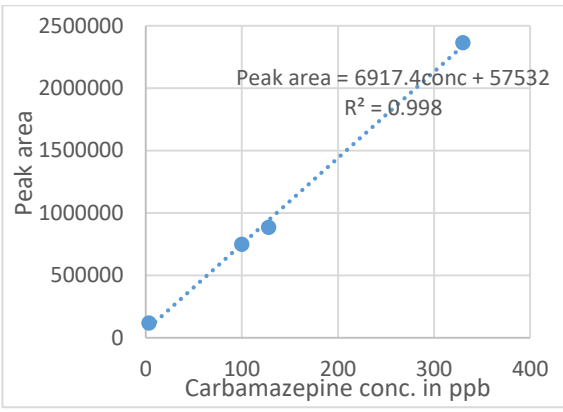


**Figure 10. Chromatograms of wastewater samples analysis for acetaminophen a) CHUK (1) b) CHUK (2) c) Masaka (3)**

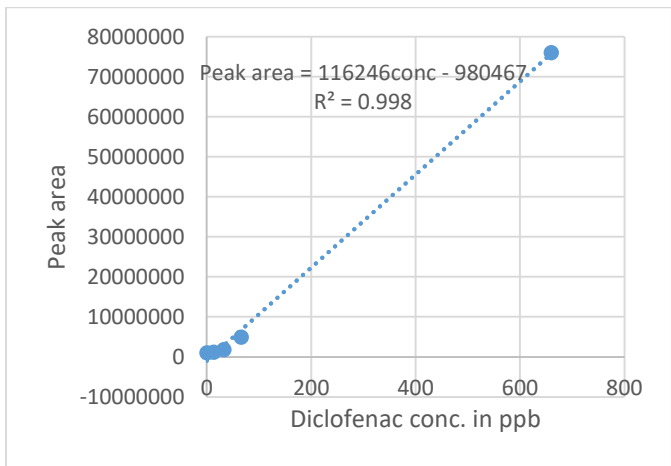
Calibration standards curve for each pharmaceutical were prepared by diluting the standard solution for each as represented by figure; 11, 12, 13, 14, and 15. Standard solutions (1 g/L) were diluted in a range of 0.13-660.00 ppb, 0.43-66.00 ppb, 2.00-100.00 ppm, 10.00-50.00 ppm and 3.30-330 ppb for diclofenac, ibuprofen, sulfamethoxazole, acetaminophen and for carbamazepine, respectively. From these, five calibration curves with good linearity were obtained as indicated by their  $R^2$  (coefficient of determination) which are above 0.995 for each, these values obtained indicate how these curves match with the data produced and this is a good way for the identification of unknown substance in a sample [46].



**Figure 11. Calibration curve for acetaminophen** **Figure 12. Calibration curve for sulfamethoxazole**



**Figure 13. Calibration curve for carbamazepine** **Figure 14. Calibration curve for ibuprofen**



**Figure 15. Calibration curve for diclofenac**

The detection limits (LOD), limits of quantification, relative standard deviation and other parameters as shown by table 3 were calculated for 5 pharmaceuticals. Detection limits (LOD) were found to be 55.95, 38.34, 4.30, 7.34 and 7.09 ppb for diclofenac, carbamazepine, ibuprofen, sulfamethoxazole, and for acetaminophen, respectively. The limits of quantification were found to be 169.5498 ppb for diclofenac 116.1854 ppb for carbamazepine, 22.25945 ppm sulfamethoxazole 13.03347ppb for ibuprofen and 21.50477 ppm for acetaminophen. The relative standard deviations of this method were found to be 4.0742 % for ibuprofen 7.8164 % for carbamazepine 11.6% for diclofenac 5.937% for sulfamethoxazole and 7.0741 for acetaminophen. These were calculated from calibration curves produced by the standard solutions, so these indicate the repeatability of this method. The percentage recovery for all five pharmaceuticals were determined after spiking the known concentration for each with distilled water and extracted in the same way with that of the sample and were found to be 94% for acetaminophen, 89.5% for sulfamethoxazole, 76.7% for diclofenac, 88% for carbamazepine and 98.4 for ibuprofen. So the same method and parameters analyzed have been reported recently in similar study conducted and this show the efficiency of our study [43].

**Table 3. Method performance parameters**

Parameters	Acetaminophen	sulfamethoxazole	diclofenac	carbamazepine	Ibuprofen
T <sub>R</sub> (min)	2	2.3	5.7	4	5.69
Equations	$Peak\ area = 71899conc + 298307$	$Peak\ area = 93348conc + 101661$	$Peak\ area = 116246conc - 980467$	$Peak\ area = 6917.4conc - 57532$	$Peak\ area = 69408conc + 605061$
R <sup>2</sup>	0.9975	0.9989	0.9982	0.998049	0.99932
LOD	7.096573	7.345617	55.95145	38.34117	4.301046
LOQ	21.50477	22.25945	169.5498	116.1854	13.03347
RSD	7.074177	5.93761	11.6137	7.816438	4.074254
Percentage recovery	94%	89.5%	76.7%	88%	98.4%

The results of the samples analyzed show that the targeted pharmaceuticals are not in the detectable range by using HPLC with UV detector as shown by the chromatograms of wastewaters measured

with respect to that of standards, this may be caused by the use of a less-sensitive detector which was available in our laboratories. Ultraviolet detector which is also known as UV detector used during this analysis, is a simple and low cost technique which determine a very low concentrations of compounds and use a small amounts of sample, it is a non-destructive chromatographic detector and measures the amount of ultraviolet or visible light absorbed by components of the sample mixture which are eluted off by the chromatographic column, this technique is used in many fields of research including; agriculture, food analysis, clinical and pharmaceuticals as well as in environmental sample analysis, so there are many other detector apart from UV detector including MS (mass spectrometric detector), DAD (diode array detector) that minimize some drawbacks and with high detection capacity [48].

Pharmaceuticals and other samples from different field such as agriculture, clinical and environment analyzed by DAD detection and MS have shown the presence of the targeted compounds in the sample analyzed, from the study conducted in south Nigeria in wastewater from three wastewater treatment plants have shown the presence of non-steroidal anti-inflammatory drugs such as diclofenac and ibuprofen, these were detected at a level of 166.1  $\mu\text{g/l}$  and 62.0  $\mu\text{g/l}$  respectively [41]. There are also the determined pharmaceuticals in industries wastewater such as trimethoprim (TMP), sulfadiazine (SDIAZ) enrofloxacin (ENRO), oxytetracycline (OTC), sulfaguanidine (SGUA), sulfamethazine (SMETH), and penicillin G/procaine (PGP) by using HPLC with DAD, the results from this study confirmed the presence of some of these pharmaceuticals in wastewater from industries [49]. So HPLC with MS detector and HPLC with DAD provide effectiveness in determination of pharmaceuticals in wastewater when we compare with HPLC with UV detector. Pharmaceuticals like non-steroidal anti-inflammatory drugs are frequently detected in wastewater all around the world in aquatic environment, wastewater streams and this is due to the wastes from hospitals, pharmaceuticals industries and shops that are always discharged in water streams with insufficient treatment [50].

These NSAIDS analyzed poses many different harmful effects after reaching in the environment, many of these analyzed are harmful to the aquatic organisms and they cause some negative effects to them such as the damages to the fish eggs and embryo, the lipids oxidative degradation, protein denaturation, genetic disorders in the living organisms and affect the development and normal growth of embryo and larva in zebra fish and other species, this occur up on exposure to the low

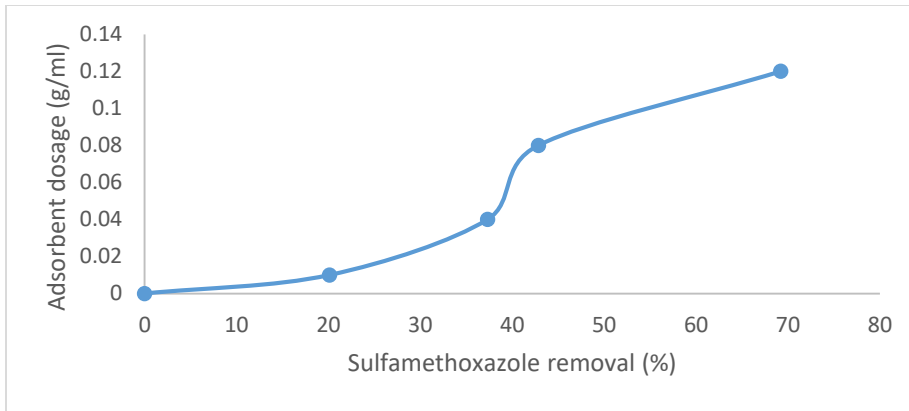
amount which is at low level [51]. So there are many different ways for treatment of this water that contain these pharmaceuticals like non-steroidal anti-inflammatory drugs in wastewater and here we have attempted one of the method of adsorption by using activated carbon charcoal as adsorbent as shown below to remove these non-steroidal anti-inflammatory drugs in the synthetic wastewater produced, and this has shown the effectiveness for removing these pharmaceuticals [52].

#### **4.1. Removal of pharmaceuticals in synthetic wastewater by using activated carbon as the adsorbent.**

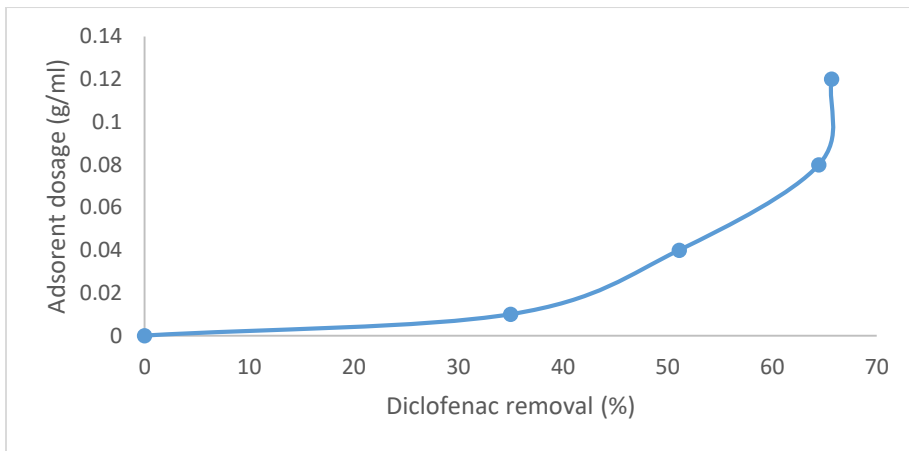
The activated carbon which is a solid adsorbent provide the better ways of removing these pharmaceuticals in wastewater by the adsorption in its pores, this is taken as the most efficient way in the treatment of the wastewater contaminated by the pharmaceutical products, it is a natural way which is very cheap after advanced oxidation process and others methods as it uses the natural products like wood, so during the use of this type of adsorbent the amount adsorbed from the waste increase as the amount of adsorbent also increase, and this is due to the increase of the site for adsorption. Also the amount adsorbed increase as the temperature of adsorbent increase due to the increase of the diffusion rate [53].

#### **4.2. Effects of adsorbent dosage**

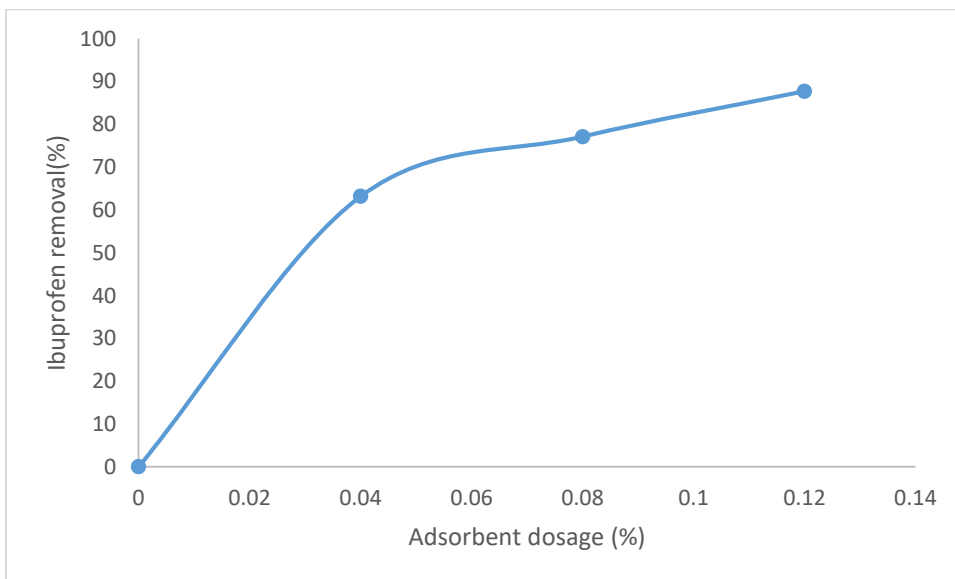
The effect of activated carbon charcoal adsorbent dosage to the adsorption of sulfamethoxazole, acetaminophen, diclofenac, ibuprofen and carbamazepine residues in synthetic wastewater at room temperature is shown by the figure. 16 (a) 16 (b) 16 (c) 16 (d) 16 (e), the adsorbent amount was varied between 1g of adsorbent and 3g in 25ml of synthetic wastewater. The initial concentration in synthesized wastewater was 411.12 ppm for sulfamethoxazole, 1256.04 ppm for acetaminophen, 122.47 ppb for diclofenac, 116.21 ppb ibuprofen and 333.3 ppb for carbamazepine. The percentage removed of the residues here also show that increase as the dosage of adsorbent used increase and was calculated by using this relation; % removal= ((Initial concentration- concentration after adsorption)/Initial concentration) ×100.



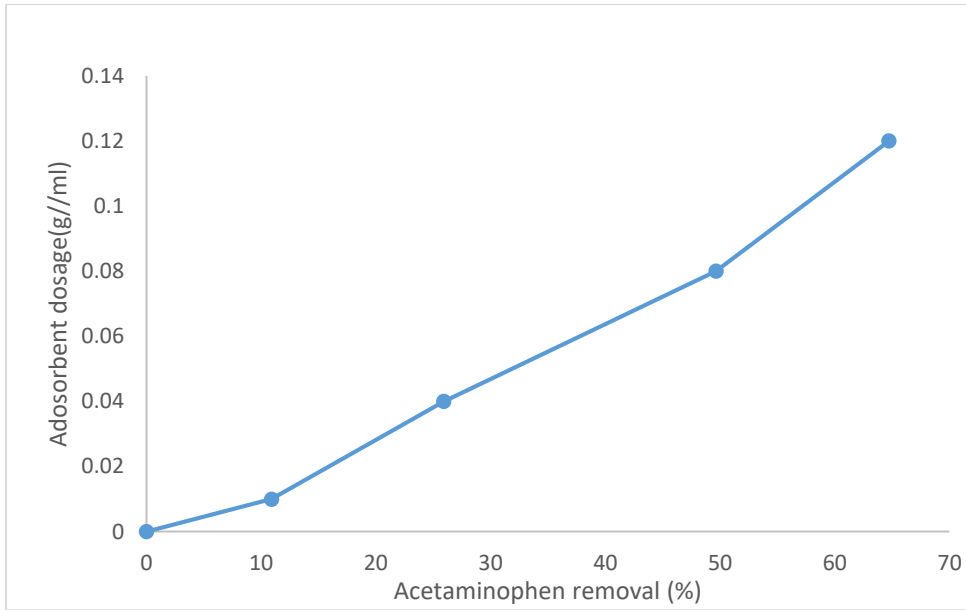
**Figure 16. Effect of removing pharmaceuticals in synthetic wastewater by dosage (sulfamethoxazole)**



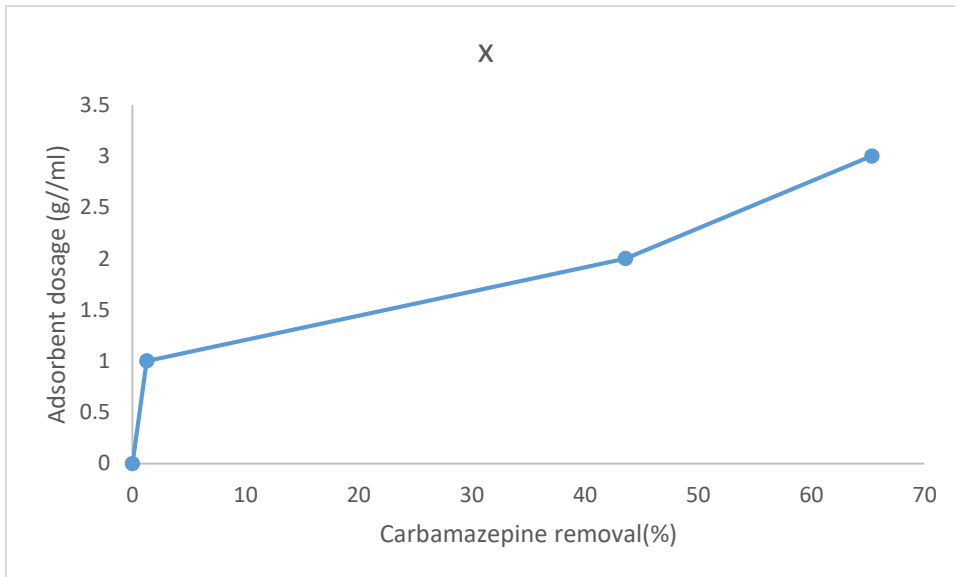
**Figure 17. Effect of removing pharmaceuticals in synthetic wastewater by dosage (Diclofenac)**



**Figure 18. Effect of removing pharmaceuticals in synthetic wastewater by dosage (Ibuprofen)**



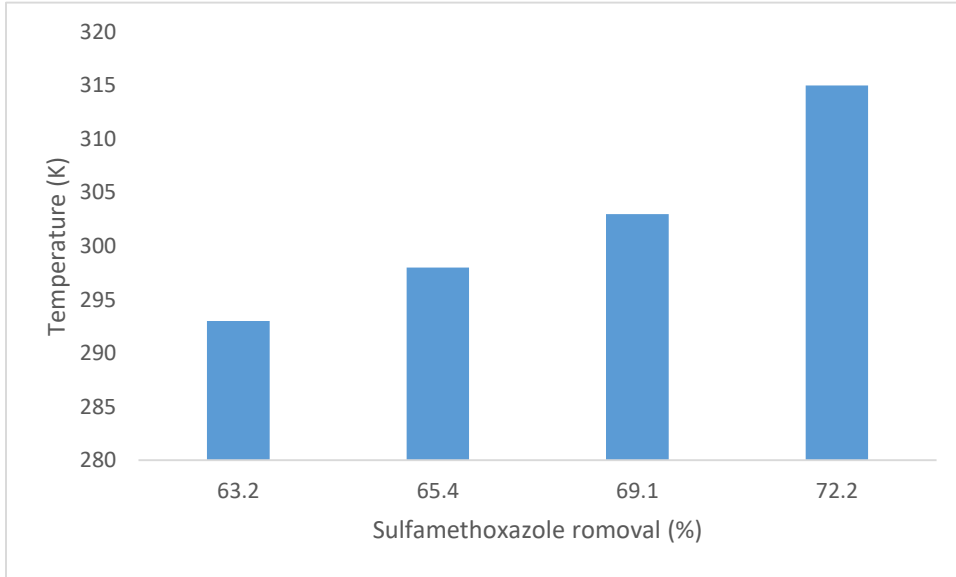
**Figure 19. Effect of removing pharmaceuticals in synthetic wastewater by dosage (Acetaminophen)**



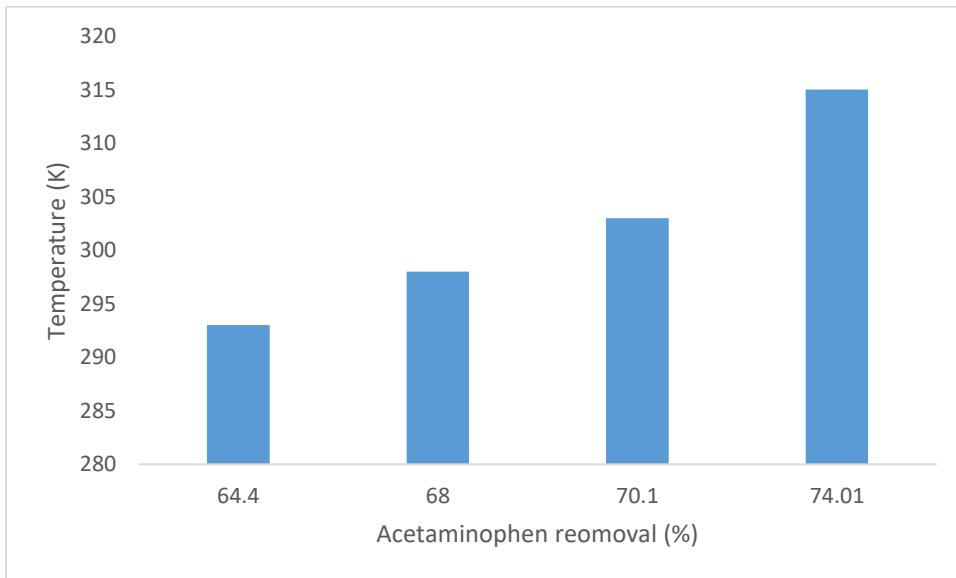
**Figure 20. Effect of removing pharmaceuticals in synthetic wastewater by dosage (Carbamazepine)**

### 4.3. Effects of temperature to the residues adsorption

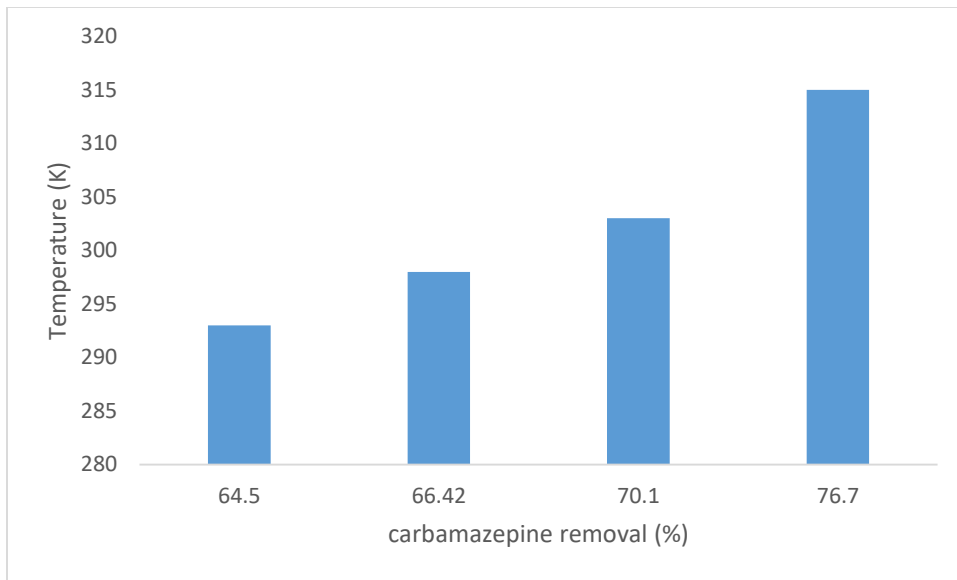
The effects of temperature on pharmaceuticals removal in wastewater are shown by the figures 17 (a) 17 (b) 17 (c) 17 (d) 17 (e), adsorption performed at four different temperature ranges which are; 293 K, 298 K, 300 K and 315 K in the same amount of adsorbent. At 315 K a big amount was removed compared to the other temperature values and these emphasis that as the temperature increase the adsorption also increase [52].



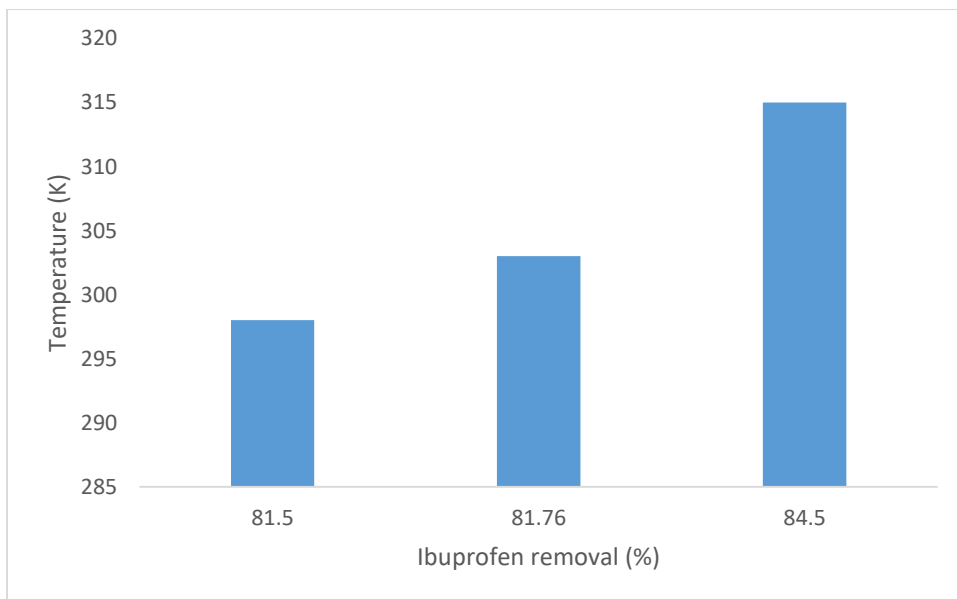
**Figure 21. Effect of temperature on the removal of pharmaceuticals in synthetic wastewater (Sulfamethoxazole)**



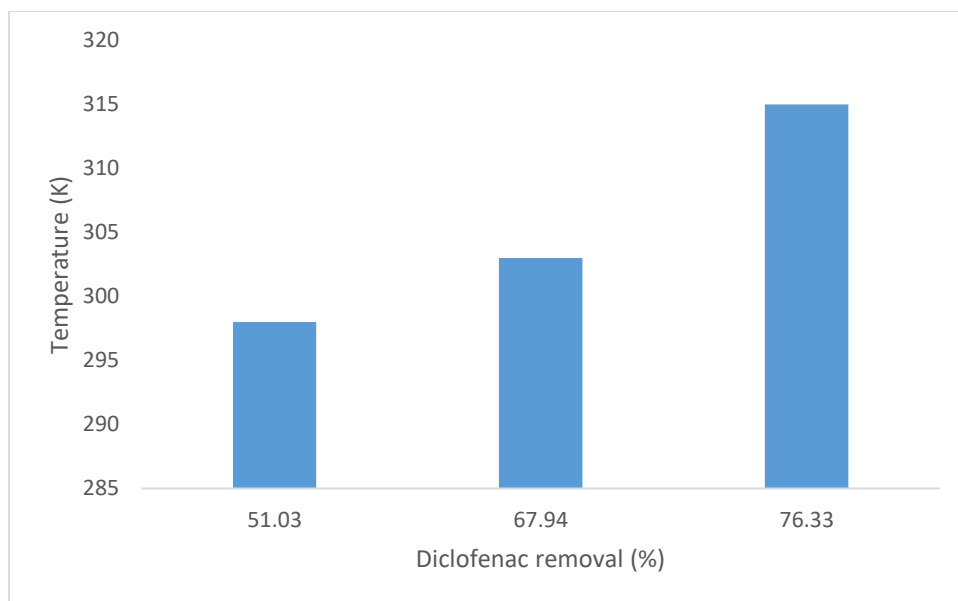
**Figure 22. Effect of temperature on the removal of pharmaceuticals in synthetic wastewater (Acetaminophen)**



**Figure 23. Effect of temperature on the removal of pharmaceuticals in synthetic wastewater (Carbamazepine)**



**Figure 24. Effect of temperature on the removal of pharmaceuticals in synthetic wastewater (Ibuprofen)**



**Figure 25. Effect of temperature on the removal of pharmaceuticals in synthetic wastewater (Diclofenac)**

Adsorption by adsorbent such as activated carbon is a low cost method compared to the other techniques [54]. Activated carbon is effective adsorbent to remove pharmaceuticals in wastewater and this is confirmed by the removal of N-Vinylpyrrolidone by adsorption from polyvinylpyrrolidone pharmaceutical due to the trace amount of this N-vinylpyrrolidone cause odor and discoloration, in this study the adsorption of N-Vinylpyrrolidone were performed at different dosages of adsorbent and at different ranges of temperature, from these the high amount of N-Vinylpyrrolidone was adsorbed as the amount of adsorbent also increases, in terms of temperature also, within all ranges of temperature for adsorption a high amount of N-Vinylpyrrolidone was adsorbed only at range of high temperature than the others which is a similar report to our study [52]. There are the others parameters that affect the adsorption like pH contact time and so on, pH is a major influence on adsorption process, in fact for example when adsorbent has neutral charges, at a pH below adsorbent surface is positively charged and at pH above adsorbent is negatively charged and this will determine electrostatic attractions or repulsions between the adsorbent and the adsorbate, with time the adsorption is rapid in the first minutes and slowed down after and these is due to the porous that are fouled as the adsorption process progress [54].

## **CHAPTER 5. CONCLUSIONS AND RECOMMENDATIONS**

### **5.1. Conclusions**

Acetaminophen, ibuprofen, diclofenac, sulfamethoxazole and carbamazepine residues were determined from wastewater of CHUK and Masaka hospitals in Kigali city by using high performance liquid chromatography with UV detector, from the study conducted, the chromatograms of the results found from these sample indicate that they are not detected when we use HPLC with UV detector and these can be because they have undergone conjugation with other substances or metabolized to give different metabolites according to the different peaks that are formed in the wastewater samples. Also, while removing these pharmaceuticals in synthetic wastewater it has been realized that as the amount of adsorbent and temperature increase is the more they are removed. These were confirmed after the injection of samples in HPLC with UV detector machine with respect to the mobile phase and the wavelength for each standard. The pharmaceuticals assessed pose a high threat to the aquatic environmental organisms when they reach in water according to the literatures.

### **5.2. Recommendations**

The efficient wastewater treatment and other advanced technologies for treatment are therefore recommended so as to reduce the amount of the pharmaceutical residues that are discharged in the environment, and also the continuous assessment of these water from the hospitals should be conducted periodically to look for the level of these pharmaceuticals in water. Also HPLC with a highly sensitive detector which like MS (mass spectrometer) should be used for the next studies as it can detect the very low concentrations of these pharmaceuticals in wastewater than UV detector, also the metabolites and conjugates that come from these pharmaceuticals should be assessed to be aware if they have been transformed into those products, this is due to the different peaks that are formed in the sample. There is also the advanced method of extraction that can be used such solid phase extraction which can provide the best way of sample extraction during the study than liquid-liquid extraction method which has been used during this study.

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## **APPENDIX**

### **Water quality management situation in RWANDA**

#### **The constitution and the Law on Environment**

The right of every citizen to live in a sanitary and healthy environment is emphasized in the Republic of Rwanda's 2015 constitution amendment. The same constitution assigns the responsibility of preserving, defending, and promoting the environment to the people of Rwanda, but the government is responsible for ensuring its general preservation (See Articles 22, 53, and 169 of the constitution)

#### **Law on the environment**

The protection of water resources is outlined in Law on Environment (No 48/2018 of 13/08/2018 ) Articles 11, 12, 37, and 40 in order to maintain the amount and quality of waterbodies like, rivers, lakes, and groundwater, Articles 47, 48, and 49 provide administrative sanctions for polluting and harming wetlands, changing the nature of wetlands, and breaking required distances from wetlands or waterbodies, whereas Article 42 outlines banned conduct in wetlands and protected areas. The Ministerial Order N° 004/16.01 of 24/05/2013 establishing the list of water contaminants included an appended list of inorganic physical-chemical, organoleptic, radionuclide, and biological pollutants. a ministerial Order from 2013.

#### **Rwanda Water Resources Law**

The law governing the use and management of Rwanda's water resources was published in the official gazette in 2018 as Law N°49/2018 of August 13, 2018. It offers a precise framework for the guiding ideas of integrated water resources management, such as pollution avoidance and the "user pays" and "polluter pays" tenets. Additionally, it stipulates that it is an offense to pollute water bodies by disposing of, spilling, or depositing chemicals of any kind that are above the level that is bearable for human health or aquatic life (art. 37), and it sets penalties for violators

#### **Institutions involved in water quality management**

Information on the gathering and administration of water quality data is scarce in Rwanda. Water quality sampling has been found to have discrepancies in terms of sampling locations, frequency, and even the variables to be monitored. The University of Rwanda, in partnership with the previous Ministry of Natural Resources and/or the former Rwanda Natural Resources Authority (RNRA),

gathered some data on water quality. The Ministry of Environment, the Ministry of Land and Forestry, the Ministry of Agriculture and Animal Resources, the Ministry of Health, the Ministry of Infrastructure, the Rwanda Water Resources Board (RWB), Rwanda Green Fund (FONERWA), Water and Sanitation Corporate (WASAC), Rwanda Utility Regulatory Authority (RURA), Rwanda Standards Board (RSB), Rwanda Environment regulation Authority (REMA), and Water and Sanitation Corporate (WASAC) are all directly or indirectly involved in the regulation of water quality in Rwanda. In addition, continuous changes of the public institutions, for example, recent restructuring in MINIRENA and establishment of RWB, RLMUA and RMB from RNRA can delay meeting the targets for water quality management as a result of budget allocations to the various institutions. However, as some of the institutions that are presented below are still new, this institutional arrangement will be adjusted as more information becomes available about their mandates, and roles and responsibilities

## **Water quality Pollutants**

### **Emerging pollutants**

There are some new pollutants that may be of concern, but not enough is known about how they are faring in Rwanda. These are frequently found at low concentrations, are challenging to find, and require sophisticated analytical tools for sample analysis. Endocrine disrupting substances (EDS), persistent organic pollutants (POPs), and nanoparticles are a few among them. Before management methods can be devised, study is necessary to better understand the severity and scope of new contaminants in Rwanda, as is the case in many developing nations. In the meanwhile, the management of these contaminants should take a preventive approach.

### **Endocrine disrupting chemicals**

Endocrine disrupting chemicals (EDCs) are substances that affect both people and wildlife's endocrine systems. Pharmaceutically active compounds (PhACs) are substances that cause humans to respond to drugs. EDCs and PhACs are not mutually exclusive categories because some PhACs are also EDCs, but not all. "An exogenous substance or mixture that alters the function(s) of the endocrine systems and subsequently causes adverse health effects in an individual" is the definition of an EDC. The ability of a wide variety of compounds to interfere with the endocrine systems has been disc

covered or is thought to exist. Pharmaceuticals and personal care products contain a significant amount of chemical contaminants that can come from human use and excretion, veterinary applications of a range of products, including prescribed counter medications, and fungicides and disinfectants used in domestic, agricultural, industrial, and livestock practices. Continuous introduction of PhACs, PCPs, and their metabolites into the aquatic environment has resulted in detectable amounts that have the potential to damage drinking water supplies, ecosystems, and human health. EDCs are typically connected to big cities where there is a high population density.

### **Wastewater treatment works (WWTWs)**

If wastewater treatment works (WWTWs) that discharge treated effluent into surface water streams do not exceed effluent regulations, they are significant point sources of pollution. However, their combined effects might also be considerable if there is a high density of WWTWs that are all compliant with effluent requirements. There are approximately 161 wastewater treatment systems in Rwanda, with the majority of them centered in Kigali City (roughly 119 of the 161 WWTWs), according to a thorough evaluation of these systems conducted in 2016 for REMA. To treat the wastewater from a hospital, hotel, resort, training facility, office complex, etc., these systems were often small and frequently on-site.