

**Removal of antiretrovirals using low-cost adsorbents:  
adsorption kinetics, adsorption isotherms and  
thermodynamics studies**



**LINDOKUHLE ANELE SIMELANE**

**Removal of antiretrovirals using low-cost adsorbents:  
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thermodynamics studies**



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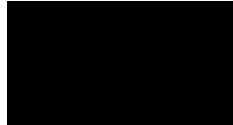
**A dissertation submitted to  
The School of Physics and Chemistry  
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# Declaration

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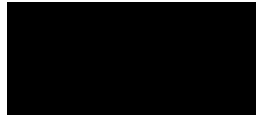
I Lindokuhle Anele Simelane, declare that this project research is my original work entirely, except where it is stated otherwise, and other people works included in this work were acknowledged through citations. This dissertation has not been submitted for any other degree or at any other universities for examination.

(Signature of candidate)



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(Signature of Supervisor)



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Date

April 2023

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## Abstract

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The current study was directed to the synthesis and application of low-cost adsorbent for the removal of antiretroviral drugs (ARVDs) such as nevirapine, abacavir and efavirenz in wastewater samples. The study involved the modification and application of liquid chromatography photo diodearray (LC-PDA) for the detection of the ARVDs of interest. The good separation of ARVDs was achieved using a gradient elution 50 % ACN: 50 % H<sub>2</sub>O (0-2 minutes), 70 % ACN: 30 % H<sub>2</sub>O (3-20 minutes). The macadamia nutshells, *Platanus acerifolia* leaves (London plane) were explored as easily accessible and eco-friendly adsorbents. The single synthetic route and high surface area of the polymer of intrinsic microporosity number-1 (PIM-1) were the distinct properties that were ideal for exploring this adsorbent for removal of ARVDs in wastewater samples. The adsorbents were synthesized and characterized using Fourier transform infrared spectroscopy (FTIR), Scanning electron microscopy (SEM), Brunauer Emmett Teller (BET), Powder X-ray diffraction (PXRD). The results obtained from macadamia nutshell and *Platanus acerifolia* adsorbent for FTIR characterization were functional groups such O-H, C=O and C=C and many others whereas *Platanus acerifolia* adsorbent had additional N-H from in addition to one obtained in macadamia adsorbent. The PIM-1 showed CN, C=O and C-H functional groups. SEM showed rod-folded structure and flaky-folded structure for macadamia nutshell adsorbent and *Platanus acerifolia* leaves adsorbent respectively, whereas PIM-1 exhibited microporous to mesoporous pore on adsorbent surface. The BET showed a surface area, pore diameter and pore volume of 0.1180 m<sup>2</sup>/g, 27.98 nm, and 8.3×10<sup>-5</sup> cm<sup>3</sup>/g for macadamia nutshells adsorbent and 1.14 m<sup>2</sup>/g, 0.0024 cm<sup>3</sup>/g and 4.09 nm for *Platanus acerifolia* leaves adsorbent. The PIM-1 had a surface of 557.39 cm<sup>2</sup>/g, pore volume 0.4123 cm<sup>3</sup>/g and pore diameter 2.96 nm. The PXRD of macadamia and *Platanus acerifolia* adsorbents had native crystalline cellulose structure whereas PIM-1 had an amorphous material. These characterization results indicated that the adsorbents have the potential to efficiently remove the ARVDs from in contaminated wastewater.

Prior to the application of adsorbents, parameters such as adsorption time (5-240 minutes), solution pH (2-10), initial concentration (0.2-2 mg/L), adsorbent mass dosage (0.2-10 mg) and adsorption temperature (15-40°C) were investigated to access the removal efficiency of all the synthesized adsorbents on their ability to remove ARVDs in wastewater samples. Under optimum conditions the adsorption was conducted using 10 mg of the adsorbent in 10 mL wastewater sample spiked at

a concentration 1.0 mg/L, at a pH of 7 and stirred at 150 rpm at 30°C. These conditions yielded a removal efficiency greater than 80 %, 90 % and 86 % using macadamia nutshells, *Platanus acerifolia* leaves and PIM-1 adsorbent, respectively in all ARVDs of interest.

The study of adsorption kinetics, adsorption isotherms and thermodynamic model was essential for designing an efficient adsorption process to remove ARVDs which are pollutants of emerging concern. The results obtained showed that pseudo-second-order model well defined the kinetic data, and the adsorption isotherms was well fitted in Langmuir isotherm and adsorption process was exothermic in nature for macadamia nutshells and *Platanus acerifolia* leaves adsorbent. For PIM-1 adsorbent, the pseudo-second-order was dominant, and the adsorption isotherm was well defined by Freundlich model. Thermodynamic parameters showed that the adsorption was thermodynamically favored, spontaneous, and exothermic in nature. The adsorbents were then applied under optimum conditions and the amount adsorbed of ARVDs from wastewater samples were 94.41, 88.84 and 83.06 mg/g for nevirapine, abacavir and efavirenz respectively for macadamia nutshell adsorbent. For *Platanus acerifolia* leaves adsorbent, 97.56, 84.75 and 81.56 mg/g amount adsorbed of nevirapine, abacavir and efavirenz. On the other hand, PIM-1 adsorbent had an adsorption capacity of 83.65, 93.83 and 94.56 mg/g amount for nevirapine, abacavir and efavirenz, respectively.

Overall, the macadamia nutshells, *Platanus acerifolia* leaves and PIM-1 adsorbents have illustrated to be efficient and cost-effective adsorbents for removal ARVDs in wastewater samples. However, the two agricultural adsorbents, macadamia nutshell and *Platanus acerifolia* leaves adsorbents could be highly recommended since their usage is able to reduce land and water pollution which is compromises water quantity which is already at stake across the globe.

**Keywords:** antiretrovirals, low-cost adsorbents, kinetics, isotherm, thermodynamics

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“The distance between a goal and achievement is discipline.”

-Unknown

## **Dedication**

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To my brother Themba Malibongwe Ndlangamandla

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## Glossary

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ARVDs	antiretrovirals drugs
HIV-1	human immunodeficiency virus type 1
FTIR	fourier infrared spectroscopy
BET	brunauer Emmett Teller
PXRD	powder Xray diffraction
SEM	scanning electron microscopy.
PIM-1	polymer of intrinsic microporosity number-1
MCN	macadamia nutshell
WWTP	wastewater treatment plants
HCl	hydrochloric acid
NaOH	sodium hydroxide
LC-PDA	liquid chromatography photo diode array
LC-MS	liquid chromatography mass spectrometry
NNRTI	non-nucleoside reverse transcriptase inhibitors
NRTI	nucleoside reverse transcriptase
PI	protein inhibitors
AC	activated carbon
NF	nanofiltration
RO	reverse osmosis
MB	methylene blue
FDA	food drug administration

# Chapter One

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## 1.1 Introduction

Antiretrovirals (ARVDs) are therapeutic medication for treatment of retroviral infections such human immunodeficiency virus type 1 (HIV-1). The ARVDs do not eradicate the HIV virus but it inhibits the further replication of the virus, prevents the attack by opportunistic diseases and infections in an infected people, and increases life expectancy of infected people (Gökengin et al., 2016, Adeola & Forbes et al., 2022). Like other pharmaceutical compounds, antiretroviral drugs are not entirely broken down in body as a result, they are eliminated as faecal waste and urine thus they are transported in the wastewater treatment plants through the sewer. Due to treatment process's inability to remove them completely, they are released with the treated effluent into surface water which could result to potential threat to human and animal health (Schoeman et al., 2017). Antiretrovirals drugs are designed to be stable and produce pharmacological response even in trace concentration which makes them to accumulate and be persistent in the environment. Therefore, there has been an increase in the detection of antiretrovirals in the environment (Schoeman et al., 2017, Afafe et al., 2018).

The continual excretion of incompletely metabolized ARVDs into non-target species such as fish could affect reproduction and metabolism of these species (Mlunguza et al., 2020a). Zidovudine and abacavir antiretroviral drugs are associated with mania and psychosis which are central nervous system disturbances in human (Calmy et al., 2009). Toxic epidermal and skin rash are mild effects cause by nevirapine which is commonly affects infants diagnosed with HIV virus (Tchetnya et al., 2018). The continual exposure to antiretrovirals is likely to cause feminization of fish and amphibians. The abacavir ARVD has been reported to cause toxicity to green algae which is a major concern since green algae is the main precursor of aquatic systems. As a results, of these toxicological effects of the antiretroviral drugs, it is thus of paramount importance to constantly monitor them and to find eco-friendly adsorption methods to remove them in polluted water systems. The adsorption mechanism has been the most prominent method use for elimination of numerous pharmaceuticals compounds including ARVDs in aquatic environments (Abdullah et al., 2011, De Andrade et al., 2018). The adsorption phenomenon is facilitated by physical or chemical interactions between the adsorbent and adsorbate thus leads to removal of target species in aqueous solution. Parameters such time, pH, mass dosage, concentration and temperature are very

essential to assess the removal efficiency of the adsorption process, which were investigated in study. The high protein of macadamia nuts and extensive application in body lotion and heavy cream production leads to the accumulation of nutshell as waste materials (Marketing et al, 2019). The anti-microbial and anti-inflammatory traits of *Plantaus acerifolia* leaves has led to extensive plantations of these trees. As a results, of the highly availability and easy accessibility of waste material this has led to improve bio-circular economy through application of the waste materials as adsorbent to remove ARVDs in wastewater samples that are of much concern. The easy synthetic route and the excellent gas storage of PIM-1 would be explored also a candidate for removal of ARVDs due to good packing structures (Mason et al., 2014). The combinational investigation of adsorption kinetics, adsorption isotherms and thermodynamics studies were critical to evaluate the adsorption process, gain more insight about reaction behavior and understand the adsorption mechanism. These mentioned above investigations were vital to design an effective adsorption process of ARVDs in wastewater.

## **1.2 Problem statement**

The continual detection of ARVDs in water sources due to their extensive application as first-line treatment against retroviral infections is becoming a major concern. Antiretrovirals similar many pharmaceuticals are designed to stable and produce pharmacological response even in trace concentrations. As a results, upon oral administration in the body they are partial metabolized thus are release via sewage systems as metabolites or original compounds. These pharmacological properties make ARVDs to be very persistent and bioaccumulative which is major threat to human and animal health (De Andrade Aragão et al., 2020). These metabolites or original compounds are likely to feminizations of fish and amphibians and alteration of physiology in tuna fish (De Andrade et al., 2018). The continual exposure to ARVDs could lead to genotoxicity, endocrine disruption and aqua toxicity (De Andrade et al., 2018). Studies have shown that inefficiency of current wastewater treatment methods to remove ARVDs in wastewater is the major contributor to water sources pollution which is likely to cause adverse effects. The constant detection of ARVDs in water bodies are a main threat to water quality which could exacerbates the accessibility to clean and quality water which is already a major through around the globe (Abafe et al., 2018).

As a result, the scientific community has explored a variety of adsorbent to remove ARVDs from wastewater. However, most of these adsorbents are costly, and hard to regenerate resulting in the impracticality to be applied in the adsorption process, also they require more preparatory steps. Therefore, new alternative adsorbents are required to remove these compounds of emerging concern. The aim of this work was therefore to mitigate these limitations. In this respect, the macadamia nutshells, *Platanus acerifolia* leaves which are agricultural waste adsorbents were explored as alternative to remove ARVDs in wastewater. These were selected as they are highly abundance, eco-friendly and cost-effective adsorbent. Also, the polymeric material (polymer of intrinsic microporosity number-1, PIM-1) was explored due to its high abundance of  $\pi$ -electrons from phenols and high surface area. This could result to high removal efficiency as pollutants would have more binding sites. Furthermore, PIM-1 has a single synthetic route with mild preparatory conditions.

## **1.3 Aim and objectives**

### **1.3.1 Aim**

The aim of this study is to synthesize and apply low-cost adsorbent for removal of antiretrovirals in wastewater.

### **1.3.2 Objectives**

The objectives were:

1. To optimize the LC-PDA method for analysis of antiretroviral drugs.
2. To synthesize and characterize low-cost adsorbents using, FTIR, SEM, BET and PXRD techniques
3. To optimize the conditions that will allow high adsorption efficiency of the selected antiretroviral drugs by the synthesized adsorbents.
4. To apply the synthesized adsorbents under optimal conditions for the removal of antiretroviral drugs from wastewater.
5. To compare the removal efficiency of the synthesized adsorbent.

## **1.4 Research questions**

- Which LC-PDA parameters need to be optimized to improve the separation of the selected ARV
- Will acid or base modification of the adsorbents activate their functional groups and enhance their adsorption efficiency?
- Which parameters need to be optimized to improve the adsorption of the ARVDs from wastewater?
- Is it acid or base modified adsorbent that will be more effective in adsorbing the ARVDs of interest?
- Which is the most efficient adsorbent (macadamia nutshell, *Plantaus acerifolia* and PIM-1) for removal of the selected antiretroviral drugs in wastewater samples?

## 1.5 Research justification

The continual detection of ARVDs in environment and aquatic species is worrisome concern. South Africa has about 7.9 million people who are infected by the HIV virus, this makes about 13.78 % of the country population. There are about 4.4 million of infected people which about 60 % who are already in the ARVDs treatment program which makes, South African the largest ARVDs program in world (Nibamureke et al., 2019, Adeola & Forbes et al., 2022).are released with urine and faecal to coordinated wastewater treatment which is a main water supply of water for commercial and domestic usage. Also, the environmental persistence of ARVDs could induce toxicity to non-target species such as fish and a potential risk to humans. As a result, there is a sense of urgency from scientific community to find efficient adsorbents to remove the ARVDs in polluted water. Hence, this study seeks to explore macadamia nutshells, *Platanus acerifolia* leaves and PIM-1 as easily accessible and eco- friendly methods to remove ARVDs in wastewater samples. The use of macadamia nutshells, *Platanus acerifolia* leaves are in high abundance and could promote circular economy and reduce pollution. Many reported studies on the application of macadamia nutshells (Ntuli, 2017, Ma et al., 2019), *Platanus acerifolia* leaves (Wang et al., 2015, Liu et al., 2020) and PIM-1 (Pim et al., 2015, Peng et al., 2016) as adsorbents are removal of heavy metals, pesticides and phenolics compounds which is indicative of novelty of the current study whereby we shall explore removal of ARVDs in wastewater samples use these adsorbents.

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## Chapter Two: Literature Review

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### 2. Introduction

#### 2.1.1 Antiretrovirals drugs (ARVDs)

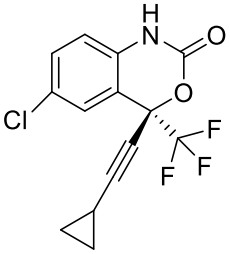
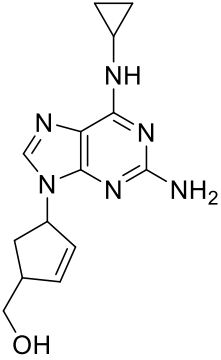
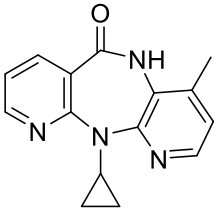
Antiretrovirals drugs (ARVDs) are therapeutic medications used for the treatment of retroviral infections, the human immunodeficiency virus type 1 (HIV-1). The HIV virus attacks the CD4-T cells whose main aim is to provide body immunity against various infections and diseases (Ncube et al., 2018, Ngumba et al., 2016). The ARVDs medications do not completely remove the HIV-1 virus but it prevents the further replication of the virus. In addition, ARVDs prevents the susceptibility of the infected person to virus opportunistic diseases and infections. Unused drugs and expired drugs are often poorly disposed as a result are found in drainage systems and eventually to water sources (Abafe et al., 2018, Adeola & Forbes et al., 2022). Main sources of ARVDs in the environment are ground water, surface water, infiltrated pit latrines and wastewater treatment plants (WWTPs). Antiretroviral drugs are classified by their mode of action which include nucleoside reverse transcriptase inhibitors (NRTI), non-nucleoside reverse transcriptase inhibitors (NNRTI), and protease inhibitors (PI) (Arts & Hazuda et al., 2012). Nucleoside/ Nucleotide reverse transcriptase inhibitors (NRTI) were among the first line of treatment of HIV virus that was licensed by Food Drug Administration (FDA), a drug regulatory authority in the United States of America (Young et al., 1988). This class of compounds requires a host cell and phosphorylation to function via cellular kinases before binding for antiretrovirals effect (Arts & Hazuda et al., 2012). Efavirenz is an example of compounds that belongs to NRTI which has been used against treatment of HIV virus for a long period of time. Efavirenz has evolved to be another key component for a number of efficacious treatment cocktails used as either a prescribed drug or as add-on for various combinational drugs such lamivudine and zidovudine (Gulick et al., 2006, Butanda-Ochoa et al., 2017) Moreover, efavirenz has illustrated to have a virologic efficacy and remains the widely ARVDs of choice against the rapid replication of retroviral infections such HIV type-1.

Non-nucleoside reverse transcriptase (NNRT) is a class of compounds that alters the inhibition of transcriptase through binding to enzyme at a site different from nucleoside binding component (Smith et al., 2007). Nevirapine is prominent compound of the NNRT which used with a combination of several compounds as a treatment against the further replication of retroviral viruses such HIV. The high bounding effect to plasma proteins and high adsorptive ability on the gastrointestinal tract make it to be rapidly adsorbed by the blood stream and be distributed throughout the body. The nevirapine compound is extensively metabolized by cytochrome P450 enzymes which is the reason they can found in the urine metabolites (Liao et al., 1987).

Protease inhibitors (PI) - prevents the further replication of HIV virus by breaking down structural proteins which are responsible for morphogenesis and assembly of particles of the virus (Lu et al., 2008). PI occupy the active site of HIV-1 protease thus hinders the attachment to the processing site which it wants to cleave to become a mature viral particle. By preventing this step, the virus could not further replicate. Protease enzymes are critical for viral maturation in the HIV cycle (Lv et al., 2015). PI block the protease enzyme activity thus prevents the assembly of new viral particles. This class of compound is used with combinatory ARVDs to reduce transmission, reduce symptoms, keeps the immune system intact (Arts & Hazuda et al., 2012).

The physiochemical properties influence the ability of ARVDs to solubilize in the aqueous media. If the solution pH is higher than the AVRVDs pka, it could result to their poor adsorption from the solution due to that the ARVD compounds are likely to hydrolyze and be in anionic form. In addition, the lower log  $K_{ow}$  could result to high solubility which could enhance the removal of species in solution. The physical properties for the ARVDs of interest are shown in (**Table 2.1**). Abacavir and nevirapine have lower log Kow hence have high solubility in water. Efavirenz has a low (log Kow 4.15) and a lower solubility of (10 mg/L) which is to cause easy diffusion of the compounds into the aqueous phase hence it could have a high removal efficiency compared to rest of the compounds of under investigation (Versteeg et al., 2014, Madikizela et al., 2016).

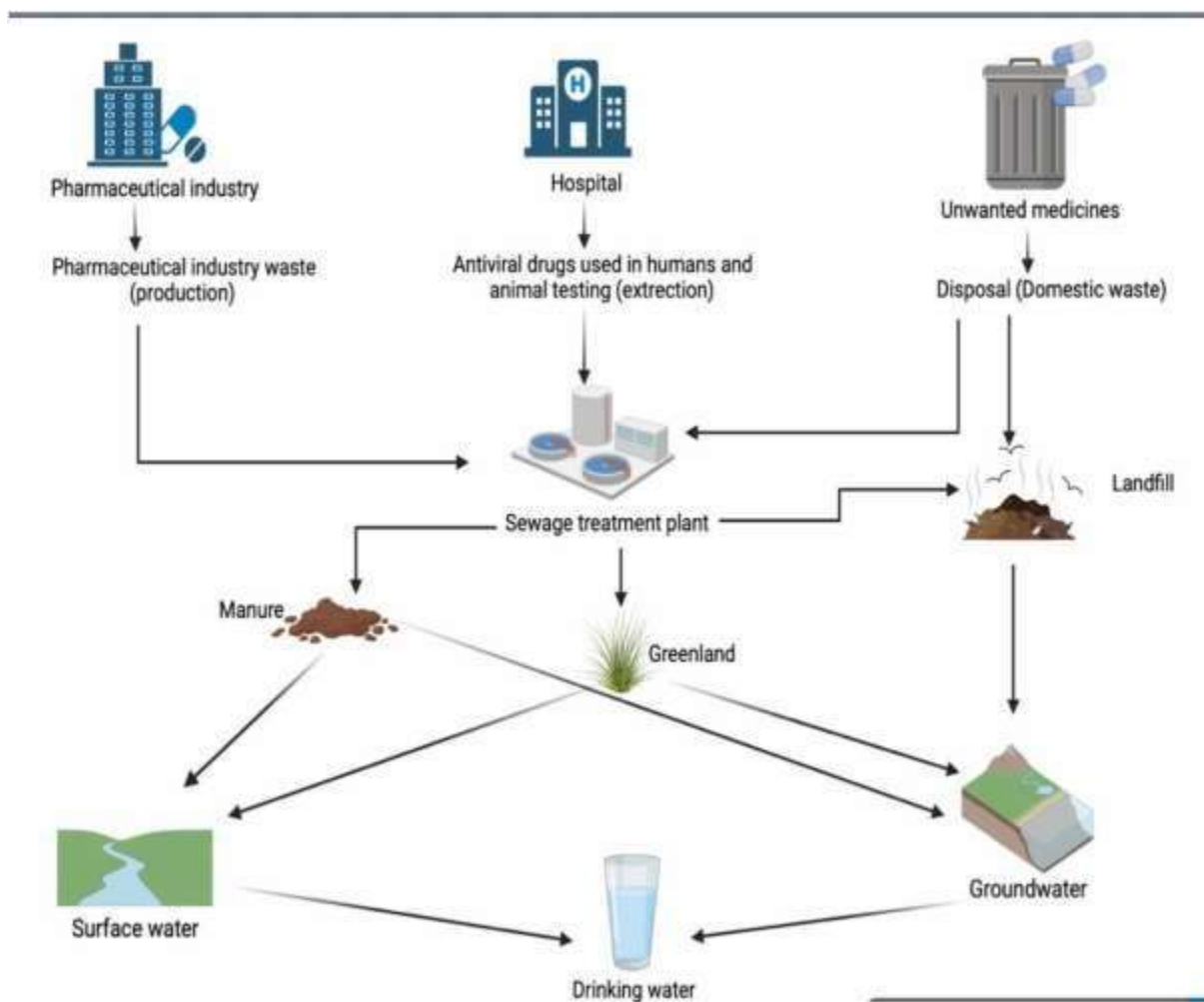
**Table 2.1: Physio-chemical properties of three antiretroviral of interest to be studied**

Name	Chemical Structure	Log K <sub>ow</sub>	pKa	Solubility mg/L	Reference
Efavirenz		4.15	12.52	10	(Adeola et al., 2021)
Abacavir		1.45	5.77	77	(Eryildiz et al., 2020)
Nevirapine		3.89	5.06	100	(Pereira et al., 2023).

### 2.1.2 Fate of antiretroviral drugs in the environment

The over-usage of antiretroviral drugs is increasing due to considerable number of people of already infected by the HIV virus. Evidence in literature has shown that many pharmaceutical compounds including ARVDs are partially metabolized and excreted as original compounds or as metabolites via urine and faecal waste and reach wastewater treatment plants (WWTPs) which are a source of water for domestic and commercial practices (Abafe et al., 2018a, Nibamureke et al., 2019, De Andrade Aragão et al., 2020). The main point source of ARVDs into wastewater treatment plants are discharges from pharmaceutical industry effluent, hospital influent waste and unwanted or expired medicines (domestic waste)(Jain et al., 2013).

The effluent water from wastewater treatments plants can be used for irrigation while the biosolids from sewage sludge can be used as manure for agricultural purposes which could results to adsorption of ARVDs by crops and eventually be ingested by human (Azzouz & Ballesteros et al., 2012). The biosolids from landfill waste or farming fields could be transported to rivers and dams through surface runoff and pollute water sources and can eventually reach drinking water where human beings can unintentionally consume them. The ARVDs could also be distributed into the environment through diffuse sources such as leaching of septic tanks and infiltration of pit latrines into ground water (Ngumba et al., 2020). The ARVDs have also been known as pseudo-persistent pollutants due their continual release into the environment. The **(Figure 2.1)** gives an insight on how pharmaceutical compounds including ARVDs are transported to water sources and eventually to drinking water. The continual addition of ARVDs in water sources compromises water quality and could have a significant impact to aquatic species and pose a potential to human health.



**Figure 2.1:** Pharmaceutical compounds of fate in the environment (Eryildiz et al., 2020)

### 2.1.3 Effects of ARVDs in human and aquatic life

The continual exposure to ARVDs through various routes is an emerging concern for animals and human health. The constant detection of ARVDs in food sources and drinking water could result into unplanned consumption by humans and thus leads to development of resistant strains of HIV-1 to current treatment drugs. This may have additive effects to human and animal health as new drugs could be required to combat the replication retroviral infections (Nibamureke et al., 2019). For instance, ARVD drug like abacavir is associated with psychosis and mania which are mild nervous system disturbance, while efavirenz may cause insomnia, vivid dreams, and irritability (Abers et al., 2014). Nevirapine is likely to cause liver toxicity to nontarget species such to fish and amphibians (Memmert et al., 2013, Schoenfuss et al., 2016).

The continual exposure could lead to ARVDs adverse effects such fever, fatigue, hepatic steatosis, pancreatitis and heart diseases and headache. These effects may be evident through bioaccumulation of ARVDs in water sources, overdose, and drug abuse over a long period of time (Calmy et al., 2009, Ncube et al., 2018). ARVDs are believed to have cause toxicity to algae which is a main precursor for all aquatic systems. Moreover, feminization and alternation of physiological structure daphnids and fish has been reported because of continual exposure of nevirapine and abacavir to these species.

The inefficiency of wastewater treatment plants to remove ARVDs would continue to be a major threat to accessibility to clean and fresh drinking water. The availability of clean and fresh water has been a crisis due to increase in urbanizations, severe droughts, and climate change. Drastic measures have been explored to fight against water scarcity such harvesting of rainwater, reclaiming water from storm water and recycling of water from wastewater. Since there has a growing trend of water scarcity, effluent water from wastewaters treatment plants have been used as alternative of water supply for domestic and commercial practices. Since the wastewater treatment plants receives large amount of for therapeutic compounds such as ARVDs and veterinary medicines, the water scarcity led to usage of water from treatment plants could lead to a directly introduction of pharmaceutical to soil when the water is used for irrigation purposes. These compounds could be adsorbed by crops which are a major source of food for human. Moreover, sewage sludge used biosolids as manure to grow agricultural produce which could add more concentration of ARVDs in the soil where agricultural produce obtains their nutrients for growth (González García et al., 2018). Furthermore, the applied biosolids could be carried be through process such surface runoff into rivers and dams which are major of water for domestic purpose and commercial practices (Madikizela et al., 2017, Ncube et al., 2018).

Aquatic plants have the ability adsorb pharmaceutical including ARVDs through roots, stems, and leaves (Shakir et al., 2017). A study conducted by Mlunguza and co-workers (Mlunguza et al., 2020b), showed the ability of ARVDs compounds to bio-accumulate on hyacinth plants which yielded about (8.7-29.6  $\mu\text{g}/\text{kg}$ ). Akenga and co-workers (Akenga et al., 2021), reported on accumulation and uptake of ARVDs by a lettuce through the roots and stem about (691-3463  $\text{ng}/\text{g}$ ). The study showed the potential toxicity effects on lettuce which was mass reduction due exposure ARVDs contaminated water. The result obtained are evidence that ARVDs could produce toxicological effects even in trace concentrations. A study on bioaccumulation and bio- translocation to roots, stem and fruit indicated that beetroots, spinach, and tomato has 55 %, 48 % and 48 % of abacavir, respectively. In addition, the roots of spinach adsorbed 40.21 %, 18.43 % of spinach stem and 6.77 % in the spinach soil (Kunene &

Mahlambi et al., 2023). This is an indicative that roots can adsorb ARVDs from contaminated soils and translocate to stem, leaves aerial parts of the plants tissue.

#### **2.1.4 Occurrence of ARVDs in wastewater worldwide**

Wastewater treatment plants receives higher amounts of pharmaceutical compounds including antiretroviral drugs from domestic and industrial effluent water. As the treatment plants were not designed to remove these compounds, they are partially removed and thus be released with the treated effluent into the receiving waters. For this reason, the wastewater treatment plants have been reported to contribute towards surface water pollution. (**Table 2.2**) shows the concentration of some ARVDs obtained in wastewater influent and effluent worldwide. From the data, efavirenz and nevirapine have been mostly assessed and have higher concentration in African countries in both influent and effluent. Nevirapine's highest concentration in the effluent (3000 ng/L) was detected in South Africa (Abafe et al., 2018), while efavirenz (100 ng/L) was detected in Kenya (K'oreje et al., 2016). The high concentration obtained of nevirapine and efavirenz is due to that these compounds are an integral part of most efficacious treatment cocktails of HIV (Gulick et al., 2006). These higher concentrations are due to the surge of HIV infections among African countries, and these ARVDs are the commonly used as a first-line of treatment against HIV virus (Mlunguza et al., 2020).

The lower concentrations detected in the overseas countries like Germany could be attributed to legislative measures that govern the production and disposal of ARVDs compounds in environment (Ngqwala & Muchesa et al., 2020). The detection of ARVDs in effluent water all over the world indicates the inefficiency of the wastewater treatment current employed processes to completely remove them (Adeola & Forbes., 2022) which is a major concern. Hence, there is a need of sensitive and affordable methods for removal of these compounds in wastewater. This is due to that the continual detection of ARVDs in the environment is evidence of the pollution in aquatic environment which may have a potential long-term effect to human as ARVDs could unintentionally ingested leading to their resistance by the human body

**Table 2.2: Maximum ARVDs concentrations (ng/L) obtained in influent and effluent water around the world**

<b>Antiretrovirals</b>	<b>Name of WWTP</b>	<b>Country</b>	<b>Influent</b>	<b>Effluent</b>	<b>Reference</b>
Efavirenz	Dondora	Kenya	780	100	K'oreje et al., 2016
	Kiast		1020	110	
	Northern	South Africa	140	93.1	Mtolo et al., 2019
Nevirapine	Northern	South Africa	24000	20000	Abafe et al., 2018
	Phoenix		34000	30000	
	Jyvaskyla	Finland	19	10	Ngumba et al., 2016
	Ruhr	Germany	32	22	Abafe et al., 2018
Zidovudine	DEWATS	South Africa	53	0.5	Abafe et al., 2018
	Ruhr	Germany	380	564	Prasse et al., 2010
Emtricitabine	Western Cape WWTPs	South Africa	172	41.7	Mosekiemang et al., 2019
Ritonavir	DEWATS	South Africa	43	17	Abafe et al., 2018

### **2.1.5 Techniques for removal of pharmaceuticals from aqueous media**

Numerous techniques have been explored of the removal for emerging water pollutants. Physico-chemical process like filtration, sedimentation, floatation, and coagulation are economically viable and have been employed in various water treatment stages for removal of various water contaminants (Suarez et al., 2009, De Andrade et al., 2018). Although, these methods have found vast application for the removal of other emerging pollutants, they are inefficient in the removal of ARVDs such as abacavir and zidovudine due their high chemical stability. Some of the emerging pollutants such as ARVDs has the ability to produce side products with adverse effects than original compounds if incorrect methods are used for their removal. In addition, methods like ozonation are efficient in removal pharmaceuticals compounds however, they are energy intensive and due to energy crisis, which looming around the world they are applicability may be limited.

Membrane separation methods have also been widely used for removal of micropollutants such as antibiotics and veterinary medicines in aqueous environment (Luo et al., 2014). These includes reverse osmosis (RO) and nanofiltration (NF) which have been successful employed for removal of many pharmaceutical compounds with removal efficiency about 94 to 100% (De Andrade et al., 2018). However, they have complex operational process and membrane replacement is expensive. Moreover, their application in the removal of pharmaceutical is also governed by polarity, hydrophobicity, charge and the competition between anions and cations in solution (Yoon et al., 2006, De Andrade et al., 2018). Besides the complex operational process these methods could produce side-products with high toxicity even to original compounds and high energy consumption. On the other hand, adsorption method has numerous advantage such as simplicity in design, low energy consumption, mild operation conditions and minimal or no side products. This has made adsorption to be a prominent method used for elimination of numerous water contaminants such ARVDs (Seo et al., 2016, Adeola & Forbes et al., 2022).

### **2.1.6 Adsorptive phenomenon for removal of pharmaceutical**

Adsorption phenomenon refers to transference and accumulation in the interfacial layer of fluid phases via physical or chemical interactions (Dessie Sintayehu et al., 2016, Ntuli et al., 2017). Adsorption of the adsorbate can take place in two mechanism which are: physical (physisorption)

and chemical (chemisorption) adsorption. Physisorption process is driven by the inter-molecular attractive forces (Van der Waals) forces between adsorbate and adsorbent (Tan & Hameed et al., 2017). The physisorption is quick even though diffusion into the pores may be time-consuming. The porosity of the adsorbent is essential in this kind of adsorption more than the surface area as the pore volume and pore size determine the adsorption capacity. In addition, the pore volume and pore size properties, the activation energy can be used as a parameter to measure the interaction between the adsorbate and adsorbent. The activation energy of physical adsorption must within a range of 5-40 kJ/mol (Farhan et al., 2013).

The formation of strong chemical bond that could involve the sharing or transfer of electrons through interactive forces such covalent bonding between adsorbate and adsorbent is described as chemisorption (Tan & Hameed et al., 2017). The sharing of electrons or transfer of electrons could result to a change of the ionic state or form of the adsorbate. It's not an easily reversible process and as heat applied may result to bond breaking and new bond formation. Chemisorption is dependent solely on the adsorption sites that are present on the surface of the adsorbent where the pharmaceuticals can bind. Chemisorption also requires high activation energy to take place. When activation energy ranges from (40–620 kJ/mol), it is classified as chemical adsorption (Ntuli et al., 2017).

### **2.1.7 Commonly used adsorbents**

Adsorptive materials such as activated carbon (AC), clays, silica, composites, alumina, and zeolites and others have been explored for the removal of various micropollutants such antibiotics, pesticides, and pharmaceuticals from water sources (Rakić et al., 2015, Rakhym et al., 2020). The motivation on exploring these adsorbents for removal of water pollutants are their distinct functional groups that could interact with various compounds that can enhance their removal. The activated carbon developed from *Ficus carica* bast have been effectively used for removal of methylene blue (MB) where about 63.31 mg/g was removed from industrial effluent sample (Pathania et al., 2017). In addition, the (AC) synthesized from *Vernonia amygdalina* wood was used for adsorption of acetic acid whereby about 85 % of acetic acid was removed (Dessie Sintayehu et al., 2016). The removal of atenolol and diclofenac was successfully investigated whereby 60 % of these compounds was removed in sewage water samples using alumina as an adsorbent. All these is an indication of the ability of some of the mentioned adsorptive material to remove compounds in aqueous media that could be a potential threat to human and animal health.

Nanofibers were successfully synthesized and applied for the removal ARVDs whereby the amount adsorbed ranged from (72.5-189.1 mg/g) and (64.9-174.0 mg/g) (Kebede et al., 2019) in effluent and influent respectively. The high porous structure, accessible surface and high adsorption capacity of the aforementioned adsorbents has made them to have a vast application in removal of water contaminants (Ma et al., 2014).

Over the years, the polymer of intrinsic microporosity number-1 (PIM-1) has evolved as a novel class of polymeric compounds that has been prominently applied as an adsorbent for removal of phenol (Budd et al., 2004) and dye (Pim et al., 2015) in polluted aquatic environment. The nitrile functional group on its backbone is very essential because it could be functionalized to various functional groups that used to adsorb target species in polluted water. Some of the outstanding features of PIM-1 are high affinity to molecule and high free volume which could be essential for adsorption of various aqueous contaminants (Zhang et al., 2016). The PIM-1 has an inefficient packing of non-network polymer chain with rigid and contorted structure which improves the surface area that can enhance the adsorption of target pollutants. The PIM-1 illustrated to be an excellent adsorbent in removal of antibiotics whereby antibiotics such amoxicillin, ciprofloxacin showed about 80 % of removal efficiency from wastewater treatment samples (Alnajrani & Alsager et al, 2020). The high surface area, high adsorptive rate, processability and tailorable backbone has made a PIM-1 a potential good for eliminating micropollutants (Mason et al., 2014, Halder et al., 2018, Pan et al., 2018).

Agricultural adsorbents from material such as leave, bark, shells, pit, bagasse, contain organic compounds. On the other inorganic compounds such as lignin, cellulose, alkaloids, proteins, red mud, and minerals have been used for elimination of various water pollutants (Mahvi et al., 2007, Phele et al., 2019). These are highly abundance, low-cost, and easily accessible agro-industrial adsorbents which offer environmental advantages in comparison with conventional adsorbents, including renewable nature and reduction of waste in the environment. The agricultural waste adsorbents have various components such hydrocarbons, lignin, lipids, and cellulose (Bhatnagar & Sillanpa et al., 2010, DeGisi et al., 2016) which possess various functional groups such as N-H, O-H, C=C, C-H essential for the removal of pollutants in water. A study revealed that Antunes and co-workers, explored Isabel grape bagasse produced during wine production which showed to be an effective adsorbent for eliminating diclofenac (76.98 mg/g) from water (Antunes et al., 2012).

Balarak and co-workers, reported on removal of ciprofloxacin from wastewater whereby about 96.5 % removal efficiency was achieved (Balarak et al., 2017). The various material from agricultural waste possesses functional groups which through various mechanism like complexation and valence electron sharing interact with pharmaceuticals and various pollutant that leads to their removal in wastewater.

On the other hand, Macadamia nuts has become a notable and fastest growing crop in the agricultural industry. A hot subtropical climate with no humidity is an essential climate for macadamia plantations to grow. The macadamia trees may take about five to twelve years before it can produce the nuts for about 40 years. The climate of Limpopo, KwaZulu-Natal and Mpumalanga is ideal for macadamia plantations in South Africa. South Africa is third largest producer of macadamia nuts around the globe behind Australia (where they were originally produced) and Hawaii (Phele et al., 2019). The increase in the production of macadamia in South Africa has made it the largest exporter of macadamia nuts. Macadamia nuts have found their vast applications in formulations chemistry where they are used for making heavy creams, sun screens and widely used in baking, ice cream and snack food industries (Taylor et al., 2007, Lambaard et al., 2019). Macadamia nuts have a cushiony skin feel and high oxidative stability which makes it suitable in making personal care products. They are also a source of vitamin such iron, calcium and zinc and are a reliable source of energy. The macadamia nuts are a super energy source and sweet taste and has been recommended to low-risk heart diseases upon consumption. On the other hand, plantations of macadamia have opened employment opportunities whereby about 12500 full-time workers in across the industry. The increase in the production of macadamia plants has led to increase in the accumulation of macadamia nutshells where indiscriminately disposal of nutshell could result to environmental pollution (Taylor et al., 2007, Duncan et al., 2014). Also, macadamia nutshells have been used as an adsorbent for removal of Endrin (91 %) and 4,4-DDT (85 %) (Phele et al., 2019). In addition, (Ntuli et al., 2017) reported on the application of macadamia for removal of traces heavy metals in the aqueous media. The removal efficiency obtained for Cr(VI) was 65 %, Cu(II) 50 % and Cd (II) 30 %. The results obtained are an indicative that macadamia is an ideal adsorbent for removal of emerging contaminants in aqueous media.

*Platanus acerifolia* leaves (London plane tree) are high abundance, and easily accessible adsorbent that has attracted an intention to be applied for removal of different contaminants in aqueous media. *Platanus acerifolia* are perennial deciduous tree, that originated in Southeast Europe to India including Iran and Turkey (Talip et al., 2009, Devi et al., 2019). The first plantations of *Platanus acerifolia* trace back as early as spring of 1987 and 1988 in Transvaal near Pretoria. Since then, South Africa has a wide spread of *Platanus acerifolia* plantations across the county, whereby about 20 to 60 % of leaves are shed down resulting to large municipal solid waste (Swart & Wingfield et al., 2014). The *Platanus acerifolia* leaves possess numerous cytotoxic, anti-inflammatory and antioxidant properties. There are flavonoids compounds such as luteolin, pitot, granuloma and kaempferol which are found *Platanus acerifolia* leaves. The leaves constituents of antioxidants such phenols, tannins, and vitamins. Several components of leaves are esters of phytol with fatty acids and tocopherol derivatives (Devi et al., 2019). Most of mentioned compounds have high dominance of delocalised,  $\pi$ -conjugated system and a strong coordinate oxygen atom which could form spatial conformation with target compounds (Yang et al., 2013). The presence of these  $\pi$ -conjugated systems make *Platanus acerifolia* leaves a suitable candidate for removal of hazardous compounds in aquatic environments. The high surface area, high carbon content and abundance of functional groups such N-H, O-H, C=C and many more, makes the *Platanus acerifolia* leaves as excellent adsorbent for the removal of water pollutant such heavy metals (Dai et al., 2020). The high presence of these functional groups could lead to possibility of  $\pi$ - $\pi$  interaction, electrostatic attraction forces, hydrogen bonding that can enhance the removal of micro-contaminants in water bodies. This could be the best alternative to most prominent candidate used which is activated carbon adsorbent which is relatively expensive and low reusability (Mahvi et al., 2007). *Platanus acerifolia* leaves were explored whereby 557.05 mg/g of p-nitrophenol was adsorbed in wastewater (Ma et al., 2019). There are various advantages of macadamia nutshells and *Platanus acerifolia* leaves as adsorbents compared to other adsorbents such (1) low-cost (2) eco-friendly in nature (3) high efficiency (4) widely used for a variety of adsorbents (5) large surface area (6) low-energy consumption. The various attributes make the adsorbent to have application to removal of water contaminants. Hence the current study seeks to explore these adsorbents would explore to remove antiretrovirals in wastewater samples.

To achieve efficient removal of pollutants, it is important that adsorption parameters such

adsorption time, solution pH, mass dosage, initial concentration and adsorption temperature be optimized to obtain the optimum conditions. A minimum time with highest removal efficiency is critical in the adsorption process of target species and to gain insight about the adsorption kinetics. The solution pH is responsible for influencing the degree of ionization of compounds and surface properties of adsorbent which is crucial for adsorption of compounds. The availability of the adsorptive sites is governed by the adsorbent mass dosage whereby an increase in mass dosage increases the availability of active sites. The initial concentration is an essential parameter for evaluating mass transfer of the target compounds. To gain more insight about the ability of the adsorbent to adsorb pollutants, the adsorption kinetic, adsorption isotherms, thermodynamic studies are critical to be investigated.

## **2.2 Adsorption kinetics, adsorption isotherms and thermodynamic studies**

### **2.2.1 Adsorption kinetics**

Kinetic study is essential for evaluating the adsorption rate and controlling the adsorption mechanism which could be limited by different mass transfer resistances which is influenced by temperature, pressure conditions and nature of adsorbent. Solid material is characterized by two main resistances: resistance to external diffusion (intraparticle) that is related to mass transfer from bulk fluid to external surface and intraparticle diffusion, related to mass from external surface to internal porous structure (De Andrade et al., 2018). Several models have been explored for examining potential rate determining steps and adsorption mechanisms. Pseudo-first-order, pseudo-second-order and Intraparticle diffusion which is defined by following equations (2.1), (2.2) and (2.3).

$$\ln(q_e - qt) = \ln(q_e - K_1) \quad (2.1)$$

$$\frac{t}{q_e} = \frac{t}{K_2 q_e^2} + \frac{t}{q_e} \quad (2.2)$$

$$q_e = K_{id}t^{1/2} + C_i \quad (2.3)$$

where  $q_e$  (mg/g) is the amount adsorbed at equilibrium, and  $q_t$  (mg/g) amount of ARVDs is time  $t$  (min). A plot of  $\log (q_e - q_t)$  against time  $t$  that yield  $K_1$  and  $q_e$  values from slope and intercept respectively for a pseudo-first-order model Furthermore,  $K_1$  ( $\text{min}^{-1}$ ) and  $K_2$  ( $\text{g} (\text{min mg})^{-1}$ ) are rate constants of pseudo-first-order and pseudo-second-order,  $K_{id}$  ( $\text{mg} (\text{g}^{-1} \text{min}^{-1/2})$ ) is a diffusion rate constant and  $C_i$  is a boundary layer constant. Moreover, a plot of  $(t/q_t)$  against  $t$  gives  $(1/q_e)$  as slope and  $(1/K_2q_e^2)$  as intercept from which  $K_2$  can be obtained.

### 2.2.2 Adsorption isotherms

The adsorption isotherms modelling is an essential method for proper evaluation and design adsorptions systems. The dynamic adsorption equilibrium is critical aspect for access the isotherm adsorption. The dynamic equilibrium is obtained where the adsorption and desorption rate are equivalent. In this instance the chemical potential is the same since the global mass transfer of the solute is zero. The commonly applied adsorption isotherms are Langmuir, Freundlich and Temkin models defined by equations (2.4), (2.5), and (2,6)

$$\frac{C_e}{q_e} = \frac{1}{q_e K} + \frac{C_e}{q_m} \quad (2.4)$$

equilibrium (mg/g),  $C_e$  is the concentration at the equilibrium of antiretroviral (mg/L),  $q_m$  is the maximum theoretical capacity (mg/g) and  $K(L/mg)$  is the Langmuir constant that correlates to the binding sites. The constant of Langmuir is obtained by plotting the slope and the intercept of the plots which are plot of  $C_e/q_e$  against  $C_e$ . Moreover, the Freundlich model was also employed, which is defined by equation (2.5), (Abdel Rahman et al., 2017).

$$\log q_e = \log K_F + \frac{1}{n} \log C_e \quad (2.5)$$

Freundlich has two constants  $K_F$  and  $n$  which gives an insight about the heterogeneity degree of surface sites. The constant could be obtained through and intercept of the plot of  $\log q_e$  against  $\log C_e$ . The Temkin model could be defied by the following equation (2.6).

$$q_e = B_1 \ln K_T + B \ln C_e \quad (2.6)$$

### 2.2.3 Thermodynamic studies

Adsorption kinetics, adsorption isotherm and thermodynamic studies more insight about the nature of the adsorption process. Thermodynamics parameters Gibbs Energy ( $\Delta G^\circ$  kJ/mol), enthalpy ( $\Delta H^\circ$ , kJ/mol) and ( $\Delta S^\circ$ , J (mol. K) are expressed by the following equations.

$$D = \frac{q_e}{C_e} \quad (2.7)$$

where  $q_e$  is the number of antiretrovirals adsorbed by the adsorbent (mg/g) at equilibrium, and  $C_e$  is the equilibrium concentration of antiretrovirals in (mg/L).

$$\ln D = \frac{\Delta S^\circ}{R} + \frac{\Delta H^\circ}{RT} \quad (2.8)$$

$$\Delta G = \Delta H^\circ - T\Delta S^\circ \quad (2.9)$$

where  $R$  is a gas constant (8.314 J/mol K),  $T$  is the absolute temperature (K),  $\Delta H^\circ$  and  $\Delta S^\circ$  could be obtained from the slope and intercept of  $\Delta G^\circ$  vs  $1/T$ . Adsorption is favorable and spontaneous at a given temperature when  $\Delta G^\circ < 0$ . The value of  $\Delta H^\circ < 0$  is an indication that the adsorption process is exothermic and involves physical or chemical adsorption or both occur simultaneously. In contrast, endothermic process occurs whereby ( $\Delta H^\circ > 0$ ). Positive value of  $\Delta S^\circ$  is an indication that there is an increasing in randomness which could be associated to translational energy that gained by displaced solvents is greater than adsorbed molecule.

In a study conducted by Kebede and co-workers (Kebede et al., 2020), the pseudo-first-order and pseudo-second-order kinetics models were explored to access the adsorption process of ARVDs by the nanofibers. The obtained correlation coefficients (0.998-1.00) indicated that the adsorption process is best described by the pseudo-second-order while the closeness of the  $q_{e,exp}$  and  $q_{e,cal}$  indicated that pseudo-second-order is also the rate determining step. This conclusively revealed that the rate determining step in the adsorption of these ARVDs is governed by chemisorption process. Fitting the experimental data from intra-particle diffusion showed that the data did not pass through the origin suggesting that the intraparticle diffusion is not the rate determining step but could be other kinetic models.

The adsorption isotherms studies showed that the Langmuir dimensionless equilibrium ( $R_L$ ) was less than one and greater than zero indicating the favourability of the adsorption process. The heterogeneity ( $1/n$ ) of Freundlich indicated the favourability of adsorption. The correlation coefficients ( $R^2$ ) indicated that both models favoured the adsorption. However, the correlation coefficients ( $R^2$ ) best describe the adsorption process which is an indicative that the adsorption process occurred on a multilayer heterogeneous surface. The thermodynamic studies indicated that adsorption process was spontaneous and thermodynamically favoured. The adsorption process was exothermic in nature and showed an irregular increase in randomness in ARVDs-adsorbent interaction which was confirmed by  $\Delta H^\circ$  negative value and  $\Delta S^\circ$  positive value. These results showed that the combination investigation of adsorption kinetics, adsorption isotherms and thermodynamic studies is critical for determination of the adsorption process. The obtained results from this investigation are a clear indication of the importance investigating adsorption kinetics, adsorption isotherms and thermodynamic studies to design an effective adsorption process.

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This dissertation is presented in a form of paper publications. The experimental process is detailed in each of the written papers.

**Paper 1** presented as Chapter 3: Removal of antiretroviral drugs from wastewater using activated macadamia nutshells: adsorption kinetics, isotherm, and thermodynamic studies.

**Paper 2** presented as Chapter 4: Exploration of *Platanus acerifolia* Leaves on the adsorption of abacavir, efavirenz and nevirapine from wastewater: adsorption kinetics, isotherm, and thermodynamic studies.

**Paper 3** presented as Chapter 5: Kinetics, isotherms, and thermodynamic studies for efficient adsorption of selected antiretroviral drugs from wastewater using polymer of intrinsic microporosity number-1

## Chapter Three

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### **Removal of antiretroviral drugs from wastewater using activated macadamia nutshells: adsorption kinetics, isotherms, and thermodynamic studies**

#### **Abstract**

Pharmaceuticals compounds including antiretroviral drugs (ARVDs) have been extensively employed in health care for the improvement of the quality of life and lifecycle longevity. However, the incomplete digestion of ARVDs in the human body results in substantial amounts entering the wastewater treatment plants where they are incompletely removed leading to their continuous introduction to water sources resulting in health effects. Therefore, in this work, the removal efficiency of modified macadamia nutshell was explored for the first time as an easily accessible and low-cost adsorbent for the removal of ARVDs in water. Fourier transform infrared spectroscopy (FTIR) showed the presence of functional groups such as O-H, C=O, and C=C on the surface of the modified adsorbents which are responsible for binding with the ARVDs. Scanning electron microscopy (SEM) showed that the adsorbents surface has long rod-folded and elongated structure for both acid (hydrochloric acid) and base (sodium hydroxide) modified macadamia adsorbents. Brunauer Emmett Teller (BET) indicated a surface area, pore diameter, and pore volume of 0.1180 m<sup>2</sup>/g, 27.98 nm, and 8.3×10<sup>-5</sup> cm<sup>3</sup>/g, respectively for base activated macadamia adsorbent and 0.7468 m<sup>2</sup>/g, 7.88 nm, 1.47×10<sup>-4</sup> m<sup>3</sup>/g, respectively for acid activated macadamia adsorbent. Powder X-ray diffraction (PXRD) of both adsorbents showed a native crystalline cellulose structure. A batch adsorption studies showed the adsorption was above 80 % when 10 mg of the adsorbent in 10 mL of water sample with a pH of 7 was agitated for 90 minutes at a temperature of 30°C. The adsorption was highly favoured by acid-modified macadamia nutshell adsorbent. Eventhough, the experimental data fitted both Freundlich and Langmuir adsorption isotherms, the equilibrium behaviour was explained and described better by the Langmuir. The pseudo- second- order model well predicted the kinetic behaviour. The intraparticle diffusion was found to be involved in the adsorption process, however, it was not the rate-limiting step. The obtained results in the current study illustrated that macadamia acid modified was an effective and low-cost adsorbent for the removal of the selected ARVDs in wastewater.

**Keywords:** antiretrovirals, low-cost adsorbents, kinetics, isotherm, thermodynamics

### **3.1 Introduction**

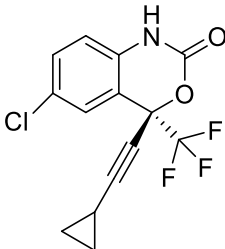
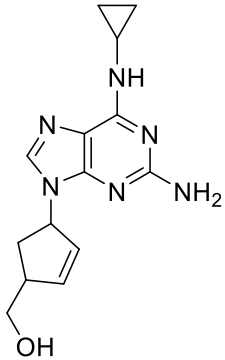
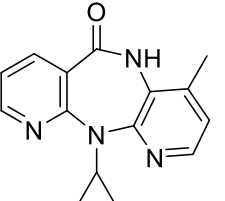
#### **3.1.1 Antiretrovirals drugs (ARVDs)**

Antiretroviral drugs (ARVDs) are therapeutic agents used for the treatment of retroviral infections, specifically the human immunodeficiency virus type1 (HIV-1) (Ngumba et al., 2016, Adeola et al., 2021). The ARVDs like many other pharmaceuticals are designed to be stable and persistent to avoid their degradation before reaching the target organ. The persistence of ARVDs is likely to result in them being excreted either as metabolites or unchanged parent compounds as they are not completely metabolized in the body (Prasse et al., 2010). The excreted ARVDs reach the wastewater treatment plants (WWTPs) where the treatment process is not designed to entirely remove and eliminate them. The ARVDs are therefore continuously detected in wastewater influent and effluent, leading to their discharge into the surface water where they can be potentially transferred to drinking water (Kebede et al., 2020). The presence of ARVDs in water bodies threatens human health and the ecosystem as it could result in aqua-toxicity, genotoxicity and in pathogenic resistance (Beere et al., 2010, Morais et al., 2018). South Africa has the highest number of people infected by HIV which is about 7.9 million which is about 13.78 % of the country population. In addition, about 19.5 % of the infected people are in age of 15-49 (Govere-Hwenje et al., 2022). Among ARVDs, nevirapine, abacavir and efavirenz have been used as first line treatment against HIV virus which could result into their continual realize in the water source (Mbuagbaw et al., 2016, Afafe et al., 2018, Nibamureke et al., 2019). The continual detection of the ARVDs is due to the inefficiency of conventional methods to efficiently remove the ARVDs in wastewater treatment plants. Adsorption method has been the most prominent method used for adsorption of water contaminants due their design simplicity, low-cost maintenance and unlikely to generate by-products (Konig-Peter et al., 2014, Adrande et al., 2018). Activated carbon has been widely employed for the adsorption of various pollutants. However, it is costly and hard to regenerate, resulting in the impracticality of the adsorption process. Therefore, highly efficient and cost- effective methods are needed as alternative replacements for pollutants removal from the environment (Sotelo et al., 2013, Phele et al., 2019).

In the study conducted by Abdel-Rahman and co-workers (Abdel Rahman et al., 2017), the modification of the bio-adsorbent (*Delonix regia*) with an acid improved its ability to adsorb lead from water. The nanofibers were synthesized and applied on the removal of ARVDs and other pharmaceuticals in wastewater (Kebede et al., 2020). The current study therefore reports on the modification and application of macadamia nutshells as an effective and low-cost adsorbent for the removal of antiretrovirals (abacavir, efavirenz, nevirapine) from wastewater. Macadamia nutshell (MCN) was therefore selected as the bio-adsorbent for these ARVDs removal from wastewater because it has been reported to be supreme for the adsorption studies as it contains lignocellulosic characteristics which possess several functions which could interact with micropollutants (Morifi et al., 2022). South Africa is the third largest producer of macadamia nuts around the globe. Hence, the increase in the growth of macadamia plantations continuously leads to an increase in the accumulation of nut shells waste which is a concern in environment as it leads to environment water pollution (Vinet & Zhedanov et al., 2011, Morifi et al., 2022). The macadamia nutshells have fascinating features, like high percent of fixed carbon, high cracking pressure and possibility to be turned into fine powder, which improves its surface area. The macadamia nutshells are considered as residue without a proper destination in the nuts processing industries. Therefore, the success of this work will result in the reduction of waste by converting it into future valuable product, thus promoting a circular economy. To the best of our knowledge, these studies were conducted for the first time to assess macadamia nutshell for removal of ARVDs. Parameters such as time, pH, concentration, adsorbent mass and temperature were assessed to determine the ability of synthesized adsorbent to remove ARVDs. To evaluate adsorption process, adsorption mechanism and adsorption behaviour the kinetics models, isotherm models, and thermodynamics studies were investigated. To improve and activate the existing functional groups improve the removal of macadamia it would be modified with acid or base to activate the available function groups on its surface.

The physio-chemical properties of ARVDs of interest has an essential role on ability of the adsorbent to remove these compounds in aquatic environment. The lower the  $\log K_{ow}$  the higher the solubility vice versa. The  $pK_a$  than  $pH$  the compounds would hydrolyse and be found in their anionic form which could result to poor adsorption. The efavirenz is likely to have a high removal efficiency due to it has a low  $\log K_{ow}$  and lower solubility hence it is more likely to diffuse in water (Versteeg, 2014, Madikizela et al., 2016).

**Table 3.1: Physio-chemical properties and structure of nevirapine, abacavir and efavirenz**

Name	Structure	Log K <sub>ow</sub>	Solubility mg/L	Molecular units (g/mol)	pK <sub>a</sub>	Reference
Nevirapine		3.89	100	266.30	pK <sub>1</sub> =5.06	(Wood et al., 2015)
Abacavir		1.45	77	286.39	pK <sub>1</sub> =5.77	(Wood et al., 2015)
Efavirenz		4.15	10	315.68	pK <sub>1</sub> =12.52	(Wood et al., 2015)

## 3.2 Experimental

### 3.2.1 Chemical reagent

All the solvents used (acetonitrile, acetone, methanol, acetic acid, 0.1 M sodium hydroxide, 0.1 M hydrochloric acid) were of HPLC grade and purchased from Sigma Aldrich (Steinheim, Germany). The ARVDs standards of (nevirapine, abacavir, and efavirenz) were purchased from J&H Chemical Ltd (Hangzhou Zhejiang China).

### 3.2.2 Instrumentation

The analysis was done using Shimadzu Liquid Chromatography (LC 2020) from Shimadzu (Tokyo, Japan). The C<sub>18</sub> analytical column (3.0 μm × 4.6 μm × 150 μm ID) was employed for separation of the ARVDs with a temperature of 30°C. The gradient elution used was 0-2 minutes

(50 % ACN: 50 % H<sub>2</sub>O) and 3-20 minutes (70 % ACN:30% H<sub>2</sub>O). The photodiode array (PDA) was used for data acquisition at wavelengths of 225, 254, and 287 nm. The macadamia nutshell were ground using MRC SMM450 sample mill and sieved into 250 µm using King test VB 200/300 sieve shaker (DLD Scientific, Durban, South Africa). Once sample preparations were done, they were shaken using FMH SHKO 20 rotary orbital shaker (DLD Scientific, Durban, South Africa) at 150 rpm for 90 minutes.

### **3.2.3 Preparation of standards**

The stock solution was prepared by dissolving 10 mg of each ARVD compound in acetonitrile to make up a concentration of about 100 mg/L. The concentration range of (0.5 to 1.0 mg/L) from the stock solution was used for the calibration of the LC-PDA instrument.

### **3.2.4 Sampling and sample preparation**

The wastewater samples were collected during the summer season in the Darville wastewater treatment plant with coordinates -29,601°, -30.428° in Pietermaritzburg and Umbilo wastewater with coordinate -29.845°, -30.982° in Durban, South Africa. The samples were collected using a dark brown bottle and stored in a cooler box. Thereafter, the samples were transported to the laboratory refrigerated at a temperature of 4°C.

The macadamia nut shells were collected from Department of Agriculture in Hilton, Pietermaritzburg. They were rinsed with tap water and left to dry in an oven at 105°C overnight. The shells were then crushed and sieved through a 250 µm sieve shaker. The shell powder was then soaked in ultrapure water and agitated for 3 hours with a stir bar, followed by drying in an oven for 24 hours. Thereafter, 20 g of the powder was acid modified in 250 mL of 0.1 M HCl and then agitated at room temperature for 3 hours followed by vacuum filtration using Whatman filter paper 90 mm. The excess or unreacted HCl was rinsed with 10 mL of ultrapure water, and the powder was left to dry in an oven overnight (Ntuli et al., 2017) thereafter it applied in series of adsorption studies. The base-modified macadamia was prepared using the same procedure and replacing the 0.1M HCl with 0.1 M NaOH.

### 3.2.5 Batch of adsorption experiment

The experiments were done in triplicates ( $n = 3$ ) and blanks were also prepared. The experimental conditions optimized as follows; the adsorbent mass (2-10 mg), contact time (5-240 minutes), solution pH (2-10), ARVDs sample concentration (0.2-2.0 mg/L) and temperature (5-40°C). The amount of adsorbed ARVDs was obtained by ( $q_e$ ) at a time ( $q_t$ ) and the removal percentages (R.E%) were obtained equations (3.1), (3.2) and (3.3) respectively.

$$q_e = \frac{C_o - C_e}{m} \times V \quad (3.1)$$

$$q_t = \frac{C_o - C_t}{m} \times V \quad (3.2)$$

$$(R.E\%) = \frac{C_o - C_t}{m} \times 100\% \quad (3.3)$$

Where  $C_o$  is the initial concentration in (mg/L),  $C_e$  is the concentration at equilibrium (mg/L) whereas  $C_t$  is the concentration at a time at any given point, ( $m$ ) is the adsorbent mass (mg) and  $V$  is the amount of volume of the sample in (L)

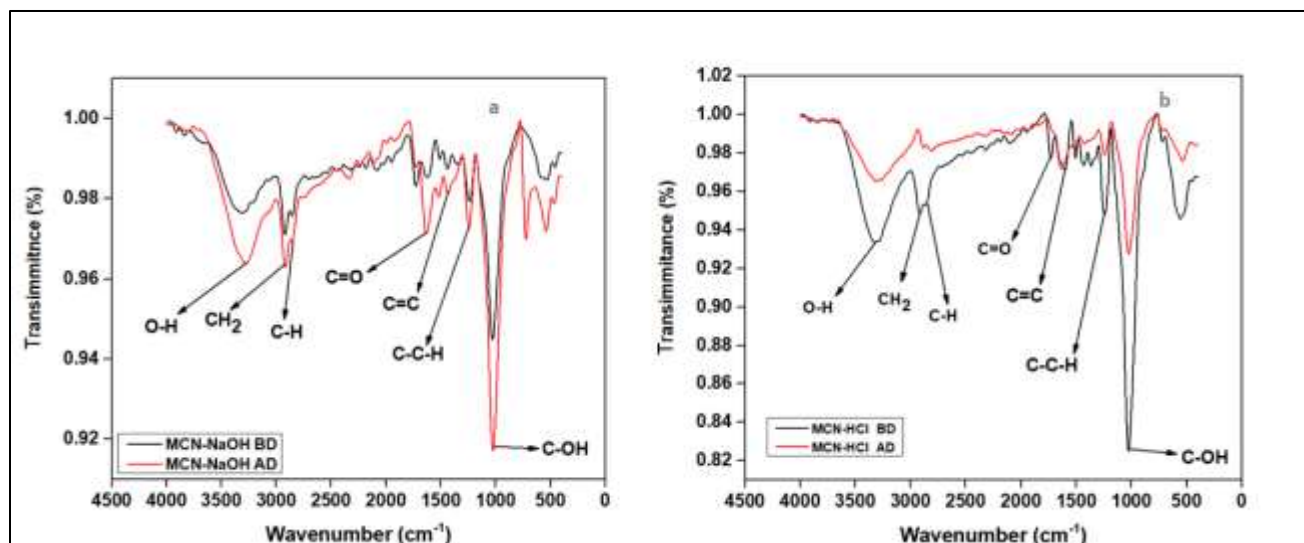
## 3.3 Results and Discussion

### 3.3.1 Fourier infrared spectroscopy (FTIR)

The FTIR was used for the identification of functional groups present in the adsorbents that could be responsible for interaction with ARVDs (Abdel Rahman et al., 2017). The acid-modified adsorbent showed a wide band around  $3330 \text{ cm}^{-1}$  which is ascribed to the O-H group before the adsorption process, which shifted to  $3311 \text{ cm}^{-1}$  after adsorption (**Figure: 3.1a**). The wide O-H functional group could be attributed to cellulose or hemicellulose from a plant material (Zhao et al., 2013). This was also observed in base-modified adsorbent whereby the wide band of the O-H group shifted from  $3341$  to  $3328 \text{ cm}^{-1}$  after adsorption (**Figure: 3.1b**). The increases intensity of the O-H band for base modification could be attributed to the addition of OH ions from sodium hydroxide to the existing OH stretch from the adsorbent. The shift in peak bands and decrease in intensity after adsorption confirms the participation of the functional groups in the interaction with ARVDs which resulted in their removal from water.

A weak vibration at  $1727 \text{ cm}^{-1}$  and  $1730 \text{ cm}^{-1}$  (**Figure 3.1a and 3.1b**) showed a carbonyl functional group (Jimoh et al., 2012). The presence of the peak at  $1433 \text{ cm}^{-1}$  and  $1512 \text{ cm}^{-1}$  (**Figure**

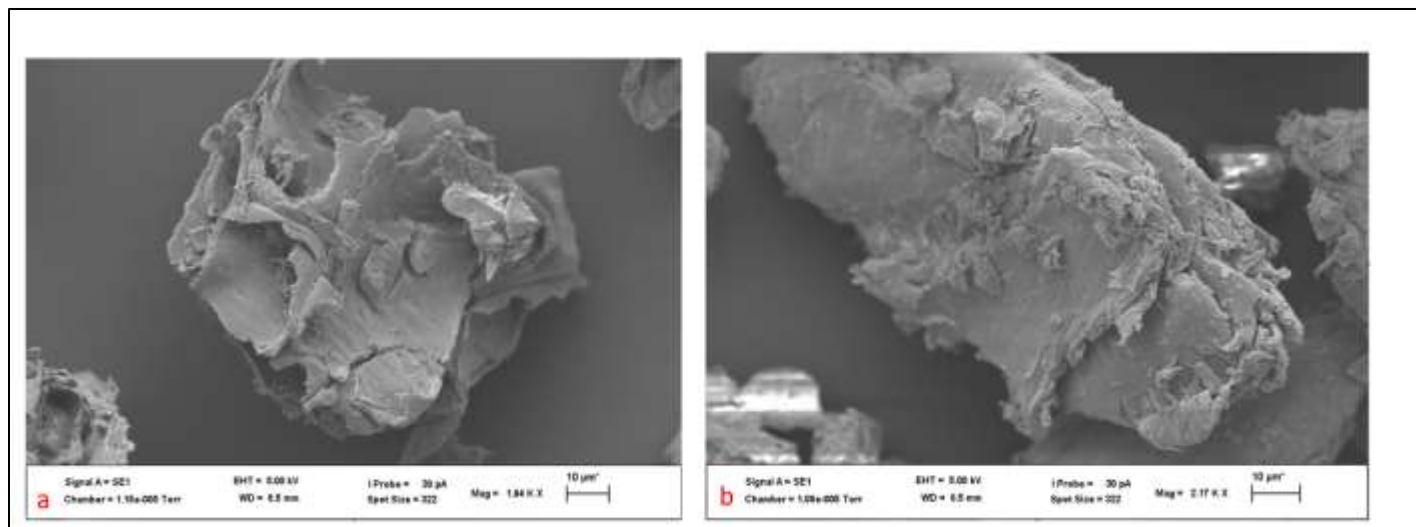
**3.1b)** is ascribed to CO, OH, and C-OH functional groups which shifted to 1426 and 1507 $\text{cm}^{-1}$  after adsorption. The bands around 1257 and 1247  $\text{cm}^{-1}$  were ascribed to a carboxylic acid whereas the bands around 1028 and 750  $\text{cm}^{-1}$  (**Figure 3.1a and 3.1b**) were an indication of C-OH on phenolic groups (Agarwal et al., 2016). All the wavelengths shift observed confirmed the participation of the functional in adsorbing the ARVDs from water.



**Figure 3.1:** FTIR spectra of activated macadamia MCN-NaOH (a) and MCN-HCl (b) adsorbent

### 3.3.2 Scanning electron microscope (SEM)

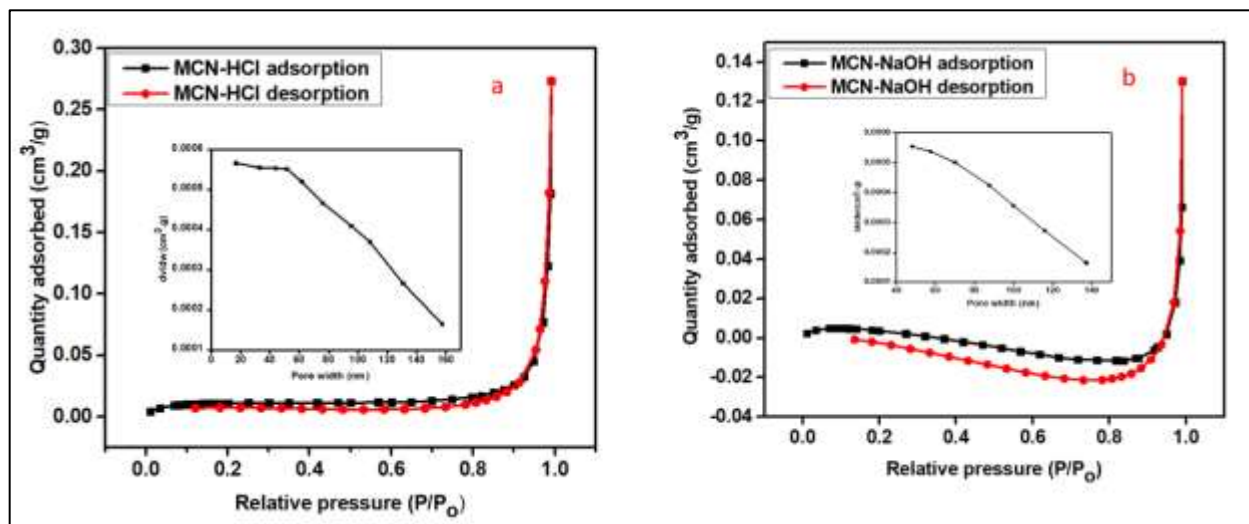
The SEM was used to observe the surface morphology of the adsorbents which gives information regarding surface texture, sample composition, and sample orientation (Ntuli et al., 2017). The surface of both acid and base-modified macadamia adsorbents showed a spherical opening and a multilayer long rod-folded structure that is typical of a plant cell (**Figure 3.2a and 3.2b**). The adsorbent also consists of a laminar surface with wrinkles and smaller abrasive layers which are similar to one that was reported by (Ntuli et al., 2017). The adsorbent produces a fine powder, but it was able to maintain its elongated structure which confirms that the sorbent kept its lignocellulose shape from a plant cell (Rincon-Silva et al., 2016). All the characteristics would assist the ability of the adsorbent to remove ARVDs in wastewater samples. Hence, the modification of the adsorbent is essential to activate the functional groups on the surface of the adsorbent which eventually improves its ability to remove the ARVDs in water samples.



**Figure 3.2:** SEM micrographs of the macadamia adsorbents modified with HCl (a) and NaOH (b) adsorbent.

### 3.3.3 Brunauer Emmett Teller (BET)

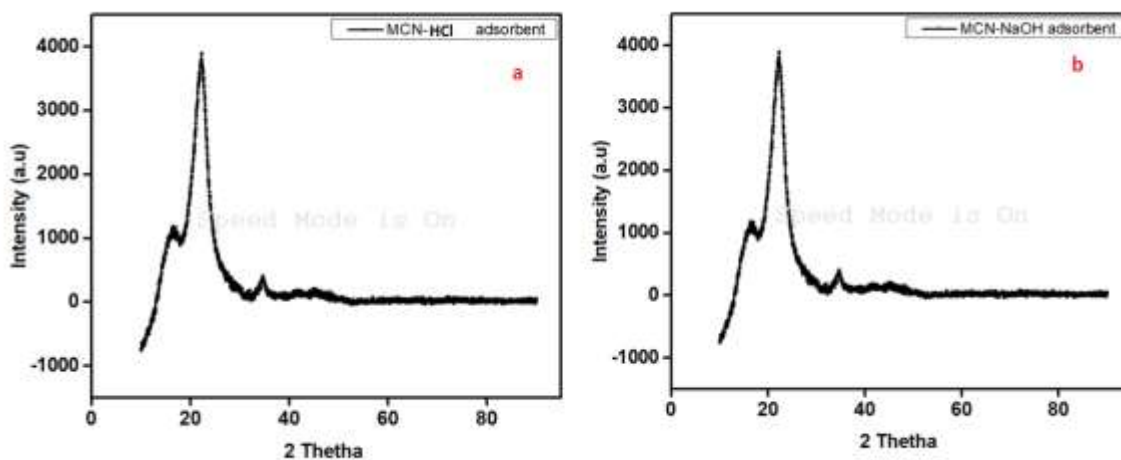
The BET analysis showed that the surface area, pore diameter, and pore volume were  $0.1180 \text{ m}^2/\text{g}$ ,  $27.989 \text{ nm}$ ,  $8.3 \times 10^{-5} \text{ cm}^3/\text{g}$ , respectively for base modified macadamia and  $0.7468 \text{ m}^2/\text{g}$ ,  $7.878 \text{ nm}$ , and  $1.47 \times 10^{-4} \text{ cm}^3/\text{g}$ , respectively for acid modified macadamia adsorbent. From this observation we can conclude that acid modified adsorbent had improved surface area compared to base modified. This observation is similar to one reported by (Nekhavambe et al., 2022). The  $\text{N}_2$  adsorption/desorption isotherms, indicated that both adsorbents exhibited a type-III isotherm (**Figure 3.3a and 3.3b**), which is mostly exhibited by crystalline materials (Yuen et al., 2008). Moreover, the acid-modified showed a closed loop whereas the base modified showed a semi-closed loop. The pore distribution of both adsorbents showed a rapid increase at relatively low pressure which is an indication of the presence of micropores with hysteresis loop found in medium relative pressure which are results of mesopores (Ma et al., 2019). These properties are essential for the ability of the adsorbent to remove the antiretrovirals from wastewater samples.



**Figure 3.3:** N<sub>2</sub> Adsorption/ desorption of the macadamia adsorbents modified with HCl (a) and NaOH (b), their corresponding pore size distribution.

### 3.3.4 Powder X-ray diffraction (PXRD) analysis

The X-rays diffraction showed major distinct peaks at  $2\theta = 17.45, 22.18,$  and  $34.48^\circ$ , and  $2\theta = 17.26, 22.74$  and  $34.68^\circ$  for acid and base modified macadamia sorbents, respectively (**Figure 3.4a and 3.4b**). These diffractions are an indication of native crystalline cellulose (C<sub>6</sub>H<sub>12</sub>O<sub>6</sub>), (Nekhavambe et al., 2022) which agrees to what was observed using SEM (**Figure 3.4a and 3.4b**). There are nor distinct differences observed on values of  $2\theta$  for both acid and base- modified adsorbents.

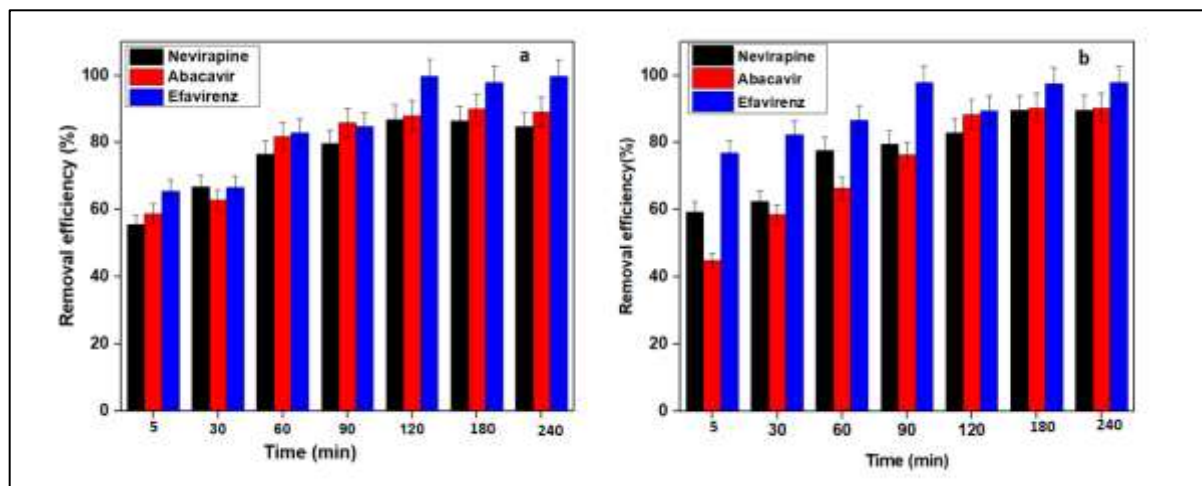


**Figure 3.4:** PXRD diffraction patterns for MCN-HCl (a) and MCN-NaOH (b) adsorbent

### 3.4. Batch of adsorption experiments

#### 3.4.1 Effect of contact time

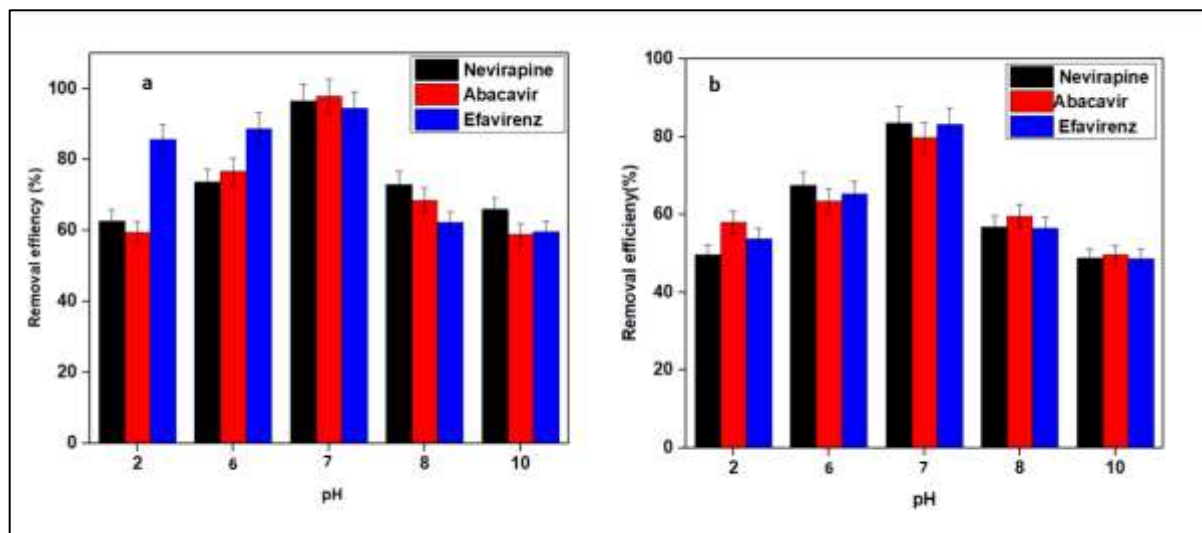
The effect of contact time was varied from (5 to 240 minutes). Both macadamia adsorbents modified with HCl and NaOH, the amount of the ARVDs removed increased with an increase in contact time, and equilibrium was reached at 90 minutes (**Figure 3.5a and 3.5b**). As a result, 90 minutes was considered the optimum time and was used throughout the experiments. This trend could be attributed to enough time for the ARVDs to interact with the available active sites on the surface of the adsorbent (Agarwal et al., 2016, Abdel Rahman et al., 2017). After the equilibrium, there is a reduction in the removal of ARVDs which could be a consequence of the saturation of active sites on the sorbent. The HCl-modified adsorbent had high removal efficiency. Nevirapine has two electron pairs on the nitrogen atoms in the pyridine aromatic structure which could lead to a possibility of covalent bonding or electrostatic interactions between the ARVD and the adsorbent. The adsorption energies of compounds increase with an increase in  $\pi$ -rings (Alnajrani & Alsageret et al., 2020). Resulting to many  $\pi$ -rings from pyrimidine and the attached imidazole in the nevirapine structure, there is a possibility of  $\pi$ - $\pi$  interactions, hydrophobic interaction, and H-bonding that will enhance the adsorption of abacavir by the functionalized adsorbents. However, efavirenz had high removal efficiency even at low contact time. The N-H functional group and  $\pi$  bonds in the chloro-benzene ring in efavirenz could facilitate  $\pi$ - $\pi$  interactions and hydrophobic interaction hence improving the adsorption of efavirenz. Moreover, efavirenz has a lower water solubility compared to the other investigated ARVDs thus it is likely to be removed faster (Adeola et al., 2021). The acid modified adsorbent illustrated an improved removal efficiency than the base modified adsorbent. This is attributed to high dominance of  $H^+$  ions, that protonate the negatively charged ions on the adsorbent surface and easily bind to ARVDs of interest which are nevirapine, abacavir and efavirenz, respectively.



**Figure 3.5:** Effect of contact time on the adsorption efficiency of the macadamia adsorbents modified with HCl (a) and NaOH (b). Adsorption conditions: sample pH - 7, adsorbent mass - 10mg, sample volume - 10 mL, initial concentration - 1.0 mg/L, agitation speed - 150 rpm.

### 3.4.2 Effect of pH

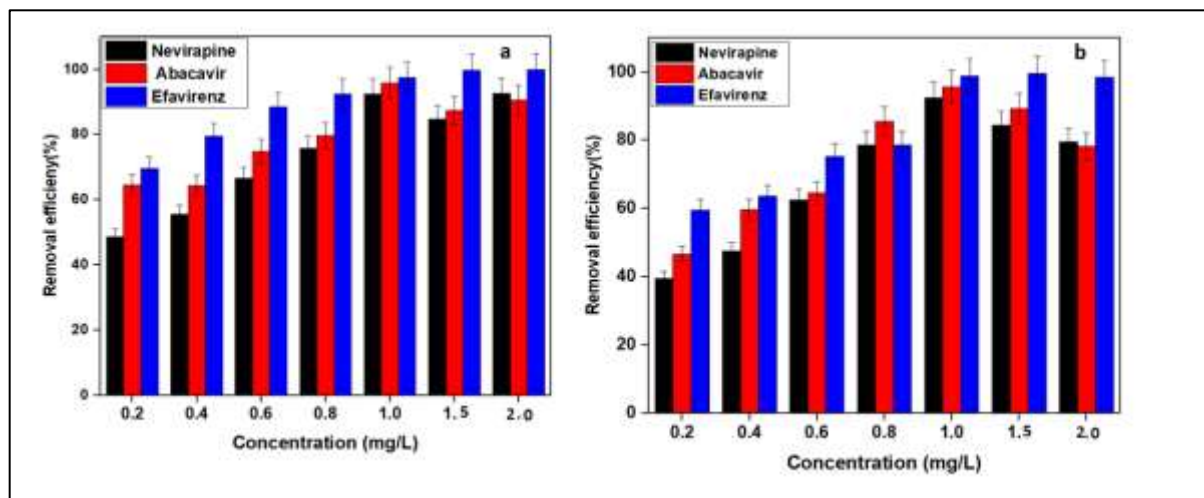
The influence of sample pH was assessed due to its ability to affect the surface properties as well as the ionic species of a solution and thus impact the adsorption efficiency (Budinova et al., 2009). The pH of the solution was varied from solution pH of 2 to 12. The removal efficiency of ARVDs increased as pH increased and reached an optimum at pH 7 units for nevirapine, abacavir, and efavirenz (**Figure 3.6a and 3.6b**). This attribute could be a consequence that surface charge density decreases with an increase in pH thus increase the rate of adsorption (Bhatti et al., 2012). The pKa values of nevirapine, abacavir and efavirenz was 5.06, 5.77 and 12.52, respectively. When observing this trend its evident that the pKa is high than pH. The consequence of that that the compounds are likely to protonate the negatively ions thus increasing in removal efficiency. After optimum pH of 7 there is a decrease in removal efficiency. The decrease in removal efficiency at a pH above 7 could be attributed to the dominance of OH<sup>-</sup> ions that could lead electrostatic repulsive forces from the negatively charged ions of adsorbents (Netpradit et al., 2003, Al-Degs et al., 2008, Jimoh et al., 2012).



**Figure 3.6:** Effect of sample pH on the adsorption efficiency of the macadamia adsorbents modified with HCl (a) and NaOH (b). Adsorption conditions: contact time 90 minutes, adsorbent mass - 10 mg, sample volume - 10 mL, initial concentration - 1 mg/L, agitation speed -150 rpm.

### 3.4.3 Effect of initial concentration

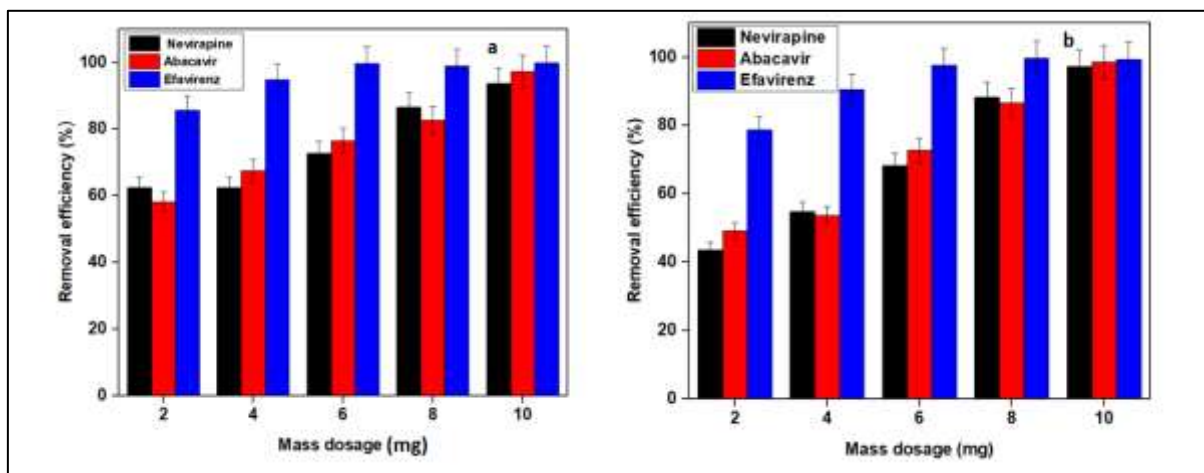
The effect of initial solution concentration on the removal efficiency of ARVDs varies between (0.2-2.0 mg/L). Initial solution concentration is an essential aspect to be considered to overcome the mass transfer resistance between aqueous media and solid phases (Bhatti et al., 2012). The increase in initial concentration increases the high possibility to overcome mass transfer resistance as a result it increases the removal efficiency (**Figure 3.7**). Moreover, the mass transfer driving forces enhance the adsorption of ARVDs target compounds. The increase in removal efficiency could be attributed to fast pore diffusion into intraparticle matrix combined with fast diffusion on external surface of the adsorbent which leads to rapid removal of target species in solution (Ho & Chiang et al., 2001). However, beyond the 1.0 mg/L concentration there was a decrease in removal efficiency which could be attributed to the saturation of active sites.



**Figure 3.7:** Effect of initial concentration on the adsorption efficiency of the macadamia adsorbents modified with HCl (a) and NaOH (b). Adsorption conditions: contact time – 90 minutes, adsorbent mass - 10 mg, sample volume - 10 mL, sample pH - 7, agitation speed -150 rpm.

### 3.4.4 Effect of mass dosage

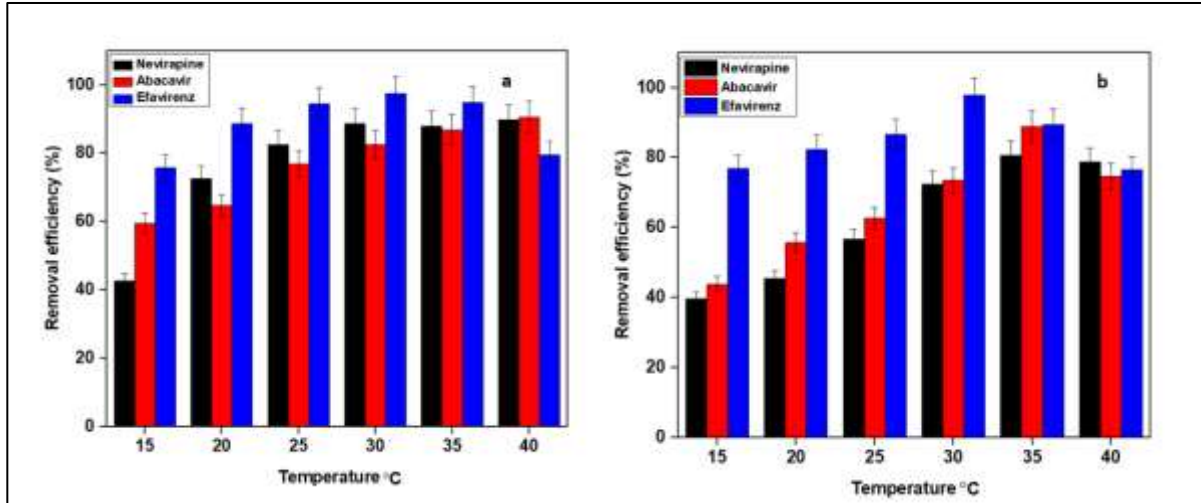
The effect of mass dosage of adsorbent was therefore investigated on both adsorbent between (2-10 mg). The removal efficiency of the adsorbent rapidly increased with an increase in mass dosage (**Figure 3.8a and 3.8b**). The observed trend could be due to that increasing in the availability of the active sites for ARVDs to be adsorbed. (Nekhavambe et al., 2022), reported a similar trend in the application of macadamia nutshell in fluorine bio-sorption and antimicrobials potency removal whereby an increase in macadamia nutshell adsorbent showed an increase in removal efficiency of fluoride adsorption. The highest removal efficiency was observed around 10 mg whereby all the target species showed results about 90 % , hence 10 mg was used for all subsequent experiments.



**Figure 3.8:** Effect of mass dosage on the adsorption efficiency of the macadamia adsorbents modified with HCl (a) and NaOH (b). Adsorption conditions: contact time – 90 minutes, initial concentration - 1 mg/L, sample pH -7, sample volume – 10 mL, agitation speed – 150 rpm

### 3.4.5 Effect of temperature

The influence of adsorption temperature was examined between (15-40°C). The removal efficiency gradually increases with an increase in temperature (**Figure 3.9a and 3.9b**). This observation indicated that ARVD molecules tend to move from the solid phase to the bulk phase with an increase in temperature which leads to an increase in removal efficiency. The high molecular weight of efavirenz could be a consequence of easily movement of the compounds from solid to bulk phase hence it has a high removal efficiency (Gupta et al.,1998, Ho & Chiang, 2001). This could be a consequence of an acceleration of existing slow adsorption steps or activation of some actives on the surface of the adsorbent (Hashem et al., 2007, Kebede et al., 2020).



**Figure 3.9:** Effect of temperature on the adsorption efficiency of the macadamia adsorbents modified with HCl (a) and NaOH (b). Adsorption conditions: contact time – 90 minutes, adsorbent mass - 10 mg in 10 mL, initial concentration – 1 mg/L, sample pH - 7, agitation speed – 150 rpm

### 3.5 Adsorption kinetics, Adsorption isotherms and Thermodynamics studies

#### 3.5.1 Adsorption kinetics

To understand the mechanism of adsorption, kinetic models such as the pseudo-first order, pseudo-second order (Salem & Akbari et al., 2011), and interparticle diffusion (Wang et al., 2012) were assessed using the equations (3.4), (3.5), and (3.6), respectively.

$$\ln(q_e - q_t) = \ln(q_e - K_1) \quad (3.4)$$

$$\frac{t}{q_e} = \frac{1}{K_2 q_e^2} + \frac{t}{q_e} \quad (3.5)$$

$$q_e = K_{id} t^{1/2} + C_i \quad (3.6)$$

where  $q_e$  (mg/g) is the amount adsorbed at equilibrium, and  $q_t$  (mg/g) amount of ARVDs in time  $t$  (min). Furthermore,  $K_1$  ( $\text{min}^{-1}$ ) and  $K_2$  ( $\text{g}(\text{min mg})^{-1}$ ) are rate constants of pseudo-first and pseudo-second-order,  $K_{id}$  ( $\text{mg}(\text{g}^{-1} \text{min}^{-1/2})$ ) is a diffusion rate constant and  $C_i$  is a boundary layer constant. The experimental data in (Figure 3.5) was fitted in these kinetic models and the results obtained are shown in Table 3.1. The slope, intercepts, and constant of the pseudo-first order and pseudo-second order model ( $K_1$  and  $q_e$ ) were obtained by plotting  $\log(q_e - q_t)$  vs  $t$ . Furthermore, the plot of  $q_t$  vs  $t$  gave the second order rate constant ( $K_2$ ) whereby  $q_e$  was calculated by slope of Eq.(3.5).

The correlation of pseudo-first-order ( $R^2 = 0.872-0.994$ ) and pseudo second-order ( $R^2 = 0.940-0.996$ ) kinetics possess high correlation coefficients value for both acid and base modified adsorbents. However, the  $q_{e,cal}$  and  $q_{e,exp}$  for acid and basic modified were close to each other in the second order which is an indication that the experimental data is well described pseudo-second-order kinetic model. This behaviour could be an indication that the pseudo second-order is the rate-determining in the adsorption of ARVDs. Although the experimental data fitted well in the pseudo-second-order model, that could not fully describe the adsorption mechanism of target compounds.

Therefore, to mitigate this limitation the intraparticle diffusion model was employed which indicates a rate-determining step if a plot of  $q_t$  vs  $t^{1/2}$  yields a straight line. The intraparticle diffusion was calculated using Eq. (3.6) where  $K_1$  is the intraparticle diffusion constant ( $\text{g/mg min}$ ) and  $(C_i)$  is an intercept of the plot which reflects on surface adsorption. When fitting the kinetic data, it was observed that the plot did not pass through the origin, which is an indication that intraparticle diffusion is not the only rate-determining step, there could be a possibility of other kinetic model that operating on adsorption process simultaneously.

**Table 3.1: Adsorption kinetics adsorption of ARVDs**

	Parameters	MCN					
		Nevirapine		Abacavir		Efavirenz	
		HCl-modified	NaOH-modified	HCl-modified	NaOH-modified	HCl-modified	NaOH-modified
First -order	$q_e(\text{mg g}^{-1})_{\text{exp}}$	23.76	18.89	31.68	24.87	49.36	18.89
	$q_e(\text{mg g}^{-1})_{\text{cal}}$	20.76	16.87	35.57	18.87	58.36	13.67
	$K_1 (\text{min}^{-1})$	0.0321	0.0004	0.0406	0.0005	0.0320	0.0005
	$R^2$	0.994	0.925	0.979	0.962	0.946	0.872
Second-order	$q_{e2}(\text{mg g}^{-1})$	22.16	16.80	29.16	21.004	55.16	17.396
	$K_2 (\text{min}^{-1})$	0.0113	0.2571	0.0198	0.0079	0.0326	0.1153
	$R^2$	0.996	0.992	0.998	0.940	0.972	0.990
Intra-particle	$K_{\text{diff}}(\text{mg}(\text{g}^{-1} \text{min}^{-1/2}))$	8.793	0.9194	0.2879	0.8914	0.6855	0.9653
	$C(\text{mg g}^{-1})$	3.767	6.6960	2.866	4.0015	10.885	4.0518
	$R^2$	0.997	0.9573	0.882	0.9902	0.990	0.989

### 3.5.2 Adsorption studies

To investigate the concentration of the adsorbate and the number of ARVDs adsorbed on the surface of the adsorbent, Adsorption isotherms models which were Langmuir and Freundlich, Temkin were explored. The Langmuir model was assessed using equation (3.7) (Treated & Studies et al., 2011).

### 3.5.3 Adsorption studies

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$$\frac{C_e}{q_e} = \frac{1}{q_e K} + \frac{C_e}{q_m} \quad (3.7)$$

where ( $q_e$  is adsorption capacity at equilibrium (mg/g),  $C_e$  is the concentration at the equilibrium of antiretroviral (mg/L),  $q_m$  is the maximum theoretical capacity (mg/g) and  $K$  (L/mg) is the Langmuir constant that correlates to the binding sites. The constant of Langmuir is obtained by plotting the slope and the intercept of the plots which are  $1/q_e$  versus  $1/C_e$ . The Freundlich model was calculated using equation (3.8), (Agarwal et al., 2016).

$$\log q_e = \log K_F + \frac{1}{n} \log C_e \quad (3.8)$$

In this instance,  $K_f$  is the Freundlich constant whereas  $n$  is the constant that gives the heterogeneity degree of surface sites. The constant could be obtained through the slope and intercept of the plot of  $\log q_e$  against  $\log C_e$ . The Temkin model was described using equation (3.9), (Oladoja et al., 2008).

$$q_e = B \ln K T + B \ln C_e \quad (3.9)$$

The Langmuir and Freundlich isotherms equilibrium constants and other parameters of the isotherms are shown in (**Table 3.2**). The results obtained showed that the Langmuir equilibrium constant ( $R_L$ ) is greater than zero and less than one, which indicates the favourability of the adsorption and a strong affinity between the adsorbate and adsorbent (Kebede et al., 2020). The value of heterogeneity factor  $1/n$  indicates that Freundlich is favourable where the adsorption mechanism displayed highly curved isotherms ( $1/n > 0.70$ ) and normal isotherms ( $1/n < 0.70$ ). The normal isotherm was the most common isotherm in the adsorption process of the selected ARVDs.

However, the  $q_{e\text{call}}$  and  $q_{e\text{exp}}$  of the Langmuir were closer to each other thus it can be concluded that the adsorption of ARVDs is consistent with the Langmuir model. The consistency of the Langmuir model suggests that the adsorption occurred on a homogenous surface. These findings are similar to a report whereby *Plantaus orientalis* leaves were used to adsorb p-nitrophenol in wastewater (Ma et al., 2019). Temkin model showed  $R^2$  greater than 0.997 for nevirapine and abacavir whereas efavirenz had  $R^2$  less than 0.957.

**Table 3.2: Adsorption isotherms Langmuir, Freundlich, and Temkin for analysis of ARVDs**

		HCl-modified	NaOH-modified	HCl-modified	NaOH-modified	HCl-modified	NaOH-modified
Langmuir	$q_{\text{max}}$ (mg/g)exp	26.54	8.56	34.56	10.85	36.58	15.56
	$q_{\text{ex}}$ (mg/g)cal	27.44	10.79	35.52	14.25	38.17	20.79
	$K_L$ (L mg <sup>-1</sup> )	0.253	0.090	0.235	0.038	0.075	0.005
	$R_L$	0.790	0.236	0.590	0.203	0.970	0.923
	$R^2$	0.999	0.944	0.997	0.902	0.979	0.994
	1/n	0.215	0.134	0.174	0.739	0.223	1.032
Freundlich	$K_F$ (L mg <sup>-1</sup> )	2.25	5.45	2.54	4.35	0.088	1.342
	$R^2$	0.997	0.887	0.997	0.890	0.998	0.908
Temkin	KT (g/L)	12.99	8.79	9.670	6.931	4.490	2.231
	B	61.89	31.58	63.79	45.56	62.27	29.86
	$R^2$	0.999	0.905	0.933	0.915	0.967	0.872

### 3.5.4 Thermodynamic studies

The spontaneity and the feasibility of adsorption of antiretrovirals can be studied through calculations of thermodynamic parameters such as Gibbs free energy change  $\Delta G^\circ$ , enthalpy change  $\Delta H^\circ$ , and entropy change  $\Delta S^\circ$ . The variation of temperature with a distribution coefficient  $D$  could be used to make thermodynamic parameters using equation (3.10).

$$D = \frac{C_e}{q_e} \quad (3.10)$$

$$\ln D = \frac{\Delta S^\circ}{R} + \frac{\Delta H^\circ}{RT} \quad (3.11)$$

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ \quad (3.12)$$

where  $q_e$  is the number of antiretrovirals adsorbed by the adsorbent (mg/g) at equilibrium, and  $C_e$  is the equilibrium concentration of antiretrovirals in (mg/L). The  $\Delta H^\circ$ ,  $\Delta S^\circ$ , and  $\Delta G^\circ$  can then be calculated according to equations (3.11) where  $R$  is a gas constant (8.314 J/mol K),  $T$  is the absolute temperature (K),  $\Delta H^\circ$  and  $\Delta S^\circ$  could be obtained from the slope and intercept of  $\Delta G^\circ$  vs  $1/T$ . The thermodynamics studies were conducted by varying temperatures from (288, 298, 303, 313, and 333 K).

**Table 3.3** shows  $\Delta G^\circ$ ,  $\Delta H^\circ$  and  $\Delta S^\circ$  values obtained from a plot of  $\ln K_c$  vs  $t^{-1}$  and other parameters. The value of  $\Delta G^\circ$  was found to be negative and showed to be increasing as the temperature increases which signifies that the adsorption process is spontaneous and thermodynamically favoured. The negative values of  $\Delta H^\circ$  and positive  $\Delta S^\circ$  indicated that the adsorption process was exothermic in nature and ARVDs-adsorbent indicated an increase in irregular randomness. Furthermore,  $\Delta H^\circ$  values for both adsorbents showed that nevirapine and abacavir followed chemisorption model (40-620 kJ mol<sup>-1</sup>) while efavirenz followed physisorption (5-40 kJ mol<sup>-1</sup>), (Ntuli et al., 2017). The base modified adsorbent showed to be more spontaneous due to rapid increase in a magnitude of  $\Delta G^\circ$  upon rising temperature for ARVDs.

**Table 3.3: Thermodynamic studies for acid and base adsorbent for adsorption of ARVDs**

T (K)		$\Delta G^\circ$ (kJ mol <sup>-1</sup> )					$\Delta H^\circ$	$\Delta S^\circ$	R <sup>2</sup>
		288	298	303	313	333	(kJmol <sup>-1</sup> )	(Jmol <sup>-1</sup> k <sup>-1</sup> )	
Nevirapine	HCl	-11.46	-11.80	-11.97	-12.32	-13.02	-144.33	3.48	0.947
	NaOH	-77.22	-76.61	-80.20	-82.45	84.98	-86.62	23.91	0.947
Abacavir	HCl	-46.45	-47.77	-48.43	-49.73	-52.35	-88.35	1.31	0.995
	NaOH	-61.34	-63.02	-65.54	68.89	-70.35	-130.10	1.68	0.997
Efavirenz	HCl	-6.24	-8.50	-13.77	-11.09	-11.77	-9.52	23.67	0.983
	NaOH	-34.43	-34.50	-34.60	-34.75	-34.87	-32.43	29.46	0.998

HCl - acid modified macadamia adsorbent.

NaOH - base modified macadamia adsorbent

### 3.5.5 The effect of adsorbent modification on the antiretroviral drugs removal efficiency

The optimized conditions from the study were applied for the removal of ARVDs in wastewater samples their removal efficiency was compared between raw macadamia nut shells adsorbent, and acid modified, and base modified macadamia adsorbents as illustrated by (Table 3.4). The initial concentration of wastewater samples was 1 ppm The unmodified macadamia adsorbent showed to have lower removal efficiency indicating that chemical modification influences the adsorbent's efficiency to remove the ARVDs. This observation could be attributed to inactivated functional groups on the surface of the unmodified adsorbents which plays crucial role in adsorption mechanisms, thus enhances the removal of the target compounds in water samples.

The higher removal efficiency was observed on the effluent water sample compared to the influent sample. This observation could be a consequence of competition of pollutants on the active sites due to matrix effects (Kebede et al., 2020). The matrix effect may lead to either a loss or an enhancement in the efficiency of ARVDs removal from wastewater samples. Both raw and base modified illustrated some of degree of adsorption however, it evident that acid had high removal efficiency.

**Table 3.4: Effect of unmodified adsorbent macadamia for removal of ARVDs**

Target compounds	Modified MCN-HCl q <sub>e</sub> (mg/g)	Modified MCN- NaOH q <sub>e</sub> (mg/g)	Raw MCN q <sub>e</sub> (mg/g)
Nevirapine	94.41	88.56	62.43
Abacavir	88.84	78.63	69.87
Efavirenz	83.06	79.56	43.67

### 3.6 Conclusion

In this study, macadamia nutshell was successfully modified and applied as an easily accessible and low-cost adsorbent for the removal of ARVDs in real samples. The characterization of the adsorbents showed functional group such as C=C, C-OH for both acid and base modified. The obtained functional were essential for facilitation of electrostatic interaction,  $\pi$ - $\pi$  interaction which promoted the removal of ARVDs of interest. The optimum conditions were a contact time of 90 minutes, pH 7, initial concentration 1.0 mg /L, adsorbent mass 10 mg. The macadamia nutshell modification was essential as it improved the adsorption capacity of the adsorbent before it was applied to water samples. The optimum removal efficiency of the target compounds from the optimized method ranged from (69.64-96.32 mg/g). From the obtained results evident that macadamia nutshell was an excellent adsorbent for removal of ARVDs wastewater samples. The kinetic data fitted better on the second order compared to the first-order. The experimental data showed that the Langmuir model was more favourable. Temkin model had  $R^2$  close to 1 which indicated that there was a strong affinity between adsorbate and adsorbent. The thermodynamic studies showed that ( $\Delta H^\circ$ ) negative and ( $\Delta S^\circ$ ) were negative indicating that the adsorption process was exothermic, and an irregular randomness drove ARVDs-adsorbent interaction. Generally, the acid modified macadamia became a low-cost and effective adsorbent for the removal of selected ARVDs in water samples.

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## Chapter Four

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### **Exploration of *Platanus acerifolia* Leaves on the adsorption of abacavir, efavirenz and nevirapine from wastewater: adsorption kinetics, isotherm, and thermodynamic studies.**

#### **Abstract**

An increase in pharmaceuticals production and formulation, patient use, use in food production and improper disposal of expired or unused drugs has led to frequent detection of pharmaceuticals drugs including antiretrovirals (ARVDs) in the environment. This detection of ARVDs has become an emerging concern due to the threat it possesses to human and the environment. The current study therefore explored modified *Platanus acerifolia* leaves (London plane ) as an easily accessible and low-cost adsorbent for removal (ARVDs) (nevirapine, abacavir and efavirenz) in wastewater. The *Platanus acerifolia* adsorbent showed N-H, O-H and C=O functional groups when characterized using FTIR. SEM analysis showed flaky-folded semi-circle with porous microstructure for both base and acid modified *Platanus acerifolia* adsorbents. The PXRD technique revealed major peaks of  $2\Theta = 18.26, 23.86, 36.44^\circ$  for base modified whereas acid modified showed  $2\Theta = 18.26, 23.44$  and  $36.33^\circ$  which are ascribed to native crystalline structure. The BET analysis showed surface area of  $1.14 \text{ m}^2/\text{g}$ , pore volume  $0.0024 \text{ cm}^3/\text{g}$  and pore diameter  $4.09 \text{ nm}$  for base modified. Moreover, acid modified has surface  $3.83 \text{ m}^2/\text{g}$ , pore volume  $0.039 \text{ cm}^3/\text{g}$  and pore diameter  $8.45 \text{ nm}$ . The optimum adsorption conditions were contact time of 90 minutes, pH 7 concentration  $1.0 \text{ mg/L}$ , mass dosage of 10 mg. Pseudo-second-order was better fitted the kinetic data. The adsorption was observed to follow the Langmuir model since the  $q_e \text{ cal}$  and  $q_e \text{ exp}$  were found to be closer to each other on both acid and base modified adsorbents. Thermodynamic studies showed that the adsorption process was spontaneous since  $\Delta H^\circ$  was found to be negative, and the observed positive  $\Delta S^\circ$  implies that the adsorption is exothermic in nature.

**Keywords:** pharmaceuticals, antiretrovirals, low-cost, kinetics, isotherm, thermodynamics

## **4.1 Introduction**

### **4.1.1 Antiretroviral drugs (ARVDs)**

Antiretrovirals (ARVDs) are curative pharmaceuticals compounds which are primarily employed for the treatment against human immunodeficiency virus type-1 (HIV-1), (P. Kunene et al., 2022, Ncube et al., 2018). The virus increases the vulnerability or susceptibility to various infections and diseases by attacking the CD4-T cells whose main aim is to provide body with immunity in numerous diseases and infections (Gökengin et al., 2016) diseases and infections (Gökengin et al., 2016, Ngumba et al., 2016). Even though the HIV virus is not completely removed by the ARVDs, it is prevented from further replication which leads to the improvement of life expectancy (Ncube et al., 2018). However, the ARVDs are partially metabolized in the body upon being administered, resulting to their excretion with urine and faecal waste. Subsequently through engineered sanitation systems they are able to enter into wastewater treatment plants (WWTPs) which is a main supplier of water for domestic and commercial practices, (Tambosi et al., 2010). The hospital influents, municipal waste, domestic use, and improper disposal of expired drugs, also contributes towards the ARVDs reaching the WWTPs. Therefore, the presence of ARVDs have been constantly detected in wastewater influents and effluents (Wood et al., 2015, Kebede et al., 2020, Adeola et al., 2021) surface water (Freitas & Radis-Baptista., 2021), ground water (Liu et al., 2020), and drinking water. The frequent detection the ARVDs in these sources continues to raise concern with regards to their potential impact on the environment and public health systems. The adverse effects likely to be caused by ARVDs presence in water include potential antimicrobial resistance, alteration of physiology in amphibians, toxicity to aquatic fauna, endocrine disruptions, and cancer prevalence in humans (De Andrade et al., 2018, Morais et al., 2018, Freitas & Radis-Baptista et al., 2021).

As a result of the frequent detection of ARVDs in wastewater effluents, the WWTPs have been identified as one of the main sources of environmental pollution by these emerging pollutants. This indicates the ineffectiveness of current and existing methods in wastewater treatment to remove these compounds. Therefore, there is an urgency to develop efficient and affordable methods that can be utilized to remove ARVDs from water sources. Consequently, the efficient removal of pharmaceutical compounds in water bodies require innovative methods such as adsorption (Phele et al., 2019). Several studies have been explored for the removal of ARVDs from water which

include the use of nanofibers (Kebede et al., 2020), the activated carbons like graphene (Adeola et al., 2021). However these methods are not green and eco-friendly methods. On the other hand, there is an increasing interest on the development of greener adsorbents that will not generate toxic by-products that resulting to more adverse environmental effects (Ngumba et al., 2016). Even though the HIV virus is not completely removed by the ARVDs, it is prevented from further replication which leads to the improvement of life expectancy (Ncube et al., 2018). However, the ARVDs are partially metabolized in the body upon being administered, resulting to their excretion with urine and faecal waste. Subsequently through engineered sanitation systems they are able to enter into wastewater treatment plants (WWTPs) which is a main supplier of water for domestic and commercial practices, (Tambosi et al., 2010). The frequent detection of the ARVDs in these sources continues to raise concern with regards to their potential impact on the environment and public health systems. The adverse effects likely to be caused by ARVDs presence in water include potential antimicrobial resistance, alteration of physiology in amphibians, toxicity to aquatic fauna, endocrine disruptions, and cancer prevalence in humans (DeAndrade et al., 2018, Morais et al., 2018, Freitas & Radis-Baptista et al., 2021).

As a result of the frequent detection of ARVDs in wastewater effluents, the WWTPs have been identified as one of the main sources of environmental pollution by these emerging pollutants. This indicates the ineffectiveness of current and existing methods in wastewater treatment to remove these compounds. Therefore, there is an urgency to develop efficient and affordable methods that can be utilized to remove ARVDs from water sources. Consequently, the efficient removal of pharmaceutical compounds in water bodies require innovative methods such as adsorption (Phele et al., 2019). Several studies have been explored for the removal of ARVDs from water which include the use of nanofibers (Kebede et al., 2020), the activated carbons like graphene (Adeola et al., 2021). However these methods are not green and eco-friendly methods. On the other hand, there is an increasing interest on the development of greener adsorbents that will not generate toxic by-products that resulting to more adverse environmental effects.

Accordingly, the vegetal mass (roots, rice husk, wood, seeds, and leaves) has been explored as a promising greener source of materials for the adsorption of pharmaceuticals from aqueous samples (Sharma et al., 2011, Phele et al., 2019). The current study therefore seeks to explore *Platanus acerifolia* leaves (London Plane ) as an adsorbent for adsorption of efavirenz, abacavir, and nevirapine from wastewater.

The *Platanus acerifolia* leaves commonly known as the king of the street's trees, is a widely planted tree especially in urban landscape across the globe, producing larger amount deciduous leaves in winter and autumn, which accumulate a lot of waste (Liu et al.,2020). Currently, the deciduous leaves are eliminated as landfill which could lead to environmental pollution and groundwater eutrophication. The *Platanus acerifolia* has been reported to have numerous flavonoid compounds such kaempferol, luteolin, pitot granuloma, etc., (Yang et al., 2013).

Furthermore, there are other flavanols, chalcones and phenolcarboxylic acids which exhibit various levels of bioactivity (Creuzet et al., 1988). These compounds have a high dominance of de-localised, complete  $\pi$ - conjugated system and strong coordinate oxygen atoms, with a spatial configuration to form chelating agents with target compound (Valko et al., 2006, Yang et al., 2022). The high dominance of  $\pi$ -conjugated systems led to  $\pi$ - $\pi$  interaction that enhances the removal of ARVDs in wastewater samples. In addition, the presence of strong coordinate of oxygen could result to hydrogen bonding and electrostatic attractive interaction which are essential for water pollutants removal. *Platanus acerifolia* leaves have been explored as an adsorbent for removal of methylene blue (Pathania et al., 2017, Peydayesh, Rahbar-Kelishami et al., 2015). On the other hand, biochar derived from *Platanus acerifolia* leaves has been able to remove about 96.34 % of ibuprofen in wastewater samples (Yang et al., 2022).

South Africa has a wide spread of *Platanus acerifolia* plantations whereby about 20 to 60 % of leaves are shed down resulting to large municipal solid waste (Swart & Wingfield et al., 2014). Therefore, on the success of this current study will result in the conversion of *Platanus acerifolia* leaves waste into future valuable product, while promoting eco-friendly environment. The *Platanus acerifolia* leaves were modified with acid or base with the aim of improving their adsorptive capacity which was then assessed by conducting adsorption kinetics, isotherm, and thermodynamics studies. To the best of our knowledge the adsorption of ARVDs in wastewater was explored with this type of adsorbent for first time in this study. This work will therefore contribute towards increasing knowledge, while its closes the existing gaps within the field.

**Table 2.1** in **Chapter 2** shows the ARVDs of interest and their physio-chemical properties that explored for removed by *Platanus acerifolia* leaves adsorbent.

## **4.2 Experimental procedure**

### **4.2.1 Chemicals and Standards**

Solvents such as acetonitrile and 0.1M hydrochloric acid were purchased Merck (Darmstadt, Germany). Acetonitrile (HPLC grade) was purchased in Sigma-Aldrich (Stenheim, Germany). The ARVDs standards (abacavir, efavirenz, nevirapine) were purchased from J & H Chemical Ltd (Hangzhou Zhejiang, China).

### **4.2.2 Sampling areas**

*Platanus acerifolia* leaves were collected from the University of KwaZulu-Natal in Pietermaritzburg campus (South Africa) in August 2022. The leaves were hand-picked and stored in a brown card box at room temperature. The wastewater was sampled in summer season in Mhlathuzana with GPS coordinate -30.307°, -30.997° and Amanzimtoti wastewater treatment plant whereby the GPS coordinate -30.007°, -30.917°, whereby both effluent and influent were collected. The sample were collected in dark brown bottles, stored in a cooler box with ice. The samples were then transported to the laboratory where they were stored in the refrigerator 4°C. The sample were collected in triplicates to get a fully representation of the studied area

### **4.2.3 Sample preparation**

The *Platanus acerifolia* leaves were washed with tap water and left to dry overnight at a temperature of 25 °C. The leaves were grinded to produce to a fine powder and sieved at a 250 µm. The fine powder was soaked in ultrapure water and agitated for 3 hours with continuous stirring, thereafter, left to dry in oven overnight at a temperature of 105 °C. A 20 g portion of fine powder of the *Platanus acerifolia* leaves was modified whereby 0.1 M of HCl (10 mL) was added and then filled with ultrapure water to make up 250 mL. This was agitated for about 3 hours and thereafter, filtered with Whatman filter paper 90 mm. The unreacted 0.1 M of HCl was washed with 10 mL of ultrapure water and the fine powder was left to dry in the oven at 105 °C for 24 hours

The *Platanus acerifolia* leaves were grinded using MRC SMM450 sample mill and sieved into 250  $\mu\text{m}$  using King test VB 200/300 sieve shaker (DLD Scientific, Durban, South Africa). Once sample preparation was done there were shaken using FMH SHKO 20 rotary orbital shaker (DLD Scientific, Durban, South Africa) at 150 rpm for 90 minutes.

#### **4.2.4 Instrumentation**

Shimadzu Liquid chromatography mass spectrometry with Shim-Pack GIST C18 column (3.5  $\mu\text{m}$   $\times$  4.6 mm  $\times$  150 mm ID) purchased from Tokyo, Japan was utilized for the analysis of ARVDs. The column temperature was kept at 30°C. The LC-MS in gradient elution method employed was 0-2 minutes (50 % ACN: 50 % H<sub>2</sub>O) and 3-20 minutes (70 % ACN: 30 % H<sub>2</sub>O). The effect of wavelengths was investigated at 225, 254, and 287 nm.

#### **4.2.5 Preparation of standards**

The standards with a concentration range of 0.2 to 2.0 mg/L were prepared from the stock solution and used to calibrate the Liquid Chromatography Photodiode-Array (LC-PDA) instrument. A stock solution was made through dissolving of 10 mg of ARVDs (nevirapine, abacavir and efavirenz) to make a 100 mg/L concentration.

#### **4.2.6 Batch of adsorption experiment**

The adsorption capacity of the functionalized *Platanus acerifolia* leaves for ARVDs was investigated in a series of adsorption experiments. The adsorption parameters investigated were contact time (5-240 min), solution pH (2-10), and mass dosage (2-10 mg), concentration (0.2 -2.0 mg/L) and temperature (5-40°C). The experiments were done in triplicates (n =3) and blanks were also prepared. The amount of adsorbed ARVDs was obtained by ( $q_e$ ) at a time ( $q_t$ ) and the removal percentages (R.E%) were obtained equations (4.1), (4.2) and (4.3) respectively.

$$q_e = \frac{C_o - C_e}{m} \times V \quad (4.1)$$

$$q_e = \frac{C_o - C_t}{m} \times V \quad (4.2)$$

$$(R. E\%) = \frac{C_o - C_t}{m} \times 100\% \quad (4.3)$$

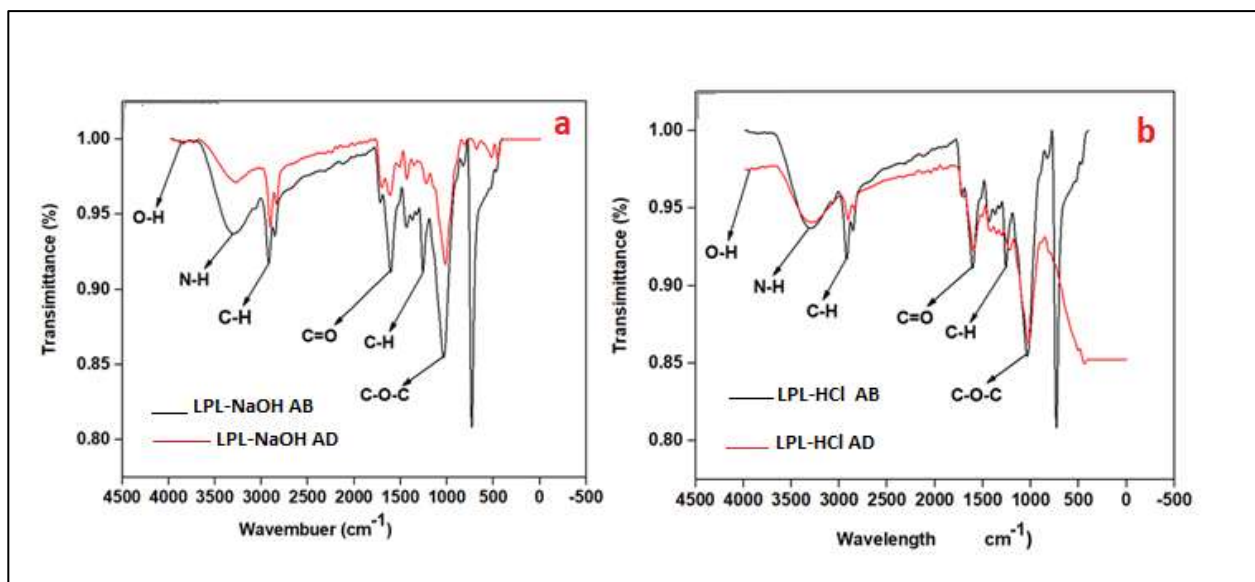
Where  $C_o$  is the initial concentration in (mg/L),  $C_e$  is the concentration at equilibrium (mg/L) whereas  $C_t$  is the concentration at a time at any given point, (m) is the adsorbent mass (mg) and V is the amount of volume of the sample in (mL).

## 4.3 Results and Discussion

### 4.3.1 Fourier infrared spectroscopy (FTIR)

The FTIR technique was used to identify the functional groups present in the modified *Platanus acerifolia* leaves adsorbent, which have a potential to adsorb the antiretrovirals in wastewater. For a base modified material (before adsorption) a broad band around  $3283.52 \text{ cm}^{-1}$  is ascribed to N-H stretching peak of hydrogen bond in the materials (**Figure 4.1**) (Kutbay & Akfirat., et al 2015). After adsorption it was observed that the wavenumber of band decreases to  $3277.34 \text{ cm}^{-1}$  as well as its intensity. A similar observation was evident in the acid modified whereby the broad band  $3465.23 \text{ cm}^{-1}$  showed a decrease in wavenumber of  $3374.35 \text{ cm}^{-1}$  and intensity. The shifts in the intensity of functional groups could be attributed to the interaction between the adsorbents and ARVDs which could lead to their removal (Liang et al., 2010). A very weak band around  $3672.67 \text{ cm}^{-1}$  corresponds to a stretching vibration of an O-H stretching bent vibration of the material, hydrogen bonded intermolecular alcohol. A sharp peak around  $2965.45 \text{ cm}^{-1}$  ascribed to stretching vibration of C-H in a methyl group. The peak found around  $1721.30 \text{ cm}^{-1}$  and  $1729.47 \text{ cm}^{-1}$  for base and acid correspond to carbonyl functional group. A weak peak located around  $1443.12$  and  $1364.70$  is ascribed to C-H of methyl group. The C-O-C stretching of cellulose found around  $1029.04 \text{ cm}^{-1}$  and  $1016.65 \text{ cm}^{-1}$  (Bulut & Aydin et al., 2006) for base and acid respectively. Changes in characteristic bands observed in the FTIR whereby some peaks disappeared and C=O and C-H shifted is an indication of several functional group's involvement on the adsorption of ARVDs

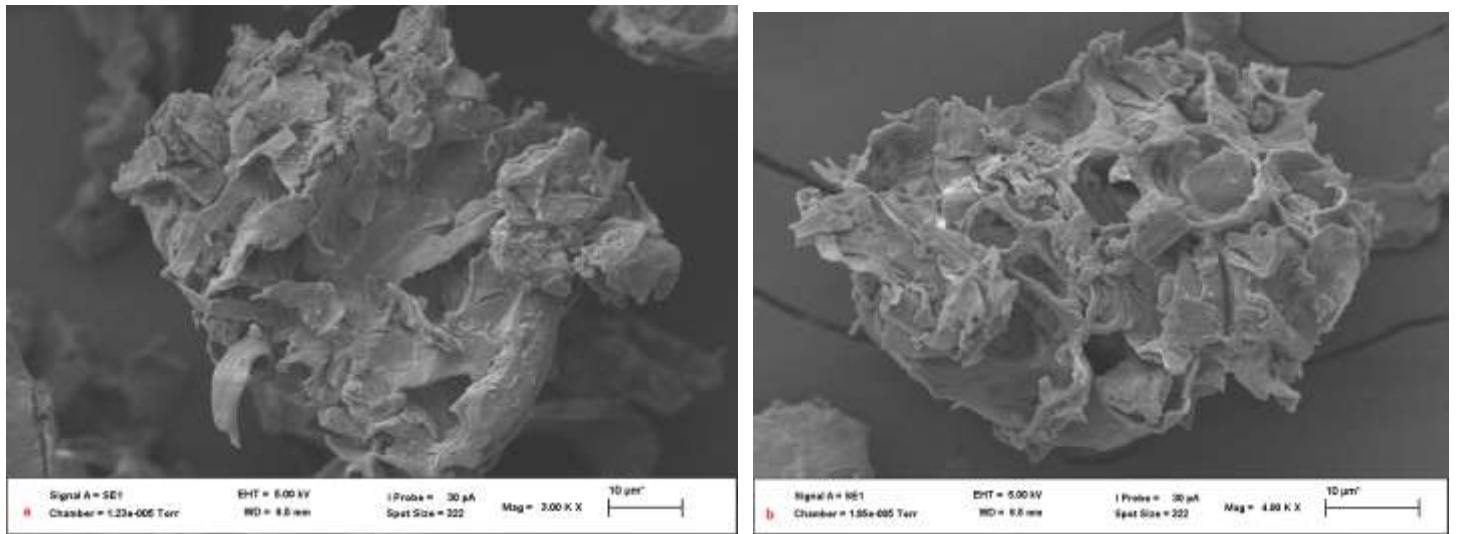
(Mahvi et al., 2007). There is no difference between the based and acid due to that both adsorbents was able to retain its lignocellulose structure besides that N-H from base modified was more broad than acid modified. The treatment with both acid and base would affect the ability of the to protonate or donate its electrons to remove the target species.



**Figure 4.1:** FTIR micrographs of *Platanus acerifolia* -NaOH (a) and *Platanus acerifolia* -HCl (b) adsorbent BD – before adsorption, AD – after adsorption

#### 4.3.2 Scanning electron microscopy (SEM)

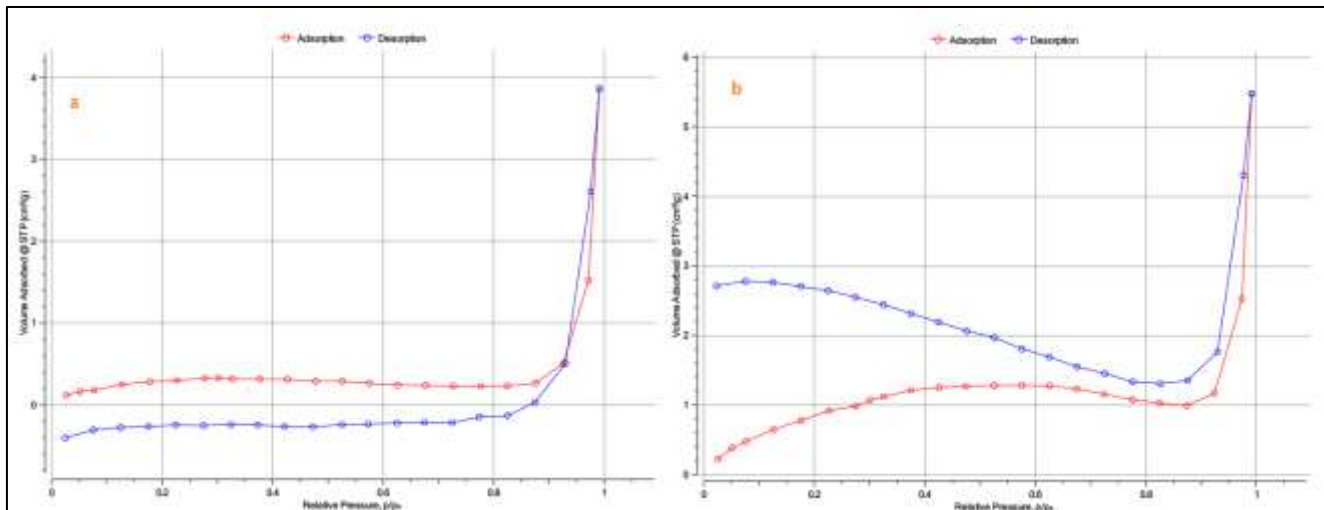
The SEM analysis showed that both base and acid modified *Platanus acerifolia* adsorbents have a semi-circle microstructure and porous surface (**Figure 4.1**) which are expected to provide suitable binding sites for ARVDs compounds. The SEM images of both adsorbents also revealed a flaky-folded irregular and rough-structure which is commonly found in plant materials. A similar observation whereby an irregular and rough surface was reported on adsorption of methylene blue by *Platanus orientalis* in aqueous solution (Peydayesh & Rahbar-Kelishami et al., 2015).



**Figure 4.2:** SEM micrographs of LPL-NaOH (a) and LPL-HCl (b) adsorbent

### 4.3.3 Brunauer Emmett Teller (BET)

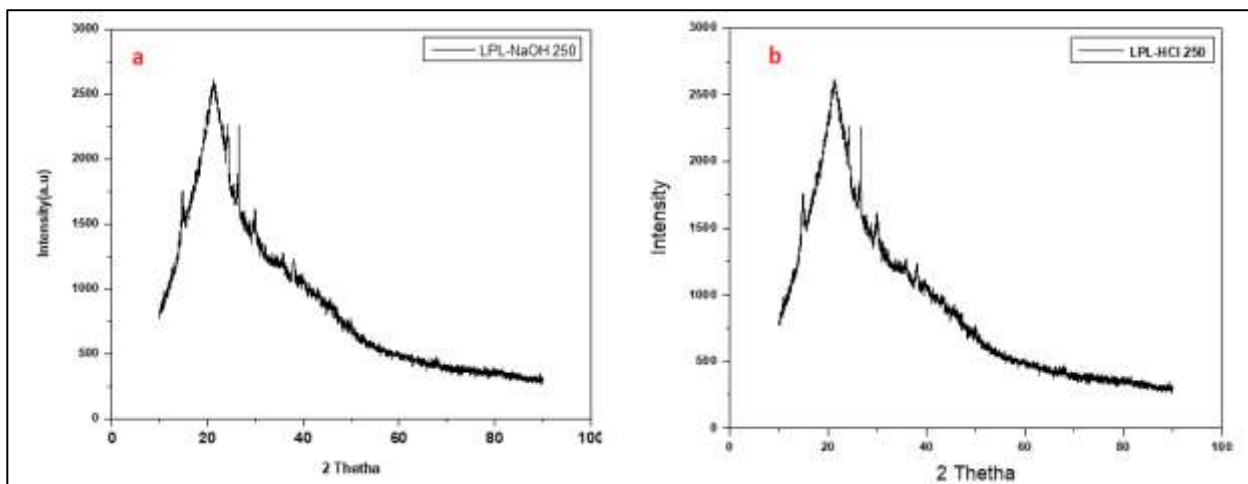
The surface area evaluated using the BET method with nitrogen adsorption isotherms showed a surface area of  $1.14 \text{ m}^2/\text{g}$ , pore volume  $0.0024 \text{ cm}^3/\text{g}$  and pore diameter  $8.45 \text{ nm}$  for a base modified *Platanus acerifolia*. The acid modified *Platanus acerifolia* adsorbent had a surface area of  $3.83 \text{ m}^2/\text{g}$ , pore volume  $0.0039 \text{ cm}^3/\text{g}$  and diameter  $4.09 \text{ nm}$ . The unmodified surface area  $0.65 \text{ m}^2/\text{g}$ , pore volume  $0.010 \text{ cm}^3/\text{g}$  and pore diameter  $4.67 \text{ nm}$ . The acid modified adsorbent showed more improve surface area, this attribute could lead to high adsorption efficiency. The  $\text{N}_2$  adsorption/ desorption of both adsorbents showed a type-V with parallel pores. The adsorption /desorption shows a more parallel size between 0.4 and 0.6 ( $p/p_0$ ) (**Figure 4.3**) which is an indication that more  $\text{N}_2$  gas adsorbed into the free state due to the special pore structure (Yue et al., 2019).



**Figure 4.3:** BET micrographs of *Platanus acerifolia* -NaOH (a) and *Platanus acerifolia* -HCl (b) adsorbent.

#### 4.3.4 Powder X-ray diffraction (PXRD)

PXRD showed that the modified adsorbents exhibit  $2\theta = 18.76, 23.86$  and  $36.44^\circ$  for a base modified *Platanus acerifolia* adsorbent and  $2\theta = 18.26, 23.44$  and  $36.33^\circ$  for acid modified adsorbent (**Figure 4.4**). The major distinct diffraction peaks observed are ascribed to native crystalline cellulose ( $C_6H_{12}O_6$ ) structure. The mixture of broad and sharp peaks could be attributed to a mixture of amorphous and crystalline nature of the adsorbents (Rai et al., 2016).

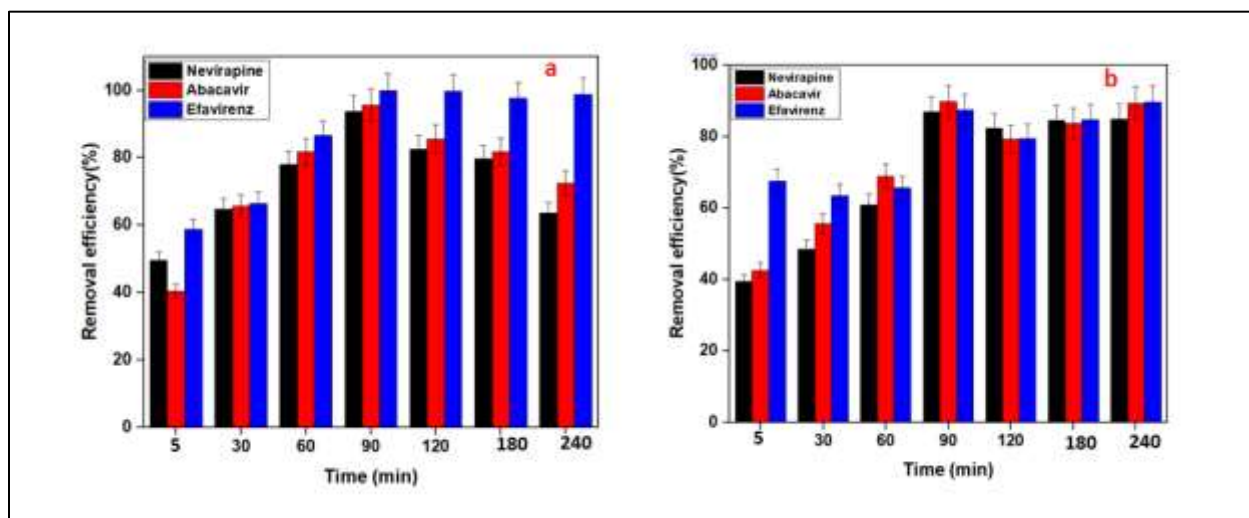


**Figure 4.4:** PXRD micrographs of *Platanus acerifolia* -NaOH (a) and *Platanus acerifolia* -HCl (b) adsorbent

## 4.4 Batch of adsorption experiments

### 4.4.1 Effect of contact time

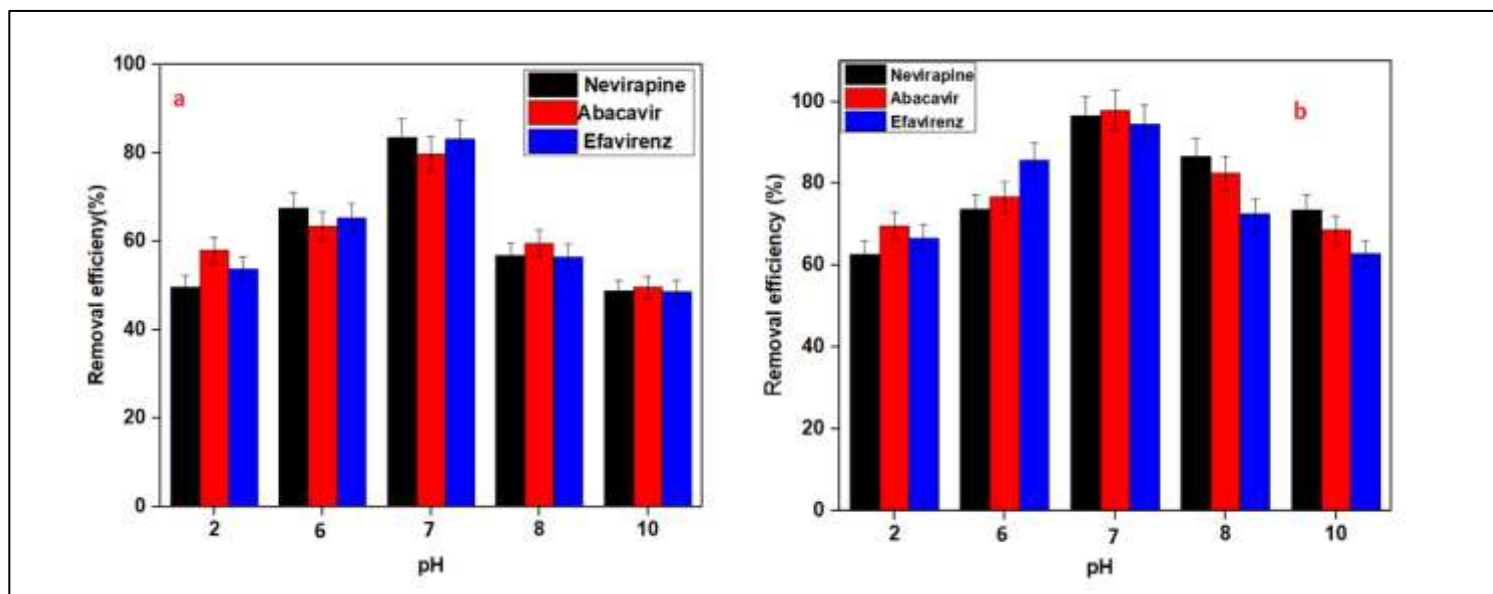
The effect of contact time on the adsorption capacity of *Platanus acerifolia* was varied between (5-240 minutes). The rate of removal of ARVDs showed an increase with increase in contact time (Figure 4.5). The base modified adsorbent shows a rapid increase in adsorption of all the ARVDs up to 90 minutes. This was followed by a gradually decrease in the ability of the adsorbent to remove the ARVDs which was more pronounced for abacavir and nevirapine especially in the base modified adsorbent. The increase in adsorption at the start of the adsorption process could be due to that adsorbent sites are vacant and solute gradient concentration is very high. However, as the contact time is prolonged there is more interaction between the ARVDs and the adsorbent resulting to the saturation of the vacant sites where the ARVDs could no longer be adsorbed thus reducing adsorption (Liang et al., 2010). The removal efficiency shows a fluctuation with an increase with time which could be attributed to alteration of the matrix effect thus affect the consistency on adsorption of analytes. The adsorption time of 90 minutes was taken as optimum and was applied through the study.



**Figure 4.5:** Effect of time on adsorption efficiency of ARVDs on *Platanus acerifolia* -NaOH(a) and *Platanus acerifolia* -HCl (b) adsorbents. Adsorption conditions: sample pH - 7, adsorbent mass - 10 mg, sample volume - 10 mL, initial concentration -1mg/L, agitation speed - 150 rpm

#### 4.4.2 Effect of pH

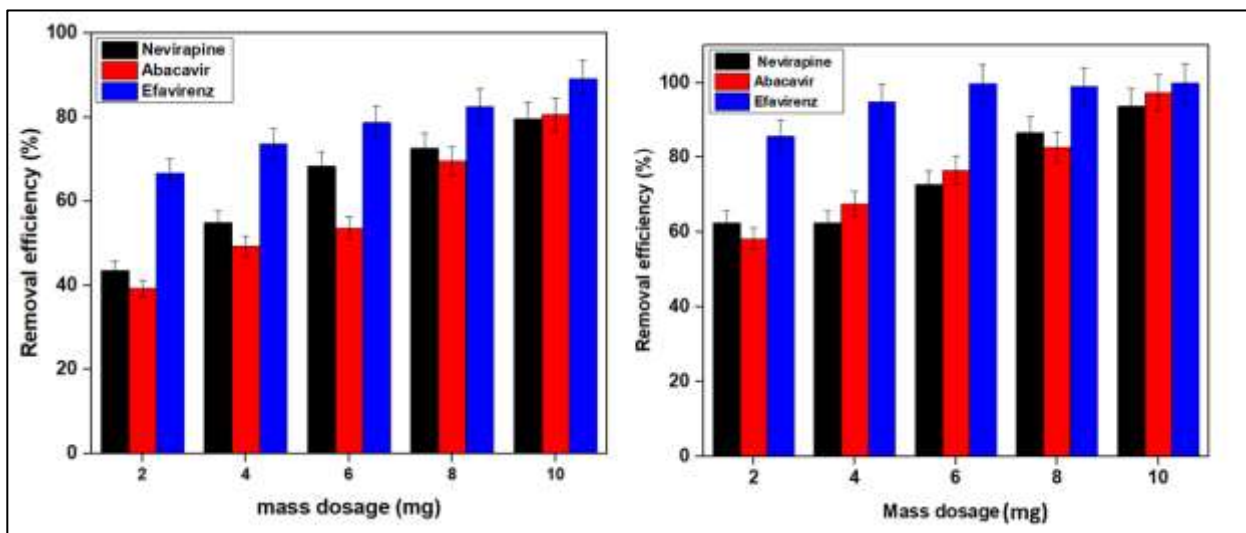
The influence of pH on the surface charge of *Platanus acerifolia* adsorbent, and adsorption of the ARVDs from the wastewater samples was investigated at pH 2-10. The rate of adsorption of ARVDs increases with an increase in pH with a maximum obtained around pH 7 (**Figure 4.6**), which was then employed in subsequent experiment. This observation could be attributed that the surface charge of functional groups increases with increase in pH, thus increases the electrostatic forces leading to increase in the rate of adsorption (Bhatti et al., 2012, Budinova et al., 2009). The pKa of nevirapine, abacavir and efavirenz are (5.06, 5.77 and 12.5) (Qwane et al., 2020, Adeola et al., 2021). The decrease in removal efficiency after optimum pH could be attributed to the pH is high than the pKa as a consequence of that the ARVDs of interest tends to hydrolyze thus the compounds exist in anionic form hence there is decrease in removal efficiency (Madikizela et al., 2016).



**Figure 4.6:** Effect of pH on adsorption efficiency of ARVDs on *Platanus acerifolia* -NaOH (a) and *Platanus acerifolia* -HCl (b) adsorbents. Adsorption conditions: adsorbent mass - 10 mg, sample volume - 10 mL, initial concentration - 1mg/L, agitation speed - 150 rpm

#### 4.4.3 Effect of mass dosage

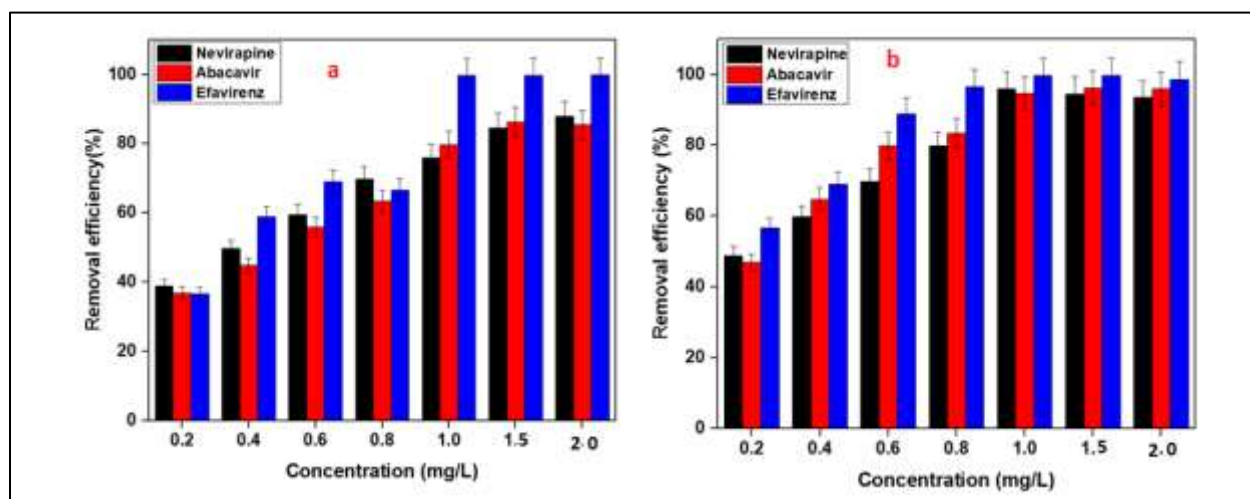
Mass dosage has a significant influence on ability of the adsorbent to remove target species. There is a steady increase in adsorption of ARVDs as mass dosage increase from 2 to 10 mg (**Figure 4.7**). This trend could be due to availability of more active sites and greater availability of specific surface on the adsorbent. The high removal efficiency in acid modified could be attributed to the easy protonation of nevirapine, abacavir and efavirenz under acidic media which promotes the ionic interaction thus leads to increase in removal efficiency (Al-Degs et al., 2008). The increase in mass dosage implies that more surface area is made available and therefore the total number of number of sites increases. As a result, the removal efficiency would increase as the target species would have more active sites to interact thus lead to their removal in the aqueous solution.



**Figure 4.7:** Effect of mass dosage on adsorption efficiency of ARVDs on *Platanus acerifolia* - NaOH (a) and *Platanus acerifolia* -HCl (b) adsorbent. Adsorption conditions: sample pH -7, sample volume – 10 mL, initial concentration - 1mg/L, agitation speed - 150 rpm

#### 4.4.4 Effect of initial concentration

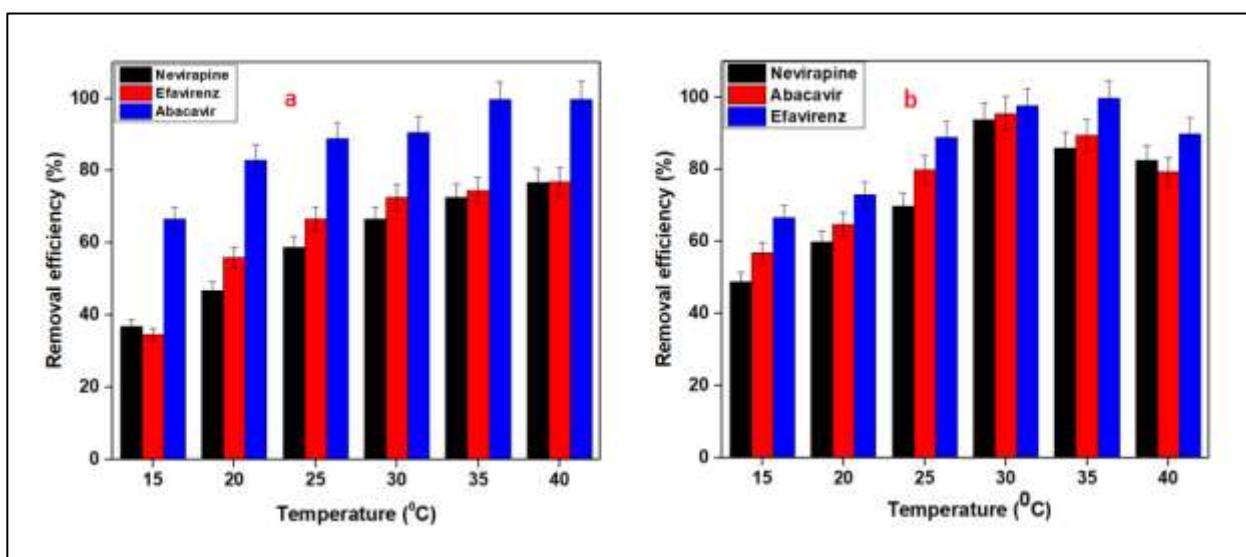
The initial concentration effect was varied from (0.2-2.0 mg/L), (**Figure 4.8**). An increase in concentration result to increase in adsorption capacity. Furthermore, the increase in concentration increases mass transfer resistance which the driving force on ability of adsorbent to interact with antiretrovirals. The mass transfer resistance governs the strong attraction between the ARVDs compounds and the modified *Platanus acerifolia* adsorbents, whereby a fast diffusion on the external surface and fast diffusion into the intraparticle matrix is essential for elimination of these compounds in polluted water samples. The base and acid showed a steady increase in removal efficiency until and optimum of 1.0 mg/L and 1.5 mg/L respectively. After the optimum concentration the removal efficiency is constant which could be attributed to saturation of active sites (Auta & Hameed et al., 2011). A similar behaviour was reported on adsorption of methylene blue by tea leaves (Dakhil et al., 2013).



**Figure 4.8:** Effect of concentration on adsorption efficiency of ARVDs on *Platanus acerifolia*-NaOH(a) and *Platanus acerifolia* -HCl (b) adsorbents. Adsorption conditions: sample pH-7, adsorbent mass – 10 mg, sample volume - 10 mL, agitation speed – 150 rpm.

#### 4.4.5 Effect of temperature

The temperature was investigated from a range of (15-40°C). The rate of diffusion of adsorbate species from external boundary into internal pores of adsorbent particle is known to increase by an increase in temperature (Hameed & Ahmad et al., 2009). Hence, there is increase in removal efficiency up on temperature increase. Furthermore, increase temperature change can improve the adsorption capacity through the increase in mobility of ARVDs molecules. As a result, there is an increase in removal efficiency as temperature increases as depicted by (Figure 4.9a and 4.9b) which be a consequence of increase in average kinetic energy of molecules thus leads to effective collision. A similar observation was reported by adsorption of acid dye by activated clay (Ho & Chiang et al., 2001).



**Figure 4.9:** Effect of temperature on adsorption efficiency of ARVDs on *Platanus acerifolia* - NaOH (a) and *Platanus acerifolia*-HCl (b) adsorbents. Adsorption conditions: sample pH-7, adsorbent mass -10mg, sample volume - 10 mL, initial concentration -1mg/L, agitation speed -150 rpm.

## 4.5 Adsorption isotherms, Adsorption kinetics and Thermodynamics studies

### 4.5.1 Kinetics studies

Pseudo-first-order, pseudo-second-order and interparticle diffusion kinetic models were conducted to evaluate the adsorption process *Platanus acerifolia* adsorption (Salem & Akbari, 2011, Wang et al., 2012) which were assessed using the Eqs (4.4), (4.5), and (4.6), respectively.

$$\ln(q_e - q_t) = \ln(q_e - K_1) \quad (4.4)$$

$$\frac{t}{q_e} = \frac{1}{K_2 q_e^2} + \frac{t}{q_e} \quad (4.5)$$

$$q_e = K_{id} t^{1/2} + C_{id} \quad (4.6)$$

where  $q_e$  (mg/g) is the amount adsorbed at equilibrium, and  $q_t$  (mg/g) amount of ARVDs is time  $t$  (min). Furthermore,  $K_1$  ( $\text{min}^{-1}$ ) and  $K_2$  ( $\text{g} (\text{min mg})^{-1}$ ) are rate constants of pseudo-first and pseudo-second-order,  $K_{id}$  ( $\text{mg} (\text{g}^{-1} \text{min}^{-1/2})$ ) is a diffusion rate constant and  $C_i$  is a boundary layer constant. Adsorption kinetics are essential aspect for evaluating adsorption process. A plot of  $\text{Log}(q_e - q_t)$  against time ( $t$ ) that yield  $K_1$  and  $q_e$  values from slope and intercept respectively for a pseudo-first-order model. Moreover, a plot of  $(t/q_t)$  against ( $t$ ) gives  $(1/q_e)$  as slope and  $(1/K_2 q_e^2)$  as intercept from which  $K_2$  can be obtained. The correlation coefficients values obtained by fitting the experimental data were high in pseudo-second-order with  $R^2$  values range from ( $R^2 = 0.976-0.998$ ) compared to pseudo-first-order ( $R^2 = 0.937-0.974$ ) (**Table 4.1**). In addition, the adsorption capacity calculated ( $q_e$  cal) for pseudo- second-order model were close to  $q_e$  exp. Deductions from kinetic model shows that the adsorption of ARVDs followed a pseudo-second- order kinetic model however, this could not explain the reaction mechanism. Therefore, the intraparticle diffusion was employed to combat this limitation. Fitting the kinetic data on intraparticle diffusion equation showed that it does not pass through the adsorption of ARVDs showed that the rate constant  $K_{diff}$  is almost similar across the base and acid in all ARVDs compounds.

#### 4.1: Kinetic constants of nevirapine, abacavir and efavirenz

Parameters	Nevirapine		Abacavir		Efavirenz		
	HCl modified	NaOH modified	HCl modified	NaOH modified	HCl modified	NaOH modified	
First-order	$q_e(\text{mg/g})_{\text{exp}}$	35.45	79.56	48.56	39.56	35.56	36.56
	$q_e(\text{mg/g})_{\text{cal}}$	39.24	34.52	57.56	36.16	29.69	32.22
	$K_1 (\text{min}^{-1})$	0.00234	0.0042	0.0019	0.002	0.0249	0.0019
	$R^2$	0.974	0.967	0.921	0.936	0.917	0.937
Second-order	$q_{e2}(\text{mg/g})$	45.52	78.87	51.02	51.02	10.45	34.56
	$K_2 (\text{min}^{-1})$	0.565	$1.21 \times 10^{-3}$	65.45	$4.09 \times 10^{-3}$	0.235	$2.83 \times 10^{-3}$
	$R^2$	0.998	0.976	0.997	0.986	0.998	0.976
Intra-particle diffusion	$K_{\text{diff}}$ ( $\text{mg g}^{-1} \text{min}^{-1/2}$ )	1.07	1.12	1.08	1.09	1.04	1.06
	$C (\text{mg g}^{-1})$	1.12	3.90	3.56	3.56	1.03	2.01
	$R^2$	0.990	0.974	0.980	0.937	0.978	0.920

#### 4.5.2 Adsorption isotherms

The Langmuir, Freundlich and Temkin models were applied to study the reaction behaviour. The Langmuir kinetic model was investigated using equation (4.7).

$$\frac{C_e}{q_e} = \frac{1}{q_e K} + \frac{C_e}{q_m} \quad (4.7)$$

where ( $q_e$ ) is adsorption capacity at equilibrium (mg/g),  $C_e$  is the concentration at the equilibrium of antiretroviral (mg/L),  $q_m$  is the maximum theoretical capacity (mg/g) and  $K$  (L/mg) is the Langmuir constant that correlates to the binding sites. The constant of Langmuir is obtained by plotting the slope and the intercept of the plots which are plot of  $C_e/q_e$  against  $C_e$ . Moreover, the Freundlich model was also employed, which is defined by equation (4.8), (Abdel Rahman et al., 2017).

$$\log q_e = \log K_F + \frac{1}{n} \log C_e \quad (4.8)$$

Freundlich has two constants  $K_F$  and  $n$  which gives an insight about the heterogeneity degree of surface sites. The constant could be obtained through and intercept of the plot of  $\log q_e$  against  $\log C_e$ . The Temkin model could be defied by the following equation (4.9).

$$q_e = B_1 \ln K_T + B \ln C_e \quad (4.9)$$

Adsorption isotherms gives an insight about adsorbate molecules are distributed between the liquid and solid phases when the system equilibrium is reached. Langmuir process described adsorption process in homogenous surface whereby the adsorbate is distributed in monolayers. Freundlich isotherms model describes a multilayer adsorption on a heterogenous surface. The  $R_L$  describes the favourability of the adsorption process whereby ( $0 < R_L < 1$ ) favourable ( $R_L > 1$ ) unfavourable, and linear ( $R_L = 1$ ). The smaller the  $R_L$  value the greater the affinity between the ARVDs and adsorbent. The  $R_L$  values on both base and acid modified *Platanus acerifolia* adsorbents were between 0 and 1 which implies that adsorption is favourable and a strong affinity between the ARVDs and the adsorbent exist. Moreover, the correlation coefficients of Langmuir model ( $R^2 = 0.886-0.998$ ) were high than Freundlich model ( $R^2 = 0.817-0.998$ ) whereas Temkin ( $R^2 = 0.826- 0.960$ ) across all three ARVDs was observed (**Table 4.2**). In addition, the  $q_e$  cal and  $q_e$  exp were

closer other on both acid and base modified *Platanus acerifolia* for Langmuir isotherm model. As a result, it is evident that the adsorption data is consistent with the Langmuir adsorption model which suggests that adsorption of ARVDs and *Platanus acerifolia* occurs in a monolayer surface. A similar trend whereby the kinetic data fitted in pseudo-second-order and adsorption isotherms followed Langmuir model was reported on adsorption of ARVDs using nanofibers (Kebede et al., 2020).

**Table 4.2: Adsorption isotherms Langmuir, Freundlich, and Temkin for analysis of ARVDs**

Parameters	Nevirapine		Abacavir		Efavirenz		
	HCl Modified	NaOH modified	HCl modified	NaOH modified	HCl modified	NaOH modified	
$q_{eexp}(mg/g)$	106.24	23.45	78.56	81.23	102.86	96.02	
Langmuir	$q_{max}, (mg/g)$	98.92	18.39	63.42	76.22	81.05	10.30
	$K_L (Lmig^{-1})$	$8.0 \times 10^{-3}$	0.15	0.014	0.21	0.15	0.015
	$R_L$	0.89	0.45	0.78	0.58	0.75	0.49
	$R^2$	0.998	0.886	0.987	0.917	0.998	0.996
	$1/n$	0.40	0.48	0.28	0.38	0.35	0.46
Freundlich	$K_F$	66.68	50.42	84.09	53.91	68.03	52.81
	$R^2$	0.886	0.817	0.932	0.987	0.984	0.945
	$K_T (g/L)$	1.68	5.67	5.03	7.28	1.85	4.80
Temkin	B	20.74	29.16	30.51	25.78	24.89	24.89
	$R^2$	0.826	0.962	0.944	0.956	0.978	0.960

### 4.5.3 Thermodynamic studies

The standard free energy  $\Delta G^\circ$ , enthalpy change  $\Delta H^\circ$  and entropy changes  $\Delta S^\circ$  are essential parameters in understanding the feasibility of the adsorption process. Gibb's free energy is studied using equation (4.12). The variation of temperature with a distribution coefficient D could be used to make thermodynamic parameters using equation (4.10)

$$D = \frac{C_e}{C_e} \quad (4.10)$$

where  $q_e$  is the number of antiretrovirals adsorbed by the adsorbent (mg/g) at equilibrium, and  $C_e$  is the equilibrium concentration of antiretrovirals in (mg/L).  $\Delta H^\circ$ ,  $\Delta S^\circ$ , and  $\Delta G^\circ$  can then be calculated according to equations (4.11, and 4.12).

$$\ln D = \frac{\Delta S^\circ}{R} - \frac{\Delta H^\circ}{RT} \quad (4.11)$$

$$\Delta G = \Delta H^\circ - T\Delta S^\circ \quad (4.12)$$

where R is a gas constant (8.314 J/mol K), T is the absolute temperature (K),  $\Delta H^\circ$  and  $\Delta S^\circ$  could be obtained from the slope and intercept of  $\Delta G^\circ$  vs 1/T. The thermodynamics studies were conducted by varying temperatures from (288, 298, 303, 313, and 333 K).

A plot of  $\ln D$  against 1/T was used to calculate the values of  $\Delta H^\circ$  and  $\Delta S^\circ$  and standard Gibbs energy was evaluated by equation (4.12). The negative value of  $\Delta G^\circ$  increased with an increase in temperature which implies that the adsorption was spontaneous and thermodynamically favoured. Moreover, the spontaneity increases with an increase of temperature for all the ARDs under investigation. In addition, the negative values  $\Delta H^\circ$  and positive  $\Delta S^\circ$  implies that adsorption of ARVDs is exothermic in nature and ARVDs-*Platanus acerifolia* interaction consist of increase in randomness. The values of  $\Delta H^\circ$  were less than 40 kJ mol<sup>-1</sup> for nevirapine, abacavir and efavirenz which implies that physical adsorption was dominant through the study. Furthermore, the positive values of entropy changes  $\Delta S^\circ$  describes the random nature of adsorption process at solid/solutions interface and the affinity of *Platanus acerifolia* leaves on ARVDs adsorption (Saltali et al., 2016, Pathania et al., 2017).

#### 4.5.4 The effect of adsorbent modification on the antiretroviral drugs removal efficiency

The effect of adsorbent modification was evaluated by using the raw, acid modified and base modified *Platanus acerifolia* adsorbent under optimum conditions to assess the removal efficiency of the AVRDS from wastewater. The results (**Table 4.4**) showed that modification of the *Platanus acerifolia* is essential for activation of the functional groups on the surface of the adsorbent is plays a mechanistic role in the adsorption of ARVDs in wastewater. The unmodified adsorbent had lower amount adsorbed compared to modified adsorbents. The effluent samples had higher amount adsorbed compared to the influent wastewater samples. This could be due to matrix effect, whereby there is a possibility of pollutants to compete for active sites on surface of the adsorbent. Moreover, the *Platanus acerifolia* superiority in adsorption could attributed to distinct interactions such aggregation thus resulting in high adsorbent adsorption (Bhatti et al., 2012).

**Table 4.3: Thermodynamic studies of *Platanus acerifolia* acid and base adsorbent for adsorption of ARVDs**

		$\Delta G^\circ$ (kJ mol <sup>-1</sup> )					$\Delta H^\circ$	$\Delta S^\circ$	$R^2$
T (K)		288	298	303	313	333	(kJmol <sup>-1</sup> )	(Jmol <sup>-1</sup> k <sup>-1</sup> )	
Nevirapine	HCl	-17.17	-17.47	-17.47	-17.56	-17.98	-29.03	34.99	0.923
	NaOH	-17.41	-18.56	-18.56	-19.79	-11.03	-20.42	55.77	0.978
Abacavir	HCl	-14.20	-15.83	-16.49	-16.71	-17.14	-27.20	41.50	0.919
	NaOH	-16.24	-16.47	-16.78	-16.89	-16.89	-18.18	31.70	0.921
Efavirenz	HCl	-13.47	-13.47	-14.46	-14.99	-15.38	-24.47	46.23	0.918
	NaOH	-16.52	-14.25	-15.85	-16.38	-17.42	-36.38	52.38	0.975

HCl - acid modified macadamia adsorbent.

NaOH - base modified macadamia adsorbent

**Table 4.4: Effect of Raw *Platanus acerifolia*, *Platanus acerifolia* -NaOH and *Platanus acerifolia* - HCl for adsorption of ARVDs**

Target compounds	<i>Platanus acerifolia</i>	<i>Platanus acerifolia</i> - NaOH	<i>Platanus acerifolia</i> - HCl
	HCl ( $q_e$ )	NaOH ( $q_e$ )	Raw $q_e$ (mg/g)
Nevirapine	97.56	89.63	72.53
Abacavir	84.75	84.63	68.96
Efavirenz	81.56	81.56	63.23

#### 4.6 Conclusion

The *Platanus acerifolia* leaves were functionalized and applied as effective and low-cost adsorbent for the removal of ARVDs in real samples. From the kinetic data of both adsorbent the pseudo-second-order ( $R^2=0.976-0.998$ ) was better compared pseudo-first-order ( $R^2=0.937-0.974$ ) kinetic model. Adsorption isotherms showed that the Langmuir ( $R^2=0.886-0.998$ ) model best described the adsorption process than Freundlich ( $R^2=0.817-0.998$ ) model. The value of  $\Delta G^\circ$  increased upon increasing temperature which is an indication process is spontaneous and thermodynamically favoured. Moreover, the value  $\Delta H^\circ$  negative and  $\Delta S^\circ$  positive which implies that adsorption process is exothermic in nature and the ARVDs-adsorbents interaction was an increase irregular of randomness. These observations were confirmed by thermodynamic studies. The activated *Platanus acerifolia* leaves adsorbent demonstrated to be an effective and low-cost adsorbent as 10 mg of the adsorbent was able to remove an optimum amount of about 90 % of all the target analytes. In addition, the adsorbent showed to be promising adsorbent to be applied for the removal of antiretrovirals in polluted wastewater, thus improving the water quality which is very essential for living organisms and biological process.

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## Chapter Five

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### **Kinetics, isotherms, and thermodynamic studies for efficient adsorption of selected antiretroviral drugs from wastewater using polymer of intrinsic microporosity number-1**

#### **Abstract**

In recent years, the ever-increasing detection of pharmaceutical compounds including antiretrovirals (ARVDs) in water bodies has been an emerging concern. As a result, the research topics on the removal of these emerging pollutants from aqueous environments have been relevantly growing. This is due to that these pollutants may adversely affect humans and animals even at trace levels of concentrations. The current study therefore explored the polymeric materials of intrinsic microporosity number-1 (PIM-1) for the removal of ARVDs from the wastewater samples. The structure, morphology, and porosity of the PIM1 was assessed using Fourier-transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), Powder X-ray diffraction (PXRD), Brunauer, Emmett and Teller (BET). The FTIR characterization revealed distinct functional groups such as C-H, C-N, C=O which are critical for interaction of ARVDs with the adsorbent. The characterization by SEM showed the polymer contains microporous to mesoporous pores on its surface. PXRD patterns showed  $2\theta = 21.34^\circ$  and  $36.48^\circ$  which indicated an amorphous material. Brunauer, Emmett and Teller (BET) had a surface of  $557.39 \text{ cm}^2/\text{g}$ , pore volume  $0.4123 \text{ cm}^3/\text{g}$  and pore diameter  $2.96 \text{ nm}$  which are essential on adsorption of ARVDs by PIM-1. The effect of time, pH, initial concentration, mass dosage and adsorption temperature were investigated for their influence on the removal of ARVDs from wastewater. The contact time of 60 minutes, pH 7, concentration of  $1.0 \text{ mg/L}$  of sample, mass dosage of  $10 \text{ mg}$  of adsorbent and a temperature of  $30^\circ\text{C}$  gave optimum removal efficiency above 86 % for nevirapine, abacavir and efavirenz. Kinetic data fitted well with the pseudo-second-order kinetic model ( $R^2 = 0.925-0.997$ ) compared to pseudo-first-order ( $R^2 = 0.654-0.991$ ). The isotherm of ARVDs adsorption of PIM-1 confirmed that Freundlich model has a great coefficient correlation ( $R^2 = 0.978-0.999$ ) which implied that physio-chemical adsorption of ARVDs was dominant in the heterogeneous surface of PIM-1. The value of  $\Delta G^\circ$  increase in magnitude upon increasing temperature which is an indicative that the adsorption process was spontaneous and thermodynamically favoured. The negative value of  $\Delta H^\circ$  was an indicative that adsorption process was exothermic and  $\Delta S^\circ$  was positive which implied that an irregular increase of randomness in the adsorption of ARVDs. Generally, the PIM-1 adsorbent showed to be an effective and eco-friendly adsorbent for removal of ARVDs in

wastewater.

**Keywords:** polymer intrinsic microporosity, antiretrovirals, low-cost, kinetics, isotherm, thermodynamics

## **5.1 Introduction**

### **5.1.1 Antiretrovirals drugs (ARVDs)**

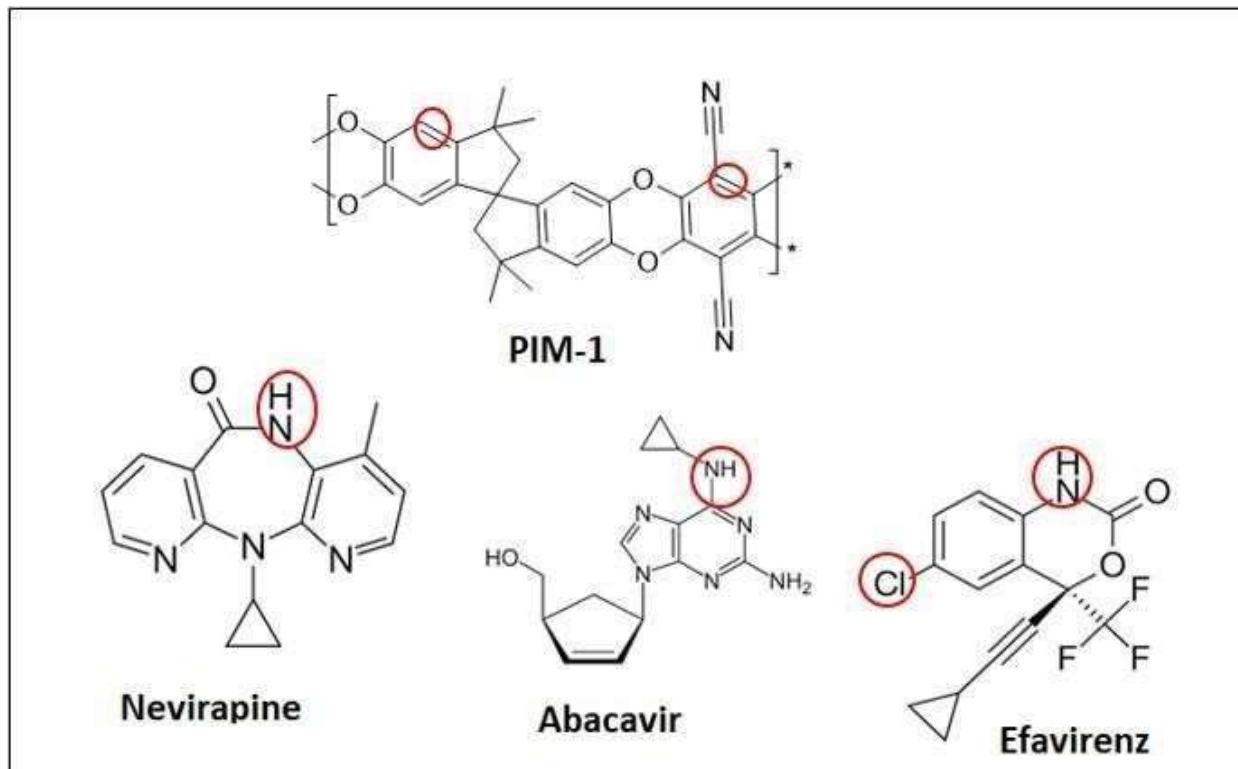
Antiretrovirals drugs (ARVDs) are therapeutic agents used for treatment of retroviral infections such as HIV-1, commonly known as HIV virus. The virus mainly attacks the CD4-T cells that prevents the vulnerability of the immune system against infections and diseases (Adeola & Forbes., 2022, Ncube et al.,2018). ARVDs are useful in prolonging human health life however, the improper usage and disposal of unused or expired drugs could result in contamination of drainage systems and other water systems thus cause a threat to the environment and aquatic life (Tambosi et al.,2010). More than 90% of the ARVDs administered orally are passed out into the sewage system as faecal waste in partially metabolized or in their original form. As a results of the incomplete metabolization of ARVDs, they are excreted urine and faecal waste in their original or as metabolites thus through coordinated sewage systems are likely to reach wastewater treatment which major source of water for domestic and commercial use. ARVDs like many pharmaceuticals are biological active, persistent, and bio-accumulative, a result is likely are continually detected in several compartments of the environment (Adeola & Forbes et al., 2022, Houeto et al., 2012, de Andrade et al., 2018). The continual exposure to ARVDs is likely to cause adverse effects in human such peripheral nervous systems like neurotoxicity. Abacavir is associated with a cause nervous system disturbance such mania and psychosis (Calmy et al., 2009) whereas efavirenz mainly attacks central nervous system with toxicity such an insomnia and vivid dreams (Abers et al., 2014). Nevirapine is associated with aqua toxicity and alteration of physiology in amphibians and fish (Freitas & Radis-Baptista et al., 2021).

In the last few decades, adsorption phenomenon has become a well-established method for removal water pollutants even in trace concentration. Adsorption process is a surface phenomenon that involves the adherence of pollutants on the surface of adsorbent via chemical, physical and/or electrostatic attraction. The process mainly depends on the physicochemical properties such pH pore diameter and temperature etc on the surface of adsorbate and adsorbent (Kebede et al., 2019).

The adsorption technique has found its vast application due to simplicity of design, non-selective in nature, minimal tendency to form side products (Ahmed & Hameed, et al 2018). Numerous adsorbents have been successfully explored for removal of pharmaceutical compounds in aqueous environment including activated carbons (Rakić et al., 2015), nanofibers (Kebede et al., 2019), zeolites (De Ridder et al., 2012) and clay (Lozano-Morales et al., 2018), vegetal biomass (Phele et al., 2019). The most prominent adsorbents employed are zeolites and activated carbons due to their ideal properties microporous (< 2 nm) and mesoporous (2 -50 nm) which improves their ability to remove pollutants such as antiretrovirals in water (Braschi et al., 2010, Baccar et al., 2012). Although the clay and zeolites have been reported to be excellent adsorbents, they have great sensitivity to deactivation by irreversible adsorption. Also, they have functional groups that are highly polar, and it is not easy to explore their shape selectivity in reactions compared to hydrocarbons (Rakhym et al., 2020). Thus, it is important to find alternative adsorbents that can mimic zeolite and clay adsorbents for the removal of pollutants in aqueous media such as antiretroviral drugs. Polymeric materials have emerged to be promising and alternative adsorptive materials to remove hazardous compounds in the environment.

Polymer of intrinsic microporosity (PIM) exhibits distinct properties of amorphous, and mesoporous materials and thus has found vast application in catalysis, gas separation and adsorption (Budd et al., 2004, Alnajrani & Alsager et al., 2020). The PIM consists of distinct structural features with a backbone made of confused rings and site contortion which makes them to have high free volume since they are unable to pack nicely. Other attributes of PIM are high surface area, high thermal and chemical stability which make it a promising candidate for application in adsorption (Satilmis & Budd et al., 2014, Zhang et al., 2016). A great number of PIMs have been successfully synthesized, PIM-1 trimethylsilyl-1-propyne a novel class of polymeric compound, which has found its most application in dye (Pim et al., 2015) and phenol (Budd et al., 2004) removal in aqueous solutions. Therefore, the current study seeks to explore the PIM-1 for the first time as an adsorbent for the removal of ARVDs in wastewater. Adsorption isotherms, kinetic and thermodynamics were investigated. This was due to the fact that adsorption kinetics is essential for evaluating the adsorption process, the adsorption isotherms give more insight about the reaction behaviour between the PIM and the ARVDs target compounds. Thermodynamics describes the adsorption mechanism on the surface of the adsorbents. The PIM adsorbent and ARVDs target analytes are illustrated in **Figure 5.1**. The PIM and the target ARVDs have high density of  $\pi$

electrons which could lead to  $\pi$ -to- $\pi$  interactions, while the presence of N-H functional on the ARVDs could result to hydrogen bonding which is a strong interaction, and these can enhance the removal of ARVDs from water. Also, the chlorine and hydroxide atoms are good leaving thus could result to electrostatic attractive forces which could further improve the removal ARVDs from water.



**Figure 5.1:** Molecular structure of PIM-1 (only repeating unit) and nevirapine, abacavir, efavirenz ARVDs of interest

## 5.2 Experimental

### 5.2.1 Instrumentation

Shimadzu Liquid Chromatography (LC 2020) used for the analysis of ARVDs was from Shimadzu (Tokyo, Japan). The  $C_{18}$  analytical column ( $3.0 \mu\text{m} \times 4.6 \mu\text{m} \times 150 \mu\text{m ID}$ ) set at a temperature of  $30^\circ\text{C}$  was employed for separation of the ARVDs. The detection was acquired at wavelengths of 225, 254 and 287 nm. The LC-PDA gradient elution method of 50 % ACN: 50 %  $\text{H}_2\text{O}$  (0-2 minutes), 70 % ACN: 30 %  $\text{H}_2\text{O}$  (3-20 minutes) was used.

### 5.2.2 Chemical reagent

Solvents used (acetonitrile, methanol, acetic acid, acetone, hydrochloric acid, sodium hydroxide) were of HPLC grade and purchased from Sigma Aldrich (Steinheim, Germany). The ARVDs compounds (nevirapine, efavirenz and abacavir) were purchased from J&H Chemical Ltd (Hangzhou Zhejiang China). The standards of nevirapine, abacavir and efavirenz (10 mg each) were dissolved in 50 mL volumetric flask to make a stock solution of 100 mg/L. Varied concentration of 0.2 to 1.0 mg/L from the stock solution was used for the calibration of the (Liquid chromatography photodiode array) LC-PDA instrument. The  $K_2CO_3$  compound with a mass of 10.25 g , 30.1 mmol and 2,3,4,5,6-tetraflourophthalonitrile (6.02, 30.1mmol ) was stirred 65°C for 72 hours. On the cooling, mixture was added to water ( 300 mL) and crude product collected by filtration. Repeated precipitation from methanol gave 13.15 g with a yield of about 95 % of a yellow polymer (Budd et al., 2004).

### 5.2.3 Sampling and Sample preparation

The samples were collected in summer season (October 2022) in Amanzimtoti wastewater treatment with GPs coordinate -30.007°, -30.917° which is in South coast Durban, South Africa. The samples were collected using a darkbrown bottle and stored in a cooler box. Thereafter, the samples were transported to the laboratory where there refrigerated at a temperature of 4°C.

### 5.2.4 Batch of adsorption experiment adsorption

The removal of ARVDs using PIM-1 adsorbent was conducted using batch experiments. The factors affecting the adsorption efficiency including adsorbent's mass dosage (2-10 mg) per 10 mL of sample, contact time (5-240 min), solution pH 2 to 10 , adsorbate initial concentration (0.2- 2.0 mg/L) and adsorption temperature (5-40°C) were assessed. Blanks were also prepared and analyzed, and the experiment were done in triplicate (n=3). The amount of adsorbed ARVDs was obtained by ( $q_e$ ) at a time ( $q_t$ ) and the removal percentage (R) was obtained using equations (5.1) (5.2), and (5.3) respectively.

$$q_e = \frac{C_e - C_o}{m} \times V \quad (5.1)$$

$$q_t = \frac{C_e - C_t}{m} \times V \quad (5.2)$$

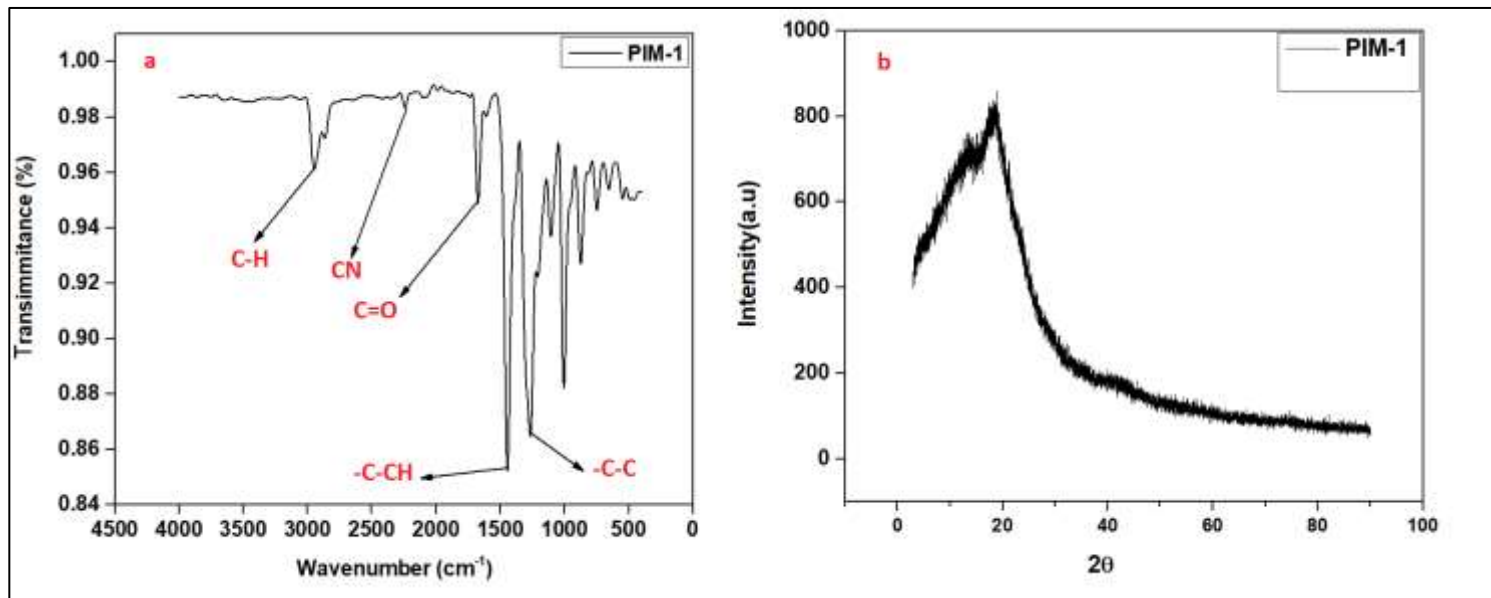
$$(R.E\%) = \frac{C_e - C_t}{m} \times V \quad (5.3)$$

$C_e$  is the concentration at equilibrium (mg/L),  $C_0$  is the initial concentration in (mg/L), whereas  $C_t$  is the concentration at a time at any given point, ( $m$ ) is the adsorbent mass (mg) and  $V$  is the amount of volume of the sample in (L).

## 5.3 Results and Discussion

### 5.3.1 FTIR and PXRD micrographs adsorbents

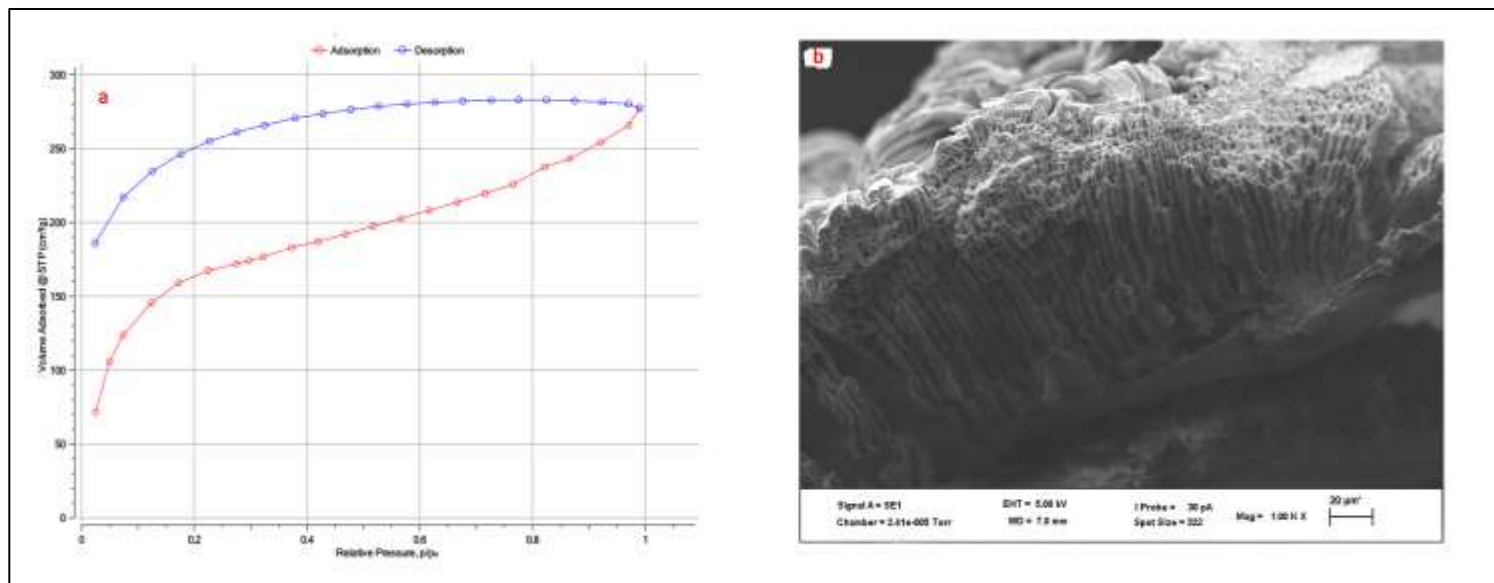
The functional groups present in PIM-1 were examined using Fourier infrared spectroscopy (FTIR) Alpha II FTIR spectrometer, Platinum ATR diamond 1 Bounce supplied by Bruker. The FTIR spectrum showed a C-H around  $2953.52 \text{ cm}^{-1}$  (**Figure: 5.2a**) band which is ascribed to an asymmetric stretching which is related to a vibration of hydrogen bond. The CN band around  $2238.94 \text{ cm}^{-1}$  is attributed to the cyanide functional group. Furthermore, the C=O band around  $1674.70 \text{ cm}^{-1}$  is ascribed to a stretching ester, ketones, and phenols group (Basiak et al., 2018). The Powder X-ray diffraction (PXRD) was Mini Flex 600 model, purchased in (Rigaku Tokyo, Japan) was employed to examine the inner structure of the PIM-1 adsorbent. The PXRD exhibits amorphous materials with  $2\Theta = 21.24$  and  $36.48^\circ$ . The diffraction patterns showed a mixture of broad and sharp peaks that can be ascribed to morphological combination of amorphous and mesoporous nature of adsorbent (**Figure: 5.2b**).



**Figure 5.2:** FTIR micrographs of PIM-1 adsorbent (a) and PXRD micrographs of PIM-1 adsorbent (b)

### 5.3.2 BET and SEM micrographs adsorbents

Nitrogen adsorption (Anton Paar GmbH, Austria) and the Brunauer Emmett and Teller (BET) model were used for surface area measurement of the adsorbents. The presence of a high surface area of 557.39 m<sup>2</sup>/g makes the PIM a promising candidate for removal of ARVDs. The average diameter of a PIM has a range of 2-50 nm (Madikizela et al., 2018) which is an indication of mesoporous structure which is essential for the adsorption of the target analytes. A pore volume of 0.4123 cm<sup>3</sup>/g and pore diameter of 2.96 nm which are significant for the adsorption of target analytes in wastewater samples. The average pore diameter is quite large than the average diameter which could improve the adsorption of target analytes. The surface area measurements are essential for the removal of ARVDs in wastewater. The PIM-1 adsorbents showed a type-I isotherm at low pressure which is a significant microporosity that enhances its adsorption. The EVO LS15 Scanning electron microscopy (SEM) (Zeiss, Germany) and Q 150R ES Sputter coater Quorum (Quorum Technologist, United Kingdom) was employed to assess the surface morphology of the adsorbents. The SEM image show numerous actives sites which makes are essential for PIM-1 for removal of ARVDs. **Figure: 5.3 (a and b)** shows the nitrogen adsorption isotherm and SEM micrographs with distinct features for adsorption, respectively

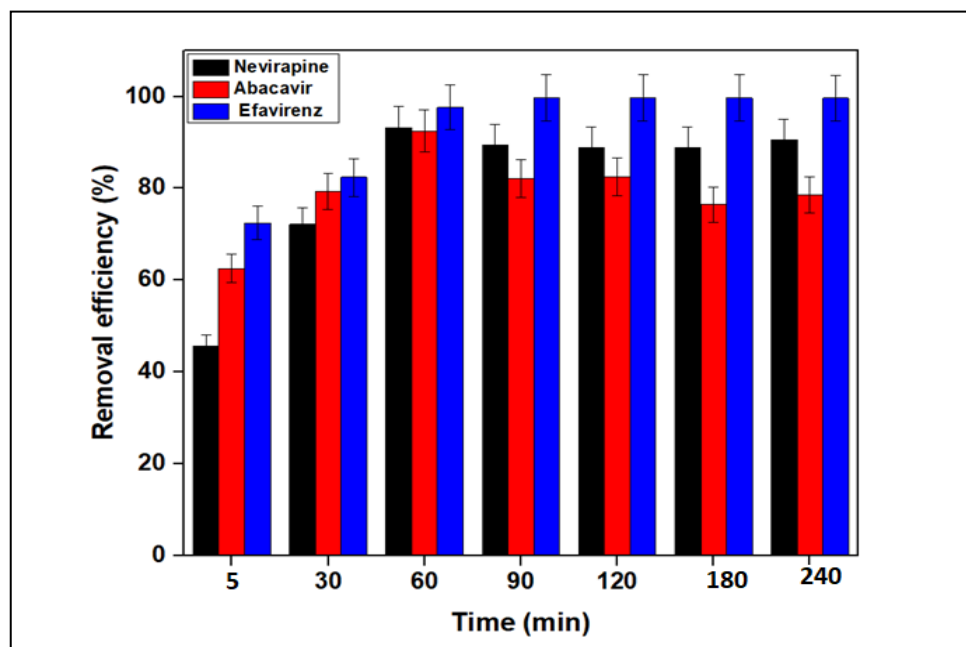


**Figure 5.3:** Nitrogen isotherm (77 K) (a) and SEM micrographs of PIM-1 adsorbent (b)

## 5.4 Batch of adsorption experiments

### 5.4.1 Effect of contact time

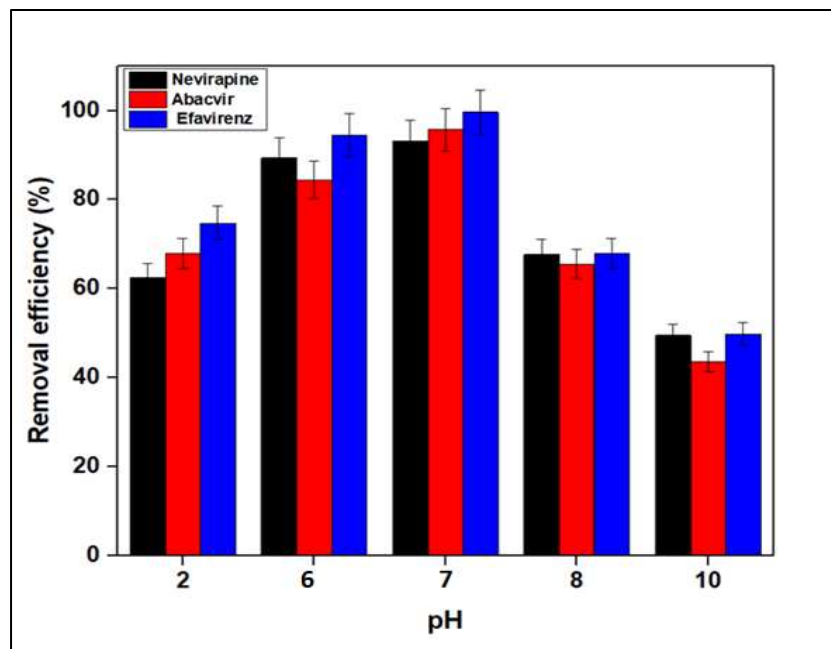
The adsorption efficiency showed an increase with increase in contact time and reaches an optimum adsorption at 60 minutes (Kebede et al., 2020), (**Figure 5.4**). The interaction between the PIM-1 and ARVDs was rapid in the first 60 minutes, beyond that there was slightly decrease to constant on adsorption of two compounds (nevirapine and abacavir), however efavirenz remained high throughout the investigated adsorption times. The optimum 60 minutes was used in the subsequent studies. The increasing adsorption of efavirenz ARVDs could be attributed to the high density of  $\pi$  electrons and chlorine attached to benzene which could lead to  $\pi$ -to- $\pi$  interactions thus leads to increase in adsorption. Additional mechanistic bonding such hydrogen bonding can be ruled out, which may be auxiliary mechanism (Peng et al., 2016).



**Figure 5.4:** Effect of time on adsorption efficiency of ARVDs by PIM-1: Adsorption conditions: sample pH - 7, adsorbent mass - 10 mg, sample volume - 10 mL, initial concentration -1mg/L, agitation speed -150 rpm

#### 5.4.2 Effect of pH

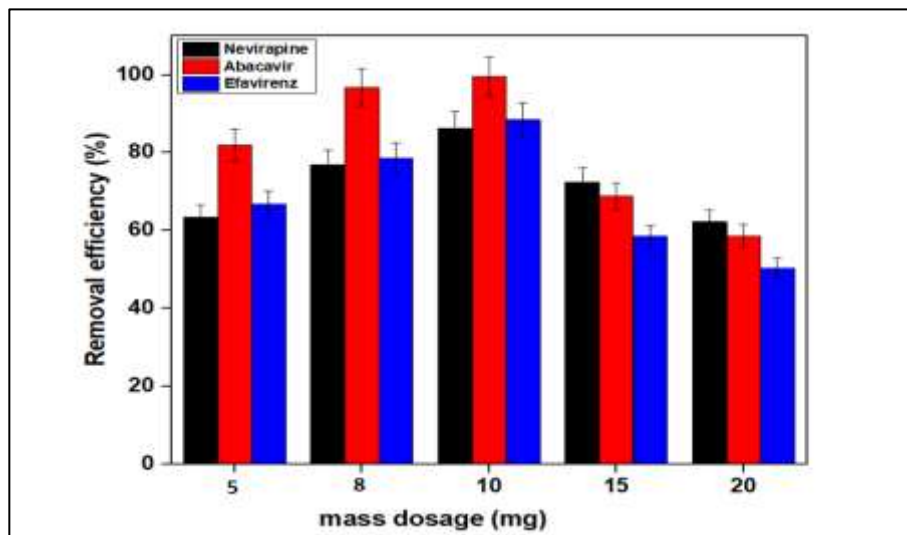
Several studies have indicated that pH is a critical aspect in the aqueous chemistry and binding sites that consequently affects the adsorption of target analytes in polluted water (Madikizela et al., 2018). The variation of the pH does not change the physio-chemical properties, but it only affects the ionic state in solution. From this observation it is evident that adsorption is pH-dependent as illustrated by (Figure 5.5). The dependence of the adsorption can be mainly related to the type and ionic state of functional groups found on surface of the adsorbent and target species in solution. As a consequence of that, in this investigation the removal efficiency increases in the acid media due to easy protonation of nevirapine, abacavir and efavirenz in acidic media thus, leads to electrostatic attraction forces that improves removal efficiency. The ionic and  $\pi$ -interaction due to high density of  $\pi$ -electrons from phenol rings from ARVDs could also improves their removal in wastewater samples. The high dominance of  $\text{OH}^-$  ions at basic pH could interact with negatively charges ions due to easily protonation could result to electrostatic repulsive forces hence, there is a decrease in removal efficiency at basic pH.



**Figure 5.5:** Effect of time on adsorption efficiency of ARVDs by PIM-1: Adsorption conditions: contact time of 60 minutes, adsorbent mass - 10 mg, sample volume - 10 mL, initial concentration - 1mg/L, agitation speed - 150 rpm

#### 5.4.3 Effect of PIM-1 mass dosage

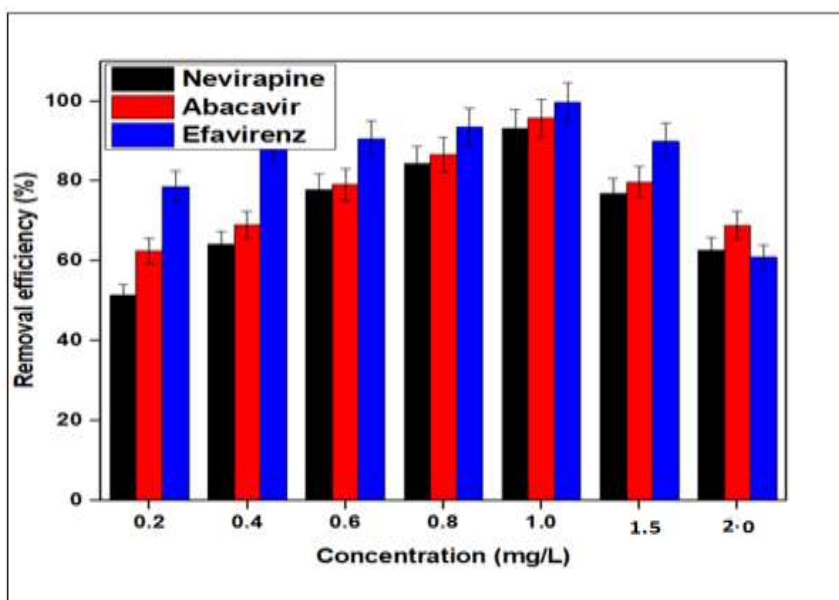
Mass dosage has a significant impact for adsorption of target compounds due to that an increase in mass dosage increases the number of available sites for adsorption. The adsorption of ARVDs onto PIM-1 rapidly increased with an increase in mass dosage from 5 to 10 mg with a removal percentage above 80% for all the studied ARVDs (**Figure 5.6**). Thereafter, a decrease in adsorption of ARVDs was observed which could be due increase in available active side at a constant concentration of ARVDs (Bhatti et al., 2012). Moreover, the decrease in removal efficiency could be attributed to overlapping or aggregation of adsorption sites, resulting in a decrease in total adsorption surface area available to ARVDs in the diffusion path length (Etim et al., 2016).



**Figure 5.6:** Effect of mass dosage of wastewater sample on adsorption efficiency of ARVDs by PIM-1: Adsorption conditions: contact time of 60 minutes, pH -7, initial concentration - 1mg/L, agitation speed - 150 rpm

#### 5.4.4 Effect of ARVDs initial concentration

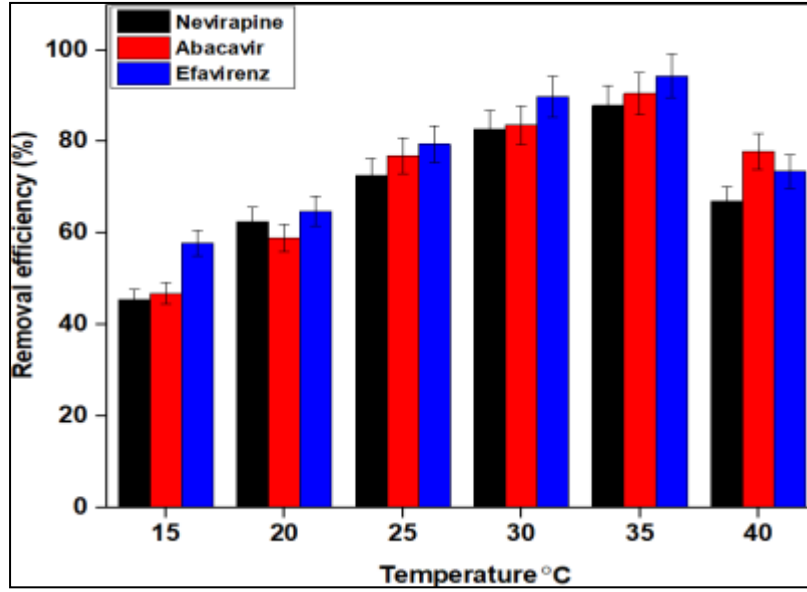
The initial concentration of ARVDs provides the driving force to overcome resistance of mass transfer of ARVDs between solid phases and aqueous media. A similar phenomenon was reported where the palm kernel fibre demonstrated to be a promising adsorbent for removal of anionic dye from wastewater (Ofomaja & Ho et al., 2007), while castor seed shell illustrated to be an excellent adsorbent for the removal of methylene blue in aqueous solutions (Hameed et al., 2008). In this work, there is a steady increase in the adsorption of ARVDs on the surface of PIM-1 adsorbent from 0.2 -1.0 mg/L (**Figure 5.7**). This could be ascribed to increase in concentration gradient which is a driving force for adsorption upon increasing initial concentration (Bhatti et al., 2012). Above a concentration of 1.0 mg/L, a decrease in adsorption of the ARVDs was observed which could be due to the limited ARVDs available for the adsorption process. The 1.0 mg/L was thus taken as the optimum concentration.



**Figure 5.7:** Effect of concentration on adsorption efficiency of ARVDs by PIM-1: Adsorption conditions: contact time of 60 minutes, pH -7, mass dosage 10 mg, sample volume - 10 mL, agitation speed -150 rpm

#### 5.4.5 Effect of temperature

The effect of temperature was investigated due to its ability change the adsorbent's adsorption capacity and thus negatively influence the adsorption of ARVDs from aqueous solution. A sharp increase in the adsorption efficiency was observed from 15-30°C (40-90%) (**Figure 5.8**) indicating that adsorption is favoured by increased temperature. The increase in temperature leads in successful collision of solute and adsorbent thus results rapid adsorption chances (Auta & Hameed et al.,2012). After the optimum temperature is obtained the adsorption capacity steadily decrease in the removal of ARVDs which could be ascribed to weakening of attractive forces on the surface of PIM-1 which is a consequence of temperature increase (Hamdaoui et al., 2006, Hameed & Ahmad el al., 2009).



**Figure 5.8:** Effect of temperature on adsorption efficiency of ARVDs by PIM-1: Adsorption conditions: contact time of 60 minutes, sample pH -7, mass dosage 10 mg, sample volume - 10 mL, initial concentration of 1.0 mg/L, agitation speed - 150 rpm

## 5.5 Adsorption kinetics, Adsorption isotherms and Thermodynamic studies

### 5.5.1 Adsorption kinetics studies

The kinetics studies were conducted to find the adsorption equilibrium time and to assess the ARVDs removal rate from the aqueous phase over time. The kinetic models such as the pseudo first-order (associated with the adsorbent's adsorption capacity), and pseudo second-order (proposes the probability of chemisorption interaction between the adsorbate and the adsorbent), and intraparticle diffusion were employed to study the behaviour of the adsorbent-adsorbate (Duarte et al., 2022, Wang et al., 2012, Ma et al., 2019) using the following equations (5.4), (5.5), and (5.6), respectively.

$$\ln(q_e - q_t) = \ln(q_e - K_1) \quad (5.4)$$

$$\frac{t}{q_e} = \frac{1}{K_2 q_2^{1/2} + C_i} \quad (5.2)$$

$$q_e = K_{id}t^{1/2} + C_i \quad (5.6)$$

where  $q_e$  (mg/g) is the amount adsorbed at equilibrium, and  $q_t$  (mg/g) amount of ARVDs is time  $t$  (min). Moreover,  $K_1$  ( $\text{min}^{-1}$ ) and  $K_2$  ( $\text{g} (\text{min mg})^{-1}$ ) are rate constants of pseudo-first and pseudo-second-order,  $K_{id}$  ( $\text{mg} (\text{g}^{-1} \text{min}^{-1/2})$ ) is a diffusion rate constant and  $C_i$  is a boundary layer constant.

To obtain a better understanding of adsorption process the kinetic model are explored. A plot of  $\log(q_e - q_t)$  against time ( $t$ ) that yield  $K_1$  and  $q_e$  values from slope and intercept respectively for a pseudo-first-order model. Furthermore, a plot of  $(t/q_t)$  against ( $t$ ) gives  $(1/q_e)$  as slope and  $(1/K_2 q_e^2)$  as intercept from which  $K_2$  can be obtained. Upon fitting the experimental data on the models, the correlation coefficient of pseudo-second-order ( $R^2 = 0.925-0.997$ ) was observed to be greater than pseudo-second-order kinetic model ( $R^2 = 0.654-0.991$ ), (**Table 5.1**). This implied that the rate determining is pseudo-second-order. A similar trend was observed whereby nanofibers were employed for adsorption of ARVDs from water where the data was fitted better in the pseudo-second-order and chemisorption was suggested to be the rate determining step of the adsorption process (Kebede et al., 2020). The intraparticle diffusion model showed that the linear plots do not pass through the origin. This an indication that the intraparticle diffusion is not the only rate determining steps but there are other kinetic models which could be simultaneously operating that control the adsorption process of ARVDs by PIM. In addition, the deviation could be attributed to difference in mass transfer between initial and final phases of the adsorption process. Furthermore, this a confirmation that adsorption of ARVDs by PIM-1 is a multi-step process involving adsorption on the external surface and diffusion into the interior (Kumar & Kumaran et al., 2005)

**Table 5.1: Kinetic constants of nevirapine, abacavir and efavirenz**

	Parameters	Nevirapine	Abacavir	Efavirenz
First order	$q_e$ (mg/g)exp	$2.75 \times 10^{-3}$	63.56	$4.45 \times 10^{-3}$
	$q_e$ (mg/g)cal	$7.41 \times 10^{-5}$	56.79	$9.23 \times 10^{-5}$
	$K_1$ (min <sup>-1</sup> )	0.5630	0.0046	3.3350
	$R^2$	0.654	0.925	
Second-order	$q_{e2}$ (mg/g)	$9.67 \times 10^{-5}$	1.065	1.770
	$K_2$ (mg(g <sup>-1</sup> min <sup>-1/2</sup> ))	$91.75 \times 10^{-6}$	1.034	0.876
	$R^2$	0.965	0.997	0.925
Intra-particle diffusion	$K_{diff}$ (mg( g <sup>-1</sup> min <sup>-1/2</sup> ))	2.210	2.460	2.430
	$C$ (mg g <sup>-1</sup> )	2.430	3.021	2.574
	$R^2$	0.825	0.998	0.985

### 5.5.2 Adsorption isotherms

To gain more insight about the reaction behaviour the Freundlich, Langmuir and Temkin model were explored. The Langmuir kinetic model was investigated using equation (5.7).

$$D = \frac{q_e}{C_e} \quad (5.7)$$

Where  $C_e$  is the concentration at the equilibrium of antiretroviral (mg/L), ( $q_e$  is adsorption capacity at equilibrium (mg/g),  $q_m$  is the maximum theoretical capacity (mg/g) and  $K$  (L/mg) is the Langmuir constant that correlates to the binding sites. The constant of Langmuir is obtained by plotting the slope and the intercept of the plots which are plot of  $C_e/q_e$  against  $C_e$ . the Freundlich model was investigated using equation (5.8), (Abdel Rahman et al., 2017).

$$\log q_e = \log K_F + \frac{1}{n} \log C_e \quad (5.8)$$

The  $K_F$  and  $n$  are the constants which gives an insight about the heterogeneity degree of surface sites. A plot of  $\log q_e$  against  $\log C_e$  is be used to obtain the two constants.

The Temkin model could be defied by the following equation (5.9).

$$q_e = B \ln K_t + B \ln C_e \quad (5.9)$$

$$R_L = \frac{1}{1 + bC_e} \quad (5.10)$$

The experimental data was fitted in Langmuir, Freundlich and Temkin model. An essential characteristic of Langmuir isotherm can be expressed by dimensionless constant called equilibrium parameter ( $R_L$ ) defined by equation (5.10). The  $R_L$  value defines the isotherm type to be unfavourable ( $R_L > 1$ ). linear ( $R_L = 1$ ), favourable ( $0 < R_L < 1$ ) or irreversible ( $R_L = 0$ ), (Jagtap et al., 2012, Martins et al., 2015). The  $R_L$  value ranged from (0.300-0.970) across all the ARVDs in this investigation indicating the favourability of nevirapine, abacavir and efavirenz under studied conditions (**Table 5.2**).

The correlation of Freundlich ( $R^2 = 0.978-0.999$ ) was greater than Langmuir ( $R^2 = 0.946-0.998$ ) thus adsorption of ARVDs was consistent with Freundlich isotherm model. The dominance of Freundlich isotherms is an indication that physio-chemical adsorption on heterogenous surface is best describes that adsorption of ARVDs by PIM-1 adsorbent. The dominance of Freundlich model implies that there is a multilayer adsorption process in the surface of the PIM polymer for removal of ARVDs in wastewater samples. Temkin model had  $R^2$  close to 1, which implies there is a strong affinity between the adsorbent and adsorbate.

**Table 5.2: Adsorption isotherms Langmuir, Freundlich, and Temkin for analysis of ARVDs**

	Parameters	ARVDs		
		Nevirapine	Abacavir	Efavirenz
Langmuir	$q_{\max}$ , cal(mg/g)	20.40	31.28	34.78
	$K_L$ (Lmig <sup>-1</sup> )	0.860	0.630	0.050
	$R_L$	0.300	0.590	0.970
	$R^2$	0.983	0.998	0.946
	1/n	1.780	0.670	0.1720
Freundlich	$K_F$	0.430	0.450	0.830
	$R^2$	0.997	0.999	0.978
	$K_T$ (g/L)	12.99	9.870	4.490
Temkin	B	56.8	52.69	46.06
	$R^2$	0.989	0.990	0.967

### 5.5.3 Thermodynamic studies

To gain more understanding of the adsorption process standard free energy  $\Delta G^\circ$ , enthalpy change  $\Delta H^\circ$  and entropy changes  $\Delta S^\circ$  are essential parameters to be evaluated. Gibb's free energy is studied using equation (5.11). The variation of temperature with a distribution coefficient D could be used to make thermodynamic parameters using equation (5.11)

$$D = \frac{q_e}{C_e} \quad (5.11)$$

where  $q_e$  is the number of antiretrovirals adsorbed by the adsorbent (mg/g) at equilibrium, and  $C_e$  is the equilibrium concentration of antiretrovirals in (mg/L).  $\Delta H^\circ$ ,  $\Delta S^\circ$ , and  $\Delta G^\circ$  can then be calculated according to equations (5.12).

$$\Delta G^{\circ} = \Delta H^{\circ} - T\Delta S^{\circ} \quad (5.12)$$

where R is a gas constant (8.314 J/mol K), T is the absolute temperature (K),  $\Delta H^{\circ}$  and  $\Delta S^{\circ}$  could be obtained from the slope and intercept of  $\Delta G^{\circ}$  vs  $1/T$ . Variation of temperatures (288, 298, 303, 313, and 333 K) is essential to conduct the thermodynamics studies.

A plot of  $\ln D$  against  $1/T$  was used to calculate the values of  $\Delta H^{\circ}$  and  $\Delta S^{\circ}$  and standard Gibbs energy was evaluated by equation (5.12). The negative values of  $\Delta G^{\circ}$  increased with an increase in temperature (**Table 5.3**) which implies that the adsorption was spontaneous and thermodynamically favoured. The values of  $\Delta H^{\circ}$  were found to be negative which implies that the adsorption of ARVDs onto the PIM-1 is exothermic in nature. The value of  $\Delta S^{\circ}$  was positive which implied an increase in randomness in the ARVDs-adsorbent interaction. All the target compounds ARVDs had  $\Delta H^{\circ}$  greater than 40 kJ mol<sup>-1</sup> which shows that the adsorption is dominated by chemisorption (Duarte et al., 2022). This observation is consistent with observation of adsorption kinetics whereby the pseudo-second-order was favoured which is an indicative of favourability of chemisorption adsorption process. A similar trend was observed where the adsorption process was favoured by chemisorption on the removal of ARVDs in wastewater using nanofibers (Kebede et al., 2020).

**Table 5.3: Thermodynamic parameters for adsorption of ARVDs**

	$\Delta G^{\circ}(\text{kJ mol}^{-1})$					$\Delta H^{\circ}$	$\Delta S^{\circ}(\text{Jmol}^{-1}\text{k}^{-1})$	$R^2$
	288	293	298	303	313	(kJmol <sup>-1</sup> )		
T (K)	288	293	298	303	313			
Nevirapine	-18.87	-40.25	-71.42	-73.43	-90.00	-91.50	46.78	0.961
Abacavir	-71.09	-86.82	-102.59	-118.36	-123.84	-68.87	31.54	0.986
Efavirenz	-45.32	-46.06	-120.63	-121.18	-183.71	-71.06	25.08	0.961

#### 5.5.4 Comparison of the adsorption efficiency of different adsorbent on removal of ARVDs

The adsorption of ARVDs from aqueous solution has been assessed using various adsorbents (**Table 5.4**). The optimum adsorption conditions for *Platanus acerifolia* and macadamia nutshells were also evaluated in the previous study. These were a contact time of 90 minutes, solution pH of 7, ARVDs initial concentration of 100.0 mg/L, adsorbent mass dosage of 10 mg and adsorption temperature of 35°C. These conditions were found to be optimum for PIM-1 except the contact time 60 minutes. From (**Table 5.4**), it is evident that nanofibers have high adsorption efficiency (111.6 -189.1 mg/g) which could be due to its large surface area. The graphene wool gave 80-84 mg/g while biofilm reactor application showed 62-94 mg/g. Nanofibers has illustrated to be efficient adsorbent for removal of antiretrovirals in wastewater (Kebede et al.,2020). However, the nanofibers require more preparatory steps and high energy consumption.

PIM-1 had received attention for removal of environmental pollutants such dyes (Peng et al., 2016, Alnajrani & Alsageret et al., 2020, Wang et al., 2022). Upon PIM-1 application for the removal of ARVDs in this work it gave 83.65-96.45 mg/g whereby the initial contraction of wastewater samples was 100 mg/L. These results illustration that PIM-1 is also a good candidate for the removal of ARVDs from water. The additional attributes of PIM-1 are that it requires one synthetic route and easy set up before applied for adsorption of ARVDs. Macadamia nutshell and *Platanus acerifolia* leaves which are generated in agricultural waste are promising adsorbent for removal of ARVDs from aqueous media. This could be due to presence of N-H and O-H functional groups which promote the hydrogen bonding between the *Platanus acerifolia* and ARVDs leading to their high adsorption. The application of these adsorbents contributes to circular-economy while simultaneously reducing environmental pollution. Furthermore, these adsorbents are eco-friendly, cost effective, easily accessible and requires minimal preparation steps prior their application. Thus, they are the potential replacements as ARVDs adsorbents for the available expensive and harmful currently used adsorbents.

**Table 5.4: Comparison adsorbents on adsorption efficiency of ARVDs in wastewater.**

	Macadamia nutshell adsorbent	<i>Platanus acerifolia</i> Leaves adsorbent	PIM-1 adsorbent	Nanofiber Adsorbent	Graphene wool	Moving bed biofilm reactor	
Reference	Previous Unpublish ed work	Previous unpublish ed work	This work	(Kebede et al., 2020)	(Adeola et al., 2021)	(Mokgope et al., 2022)	
$q_e$ (mg/g)							
	Nevirapine	94.41	78.34	83.65	189.1	84	-
Effluent	Abacavir	92.48	80.87	94.56	-	-	-
	Efavirenz	93.06	83.65	96.45	138.40	80	-
	Nevirapine	93.83	84.06	89.56	111.6	-	62
Influent	Abacavir	97.83	90.37	90.45	-	-	-
	Efavirenz	99.67	95.56	87.55	174.0	-	94

The initial concentration for wastewater samples used in the adsorption studies was 100.0 mg/L.

## 5.6 Conclusion

The PIM-1 was successfully synthesized and applied as an effective adsorbent for removal of the selected ARVDs in wastewater. The characterized by FTIR functional groups such C-N, C-H and C=O played an essential role on the ability of the adsorbent to interact with target species. An amorphous and mesoporous materials was obtained by the PXRD characterization which could be essential for removal of ARVDs in wastewater samples. The optimum conditions of contact 60 minutes, concentration 1.0 mg/L, pH 7 and mass dosage of 10 mg. The kinetic data was well fitted in pseudo-second-order, while the adsorption isotherms showed that the experimental data well fitted in Freundlich model confirming the dominance of physio-chemical adsorption in a heterogenous surface of the adsorption process. The thermodynamic studies revealed that ARVDs adsorption onto the PIM-1 is of endothermic in nature as the value of  $\Delta H^\circ$  was found to be positive. The PIM-1 became a promising candidate for the removal of ARVDs with removal efficiency above 86% for all ARVDs target compound. Generally, PIM-1 showed to be very efficient and effective in the removal of (nevirapine, abacavir and efavirenz) and the adsorption process was simple and easily applicable for removal of wastewater.

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## Chapter Six: Conclusion and Recommendations

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### 6.1 Conclusion

The macadamia nutshell, *Plantaus acerifolia* leaves and polymer of intrinsic of microporosity number-1 (PIM-1) proved to be easily accessible and cost-effective adsorbents for removal of antiretrovirals in wastewater samples. The calibration of LC-PDA method showed good accuracy with all correlation coefficients above 0.99. All adsorbents displayed a removal efficiency about 80% for all ARVDs of interest. The simplicity of preparation of macadamia and *Plantaus acerifolia* leaves as adsorbent is an added advantage.

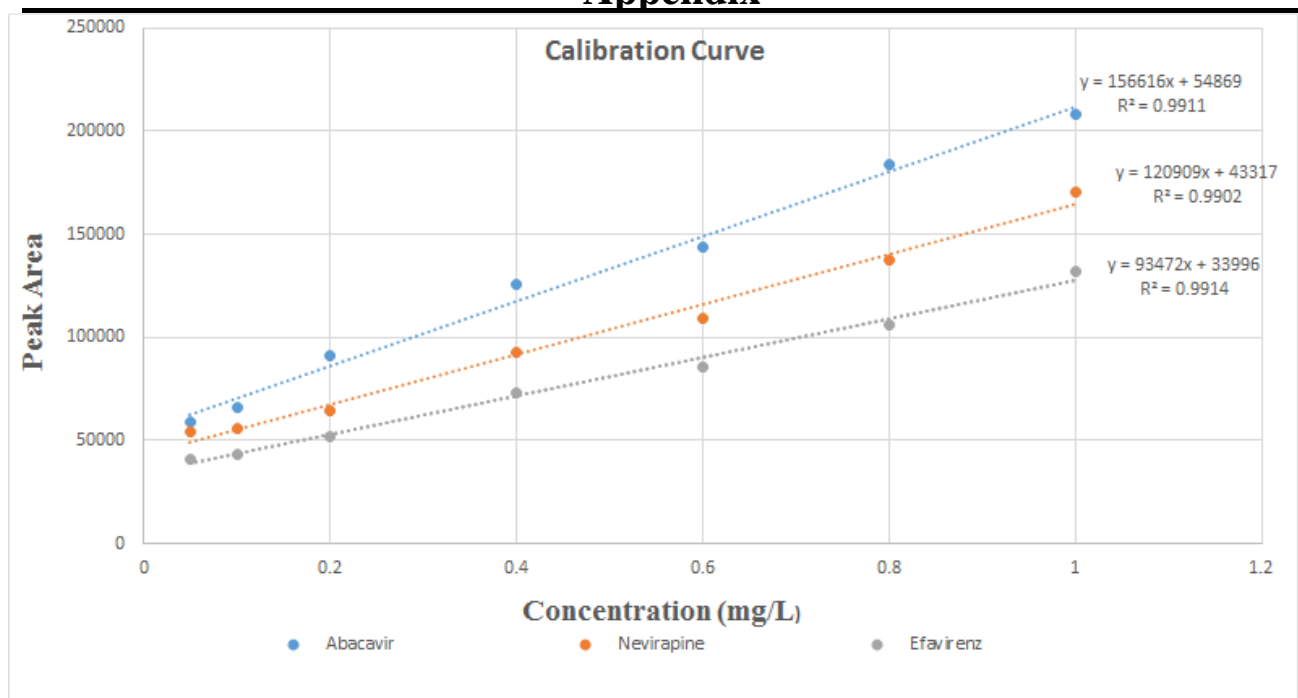
The successful synthesis and application of macadamia nutshell, *Plantaus acerifolia* leaves provided an alternative adsorbent for removal of ARVDs in wastewater samples with minimal or norside-products. This study demonstrates the potential use of natural occurring resources to resolve challenges of water pollution. Moreover, the usage of these agricultural adsorbent promoted circular economy and reduced pollution where the waste macadamia nutshell and *Plantausacerifolia* leaves could be dumped in the landfills and increase eutrophication resulting to major threat to water quality and aquatic species. Moreover, the application of PIM-1 provides an alternative usage of the polymeric materials besides its common application as a gas storage material.

Overall, the synthesis and application of macadamia nutshell, *Plantaus acerifolia* and PIM-1 illustrated as eco-friendly, effective, and cost-effective for removal of ARVDs which has a potential risk to human and animal health. Furthermore, this study promotes the application of the basic principle of chemistry. The results from this study could assist policy makers to make decisive legislation that govern the disposal of ARVDs given the extent of potential threat it possesses to human and animal health through continual exposure.

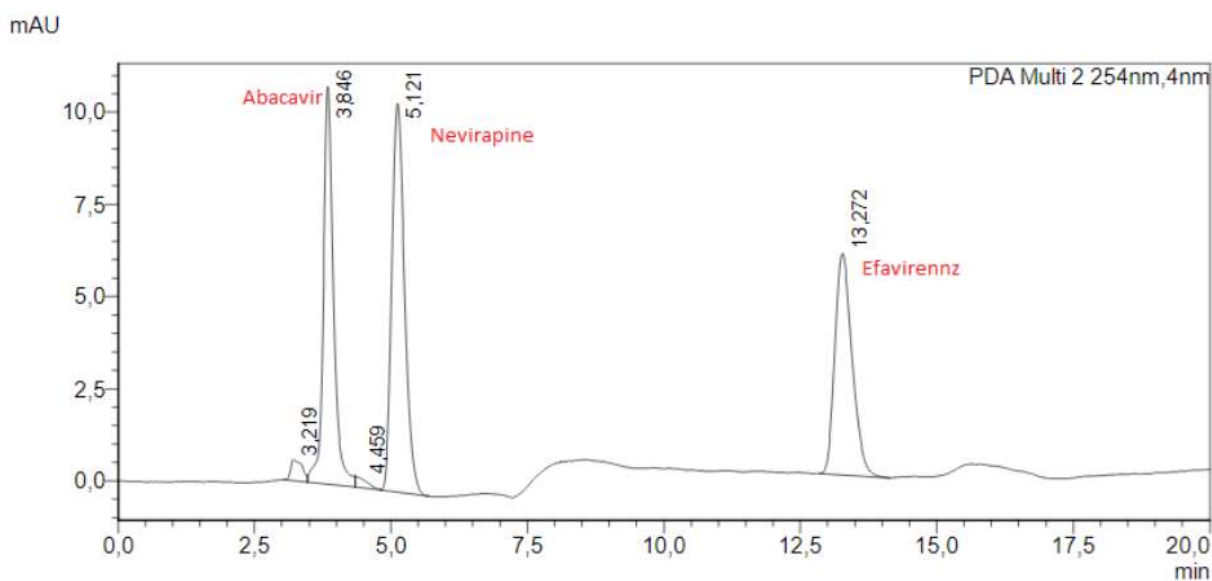
## **6.2 Recommendations and future work**

- The assessment of these synthesized adsorbents for adsorption of other potential water contaminants.
- The continual monitoring of other water pollutants and their associated potential risk to animal and human health.
- The continual assessment of ARVDs and other water pollutants in different sites in South Africa and reports on extent of pollution and effects due to continual exposure to them.
- The explore synthesis and application of different adsorbents for adsorption of ARVDs and other water contaminants.

## Appendix



**Figure A1:** Calibration curve for nevirapine, abacavir and efavirenz



**Figure A2:** Chromatogram showing the separation of abacavir, nevirapine and efavirenz under optimum conditions

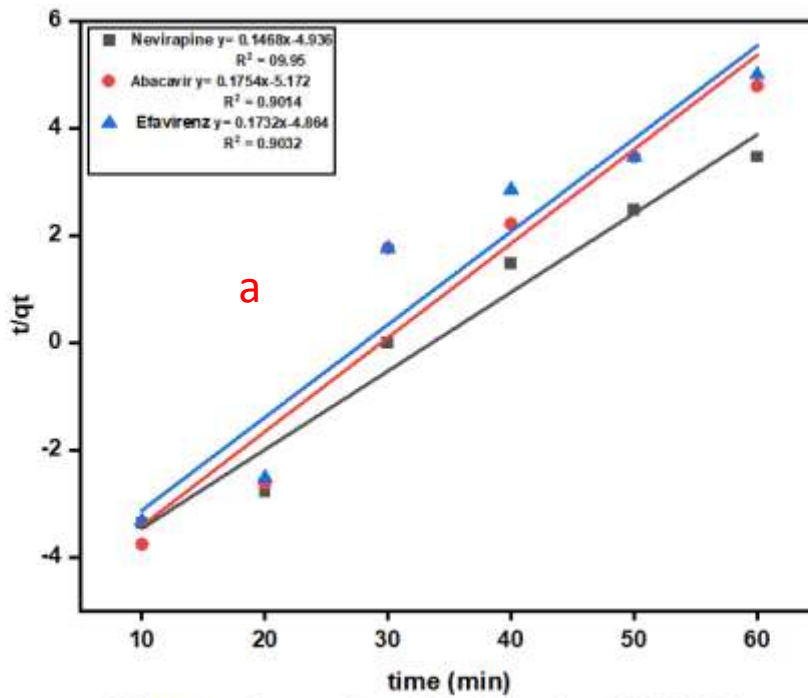


Figure : Second-order kinetics PIM-HCl

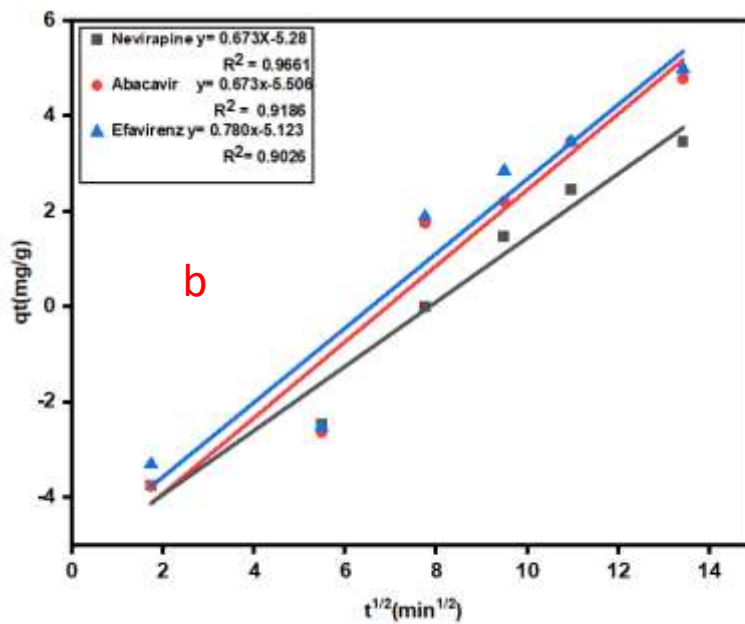


Figure : Intraparticle model of Pim-HCl for removal of ARVDs

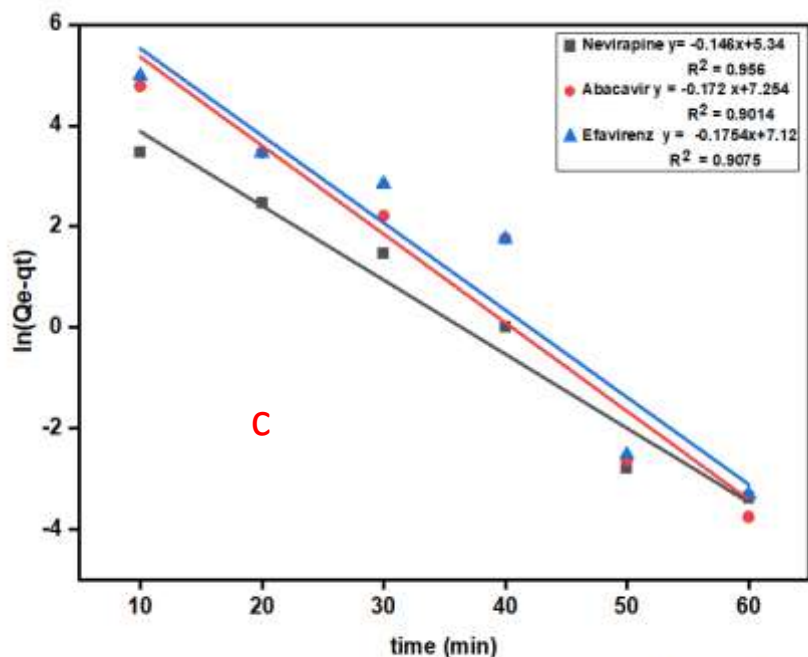
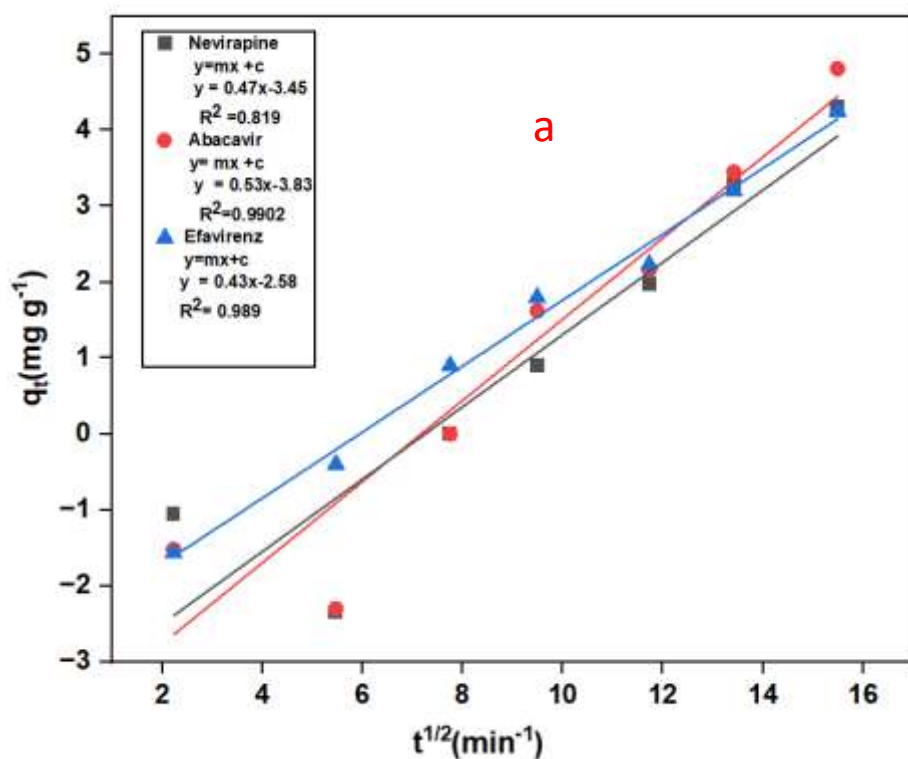
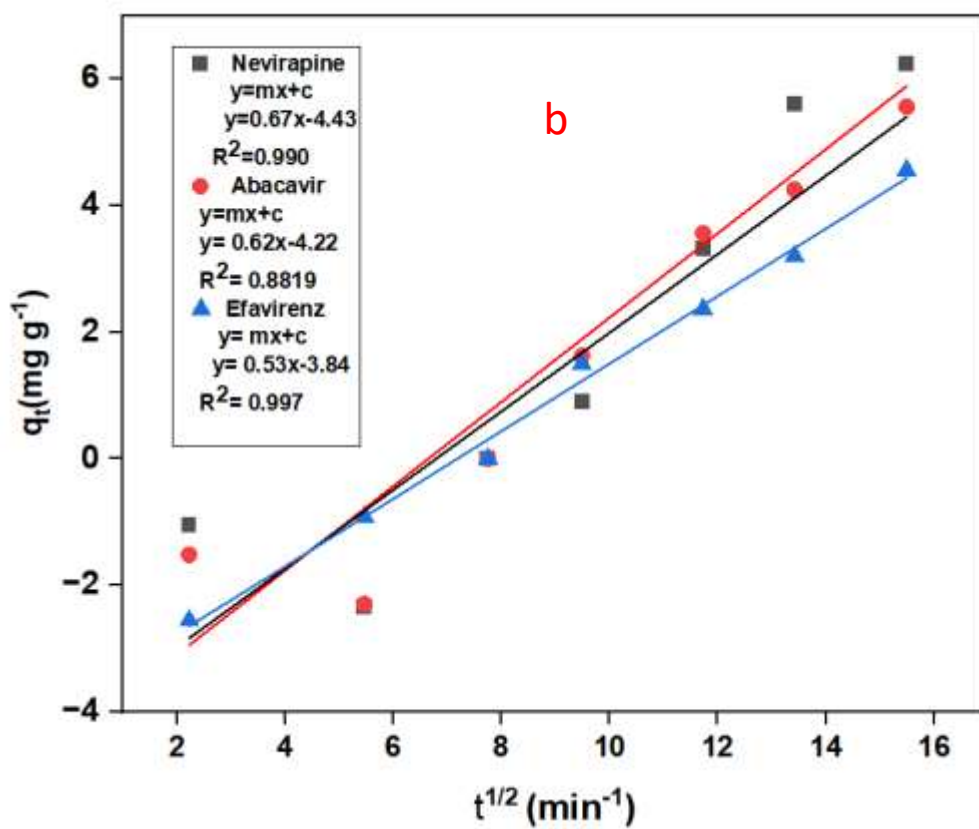


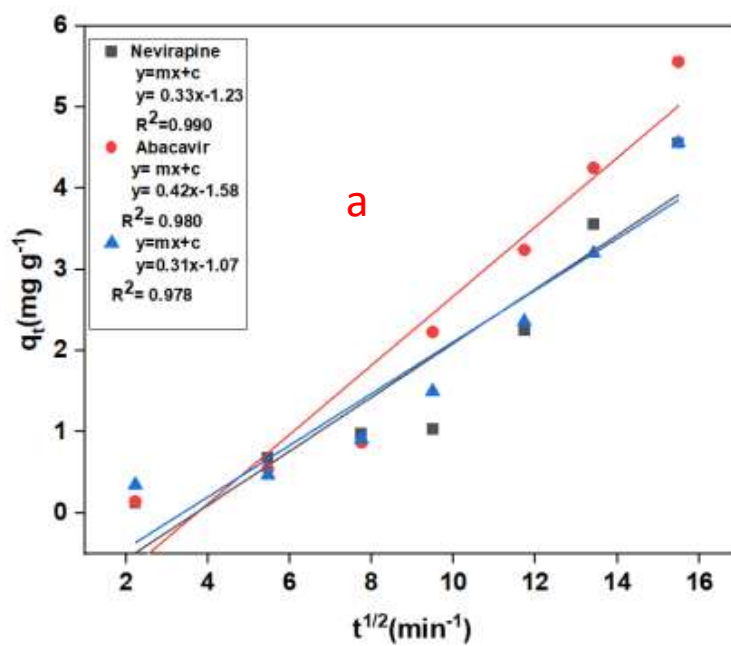
Figure : First-order PIM-HCl for removal of ARVDS

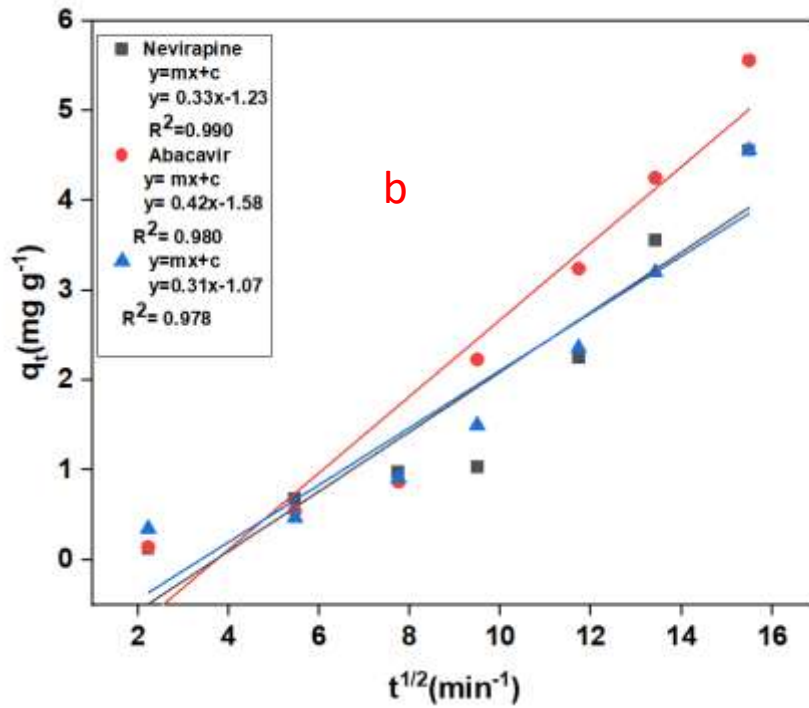
Figure A3: Kinetic parameters of polymer of microporosity number-1 (PIM-1) adsorbent pseudo-first-order (a), pseudo-second-order(b) and intraparticle diffusion(c)





**Figure A4:** Intraparticle diffusion model for MCN-NaOH (a) and MCN-HCl (b) on the ARVDs adsorption by macadamia nustshells





**Figure A5:** Intraparticle diffusion model for LPL-NaOH (a) and LPL-HCl (b) on the ARVDs adsorption by *Plantaus acerifolia* leaves as adsorbents.