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Stability Studies of Amide Containing Pharmaceuticals and Their Removal by Nano-membrane Technology, Activated Carbon and Micelles-Clay Complex

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Stability Studies of Amide Containing Pharmaceuticals and Their Removal by Nano-membrane Technology, Activated Carbon and Micelles-Clay Complex

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Dedication

This thesis is dedicated to my wonderful parents who sacrificed a lot for me to be what I am now.

I am very grateful for their unconditional love, support and prayers. Thank you for instilling in me the desire to strive for the best.

I dedicate this thesis to my dear country, Palestine. My dear land that I believe Strongly will return to us some day.

Declaration

I certify that the thesis submitted for the degree of master is the result of my own research, except where otherwise acknowledged, and that this thesis (or any part of the same) has not be submitted for a higher degree to any bother university or institution.

Signed: 

Ibrahim Ali Ibrahim Ayyad

Date: .....

Abstract

Kinetic studies on the stability of the pain killer agent, paracetamol and its metabolite-aminophenol and N-substituted benzamide derivatives in Al-Quds activated sludge demonstrated that paracetamol underwent a complete biodegradation within less than one month to provide hydroquinone via the intermediacy of *p*-aminophenol. Moreover, the results revealed that *p*-aminophenol and benzamide underwent complete biodegradation within less than one week to furnish hydroquinone and benzoic acid, respectively. The pseudo first order reaction rate constants for those processes were found to be 2.17×10^{-9} $M.s^{-1}$, 8.64×10^{-9} $M.s^{-1}$ and 7.86×10^{-9} $M.s^{-1}$, respectively. Moreover, it was found that *Pseudomonas aeruginosa*is the bacteria responsible for the biodegradation of the above mentioned amide pharmaceuticals. The efficiency of Al-Quds University wastewater treatment plant (AQU-WWTP) demonstrated that the ultrafiltration- hollow fiber unit (UF-HF) was insufficient in removing the studied amide pharmaceuticals (40% removal) and their metabolites from spiked secondary treated wastewater samples, whereas the ultrafiltration-spiral wound unit (UF-SW) (80% removal) followed by activated carbon column were quite efficient and yielded a complete removal of the pharmaceuticals (100% removal). Batch adsorption results of the amide containing pharmaceuticals: N-substituted benzamide derivatives, paracetamol and *p*-aminophenol onto activated carbon and octadecyltrimethylammonium) (ODTMA) – micelles clay complex were found to fit Langmuir and Freundlich Isotherms. In addition, the results demonstrated that the adsorption of these pharmaceuticals onto ODTMA micelles-clay complex was more efficient than activated carbon.

Acknowledgments

At the beginning and before anything I would like to thank God (Allah) for this success. As without his support I would not have managed to accomplish this treatise.

Then, I would like to thank my dear university, Al-Quds University and its professional staff that provided me with every source and advice that needed to attain my BS degree in chemistry and M.Sc. degree in the Applied and Industrial Technology Program. For this great establishment and its staff, I am grateful.

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In this special day I would like to thank all who supported me, encouraged me and had the tolerance to wait for this success to be made.

All respect, love and appreciation to all of you. Wishing all of you happiness and joy.

Jerusalem, Palestine, Jan. 2017.

Ibrahim Ali Ibrahim Ayyad

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List of Abbreviations

AQU-WWTP	Al-Quds University Wastewater Treatment Plant
AC	Activated Carbon
AOPs	Advanced Oxidation Processes
AST	After Secondary Treatment
AV	Average
BOD	Biological Oxygen Demand
BP	British Pharmacopoeia
CAD	Coronary Artery Disease
COD	Chemical Oxygen Demand
DAF	Dissolved Air Flotation
DEET	N,N-Diethyl-3-Methylbenzamide
DWW	Domestic Wastewater
EC	Electrical Conductivity
EDA	Environmental Protection Agency
FC	Fecal Coliform
HDL-C	High Density Lipoprotein Cholesterol
HF	Hollow Fiber
HPLC	High Pressure Liquid Chromatography
kD	Kilo-Dalton
LC-MS	Liquid Chromatography Mass Spectroscopy
LDL-C	Low Density Lipoprotein Cholesterol
MBR	Membrane Bio-Reactor
MF	Micro-Filtration
NAPQI	N-acetyl-p-benzoquinone imine
NF	Nano-Filtration
NMR	Nuclear Magnetic Radiation
ODTMA	Octadecyltrimethylammonium
OPA	Ortho-Phosphoric acid
PDA	Photo Diode Array
PPCPs	Pharmaceuticals and Personal Care Products
ppm	Part per million
PSD	Particle Size Distribution
RO	Reverse Osmosis
SD	Standard Deviation
SW	Spiral Wound

STP	Sewage Treatment Plants
TC	Total Coliform
TDS	Total Dissolved Solids
TOC	Total Organic Carbon
TOD	Total Oxygen Demand
TSS	Total Suspended Solids
UK	United Kingdom
UF	Ultra-Filtration
USA	United State of America
UV	Ultra Violet
WWTPs	Waste Water Treatment Plants
WWTT	Waste Water Treatment Technology
WWT	Waste Water Treatment

Chapter One

Introduction

Chapter One
Introduction

1.1 Background:

Water is a basis component for an environmental function. As the world population continues to increase, world seeks to secure supplies to meet the human needs of water, and greater dare arising in purifying water of poorer quality for reuse (Zimmo 2005).

The water sources in Palestine are very limited. Groundwater is the main source of fresh water in Palestine, where the aquifer system is distributed to three main ground water drainage basins: the first in the western part of the West Bank, and the second in the northeastern part of the West Bank, while the third is in the eastern part of the West Bank. It mostly, lies under Israeli control. The second part of the water sources in Palestine is the surface water of the Jordan River (Zahra et al., 2001. Nazer et al., 2008).

The land in Palestine is semi-arid, where 70% of the available water is used in agriculture and about 27% is used in the domestic sector, while the remainder is used in industry (Zimmo 2005). Due to the water shortage, wastewater treatment technology (WWTT) has been utilized in Palestine to protect environmental pollution (such as ground water), and reuse the treated wastewater in agriculture (Bdour et al., 2009).

Palestine as a one of the Middle East countries, less tribute to different factors as increasing population growth rate and industrializing, the increasing life style in water consumption, the wastewater treatment (WWT) is the best alternative to decrease the gap between supply and demand.

Wastewater treatment (WWT) plants in Palestine include conventional such as activated sludge, bio-filters and others slightly less conventional, such as oxidation ditches, aerated lagoons and natural treatment system such as waste stabilization ponds (Al-Tamimi et al., 2008. Mcneill et al., 2009. Bdour et al., 2009).

The wastewater as a definition is a combination of water, 99% by weight, and solid material, about 1% by weight (dissolved material and suspended material). Wastewater contains organic materials, inorganic materials and microorganisms, where these components vary according to sources (EPA 1997). The wastewater sources can be divided into two types. First, domestic wastewater (DWW), or "sewage" and this type coms from homes, commercial places, and farms. DWW can also be divided into two types: black water which originates from toilets and kitchens and is highly contaminated and grey water which originates from baths, showers, wash basins and washing machine and is generally less contaminated. Grey water makes up 40% - 60% of the total DWW volume. The second type of wastewater isindustrial wastewater which is generated and discharged from manufacturing and commercial activities (EPA 1997, Metcalf 2003).

The wastewater is classified according to physical, chemical and biological components. (1) The physical which includes total solid contents is subdivided into total suspended solids (TSS) and total dissolved solids (TDS), particle size distribution (PSD), turbidity, temperature, electrical conductivity (EC), transmittance, density, color, and odor. (2) The chemical includes organic chemical (biochemical oxygen demand (BOD), chemical oxygen demand (COD), total organic carbon (TOC), and total oxygen demand (TOD). This type also includes inorganic chemicals: salinity, hardness, pH, acidity and alkalinity, as well as concentrations of cationic ions such as ionized metals such as iron and manganese, and anionic such as chlorides, sulfates, sulfites, nitrates, and phosphates. (3) The biological includes total coliforms (TC), fecal coliforms (FC), specific pathogens, and viruses (Emmerson 1998, EPA 1997, Scott 2004,Vigneswaran 2009).

The wastewater treatment process included physical, chemical and biological process. These processes can be divided into four stages: preliminary, primary, secondary and tertiary treatment process (EPA 1997). The preliminary, primary and secondary are called conventional wastewater treatment, they included a physical process such as sieve (for screening the large object and rags) and biological process such as activated sludge (to break down and removal of organic material). Fourth stage of treatment is a tertiary process and called advanced treatment of conventional effluent. Where use a physical and chemical

process (such as ozonation, membrane filtration ...and adsorption), (EPA 1997, US.EPA 2004, Bielefeldt 2009,Okoh 2009,Acero 2010)

Activated sludge is the most widely used methodology for WWT. In this process, the microorganisms are kept in suspension forming a biological flock while aeration basin by mechanical mixers or diffused air is maintained. The load of microorganisms is preserved by a continuous return of the settled biological flocks. As organic carbon is the most important energy source, heterotrophic bacteria dominate in activated sludge systems. Several variations of the activated sludge process have been developed in order to optimize carbon, nitrogen, and phosphorous removal from the wastewater (Kämpfer et al., 1996).

Communities of prokaryotic microorganisms present in activated sludge are responsible for all of the carbon and nutrient removal from sewage and thus represent the core component of the biological wastewater treatment plant (WWTP). Consequently, a thorough knowledge of the ecology of the microbial community is required to reveal factors influencing the efficiency and stability of biological WWTP and to develop promising strategies for improved process performance (Wagner 2002). Therefore, the microbiological details, including the compositions of the microbial populations that are responsible for the mineralization processes, are very important in increasing the treatment efficiency (Kämpfer et al., 1996).

Microbial populations in WWTP are frequently analyzed either by light microscopic observation (Eikelboom 1975, Jenkins 1993) or by cultivation-dependent techniques (Ueda 1972, Seiler 1982). These approaches lead to the postulation of model organisms for the most important microbiologically driven processes in WWTP (Henze 1997). During the past decade, a variety of approaches were also developed and used to study bacterial diversity in WWTP (Wagner 2002). Extensive studies using cultivable microorganisms that require their isolation and identification were performed. Characterization of bacterial populations in the environment samples including raw wastewater using commercially available identification kits was previously documented (Kämpfer et al., 1989. Kämpfer et al., 1990. Kämpfer et al., 1996).

Several pharmaceutical compounds and their metabolites have been detected in wastewater as well as in surface and drinking water; they were found at concentrations up to µg/L level in influent and effluent samples from WWT and also in surface water. Polar pharmaceutical compounds leach through the subsoil to ground water and have been detected up to the µg/L level (Egun 2010, Yu 2006).

1.2 Selected pharmaceutical containing amide bonds

1.2.1 Paracetamol

Paracetamol (Figure 1.2-a) is available in different dosage forms such as tablets, capsules, drops, elixirs, suspensions and suppositories. Its saturated aqueous solution has a pH of about 6 and is stable with a half-life exceeding 20 years, but its stability decreases in acidic or alkaline conditions due to being slowly degraded, via a base or acid hydrolysis of the amide bond, into acetic acid and *p*-aminophenol (Figure 1.2-b). Paracetamol is metabolized primarily in the liver, into non-toxic products via three metabolic pathways (Figure 1.1). Glucoronidation is believed to account for 40-66% of the metabolism of paracetamol; and sulfation (sulfate conjugation) may account for 20-40% (Nelson 2006).N-hydroxylation and rearrangement, then GSH conjugation, account for less than 15%. The hepatic cytochrome P450 enzyme system metabolizes paracetamol, forming a minor yet significant alkylating metabolite known as NAPQI (N-acetyl-p-benzoquinone imine). NAPQI is then irreversibly conjugated with the sulfhydryl groups of glutathione. All mentioned three pathways yield final products that are inactive, non-toxic, and eventually excreted by the kidney. In the third pathway, however, the intermediate product NAPQI is toxic. NAPQI is primarily responsible for the toxic effects of paracetamol (Williams 2002).

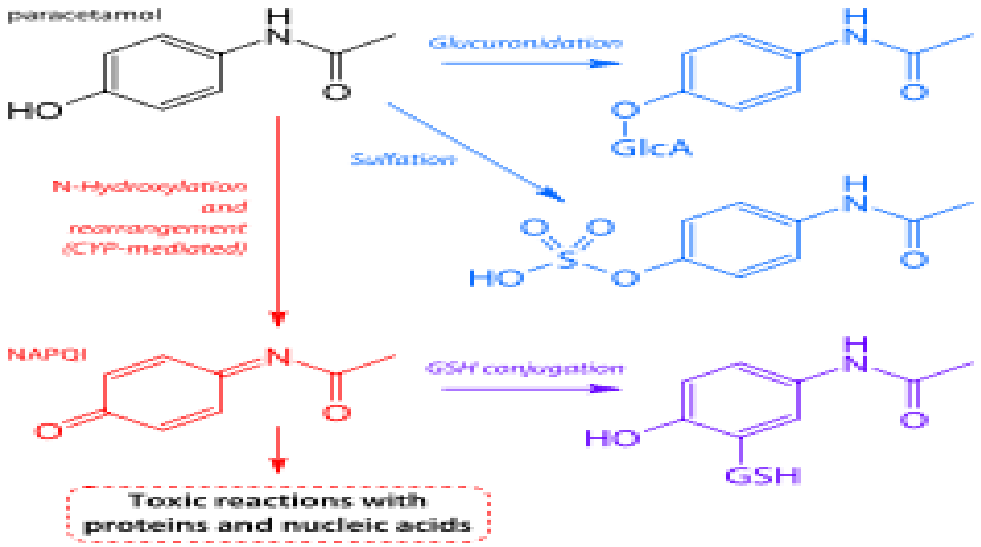

Figure 1.1 Main pathways of paracetamol metabolism, Pathways shown in blue and purple lead to non-toxic metabolites; the pathway in red leads to toxic NAPQI.

1.2.2 Benzamide

Benzamide (Figure 1.2-d) and N- substituted derivatives of benzamide are reported to possess antiemetic, antipsychotic and antiarrhythmic activities (Clark 1985, Vamecq 1997).

1.2.3 Bezafibrate

Bezafibrate **(**Figure 1.2-c) is one of the most popular compounds of the fibrate hypolipidaemic class of drugs. Its pharmacological activity consists in reducing serum triglyceride (22%) and low density lipoprotein cholesterol (LDL-C) (5%) levels and significantly raising high density lipoprotein cholesterol (HDL-C) fraction. It is widely used in the treatment of hypertriglyceridemia, which is now recognized as an independent risk factor of a coronary artery disease (CAD) (Duriez 1999). About 95% of orally administered bezafibrate is bounded by albumin and most of the absorbed drug is excreted in urine. It is known that approximately 50% of the administered dose is not completely metabolized and its unchanged form is excreted in urine within 24 hours (Abshagen 1979).

1.2.4 Atenolol

Atenolol (Figure 1.2-e) is available in different dosage forms such as tablets, oral solution and injection. It is beta-adrenergic antagonist. Atenolol is incompletely absorbed through the intestine (about 50%), but most of the absorbed dose reaches the systemic circulation. Peak blood levels are reached between two and four hours after ingestion. Unlike propranolol or metoprolol, atenolol undergoes little or no metabolism by the liver and the absorbed portion is eliminated by renal excretion. Over 85% of intravenous dose is excreted in urine within 24 hours compared with 50% for an oral dose. Only a small amount (6-16%) is protein-bound resulting in relatively consistent plasma drug levels with about a four-fold inter-patient variation. The elimination half-life of atenolol is 6 to 7 hours and there is no alteration of kinetic profile of drug by chronic administration. Following intravenous administration peak plasma levels are reached within 5 minutes. Declines from peak levels are rapid (5 to 10 fold) during the first 7 hours. Following oral doses of 50 mg or 100 mg both beta-blocking and anti-hypertensive effects persist for at least 24 hours (Wander et al., 2009).

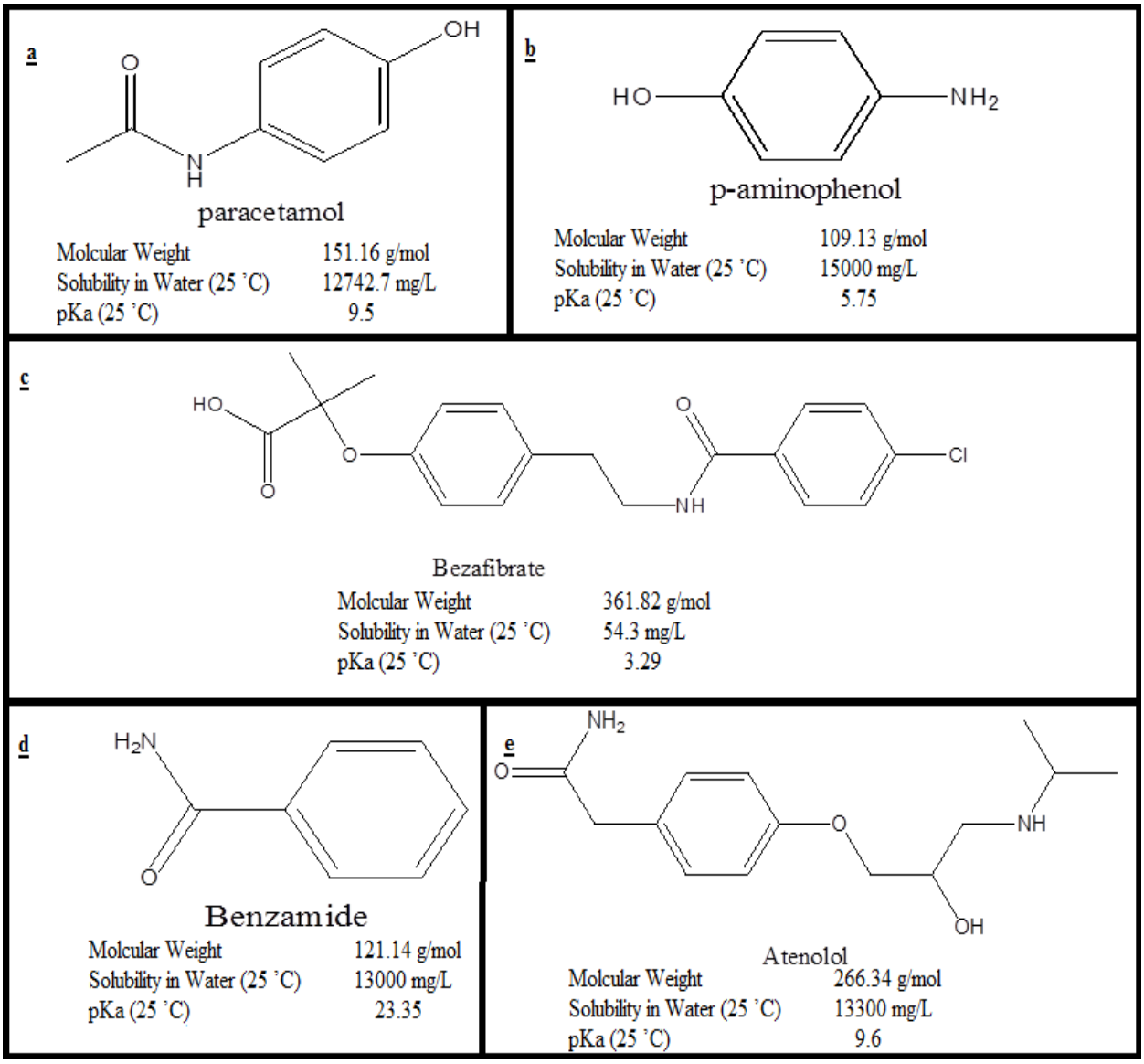

Figure 1.2: Physiochemical properties of selected pharmaceuticals, (a) Paracetamol, (b) *P*-aminophenol, (c) Bezafibrate, (d) Benzamide and (e) Atenolol. (B.P. 2009, Champman 1982).

1.3 Thesis Objectives

The main objectives of my thesis were (1) to investigate the stability of amide pharmaceuticals in wastewater (activated sludge) and (2) to study their removal along with their metabolites by micelle-clay complex and advance membranes technology.
The sub-goals of this thesis were to investigate:

- ✓ The stability of the amide pharmaceuticals in fresh water and activated sludge and to conduct comparisons between both.

- ✓ The biodegradation of the amide pharmaceutical by isolated bacteria (this bacterium was detected and isolated from AQU-WWTP sludge).

- ✓ The efficiency of the Al-Quds University wastewater treatment plant (AQU-WWTP) towards removing the amide pharmaceuticals and their degradation products.

- ✓ The removal of the amide pharmaceuticals and their degradation products using low cost adsorbent materials (micelle-clay complex and activated carbon).

1.4 Thesis Outline

This thesis consists of five chapters: the first chapter which includes the introduction and selected amide pharmaceuticals and their chemical and physical properties, the second chapter which includes literature review on the occurrence of pharmaceuticals in wastewater and fresh water and the removal methods and biodegradation of amide pharmaceuticals. The third chapter includes the materials, instrumentation and methods used in sampling, sample treatment and analysis. The fourth chapter includes the results and discussion of the stability of the amide pharmaceuticals and their removal along with their degradation products using advances membranes technology, clay micelles complex and activated carbon. The fifth chapter includes the conclusion and recommendation and the final chapter lists references.

Chapter Two

Literature Review

Chapter Two
Literature Review

2.1 Introduction.

2.1.1 Occurrence of pharmaceuticals in the environment.

The occurrence and fate of pharmaceuticals residues in wastewater and the environment have attracted an increasing interest during the last decade (Halling-Sorensen et al., 1998, Lorphensri et al., 2007, Ternes et al., 1998). Many organic compounds, such as pharmaceuticals; enter the sewage through several sources such as industrial and household effluents.

The removal of many of these pharmaceuticals during municipal WWT has been found to be incomplete (Ternes et al., 1998, Ashton et al., 2004, Carballa et al., 2004, Heberer et al., 2002, Quintana et al., 2004, Stumpf et al., 1996). When they enter a WWTP, some pharmaceuticals are either partially retained in the sludge or metabolized to more hydrophilic but still persistent forms and, therefore, pass through the WWTP and end up in the effluent (Radjenovic et al., 2007). As a result, residues of these compounds have been detected in surface water in concentrations ranging from ng/L up to mg/L level (Ternes et al., 1998, Ashton et al., 2004, Carballa et al., 2004, Buser et al., 1999, Tixier et al., 2003).

Occurrence of pharmaceuticals (such as paracetamol) and personal care products (PPCPs) in raw sewage samples collected from the Baltimore Back River WWTP (Yu et al., 2006). Reported the 9 of PPCPs in marine sediments, Brazil, at range from 52.5 ng/g to 0.71 ng/g (Beretta et al., 2014).The concentration of PPCPs range 19 ng/g – 2100 ng/g was fund in fish samples collected from different river at United States (Ramirez et al., 2009).

The reported removals of paracetamol in WWTP are varying from almost complete to 86% in municipal and 80% in hospital WWTP (Gomez et al., 2007, Jones et al., 2007, Radjenovic et al., 2009, Rosal et al., 2010, Sim et al., 2010, Stackelberg et al., 2004). Yet, the

removal is not complete since concentrations ranging from several hundred nano-grams up to 11.3 mg/L have been found in European WWTP effluents (Ternes et al., 1998, Jones et al., 2007, Rabiet et al., 2006). Other researchers found that paracetamol has been found with at concentrations of up to 6 mg/Lin European sewage treatment plants (STP) effluents, and up to 10 µg/L in natural water in USA (Kolpin et al., 2002, Sim et al., 2010), and even more than 65 µg/Lin the Tyne River in the UK, 10µg/L in surface water in the US (Kolpin et al., 2002). Rabiet et al. (2006) have detected a value of 211 ng/L of paracetamol in drinking water in France.

Bezafibrate has been found at concentrations up to 500 ng/L, 200 ng/L and 20 ng/L in influent, effluent and Ebro River in Spain, respectively (Gros et al., 2010).And record detected in concentration ranged 200 – 1600 ng/L level influent WWTP (Jelic et al., 2012). Atenolol has been frequently identified in wastewaters, where atenolol was detected in the highest concentrations, in some cases ranging up to 1 mg/L (Jelic et al., 2012).

2.1.2 Removal of pharmaceutical compounds and their metabolites

Even that pharmaceuticals residue and their metabolites are usually detectable in the environment at trace levels, the low concentration level (ngL^{-1} - μgL^{-1}) can induce toxic effects, as in the cases of antibiotic and steroids that cause resistance in natural bacterial populations or endocrine disruption effects (Herando et al., 2005). Pharmaceutical compounds are designed to interact with receptors in humans and animals, but in aquatic environment the organisms exhibiting the same enzyme receptors as humans could experience similar pharmacodynamic effects. Another issue at the ecosystem level is that for continual exposure of organisms due to continuous discharge of sewage contaminants into receiving waters (Comeau et al., 2008). Although concentrations of many pharmaceuticals residues in potable drinking water are so low and do not pose high risks to human beings, the main concern is the chronic and/or synergistic effects of the “cocktail” of pharmaceuticals that human have released to water body (Webb et al., 2003, Nikolaou et al., 2007).

The methods of treatment used for the removal of pharmaceuticals from the wastewater are the following: (a) biodegradation, (b) de-conjugation, (c) partitioning, (d) removal during sludge treatment, (e) photo-degradation, (f) membrane technology, (g) adsorbent materials (Jones et al., 2005).

(a) Biodegradation: biological degradation can take place in wastewater by means of aerobic/anaerobic microbial degradation of the drug substance leading to reduction of parent compounds and/or their metabolites during wastewater treatment (Jones et al., 2005). The microbes include bacteria, yeasts, fungi, protozoa, as well as unicellular plants and rotifers, some of these organisms have the ability to degrade some of most hazards and recalcitrant chemicals (Maria et al., 2010).

(b) De-conjugation: pharmaceuticals compounds are often metabolized in the liver, and as a consequence gluconoride and sulfate conjugates of the parent drug are excreted, de-conjugation in domestic wastewater and within sewage treatment plans (STPs), for organic compounds such as steroid hormones were occur due to the large amounts of β-glucoridase enzyme present, gluconoride and sulfate conjugates of drug compounds will be degraded by the same process, the effect will be increase the excreted contribution of the active drugs to sewage and effluents (Adriano et al., 2005).

(c) Partitioning: partitioning between the aqueous and organic biomass phase consider the key component in determining the ultimate concentration of organic pollutants. Compounds with high log $K_{o/w}$ (lipophilic molecules) values are known to sorb to sludge, while substances with lower values are more likely to stay in the aquatic phase, depending on the individual compound, and substances sorbing to solids may also be remobilized if they are not strongly bound (Jones et al., 2005).

(d) Removal during sludge treatment: drugs may also be degraded by a biotic process (Hydrolysis) during sewage treatment process. Many pharmaceutical compounds are not

thermally stable, and so might be expected to break down during processes such as compositing due to heat as well as chemical and biodegradation (Jones et al., 2005).

Removal of pharmaceutical from wastewater using microbiological processes, such as membrane bioreactor (MBR) technology was studied, the combination of DAF (dissolved air flotation) MBR-ozone oxidation process get a removal percentage range 50-95 % for the removal of some pharmaceutical such as bezafibrate (Miyoung et al., 2012). While only 10 % removal of neutral carbamazepine or basic atenolol, metoprolol and trimethoprim by activated sludge (Paxéus et al., 2004).

(e) Photo-degradation: several pharmaceutical compounds have shown to degrade due to the action of sunlight, some pharmaceuticals compounds such as diclofenac which is analgesic/anti-inflammatory drug, has been shown to degrade in aquatic environment due to ultraviolet (UV) light (Jones et al., 2005).

Due to an incomplete elimination in wastewater treatment plants (WWTPs) using the conventional treatment method, residues of pharmaceuticals and PPCPs are found in both wastewater and surface water (Adriano et al., 2005), so the improvement of this situation require the application of advanced treatment techniques, such as membrane filtration technology, many studies reported as significant efficiency of nano-filtration and reverse osmosis (Zhou et al., 2002), advanced oxidation processes (Ikehata et al., 2006), and activated carbon adsorption (Jones et al., 2005, Zhou et al., 2002).

Advanced oxidation processes (AOPs) constitute a promising technology for the treatment of wastewaters containing PPCPs. Data concerning the degradation of PPCPs by means of AOPs reported during the period January 2000–May 2007 are evaluated in a review article (Santiagoet al., 2007). Photo-catalytic degradation of sulfamethoxazole in aqueous suspension an 82% of sulfamethoxazole degradation and 23% of TOC reduction was achieved when working with 0.5 g TiO_2/L (Abellán et al., 2007). Paracetamol removal by photo-degradation using ozonation and H_2O_2/UV system was complete within 1 min in aqueous mixture at pH 5 (Andreozzi et al., 2003).

(f) Membrane technology has been applied in various fields of wastewater treatment. Micro-filtration (MF), Ultra-filtration (UF) and Nano-filtration (NF) membrane systems have already proven their advantages in terms of removal efficiency. Reverse osmosis (RO) and Activated carbon (AC) are also used in a broad range of wastewater reuse. Ultrafiltration hollow fiber membrane was less efficient to removal of naproxen, diclofenac and heavy metal Cr (VI), the RO and AC membranes were found to be complete removal (100%) of this pollutant (Karaman et al., 2012, Qurie et al., 2013). Aspirin, paracetamol and their metabolite salicylic acid and *p*-aminophenol were complete removal while pass through UF, RO and AC membranes (Khamis et al., 2011).

The wastewater treatment plant included activated sludge, UF, AC and RO, the result of overall plant membrane system showed complete removal of amoxicillin trihydrate and cefuroxime axetil (Karaman et al., 2015).

(g) Adsorbent materials: adsorption is considered to be one of the most promising techniques for wastewater treatment over the last decades. Under this term "green adsorption" it is meant the low-cost materials originated from: Agricultural sources and by-products (fruits, vegetables, foods). Agricultural residues and Wastes. Low-cost sources from which most complex adsorbents will be produced (such as activated carbons). These "green adsorbents" are expected to be inferior to the super-adsorbents complex materials as modified chitosans, activated carbons, structurally-complex inorganic composite materials etc., but their cost-potential makes them competitive (Kyzas et al., 2014).Freundlich isotherm constant for COD adsorption using three different types of activated carbon was range from 66.10 L/g to 146.30 L/g of K constant and 0.59 to 0.72 for 1/n constant (Amuda et al., 2006). The result for removal of Cr (VI) from aqueous solutions using either clay or modified clay (micelle-clay complex), indicate that modified clay (86%) was more efficient than used clay (50%) (Qurie et al.,2013).

Through continuous research, adsorption studies using two low cost adsorbents, activated carbon and positively ODTMA-complex (micelle-clay complex), revealed that both adsorbents are efficient in removing the pharmaceutical together with their biodegradation products, pesticide and toxic heavy metal Cr (VI). The adsorption isotherms were found to fit

Langmuir isotherms and the adsorption parameters were evaluated (Khamis et al., 2011, Karaman et al., 2012, Qurie et al., 2013, Karaman et al., 2015).

This thesis reports the efficiency of these advanced technologies for removal of selected pharmaceuticals, paracetamol, *p*-aminophenol, benzamide, bezafibrate and atenolol at the wastewater treatment plant at Al-Quds University which includes ultrafiltration (hollow fiber and spiral wound).

This study reports the removal of these selected pharmaceuticals (paracetamol, *p*-aminophenol, benzamide, bezafibrate and atenolol) by ultrafiltration (hollow fiber and spiral wound), their adsorption by activated carbon and clay-micelle filters, and removal by reverse osmosis technology.

2.1.3 Biodegradation of pharmaceutical compounds

Biodegradation of pharmaceutical compounds was studied (Zwiener et al., 2002, Gusseme et al., 2011, Zhang et al., 2012). This process considered the most important process for the removal of pharmaceuticals from activated sludge during the WWT. While transformation of pharmaceuticals in humans mammals has been studied extensively, the microbial degradation of pharmaceuticals in activated sludge, their degradation pathways and products, has rarely been investigated and their pathways are largely unknown (Quintana et al., 2005).

Biodegradation of pharmaceuticals was studded by batch incubation experiment using activated sludge as microbial (Yu et al., 2006), or isolated bacteria (Gusseme et al., 2011).Paracetamol with initial concentration 50, 10 and 1 mg/L of, was incubated at 25 ^{o}C, and the result showed fast biodegradation rate of paracetamol and complete biodegradation following 14 days of incubation. Biodegradation results were not sensitive to the initial concentration (Yu et al., 2006).paracetamol was underwent hydrolysis to p-aminophenol by batch incubation experiment using activated sludge (Schröder et al., 2012). In batch incubation experiment using isolated bacteria (Delftia-Tsuruhatensis and *Pseudomonas*

Aeruginosa) of 10 mg paracetamol at 28 ^{o}C in minimal medium, amide cleavage to produce p-aminophenol as intermediate to produce hydroquinone (Gusseme et al., 2011).

On the other hand, N, N-Diethyl-3-Methylbenzamide (DEET), derivative of benzamide was degraded into 3-methylbenzoate and diethylamide by amide hydrolysis through incubation with Pseudomonas putida in aerobically condition (Rivera et al., 2007).
The biodegradation of bezafibrate were studied by using activated sludge (from membrane bioreactor), with 20 mg as initial concentration, the results showed that bezafibrate was degraded to one metabolite within 5 days: the metabolite was identified as 4-chlorobenzoic acid (Quintana et al., 2005). Biodegradation of bezafibrate in activated sludge, the result showed a hydrolysis of amide bond, two products were identified as 4-chlorobenzoic acid and 4-(2-aminoethyl)-α, α-dimethyl-benzene acetic acid (Gusseme et al., 2011). Degradation of bezafibrate using isolated bacteria (pseudomonas putida): a 48% of bezafibrate was underwent biodegradation within 5 days (Yang et al., 2010).

Biodegradation of atenolol under aerobic condition in activated sludge with initial concentration 50 mg/L and 10mg/L, the produce was determined to be a microbial hydrolysis of the amide bond (Radjenovi et al., 2008).

Chapter Three

Experimental

Chapter Three
Experimental

3.1 Chemicals

All chemicals were of analytical grade. The clay used was Wyoming Na-montmorillonite SWY-2 obtained from the Source Clays Registry (Clay Mineral Society, Colombia, MO). Octadecyltrimethylammonium (ODTMA) bromide was obtained from Sigma Aldrich. Paracetamol was obtained as a gift from Bir-ziet pharmaceutical company (Ramallah-Palestine). Bezafibrate was extracted from Bezafibrate 400mg Tablets. Activated Charcoal (12-20 mesh) was obtained from Sigma (Sigma Chemical Company, USA). De-ionized water was used to prepare all solutions. Methanol, acetonitrile and water were HPLC grade and purchased from Sigma Aldrich. Magnesium sulfate, benzamide, ammonium acetate, acetic acid, atenolol, benzoic acid and *p*-aminophenol were purchased from Sigma Aldrich. Chloroform and High purity diethyl ether (> 99%) were purchased from Biolab (Israel), orthophosphoric acid (OPA) was obtained from Riedel-De Haen (Germany). Syringe Millipore filter 13 mm diameter 0.45µm Nylon membrane and peptone water were obtained from sigma Aldrich.

3.2 Instrumentation

3.2.1 High Pressure Liquid Chromatography

High Pressure Liquid Chromatography (HPLC-PDA) system consists of an alliance 2695 HPLC from (Waters), and waters Micromass® Masslynx ™ detector with Photo diode array (PDA) (Waters 2996). Data acquisition and control were carried out using Empower™ software (Waters). Analytes were separated on a 4.6 mm x150 mm C18 XBridge ®column (5 µm particle size) used in conjunction with a 4.6mmx20 µm XBridge ™ C18guard column. Microfilter was used with 0.45µm (Acrodisc® GHP, Waters).

3.2.2 UV-Spectrophotometer

The concentrations of the amide pharmaceuticals in wastewater samples were determined spectrophotometrically (UV-spectrophotometer, Model: UV-1601, Shimadzu, Japan) by monitoring the absorbance at the λ_{max} for each pharmaceutical.

3.2.3 pH meter

pH values were recorded using pH meter (model HM-30G: TOA electronics ™).

3.2.4 Centrifuge and Shaker

Labofuge®200 Centrifuge was used (230 V 50/60 Hz. CAT. No. 284811, made in Germany). Some of pharmaceuticals solutions were shaken with an electronic shaker (Bigbill shaker, Model No.: M49120-26, 220-240 V 50\60 Hz.) at 250 rpm.

3.2.5 Description of Al-Quds University Wastewater Treatment Plant (AQU-WWTP)

The AQU-WWTP collects a mixture of black, gray, and storm water. The treatment plant consists of a primary treatment (two stage primary settling basin), and a secondary treatment (activated sludge with a hydraulic retention time of 16-20 hours, coagulation and chlorination). Then, the secondary effluents introduced to the sand filter before entering the ultra-filtration membrane (Hollow fiber and Spiral wound). After the ultra-filtration process, the effluent is subjected to activated carbon column followed by a reverse osmosis (advanced treatment). Then, a blend of all effluents is used for irrigation. The ultra-filtration process is made of two small scale membrane treatment plants with a capacity of 12 m^3 /day. The first UF unit is equipped with 2 x 4 inch pressure vessels with pressure resistance up to 150 psi. Each vessel holds two separation membranes (spiral wound with 20 kD cutoffs which is equivalent to 0.01micron separation rate). The designed permeate capacity of the system is 0.5-0.8 m3/h. This Membrane can remove bacteria, suspended solids, turbidity agents, oil, and emulsions. The second unit is equipped with two pressure vessels made from Vendor (AST

technologies, model number 8000 WW 1000-2M) that houses the hollow fiber membranes with 100 kD cutoff (Vendor, AST technologies, Model no. 8000- WWOUT-IN-8080). The two units are designed to deliver 1 .5m3/h. The reverse osmosis (RO) membranes are made from thin film polyamide which consists of 1 x 4 inch pressure vessel made from composite material with pressure resistance up to 400 psi. The vessel holds two 4 inches special separation membranes (manufactured in thin film polyamide with pH range 1-11models BW30-4040 by DOW Film Tec.). Membrane antiscalent (Product NCS-106-FG, made of phosphate in water with active ingredient of phosphoric acid disodium salt) are continuously dosed to the RO feed at concentration of 4 ppm in order to prevent deposition of divalent ions. The system is designed to remove major ions and heavy metals. The designed RO permeate capacity of the system is 0.45- 0.5 m3/h (Khamis et al., 2011).

3.3 Methods

3.3.1 Micelle-clay complex preparation

The micelle-clay complex was prepared as described elsewhere (Polubesova et al., 2005). Briefly, the micelle–clay complex was prepared by stirring 12 mM of ODTMA with 10g/ L clay for 72 h. Suspensions were centrifuged for 20 min at 15000 rpm, supernatants were discarded, and the complex was lyophilized.

3.3.2 Stability of selected pharmaceutical

3.3.2.1 Stability of paracetamol and *p*-aminophenol

Stability studies were conducted either in fresh water, activated sludge or sterile peptone water containing *Pseudomonas aeruginosa*, by dissolved 100 mg of paracetamol standard or 100 mg of *p*-aminophenol standard in 1L.The solutions were incubated in water bath at a temperature of 25 ^{o}C for 14 days.

In another experiment, 100 mg, 250 mg and 500 mg of paracetamol standard was dissolved in sterile peptone water containing *Pseudomonas aeruginosa*in the same condition to achieve the variation of paracetamol concentration effect on biodegradation rate constant.

3.3.2.1.1 Sampling and sample preparation

10 ml of paracetamol or p-aminophenol samples were taken every day of incubation; all samples were centrifugation and extracted three times with ether or chloroform. The ether or chloroform extracts were combined, dried on anhydrous magnesium sulfate ($MgSO_4$), filtered and evaporated. For HPLC-PDA analysis, the dried residue after solvent evaporation was dissolved with a mixture of water: acetonitrile (water adjusted to pH 3.45 using dilute o-phosphoric acid) in a ratio (90:10 v\v) and was injected to the HPLC apparatus.

3.3.2.1.2 Stock solution and standards preparation

A- Stock solution: Stock solution was prepared by dissolving paracetamol, or *p*-aminophenol, standards in acetonitrile and water which was adjusted to pH 3.45 in a ratio (10:90) to a concentration 200 ppm.

B- Calibration curves: A 500 ml stock solution of paracetamol or *p*-aminophenol, with a final concentration of 200 ppm was prepared in (**A**). The diluted solutions that were prepared from the stock solution were: 0.5 ppm, 1 ppm, 5 ppm, 10 ppm and 100 ppm. Then, each diluted solution was extracted three times with ether or chloroform. The ether or chloroform extracts were combined, dried on anhydrous magnesium sulfate ($MgSO_4$), filtered and evaporated. For HPLC-PDA analysis, the dried residue after solvent evaporation was dissolved with a mixture of water: acetonitrile (water adjusted to pH 3.45 using dilute o-phosphoric acid) in a ratio (90:10 v\v) and was injected to the HPLC apparatus.

3.3.2.1.3 Chromatographic conditions for the separation of paracetamol and *p*-aminophenol

The optimal HPLC conditions that were efficient for the separation of paracetamol and *p*-aminophenol were: C-18 as the separation column, a mixture of water: acetonitrile (water pH adjusted to 3.45 using dilute o-phosphoric acid) (90:10 v/v) as a mobile phase, flow rate of 1.0 ml/ minute and a UV detection at a wavelength of 247 nm.

3.3.2.2 Stability of benzamide

Stability studies were conducted either in activated sludge, fresh water or sterile peptone water containing *Pseudomonas aeruginosa*, by dissolving 100 mg of benzamide in 1Liter.The solution was incubated in water bath at a temperature of $25C^{o}$ for 14 days.

3.3.2.2.1 Sampling and sample preparation

10 ml of benzamide samples were taken every day of incubation; all samples were centrifugation and extracted three times with ether or chloroform. The ether or chloroform extracts were combined, dried on anhydrous magnesium sulfate ($MgSO_{4)}$, filtered and evaporated. For HPLC-PDA analysis, the dried residue after solvent evaporation was dissolved with a mixture of water: acetonitrile (water adjusted to pH 3.0 using dilute o-phosphoric acid) in a ratio (70:30 v\v) and was injected to the HPLC apparatus.

3.3.2.2.2 Stock solution and standards preparation

A- Stock solution: Stock solution was prepared by dissolving benzamide standard in acetonitrile and water that was adjusted to pH 3.0 in a ratio (30:70) to a concentration 200 ppm.

B- Calibration curves: A 500 ml stock solution of benzamide with a final concentration of 200 ppm was prepared in (A). The diluted solutions that were prepared from the stock

solution were: 10 ppm, 50 ppm, 100 ppm and 200 ppm. Then, each diluted solution was extracted three times with ether or chloroform. The ether or chloroform extracts were combined, dried on anhydrous magnesium sulfate ($MgSO_{4)}$, filtered and evaporated. For HPLC-PDA analysis, the dried residue after solvent evaporation was dissolved with a mixture of water: acetonitrile (water adjusted to pH 3.0 using dilute o-phosphoric acid) in a ratio (70:30 v\v) and was injected to the HPLC apparatus.

3.3.2.2.3 Chromatographic conditions for the separation of benzamide and metabolite

The optimal HPLC conditions that were efficient for the separation of benzamide and metabolite were: C-18 as the separation column, a mixture of buffer: acetonitrile (Buffer solution: 0.4 g of ammonium acetate in 1L distilled water, pH adjusted to 4.2 using dilute o-phosphoric acid, buffer solution was filtered through 0.45µm and storage at 4^{o}C) (80:20 v/v) as a mobile phase, flow rate of 1.0 ml/ minute and a UV detection at a wavelength of 230 nm.

3.3.3 Efficiency of the AQU-WWTP for removal of selected pharmaceuticals.

The efficiency of different membranes (hollow fiber (HF-UF), spiral wound (SW-UF), activated carbon (AC) and reverse osmosis (RO) membranes, for the removal of selected pharmaceuticals from wastewater was studied by spiking the selected pharmaceuticals in the storage tank of the wastewater treatment plant at a concentration rang 30-45 ppm.

3.3.3.1 Spiking solutions

Dissolve 20 g of paracetamol and *p*-aminophenol, (separately), in 50 ml methanol and spike in 500 liters of activated sludge wastewater to a concentration of 40 ppm. Dissolve 17.5 g of benzamide in 50 ml methanol and spike in 500 liters of activated sludge wastewater to a concentration of 35 ppm. Dissolve 15 g of bezafibrate and atenolol, (separately), in 50 ml methanol and spike in 500 liters of activated sludge wastewater to a concentration of 30 ppm.

3.3.3.2 Stock solutions and standard preparation

A- Stock solution: Each stock solution of a selected pharmaceutical standard was prepared in a separated volumetric flask 100 ml by dissolving the compound in small amount methanol then distilled water to a concentration of 100 ppm.

B- Calibration curves: Each 100 ml stock solutions of each compound with a final concentration of 100 ppm prepared in (A) was used to prepare the following diluted solutions: 0.1 ppm, 0.5 ppm, 1 ppm, 5 ppm, 10 ppm, and 50 ppm. Then, the absorption of each solutions of each of the tested compounds was determined using UV-spectrophotometer.

3.3.3.3 Sampling and sample preparation

50 ml of samples were taken from the following points of the AQ-WWTP: (A) storage tank (before running wastewater treatment plant) (B) and (C) Brine and product of the UF/HF membrane, respectively, (D) and (E) Brine and product of the UF/SW membrane, respectively, (F) product of activated carbon, (G) and (H) Brine and product of the reverse osmosis membrane. These sampling points are shown in (Figure 3.1). Samples were treated by centrifugation and filtration through 0.45µm syringe Millipore nylon filter, then measurement the samples using UV-vis.

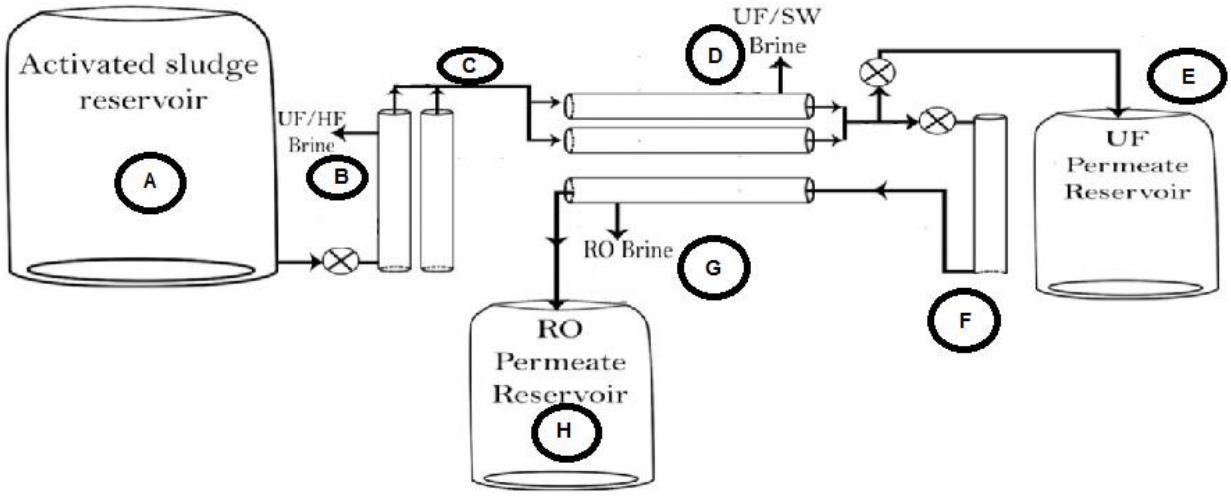

Figure 3.1: Flow diagram showing the process of AQU-WWTP which consists of UF/HF-filter (Hollow Fiber Membrane) and UF/SW-filter (Spiral Wound Membrane), Activated Carbon and RO filters (Reverse Osmosis Membrane). Sampling locations are indicated by letters.

3.3.4 Adsorption studies of selected pharmaceuticals onto micelle-clay complex and activated carbon.

3.3.4.1 Stock solution and standards preparation

A- Stock solution: each stock solution of a selected pharmaceutical standard was prepared in a separated volumetric flask 500 ml by dissolving the compound in distilled water to a concentration of 500 ppm.

B- Calibration curves: each 500 ml stock solution of each pharmaceutical with a final concentration of 500 ppm prepared in (A) was used to prepare the following diluted solutions: 1 ppm, 5 ppm, 10 ppm, 20 ppm, 50 ppm, and 100 ppm. Then, the absorption of each solution of each of the tested compounds was determined using UV-vis.

3.3.4.2 Batch adsorption studies

Batch adsorption experiment was carried out for 100 ml solutions of 10 ppm, 50 ppm, 100 ppm, 250 ppm, and 500 ppm, separately, as an initial concentration of the selected pharmaceutical. The Experiment was performed in 250 ml Erlenmeyer flasks containing 0.5 g micelle-clay complex or activated carbon (dosage 5g/L). The flasks were shaken in an electric shaker for two hours at room temperature, and then the content of the flask was centrifuged for 5 minutes and filtered using 0.45 μm syringes Millipore nylon filter. A kinetic study of the extent of adsorption was determined by conducting 100 ml solution of 50 ppm for each selected pharmaceutical, separately, in 250 ml Erlenmeyer flask containing 0.5 g of micelle-clay complex or activated carbon then samples were taking as a function of time, centrifuged all samples for 5 minutes and filtered using 0.45 μm syringe Millipore nylon filter, and finally, measuring the concentration of the solution vs. time.

Chapter Four

Results and Discussion

Chapter Four
Results and Discussion

4.1. Stability studies of selected pharmaceuticals.

4.1.1. Stability of paracetamol and *p*-aminophenol

4.1.1.1 Calibration Curve of paracetamol and *p*-aminophenol standard using HPLC method

Calibration curve was obtained by plotting area under paracetamol peak versus paracetamol concentration in ppm (Table 4.1) and area under *p*-aminophenol peak versus *p*-aminophenol concentration in ppm (Table 4.2). The method gave a linear relationship within the concentration range of 0.5–50 ppm with correlation coefficient $r^2 = 0.999$ and $r^2 = 0.997$, respectively, as shown in Figures 4.1 &4.2.

Table 4.1: Area under peak of paracetamol standard at different concentrations.

Paracetamol Concentration (ppm)	Peak Area
0.5	19653
1	57440
5	240765
10	449423
50	2232590

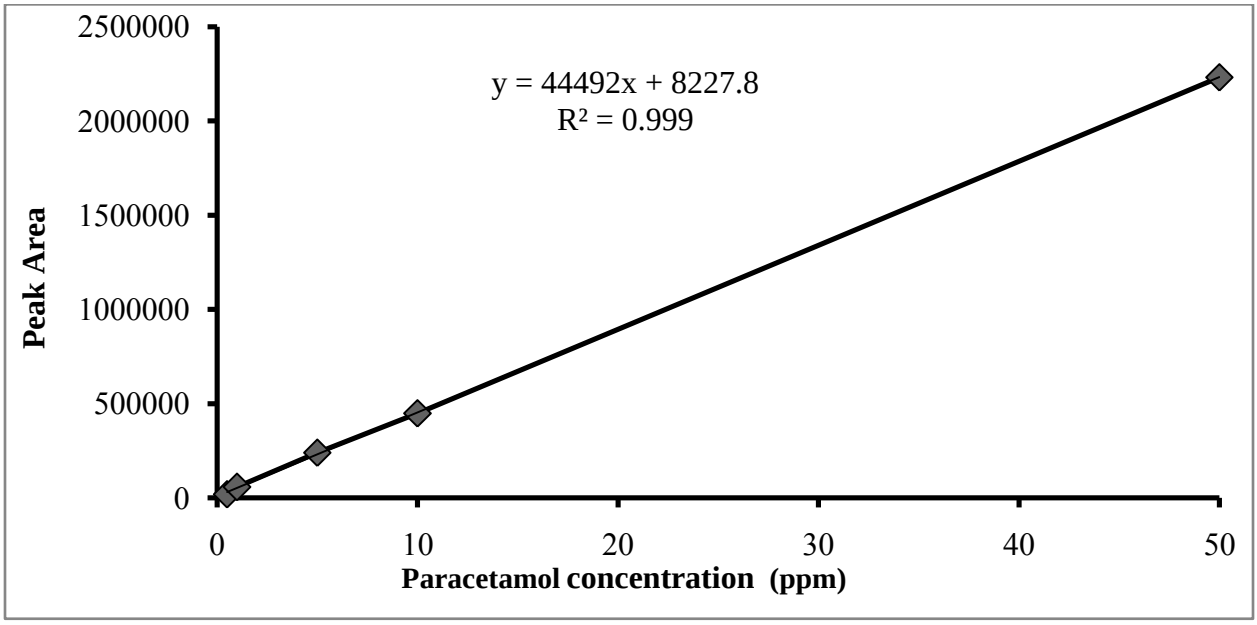

Figure 4.1: Calibration curve of paracetamol using HPLC method.

Table 4.2: Area under peak of *p*-aminophenol standard concentration.

p-Aminophenol Concentration (ppm)	Peak Area
0.5	0
1	471
5	2353
10	3260
50	15634

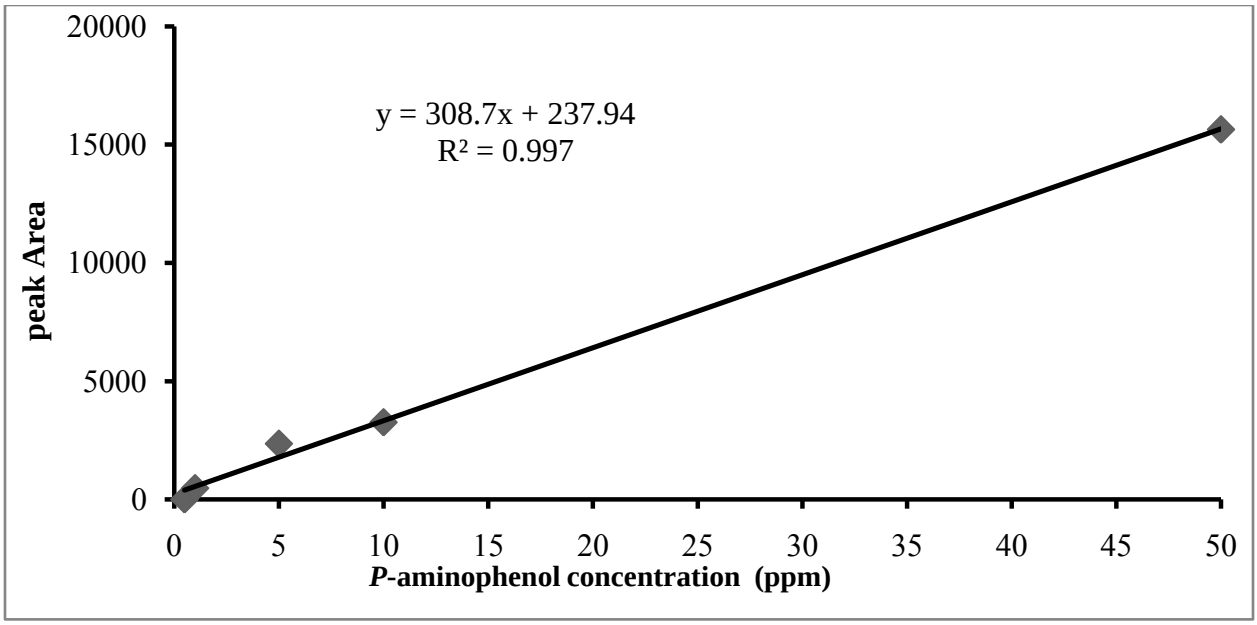

Figure 4.2: Calibration curve of *p*-aminophenol using HPLC method.

4.1.1.2 Stability of Paracetamol in fresh water.

As mentioned in the introduction section, aqueous solution of paracetamol is quite stable at room temperature. The half-life of paracetamol solutions (pH 6) lasts over 20 years, however upon heating, acidic and basic conditions its stability decreases and it degrades to furnish *p*-aminophenol and acetic acid (Nelson et al., 2006). This hydrolysis reaction was found to be carried out by enzymatic cleavage or by microwave assisted alkaline hydrolysis of amide bond (Figure 4.5).

Stability study of paracetamol in fresh water demonstrated that paracetamol was completely stable after incubation for more than one month due to high energy needed to overcome the barrier for the cleavage of its amide bond.

HPLC monitoring results of paracetamol stability in fresh water gives the same retention time (3.9 min) belongs to paracetamol standard after 30 days incubation, as shown in (Figures 4.3 & 4.4).

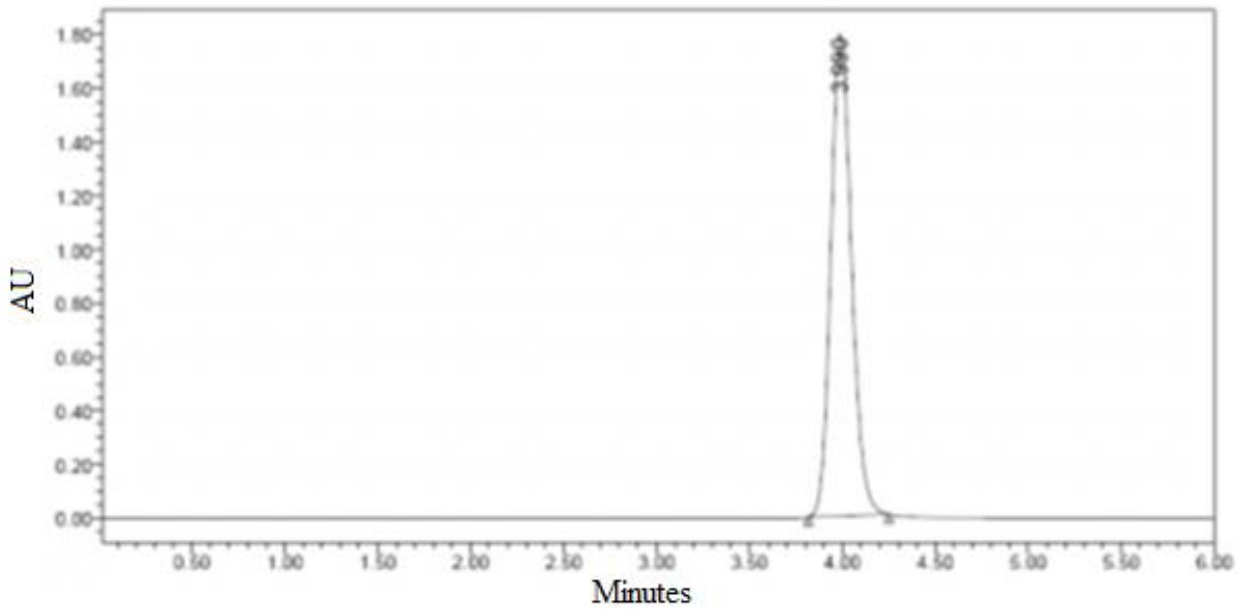

Figure 4.3: Chromatogram showing paracetamol in fresh water after 2 days incubation at 25^{o}C.

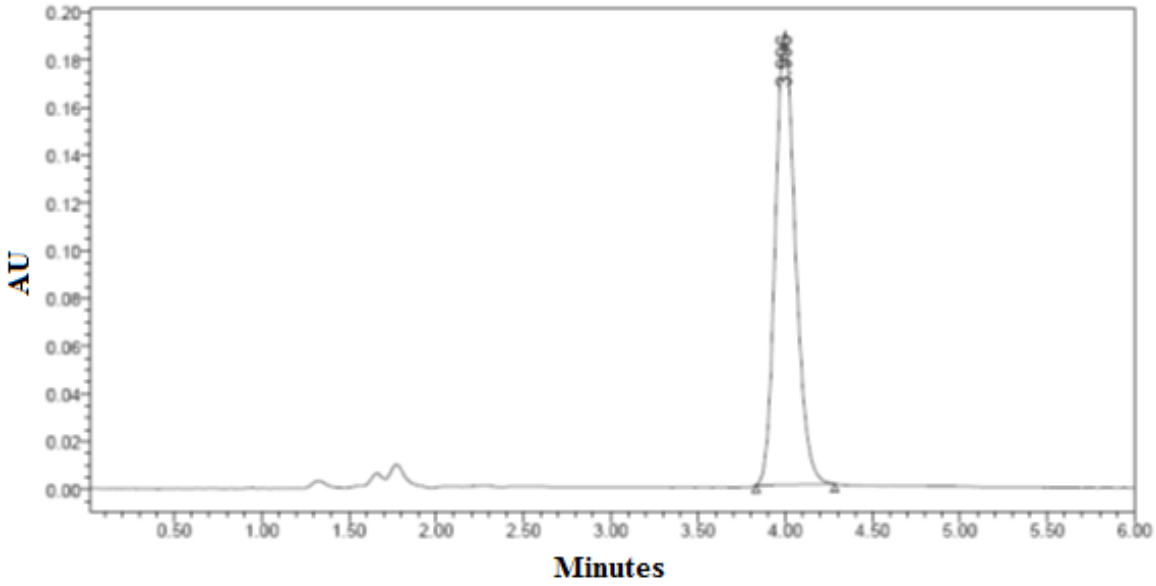

Figure 4.4: Chromatogram showing paracetamol in fresh water after 30 days incubation at 25 ^{o}C.

4.1.1.3 Stability of Paracetamol & *p*-aminophenol in activated sludge.

HPLC monitoring results of Al-Quds University sludge solutions containing paracetamol revealed a gradual degradation of paracetamol to *p*-aminophenol and acetate (Figure 4.5).

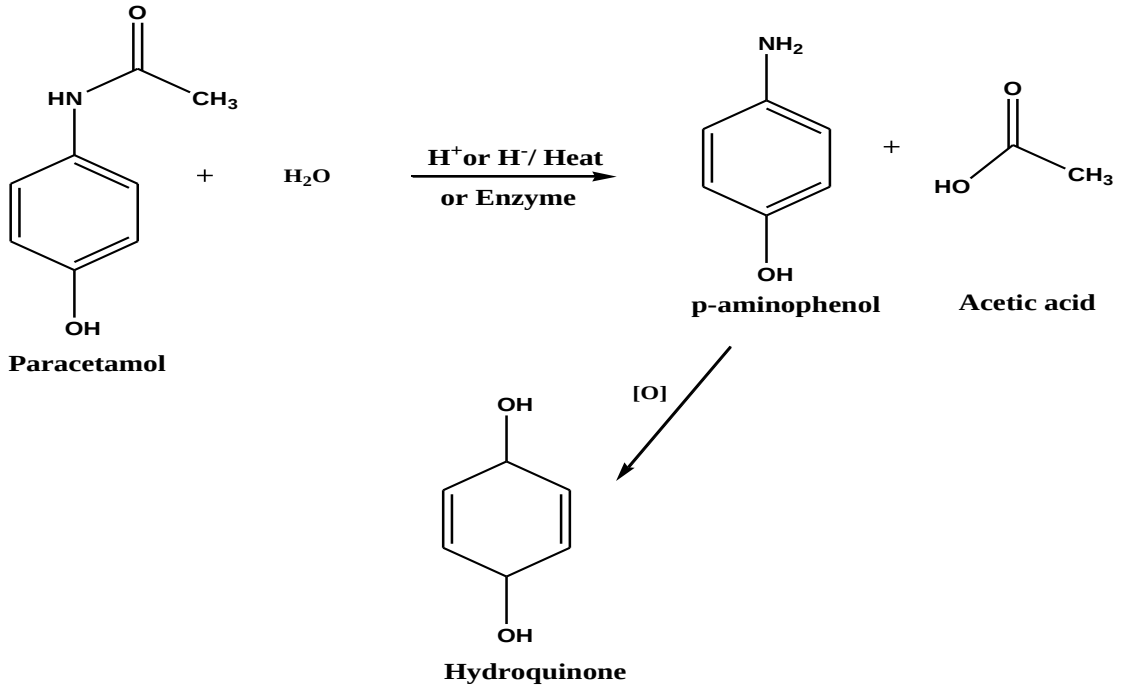

Figure 4.5: Schematic pathway for the degradation of paracetamol in Al-Quds sludge.

The degradation was demonstrated by a disappearance of a peak characterized as the reactant (paracetamol) at a retention time of 3.9 minutes and a gradual appearance of a new peak at a retention time of 1.9 minutes characterized as a product (*p*-aminophenol). Figures 4.6 and 4.7 illustrate a progress of paracetamol degradation as monitored by HPLC.

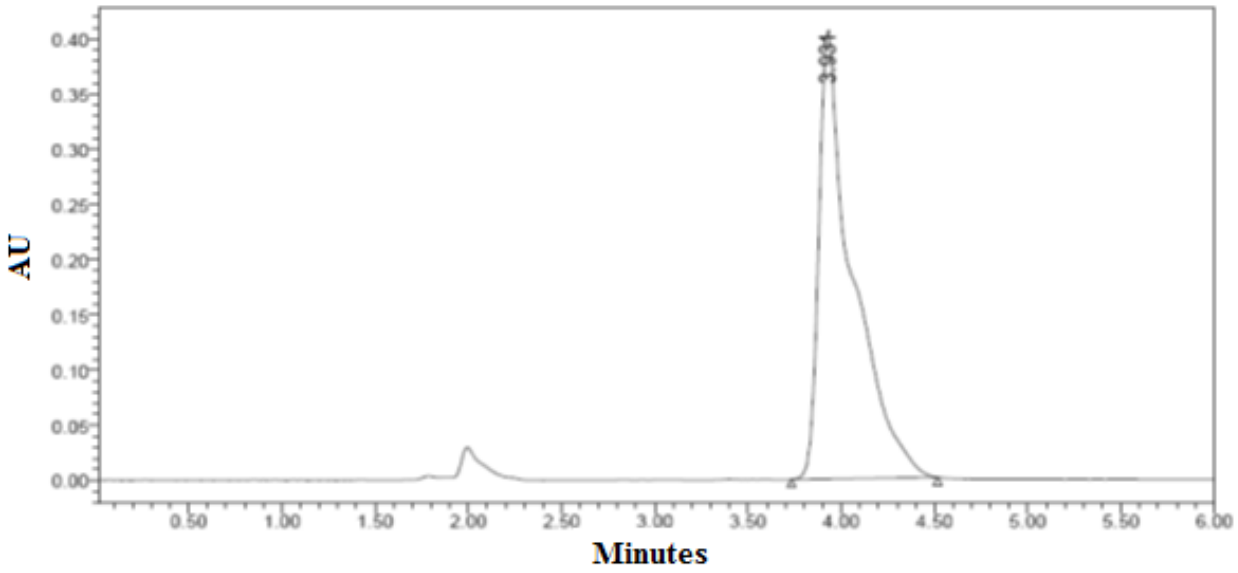

Figure 4.6: Chromatogram showing the hydrolysis of paracetamol after 2 days in presence of activated sludge at 25 ^{o}C.

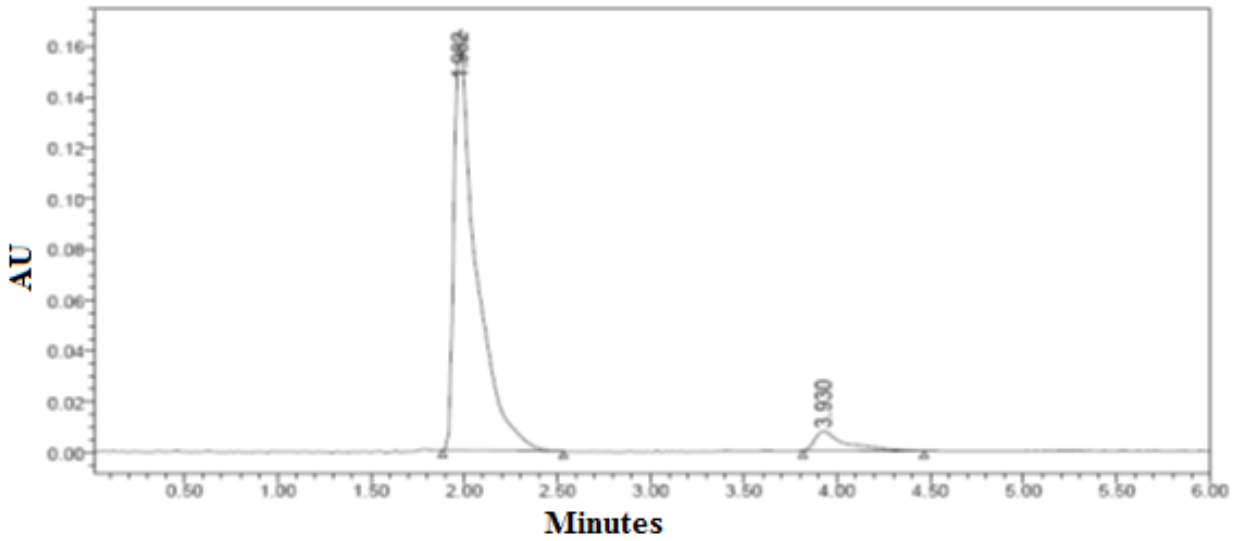

Figure 4.7: Chromatogram showing the hydrolysis of paracetamol after 7 days in presence of activated sludge at 25 ^{o}C.

Characterization of the product, *p*-aminophenol was confirmed by injecting a mixture standard solution of paracetamol and *p*-aminophenol to HPLC that gave paracetamol peak at a retention time of 3.9 minutes and *p*-aminophenol peak at a retention time of 1.9 minutes (Figure 4.8).

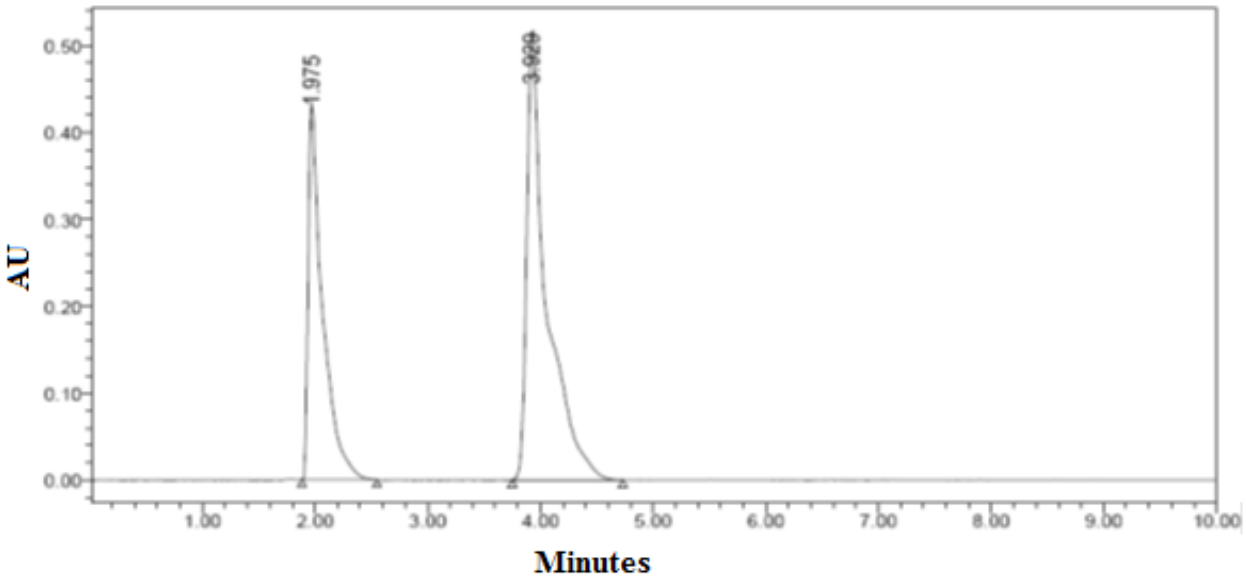

Figure 4.8: Chromatogram showing separation of a mixture paracetamol and *p*-aminophenol.

The HPLC kinetic data (Tables 4.3 and 4.4) obtained after one week monitoring was examined for linear correlation (Figures 4.9 and 4.10). A linear correlation was obtained when ln[paracetamol] and ln[*p*-aminophenol] was plotted against time with a correlation coefficient R^2 = 0.9827, R^2 = 0.9908, respectively . The pseudo first order reaction rate constants were found to be 2.17×10^{-9} $M.s^{-1}$ and 8.64×10^{-9} $M.s^{-1}$, respectively.

Table 4.3: Kinetic data for molar paracetamol concentration versus time at 25 ^{o}C.

Ln[Paracetamol] M	Time (hrs)
-7.11356425	0
-7.17295734	12
-7.48992918	24
-7.69084529	48
-7.75383443	72
-8.26910854	120
-8.7748446	168

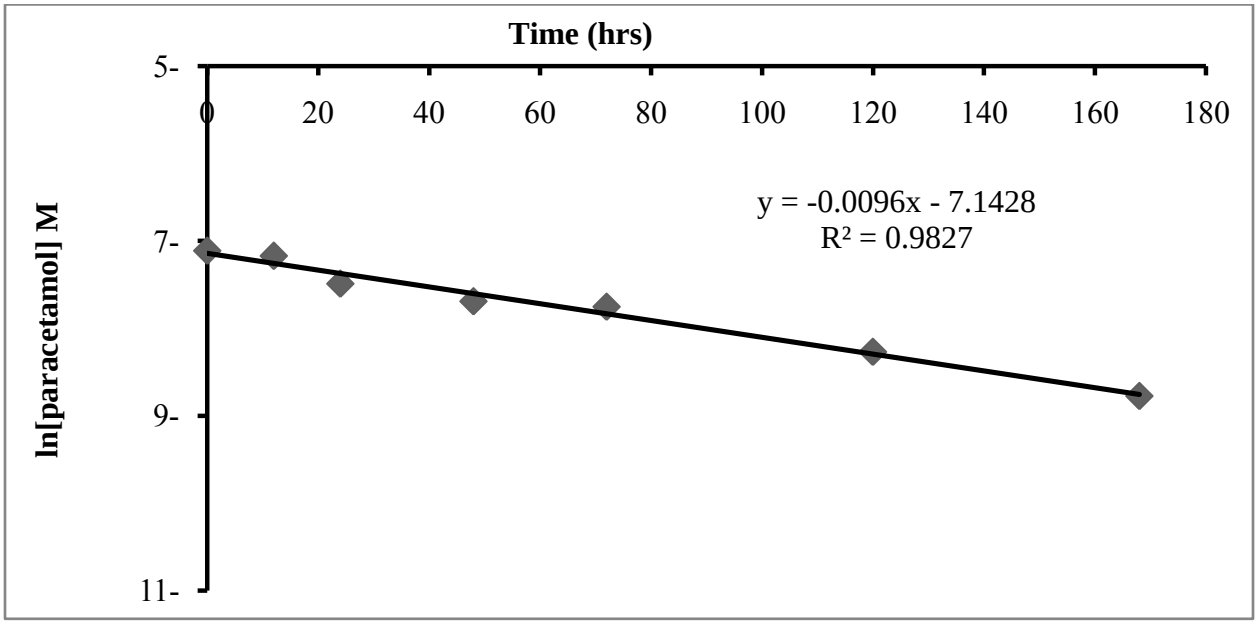

Figure 4.9: First order kinetic plot for the biodegradation of paracetamol in Al-Quds activated sludge at 25 ^{0}C.

Table 4.4: Kinetic data for molar *p*-aminophenol concentration versus time at 25 ^{o}C.

ln[*p*-aminophenol] M	Time (hrs)
-6.76534	0
-7.25666	24
-8.24042	72
-9.24073	96
-9.96466	120
-10.4217	144
-11.2532	168

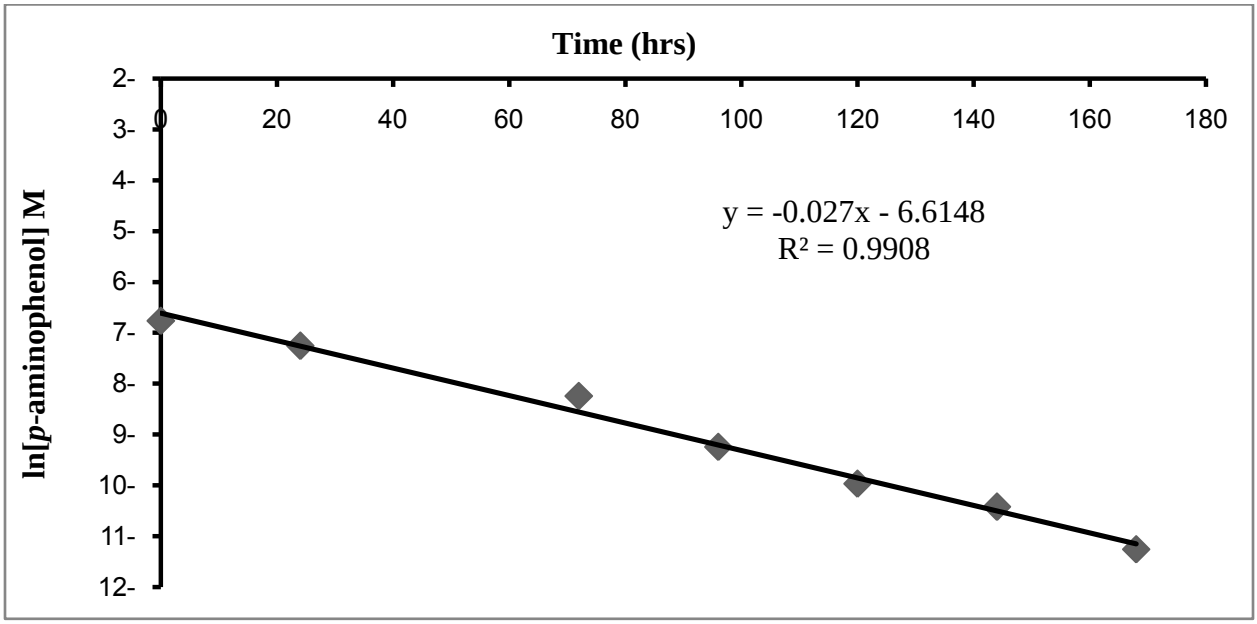

Figure 4.10: First order kinetic plot for the biodegradation of *p*-aminophenol in Al-Quds activated sludge at 25 ^{0}C.

The degradation of paracetamol in Al-Quds University sludge might be due to the presence of variety of enzymes, bacteria, heavy metals, and etc. which have the potential to play a role in catalysis of the breakdown of paracetamol amide bond.

4.1.1.4 Biodegradation of Paracetamol and *p*-aminophenol in sterile peptone water contains *Pseudomonas aeruginosa*.

Pseudomonas aeruginosa was sub-cultured from the bacteria characterized in the sludge of AQ-WWTP in sterile peptone water under complete sterile technique. The inoculated flask was incubated at 37 ºC for two hours to activate the growth of the bacteria, and then was transferred to a shaker. 200 mg paracetamol were added to the bacterial suspension having 0.5 optical densities. Paracetamol was extracted from the biological degradation reactor after 1, 2, 4, 7, 10 and 14 days. The extraction was performed using chloroform, and then liquid chromatography was performed to determine the concentrations of resulting metabolites.

As deduced by HPLC determinations paracetamol was degraded within 14 days. During paracetamol degradation, two new metabolites were detected and tentatively identified by means of LC-MS and NMR (Figure 4.5). While the first metabolite reached its maximum around seven days, the second one increased until the end of the experiment (14 days) (Figure 4.11).

Table 4.5: Kinetic biodegradation data of paracetamol and *p*-aminophenol versus time. The concentration values are repeated as a value of ± SD, SD: standard deviation of three replicates.

	Paracetamol		*p*-Aminophenol	
Time (Days)	Conc. (ppm) AV	SD	Conc.(ppm) AV	SD
0.0	100.03	2.42	0	
0.5	99.54	5.94	0	
1.0	84.45	4.73	3.17	2.92
2.0	64.59	4.77	14.29	3.26
3.0	50.93	2.26	35.06	2.72
5.0	23.01	0.79	59.81	2.09
7.0	14.38	0.38	62.85	1.76
8.0	10.01	0.19	58.56	1.56
11.0	2.90	0.17	42.09	0.71
12.0	2.38	0.07	36.63	0.92
14.0	1.63	0.29	29.67	1.11

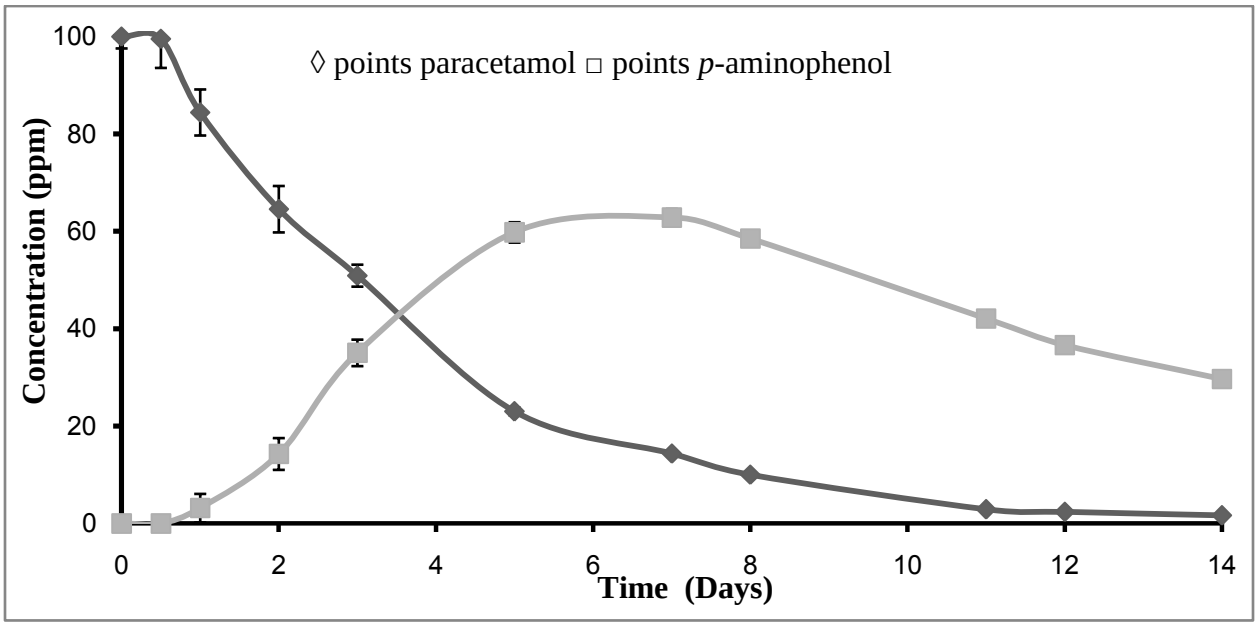

Figure 4.11: Biodegradation curve for paracetamol (white points ◊) 100 ppm initial paracetamol concentration, and *p*-aminophenol (Red points □) within 14 Days incubation at 25^{o}C. by *pseudomonas aeruginosa*. Data represent of average of triplicate measurements.

Metabolite 1 was characterized as *p*-aminophenol and the second metabolite was identified as hydroquinone. Metabolite 2 remained stable throughout the experimental period of 14 days. Transformation of paracetamol via metabolite 1 to metabolite 2 was confirmed by running a second set of experiments by which a standard solution of *p*-aminophenol was incubated with *Pseudomonas aeruginosa* in the same manner and conditions as described for paracetamol. HPLC monitoring demonstrated that *p*-aminophenol underwent degradation to hydroquinone (Figure 4.5). A complete biodegradation was achieved after 14 days of incubation with the bacteria.

It is indicated that the identification of metabolites 1 and 2 was confirmed by injecting authentic samples of *p*-aminophenol and hydroquinone that gave identical peaks to the two metabolites, respectively.

4.1.1.5 Variation of paracetamol concentration effect on biodegradation rate constant

Different paracetamol concentrations in a sterile peptone water with *Pseudomonas aeruginosa* under complete sterile technique incubated with *Pseudomonas aeruginosa* in the same manner and conditions as described above. Paracetamol was extracted from the biological degradation reactor after 1 day, 2, 4, 7, 10 and 14 days. The extraction was performed using chloroform, and then liquid chromatography was performed to determine the degradation of paracetamol.

The HPLC kinetic data (Table 4.6) obtained after one week monitoring was examined for linear correlation (Figure 4.12). A linear correlation was obtained when ln[paracetamol] was plotted against time with a correlation coefficient $R^2 = 0.994$, $R^2 = 0.972$ and $R^2 = 0.981$ respectively. The pseudo first order reaction rate constant was found to be 2.39×10^{-9} $M.s^{-1}$, 4.91×10^{-9} $M.s^{-1}$ and 5.71×10^{-9} $M.s^{-1}$, respectively.

Table 4.6: Kinetic data of different molar paracetamol concentration versus time at 25^{o}C.

	100 ppm paracetamol	250 ppm paracetamol	500 ppm paracetamol
Time (hrs)	ln[paracetamol]M	ln[paracetamol]M	ln[paracetamol]M
0	-7.32	-6.34	-5.68
12	-7.33	-6.35	-5.68
24	-7.49	-6.59	-5.82
48	-7.76	-6.79	-5.91
72	-7.99	-7.38	-5.97
120	-8.79	-8.18	-6.25
168	-9.26	-8.99	-6.81
192	-9.62	-9.21	-7.09
264	-10.86	-10.74	-7.31
288	-11.06	-11.97	-7.49
336	-11.44	-12.50	-7.71

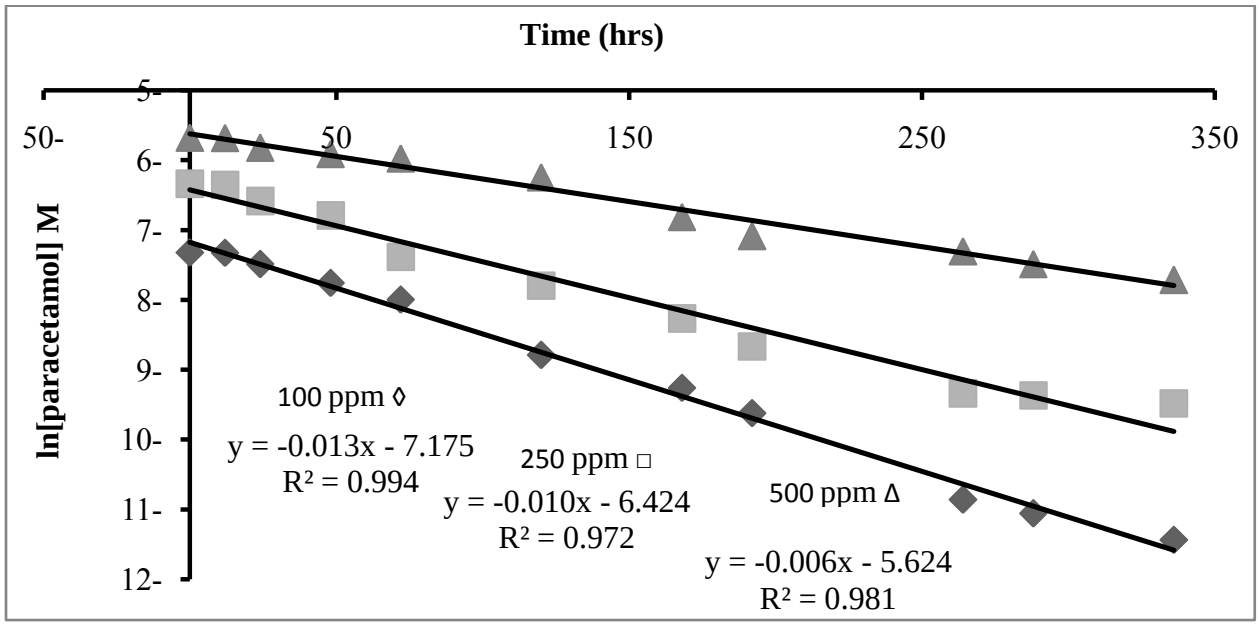

Figure 4.12: Variation the biodegradation rate of paracetamol with different concentration.

4.1.2 Stability of Benzamide

4.1.2.1 Calibration Curve of Benzamide standard using HPLC method

Calibration curve was obtained by plotting the area under benzamide peak versus benzamide concentration in ppm (Table 4.7). The plot gave a linear relation within the concentration range 10 – 200 ppm with correlation coefficient $R^2 = 0.999$, as shown in Figure 4.13.

Table 4.7: Area under the peak of standard benzamide concentration.

Benzamide Concentration (ppm)	Peak Area
0	0
10	465001
50	2437076
100	4718702
200	9505047

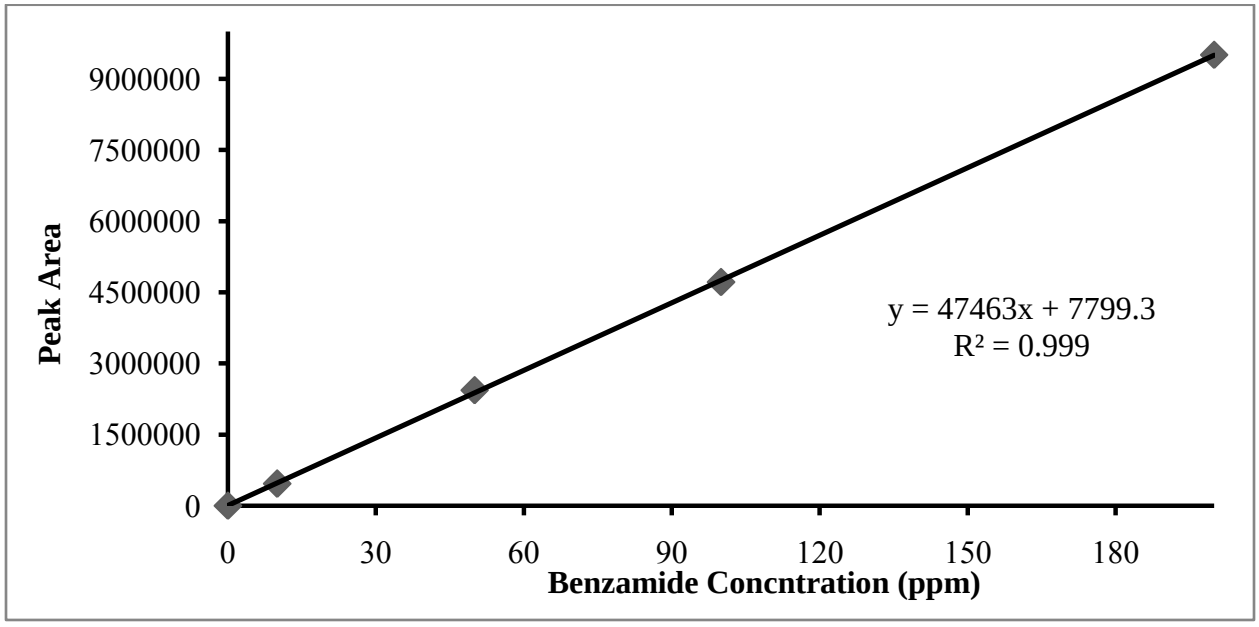

Figure 4.13: Calibration curve of benzamide using HPLC method.

4.1.2.2 Stability of Benzamide in fresh water.

In this experiment, as in paracetamol, benzamide was stable in aqueous media, where monitoring by HPLC showed the benzamide peak at a retention time 3.3 min after one day and 7 days incubation without being changed (Figures 4.14 and 4.15).

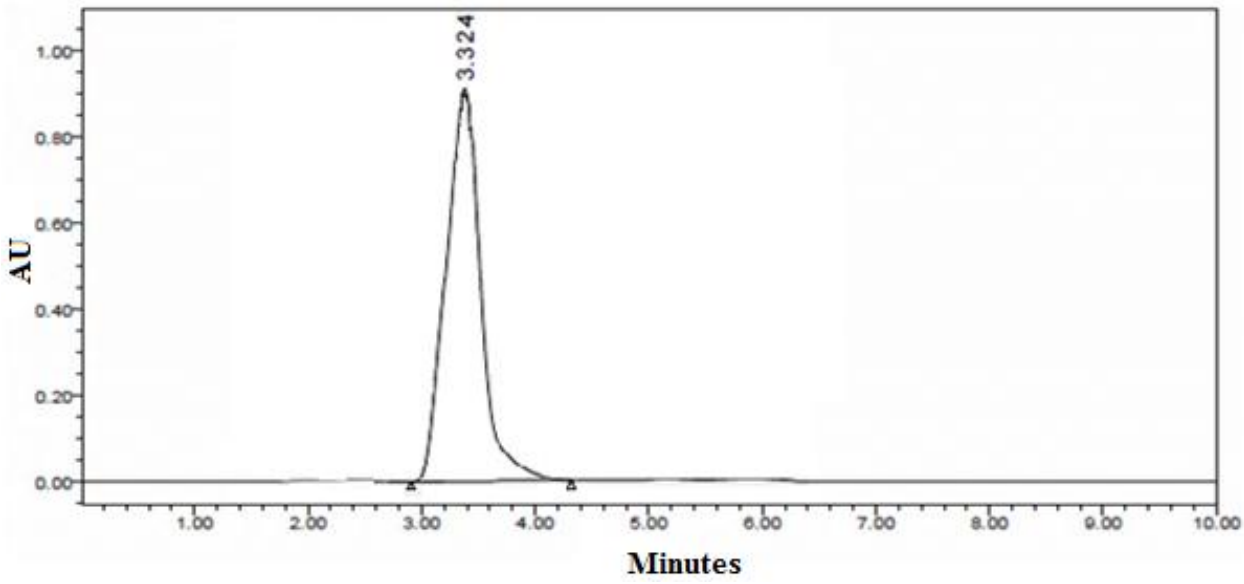

Figure 4.14: Chromatogram showing a stability of benzamide in fresh water after 2 days incubation at 25 ^{o}C.

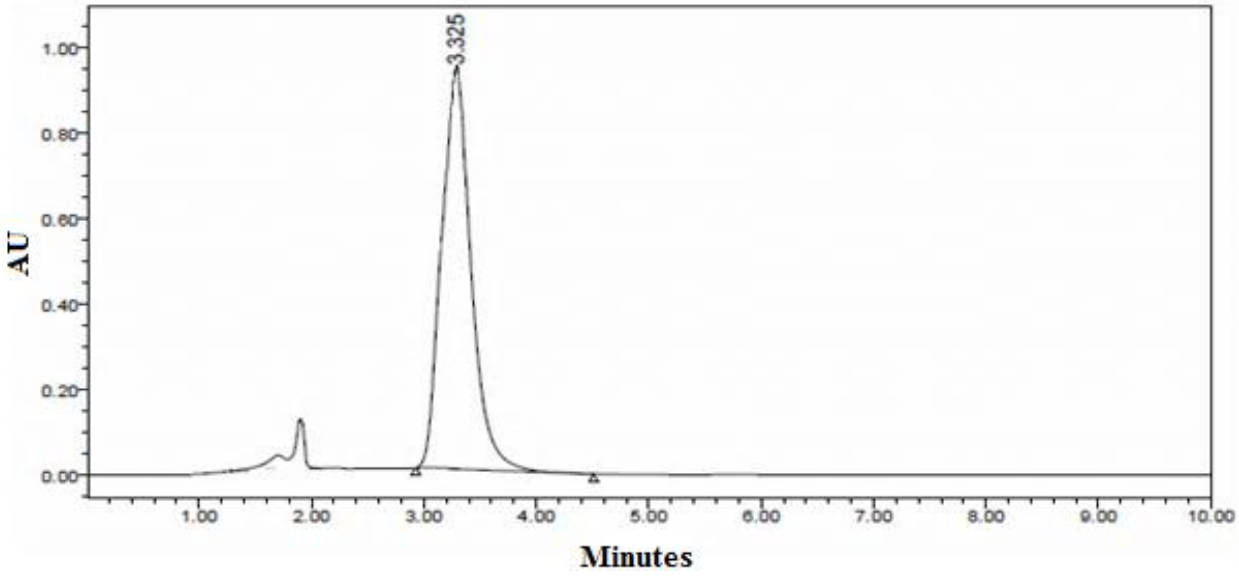

Figure 4.15: Chromatogram showing a stability of benzamide in fresh water after 7 days incubation at 25 ^{o}C.

4.1.2.3 Stability of Benzamide in activated sludge

Benzamide was revealed a gradual degradation to benzoic acid (Figure 4.16) within six days incubation at 25^{o}C in activated sludge. The degradation was demonstrated by a disappearance of a peak characterized as the reactant (benzamide) at a retention time of 3.3 minutes and a gradual appearance of a new peak at a retention time of 4.6 minutes characterized as benzoic acid, degradation product (Figure 4.19). Figures 4.17 and 4.18 illustrate a progress of benzamide degradation as monitored by HPLC.

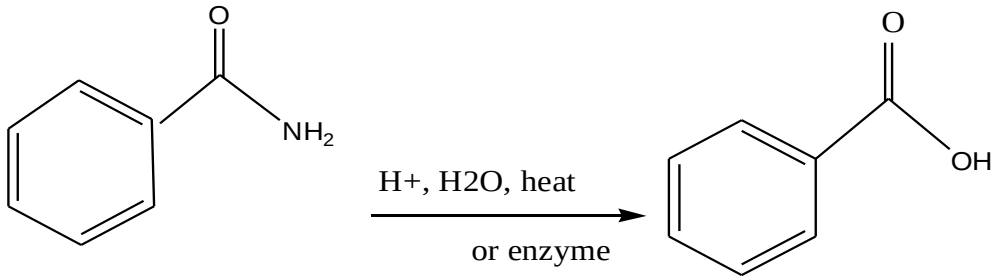

Figure 4.16: Schematic pathway for a degradation of benzamide in Al-Quds sludge and by *Pseudomonas aeruginosa* bacteria**.**

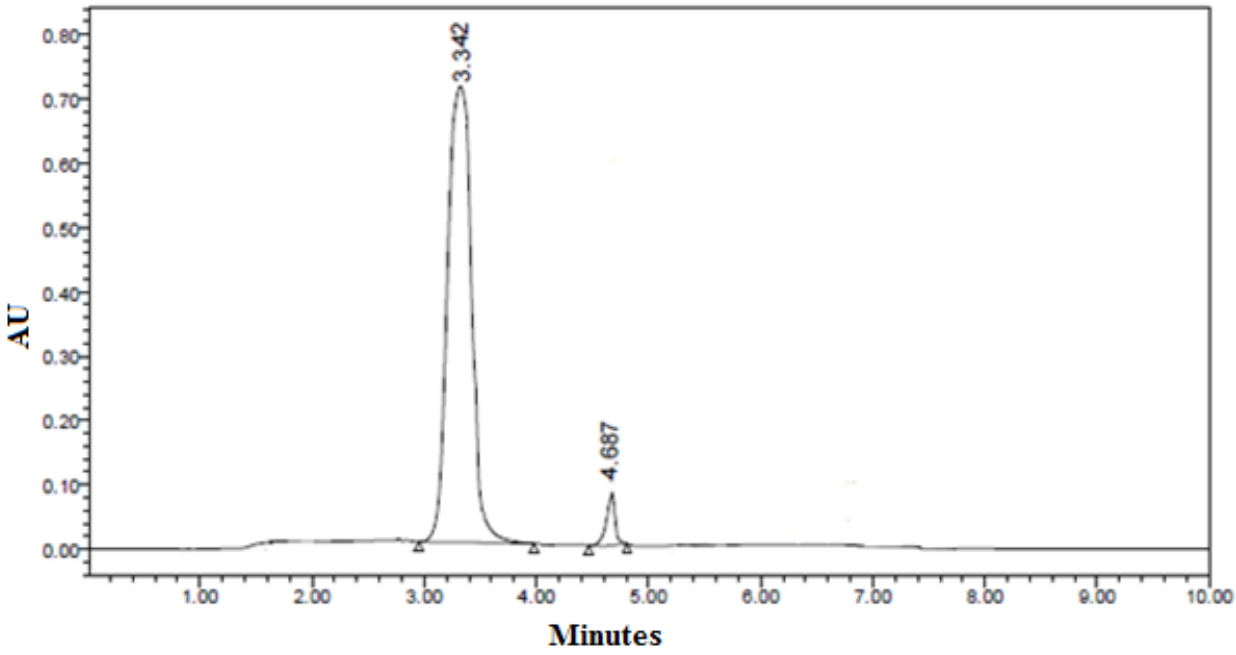

Figure 4.17: Chromatogram showing a hydrolysis of benzamide in activated sludge after 2 days in presence of activated sludge at 25^{o}C.

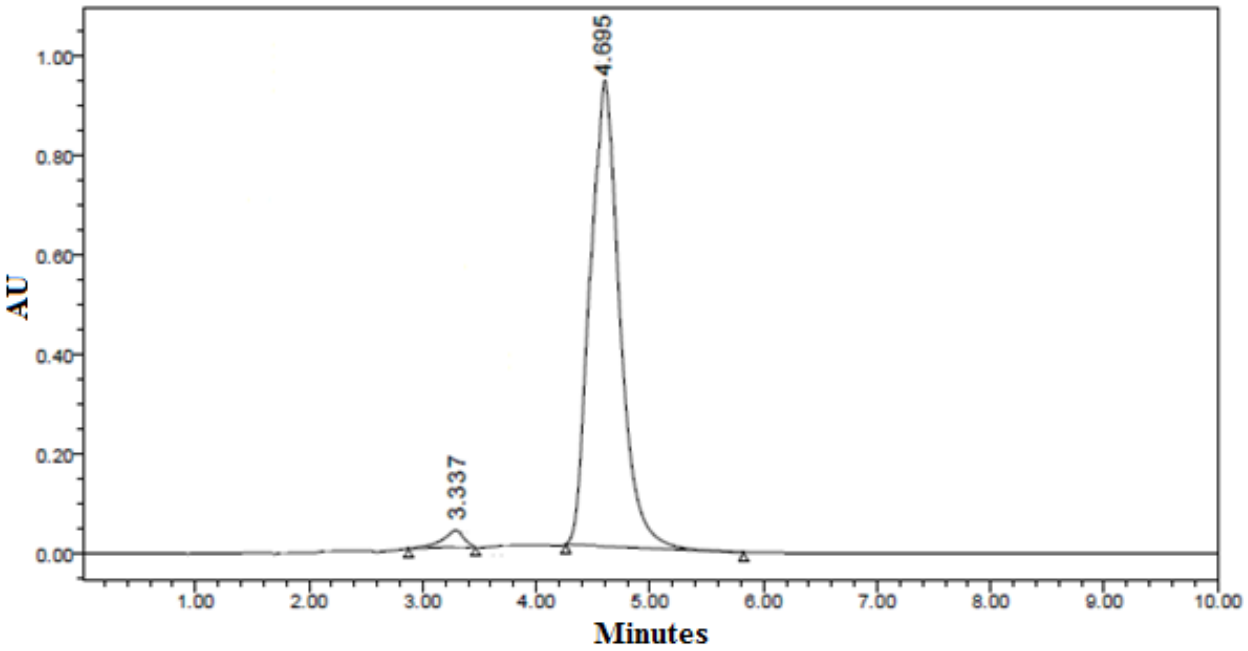

Figure 4.18: Chromatogram showing a hydrolysis of benzamide in activated sludge after 6 days in presence of activated sludge at 25^{o}C.

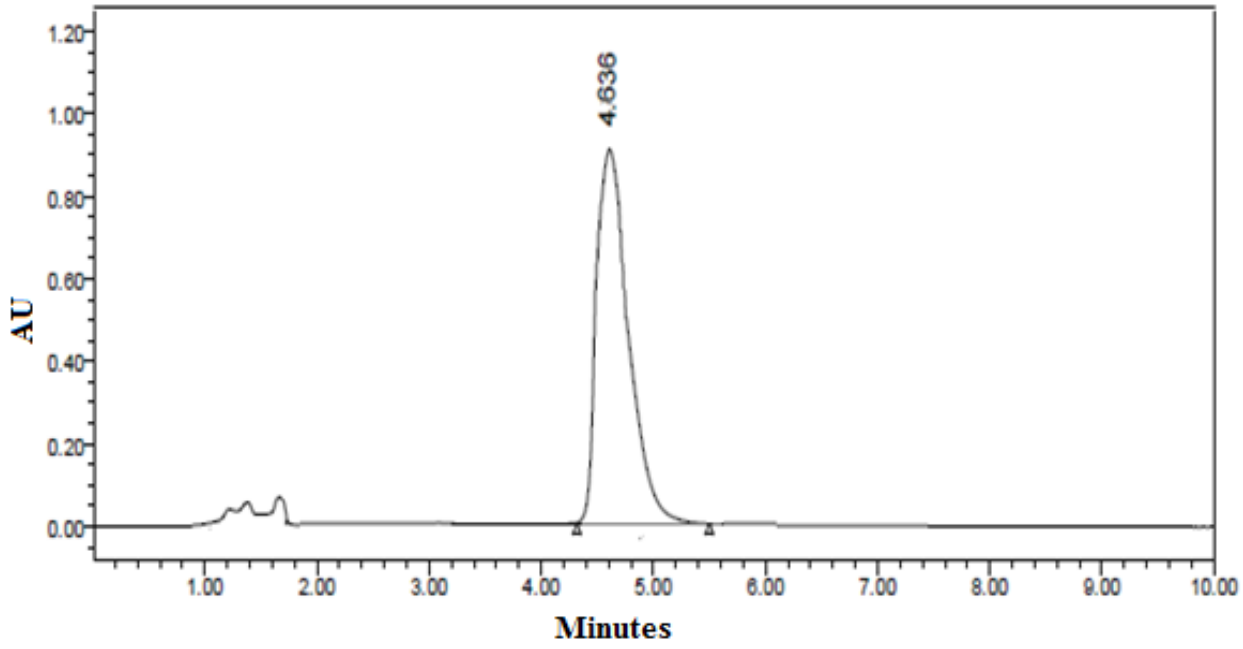

Figure 4.19: Chromatogram showing a benzoic acid standard.

4.1.2.4 Biodegradation of Benzamide in sterile peptone water contains *Pseudomonas aeruginosa*.

Pseudomonas aeruginosa was sub-cultured from the bacteria characterized in the sludge of AQU-WWTP in sterile peptone water under complete sterile technique. The inoculated flask was incubated at 37 ºC for two hours to activate the growth of the bacteria, and then was transferred to a shaker. 100 mg benzamide were added to the bacterial suspension having 0.5 optical densities. The product (metabolite) was extracted from the biological degradation reactor after 1, 2, 3, 4, 5, 6 and 7 days. The extraction was performed using chloroform, and then liquid chromatography was performed to determine the concentrations of resulting metabolites.

As deduced by HPLC determinations benzamide was degraded within 6 days (Figure 4.21). During benzamide degradation, new metabolite was detected and tentatively identified by means of LC-MS and NMR as benzoic acid (Figure 4.16). The HPLC kinetic data (Table 4.8) obtained after one week monitoring was examined for linear correlation (Figure 4.20). A linear correlation was obtained when ln[benzamide] was plotted against time with a correlation coefficient $R^2 = 0.938$. The pseudo first order reaction rate constant was found to be 7.86×10^{-9} $M.s^{-1}$.

Table 4.8: Kinetic data of molar benzamide concentration versus time at 25 ^{o}C.

Time (hrs)	ln [Benzamide] M
0	-7.0884
24	-7.10198
48	-7.53037
72	-8.71401
96	-9.26353
120	-10.48
144	-11.8459

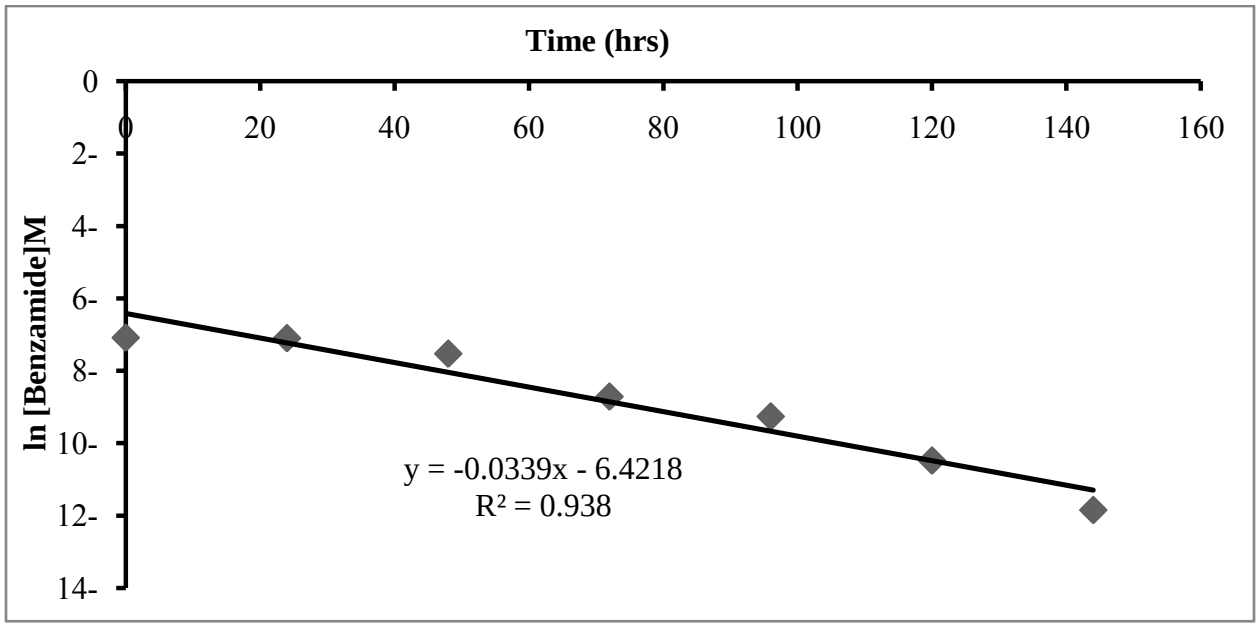

Figure 4.20: First order kinetic plot for the biodegradation of benzamide in *pseudomonas aeruginosa* at 25 ^{0}C.

Table 4.9: Kinetic data of benzamide biodegradation versus time at 25^{o}C.

Time (Days)	Benzamide Concentration (ppm) AV	±SD
0	101.11	5.92
1	99.76	8.01
2	64.99	5.69
3	19.89	6.69
4	11.49	2.39
5	3.40	0.82
6	0.89	0.73

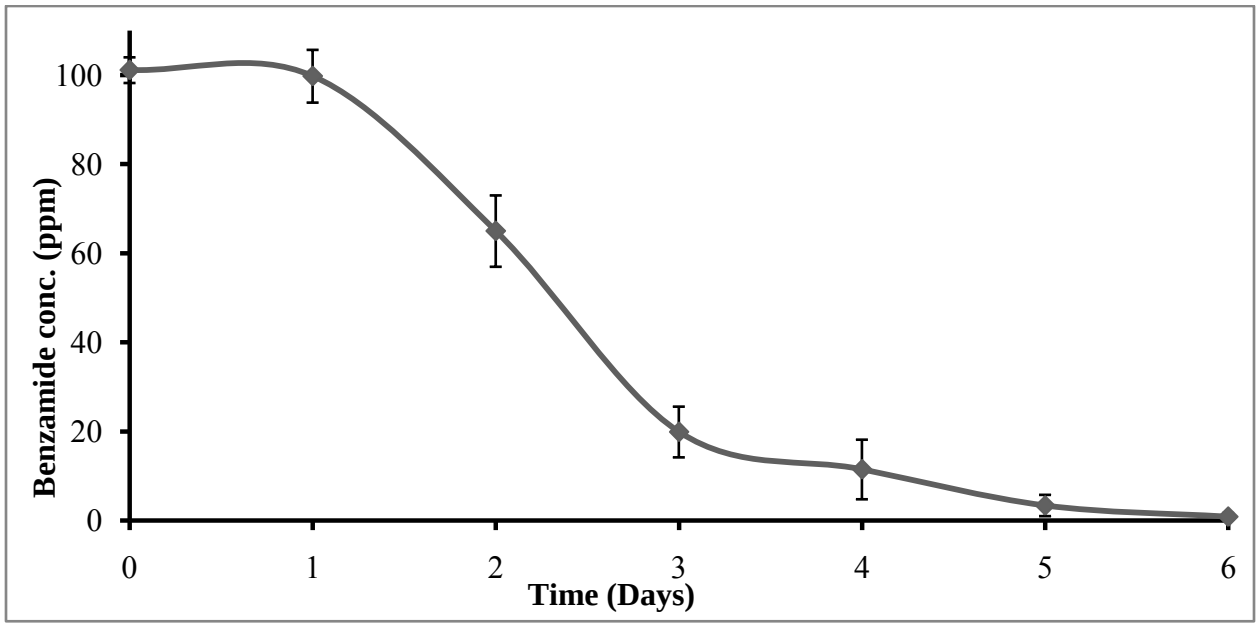

Figure 4.21: Benzamide concentration decay versus time when incubated with *pseudomonas aeruginosa* at 25 ^{0}C. Data represent of average of triplicate measurements.

4.2 Efficiency of AQU-WWTP for the removal of selected pharmaceuticals.

4.2.1 Removal of Paracetamol

4.2.1.1 Calibration curve of paracetamol standard using UV-spectrophotometer method

Calibration curve was obtained by plotting absorbance of paracetamol versus paracetamol concentration in ppm at 245 nm wavelengths (Table 4.10). The method gave a linear correlation within the concentration range 0.1– 50 ppm with correlation coefficient r^2 = 0.996, as shown in Figure 4.22.

Table 4.10: Standard of paracetamol concentration versus absorbance.

Concentration (ppm)	Absorbance
0	0
0.1	0.007
0.5	0.021
1	0.032
5	0.154
10	0.301
50	2.158

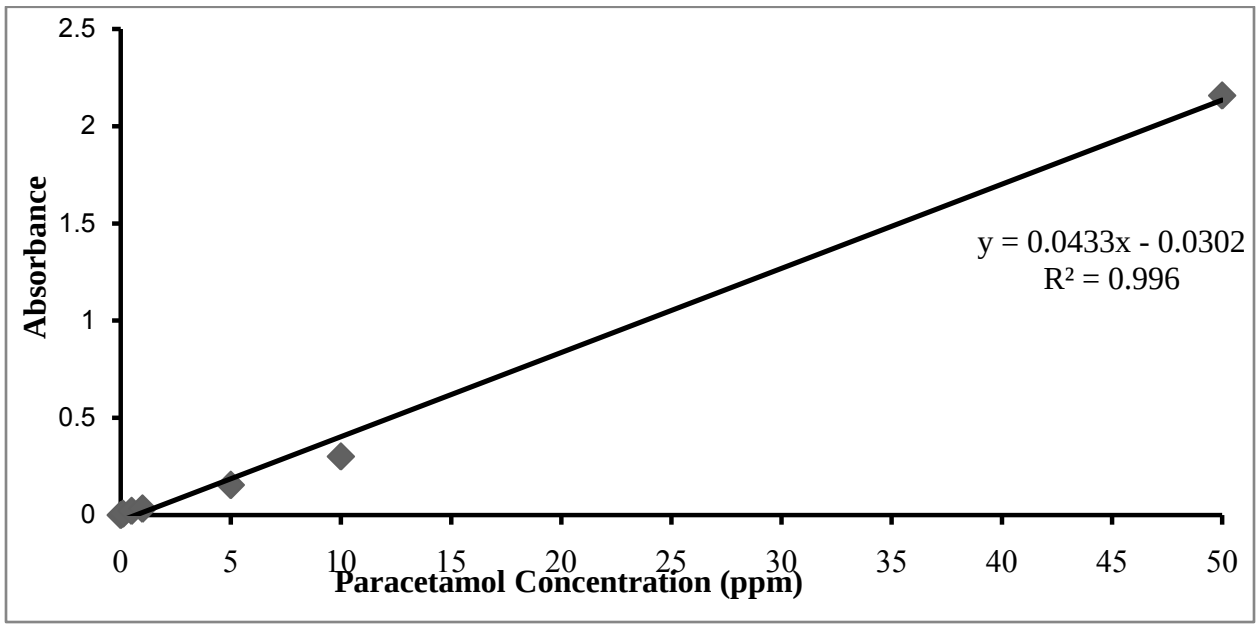

Figure 4.22: Calibration curve of paracetamol using UV-spectrophotometer method.

4.2.1.2 AQU-WWTP efficiency for paracetamol removal

The efficiency of AQU-WWTP for paracetamol removal was studied. The result demonstrated that paracetamol was 46% removed at the hollow fiber membrane, while about 84% of paracetamol was removed at the spiral wound membrane, (Table4.11). At the activated carbon adsorbent point of the wastewater treatment plant, 99% of paracetamol was removed. The results also indicated that a complete removal (100%) of paracetamol was achieved through the reverse osmosis membranes (RO).

Table 4.11: Percentage removal of paracetamol after passing through the UF-HF, UF-SW, AC and RO of AQU-WWTP membranes.

Parameter		Paracetamol Concentration (ppm)	% Removal
Before addition (Blank)		0	
After addition (Inlet)		46.27 ± 1.64	
Ultra-Filtration-Hollow Fiber	Product	24.76 ± 2.97	46
	Brine	22.75 ± 1.79	
Ultra-Filtration-Spiral Wound	Product	7.61 ± 1.56	84
	Brine	14.26 ± 0.33	
Activated Carbon		0.15 ± 0.06	99
Reverse Osmosis	Product	0	100
	Brine	0.14 ± 0.11	

4.2.2 Removal of *P*-aminophenol

4.2.2.1 Calibration curve of *p*-aminophenol standard using UV-spectrophotometer method

Calibration curve was obtained by plotting absorbance of *p*-aminophenol versus *p*-aminophenol concentration in ppm at 245 nm wavelength (Table 4.12). The method gave a linear relation within the concentration in the range 0 – 50 ppm with correlation coefficient r^2 = 0.999, as shown in Figure 4.23.

Table 4.12: Standard *p*-aminophenol concentration versus absorbance

Concentration (ppm)	Absorbance
0	0
0.1	0.001
0.5	0.021
1	0.072
5	0.254
10	0.381
50	2.158

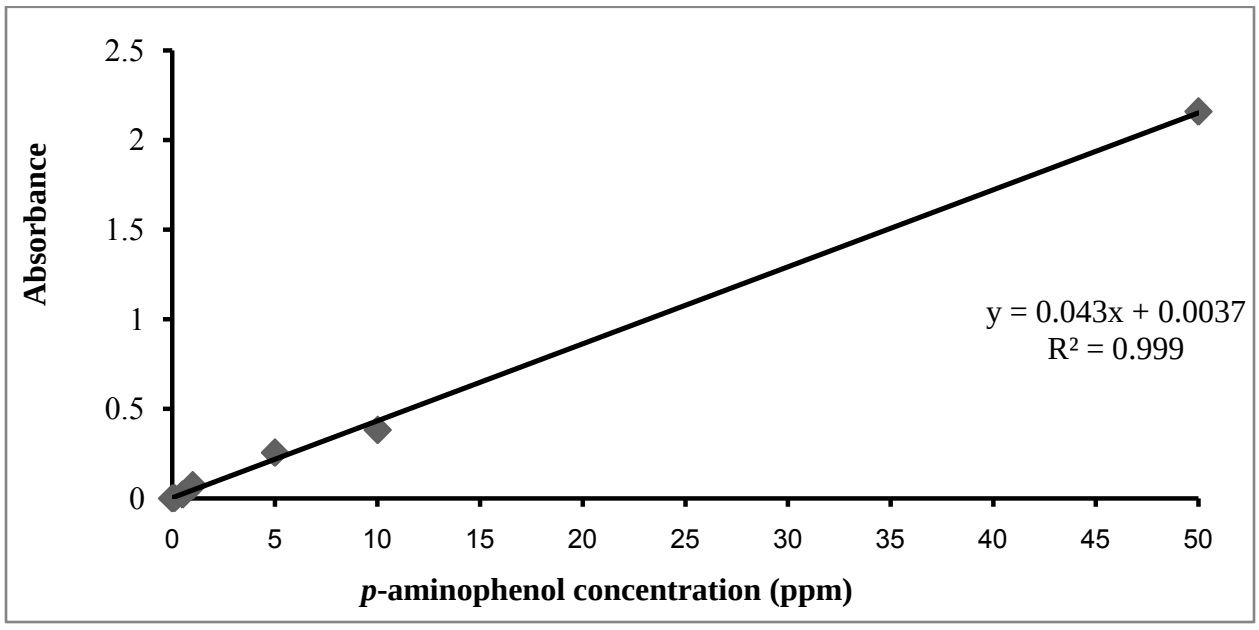

Figure 4.23: Calibration curve of *p*-aminophenol using UV-spectrophotometer method.

4.2.2.2 AQU-WWTP efficiency for *p*-aminophenol removal

The efficiency of AQU-WWTP for *p*-aminophenol removal was studied. The results demonstrated that p-aminophenol was 43% removed at the hollow fiber membrane, while about 80% of *p*-aminophenol was removed at the spiral wound membrane, (Table4.13). The results also indicated that a complete removal (100%) of *p*-aminophenol was achieved after passing through the activated carbon and reverse osmosis membranes (RO), respectively.

Table 4.13: Percentage removal of *p*-aminophenol after passing through the UF-HF, UF-SW, AC and RO of AQU-WWTP membranes.

Parameter		*p*-aminophenol Concentration (ppm)	% Removal
Before addition (Blank)		0	
After addition (Inlet)		49.53 ± 1.07	
Ultra-Filtration-Hollow Fiber	Product	28.15 ± 0.72	43
	Brine	22.75 ± 1.79	
Ultra-Filtration-Spiral Wound	Product	9.96 ± 0.65	80
	Brine	13.35 ± 0.46	
Activated Carbon		0	100
Reverse Osmosis	Product	0	100
	Brine	0	

4.2.3 Removal of Benzamide

4.2.3.1 Calibration curve of benzamide standard using UV-spectrophotometer method

Calibration curve was obtained by plotting absorbance of benzamide versus benzamide concentration in ppm at 226 nm wavelength (Table 4.14). The method gave a linear relation within the concentration range 0.1 – 50 ppm with correlation coefficient r^2 = 0.998, as shown in Figure4.24.

Table 4.14: Standard benzamide concentration versus absorbance

Concentration (ppm)	Absorbance
0	0
0.1	0.012
0.5	0.031
1	0.053
5	0.159
10	0.226
50	1.315

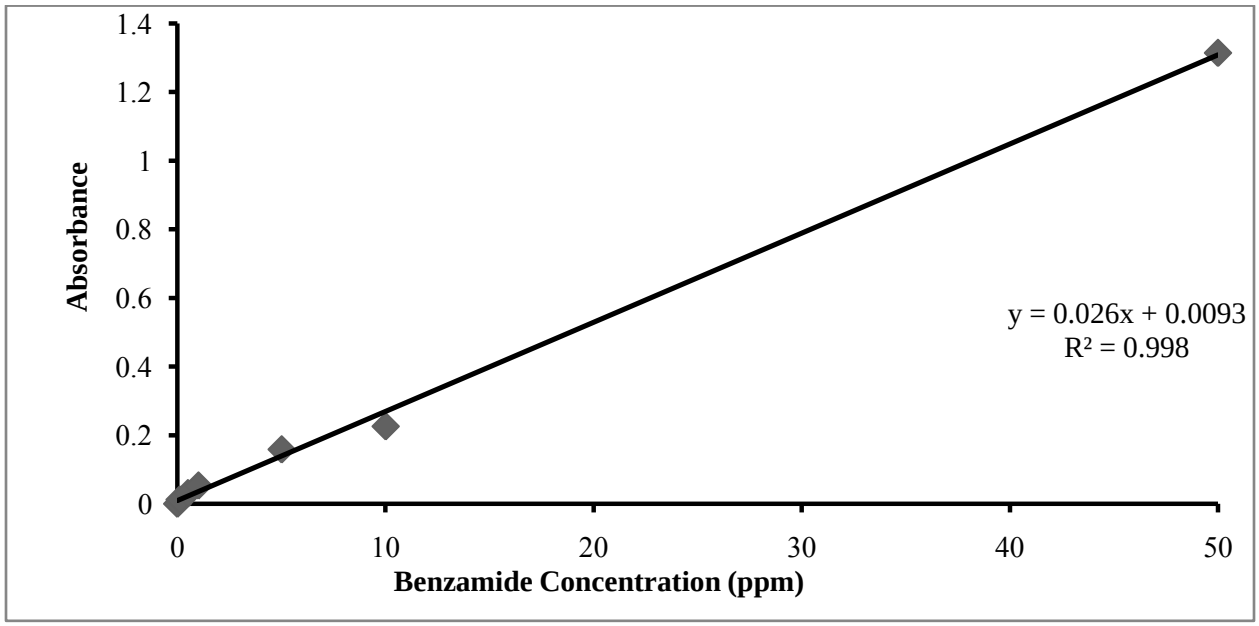

Figure 4.24: Calibration curve of benzamide using UV-spectrophotometer method.

4.2.3.2 AQU-WWTP efficiency for benzamide removal

The efficiency of AQU-WWTP for benzamide removal was studied. The result demonstrated that benzamide was 40% removed at the hollow fiber membrane, while about 86% of benzamide was removed at the spiral wound membrane, (Table4.15). The results also indicated that a complete removal (100%) of benzamide was achieved after passing through the activated carbon and reverse osmosis membranes (RO), respectively.

Table 4.15: Percentage removal of benzamide after passing through the UF-HF, UF-SW, AC and RO stages of AQU-WWTP.

parameter		Benzamide Concentration (ppm)	% Removal
Before addition (Blank)		0	
After addition (Inlet)		34.70 ± 0.82	
Ultra-Filtration-Hollow Fiber	Product	20.96 ± 188	40
	Brine	13.49 ± 1.49	
Ultra-Filtration-Spiral Wound	Product	4.92 ± 0.96	86
	Brine	10.12 ± 1.21	
Activated Carbon		0	100
Reverse Osmosis	Product	0	100
	Brine	0	

4.2.4 Removal of Bezafibrate

4.2.4.1 Calibration curve of bezafibrate standard using UV-spectrophotometer method

Calibration curve was obtained by plotting the absorbance of bezafibrate versus its concentration in ppm at 231 nm wavelength (Table 4.16). The method gave a linear relation within the concentration range of 0.1 – 10 ppm with correlation coefficient R^2 = 0.998, as shown in Figure 4.25.

Table 4.16: Standard bezafibrate concentration versus absorbance

Concentration (ppm)	Absorbance
0	0
0.1	0.019
0.5	0.047
1	0.126
5	0.431
10	0.852

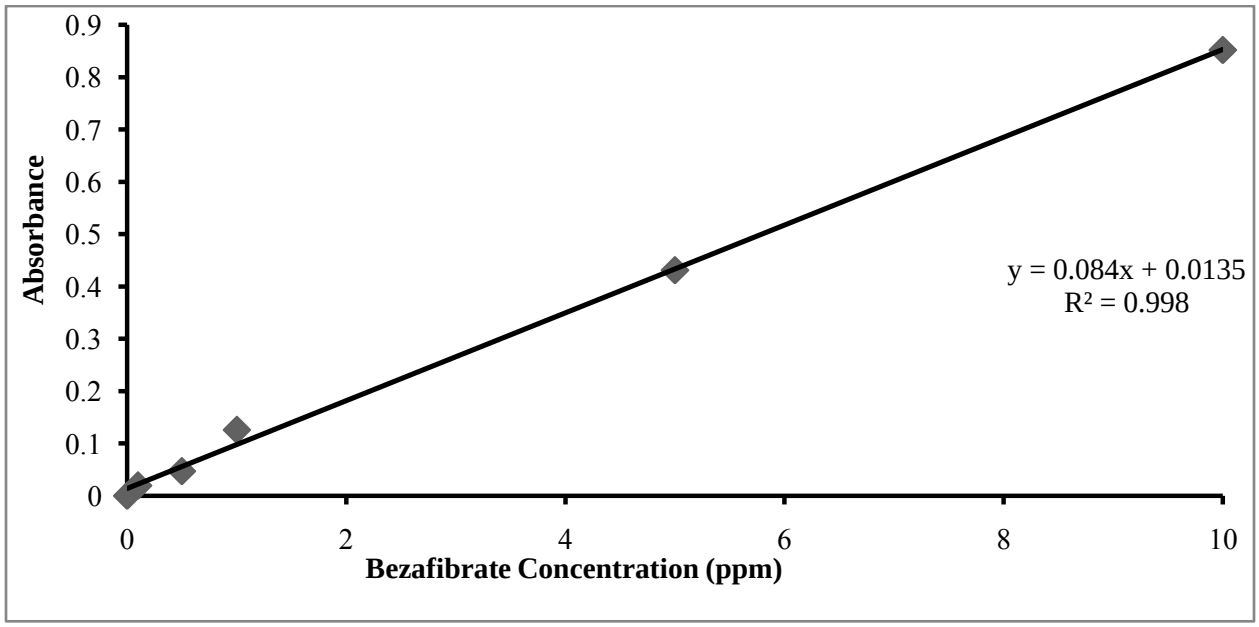

Figure 4.25: Calibration curve of bezafibrate using UV-spectrophotometer method.

4.2.4.2 AQU-WWTP efficiency for bezafibrate removal

The efficiency of AQU-WWTP for bezafibrate removal was studied. The result demonstrated that bezafibrate was 52% removed at the hollow fiber membrane, while about 95% of bezafibrate was removed at the spiral wound membrane (Table4.17). The results also indicated that a complete removal (100%) of bezafibrate was achieved after passing the pharmaceutical through the activated carbon and reverse osmosis membranes (RO), respectively.

Table 4.17: Percentage removal of bezafibrate after passing through the UF-HF, UF-SW, AC and RO of AQU-WWTP membrane.

Parameter		Bezafibrate Concentration (ppm)	% Removal
Before addition (Blank)		0	
After addition (Inlet)		29.19 ± 1.05	
Ultra-Filtration-Hollow Fiber	Product	14.09 ± 0.80	52
	Brine	11.26 ± 0.55	
Ultra-Filtration-Spiral Wound	Product	1.59 ± 0.69	95
	Brine	8.59 ± 1.49	
Activated Carbon		0	100
Reverse Osmosis	Product	0	100
	Brine	0	

4.2.5 Removal of Atenolol

4.2.5.1 Calibration curve of atenolol standard using UV-spectrophotometer method

Calibration curve was obtained by plotting the absorbance of atenolol versus its concentration in ppm at 273 nm wavelength (Table 4.18). The method gave a linear relation within the concentration range 0.1 – 50 ppm with a correlation coefficient of r^2 = 0.999, as shown in Figure 4.26.

Table 4.18: Standard atenolol concentration versos absorbance

Concentration (ppm)	Absorbance
0.1	0.009
0.5	0.026
1	0.052
5	0.15
10	0.341
50	1.632

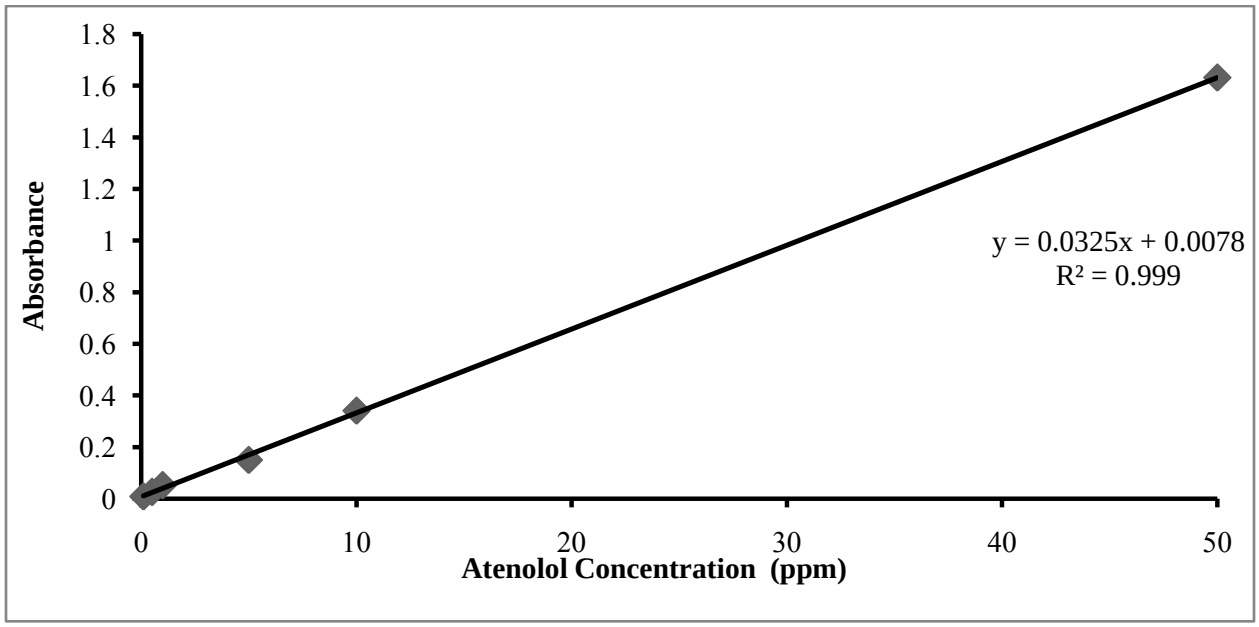

Figure 4.26: Calibration curve of atenolol using UV-spectrophotometer method.

4.2.5.2 AQU-WWTP efficiency for atenolol removal

The efficiency of AQU-WWTP for atenolol removal was studied. The results demonstrated that atenolol was 44% removed at the hollow fiber membrane, while about 96% of atenolol was removed at the spiral wound membrane (Table 4.19). The results also indicated that a complete removal (100%) of atenolol was achieved after passing through the activated carbon and reverse osmosis membranes (RO), respectively.

Table 4.19: Percentage removal of atenolol after passing through the UF-HF, UF-SW, AC and RO of AQU-WWTP membranes.

Parameter		Atenolol Concentration (ppm)	% Removal
Before addition (Blank)		0	
After addition (Inlet)		31.39 ± 0.53	
Ultra-Filtration-Hollow Fiber	Product	17.53 ± 1.19	44
	Brine	11.33 ± 0.67	
Ultra-Filtration-Spiral Wound	Product	1.75 ± 0.96	96
	Brine	13.69 ± 1.79	
Activated Carbon			100
Reverse Osmosis	Product		100
	Brine		

4.3 Adsorption studies of selected pharmaceuticals into micelle-clay complex and activated carbon

Herein, results for the removal of paracetamol and its metabolite, *p*-aminophenol in suspension by a micelle-clay complex in comparison with activated carbon are presented. The micelles of the organic cation octadecyltrimethylammonium (ODTMA) interact with negatively charged clay (montmorillonite) at optimal ratios (Polubesova 2005, 2006). The complex has a very large surface area per weight; it includes large hydrophobic parts and has an excess of a positive charge, about half of the exchange capacity of the clay. X-ray diffraction, electron microscopy and adsorption experiments indicated that the material characteristics of the micelle-clay complex are different from those of an organo-clay complex, which is formed by adsorption of the same organic cation as monomer (Mishael 2002). The micelle-clay is ideally suited for the adsorption of anionic organic molecules e.g., herbicides (Polubesova 2005), humic acid, dissolved organic matter (DOM) (Radian 2011), certain antibiotics (Polubesova 2006, Karaman 2012), as well as certain inorganic anions, such as perchlorate (Nir 2015). Filters filled with a micelle-clay complex mixed with sand were employed to study the ability of the mixture adsorbents in removing a variety of pharmaceuticals (Karaman 2012, Awwad 2015).

4.3.1 Adsorption of paracetamol & *p*-aminophenol

4.3.1.1 Kinetic Adsorption.

Figures 4.27 and 4.28 and Tables 4.21 and 4.22 demonstrate a decrease in paracetamol and p-aminophenol concentrations, respectively, with function of time using either micelle-clay complex or activated carbon. This revealing that micelle-clay complex is efficient for paracetamol and *p*-aminophenol removal.

Table 4.20: Kinetic data for the removal of paracetamol into micelle-clay complex and activated carbon.

Adsorbent	Micelle-Clay Complex	Activated Carbon
Time (minutes)	Concentration (ppm)	Concentration (ppm)
0	50.13 ± 1.20	50.29 ± 1.51
2	23.85 ± 1.62	17.89 ± 2.63
5	13.76 ± 1.95	8.15 ± 1.90
10	8.59 ± 2.13	3.94 ± 2.16
20	1.89 ± 1.03	1.49 ± 0.93
30	1.66 ± 1.08	0.99 ± 0.08
40	1.24 ± 1.11	0.67 ± 1.01
60	0.71 ± 0.07	0.32 ± 0.07
80	0.27 ± 0.03	0.16 ± 0.03
100	0.32 ± 0.10	0.04 ± 0.03
120	0.24 ± 0.14	0.02 ± 0.08

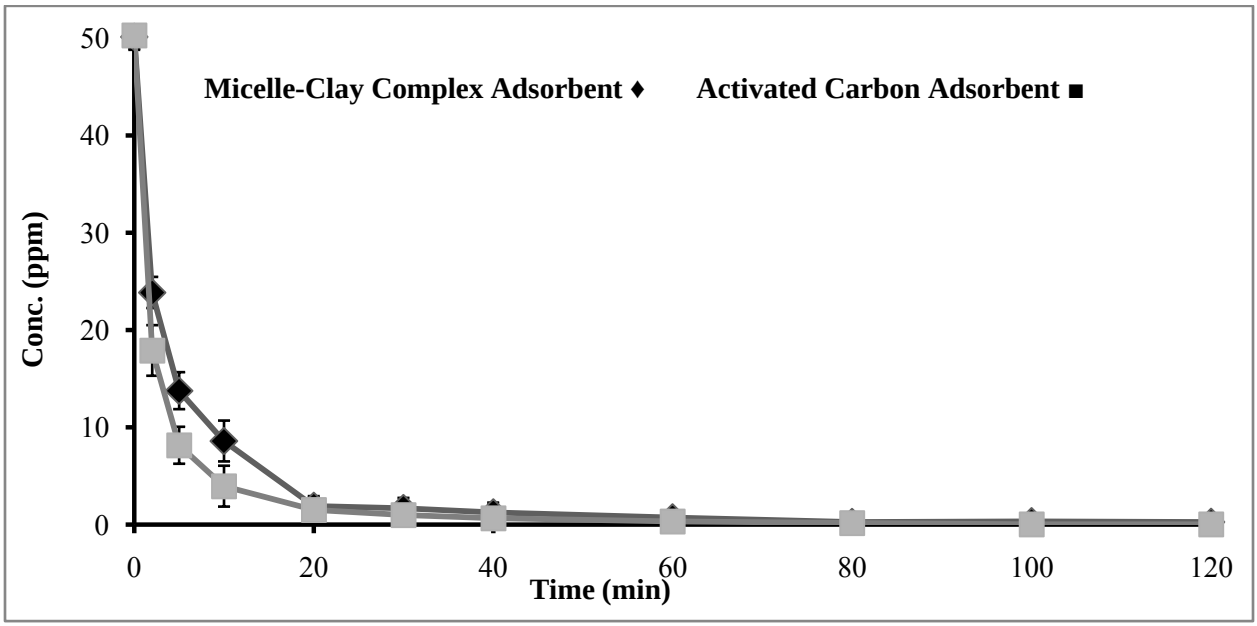

Figure 4.27: Kinetic adsorption of paracetamol into the Micelle-Clay complex (♦) and activated carbon (■). Temp. = 25.0 ^{o}C, and adsorbent dosage = 5.0 g/L.

Table 4.21: Kinetic data for the removal of *p*-aminophenol into micelle-clay complex and activated carbon.

Adsorbent	Micelle-Clay Complex	Activated Carbon
Time (min)	Conc. (ppm)	Conc. (ppm)
0	51.73 ± 2.40	51.49± 2.50
2	44.40± 1.83	42.79±3.83
5	33.61± 2.42	29.26± 3.61
10	11.17 ± 1.61	4.68± 2.90
20	2.45 ± 1.04	1.66± 1.82
30	1.87 ± 1.52	1.29± 1.20
40	1.36 ± 0.85	1.03± 0.85
60	1.33± 0.04	0.87± 0.30
80	1.49± 0.18	0.59± 0.24
100	1.43 ± 0.69	0.54± 0.93
120	1.45 ± 0.57	0.38± 0.79

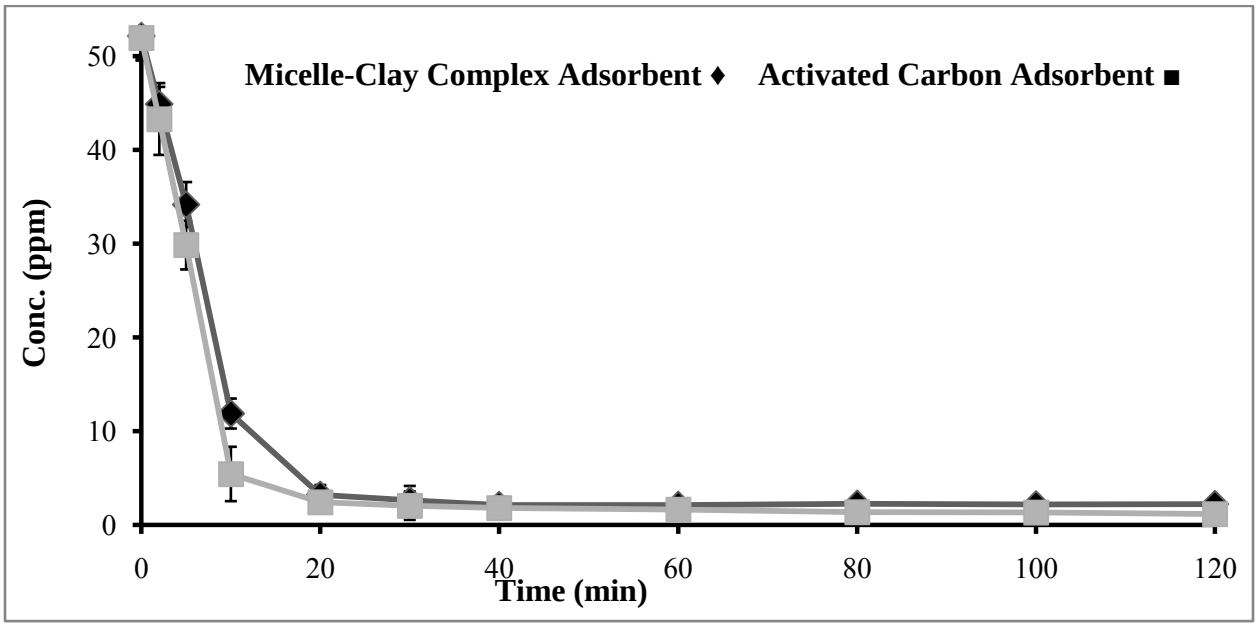

Figure 4.28: Kinetic adsorption of *p*-aminophenol into the Micelle-Clay complex (♦) and activated carbon (■). Temp. = 25.0 ^{o}C, and adsorbent dosage = 5.0 g/L.

4.3.1.2 Adsorption Isotherm

The adsorption of selected pharmaceuticals onto a clay micelles complex and charcoal was analyzed by the Langmuir isotherm equation as shown below:

$$\frac{Ce}{Qe} = \frac{1}{K*Qmax} + \frac{Ce}{Qmax} \qquad (1)$$

Where:

C_e: equilibrium concentration of (solute, e.g., paracetamol) (ppm).

Q_e: equilibrium mass of adsorbed selected pharmaceuticals per gram of absorbent (mg/g).

K: Langmuir affinity constant (L/mg).

Q_{max}: Maximum amount of solute adsorbed per gram of micelle- clay complex, or charcoal (mg/g).

Adsorption of paracetamol is well described by Langmuir adsorption isotherm as shown by the plot of $C_e\backslash Q_e$ versus C_e (Table 4.23, Figure 4.29). The correlation coefficient values (R^2) obtained by the two adsorbents were summarized in Table 4.22.The calculated Q_{max} and K values for the removal of the paracetamol (Table 4.22) are 47.17 ± 6.21 mg/ g and 0.054 ±0.007 L/mg, respectively using micelle-clay complex. The corresponding values in the case of activated carbon are Q_{max} =46.73 ± 4.05 mg/g and K= 0.391 ± 0.020 L/mg, this indicates that no significant difference between the activated carbon and micelle-clay complex, the affinity coefficient, k, for the activated carbon was larger than that for micelle-clay complex.

Table 4.22: Langmuir constant (Q_{max}& K) and correlation coefficient for adsorption isotherm of paracetamol into micelle-clay complex and activated carbon.

	Adsorbent	Q_{max} (mg/g)	K (L/mg)	R^2
Paracetamol	Micelle-Clay Complex	47.17 ± 6.21	0.05 ±0.02	0.974
	Activated Carbon	46.73 ± 4.05	0.39 ± 0.20	0.965

Table 4.23: Langmuir isotherm parameter for adsorption of adsorbate paracetamol into micelle-clay complex and activated carbon as adsorbent.

Micelle-Clay Complex		Activated Carbon	
C_e (ppm)	C_e/Q_e (g/L)	C_e (ppm)	C_e/Q_e (g/L)
0.29	0.30	-0.004	-0.005
1.29	0.26	0.02	0.004
6.02	0.64	0.73	0.07
24.08	1.07	9.42	0.39
95.69	2.37	45.30	0.99

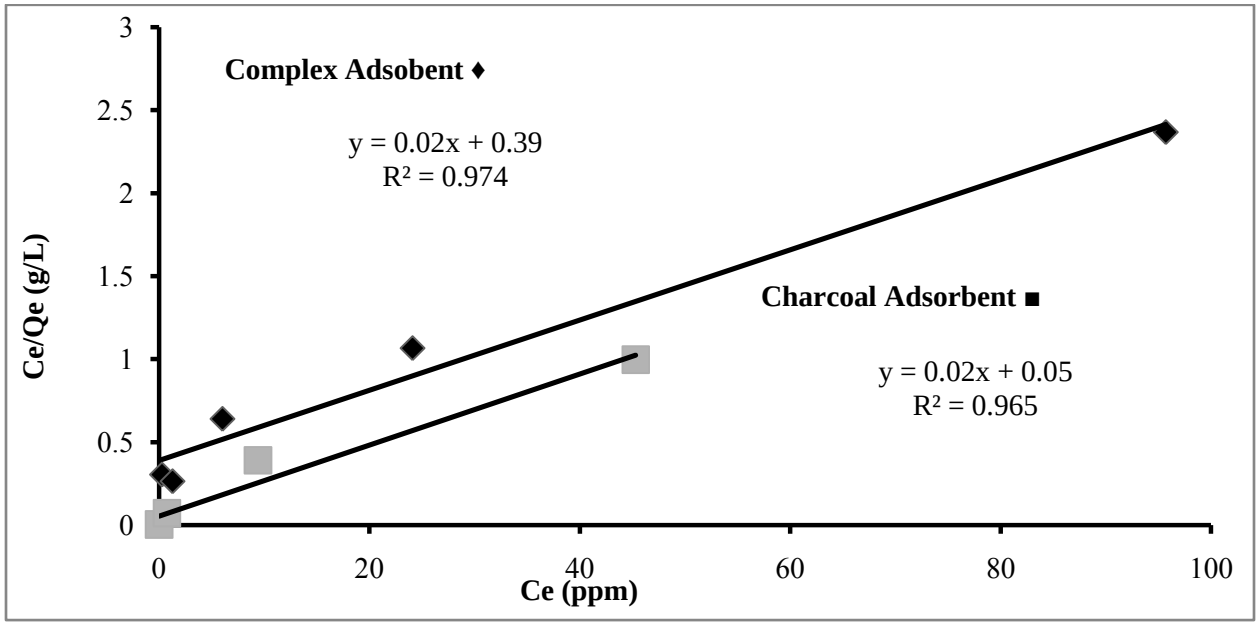

Figure 4.29: Plot of Langmuir isotherm for the adsorption of paracetamol into the micelle-clay complex (♦) and activated carbon (■). Contact time = 2 h, Temp. = 25.0 °C, and adsorbent dosage = 5.0 g/L.

Adsorption of *p*-aminophenol is well described by Langmuir adsorption isotherm as shown by the plot of $C_e\backslash Q_e$ versus C_e (Table 4.25 and Figure 4.30). The correlation coefficient values (R^2) obtained by the two adsorbents were summarized in Table 4.24. The Q_{max} and K values determined for the removal of the *p*-aminophenol (Table 4.24) are 44.25 ± 5.28mg/g and 0.033 ±0.019 L/mg, respectively using micelle-clay complex. The corresponding values in the case of activated carbon are Q_{max} = 50.00 ± 7.32 mg/g and K= 0.033 ± 0.002 L/mg. The Q_{max} for micelle-clay complex was higher than that for the activated carbon, the affinity coefficient, k, for both micelle-clay complex and activated carbon was equal.

Table 4.24: Langmuir constant and correlation coefficient for adsorption isotherm of *p*-aminophenol into micelle-clay complex and activated carbon.

	Adsorbent	Q_{max} (mg/g)	K (L/mg)	R^2
P-aminophenol	Micelle-Clay Complex	44.25 ± 5.28	0.033 ±0.019	0.945
	Activated Carbon	50.00 ± 7.32	0.033 ± 0.002	0.962

Table 4.25: Langmuir isotherm parameter for adsorption of adsorbate *p*-aminophenol into micelle-clay complex and activated carbon as adsorbent.

Micelle-Clay Complex		Activated Carbon	
C_e (ppm)	C_e/Q_e (g/L)	C_e (ppm)	C_e/Q_e (g/L)
0	0	0	0
4.05	0.88	1.75	0.36
8.12	0.88	6.33	0.68
33.70	1.56	28.17	1.27
134.60	3.68	117.58	3.07

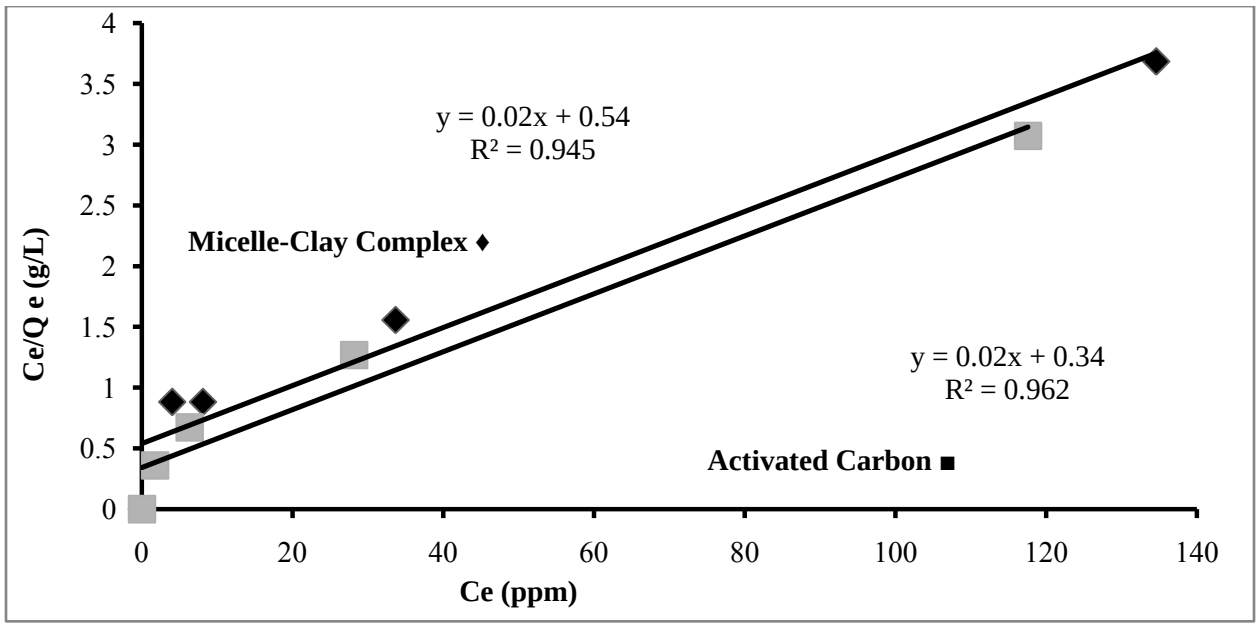

Figure 4.30: Plot of Langmuir isotherm for the adsorption of *p*-aminophenol into the micelle-clay complex (♦) and activated carbon (■). Contact time = 2 h, Temp. = 25.0 ^{o}C, and adsorbent dosage = 5.0 g/L.

The adsorption of paracetamol and *p*-aminophenol were analyzed as well by Freundlich isotherm equation:

$$\log Qe = \log k + \frac{1}{n} logCe \qquad (2)$$

C_e: equilibrium concentration of adsorbate (ppm).

Q_e: equilibrium mass of adsorbed selected pharmaceuticals per gram of absorbent (mg/g).

K and n: Freundlich parameter constant.

Adsorption of paracetamol is well described by plot log (Q_e) versus log (C_e) (Table 4.27). The correlation coefficient values (R^2) obtained by the two adsorbents are summarized in Table 4.26.The fitted equilibrium data in Freundlich isotherm expression is shown in Figure 4.31. It is observed that the equilibrium data fitted very well in Freundlich expression with very high correlation coefficients, thus confirming the applicability of the isotherm. For using activated carbon a larger value of k indicates good adsorption efficiency, while a larger value of 1/n for micelle-clay complex indicates a larger change in effectiveness over different equilibrium concentrations.

Table 4.26: Freundlich constant and correlation coefficient for the adsorption isotherm of paracetamol into micelle-clay complex and activated carbon

	Adsorbent	1/n	K	R^2
Paracetamol	Micelle-Clay Complex	0.62 ± 0.47	2.87 ± 1.09	0.965
	Activated Carbon	0.28 ± 0.02	13.49 ± 2.96	0.968

Table 4.27: Freundlich isotherm parameter for adsorption of adsorbate paracetamol into micelle-clay complex and activated carbon as adsorbent.

Micelle-Clay Complex		Activated Carbon	
log (C_e)	log (Q_e)	log (C_e)	log (Q_e)
-0.53	-0.01		
0.11	0.69	-1.73	0.69
0.78	0.97	-0.13	0.99
1.38	1.35	0.97	1.38
1.98	1.61	1.66	1.66

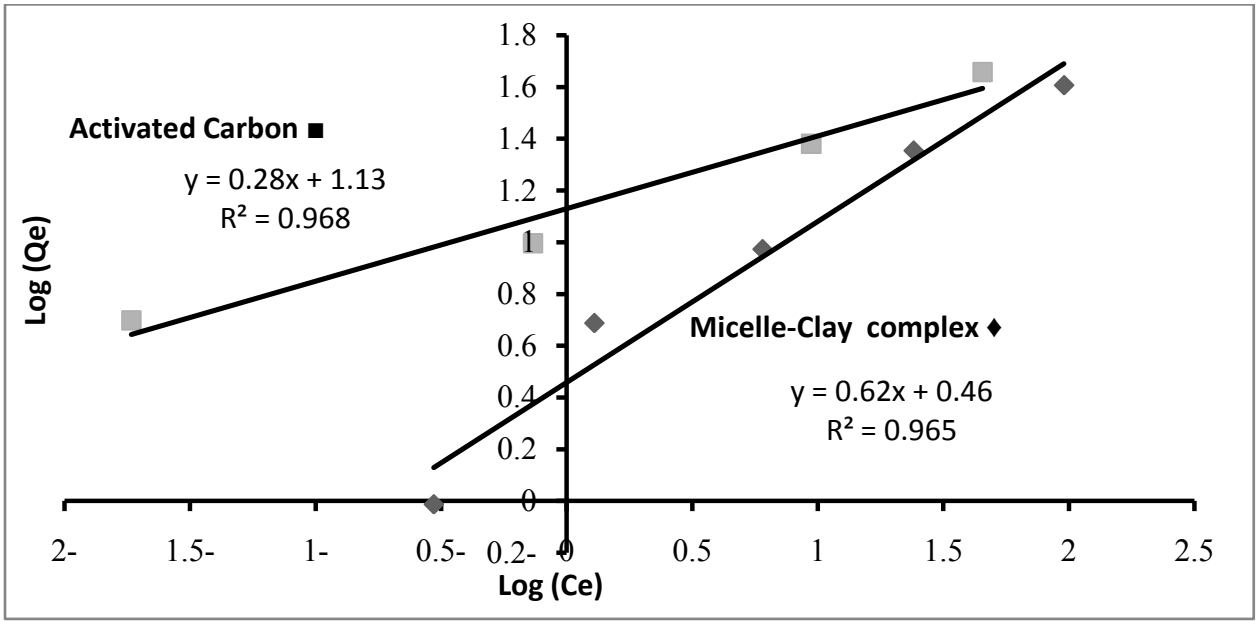

Figure4.31: Plot of Freundlich isotherm for the adsorption of paracetamol into the Micelle-Clay complex (♦) and activated carbon (■). Contact time = 2 h, Temp. = 25.0^{o}C, and adsorbent dosage = 5.0 g/L.

Adsorption of *p*-aminophenol is well described by plot log (Q_e) versus log (C_e), (Table 4.29). The correlation coefficient values (R^2) obtained by the two adsorbents are summarized in Table4.28.The fitted equilibrium data in Freundlich isotherm expression is shown in Figure4.32. It is observed that the equilibrium data fitted very well in Freundlich expression with high correlation coefficients, thus confirming the applicability of the isotherm. The values of k and 1/n indicate that no significant different for both micelle-clay complex and activated carbon.

Table 4.28: Summarized the Freundlich constant and correlation coefficient for adsorption isotherm of *p*-aminophenol into micelle-clay complex and activated carbon.

	Adsorbent	1/n	K	R^2
p-aminophenol	Micelle-Clay Complex	0.67 ± 0.38	1.77 ± 0.83	0.948
	Activated Carbon	0.69 ± 0.20	1.95 ± 0.98	0.984

Table 4.29: Freundlich isotherm parameter for adsorption of adsorbate *p*-aminophenol into micelle-clay complex and activated carbon as adsorbent.

Micelle-Clay Complex		Activated Carbon	
log (C_e)	log (Q_e)	log (C_e)	log (Q_e)
-0.15	-0.03	-0.34	-0.02
0.39	0.68	0.51	0.67
0.95	0.96	0.85	0.97
1.53	1.33	1.46	1.34
2.13	1.56	2.02	1.59

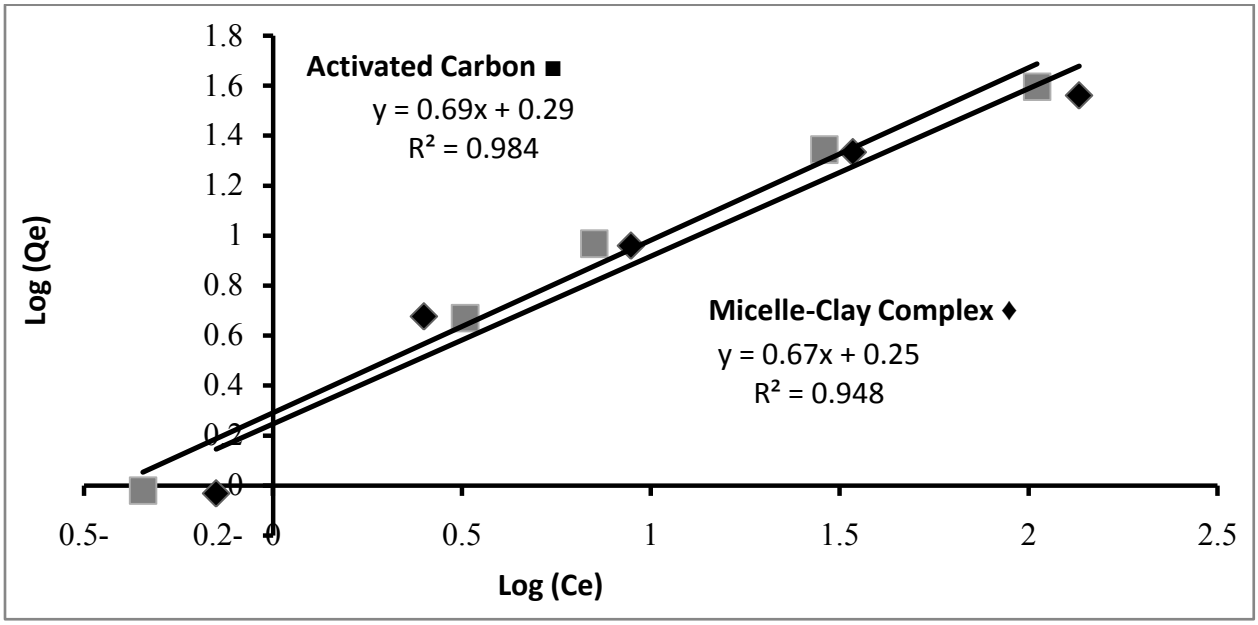

Figure 4.32: Plot of Freundlich isotherm for the adsorption of *p*-aminophenol into the Micelle-Clay complex (♦) and activated carbon (■). Contact time = 2 h, Temp. = 25.0 ^{o}C, and adsorbent dosage = 5.0 g/L.

4.3.2 Adsorption of benzamide

4.3.2.1 Kinetic Adsorption.

Figure 4.33shows a decrease in benzamide concentration versus time when adsorbed by either micelle-clay complex or activated carbon. This reveals that micelle-clay complex and activated carbon are efficient for benzamide removal.

Table 4.30: Kinetic data for the removal of benzamide into micelle-clay complex and activated carbon.

Adsorbent	Micelle-Clay Complex	Activated Carbon
Time (minutes)	Concentration (ppm)	Concentration (ppm)
0	51.79 ± 2.71	49.72 ± 3.68
1	38.57 ± 3.11	35.45 ± 2.13
5	26.29 ± 2.83	20.37 ± 3.90
10	10.87 ± 1.97	5.87 ± 2.77
20	3.14 ± 1.02	2.33 ± 0.28
40	3.26 ± 1.42	1.68 ± 0.54
60	2.03 ± 1.69	1.10 ± 0.96
80	0.99 ± 0.14	0.45 ± 0.42
100	0.87 ± 0.51	0.57 ± 0.16
120	1.07 ± 0.09	0.49 ± 0.95

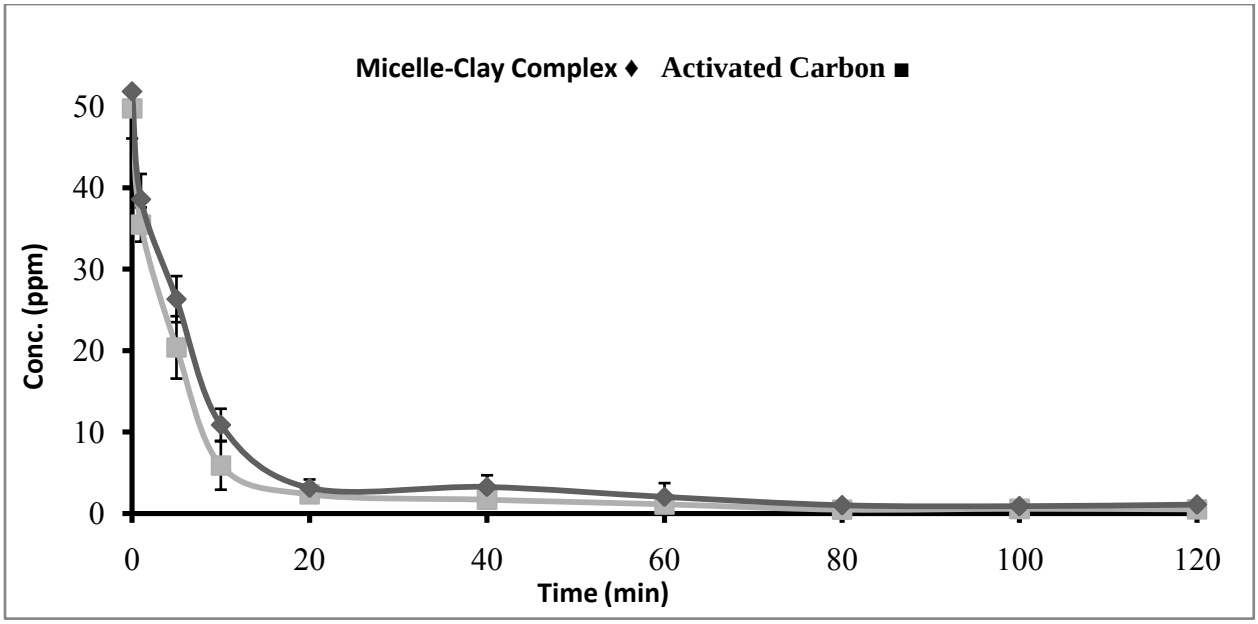

Figure 4.33: Kinetic adsorption of benzamide into the micelle-clay complex (♦) and activated carbon (■). Temp. = 25.0 ^{o}C, and adsorbent dosage = 5.0 g/L.

4.3.2.2 Adsorption Isotherm

Adsorption of benzamide was described by Langmuir adsorption isotherm as shown by the plot of $C_e\backslash Q_e$ versus C_e (Table 4.32 and Figure 4.34). The correlation coefficient values (R^2) obtained by the two adsorbents are summarized in Table4.31.The Q_{max} and K values determined for the removal of the benzamide using micelle-clay complex (Table 4.31) are 87.72 ± 10.60 mg/g and 0.04 ± 0.01 L/mg, respectively. The corresponding values in the case of activated carbon are Q_{max} = 93.46 ± 8.04 mg/g and K= 0.46 ± 0.07 L/mg. The Q_{max} for micelle-clay complex was smaller than that for the activated carbon, the affinity coefficient, k, for activated carbon was 11 fold larger than micelle-clay complex.

Table 4.31: Langmuir constant and correlation coefficient for the adsorption isotherm of benzamide into micelle-clay complex and activated carbon.

	Adsorbent	Q_{max} (mg/g)	K (L/mg)	R^2
Benzamide	Micelle-Clay Complex	87.72 ± 10.60	0.04 ±0.01	0.983
	Activated Carbon	93.46 ± 8.04	0.46 ± 0.07	0.996

Table 4.32: Langmuir isotherm parameter for adsorption of adsorbate benzamide into micelle-clay complex and activated carbon as adsorbent.

Micelle-Clay Complex		Activated Carbon	
C_e (mg/L)	C_e/Q_e (g/L)	C_e (mg/L)	C_e/Q_e (g/L)
0.45	0.24	0.01	0.004
2.79	0.29	0.23	0.02
8.29	0.45	0.59	0.03
36.28	0.85	4.65	0.09
130.47	1.77	48.79	0.54

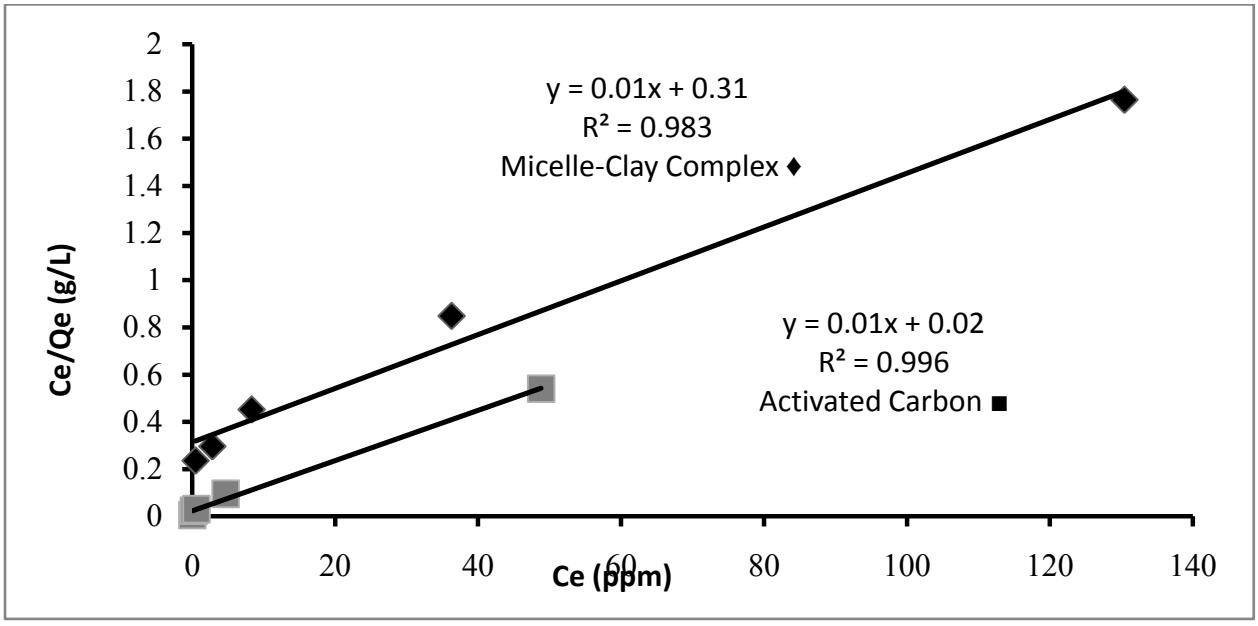

Figure 4.34: Plot of Langmuir isotherm for the adsorption of benzamide into the micelle-clay complex (♦) and activated carbon (■). Contact time = 2 h, Temp. = 25.0 ^{o}C, and adsorbent dosage = 5.0 g/L.

Adsorption of benzamide was described by plot log (Q_e) versus log (C_e) (Table 4.34). The correlation coefficient values (R^2) obtained by the two adsorbents are summarized in Table4.33.The fitted equilibrium data in Freundlich isotherm expression is shown in Figure 4.35. It is observed that the equilibrium data fitted very well in Freundlich expression with very high correlation coefficients, thus confirming the applicability of the isotherm. For using activated carbon a larger value of k indicates good adsorption efficiency, while a larger value of 1/n for micelle-clay complex indicates a larger change in effectiveness over different equilibrium concentrations.

Table 4.33: Freundlich constant and correlation coefficient for adsorption isotherm of benzamide into micelle-clay complex and activated carbon.

	Adsorbent	1/n	K	R^2
Benzamide	Micelle-Clay Complex	1.15 ± 0.88	43.21 ± 7.03	0.975
	Activated Carbon	0.64 ± 0.49	157.91 ± 14.51	0.891

Table 4.34: Freundlich isotherm parameter for adsorption of adsorbate benzamide into micelle-clay complex and activated carbon as adsorbent.

Micelle-Clay Complex		Activated Carbon	
log (Q_e)	log (C_e)	log (Q_e)	log (C_e)
0.28	-0.63	0.30	-2.32
0.98	-0.53	0.99	-1.63
1.26	-0.34	1.29	-1.53
1.63	-0.07	1.69	-1.02
1.87	0.25	1.96	-0.27

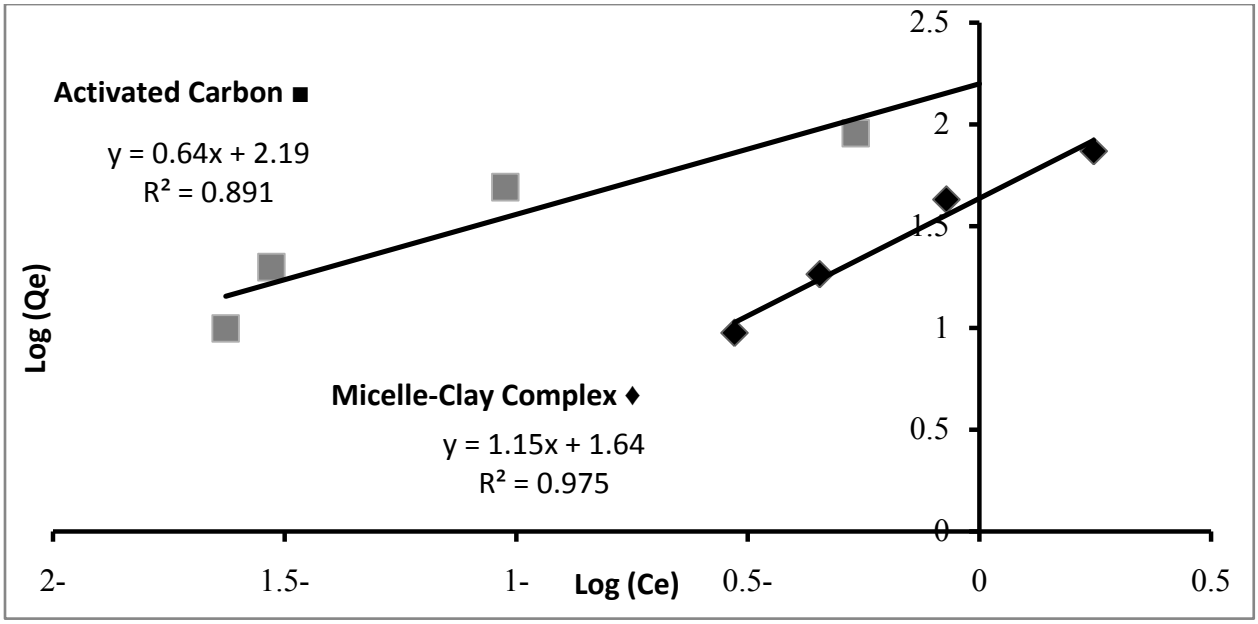

Figure 4.35: Plot of Freundlich isotherm for the adsorption of benzamide into the micelle-clay complex (♦) and activated carbon (■). Contact time = 2 h, Temp. = 25.0 ^{o}C and adsorbent dosage = 5.0 g/L.

4.3.3 Adsorption of bezafibrate

4.3.3.1 Kinetic adsorption.

Figure 4.36 shows a decrease in bezafibrate concentration with time using either micelle-clay complex or activated carbon. This reveals that activated carbon and micelle-clay complex are efficient for bezafibrate removal.

Table 4.35: Kinetic data for the removal of bezafibrate by micelle-clay complex and activated carbon.

Adsorbent	Micelle-Clay Complex	Activated Carbon
Time (minutes)	Concentration (ppm)	Concentration (ppm)
0	47.26 ± 2.25	48.61 ± 4.01
1	42.19 ± 3.07	38.03 ± 2.67
2	40.34 ± 3.91	29.91 ± 5.01
5	27.19 ± 2.14	17.81 ± 2.19
10	16.22 ± 1.44	7.26 ± 2.02
20	6.10 ± 0.79	3.79 ± 1.08
40	3.24 ± 1.01	1.42 ± 2.31
60	3.28 ± 0.97	1.58 ± 0.97
80	2.10 ± 1.09	1.55 ± 0.48
100	2.04 ±1.22	1.52 ± 1.9
120	2.10 ± 1.04	1.55 ± 1.68

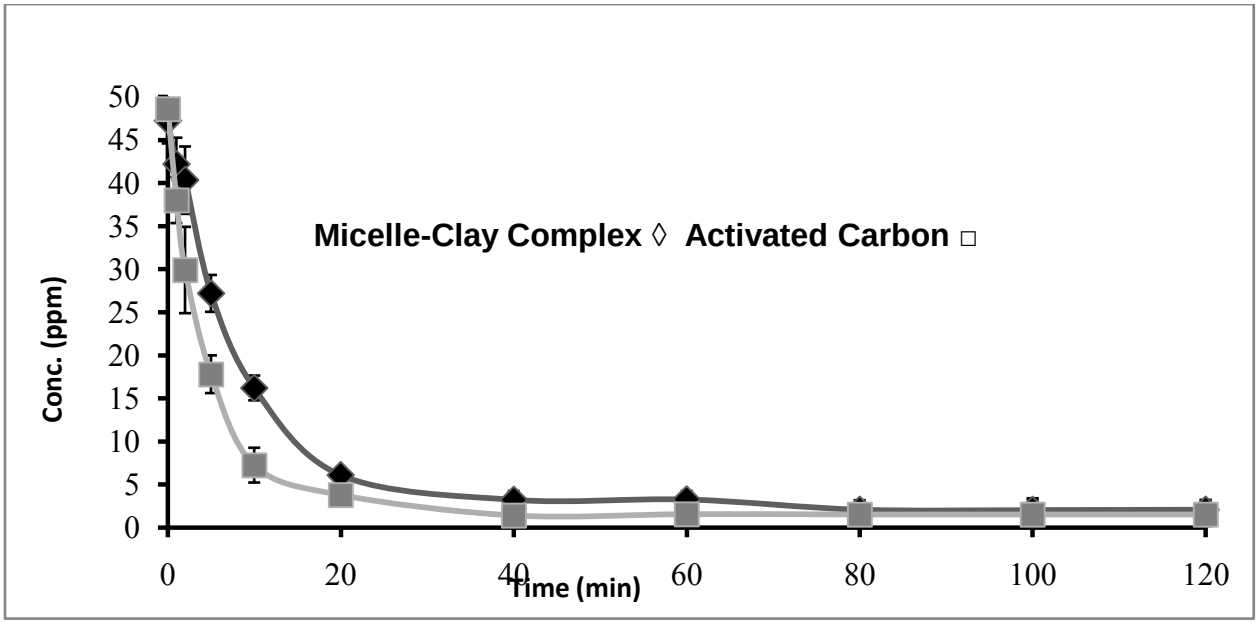

Figure 4.36: Kinetic adsorption of bezafibrate by the Micelle-Clay complex (♦) and activated carbon (■).Temp. = 25.0 ^{o}C, and adsorbent dosage = 5.0 g/L.

4.3.3.2 Adsorption Isotherm

Adsorption of bezafibrate was described by Langmuir adsorption isotherm as shown by the plot of $C_e\backslash Q_e$ versus C_e (Table 4.37 and Figure 4.37). The correlation coefficient values (R^2) obtained by the two adsorbents are summarized in Table4.36.The Q_{max} and K values determined for the removal of the bezafibrate using Micelle-Clay complex (Table 4.36) are88.49 ± 6.23mg/g and0.03 ±0.01L/mg, respectively,. The corresponding values in the case of activated carbon are Q_{max}= 82.64 ± 9.97mg/g and K = 0.12 ± 0.01L/mg. The Q_{max} for micelle-clay complex was higher than that for the activated carbon, the affinity coefficient, K, for activated carbon was 3 fold higher than for micelle-clay complex.

Table 4.36: Langmuir constant and correlation coefficient for adsorption isotherm of bezafibrate by micelle-clay complex and activated carbon.

	Adsorbent	Q_{max} (mg/g)	K (L/mg)	R^2
Bezafibrate	Micelle-Clay Complex	88.49 ± 6.23	0.03 ± 0.01	0.991
	Activated Carbon	82.64 ± 9.97	0.12 ± 0.01	0.973

Table 4.37: Langmuir isotherm parameter for adsorption of adsorbate bezafibrate into micelle-clay complex and activated carbon.

Micelle-Clay Complex		Activated Carbon	
C_e (mg/L)	C_e/Q_e (g/L)	C_e (mg/L)	C_e/Q_e (g/L)
0.60	0.32	0.10	0.05
3.72	0.40	0.69	0.07
6.95	0.37	1.89	0.09
36.85	0.86	25.96	0.58
134.12	1.83	105.79	1.34

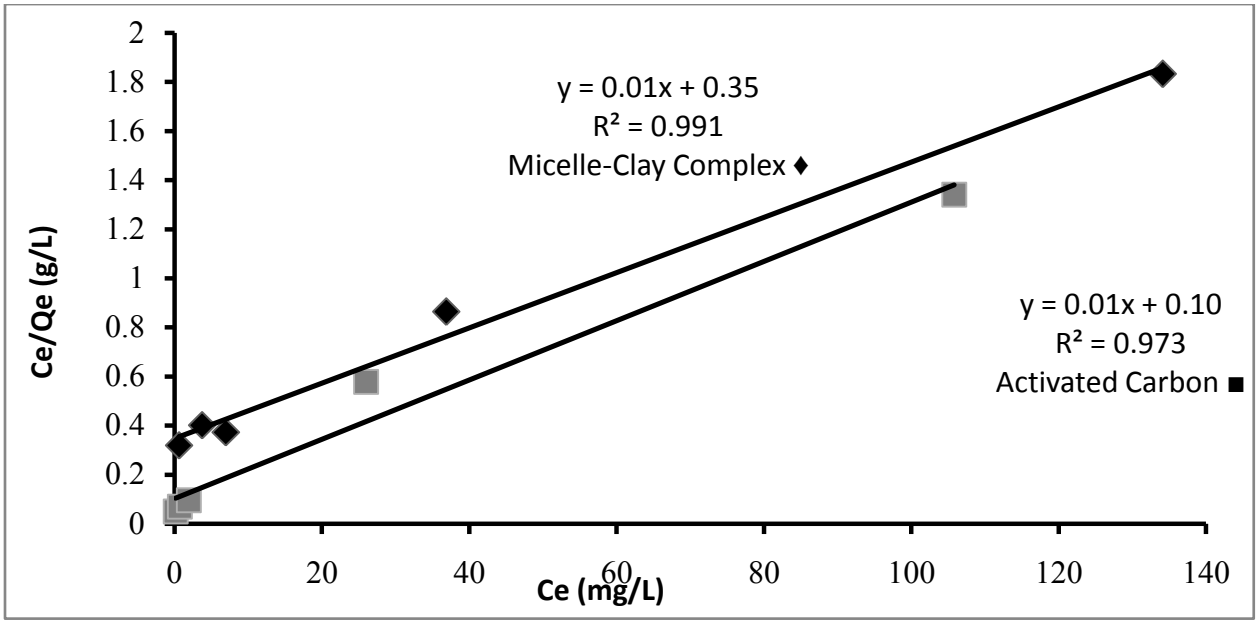

Figure 4.37: Plot of Langmuir isotherm for the adsorption of bezafibrate into the micelle-clay complex (♦) and activated carbon (■). Contact time = 2 h, Temp. = 25.0 ^{o}C, and adsorbent dosage = 5.0 g/L.

Adsorption of bezafibrate was described by plot log (Q_e) versus log (C_e) (Table 4.39). The correlation coefficient values (R^2) obtained by the two adsorbents are summarized in Table4.38. The fitted equilibrium data in Freundlich isotherm expression is shown in Figure 4.38. It is observed that the equilibrium data fitted very well in Freundlich expression with very high correlation coefficients, thus confirming the applicability of the isotherm. For using activated carbon a larger value of K indicates good adsorption efficiency, while a larger value of 1/n for micelle-clay complex indicates a larger change in effectiveness over different equilibrium concentrations.

Table 4.38: Freundlich constant and correlation coefficient for adsorption isotherm of bezafibrate into micelle-clay complex and activated carbon.

	Adsorbent	1/n	K	R^2
Bezafibrate	Micelle-Clay Complex	0.67 ± 0.07	3.49 ± 1.34	0.964
	Activated Carbon	0.50 ± 0.29	9.32 ± 1.91	0.947

Table 4.39: Freundlich isotherm parameter for adsorption of bezafibrate into micelle-clay complex and activated carbon.

Micelle-Clay Complex		Activated Carbon	
log (C_e)	log (Q_e)	log (C_e)	log (Q_e)
-0.22	0.27	-0.99	0.29
0.57	0.97	-0.16	0.99
0.84	1.27	0.28	1.29
1.57	1.63	1.41	1.65
2.13	1.86	2.02	1.89

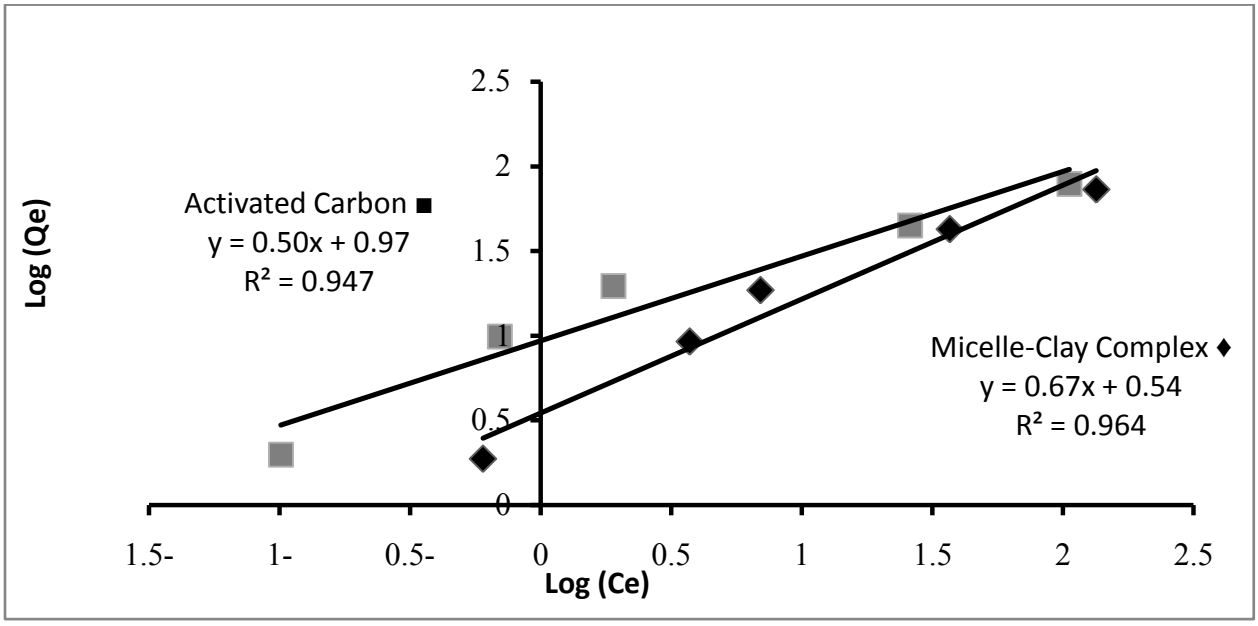

Figure 4.38: Plot of Freundlich isotherm for the adsorption of bezafibrate into the micelle-clay complex (♦) and activated carbon (■). Contact time = 2 h, Temp. = 25.0 ^{o}C and adsorbent dosage = 5.0 g/L.

4.3.4 Adsorption of Atenolol

4.3.4.1 Kinetic adsorption.

Figure 4.39 shows a decrease in atenolol concentration versus time using either micelle-clay complex or activated carbon. This reveals that both activate carbon and micelle-clay complex are efficient for atenolol removal.

Table 4.40: Kinetic data for the removal of atenolol into micelle-clay complex and activated carbon.

Adsorbent	Micelle-Clay Complex	Activated Carbon
Time (minutes)	Concentration (ppm)	Concentration (ppm)
0	49.23 ± 0.93	48.92 ± 1.04
1	47.84 ± 1.81	38.03 ± 2.94
2	42.72 ± 2.75	29.91 ± 2.07
5	36.73 ± 2.92	23.98 ± 3.78
10	20.62 ± 1.91	13.43 ± 2.91
20	9.82 ± 3.31	4.42 ± 2.55
40	7.35 ± 2.01	2.35 ± 3.74
60	3.12 ± 1.04	1.27 ± 0.92
80	2.81 ± 0.93	0.62 ± 0.02
100	2.69 ± 1.13	0.59 ± 0.93
120	3.12 ± 2.05	0.71 ± 0.07

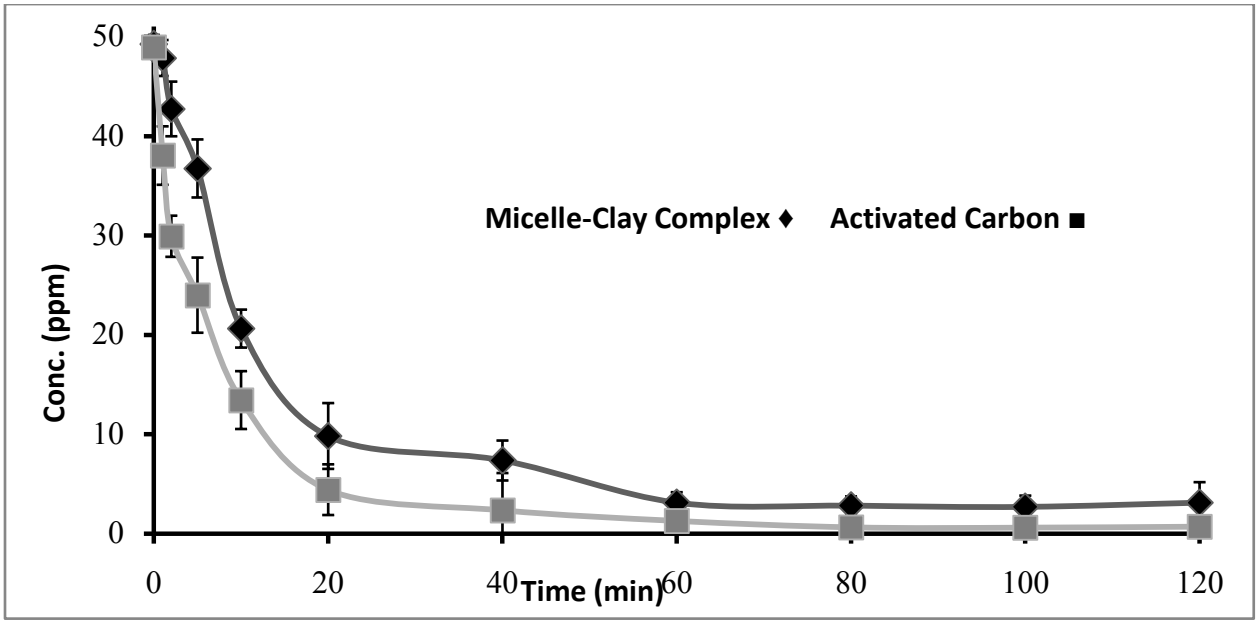

Figure 4.39: Kinetic adsorption of atenolol onto the micelle-clay complex (♦) and activated carbon (■). Temp. = 25.0 ^{o}C, and adsorbent dosage = 5.0 g/L.

4.3.4.2 Adsorption Isotherm

Adsorption of atenolol was described by Langmuir adsorption isotherm as shown by the plot of $C_e\backslash Q_e$ versus C_e (Table 4.42 and Figure 4.40). The correlation coefficient values (R^2) obtained by the two adsorbents are summarized in Table4.41.The Q_{max} and K values determined for the removal of the atenolol using micelle-clay complex(Table 4.41)are 91.74 ± 5.91 mg/g and 0.01±0.02 L/mg, respectively. The corresponding values in the case of activated carbon are Q_{max} = 75.76 ± 8.53 mg/g and K = 0.05 ± 0.01 L/mg. The Q_{max} for micelle-Clay complex was higher than that for the activated carbon, the affinity coefficient, K, for activated carbon was 5 fold higher than for micelle-clay complex.

Table 4.41: Langmuir constant and correlation coefficient for adsorption isotherm of atenolol onto micelle-clay complex and activated carbon.

	Adsorbent	Q_{max} (mg/g)	K (L/mg)	R^2
Atenolol	Micelle-Clay Complex	91.74 ± 5.91	0.01 ±0.02	0.971
	Activated Carbon	75.76 ± 8.53	0.05 ± 0.01	0.995

Table 4.42: Langmuir isotherm parameter for adsorption of adsorbate atenolol onto micelle-clay complex and activated carbon as adsorbent.

Micelle-Clay Complex		Activated Carbon	
C_e (mg/L)	C_e/Q_e (g/L)	C_e (mg/L)	C_e/Q_e (g/L)
2.34	1.53	0.38	0.19
12.87	1.73	2.59	0.27
30.44	2.19	8.16	0.44
77.12	2.23	34.04	0.79
224.27	4.07	160.81	2.37

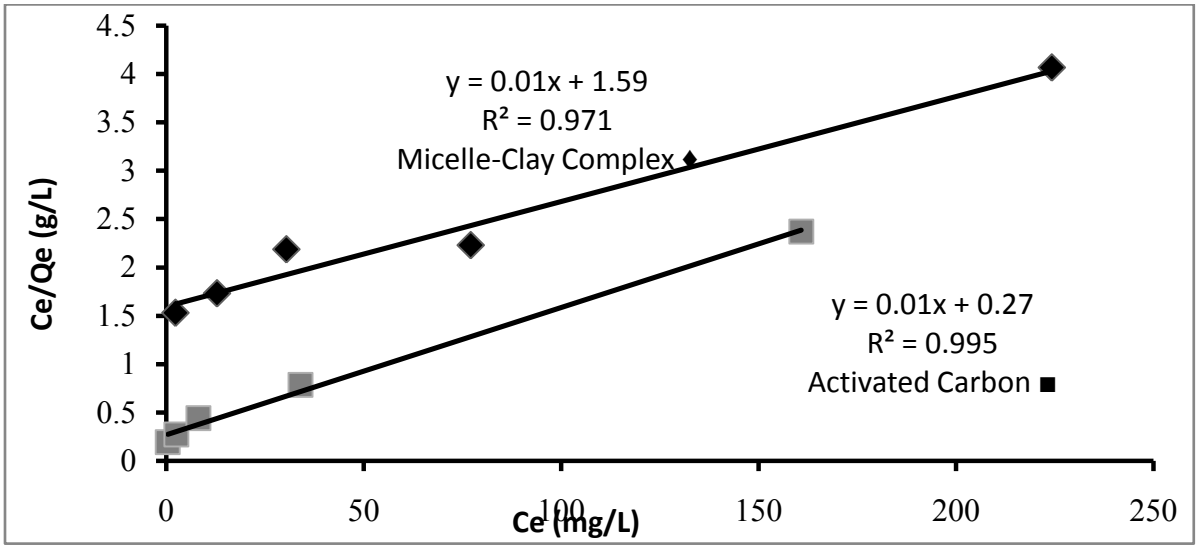

Figure 4.40: Plot of Langmuir isotherm for the adsorption of atenolol onto the micelle-clay complex (♦) and activated carbon (■). Contact time = 2 h, Temp. = 25.0 ^{o}C, and adsorbent dosage = 5.0 g/L.

Adsorption of atenolol is well described by plot log (Q_e) versus log (C_e) (Table 4.44). The correlation coefficient values (R^2) obtained by the two adsorbents are summarized in Table4.43. The fitted equilibrium data in Freundlich isotherm expression is shown in Figure 4.41. It is observed that the equilibrium data fitted very well in Freundlich expression with very high correlation coefficients, thus confirming the applicability of the isotherm. For using activated carbon a larger value of K indicates good adsorption efficiency, while a larger value of 1/n for micelle-clay complex indicates a larger change in effectiveness over different equilibrium concentrations.

Table 4.43: Freundlich constant and correlation coefficient for adsorption isotherm of atenolol into micelle-clay complex and activated carbon.

	Adsorbent	1/n	K	R^2
Atenolol	Micelle-Clay Complex	0.80 ± 0.19	0.87 ± 0.14	0.987
	Activated Carbon	0.59 ± 0.02	4.47 ± 1.09	0.968

Table 4.44: Freundlich isotherm parameter for adsorption of atenolol onto micelle-clay complex and activated carbon.

Micelle-Clay Complex		Activated Carbon	
log (C_e)	log (Q_e)	log (C_e)	log (Q_e)
0.37	0.18	-0.43	0.28
1.11	0.87	0.41	0.98
1.48	1.14	0.91	1.26
1.89	1.54	1.53	1.64
2.35	1.74	2.21	1.83

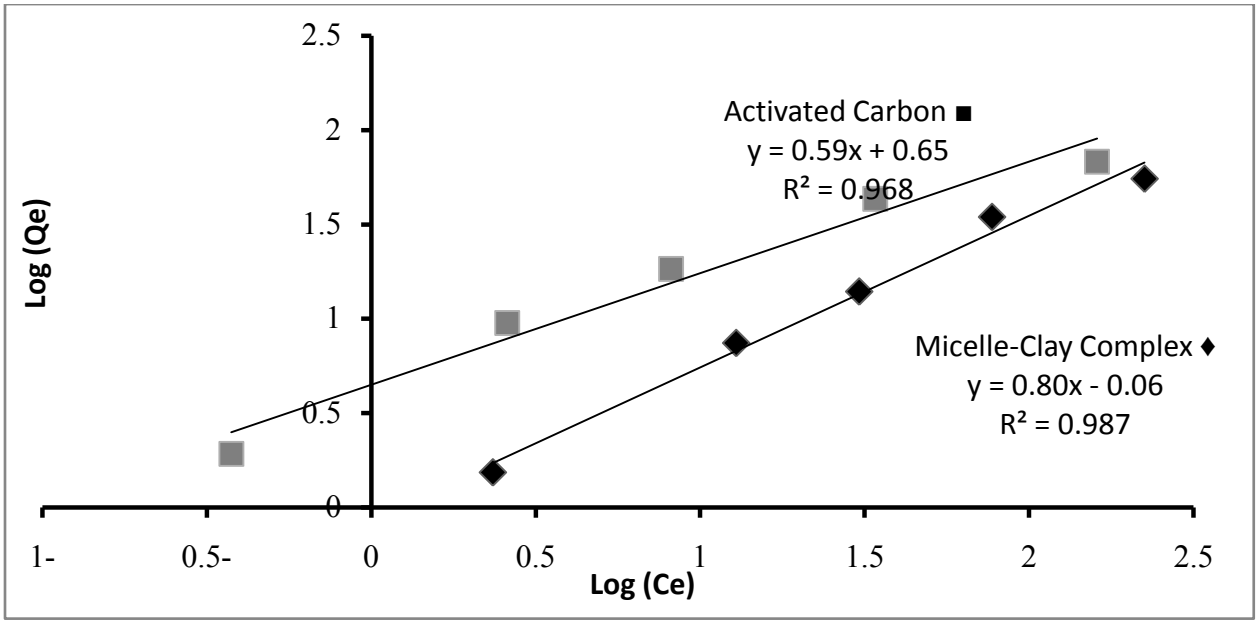

Figure 4.41: Plot of Freundlich isotherm for the adsorption of atenolol into the micelle-clay complex (♦) and activated carbon (■). Contact time = 2 h, Temp. = 25.0 ^{o}C and adsorbent dosage = 5.0 g/L.

Chapter Five

Conclusions and Recommendations

Chapter Five
Conclusions and Recommendations

5.1 Conclusions

The stability results for the selected pharmaceuticals (paracetamol, *p*-aminophenol and benzamide); in activated sludge wastewater and suspended *pseudomonas aeruginosa* (bacteria which was isolated from AQ-WWTP) demonstrate that the amide bond contained in these compounds is cleaved by enzymatic bacteria. The resulted metabolites were identify and characterized by 1H-NMR and LC-MS.

Biodegradation of paracetamol revealed the formation of *p*-aminophenol (metabolite-1) which underwent biodegradation to hydroquinone (metabolite-2). On the other hand, benzamide underwent biodegradation to benzoic acid as a final metabolite.

The ultrafiltration (hollow fiber and spiral wound membranes) used for the removal of selected pharmaceuticals (paracetamol, *p*-aminophenol, benzamide, bezafibrate and atenolol), has shown a removal of 40 – 80%, whereas, the activated carbon and reverse osmosis membranes were very efficient in removing these pharmaceuticals (~ 99.9%). Hence, we conclude that an activated carbon filter can be efficient in removing these pharmaceuticals without the need of expensive methods such as a reverse osmosis membrane.

The adsorption isotherms were found to fit Langmuir and Freundlich isotherms and the corresponding adsorption parameters were evaluated. The adsorption kinetics and parameters strongly suggest that integrating clay-micelle filters within Al-Quds wastewater treatment plant is a promising technology for an efficient removal of the studied pharmaceuticals (paracetamol, *p*-aminophenol, benzamide, bezafibrate and atenolol) and their degradation products.

5.2 Recommendations

Of the most important recommendations that should be taken into account are the following:

- ✓ Application of micelle clay complex filter in large scale waste water treatment plant.
- ✓ Increasing the public awareness toward the effect of pharmaceutical disposal on environment.

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دراسة ثباتية الادوية التي تحتوي على روابط اميدية في الحماة النشطة, كفائة تقنية الاغشية المتقدمة, الكربون النشط ومركب ميسل الصلصال المعقد في ازالة هذه الادوية

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الملخص:

اظهرة الدراسة الحركية لثباتية مسكن الآلام الباراسيتامول, البارأمينو فينول والبنزأميد انها خضعت للتحليل البيولوجي في الحمأة النشطة, حيث ان الباراسيتامول تحلل إلى بارأمينو فينول في اقل من شهر وبعوائد عالية, ايضا تحلل البارأمينو فينول والبنزأميد بأقل من اسبوع إلى هيدروكوينون وحامض البنزويك وبعوائد عالية, على التوالي. وبثابت معدل سرعة تفاعل التحلل (2.17×10^{-9}, 8.64×10^{-9}, 7.86×10^{-9} مولارية لكل ثانية). علاوة على ذلك, تم التحقق من اوصاف البكتيريا الموجودة في الحماة النشطة الخاصة بمحطة معالجة المياه العادمة في جامعة القدس, وقد تبين ان Pseudomonas aeruginosais هي المسؤولة عن تحلل الادوية الاميدية. ان اختلاف تركيز الباراسيتامول (100, 250, 500 جزء في المليون) لم يظهر اختلاف ملحوظ في ثابت معدل سرعة تفاعل التحلل (2.39×10^{-9}, 4.91×10^{-9}, 5.71×10^{-9} مولارية لكل ثانية), على التوالي. تبين من خلال هذه الدراسة مدى كفائة وحدات محطة معالجة المياه العادمة في جامعة القدس, في ازالة هذه المركبات ومنتجاتها وكانت النتائج على النحو التالي: Hollow Fiber Membrane لم تكن كافية في ازلة المركبات الصيدلانية ومنتجاتها, حيث لم تتجاوز نسبة الازالة 40% في حين اظهرة Spiral Wound Membrane بنسبة ازالة وصلت 80%, ويليها الذي اظهر Activated Carbon ازلة كاملة بنسبة 100% تقريباً.

نتائج دراسة كفائة Micelle-Clay Complex and Activated Carbon من خلال دفعه تجريبية مخبرية وبدرجة حرارة 25 مئوية, حيث اظهرة فعالية كبيرة في ازالة هذه المركبات ومنتجاتها, وقد طابقة بشكل كامل Langmuir and Freundlich Isotherms .