

An-Najah National University

Faculty of Graduate Studies

Adsorption of Some Fluoroquinolones on Selected Adsorbents

By

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the Degree of Master of Science in Chemistry, Faculty of Graduate
Studies, An - Najah National University, Nablus, Palestine.**

2010

S.M. Khalaf

DEDICATION

SUBMITTED WITH GRATEFUL RECOGNITION &
APPRECIATION TO MY GREAT MOTHER & MY
WONDERFUL FATHER,
TO MY BROTHERS, SISTERS & THEIR FAMILIES.

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TO MY BROTHERS, SISTERS & THEIR FAMILIES.

TO ALL TEACHERS IN MY ENTIRE LIFE.

TO MY BELOVED RASEEL.

TO MY FRIENDS.

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Respectfully yours

Areej Hattab

الإقرار

أنا الموقع أدناه مقدم الرسالة التي تحمل العنوان:

Adsorption of Some Fluoroquinolones on Selected Adsorbents

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Adsorption of Some Fluoroquinolones on Selected Adsorbents

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Abstract

The adsorption of some fluoroquinolones (antibiotics) such as: Gemifloxacin Mesylate and Levofloxacin Hemihydrate using selected adsorbents such as charcoal, kaolin, silica gel and alumina was carried out in terms of initial pH, residence time, initial concentration of drug (adsorbate), weight of adsorbent, temperature and affinity of the solute to the adsorbent. The adsorption was determined by measuring concentration of the drug both before and after the attainment of equilibrium, with the aid of UV-visible spectrophotometer. Gemifloxacin absorbs at 343nm and at 340nm, where Levofloxacin absorbs at 294nm and at 288nm, in acidic and basic pH respectively.

For equilibrium studies, two adsorption isotherms were used, Freundlich and Langmuir, the later fitted most data very well.

Maximum adsorption capacity for Gemifloxacin into charcoal was 137mg/g compared to 0.04 mg/g with kaolin. For Levofloxacin with charcoal was 87mg/g more than that with kaolin which was 0.26mg/g.

The amount adsorbed at equilibrium decreases as adsorbate's concentration increases and as the weight of adsorbent increases the amount of drug adsorbed increases.

pH played a significant role in the adsorption especially with silica and alumina. Maximum amount of Gemifloxacin adsorbed onto silica occurred at pH=7 and with alumina at pH=6 respectively. With charcoal adsorption of GEMX was more in the acidic medium than in basic and the maximum adsorption was at pH=6 and at neutral pH for kaolin. LEVX adsorption with charcoal and kaolin was at about pH=7 and was in acidic pH more than basic pH.

Thermodynamics parameters showed that adsorption process was exothermic and spontaneous as ΔG° and ΔH° had negative values, ΔS° was positive.

CHAPTER ONE

INTRODUCTION

1. INTRODUCTION

1.1 Fluoroquinolones Overview

Fluoroquinolones are synthetic broad-spectrum antibiotics, subset from the major family (Quinolones). They form a precious and unique group among the present bactericidal drugs used in both hospital, community sectors and veterinary medicine. They have made a major influence on the field of antimicrobial chemotherapy with the introduction of several new quinolones having improved properties particularly in recent years.^[1]

Fluoroquinolones have many privileges that enabled them to share the attributes of an ideal antibiotic. They possess excellent activity against a wide range of both Gram-positive and Gram-negative bacteria, high potency, good bioavailability, oral and intravenous formulations, a large volume of distribution and a low binding to plasma proteins that allows them to cross membranes and reach the most remote parts of the body at concentrations above the minimum inhibitory concentrations (MIC's) of most pathogens and a low incidence of side-effects.^[2]

In 1934 Hans Andersag discovered chloroquine (4-aminoquinoline drug); used in treatment and prevention of malaria.^[3]

Later in 1962 George Leshner and coworkers discovered Nalidixic acid (1, 8- naphthyridine derivative) in a distillate during an attempt at chloroquine research and purification. Nalidixic acid possessed an antibacterial activity.^[3]

1.1.1 Generation and Development of Quinolones

Nalidixic acid is the parent of quinolones, its introduction for clinical use in 1967 marks the beginning of quinolone development and use, it has possessed important efficiency in the treatment of bacterial infection but its usage was limited to the treatment of Gram-negative urinary tract infections (UTIs).^[4]

Modification in the naphthyridone nucleus of nalidixic acid as shown in (Fig.1.1) to produce a series of more active compounds: including oxolinic acid (Fig.1.2), pipemidic acid (Fig.1.3) and cinoxacin (Fig.1.4).^[5]

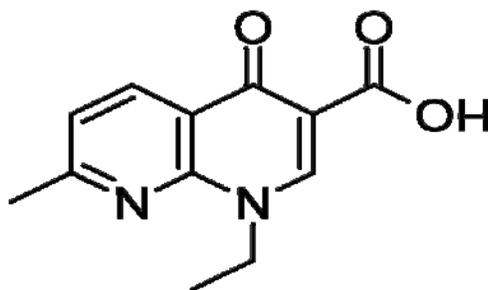


Figure 1.1: Chemical Structure of Nalidixic Acid

(1-ethyl-7-methyl-4-oxo- [1, 8] naphthyridine-3-carboxylic acid)

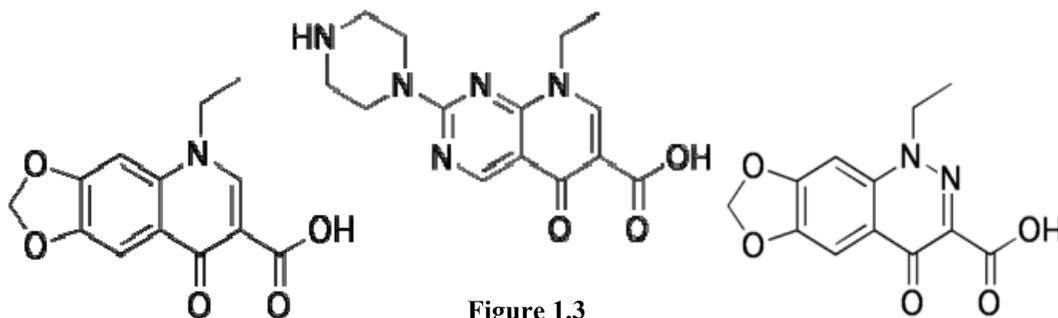


Figure 1.2

Figure 1.2: Chemical Structure of Oxolinic Acid.

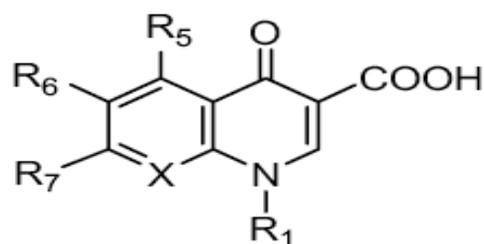
Figure 1.3: Chemical Structure of Pipemidic Acid.

Figure 1.4

Figure 1.4: Chemical Structure of Cinoxacin.

The structure of quinolones as shown in (Fig.1.5) has been developed along two pathways:

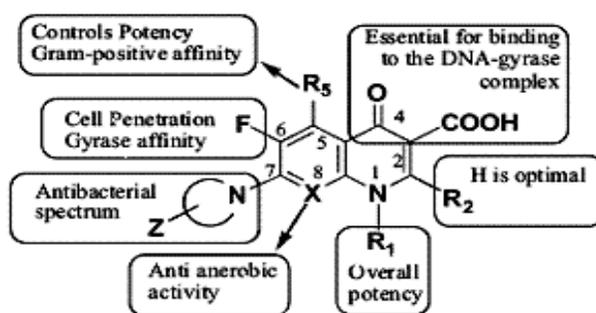
- 1- Naphthyridones: with the original naphthyridine core of nalidixic acid identified by a nitrogen atom at position 8 (X=N).
- 2- Fluoroquinolones: in which a carbon atom at position 8 (X=C) instead of nitrogen of the naphthyridine nucleus and with a fluorine atom at position 6. [6]



quinolones: X = CH or C-R₈
 naphthyridones: X = N

Figure 1. 5: Common Structure of 4-Quinolones

Each site in the fluoroquinolone (Fig.1.6) plays a role in the activity and potency. [5]



R₁= Et, cyclopropyl, halo substituted aromatic ring , etc.
 R₂= H, -SMe, or R₁& R₂ may join to form a ring.
 R₅= H, -NH₂ , -OMe
 X= N, CH, CF, C-OMe, or X & R₁ may join to form a ring.
 Z= attached group to cycloalkylamine ring.

Figure 1.6: Common Structural Features of Quinolones

Flumequine (Fig.1.7) was the first fluoroquinolone be developed in 1976, but stopped to be used after reporting its ocular toxicity.^[7]

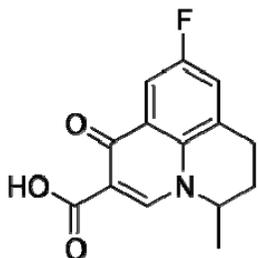


Figure 1.7: Chemical Structure of Flumequine

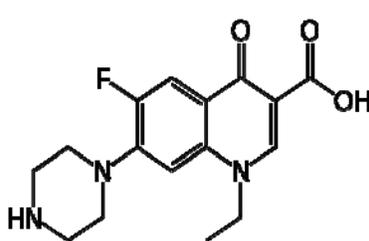


Figure 1.8: Chemical Structure of Norfloxacin

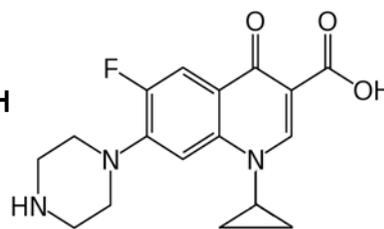


Figure 1.9: Chemical Structure of Ciprofloxacin

In 1978 norfloxacin (Fig.1.8) was developed with a 6-fluorinated quinolone and a piperazinyl side-chain at position 7. Later, during the 1980s, a great number of fluoroquinolones were developed and the best one was ciprofloxacin (Fig.1.9); an agent that has a wider spectrum of antibacterial activity and effective in the treatment of many types of infections especially respiratory infections. In particular, against Gram-negative bacteria, but not against Gram-positive bacteria or anaerobes, that made increasing the activity against Gram-positive pathogens the goal in fluoroquinolone development during the last few years, so newer agents were developed. Moxifloxacin is the most recent and most potent fluoroquinolones.^[6]

Naphthyridone derivatives emerged in parallel with the moxifloxacin lineage, enoxacin and tosufloxacin were the first naphthyridones and gemifloxacin is the most recent.^[6]

Quinolones can be classified into four generations based on their antimicrobial activity development with time, as shown in (Table 1.1).^[8]

Table 1.1: Development of Quinolones' Generations

	1970	1980	1990	2000
PARENT	FIRST	SECOND	THIRD	FOURTH
Nalidixic Acid	Cinoxacin Oxolinic Acid Piromidic Acid Pipemidic Acid Rosoxacin Flumequine	Norfloxacin	Sparofloxacin	Trovafloracin Clinafloracin Gemifloracin
		Fleroxacin	Grepafloxacin	
		Ciprofloxacin	Gatifloxacin	
		Enoxacin	Moxifloxacin	
		Lomefloxacin	Balofloxacin	
		Ofloxacin	Levofloxacin	
		Nadifloxacin	Pazufloxacin	
		Pefloxacin	Temafloxacin	
		Rufloxacin	Tosufloxacin	

1.1.2 Therapeutic Indications for Quinolone Antibiotics

Fluoroquinolones are used in human medicine against a variety of bacterial diseases and are indicated in the treatment of local and systemic diseases caused by a wide range of Gram-positive and Gram-negative bacteria, mycoplasma and chlamydia or resistant to other antibiotics. Physicians prescribe these drugs in uncomplicated and complicated urinary tract infections, pyelonephritis, skin and skin-structure infections, urethral and cervical chlamydial and gonococcal infections, bone and joint infections, infectious diarrhea, typhoid fever, inflammation of the prostate

(prostatitis), serious ear infections, acute sinusitis, acute purulent exacerbations of chronic bronchitis, lower respiratory tract infections, community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), intra-abdominal infections, gynecologic and pelvic infections, nosocomial pneumonia (NP), otitis externa, ophthalmitis, some sexually transmitted diseases (STDs), tuberculosis and some infections that affect people with acquired immunodeficiency syndrome (AIDS). Some fluoroquinolones have been used before surgery for prophylaxis (prevention of infection), and some have been studied for their usefulness in eye surgery and surgery of the biliary tract. ^[9, 10]

The Health Protection Agency in United Kingdom recommends ciprofloxacin in treatment for respiratory and gastrointestinal anthrax and currently for prophylaxis of anthrax infection caused by *Bacillus anthracis*, but gatifloxacin appeared to be more effective than moxifloxacin or ciprofloxacin at similar doses for early post-exposure treatment of murine systemic anthrax. ^[11]

Recently, fluoroquinolones are concerned as a class of antimicrobial drugs, which is widely used in veterinary medicine: enrofloxacin; marbofloxacin; norfloxacin nicotinate; difloxacin and danofloxacin have been used in dogs for complicated and uncomplicated urinary tract infections, mycobacterial infections, prostatitis and osteomyelitis. ^[12]

In swine fluoroquinolones are used to treat swine colibacillosis and in poultry for colibacillosis, poultry mycoplasmosis and other poultry

bacterial and mycobacterial diseases and for treating pneumonia and diarrhea in cattle and swine. [12]

1.1.3 Mechanism of Action

Fluoroquinolones block bacterial DNA synthesis as shown in (Fig.1.10) by binding and inhibiting the activity of two related but distinct targets within the bacterial cell: one enzyme is DNA gyrase (Type II topoisomerase); is the target for many Gram-negative bacteria and the other enzyme is topoisomerase IV; is the target for many Gram-positive bacteria. The block results in preventing of replication and transcription, thereby rapid bacterial death. [13, 14]

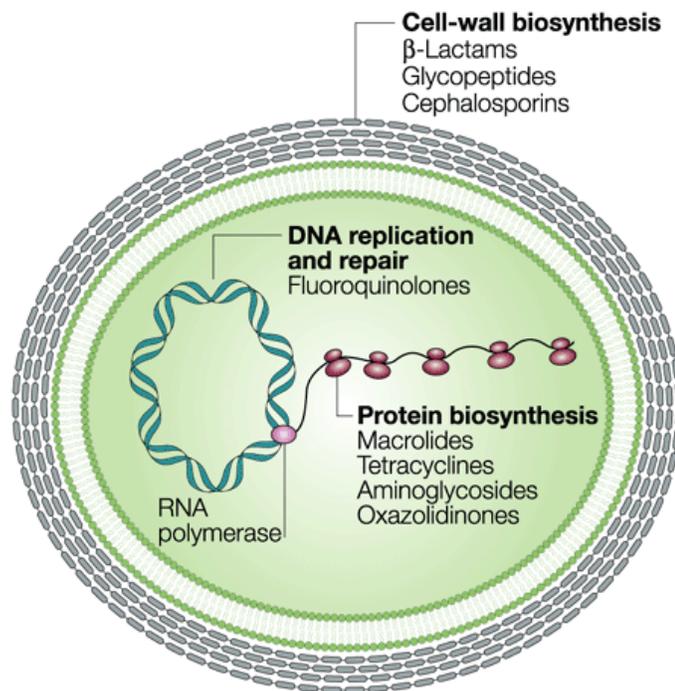


Figure 1.10: Scheme of Fluoroquinolone Target within Bacteria. [14]

1.1.4 Side Effects of Fluoroquinolones

Fluoroquinolones are generally safe and well-tolerated antibiotics, which may cause mild but not life-threatening adverse effects; generally related to the gastro intestinal disturbances such as: vomiting, diarrhea and abdominal pain. Disturbances of Central Nervous System (CNS) are also common, these symptoms include dizziness, headache, drowsiness, and less common are restlessness, depression, somnolence or insomnia, sleep disorders, agitation and vision changes may be seen, if the patients have predisposing factors such as seizure disorder, head trauma, anoxia and metabolic disturbances or concomitant therapy with specific interacting drugs (theophylline, nonsteroidal anti-inflammatory drugs (NSAIDs)).^[15, 16]

Fluoroquinolones have been reported to be phototoxic, so caution must be taken from direct and indirect exposure to sunlight during the therapy period. The symptoms of phototoxicity range from mild erythema of sun-exposed areas to severe bullous eruptions.^[15, 16]

Fluoroquinolones have a hepatic side effect: they may cause liver enzyme abnormalities in 2-3% of patients who receive them, but usually mild and reversible when the drug is discontinued.^[15, 16]

Arthropathy occurred within the first few days of therapy with these agents in approximately 1% of patients especially younger than 30 years but the symptoms resolve within days to weeks after discontinuing the drug, the signs of arthropathy may be joint pain, stiffness and swelling weight-bearing joints particularly knees.^[15, 16]

Recently, the possibility of tendinitis and tendon rupture when receiving fluoroquinolones are taken in consideration. Prolongation of the electro-cardiograph (ECG)-derived corrected QT (QTc) interval may occur within fluoroquinolones therapy. Immunologically: 0.6-1.4% of patients showed hypersensitivity reactions to fluoroquinolones. ^[15, 16]

1.1.5 Drug Interactions

Fluoroquinolones form insoluble chelation complexes in the gastrointestinal tract if taking them with drugs containing metals (e.g. antacids containing aluminum, calcium or magnesium salts, dietary supplements containing iron), which will inhibit drug absorption. ^[17]

Chelation is more with aluminum and magnesium-containing products than with products containing calcium, iron or zinc. However, the resulting decrease in fluoroquinolone absorption with all of these products increases the possibility of therapeutic failure, so an interval of two hours before or two to six hours after these medications must be when taking fluoroquinolones. ^[17]

Some quinolones slowing theophylline metabolism and some interacts with warfarin causing greater anticoagulant effect.

Fluoroquinolones especially grepafloxacin and sparfloxacin are contraindicated with antidepressants, antiarrhythmics or other drugs prolonging the QTc interval. ^[17]

1.1.6 Gemifloxacin Mesylate

1.1.6.a Chemical Name of Gemifloxacin Mesylate (IUPAC Name)

The chemical name of Gemifloxacin mesylate is (R, S)-7-(3-amino methyl-4-syn-methoxyimino-1-pyrrolidinyl)-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridone-3-carboxylic acid methanesulfonate.^[18]

1.1.6.b Molecular Formula and Weight of Gemifloxacin Mesylate

Gemifloxacin, a compound related to the fluoroquinolone class of antibiotics, is available as the mesylate salt in the sesquihydrate form. Gemifloxacin mesylate is a white to light brown solid with a formula of $(C_{19}H_{24}FN_5O_7S)$ and M. wt. = 485.49 g/mol.^[19]

1.1.6.c Chemical Structure of Gemifloxacin Mesylate

Gemifloxacin is a synthetic fluoronaphthyridine antibiotic. The structure is shown in (Fig.1.11).^[20]

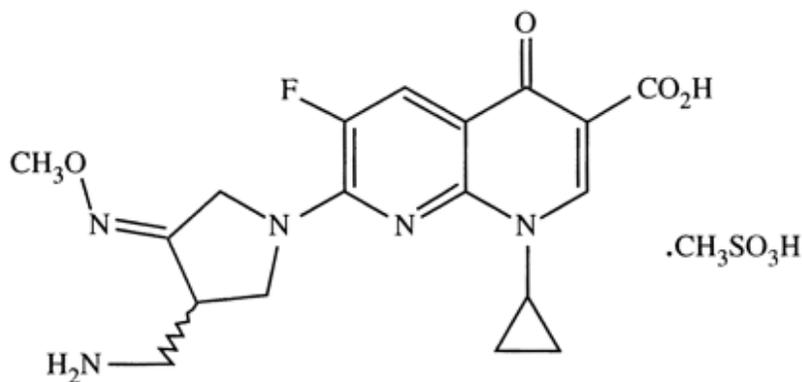


Figure 1.11: Chemical Structure of Gemifloxacin Mesylate

1.1.6.d Clinical Use of Gemifloxacin Mesylate

Gemifloxacin (SB-265805; LB-20304) is a new fluoroquinolone, was approved in April 2003 by the Food and Drug Administration (FDA) for the treatment of mild to moderate community acquired pneumonia. Gemifloxacin noticeably potent, highly efficient and low resistant bactericidal agent compared to the currently marketed quinolones. [21, 22, 23]

According to standards reference methods of the National Committee for Clinical Laboratory, gemifloxacin when compared with ciprofloxacin, levofloxacin, ofloxacin, sparfloxacin and trovafloxacin against over 800 pathogens most from blood stream infections; was the most active agent against Gram-positive species including strains observed to be resistant to other fluoroquinolones [multidrug-resistant strains (MDRSP)], as Staphylococci (Staphylococcus aureus and Staphylococcus epidermidis), Escherichia coli and Pseudomonas aeruginosa, Enterobacteriaceae, Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, Mycoplasma pneumoniae, Chlamydia pneumoniae, Klebsiella pneumoniae and acute bacterial exacerbations of chronic bronchitis (ABECB) due to S. pneumoniae, H. influenzae, Haemophilus parainfluenzae and M. catarrhalis. [21, 22, 23]

Animal studies suggest that LB20304 may be safer and less epileptogenic than ciprofloxacin. Gemifloxacin has been reported to be safe and the only side effect was rash. [21, 22, 23]

1.1.7 Levofloxacin Hemihydrate

A synthetic broad-spectrum antibacterial agent for oral and intravenous administration. Chemically, Levofloxacin is chiral fluorinated carboxyquinolone and it is the pure (-) - (S) - enantiomer of the racemic drug substance ofloxacin. [24]

1.1.7.a Chemical Name of Levofloxacin Hemihydrate (IUPAC Name)

Chemically Levofloxacin Hemihydrate is (-) - (S) -9- fluoro-2,3-dihydro -3- methyl -10- (4-methyl-1-piperazinyl) -7- oxo-7H-pyrido[1,2,3-de]-1,4 benzoxazine-6-carboxylic acid hemihydrate. [24]

1.1.7.b Molecular Formula & Weight of Levofloxacin Hemihydrate

Levofloxacin Hemihydrate is a light yellowish - white to yellow-white crystal or crystalline powder, exists as a zwitterion at the pH conditions in the small intestine. The molecular formula is $C_{18}H_{20}FN_3O_4 \cdot \frac{1}{2} H_2O$ and its molecular weight is 370.38 g/mol. [25]

1.1.7.c Chemical Structure of Levofloxacin Hemihydrate

The structure of levofloxacin Hemihydrate is shown in (Fig.1.12). [25]

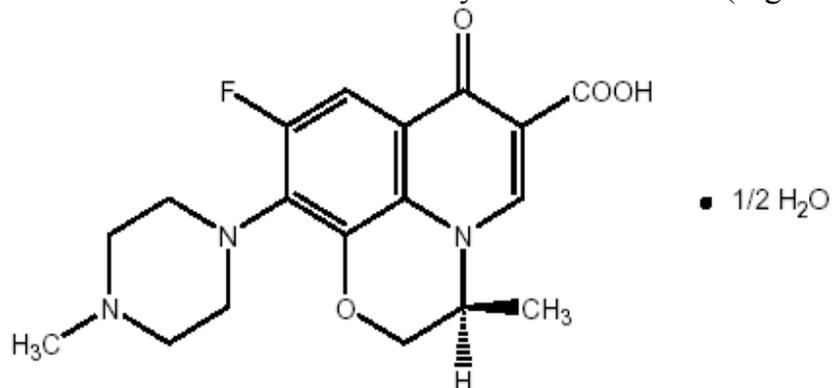


Figure 1.12: Chemical Structure of Levofloxacin Hemihydrate

1.1.7.d Therapeutic Indication of Levofloxacin Hemihydrate

Levofloxacin hemihydrate is indicated for inhalational anthrax (post-exposure) to reduce the incidence or progression of disease following exposure to aerosolized *Bacillus anthracis*, and used for the treatment of infections of the respiratory and urinary tract, skin and soft tissues. ^[26]

Levofloxacin can be the drug of choice to treat typhoid fever due to *S. typhi* because of its double features of high efficacy and lower rate of adverse reactions compared with ciprofloxacin. ^[27]

A developed product of levofloxacin hemihydrate for inhalation is currently used for the treatment of lung infections in patients with cystic fibrosis. ^[28]

Levofloxacin is effective against *Helicobacter pylori* (*H. pylori*) infection that is considered the main cause of gastritis, gastro duodenal ulcer disease and gastric cancer. ^[29]

1.2 Adsorption

1.2.1 Adsorption Process Background

The adsorption phenomena has a long history and was known in ancient times, when Scheele in 1773 and Fonata in 1777 published the first document reported some quantitative experiments of adsorption behavior of gases on charcoal, then in 1814 N.T. Saussure did many experiments onto charcoal and was the first to pay attention to systematic adsorption, the apparatus of adsorption he discovered is shown now in the exhibition of National Historical Museum in England. Chappuis studied adsorption of ammonia on charcoal at constant temperature. Bois-Reymond suggested the adsorption term and Kayser in 1881 presented the term adsorption into literature and other basic concepts in adsorption theory such as isotherm. ^[30]

1.2.2 Adsorption Process Definition

Adsorption is a surface phenomenon by which accumulation or concentration of the molecules of gas, vapor and liquid spontaneously at a contacting surface with or without undergoing chemical reaction, thereby forming a surface or interface. ^[30]

The adsorbate is the mobile molecules bound on the adsorbent surface molecules of the bulk phase at the surface being in the adsorbed state, the adsorptive is the adjacent bulk gas or liquid phase capable of being adsorbed, the localized (nonmobile) solid material is termed the adsorbent. Adsorbent has the adsorbing capacity; the whole process is called adsorption as shown in (Fig.1.13). ^[30, 32]

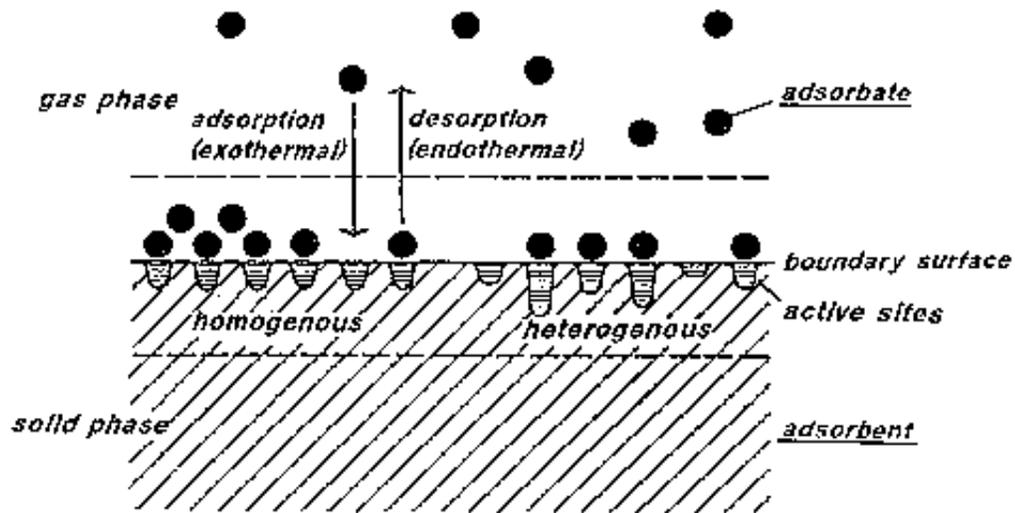


Figure 1.13: Fundamentals of Adsorption

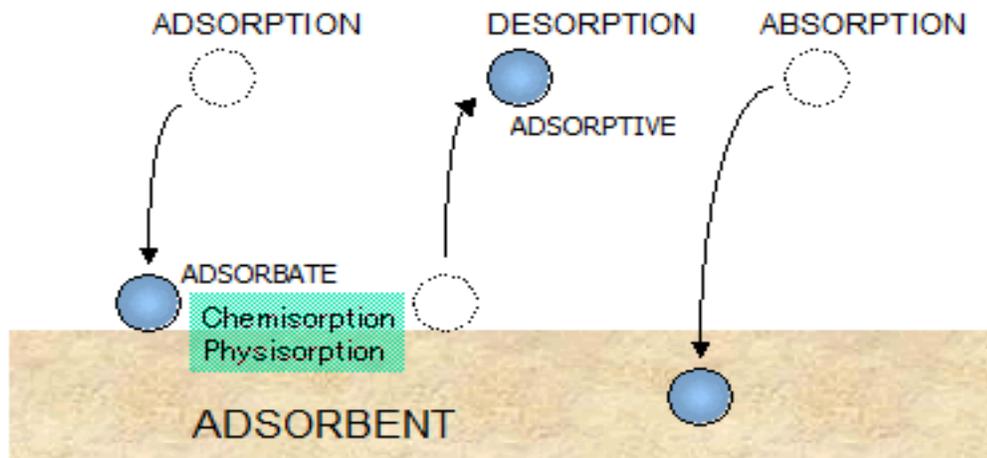


Figure 1.14: Fundamentals of Adsorption and Desorption

Desorption is a phenomenon whereby a substance is released from or through a surface, the process is the opposite of sorption as shown in (Fig.1.14). Sorption refers to adsorption and absorption together, where the molecules of a substance move from one phase to be accumulated in another phase. ^[30, 31]

1.2.3 Difference between Absorption and Adsorption.

Absorption is a physical or chemical process in which the molecules of one phase are uniformly interpenetrated among those of the other some bulk phase: gas, liquid or solid material to form a solution. However, in adsorption molecules of one phase are present at the surface of the second phase; the difference is illustrated in (Fig.1.15).^[33]

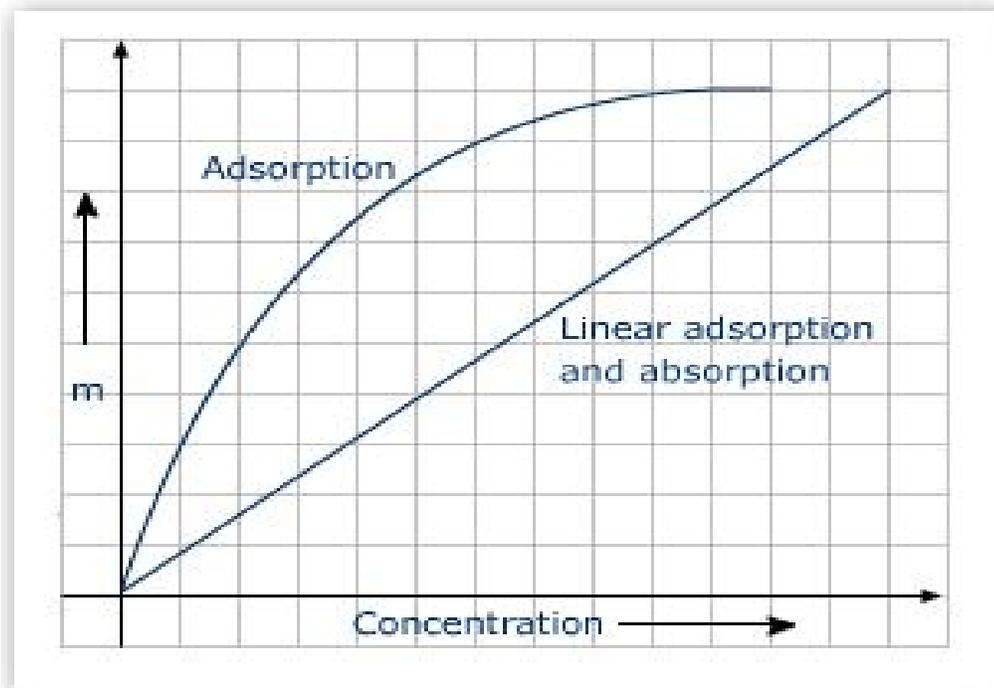


Figure 1.15: Difference between Absorption and Adsorption

m : Amount of substance moving across the interface between two phases (liquid and solid) versus concentration of the substance (solute). In adsorption amount adsorbs rapidly and slows down near equilibrium, while in absorption the amount moves at uniform rate.^[33]

1.2.4 Mechanism of Adsorption

Adsorption imbalances surface free energy that causes tension force at the surface of adsorbent. Atoms on the surface of the adsorbent are not wholly surrounded by other adsorbent hold molecules atoms and therefore can attract and of contacting adsorbate. The exact nature of the bonding depends on the details of the species involved, but the adsorption process is generally classified as physical adsorption (physisorption): a weak interaction mainly due to Van der Waals forces or chemical adsorption (chemisorption): interaction between the adsorbate and adsorbent's surface is strong characterized by electronic bonds (e.g. ionic or covalent).^[30]

1.2.5 Adsorption Isotherms

Adsorption isotherms or known as equilibrium data are the fundamental concept in adsorption science that is the correct explanation of experimental adsorption in mathematical equations or functions.^[34]

Isotherm's parameters express the surface properties and affinity of the adsorbent at known temperature and pH. The most frequently isotherms used in describing the non-linear equilibrium are: Langmuir isotherm, Freundlich isotherm and Brunauer Emmett and Teller (BET) isotherm.^[34]

1.2.5.1 Langmuir Isotherm

In 1916, Irving Langmuir was the first to develop a theoretical isotherm to describe the reaction between adsorbed gases above a solid surface at a fixed temperature; he was awarded Nobel Prize in chemistry for his work. ^[30]

Assumptions of Langmuir Model:

- 1- Monolayer adsorption: at maximum adsorption each site of free surface adsorbent can be occupied only by one adsorbate molecule, no deposition of adsorbate. ^[31, 35]
- 2- Identical adsorbent surface: adsorbent has a uniform surface and all sites are energetically equivalent, so adsorption occurs through the same mechanism. ^[31, 35]
- 3- Adsorption is localized: when a molecule adsorbed at a given site it is independent on the occupation of neighbouring sites, no movement of the adsorbate on the surface of adsorbent, but molecule can be desorbed to solution (a reversible process). ^[31, 35]
- 4- ΔH_{ads} is independent of surface coverage: enthalpy of adsorption is the same for all molecules whatever the molecules being adsorbed. ^[35, 37]

Langmuir Isotherm Expression

For adsorption of solute from a liquid, Langmuir isotherm is expressed in a plot of function at constant temperature. ^[34]

$$y_e = X / m = f * C_e \dots \dots \dots \text{(eqn.1)}$$

y_e : Equilibrium concentration of adsorbate onto adsorbent (mg/g, mol/g).

X: Mass of adsorbate in solution (moles, mg).

$$X = [C_o - C_t] * V$$

C_o : Initial concentration of adsorbate (mol/L, mg/L).

C_t : Concentration of adsorbate at time t (mol/L, mg/L).

V: Volume of adsorbate solution used (L).

M: Weight of adsorbent (mg, g).

C_e : Equilibrium concentration of adsorbate ($C_e = C_t$ t: time of equilibrium)

At equilibrium: Rate of Adsorption = Rate of Desorption

$$K_1 C_e (y_{\max} - y_e) = K_2 y_e \dots \dots \dots \text{(eqn.2)}$$

The previous equation can be rewritten as:

$$y_e = \frac{y_{\max} K_1 C_e}{K_2 + K_1 C_e} \dots \dots \dots \text{(eqn.3)}$$

With the substitution $K_A = K_1 / K_2$, the expression becomes

$$y_e = \frac{y_{\max} K_A C_e}{1 + K_A C_e} \dots \dots \dots \text{(eqn.4)}$$

y_{\max} : Constant (maximum adsorbable value of y required for monolayer adsorption (maximum capacity).

K_A : Langmuir Constant (function of enthalpy of adsorption and temperature).

For linearization of previous equation it can be rearranged to the form

$$\frac{C_e}{y_e} = \frac{1}{K_A y_{\max}} + \frac{1}{y_{\max}} C_e \quad \dots\dots\dots (\text{eqn.5})$$

or:

$$\frac{1}{y_e} = \frac{1}{y_{\max}} + \left[\frac{1}{K_A y_{\max}} \right] \cdot \frac{1}{C_e} \quad \dots\dots\dots (\text{eqn.6})$$

Using experimental data to plot any of these equations should yield a straight line, value of K_A and y_{\max} can be obtained from the slope and intercept, respectively a large value of K_A implies strong bonding of adsorbate to adsorbent at determined temperature. ^[35, 36]

The Effect of Isotherm Shape

The favourable nature of adsorption process can be expressed by a dimensionless separation factor called equilibrium parameter (R_L) as defined in (eqn.7). ^[38]

$$R_L = \frac{1}{1 + K_A C_0} \quad \dots\dots\dots (\text{eqn.7}).$$

K_A : Langmuir constant.

C_0 : Initial concentration of adsorbate in solution (g/L).

The Value of separation factor (R_L) illustrates the type of isotherm as appeared in (Table 1.2). ^[38]

Table 1.2: Type of Isotherm According to Value of (R_L)

Value of R_L	Type of Isotherm
$0 < R_L < 1$	Favourable
$R_L > 1$	Unfavourable
$R_L = 1$	Linear
$R_L = 0$	Irreversible

1.2.5.2 Freundlich Isotherm

In 1914, Freundlich popularized and justified theoretically his isotherm, so known with his name, although McBain in 1888 and Van Bemmelen and Boedecker in 1895 proposed its empirical formula. [30]

Freundlich equation (eqn.8) is widely used in mathematical description of adsorption in aqueous systems for heterogeneous surface.

The Freundlich isotherm is given by plotting the concentration of solute on the surface of an adsorbent versus the concentration of the solute in the liquid. [37]

$$y_e = X/m = K_F C_e^{1/n} \dots\dots\dots \text{(eqn.8).}$$

y_e : Equilibrium concentration of adsorbate onto solid adsorbent.

X: Mass of adsorbate (moles, mg).

m: Weight of adsorbent (mg, g).

C_e : Equilibrium concentration of adsorbate in solution.

K_F : Constant, a measure of adsorption capacity (mg/g), (mg/mg), (mol/g).

$1/n$: Constant related to heterogeneity of the surface (adsorption intensity), its value ranges from zero to one. The value of $(1/n)$ closer to zero the more heterogeneity of adsorbent's surface.

Transformation of (eqn.8) to the logarithmic form (eqn.9) is handled more conveniently.

$$\mathbf{Log\ x/m = Log\ K_f + 1/n\ Log\ C_e} \dots\dots\dots (\text{eqn.9}).$$

A straight line is obtained when plotting $\text{Log } x/m$ versus $\text{Log } C_e$ with a slope of $1/n$ and intercept of $\log K_F$.^[34, 35]

1.2.5.3 BET Isotherm

In 1938 Stephan Brunauer, Paul Emmett and Edward Teller made extension to Langmuir isotherm that failed in multilayer adsorption and dependency of ΔH_{ads} on surface coverage and created an equation applied in multilayer adsorption and in determining the total surface area of porous and finely divided adsorbents. BET model is based on the assumption that average heat of adsorption equals the heat of condensation from the second layer upwards.^[35]

Their theory is called BET theory, mathematically represented by

$$y_e = \frac{X}{m} = \frac{y_{\text{max}} K_B C_e}{(C_s - C_e) [1 + (K_B - 1) C_e / C_s]} \dots\dots\dots (\text{eqn.10})$$

And can be rearranged as given in (eqn.11)

$$\frac{C_e}{y_e (C_s - C_e)} = \frac{1}{y_{\text{max}} K_B} + \frac{(K_B - 1)}{y_{\text{max}} K_B} \cdot \frac{C_e}{C_s} \dots\dots\dots (\text{eqn.11})$$

x , m , and C_e have the same meaning as in Langmuir isotherm.

y_{\max} : Mass of adsorbate required to form a monolayer on adsorbent surface.

K_B : A constant describing the energy of interaction between the solute and the adsorbent surface related to heat.

C_s : Concentration of adsorbate when the adsorbent is saturated (bulk).

1.3 Adsorbents

1.3.1 General Requirements of Adsorbents

Adsorbents must have high abrasion resistance, high thermal stability and small pore diameters, those results in higher exposed surface area and hence high surface capacity for adsorption.

The adsorbents must also have a distinct pore structure, which enables fast transport of the gaseous vapors. ^[30, 31]

1.3.2 Adsorbents Classes

Most industrial adsorbents fall into one of three classes:

- 1- Hydrophilic (polar); including materials such as: Porous silica gel, activated alumina and kaolin. ^[30]
- 2- Hydrophobic (non-polar); including materials as: Activated carbon. ^[30]
- 3- Polymer-based compounds, polar or non-polar functional groups (semi-polar) in a porous polymer matrix such as: Polyamide. ^[30]

1.3.2.1 Activated charcoal

Activated charcoal is a black, light powder form of carbon [C] that is free from grittiness and practically insoluble in all usual solvents.

Activated charcoal is the residue from the destructive distillation of various organic materials processed properly to be extremely porous with a very large surface area, intended to confer a high adsorptive power. [38, 39]

1.3.2.2 Silica gel

Silica gel is a chemically inert, nontoxic, polar and dimensionally stable ($< 400^{\circ}\text{C}$ or 750°F) amorphous form of $[\text{SiO}_2]$. It is prepared by the reaction between sodium silicate and acetic acid, which is followed by a series of after-treatment processes such as aging, picklingetc. These after treatment methods results in various pore size distributions. [36]

1.3.2.3 Alumina

Aluminum oxide is an amphitricha oxide of aluminum with the chemical formula $[\text{Al}_2\text{O}_3]$. [36]

1.3.2.4 Kaolin

Kaolinite or "kaolin" Powder $[\text{Al}_2\text{Si}_2\text{O}_5(\text{OH})_4]$ is a clay mineral, part of the group of industrial minerals. It is a native hydrated aluminum silicate, with one tetrahedral sheet linked through oxygen atoms to one octahedral sheet of alumina octahedra. [37, 39] Kaolin has also been used topically as an emollient and drying agent. Light kaolin is an antidiarrhoeal agent and is used as food additive. [24]

Kaolin, powdered and freed from gritty particles by elutriation¹ has traditionally been used internally to control diarrhea. [37, 39]

¹ **Elutriation**, also known as **air classification**, is a process for separating lighter particles from heavier ones using a vertically-directed stream of liquid or gas (usually upwards).

1.3.3 Factors Affecting the Adsorption Process

The extent of adsorption depends on physical and chemical parameters such as:-

1. Particle size of adsorbent: smaller particle size reduces mass transfer limitation of adsorbate inside adsorbent (i.e., equilibrium is more easily achieved and more adsorption can be attained).^[40]
2. Contact time or residence time: the longer the time of contact between adsorbent and adsorbate the more complete the adsorption.^[40]
3. pH of solution: the degree of ionization of species in the solution depends on pH that affects the affinity of adsorbate to adsorbent.^[40]
4. The elemental nature of the adsorbent (polar or nonpolar).^[40]
5. Surface area of adsorbent: larger surface area implies a greater adsorbent capacity.^[41]
6. Concentration of adsorbate in the solution.^[41]
7. Amount of adsorbent used for adsorption.^[41]
8. Temperature.^[41]

1.4 Literature Review for Previous Research

Several studies were done on the interaction between Fluoroquinolones and different adsorbents, Among these are studies on the adsorption and solubility of nalidixic acid on hydrophilic polymers pharmaceutical additives including microcrystalline cellulose, ethyl cellulose, silicon dioxide and aluminium.^[42]

Recently, Sorption of four pharmaceuticals acetaminophen, 17α -ethynyl estradiol, nalidixic acid and norfloxacin to two pure minerals: silica, alumina, and a Porapak p (a hydrophobic medium) was studied. [43]

Sorption of the antibiotic ofloxacin to mesoporous and nonporous alumina Al_2O_3 and silica SiO_2 adsorbents were determined over a range of pH values (2–10) and initial concentrations (0.03–8 mM) to investigate the effects of adsorbent type and intraparticle mesopores on adsorption/desorption process. [44]

Adsorption of fluoroquinolones on pharmaceutical adsorbents was studied in-Vitro. Fluoroquinolones adsorbed on activated charcoal rapidly and attained equilibrium within 15 minutes, but onto kaolin and bentonite less rapidly and attained equilibrium within two hours. Activated charcoal and bentonite had high adsorption capacities for the fluoroquinolones while kaolin had low adsorption capacities for them. [45]

The mechanisms of reduction in absorption of levofloxacin (LVFX) by coadministration of aluminum hydroxide were studied. The partition coefficient of LVFX (0.1mM) between chloroform and phosphate buffer (pH 5.0) was reduced by 60 to 70% with the addition of metal ions such as Cu^{2+} , Al^{3+} , and Fe^{2+} (0.8mM), which indicated the formation of LVFX-metal ion chelates. However, there was no significant difference in absorption from rat intestine between the synthetic LVFX- Al^{3+} (1:1) chelate (6.75mM) and LVFX (6.75M) capacities. [46]

This study was designed to evaluate the influence of some antacids drugs like sodium bicarbonate, calcium on the availability of sparfloxacin, as concurrent administration of antacids and sparfloxacin decreases the gastrointestinal absorption of sparfloxacin and therapeutic failure may result. Calcium carbonate, aluminum hydroxide, magnesium hydroxide, magnesium carbonate, magnesium trisilicate and magaldrate were studied on BP (British Pharmacopoeia) 2003 dissolution test apparatus and were carried out in simulated gastric and intestinal juices for three hours at 37°C. The results confirmed that the dissolution rate of tablets was markedly retarded in the presence of all antacids studied, whereas magaldrate and calcium carbonate exhibited relatively higher adsorption capacities in simulated gastric juice and magnesium trisilicate and calcium hydroxide in simulated intestinal juice.^[47]

1.5 Objectives of this Study

This study is for analyzing the adsorptive behavior of some adsorbents such as: activated charcoal and kaolin for the uptake of Gemifloxacin Mesylate and Levofloxacin Hemihydrate from aqueous solution, and studying the adsorption of Gemifloxacin Mesylate as adsorbate into alumina and silica gel adsorbents.

The effect of the following parameters on adsorption process will be evaluated:

- pH value of the drug's solution.
- Concentration of the drug used.
- Temperature.
- Amount of adsorbent used.
- Contact time between adsorbent and drug (equilibrium time).
- Particle size of adsorbent.

CHAPTER TWO

MATERIALS AND METHODS

2. Materials and Methods

2.1 Fluoroquinolones (adsorbate)

Gemifloxacin Mesylate (GEMX), was obtained from LG Life Sciences, Ltd. Seoul, Korea and Levofloxacin Hemihydrate (LEVX) was obtained from UQUIFA MEXICO, S. A. DE C.V.

Certificates of analysis for the drugs are in (Appendix I: a, b).

2.2 Adsorbents

- Activated Charcoal was obtained from Sigma Aldrich.
- Kaolin was from Kempex Holland Bv.
- Silica Gel was from E. Merck, Germany.
- Alumina was from E. Merck, Germany.

Characteristics of adsorbents are shown in (Appendix II: a, b, c).

2.3 Britton – Robison Buffer

"A universal buffer used for the range pH [2-12]. Universal buffers consist of mixtures of acids of diminishing strength (increasing pK_a) so that the change in pH is approximately proportional to the amount of alkali added"^[48], it was prepared from boric acid, acetic acid and phosphoric acid and all were analytical grade.

2.4 Chemicals

All reagents such as: NaOH, HCl were analytical grade.

2.5 Instrumentation

Dual beam UV-Visible-NIR scanning spectrophotometer model Shimadzu UV-Visible -310 1PC with 1cm matched quartz cell was used for all spectral measurements.

The pH was measured with a typical pH meter (Jenway 3510, England). The samples were mixed by a Burrell Wrist-Action Shaker[®], model 75 (Burrell Corporation, Pittsburgh, PA, USA). Samples were thermo-stated in a Tuttnauer water bath (Tuttnauer Co. Jerusalem). The 33-mm Millex[®] syringe sterile filter unit with durapore membrane, pore size 0.45µm (Millipore Ireland BV) was used for filtration of samples.

2.6 Preparation of Standard Stock Solutions

A stock solution of 5×10^{-3} M GEMX was prepared via dissolving an accurately weighed 0.1213 ± 0.001 g of GEMX (M.Wt. = 485.49 g/mol) into 50ml volumetric flask, then filled by distilled water. Gemifloxacin is considered freely soluble at neutral pH (350 µg/mL at 37°C).^[19]

The stock solution was preserved by aluminum foil to keep it from exposure to light and kept ready to use at room temperature. A stock solution of 5×10^{-3} M LEVX was created via dissolving an accurately weighed 0.0925 ± 0.001 g of LEVX (M.Wt. = 370.38 g/mol) in 10ml of 0.1M HCl and completed into 50ml volumetric flask by distilled water. The solubility of levofloxacin from pH=0.6 to pH=5.8 is essentially constant (approximately 100 mg/mL). Levofloxacin is considered soluble to freely soluble in this pH range.^[25]

The stock solution was protected from light exposure by aluminum foil and kept at room temperature.²

² instructions for storage

Store at 25°C (77°F); excursions permitted to 15°C-30°C (59°F-86°F)^[18]

Stock solutions showed stability at room temperature with time, each time before doing experiments a check up test for the stock were done by measuring the absorbance of control solution.

2.7 Preparation of Buffer

Britton – Robinson Buffer consists of a mixture of:^[48]

- 0.04M H_3PO_4 .
(Equals to 2.7ml of 85% ortho-phosphoric acid (M.Wt. = 98 g/mol).
- 0.04M CH_3COOH .
(Equals to 2.3ml of 99.8% glacial acetic acid (M.Wt. = 60.05 g/mol).
- 0.04M H_3BO_3
(Equals to 2.5g of boric acid (M.Wt. = 61.83 g/mol).

Buffer stock solution was freshly prepared: graded amounts of the previous reagents were taken and brought to volume with distilled water in a 1L volumetric flask, pH was adjusted to the desired value by adding graded volume of 1M NaOH (40 g/mol) to about 200ml of buffer stock solution, and before measuring pH of the buffer, the pH meter has been calibrated with standard buffers of pH=4 & pH=7.

2.8 Absorbance Spectrum of GEMX and LVXN

Different dilutions of both stock drugs' solutions were prepared in buffer solution within the pH range of [2-12], then spectrophotometrically analyzed by scanning in the entire UV-range [200-400]nm against a blank at $25 \pm 1\text{C}^\circ$. Two GEMX solutions [$4 \times 10^{-5}\text{M}$] in buffer of pH=3 and pH=7 and two LEVX solutions [$3 \times 10^{-5}\text{M}$] in buffer of pH=4 and pH=9 were analyzed to determine absorbance spectrum of both drugs.

2.9 Preparation of the Calibration Graph

Different GEMX solutions with concentrations in the range [$0.5 \times 10^{-5} \text{M}$ - $5 \times 10^{-5} \text{M}$] and different solutions of LEVX with concentrations in the range [$0.5 \times 10^{-5} \text{M}$ - $4.0 \times 10^{-5} \text{M}$] were prepared by taking aliquots of stock standard solution [$5 \times 10^{-3} \text{M}$] of drugs into 100ml volumetric flasks completing the volumes to the mark with Britton –Robinson buffer of pH=3 for GEMX and of pH=4 for LEVX. The absorbance was measured at the maximum wavelength for each drug against a blank. ^[49]

The calibration graph was then prepared by plotting the absorbance versus the concentration of the drug. The concentration of the unknown was computed from the regression equation of the calibration graph.

The correlation coefficient (R^2) of calibration graph indicates the strength of the linearity between the variables and LOD is the lowest detectable concentration of the analyte by the method.

Activation of adsorbents:

Charcoal and kaolin were activated by drying at 110C° for five hours for charcoal and three hours for kaolin then cooled and stored in desiccator to be used later. ^[45]

Solutions of Drugs:

All the solutions that were used in adsorption process were prepared fresh daily. The solution was found to be stable for at room temperature.

2.10 Adsorption Study

2.10.1 Equilibrium Study

The general procedure for calculating equilibrium between adsorbent and adsorbate was carried out by adding constant initial amount of adsorbent into different initial concentrations of 100ml standard solutions of drugs were prepared in Britton - Robinson buffer at specific pH and inserted in 250ml conical flask that was in a thermo stated water bath at constant temperature and fixed to the shaker with adjustable moderate rate and time of contact of about 1hour before determining equilibrium time. Different aliquots of the mixture were pipetted from the flask at various intervals and filtrated by 0.45 μ m filter membrane that was an easy, rapid, clean filtration. The concentration of drug was known from measuring the absorbance of both the initial solution and the filtrate at different time intervals by spectrophotometer against a blank. The decrease in the remaining amount of adsorbate in the solution with time continues until it reaches equilibrium. ^[50]

The blank was prepared from 100ml of buffer with same pH of the sample and mixed with the same amount of adsorbent, but without drug and treated in the same way of the sample; fixed to the shaker for the same contact time and temperature and filtrated with 0.45 μ m filter membrane.

At the same time, a control solution of 100ml of the same concentration of drug prepared in buffer at same pH and temperature and same contact time then filtrated with 0.45 μ m filter membrane was analyzed to investigate that no influence of any factor other than adsorption. Blank and control

solutions showed a negligible effects when conducted for each isotherm study to detect any effects during the experimental procedure rather than adsorption.

For adsorption of GEMX onto charcoal, different concentrations of GEMX solution in the range $[1.0-5.0] \times 10^{-5} \text{M}$ at $\text{pH}=3$ mixed with $0.004 \pm 0.001 \text{g}$ charcoal at $25 \pm 1 \text{ C}^\circ$ to about 1 hour (contact time) before determining the equilibrium time, the same procedure was repeated for adsorption of GEMX with $0.01 \text{g} \pm 0.001$ of kaolin, equilibrium was reached after 1 hour between GEMX and kaolin. For adsorption of GEMX onto alumina: GEMX solutions in the range $[1.0-5.0] \times 10^{-5} \text{M}$ were prepared in buffer at $\text{pH}=7$ adsorbed onto $0.2 \pm 0.001 \text{g}$ of alumina at room temperature $[22 \pm 1 \text{C}^\circ]$ for 1hour, and for silica the same with alumina but GEMX was adsorbed onto $0.4 \pm 0.001 \text{g}$ silica gel. Equilibrium was achieved after 24 hours, but contact time between GEMX and silica and alumina was 1hour.

Different LEVX solutions in the range of $[1 \times 10^{-5} \text{M} - 5 \times 10^{-5} \text{M}]$, at $\text{pH}=4$ mixed with $0.004 \text{g} \pm 0.001$ of charcoal at $25 \pm 1 \text{C}^\circ$, and with $0.01 \pm 0.001 \text{g}$ of kaolin at $20 \pm 1 \text{C}^\circ$, amount adsorbed with time was calculated until the equilibrium was reached between LEVX and adsorbent.

2.10.2 Kinetic Study: Time Dependency

This study is to know the change in concentration of adsorbate in the solution with time, the effect of contact time on adsorption and the rate of adsorption. The experiments were carried out by adding constant amount of adsorbent into 100ml of standard solution of drug with constant initial

concentration prepared in Britton - Robinson buffer into 250ml conical flask and fixed to the thermo stated shaker, taking different aliquots of the mixture at different time intervals while shaking is contentiously, filtrated and analyzed by spectrophotometer. The filtrate after analyzing was drawn back to solution to maintain the volume. The experiment was repeated with different concentrations of both drugs with different adsorbents.

2.10.3 Effect of Adsorbate Concentration on Adsorption

The experiments were carried out by adding constant amount of adsorbent into 100ml of standard solution of drug with different initial concentrations of drugs prepared in Britton - Robinson buffer at constant pH into 250ml conical flask and mixed together in thermo-stated water bath shaker contentiously, at time of equilibrium aliquots of the mixtures were taken, filtrated and analyzed by spectrophotometer the concentration at equilibrium and the amount adsorbed was calculated versus different initial concentrations of drugs.

Amount adsorbed of GEMX solutions with initial concentrations (C_0) in the range ($1 \times 10^{-5} \text{M}$ - $5 \times 10^{-5} \text{M}$) was calculated with $0.004 \pm 0.001 \text{g}$ of charcoal and $0.01 \pm 0.001 \text{g}$ kaolin in Britton - Robinson buffer at pH=3 at $25 \pm 1^\circ \text{C}$ to the time of equilibrium (20 min) with charcoal and 1 hour with kaolin at $20 \pm 1^\circ \text{C}$. For GEMX adsorbed into $0.2 \pm 0.001 \text{g}$ alumina to the time of 1 hour at pH=7 and at $22 \pm 1^\circ \text{C}$, and for GEMX adsorbed into $0.4 \pm 0.001 \text{g}$ silica to the time of 1 hour at pH=7 and at $22 \pm 1^\circ \text{C}$.

Different solutions of LEVX in the range ($1-5 \times 10^{-5} \text{M}$) prepared in buffer at pH=4 were taken with $0.004 \pm 0.001 \text{g}$ of charcoal mixed together in

thermo-stated water bath at $20 \pm 1^\circ\text{C}$, to the time of equilibrium (20 min). For GEMX adsorbed into $0.01 \pm 0.001\text{g}$ kaolin to the time of equilibrium (1 hour) at $20 \pm 1^\circ\text{C}$ and $\text{pH}=4$.

Calculating % removal of drug = $([C_o - C_e]/C_o) * 100\%$ and amount adsorbed $X = [C_o - C_e] * v$ (v: volume of solution used) and $y_e = x/m$ (m: weight of adsorbent for the previous adsorption processes).

2.10.4 Effect of Adsorbent's Amount on Adsorption

After determining the equilibrium time, steps of adsorption study were repeated with same conditions of constant initial concentration of drugs, same pH and shaking in thermo stated shaker (constant temperature), but changing the amount of adsorbent each time. A volume of the mixture was pipetted at equilibrium, filtered and analyzed by spectrophotometer. From the initial concentration and concentration at equilibrium the amount adsorbed, % removal and the amount remaining can be calculated.

Constant initial concentration of GEMX solution at $\text{pH}=3$ versus different weights of charcoal to the time of equilibrium (20 min) at $25 \pm 1^\circ\text{C}$ were mixed to calculate the amount adsorbed of GEMX versus different weights of charcoal. Same procedure was repeated with different weights of kaolin to the time of equilibrium (1 hour). Each 100 ml of same initial concentration of GEMX $4 * 10^{-5}\text{M}$ solution was prepared in buffer at $\text{pH}=7$ and was added to different weights of alumina in a dry 250ml conical flask and were fixed to the shaker at room temperature [$22 \pm 1^\circ\text{C}$], few amounts were taken after 1 hour and filtrated by $0.45\mu\text{m}$ miller filter unit

and analyzed spectrophotometrically at λ_{\max} . The equilibrium time was for 24 hrs but we take the concentration after 1hr for simplicity, same procedure with alumina was done with silica, but more weight was taken because adsorption of GEMX to silica less than adsorption to alumina.

Each 100ml of initial concentration of LEVX solution [$3 \times 10^{-5} \text{M}$] at pH=3 was added to different weights of charcoal and kaolin in a dry 250ml conical flask and were fixed to the shaker at $20 \pm 1 \text{C}^{\circ}$, the amount adsorbed at equilibrium time was calculated.

2.10.5 Effect of pH on Adsorption

The general procedure for calculating the amount adsorbed of drug versus pH was by adding 100ml of freshly prepared solution of drug in Britton - Robinson buffer at specific pH with constant initial concentration to constant amount of adsorbent in 250ml conical flask, fixed to thermo stated shaker to the time of equilibrium, then a volume of the mixture was pipetted, filtrated and analyzed by spectrophotometer. The experiment was repeated with different pH values and the amount adsorbed of drug versus different pH was calculated.

The amount adsorbed of GEMX solutions on $0.004 \pm 0.001 \text{g}$ of charcoal versus different pH in the range (2-12), was calculated at equilibrium time (20 min) and at $25 \pm 1 \text{C}^{\circ}$. The same for Adsorption of GEMX on $0.01 \pm 0.001 \text{g}$ of kaolin but at equilibrium time (1 hour).

GEMX absorbance maximum shift from 343nm to 340nm above pH=6, the results were calculated in respect to λ_{\max} at each pH. (not shown).

For Adsorption on alumina GEMX solutions with constant initial concentration $4 \times 10^{-5} \text{M}$ were freshly prepared in buffer with different pH and mixed with $0.2 \pm 0.001 \text{g}$ of alumina for 1 hour at room temperature [$22 \pm 1 \text{C}^{\circ}$], these steps were repeated between GEMX and $0.4 \pm 0.001 \text{g}$ of silica gel and the amount adsorbed were calculated after 1 hour.

Constant initial concentration of LEVX solution $3 \times 10^{-5} \text{M}$ was prepared in buffer with different pH in the range (2-12), added to constant amount ($0.004 \pm 0.001 \text{g}$) of charcoal to 20 min, at $25 \pm 1 \text{C}^{\circ}$, then the amount adsorbed were calculated at equilibrium time at each λ_{max} repeated with kaolin $0.01 \pm 0.001 \text{g}$, the amount adsorbed were calculated at equilibrium time (1 hour) in respect to λ_{max} at each pH. (not shown). LEVX absorbance maximum shift from 294nm to 288nm above pH= 6, results were calculated in respect to λ_{max} at each pH. (not shown)

2.10.6 Effect of Temperature on Adsorption

The amount adsorbed was calculated as function of temperature generally by adding constant amount of adsorbent to 100ml solution of drug into 250ml conical flask with a constant initial concentration at constant pH then fixed to thermo stated shaker to the time of equilibrium. A volume of the mixture was pipetted, filtered and analyzed by spectrophotometer to calculate the amount adsorbed, then the previous process was repeated at different temperatures.

For adsorption of GEMX on charcoal versus temperature GEMX solution was prepared in Britton Robinson buffer at pH=3 and added to $0.004 \pm 0.001 \text{g}$ of charcoal mixed together to time of equilibrium(20 min).

The same procedure was repeated with GEMX adsorbed on 0.01 ± 0.001 g kaolin to time of equilibrium (1 hour).

For adsorption of GEMX on alumina and silica solutions of GEMX were prepared in buffer pH=7 and adsorbed onto 0.2 ± 0.001 g alumina and 0.4 ± 0.001 g silica gel to time of 1hour, amount of GEMX adsorbed was calculated versus different temperature.

Adsorption was investigated as a function of temperature and amount adsorbed of LVXN solution prepared in buffer pH=4 onto 0.004 ± 0.001 g of charcoal to the time of equilibrium (20 min), the same repeated with LEVX solution adsorbed onto 0.01 ± 0.001 g kaolin to time of 1hour.

CHAPTER THREE

RESULTS AND DISCUSSION

3. Results and Discussion

3.1 Absorbance Spectrum

3.1.1 Absorbance Spectrum of GEMX

Absorbance spectrum of GEMX solution is characterized by the maximum wavelength (λ_{\max}) = 343nm at pH=3 and λ_{\max} = 340nm at pH=7, as shown in (Fig.3.1.1).

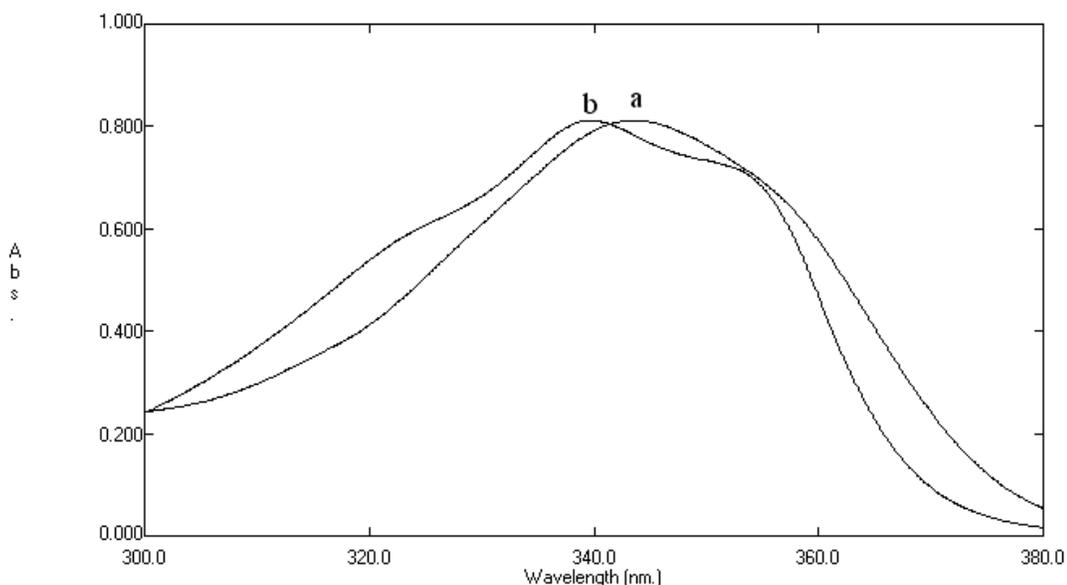


Figure 3.1.1: Absorbance Spectrum of GEMX Solution, a (pH=3) and b (pH=7)

3.1.2 Absorbance Spectrum of LVXN

Absorbance spectrum of LVXN solution is characterized by the maximum wavelength (λ_{\max}) = 294nm at pH= 4 and λ_{\max} = 288nm, as shown in (Fig.3.1.2).

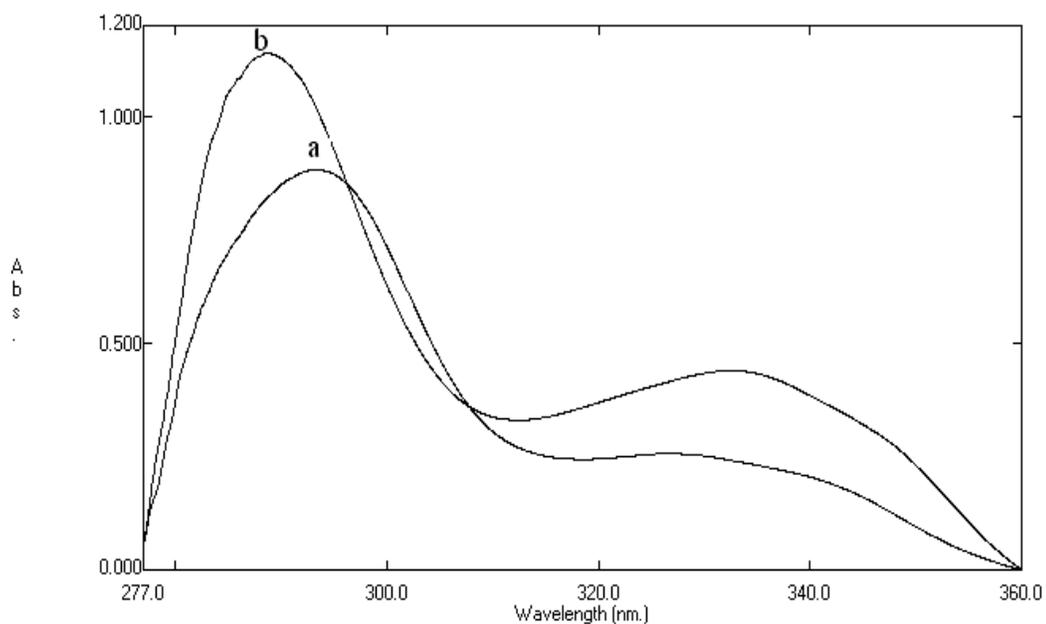


Figure 3.1.2: Absorbance Spectrum of LVXN Solution, a (pH= 4), b (pH= 9)

3.2 Calibration Graph

3.2.1 Calibration Graph for GEMX

From the calibration graph (Fig.3.2.1) the detection limit (LOD) was $0.05 \times 10^{-5} \text{M}$ and the molar absorptivity was $0.1992 \text{L.cm}^{-1}.\text{mol}^{-1}$.

The relative standard deviation (RSD) was 1.85% for 5 measurements of the absorbance of 5 samples with concentration equals to $4.0 \times 10^{-5} \text{M}$.

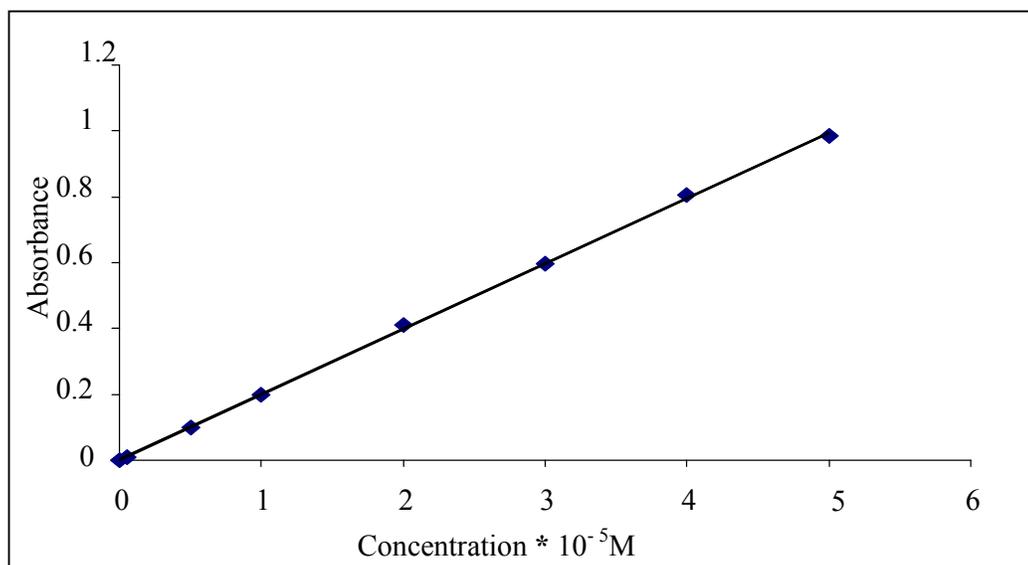


Figure 3.2.1: Calibration Graph for the Estimation of GEMX

3.2.2 Calibration Graph for LEVX

From the calibration graph (Fig.3.2.2) the detection limit (LOD) was found to be $0.05 \times 10^{-5} \text{M}$, molar absorptivity was $0.2866 \text{L mol}^{-1} \text{cm}^{-1}$ and relative standard deviation (RSD) was 1.52% for 5 measurements of absorbance of 5 samples with concentration equals to $3.0 \times 10^{-5} \text{M}$.

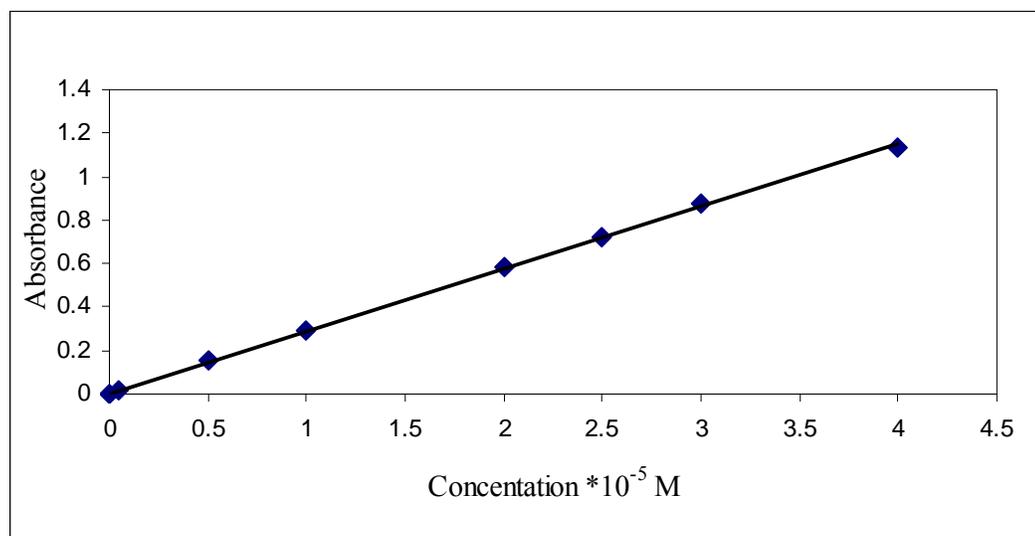


Figure 3.2.2: Calibration Graph for the Estimation of LEVX

3.3 Adsorption of GEMX on Different Adsorbents

3.3.1 Adsorption of GEMX onto Charcoal

3.3.1.a Adsorption of GEMX onto Charcoal: Time Dependency

Different initial concentrations of standard solution of GEMX adsorbed onto 0.004 ± 0.001 g charcoal, the concentration decreases with time as shown in (Table 3.3.1).

Table 3.3.1: Values of concentrations for GEMX remaining vs. time with charcoal

C₁ (ppm)	C₂ (ppm)	C₃ (ppm)	C₄ (ppm)	Time (min)
11.723	13.929	19.912	24.723	0
4.631	9.724	16.500	21.131	3
4.000	7.945	15.550	20.100	7
3.997	7.897	15.428	20.000	10
3.802	7.775	15.180	19.839	15
3.788	7.522	14.940	19.741	20
3.752	7.460	14.550	19.376	30
3.729	7.336	14.136	19.205	40

The results showed that a rapid decrease in concentration of GEMX remaining in solution was in the initial 20 min as shown in (Fig.3.3.1) until pseudo-adsorption equilibrium was reached, adsorption of GEMX continued after 30-40 min of 1 hour contact time between charcoal and GEMX until maximum adsorption was reached. The portion of GEMX participating in the long-term behavior in about 30-40 min was

insignificant as compared to that participating in the preliminary phase of rapid adsorption.

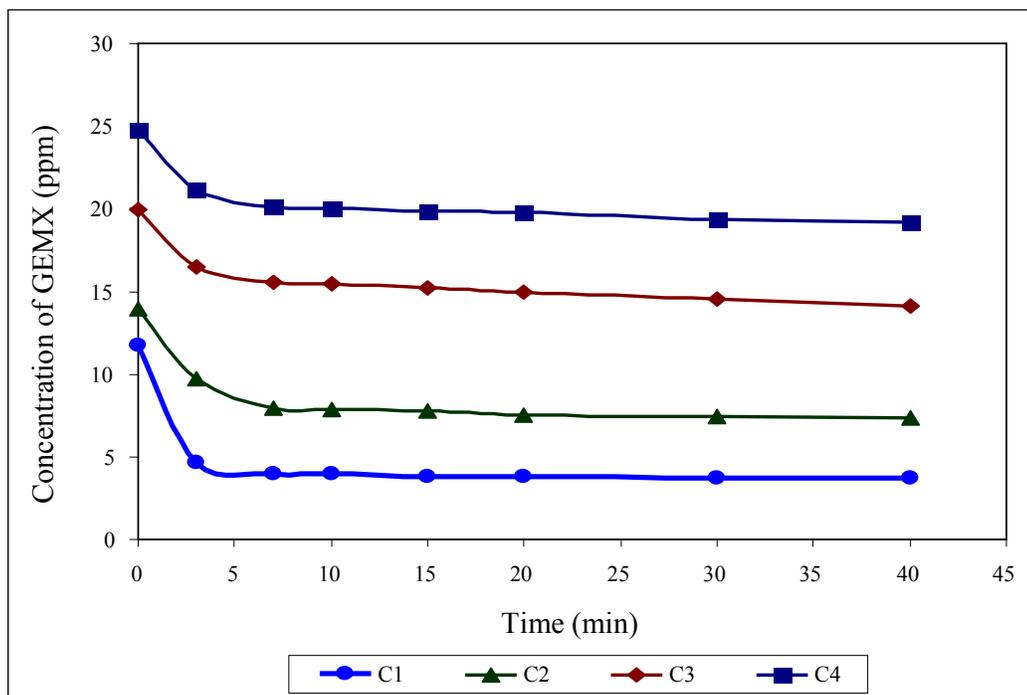


Figure 3.3.1: Concentration of GEMX remaining vs. time with charcoal

The adsorption kinetics exhibited an immediate rapid adsorption and reached pseudo_ adsorption equilibrium within a short period of 20 min. The rapid initial adsorption of GEMX is a surface phenomenon, due to anionic nature of GEMX at pH=3, the vacant sites in the charcoal particles those were filled up rapidly in the initial stages and followed a linear variation. Then a slow migration and diffusion of compound occurred and the rate of adsorption decreased drastically to reach the steady state (equilibrium), 50%-75% of GEMX is adsorbed in the first 20 min.

3.3.1.b Equilibrium Study between GEMX and Charcoal

Equilibrium concentrations for different initial concentrations of GEMX and amounts adsorbed onto charcoal were calculated as shown in (Table 3.3.2).

Table 3.3.2: Equilibrium concentrations and amounts adsorbed for GEMX on charcoal

C_o (ppm)	C_e (ppm)	y_e (mg/g)	$1/C_e$ (ppm) ⁻¹	$1/y_e$ (mg/g) ⁻¹	$\text{Log } C_e$ (ppm)	$\text{Log } y_e$ (mg/g)
11.723	3.729	199.85	0.2682	0.0050	0.570	2.301
13.929	7.336	164.83	0.1363	0.0061	0.865	2.217
15.325	9.213	152.80	0.0873	0.0065	0.964	2.184
19.912	14.136	144.40	0.0707	0.0069	1.157	2.160

Two adsorption isotherms were used to study adsorption behavior of GEMX onto charcoal clearly.

$$1\text{- Langmuir} \quad \frac{1}{y_e} = \frac{1}{y_{\max}} + \left[\frac{1}{K_A y_{\max}} \right] \cdot \frac{1}{C_e}$$

$$2\text{- Freundlich} \quad y_e = \frac{X}{m} = K_F C_e^{1/n}$$

Langmuir isotherm was obtained from the relation between $1/y_e$ vs. $1/C_e$ as shown in (Fig.3.3.2).

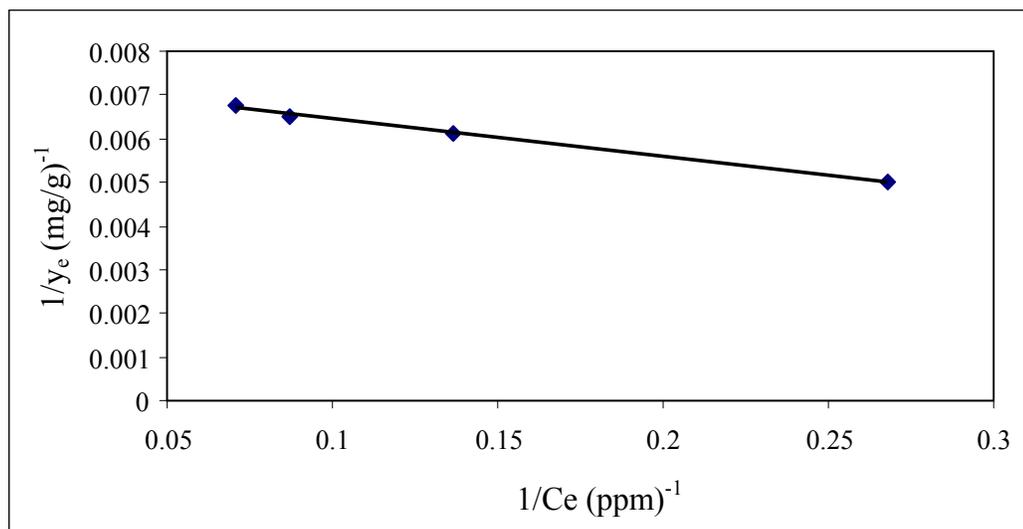


Figure 3.3.2: Langmuir isotherm for adsorption of GEMX onto charcoal

Freundlich isotherm was obtained from the relation between $\text{Log } y_e$ versus $\text{Log } C_e$ as shown in (Fig.3.3.3).

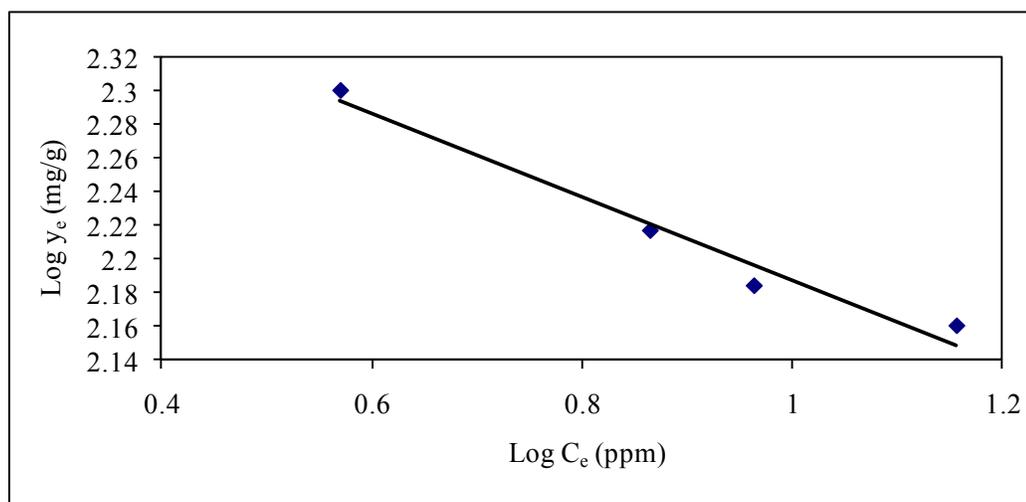


Figure 3.3.3: Freundlich isotherm for adsorption of GEMX onto charcoal

The adsorption followed Langmuir isotherm ($R^2 = 0.995$) better than Freundlich isotherm ($R^2 = 0.9695$).

From equation of Langmuir isotherm $y = -0.0087x + 0.0073$

Maximum capacity of charcoal (y_{\max})= 137 mg/g, $K_A = 0.84$ (Langmuir's constant). This maximum adsorbable value (y_{\max}) of 137 mg/g that is required for monolayer adsorption of GEMX on charcoal, shows the high binding capacity of activated charcoal that has been attributed to its high surface area .

3.3.1.c Kinetic Study between GEMX and Charcoal

Adsorption is time-dependent process so the rate of adsorption is important to evaluate the taking of GEMX by the adsorbent.

The pseudo-first order rate expression of lagergren ^[50, 51, 57] is:

$$dy/dt = K_1 (y_e - y_t)$$

y_e : Amount adsorbed of GEMX at equilibrium (mg/g).

y_t : Amount adsorbed of GEMX at time t (mg/g).

K_1 : Rate constant of pseudo first order adsorption (min)⁻¹.

Integration of the previous equation with boundaries $t = 0$ to $t = t$ gives

$$\text{Log } (y_e - y_t) = \text{Log } y_e - [k_1 \cdot t] / 2.303$$

A plot of $\text{Log } (y_e - y_t)$ versus t gave a straight line as shown in (Fig.3.3.4), with slope: 0.0949 and intercept: 0.0226.

The pseudo-second order rate constant of adsorption ($\text{g mg}^{-1} \text{ min}^{-1}$) as reported by McKay and Ho gives a linear relation: ^[50, 51, 57]

$$t/y_t = 1/ [k_2 y_e^2] + [1/y_e] t$$

y_e , y_t are amounts adsorbed of GEMX at equilibrium and at any time t respectively (mg/g), k_2 is the rate constant of pseudo-second order rate

y_e and k_2 can be determined directly from the slope: 0.0079 and intercept: 0.007 of the plot between t/y_t and t as shown in (Fig.3.3.5).

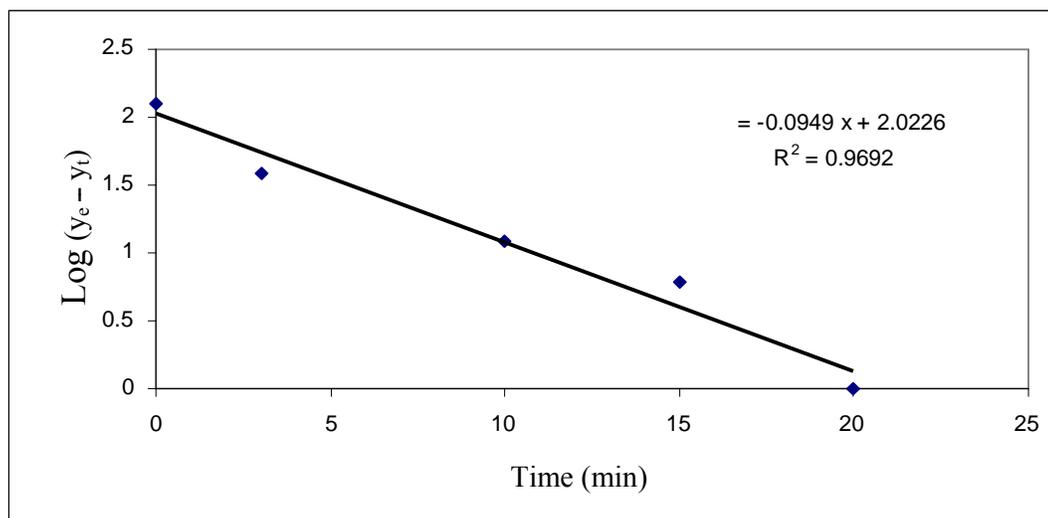


Figure 3.3.4: The pseudo first order rate expression of GEMX

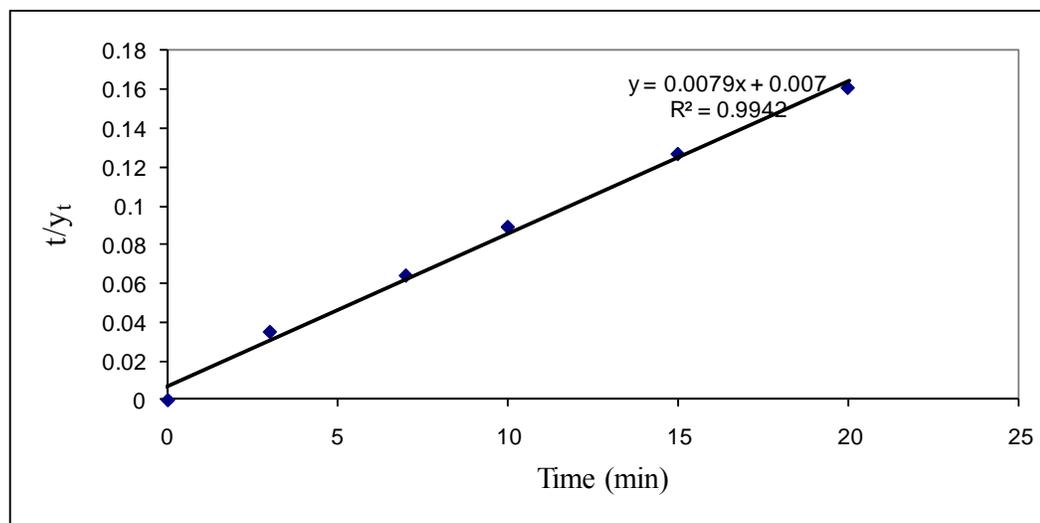


Figure 3.3.5: The pseudo second order rate expression of GEMX

From the previous plots, the calculated correlation coefficients are closer to unity in the pseudo-second order kinetics than the pseudo-first order one. From the pseudo-second rate order kinetics, adsorption process can be described $y_e=126.58 \text{ mg/g}$ and $K_2 = 0.009 \text{ g mg}^{-1} \text{ min}^{-1}$.

3.3.1.d Effect of GEMX Concentration on Adsorption.

Equilibrium concentration (C_e), amount adsorbed onto charcoal at equilibrium (y_e) and % removal of GEMX were calculated from different initial concentrations of GEMX (C_o); the values are in (Table 3.3.3).

Table 3.3.3: Values of C_e , y_e and % removal of GEMX on charcoal vs. different C_o

C_o (ppm)	C_e (ppm)	y_e (mg/g)	% removal of GEMX
11.723	3.729	199.850	68.190
13.929	7.336	164.825	42.750
15.325	9.213	152.800	38.000
19.912	14.136	144.400	29.010
24.723	19.205	137.950	22.320

As the initial concentration of GEMX increases % removal of GEMX decrease as shown in (Fig.3.3.6).

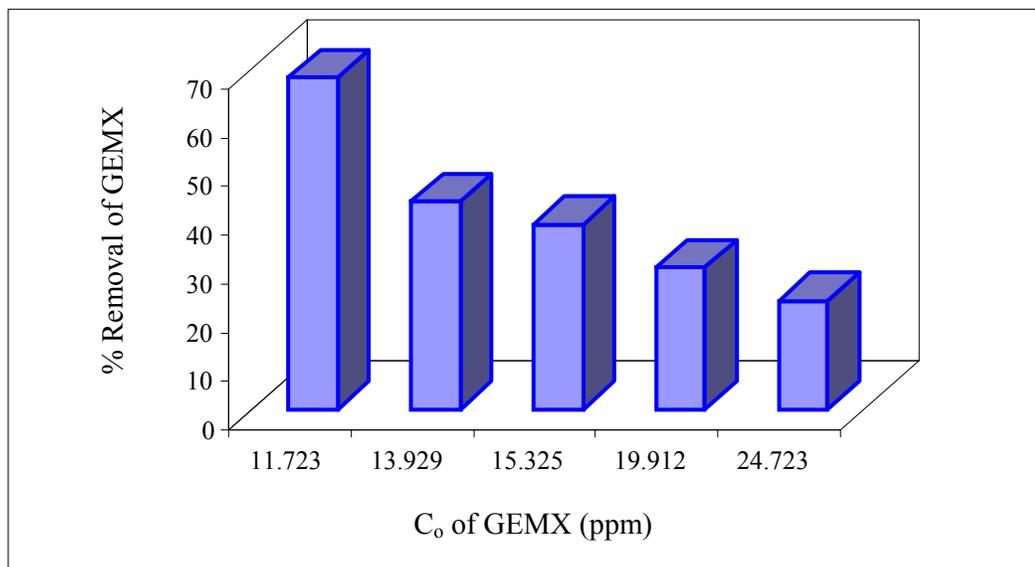


Figure 3.3.6: The % removal of GEMX by charcoal versus initial concentration of GEMX

As the initial concentration of GEMX increases the amount adsorbed decrease as shown in (Fig.3.3.7).

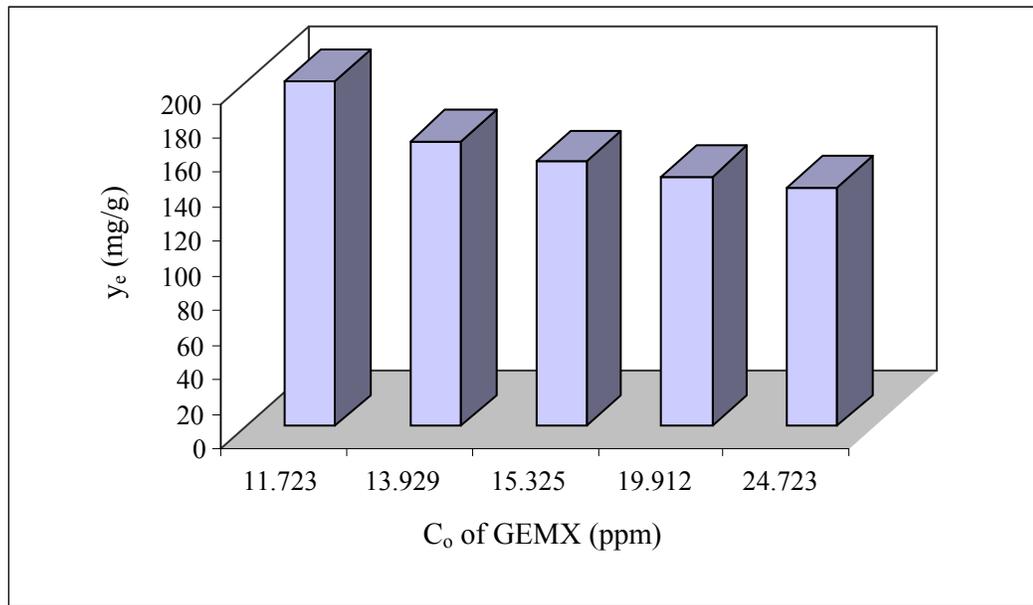


Figure 3.3.7: Amount adsorbed of GEMX by charcoal (y_e) vs. C_o of GEMX

As initial concentration of GEMX (C_o) increases y_e and % removal of GEMX decreases: at lower GEMX concentration ratio of GEMX molecules to adsorbent sites is high this is a driving force to overcome all mass transfer resistances of the adsorbate between solution and adsorbent molecules than at higher concentration, where there is saturation of adsorption sites with GEMX and higher probability of collision between GEMX molecules and more repulsion that decrease the adsorption capacity. When GEMX molecules adsorbed on the surface of charcoal they would repel each other and the incoming molecules electrostatically, hence they cannot pack densely onto the surface. This explains why Langmuir's isotherm was followed as multi-layer adsorption may not be possible. Despite such limitations, charcoal still adsorb GEMX strongly and rapidly.

3.3.1.e. Effect of Amount of Charcoal on Adsorption of GEMX

The amount adsorbed (X), equilibrium concentrations (C_e), % removal of GEMX (% y_e) and y_e of constant initial concentration of GEMX solutions (C_o) versus different weights of charcoal (m) were calculated to the time of equilibrium, as in (Table 3.3.4).

Table 3.3.4: Values of C_e , y_e and % removal of GEMX vs. weight of charcoal.

C_o (mg/L)	C_e (mg/L)	X (mg)	y_e (mg/g)	% y_e removal	m (g)
19.96	16.427	0.3533	176.65	17.70	0.002
19.91	14.964	0.4946	123.65	24.84	0.004
19.60	14.209	0.5391	89.85	27.51	0.006
19.65	12.308	0.7342	91.78	37.36	0.008
19.45	10.066	0.9384	93.84	48.25	0.010

The % removal of adsorbate and amount of GEMX adsorbed (X) increases as the amount of adsorbent increases as shown in (Fig.3.3.8), (Fig.3.3.9) respectively. The increase in the amount adsorbed can be attributed to greater surface area and more adsorption sites are available in the surface of adsorbent.

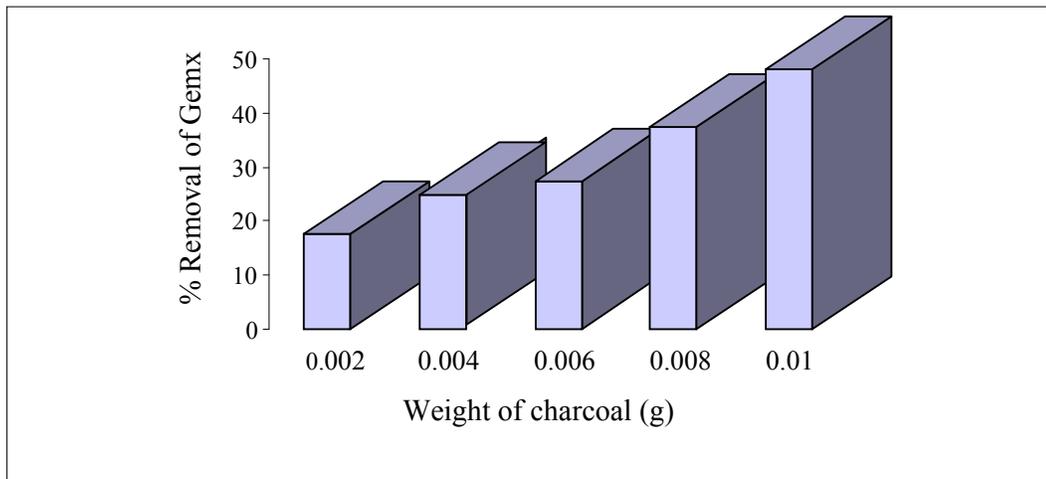


Figure 3.3.8: The % removal of GEMX by charcoal vs. weight of charcoal

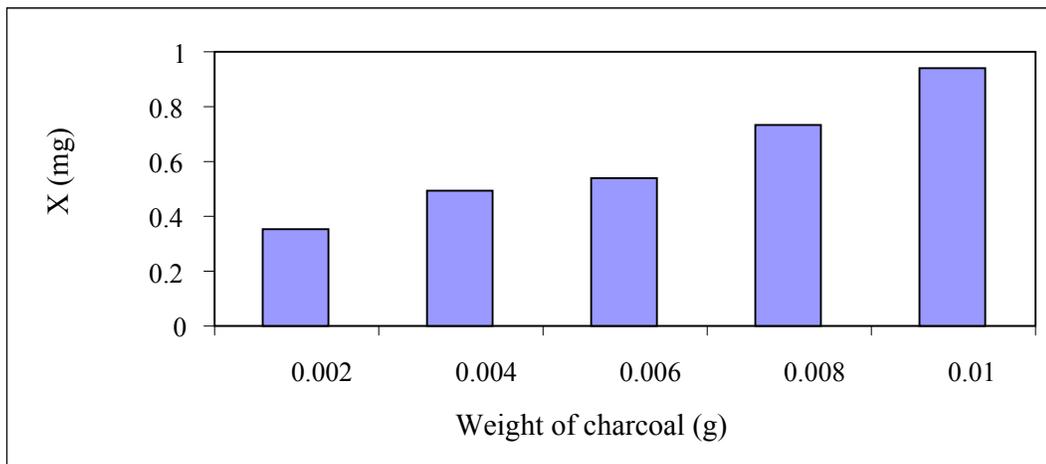


Figure 3.3.9: Amount adsorbed of GEMX (X) vs. weight of charcoal

The amount of GEMX adsorbed in respect to each weight (y_e) decreases as in (Fig.3.3.10.) but to a certain limit then it remains almost constant, because GEMX and more than 0.006g charcoal come to equilibrium with each other, although the adsorption capacity decreases may be due to overlapping and saturation of adsorbent's sites of that result in decrease in the surface area available to GEMX, when the adsorbent amount 0.002g

Adsorption capacity was high, due to higher driving force to overcome any resistance of GEMX molecules from adsorption to charcoal, because ratio of GEMX to charcoal is high.

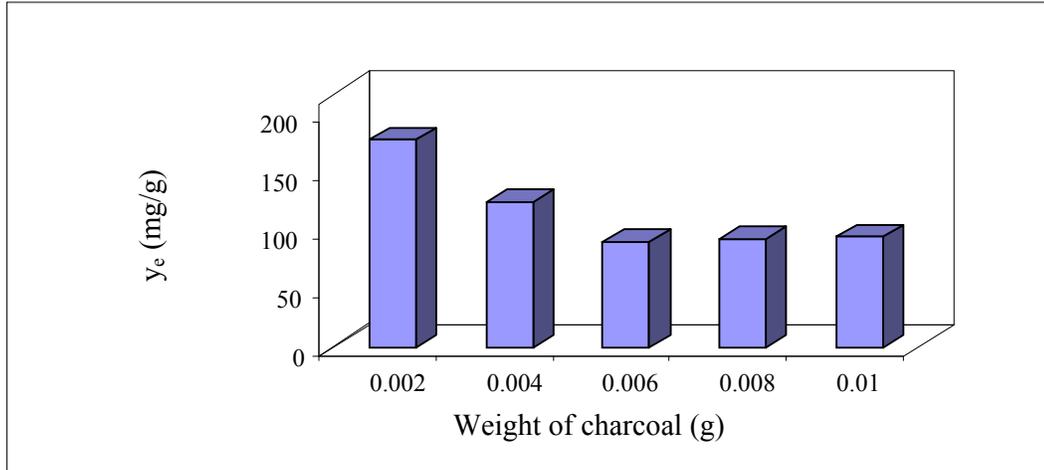


Figure 3.3.10: Amount adsorbed of GEMX by charcoal vs. weight of charcoal

3.3.1.f. Effect of pH on Adsorption of GEMX onto Charcoal

The amount of GEMX solutions with the same initial concentration adsorbed into same amount of charcoal were calculated at equilibrium time versus different pH in the range (2-12), as shown in (Fig.3.3.11).

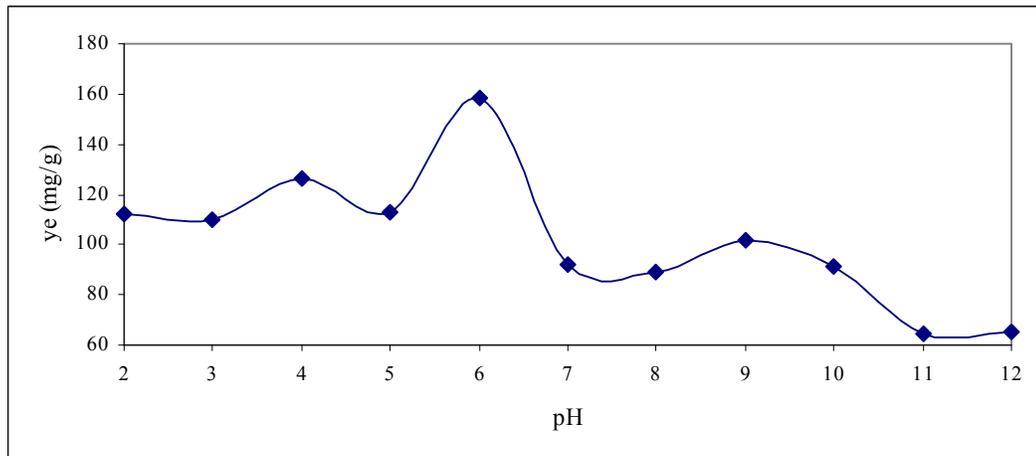


Figure 3.3.11: Amount adsorbed of GEMX onto charcoal vs. pH

The maximum adsorption of GEMX to charcoal occurred at pH=6, which was near pI of GEMX [pI: pH in the range 6.2-8.0 zwitterion fraction of GEMX > 0.7].^[52] GEMX that has two centers a carboxyl (anionic) group and a naphthyridine (cationic) one, at this pH the carboxyl group was half ionized (negatively charged) and the naphthyridine group (positively charged). The charge of the adsorbent's surface is taken in consideration charcoal is a non polar adsorbent; no charge on its surface but H⁺ ions and OH⁻ ions from the solution accumulates on its surface causing the attraction between the opposite charges and adsorbed GEMX to charcoal. The amount adsorbed was greater in acidic than in basic medium, this is because of high electrostatic attraction between the positively charged surface of charcoal because of H⁺ ions and negative charge of GEMX, as the pH increases the negative charge on the adsorbent surface will increase because OH⁻ ions increase thus decreases the positively charged sites of charcoal that will cause repulsion of negative charge of GEMX molecules.

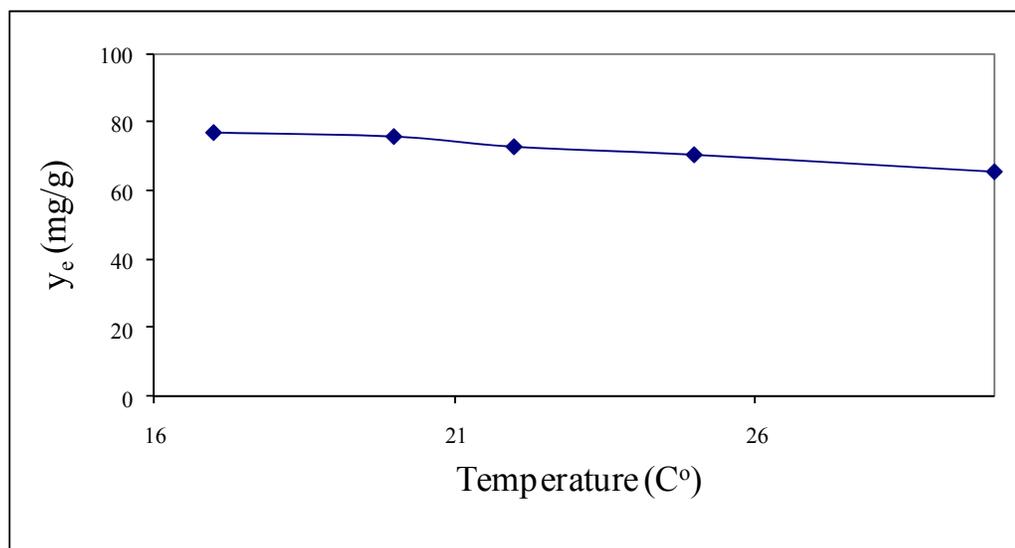
3.3.1.g. Effect of Temperature on GEMX Adsorption on Charcoal

Adsorption was investigated as a function of temperature and amount of GEMX solutions with the same initial concentration adsorbed into 0.004g of charcoal were calculated at equilibrium time versus different temperature, values in (Table 3.3.5).

Table 3.3.5: Effect of temperature on adsorption of GEMX on charcoal

Temperature		1/T k ⁻¹	C _o (ppm)	C _e (ppm)	y _e (mg/g)	K _c (L/g)	Ln K _c (L/g)
C ^o	k						
17	290	0.00345	19.58	11.891	76.89	6.466	1.867
20	293	0.00341	19.58	12.007	75.73	6.307	1.842
22	295	0.00339	19.58	12.305	72.75	5.912	1.777
25	298	0.00336	19.58	12.638	70.41	5.571	1.718
30	303	0.00330	19.58	13.066	65.47	5.011	1.612

As the temperature increased the amount of GEMX adsorbed on charcoal decreased, as shown in (Fig 3.3.12).

**Figure 3.3.12: Amount adsorbed of GEMX on charcoal vs. temperature**

Thermodynamic parameters including: standard Gibb's free energy change (ΔG°), standard entropy change (ΔS°) and standard enthalpy change (ΔH°) were determined as follows:^[50, 51]

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ \quad \dots\dots\dots (1)$$

As the system changes from standard condition to an equilibrium state: its Gibb's free energy changes from 0 to $- R T \text{ Ln } K_c$

K_c : standard thermodynamic equilibrium constant; $K_c = y_e / C_e$ (L/g).

y_e : the amount of GEMX adsorbed by the adsorbent per liter of the solution at equilibrium (mg/L), and C_e : concentration of GEMX in the solution at equilibrium (mg/L)

R: the universal gas constant (8.314 J/mol K), T (k) absolute temperature

The standard Gibb's free energy change (ΔG°) was calculated using following Gibb's equation: $\Delta G^\circ = - RT \text{ Ln } K_c \dots\dots\dots(2)$

Combining eq 1& eq 2 gives: $\text{Ln } K_c = (\Delta S^\circ/R) - (\Delta H^\circ/RT) \dots\dots\dots(3)$

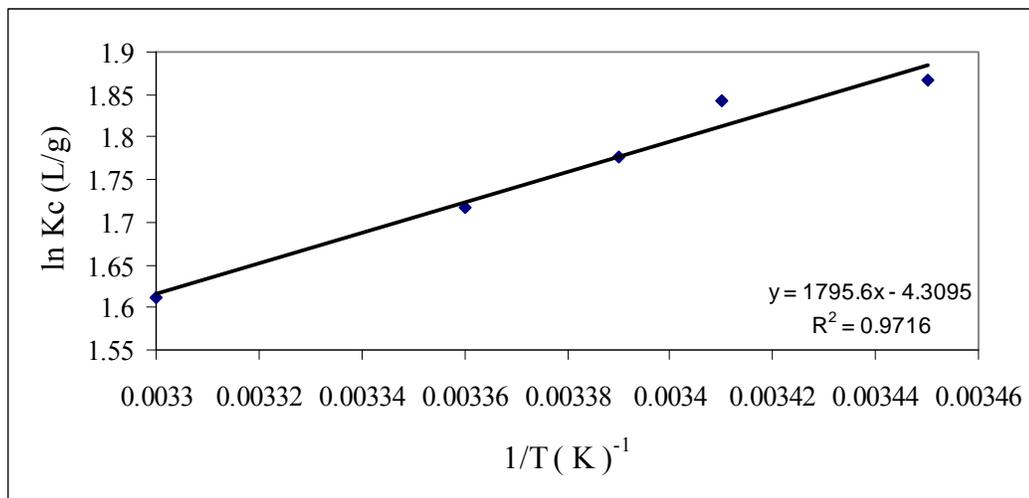


Figure 3.3.13: Standard thermodynamic equilibrium constant for GEMX on charcoal vs. temperature

The enthalpy change (ΔH°), was obtained from the slope of a linear plot between $\ln K_c$ versus $1/T$ and the entropy change (ΔS°) was calculated from the intercept of the plot as in (Fig.3.3.12)

Using Gibbs-Helmholtz equation $\Delta S^\circ = [\Delta H^\circ - \Delta G^\circ] / T$

The calculated thermodynamic parameters are shown in (Table 3.3.6)

Table 3.3.6: Thermodynamic parameters for GEMX on charcoal

Temperature (k)	Thermodynamic parameters		
	ΔG° (kJ/mol)	ΔS° (kJ/(mol))	ΔH° (kJ/mol)
290	-4.49	0.0360	-14.93
293	-4.38	0.0360	-14.93
295	-4.31	0.0360	-14.93
298	-4.20	0.0360	-14.93
303	-4.02	0.0360	-14.93

The negative values of Gibb's free energy G_o indicates that the feasibility of the adsorption process and spontaneous adsorption of GEMX to charcoal. The negative value of enthalpy H° shows that the adsorption process has an exothermic nature, and that the possibility of physical adsorption as increasing the temperature in nature of chemical effect. The total entropy change for a reaction enables us to predict feasibility. Spontaneous reactions are found to involve an increase in:

$$(\Delta S_{total}) = \Delta S_{system} + \Delta S_{surroundings}$$

But, the change in entropy of the surroundings is brought about by the enthalpy change in the system. When the system loses heat, the surroundings gain heat and vice versa.

Thus $\Delta S_{\text{surroundings}} = -\Delta H_{\text{system}}/T$. Spontaneous reactions therefore involve an increase in: $\Delta S_{\text{system}} - \Delta H_{\text{system}}/T = \Delta S_{\text{total}}$ i.e. the value of this function is positive for spontaneous changes, so $\Delta S_{\text{total}} = 0.036$ and this positive value of S° means that there is an increase in the degree of freedom and entropy of the adsorbed species.

3.3.1.h. Effect of Particle Size of Charcoal on GEMX Adsorption

The high amount adsorbed by charcoal is due to high surface area charcoal particles have as can be seen in a scanning electron micrograph of a particle of activated charcoal. Along with the tremendous surface area of charcoal there are the pores that tunnel into the actual charcoal particles as in (Fig. 3.3.14(A,B)).^[53]

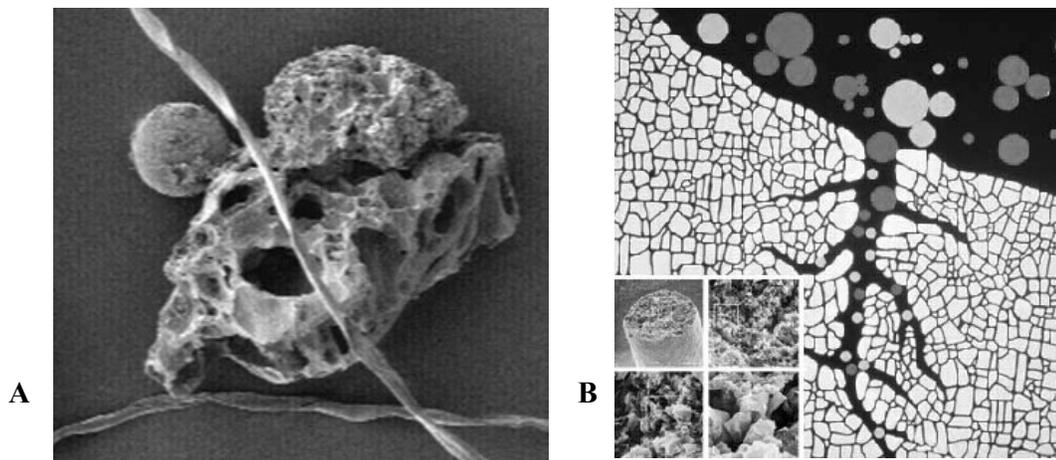


Figure 3.3.14: A: Scanning electron micrograph of a particle of activated charcoal

B: The pores that tunnel into the actual charcoal particles

3.3.2 Adsorption of GEMX onto Kaolin

3.3.2.a Adsorption of GEMX onto kaolin: Time Dependency

Different initial concentrations of standard solution of GEMX were adsorbed onto 0.01 ± 0.001 g kaolin; concentrations for GEMX remaining with time are in (Table 3.3.7).

Table 3.3.7: Values of concentration for GEMX remaining with time

C₁ (ppm)	C₂ (ppm)	C₃ (ppm)	C₄ (ppm)	Time(min)
6.15	14.43	18.34	23.9	0
5.33	14.00	16.75	22.47	5
5.17	13.30	16.40	22.23	10
4.92	13.28	16.36	21.67	15
4.85	13.23	16.23	21.58	20
4.84	13.19	16.22	21.40	30
4.80	13.16	16.20	21.12	45
4.77	12.90	16.19	21.10	60

The results showed that the decrease in concentration of GEMX remaining in solution was slow until equilibrium was reached after 1 hour contact between kaolin and GEMX as shown in (Fig.3.3.15)

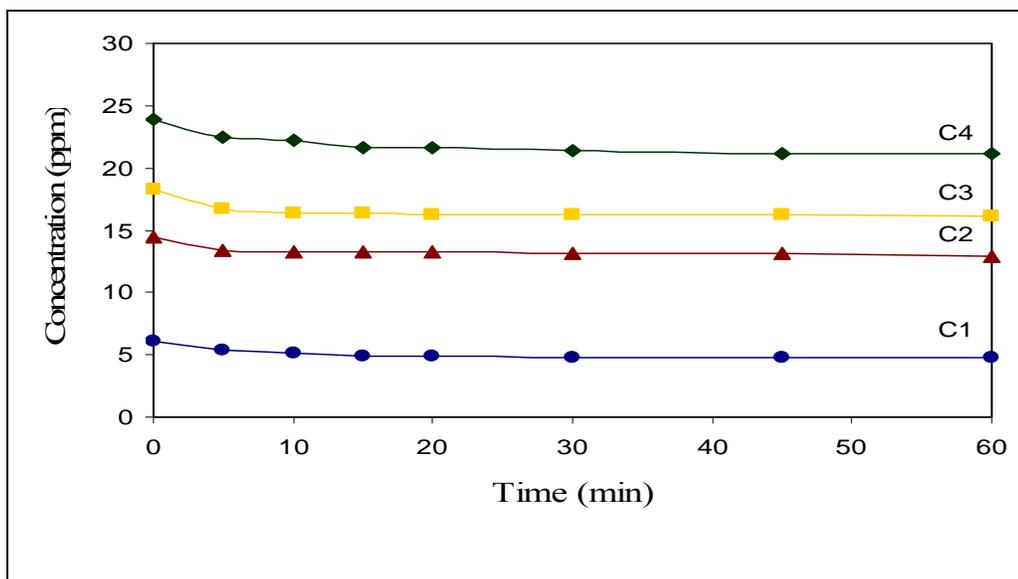


Figure 3.3.15: Concentrations of GEMX remaining vs. time with kaolin

3.3.2.b Equilibrium Study between GEMX and Kaolin

Equilibrium concentrations and amounts adsorbed for different initial concentrations of GEMX onto 0.01± 0.001g of kaolin after 1 hour were calculated as shown in (Table 3.3.8).

Table 3.3.8: Equilibrium concentrations and amounts adsorbed of GEMX onto kaolin

C_o ppm	C_e ppm	y_e mg/g	$1/C_e$ ppm ⁻¹	$1/y_e$ (mg/g) ⁻¹	Log C_e ppm	Log y_e mg/g
6.15	5.03	11.20	0.199	0.089	0.72	1.05
14.43	12.90	15.3	0.078	0.065	1.11	1.185
18.34	16.19	21.5	0.062	0.047	1.21	1.33
23.90	21.10	28	0.047	0.036	1.32	1.45

Two adsorption isotherms were used to study adsorption behavior of GEMX onto kaolin clearly, the adsorption followed Freundlich isotherm better than Langmuir isotherm because R^2 in Freundlich isotherm is nearer to unity. Langmuir isotherm was obtained from a plot of $1/y_e$ versus $1/C_e$, as in (Fig.3.3.16).

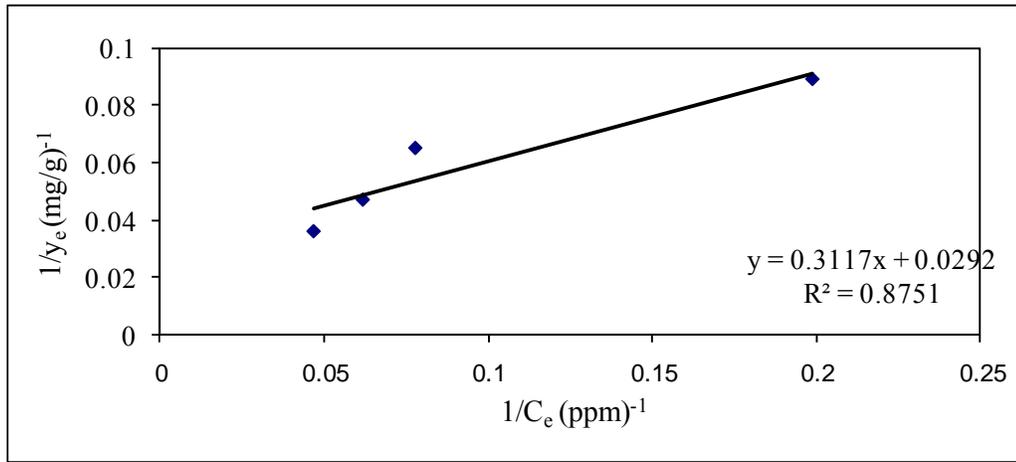


Figure 3.3.16: Langmuir isotherm for adsorption of GEMX on kaolin

Freundlich isotherm was obtained from the relation between $\text{Log } y_e$ versus $\text{Log } C_e$ as shown in (Fig.3.3.17).

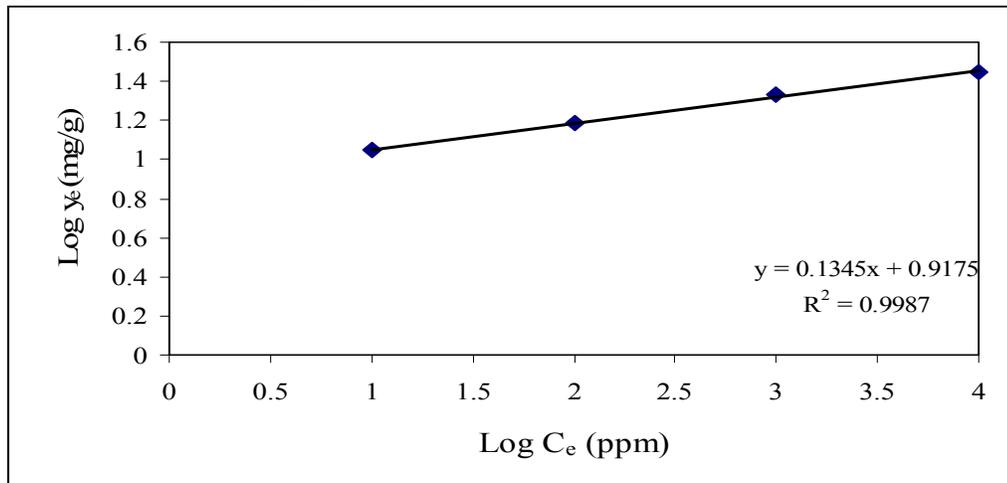


Figure 3.3.17: Freundlich isotherm for adsorption of GEMX on kaolin

From Freundlich isotherm $K_f = 0.04$ mg/g (measure of adsorption capacity). This poor adsorption capacity of kaolin has been attributed to its small surface area and weak electrostatic attraction between GEMX and kaolin, due to large particle size of kaolin and its existence as layers made the ability of adsorption so weak, as in (Fig.3.3.18).^[54]

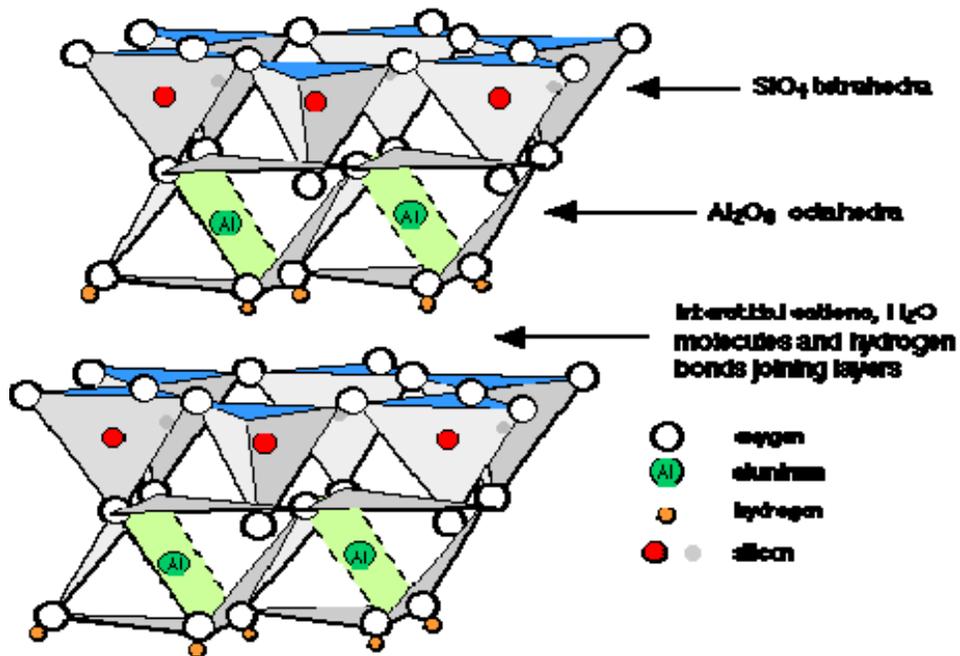


Figure 3.3.18: Structure of a clay, two layers of the stacked sheets of kaolinite

So when comparing the particle size of kaolin with that of charcoal(Fig.3.3.14), the smaller the particle size of the adsorbent the higher the surface area and so higher adsorption capacity.

3.3.2.c Effect of Amount of Kaolin on Adsorption of GEMX

The amount adsorbed of GEMX (X) and the amount adsorbed onto kaolin (y_e) and % removal of GEMX versus different weights of kaolin (m) to the time of equilibrium were calculated as in (Table 3.3.9)

Table 3.3.9: Values of C_e , X , y_e & % y_e for GEMX vs. weight of kaolin

C_o (mg/L)	C_e (mg/L)	X (mg)	y_e (mg/L)	% y_e removal	m (g)
19.29	17.91	0.138	23.00	7.15	0.006
19.29	17.75	0.204	19.25	7.98	0.008
19.29	14.48	0.481	12.03	24.93	0.040
19.29	13.07	0.622	6.22	32.24	0.100

The % removal of GEMX increases as the amount of adsorbent increases as shown in (Fig.3.3.19).

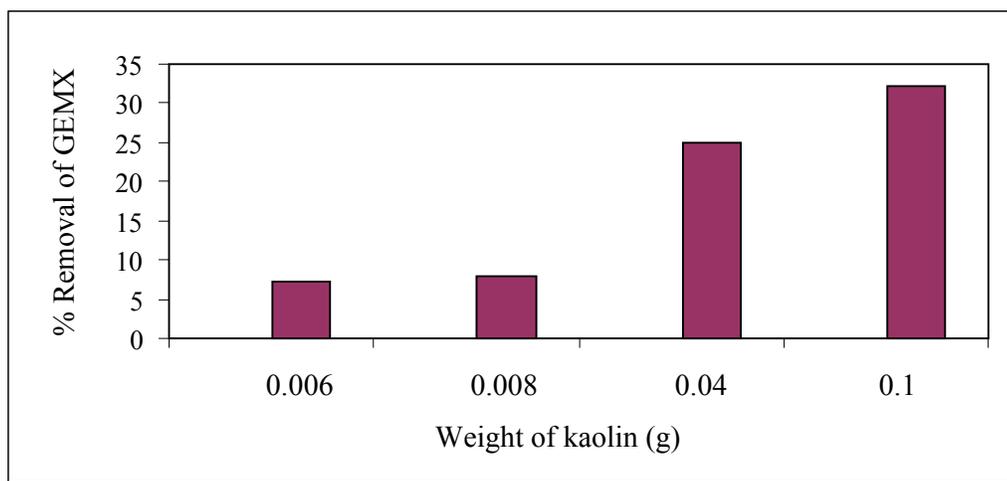


Figure 3.3.19: The % removal of GEMX on kaolin vs. weight of kaolin

The increase in amount % removal of GEMX can be attributed to availability of more adsorption sites.

The amount adsorbed of GEMX (X) increases as the amount of adsorbent increases as shown in (Fig.3.3.20).

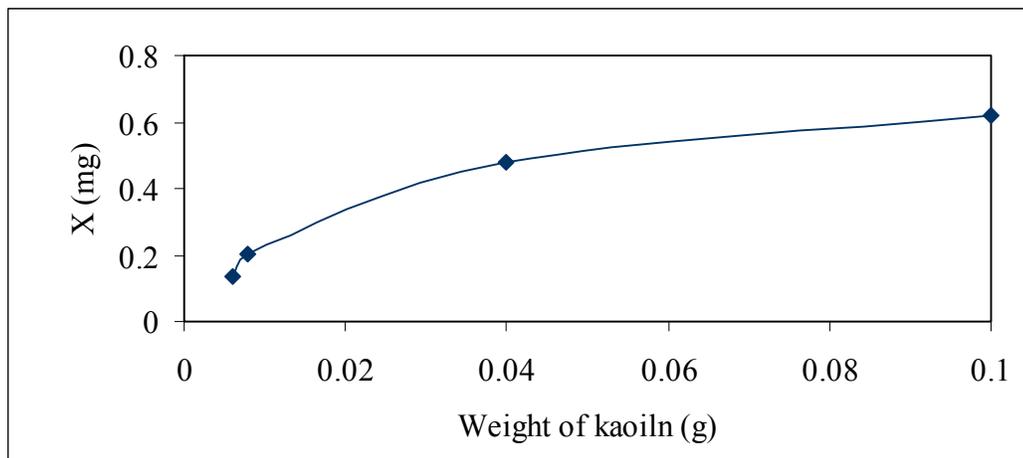


Figure 3.3.20: The amount adsorbed of GEMX on kaolin vs. weight of kaolin

Amount of GEMX adsorbed in respect to each weight (y_e) decreases as amount of kaolin used increases as in (Fig.3.3.21).

The decrease in adsorption capacity may be due to overlapping adsorbent's sites that result in decrease in the surface area available to GEMX, when the adsorbent amount 0.006g adsorption capacity was high, due to higher driving force to overcome any resistance of GEMX molecules from adsorption to kaolin.

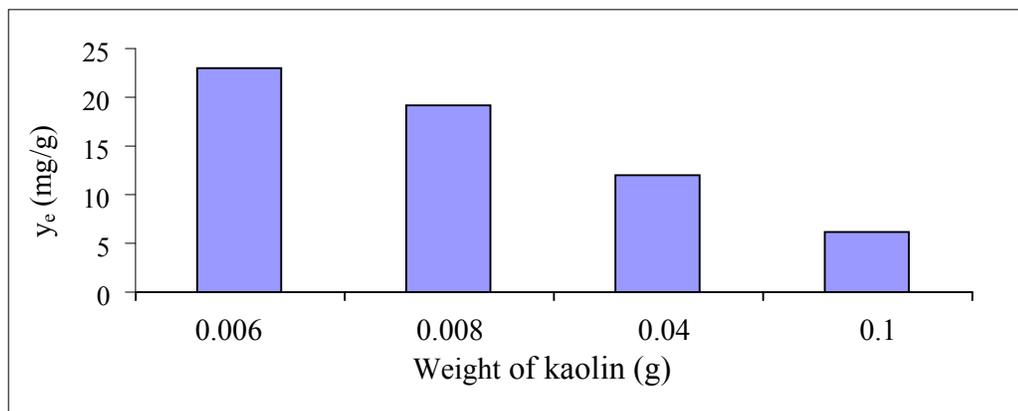


Figure 3.3.21: The amount adsorbed of GEMX on kaolin versus weight of kaolin

3.3.2.d Effect of pH on Adsorption of GEMX onto kaolin

The amount of GEMX solutions with same initial concentration adsorbed onto 0.01 ± 0.001 g of kaolin were calculated versus different pH values at 25 ± 1 C⁰, and effect of pH on adsorption extent of GEMX was investigated as shown in (Fig.3.3.22).

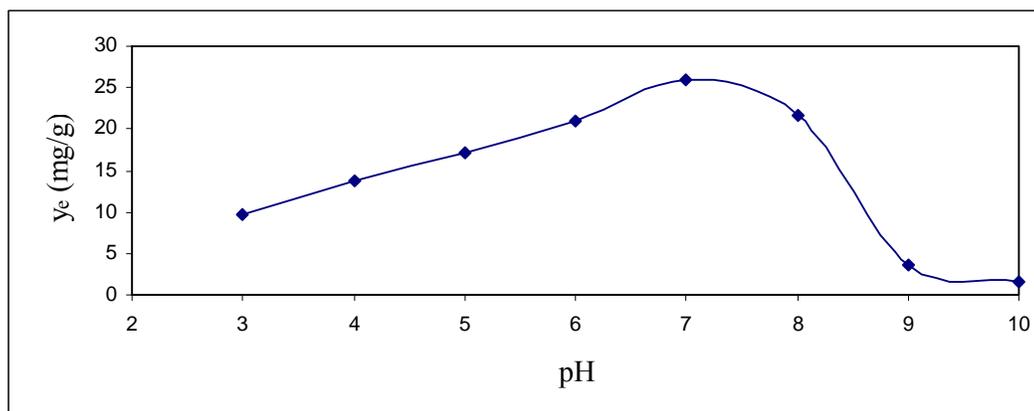


Figure 3.3.22: The amount adsorbed of GEMX on kaolin vs. pH

The result showed an increase in adsorption quantities of GEMX on kaolin clays surfaces at pH=7, due to specific and stronger attraction between the surface and the drug molecules than attraction between solvent – solute leading to an increase in the quantity adsorbed, kaolin is a polar adsorbent having both positive and negative charges and GEMX at pH=7 is in zwitterionic form so the adsorption will be the most.

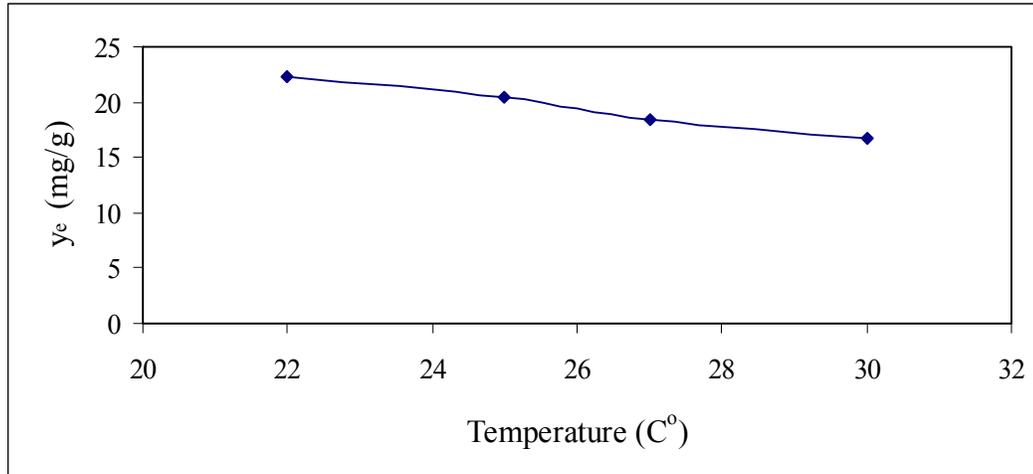
3.3.2.e Adsorption of GEMX onto kaolin versus Temperature

Adsorption was investigated as a function of temperature and amount of GEMX solutions with the same initial concentration adsorbed into 0.01 ± 0.001 g of kaolin were calculated at equilibrium time versus different temperature, values in (Table 3.3.10).

Table 3.3.10: Adsorption of GEMX on charcoal vs. of temperature

Temperature		1/T k ⁻¹	C _o (ppm)	C _e (ppm)	y _e (mg/g)	K _c (L/g)	Ln K _c (L/g)
C ^o	k						
22	295	0.00339	18.4	16.17	22.3	1.38	0.322
25	298	0.00336	18.4	16.35	20.5	1.25	0.226
27	300	0.00333	18.4	16.56	18.4	1.11	0.105
30	303	0.00330	18.4	16.72	16.8	1.005	0.005

As the temperature increased the amount of GEMX adsorbed on charcoal decreased, as shown in (Fig 3.3.23).

**Figure 3.3.23: Amount adsorbed of GEMX on kaolin versus temperature**

Thermodynamic parameters including: (ΔG°), (ΔS°) and (ΔH°) were determined from equation: $\text{Ln } K_c = (\Delta S^{\circ}/R) - (\Delta H^{\circ}/RT)$

(ΔH°) was obtained from the slope of a plot between Ln K_c versus 1/T and (ΔS°) was calculated from the intercept as shown in (Fig.3.3.24)

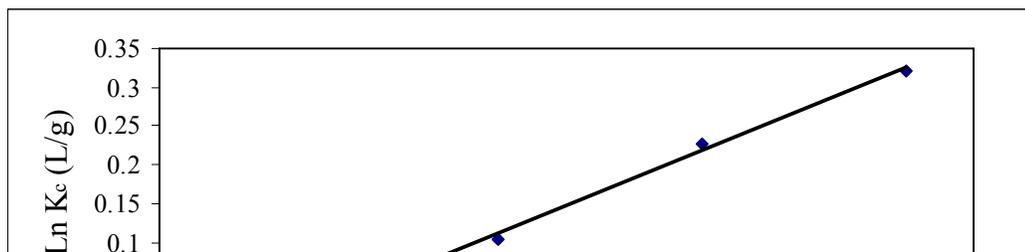


Figure 3.3.24: Standard thermodynamic equilibrium constant for GEMX on kaolin versus temperature

The calculated thermodynamic parameters are shown in (Table 3.3.11)

Table 3.3.11: Thermodynamic parameters for GEMX on kaolin

Temperature (k)	Thermodynamic parameters		
	ΔG° (kJ/mol)	ΔS° (kJ/(mol))	ΔH° (kJ/mol)
295	-58.62	0.098	-29.71
298	-58.91	0.098	-29.71
300	-59.11	0.098	-29.71
303	-59.40	0.098	-29.71

The negative values of Gibb's free energy G_o indicates spontaneous adsorption of GEMX to kaolin. The negative value of enthalpy H° shows that the adsorption process has an exothermic nature; total entropy change for a reaction enables us to predict feasibility. The change in entropy of the surroundings is brought about by the enthalpy change in the system.

When the system loses heat, the surroundings gain heat and vice versa.

Thus $\Delta S_{\text{surroundings}} = -\Delta H_{\text{system}}/T$. Spontaneous reactions therefore involve an

increase in: $\Delta S_{\text{system}} - \Delta H_{\text{system}}/T = \Delta S_{\text{total}}$ i.e. the value of this function is positive for spontaneous changes, so $\Delta S_{\text{total}} = 0.036$, a positive value of S° means that there is an increase in the degree of freedom and entropy of species.

3.3.3. Adsorption of GEMX onto Alumina

3.3.3.a Adsorption of GEMX onto Alumina: Time Dependency

Different initial concentrations of standard solution of GEMX were adsorbed onto $0.2 \pm 0.001\text{g}$ alumina, the concentration decreases with time as shown in (Table 3.3.12).

Table 3.3.12: Values of concentration for GEMX remaining with time

Time(min)	C₁(ppm)	C₂(ppm)	C₃(ppm)	C₄(ppm)	C₅(ppm)
0	6.43	10.32	14.67	20.29	23.7
5	5.75	8.54	12.99	17.81	20.23
10	5.53	8.22	12.03	16.94	19.7
20	5.52	7.86	10.81	15.32	19.29
30	5.14	7.53	10.06	15.16	18.6
45	4.99	7.08	9.71	14.22	17.73
60	4.68	6.9	9.36	14.15	17.44

The results showed that a decrease in concentration of GEMX remaining in solution with time as shown in (Fig.3.3.25) until pseudo-adsorption equilibrium was reached after 1 hour.

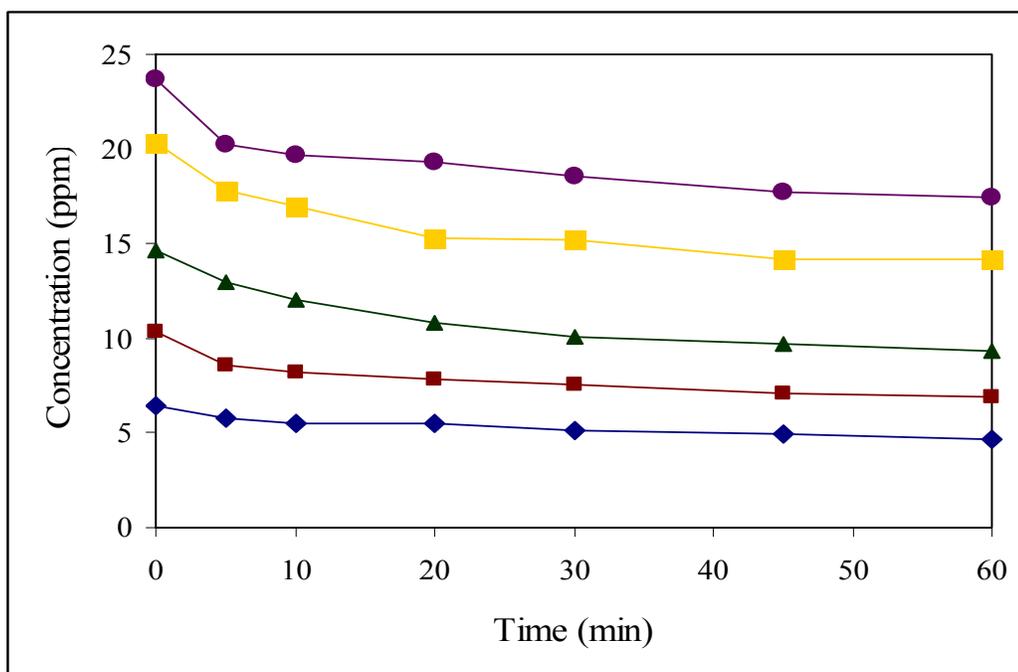


Figure 3.3.25: Concentrations of GEMX remaining vs. time with alumina

3.3.3.b Equilibrium Study between GEMX and Alumina

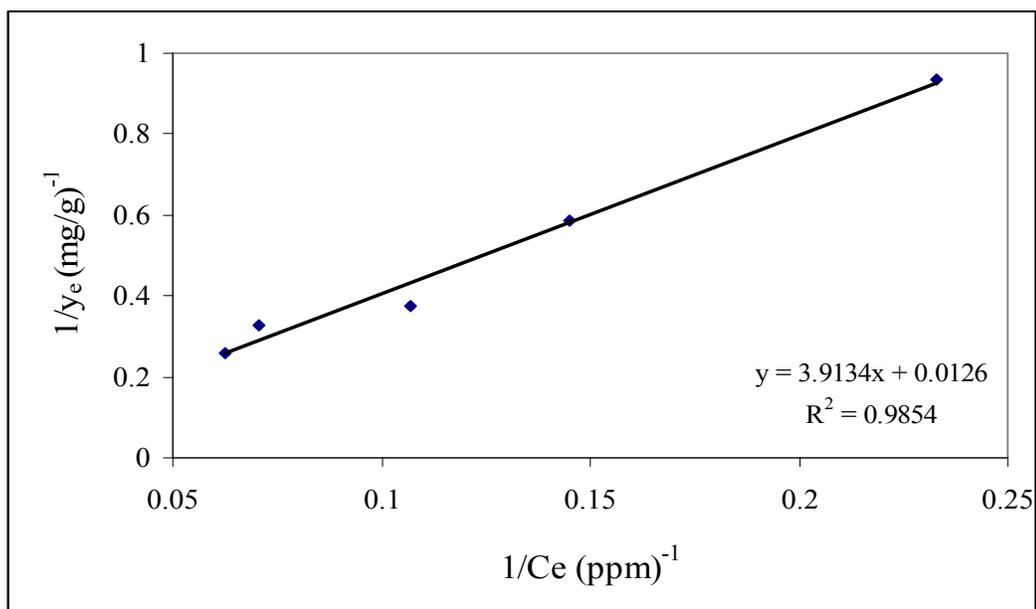
Equilibrium concentrations (C_e) and amounts of GEMX adsorbed onto alumina (y_e) were calculated, as shown in (Table 3.3.13).

Two adsorption isotherms (Langmuir & Freundlich) were used to study adsorption behavior of GEMX onto alumina clearly:

Langmuir isotherm was obtained from the relation between $1/y_e$ vs. $1/C_e$ as shown in (Fig.3.3.26), and Freundlich isotherm was obtained from the relation between $\text{Log } y_e$ vs. $\text{Log } C_e$ as shown in (Fig.3.3.27).

Table 3.3.13: Values of C_e and y_e of GEMX on adsorbed alumina

C_o Ppm	C_e ppm	y_e mg/g	$1/C_e$ ppm ⁻¹	$1/y_e$ (mg/g) ⁻¹	Log C_e ppm	Log y_e (mg/g)
6.43	4.68	0.875	0.214	1.143	0.67	-0.06
10.32	6.90	1.710	0.145	0.585	0.84	0.23
14.67	9.36	2.655	0.107	0.377	0.97	0.42
20.29	14.15	3.070	0.071	0.326	1.15	0.49
23.70	17.44	3.130	0.057	0.320	1.24	0.50

**Figure 3.3.26: Langmuir isotherm for adsorption of GEMX on alumina**

The adsorption followed Langmuir isotherm better than Freundlich isotherm because R^2 in Langmuir isotherm is nearer to unity.

From Langmuir isotherm equation: $y_{\max} = 0.26 \text{ mg/g}$, $K_A = 310.6$

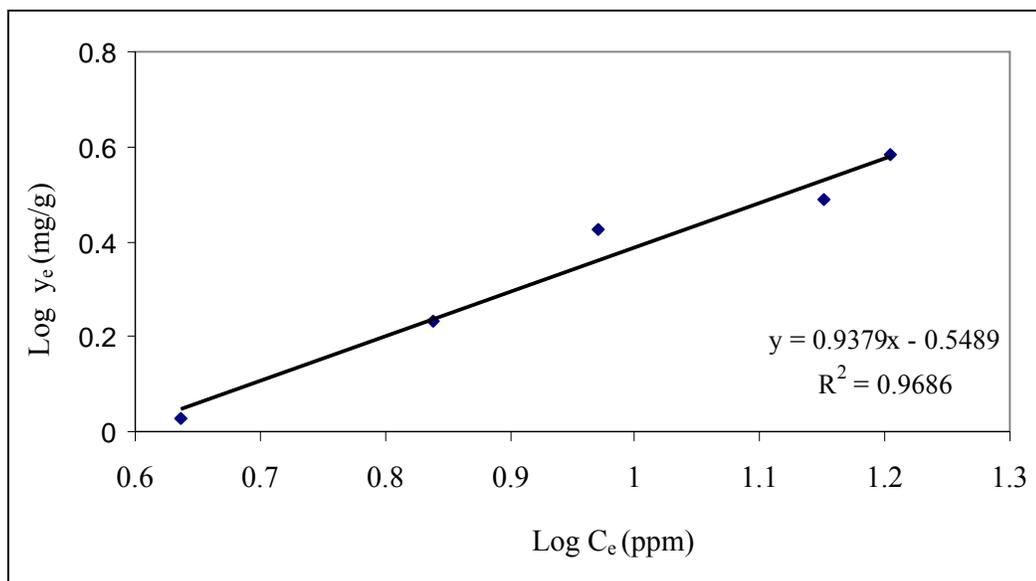


Figure 3.3.27: Freundlich isotherm for adsorption of GEMX on alumina

3.3.3.c Effect of Weight of Alumina on Adsorption of GEMX

Amount adsorbed of GEMX on alumina (y_e) and % removal ($\%y_e$) were calculated for same initial concentration of GEMX versus different weights of alumina(m), the values are in (Table 3.3.14).

Table (3.3.14): Adsorption values for GEMX vs. weight of alumina

C _o (mg/L)	C _t (mg/L)	y _e (mg/g)	% y _e removal	m (g)
20.754	18.071	13.416	12.93	0.02
20.754	17.453	8.251	15.91	0.04
20.286	13.400	6.886	33.94	0.1
20.286	13.623	3.332	32.85	0.2
20.754	9.831	2.731	50.63	0.4

The % removal of GEMX increases as the amount of alumina adsorbent increases as shown in (Fig 3.3.28). This can be attributed to greater surface area and more adsorption sites are available.

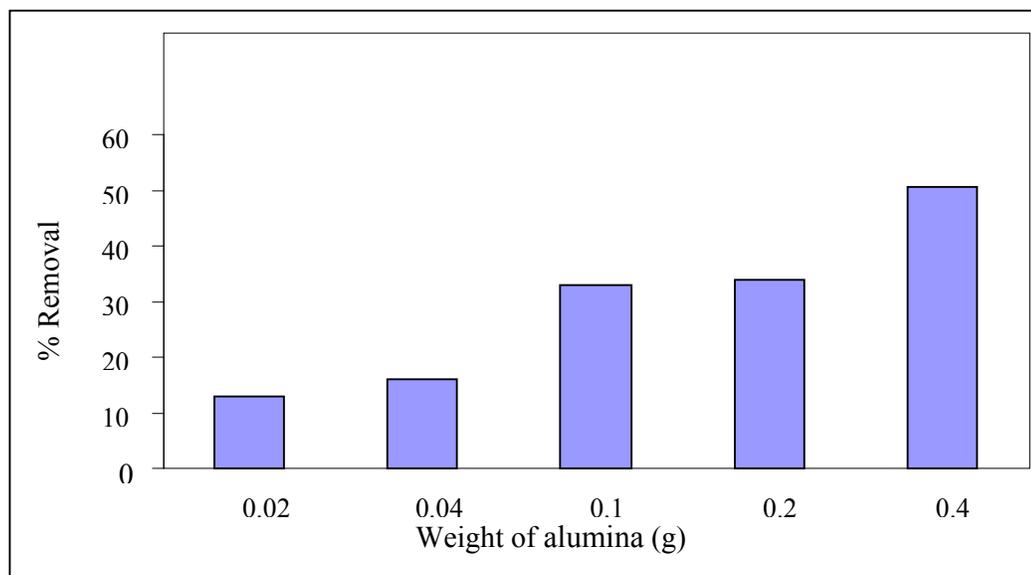


Figure 3.3.28: The % removal of GEMX vs. weight alumina

The amount of GEMX adsorbed on alumina (y_e) decreases as amount of alumina increases because alumina capacity decreases as can be seen in (Fig.3.3.29). This may be due to overlapping and saturation of adsorbent's sites of that result in decrease in the surface area available to GEMX. When adsorbent amount low the sites are freely attached to GEMX but as alumina increases condensation of sites prevent GEMX to reach to alumina and bind. 0.2g of alumina was considered the suitable weight for further studies.

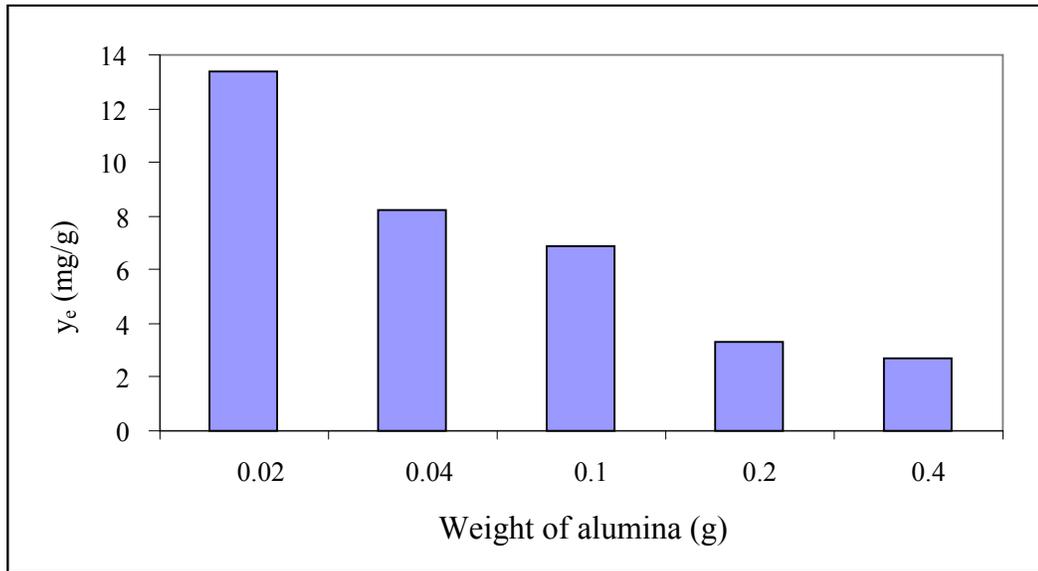


Figure 3.3.29: Amount of GEMX adsorbed vs. weight of alumina

3.3.3.d Effect of pH on the Adsorption of GEMX on Alumina

The amount of GEMX adsorbed versus pH is shown in (Fig.3.3.30).

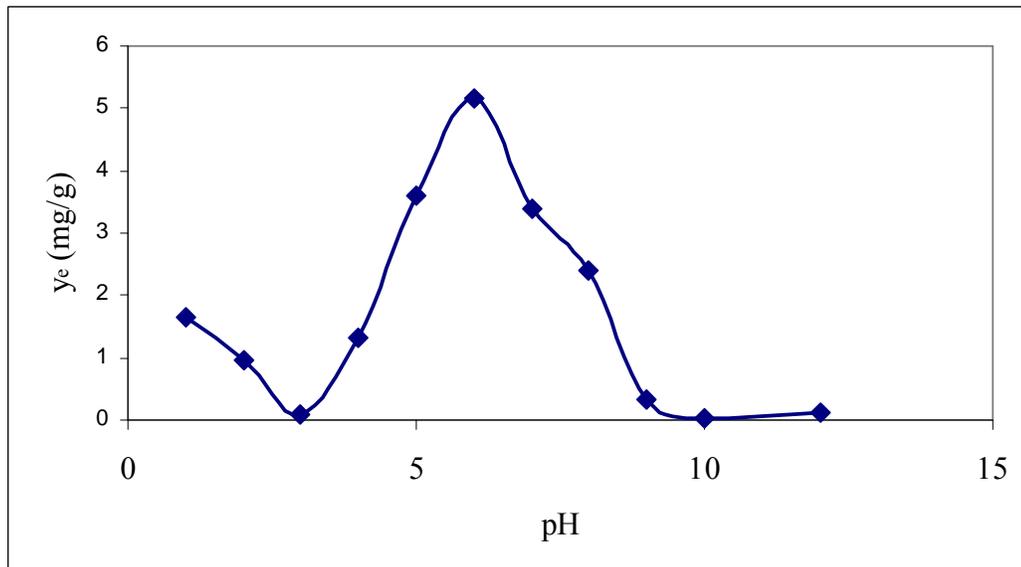


Figure 3.3.30: Amount adsorbed of GEMX onto alumina versus pH

Factors that played a role in this field are:

1- Alumina properties: point of zero charge (PZC), or isoelectric point (pI): the pH at which positive charge equals negative charge. For alumina pI at pH=5-8 (positive = negative), at pH < 5 the net charge of alumina is positive and anionic adsorption occurs and at pH > 8 the net charge of alumina is negative and cationic adsorption occurs.^[43]

2- GEMX properties (pKa: dissociation constant): GEMX has two proton binding sites (carboxyl and piperazinyll group) with pKa₁ = 5.76, pKa₂ =8.4 and pI=7.08^[52]The values were obtained from titration of GEMX against acid and alkali respectively. GEMX can exist in four forms (neutral, zwitterionic, anionic and cationic) when pH < 5.76 (the cationic form or +ve charged is dominant), at pH 5.76 - 8.40 (neutral, cationic, anionic and zwitterionic forms present) the last is dominant) and when pH > 8.40 (anionic form or -ve charged is dominant).^[52]

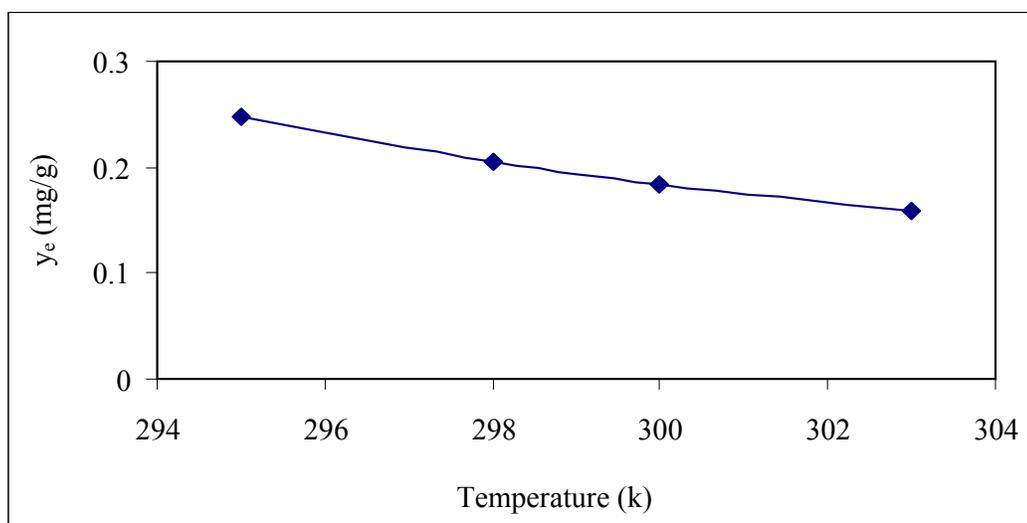
3- pH of solution: it was 7, where the zwitterionic form is dominant, causes adsorption of GEMX on alumina becomes significant at pH range (4 - 8.5), but the highest adsorption was at pH about 6, which was near the pKa₁ of GEMX, at this pKa the carboxyl group was half ionized (negatively charged and neutral charge), at pH 9 adsorption declined, where alumina had negative charge and GEMX was in anionic form.

3.3.3.e Adsorption of GEMX onto Alumina versus Temperature

Amount of GEMX adsorbed into 0.2g alumina was calculated for time of 1hour versus different temperature, values are in (Table 3.3.15)

Table 3.3.15: Adsorption of GEMX onto Alumina vs. temperature

Temperature		1/T k ⁻¹	C _o (ppm)	C _e (ppm)	y _e (mg/g)	K _c (L/g)	Ln K _c (L/g)
C ^o	k						
22	295	0.00339	20.01	13.37	3.32	0.248	-1.393
25	298	0.00336	20.01	14.19	2.91	0.205	-1.584
27	300	0.00333	20.01	14.65	2.68	0.183	-1.698
30	303	0.00330	20.01	15.17	2.42	0.159	-1.835

**Figure 3.3.31: Amount adsorbed of GEMX on alumina versus temperature.**

From A plot of Ln K_c versus 1/T, the enthalpy change (ΔH°) and the entropy change (ΔS°) were obtained as in (Fig.3.3.32).

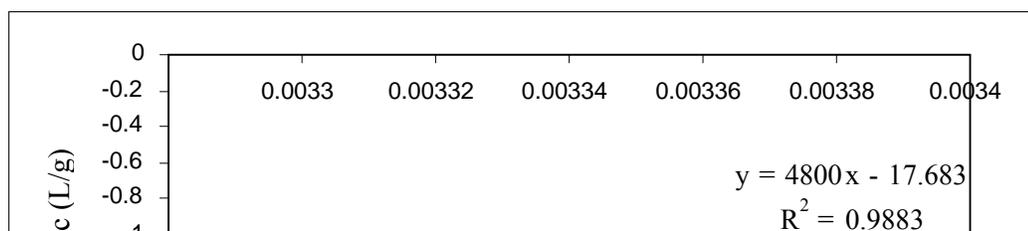


Figure 3.3.32: Standard thermodynamic equilibrium constant for GEMX on alumina versus temperature.

The calculated thermodynamic parameters are shown in (Table 3.3.16)

Table 3.3.16: Thermodynamic parameters for GEMX on alumina

Temperature(k)	Thermodynamic parameters		
	ΔG° (kJ/mol)	ΔS° (kJ/mol)	ΔH° (kJ/mol)
295	-83.265	0.147	-39.9
298	-83.706	0.147	-39.9
300	-84.000	0.147	-39.9
303	-84.441	0.147	-39.9

The negative values G° and enthalpy H° indicates the adsorption of GEMX onto alumina is spontaneous and has an exothermic nature. $\Delta S_{total} = 0.147$ and this positive value of S° means that there is an increase in the degree of freedom and entropy (as mentioned in charcoal).

3.3.4 Adsorption of GEMX onto Silica gel

3.3.4.a Effect of Weight of Silica gel on adsorption of GEMX

The amount (y_e) adsorbed on silica gel and % removal after 1 hour of same initial concentration of GEMX solutions were calculated versus weight of silica (Table 3.3.17).

Table 3.3.17: X , y_e and % removal of GEMX vs. weight of silica

C_o (mg/L)	C_t (mg/L)	X (mg)	y_e (mg/g)	% removal (% y_e)	Weight of silica (g)
19.61	17.15	0.246	2.46	12.54	0.1
19.61	16.67	0.294	1.47	15	0.2
19.61	16.12	0.349	0.87	17.8	0.4
19.61	15.58	0.403	0.4	20.6	1g

The % removal of GEMX adsorbed on silica increased as the amount of silica adsorbent increased as shown in (Fig 3.3.33)

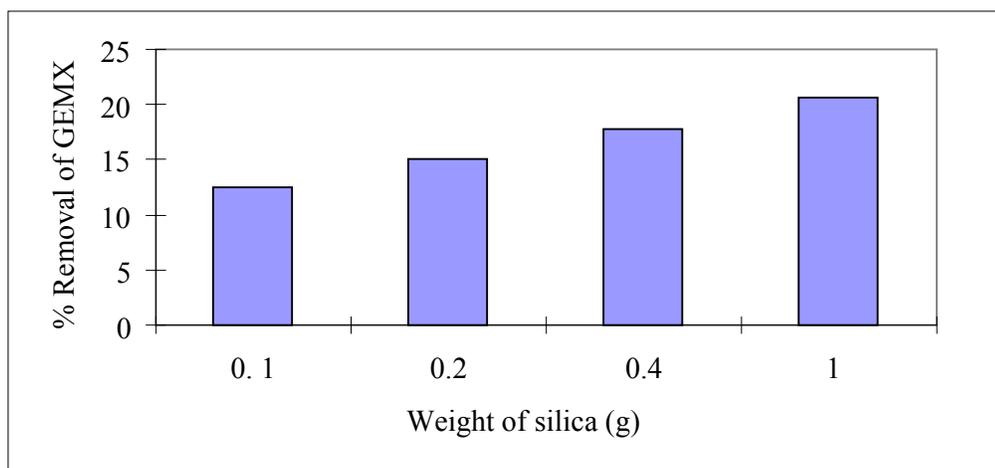


Figure 3.3.33: % y_e adsorbed of GEMX vs. weight of silica

The amount adsorbed of GEMX: X (mg) increased as the amount of silica adsorbent increased as shown in (Fig 3.3.34). This can be attributed to greater surface area and more adsorption sites are available.

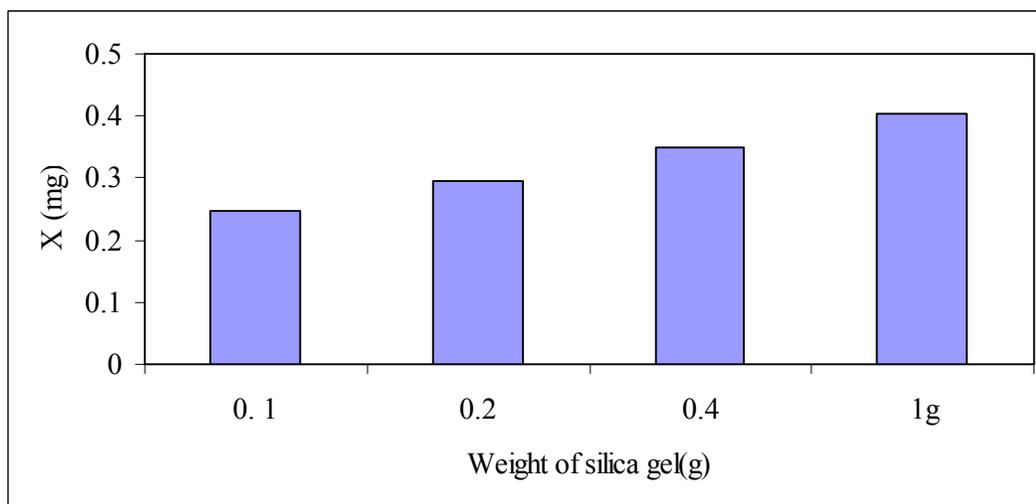


Figure 3.3.34 Amount adsorbed of GEMX (X) vs. weight of silica

The amount of GEMX adsorbed per weight of silica (y_e) decreases as the weight of silica used increases as shown in (Fig.3.3.35).

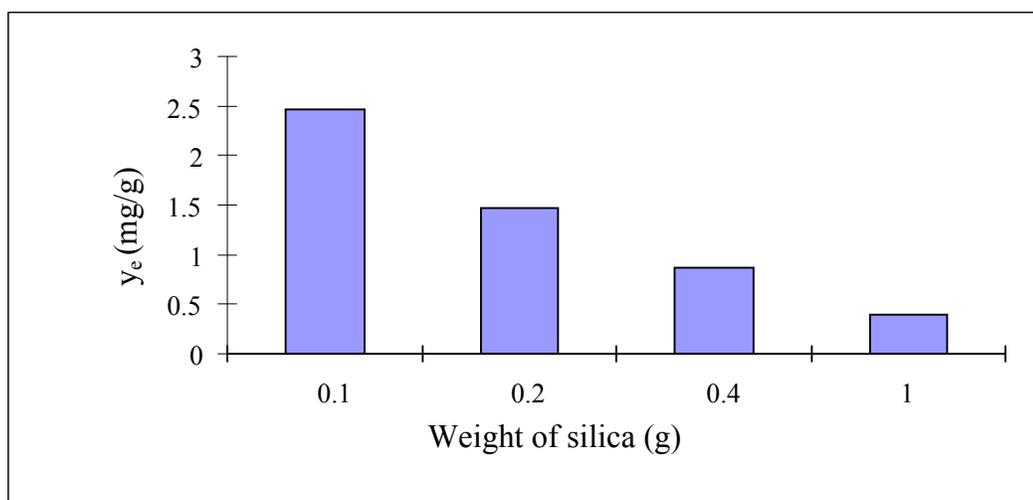


Figure 3.3.35 Amount adsorbed of GEMX per weight (y_e) vs. weight of silica

3.3.4.b Adsorption of GEMX onto Silica Gel versus Concentration

Amount adsorbed of different initial concentrations of GEMX solutions onto 0.4g silica gel at equilibrium (y_e) and % removal of GEMX were calculated, the values are in (Table 3.3.18).

Table 3.3.18: Values of C_o , C_e , y_e and % removal of GEMX on silica

C_o ppm	C_e ppm	y_e mg/g	$1/C_e$ ppm ⁻¹	$1/y_e$ (mg/g) ⁻¹	Log C_e ppm	Log y_e mg/g
5.44	4.5	0.235	0.22	4.255	0.65	-0.63
10.37	8.72	0.413	0.115	2.42	0.94	-0.38
15.20	12.7	0.625	0.08	1.6	1.1	-0.204
19.61	16.12	0.873	0.062	1.15	1.2	-0.06

The amount adsorbed of GEMX on silica gel increases as the initial concentration of GEMX increases, as shown in (Fig.3.3.37)

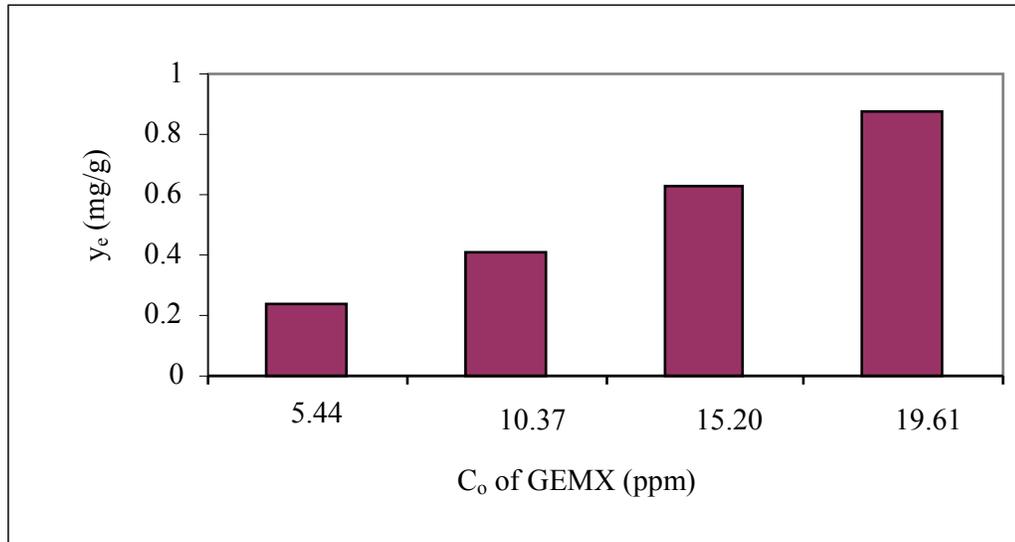


Figure 3.3.36: y_e of GEMX vs. initial concentration of GEMX (C_o)

Two adsorption isotherms (Langmuir and Freundlich) were used to study adsorption behavior of GEMX onto charcoal clearly.

Langmuir isotherm was obtained from a plot of $1/y_e$ vs. $1/C_e$ as shown in (Fig.3.3.37)

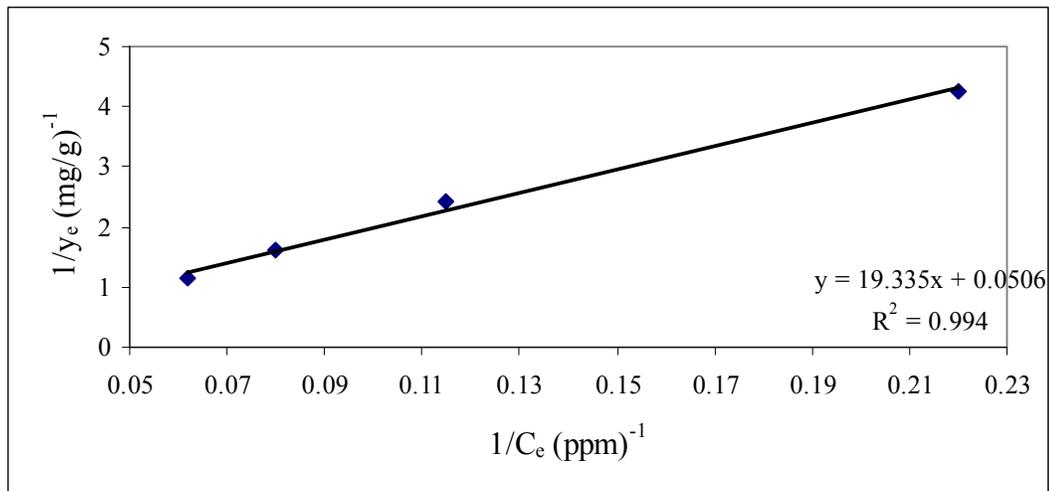


Figure 3.3.37: Langmuir isotherm for adsorption of GEMX on silica

Freundlich isotherm was obtained from a plot of $\text{Log } y_e$ versus $\text{Log } C_e$ as shown in (Fig.3.3.38).

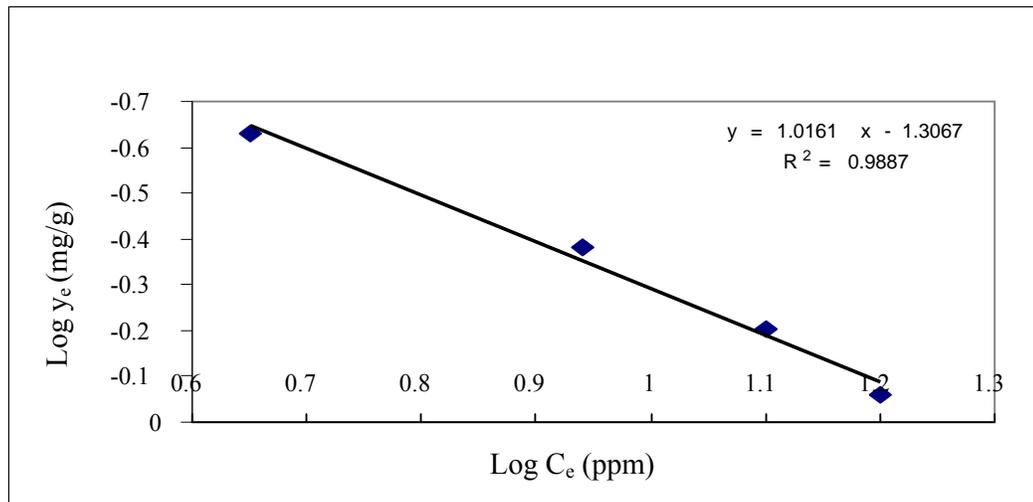


Figure 3.3.38: Freundlich isotherm for adsorption of GEMX on silica

The adsorption of GEMX onto silica followed isotherm Langmuir better than Freundlich isotherm, from Langmuir isotherm $y_{\max} = 19.76 \text{ mg/g}$

3.3.4.c Adsorption of GEMX onto Silica Gel versus pH

The amount of GEMX solutions with the same initial concentration adsorbed onto same amount of silica were calculated at equilibrium time versus different pH in the range (2-12), as shown in (Fig.3.3.38).

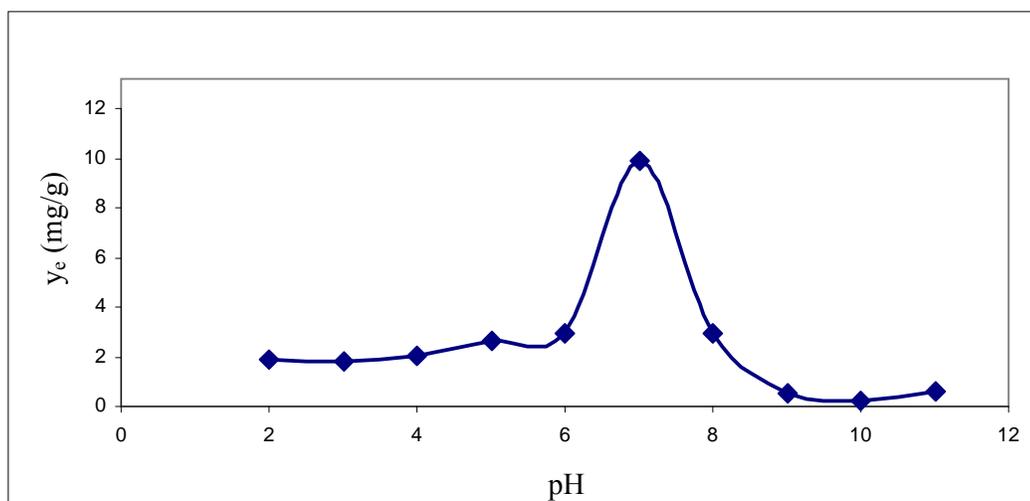


Figure 3.3.39: Amount adsorbed of GEMX onto silica gel versus pH

Adsorption to silica is significant in pH (6-8). The maximum adsorption of GEMX to silica occurred at pH=7, which is the point of zero charge of silica, where the maximum adsorption occurred zwitterions are dominant. At pH lower than 7, silica is positively charged adsorption low, and as the pH increases the silica surface became negatively charged and adsorption decreases, as noticed from the previous studies adsorption of GEMX to alumina is noticeably greater than that to silica. The cationic and zwitterionic GEMX are adsorbed to the negatively charged silica surfaces via the protonated N in the piperazinyl group.

3.3.4.d Adsorption of GEMX onto Silica Gel versus Temperature

Adsorption was investigated as a function of temperature and amount of GEMX adsorbed into 0.4g silica gel was calculated for constant initial concentration of GEMX solution, as shown in (Table 3.3.19)

Table 3.3.19: Effect of temperature on adsorption of GEMX on silica

Temperature		1/T	C _o	C _e	y _e	K _c	Ln K _c
C ^o	k	k ⁻¹	(ppm)	(ppm)	(mg/g)	(L/g)	(L/g)
22	295	0.00339	20.01	16.518	0.873	0.053	-2.94
25	298	0.00336	20.01	17.094	0.729	0.043	-3.15
27	300	0.00333	20.01	17.366	0.661	0.038	-3.27
30	303	0.00330	20.01	17.786	0.556	0.031	-3.47

As the temperature increased the amount of GEMX adsorbed on silica decreased, as shown in (Fig 3.3.40).

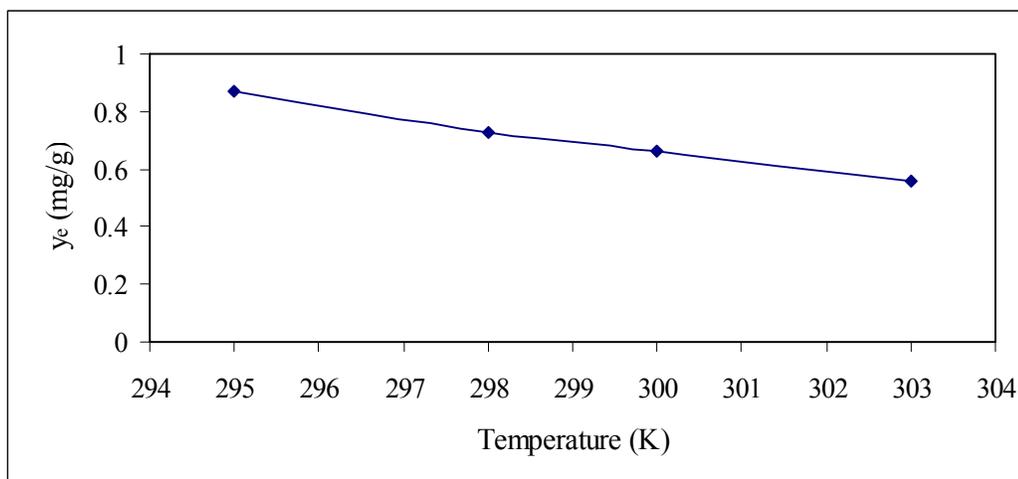


Figure 3.3.40: Amount adsorbed of GEMX on silica versus temperature.

A linear plot between $\ln K_c$ versus $1/T$, (ΔH°) and (ΔS°) was obtained from the slope and the intercept of the plot as in (Fig.3.3.41)

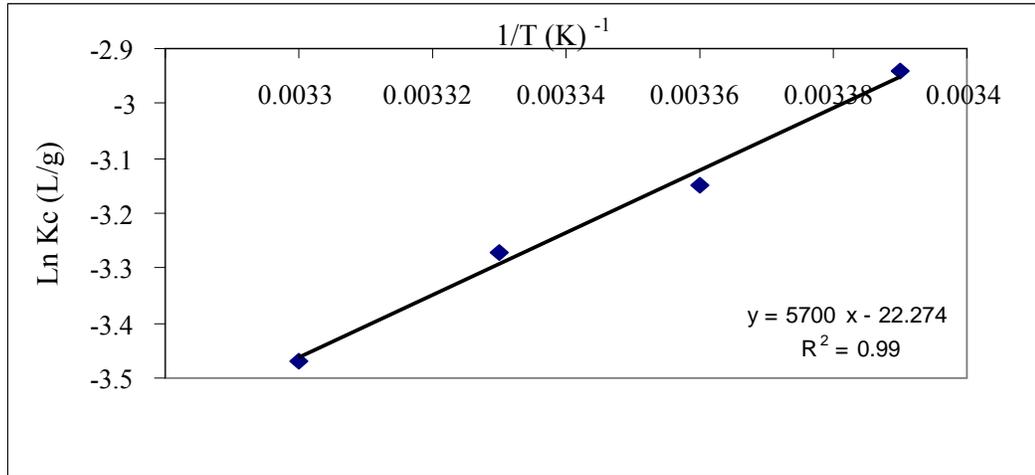


Figure 3.3.41: Standard thermodynamic equilibrium constant for GEMX on silica versus temperature.

The calculated thermodynamic parameters including:

Standard Gibb's free energy change (ΔG°), standard entropy change (ΔS°) and standard enthalpy change (ΔH°) are shown in (Table 3.3.20)

Table 3.3.20: Thermodynamic parameters for GEMX on silica

Temperature (k)	Thermodynamic parameters		
	ΔG° (kJ/mol)	ΔS° (kJ/(mol))	ΔH° (kJ/mol)
295	-101.97	0.185	-47.4
298	-102.53	0.185	-47.4
300	-102.90	0.185	-47.4
303	-103.46	0.185	-47.4

The negative values of Gibb's free energy G° and enthalpy H° indicate spontaneous, exothermic adsorption of GEMX on silica. $\Delta S_{\text{system}} - \Delta H_{\text{system}}/T = \Delta S_{\text{total}}$ Value of this function is positive for spontaneous changes, so $\Delta S_{\text{total}} = 0.185$, that positive value of S° indicates an increase in the degree of freedom and entropy of the adsorbed species

3.4 Adsorption of LEVX on different adsorbents

3.4.1. Adsorption of LEVX onto Charcoal

3.4.1.a. Adsorption of LEVX onto charcoal: Time Dependency

Values of different initial concentrations of LEVX adsorbed onto charcoal at versus time, are in (Table 3.4.1)

Table (3.4.1): Values of concentrations for LEVX remaining with time

C_1 (ppm)	C_2 (ppm)	C_3 (ppm)	C_4 (ppm)	C_5 (ppm)	Time (min)
8.01	9.45	11.36	15.38	19.08	0
4.52	6.96	8.96	11.72	16.47	5
4.08	6.24	8.57	11.25	16.37	10
4.12	5.87	8.35	10.98	16.19	15
4.04	5.61	8.17	10.82	16.14	20
3.94	5.49	8.09	10.74	16.07	25
3.79	5.19	7.83	10.57	16.01	30
3.68	4.98	7.69	10.16	15.73	45
3.62	4.93	7.61	10.08	15.65	60

The results showed that a rapid decrease in concentration of LEVX remaining in solution was in the initial 15min-20min as shown in (Fig.3.4.1) until pseudo-adsorption equilibrium was reached.

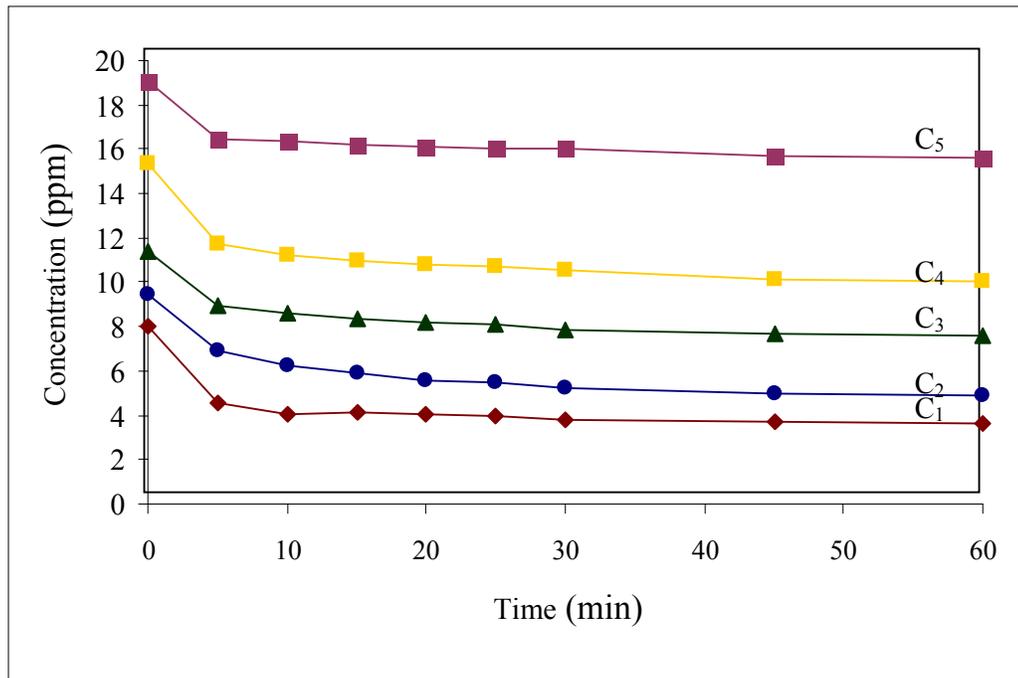


Figure (3.4.1): Adsorption of LEVX onto charcoal vs. time

Maximum adsorption was reached after 1 hour contact time between charcoal and LEVX, but the portion of LEVX participating in long-term behavior was insignificant as compared to that participating in the preliminary phase of rapid adsorption. The rapid initial adsorption of GEMX is a surface phenomenon, due to anionic nature of LEVX at pH 4, the vacant sites in the charcoal particles that held positive charge were filled up rapidly in the initial stages and followed a linear variation. Then a slow migration and diffusion of compound occurred and the rate of adsorption decreased drastically to reach the steady state (equilibrium), 60%-85% of LEVX is adsorbed in the first 20 min.

3.4.1.b Equilibrium Study between LEVX onto Charcoal

Equilibrium concentrations for different initial concentrations of LEVX and amounts adsorbed onto charcoal as shown in (Table 3.4.2)

Table (3.4.2): Equilibrium concentrations and amounts adsorbed for LEVX on charcoal

C_o (ppm)	C_e (ppm)	y_e (mg/g)	$1/C_e$ (ppm) ⁻¹	$1/y_e$ (mg/g) ⁻¹	Log C_e (ppm)	Log y_e (mg/g)
8.11	3.46	116.28	0.289	0.0086	0.539	2.066
9.80	5.68	103.09	0.176	0.0097	0.754	2.013
11.82	7.94	97.09	0.126	0.0103	0.900	1.987
19.83	16.13	92.59	0.062	0.0108	1.208	1.967

Two adsorption isotherms were used to study adsorption behavior of GEMX onto charcoal clearly.

$$1\text{- Langmuir} \quad \frac{1}{y_e} = \frac{1}{y_{\max}} + \left[\frac{1}{K_A y_{\max}} \right] \cdot \frac{1}{C_e}$$

$$3\text{- Freundlich} \quad y_e = \frac{X}{m} = K_F C_e^{1/n}$$

Langmuir isotherm was obtained from the relation between $1/y_e$ vs. $1/C_e$ as shown in (Fig.3.4.2).

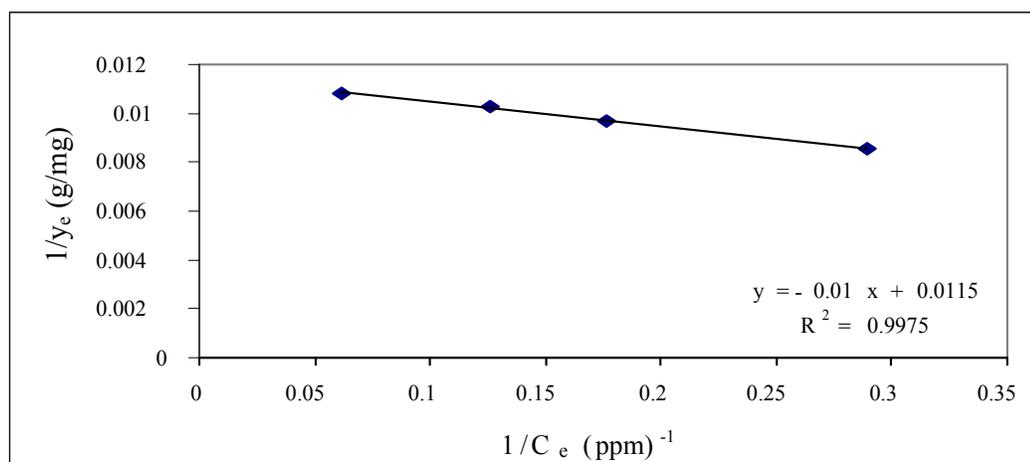


Figure 3.4.2: Langmuir isotherm for adsorption of LEVX on charcoal

Freundlich isotherm was obtained from the relation between $\text{Log } y_e$ versus $\text{Log } C_e$ as shown in (Fig.3.4.3).

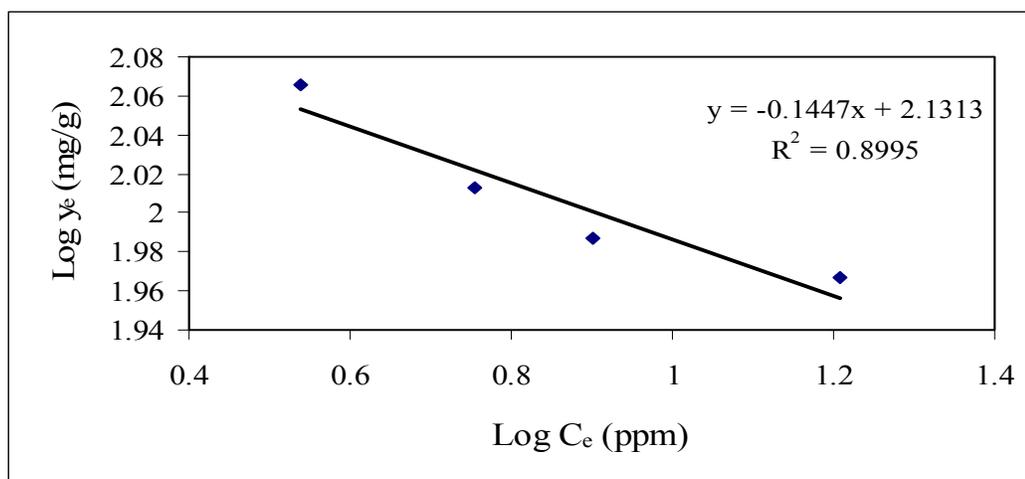


Figure 3.4.3: Freundlich isotherm for adsorption of LEVX on charcoal

The adsorption followed Langmuir isotherm ($R^2 = 0.9975$) better than Freundlich isotherm ($R^2 = 0.8995$).

From Langmuir isotherm: $y_{\text{max}} = 87$ mg/g (maximum adsorbable value of y required for monolayer adsorption (maximum capacity of adsorbent), shows the high binding capacity of activated charcoal towards LEVX and this has been attributed to high surface area of charcoal.

3.4.1.c Effect of Concentration of LEVX on Adsorption

Amount adsorbed of LEVX onto charcoal at equilibrium (y_e) and % removal of LEVX were calculated from different initial concentrations of LEVX solutions (C_o) and the equilibrium concentration of LEVX: (C_e) with charcoal, the values are in (Table 3.4.3).

Table (3.4.3): Values of C_o , C_e , y_e and % removal of LEVX on charcoal

C_o (ppm)	C_e (ppm)	y_e (mg/g)	% removal of LEVX
8.11	3.46	116.28	57.34
9.80	5.68	103.09	42.04
11.82	7.94	97.09	32.83
19.83	16.13	92.59	18.66

As the initial concentration of LEVX (C_o) increases the amount adsorbed y_e and % removal of GEMX decreases as shown in (Fig.3.4.4) and (Fig.3.4.5), at lower LEVX concentration ratio of LEVX molecules to adsorbent sites is high, and it is driving force to overcome all mass transfer resistances of the adsorbate between solution and adsorbent molecules than at higher concentration, where there is saturation of adsorption sites with LEVX and higher probability of collision between LEVX molecules adsorbed on the surface of charcoal and incoming cations electrostatically that decrease the adsorption capacity.

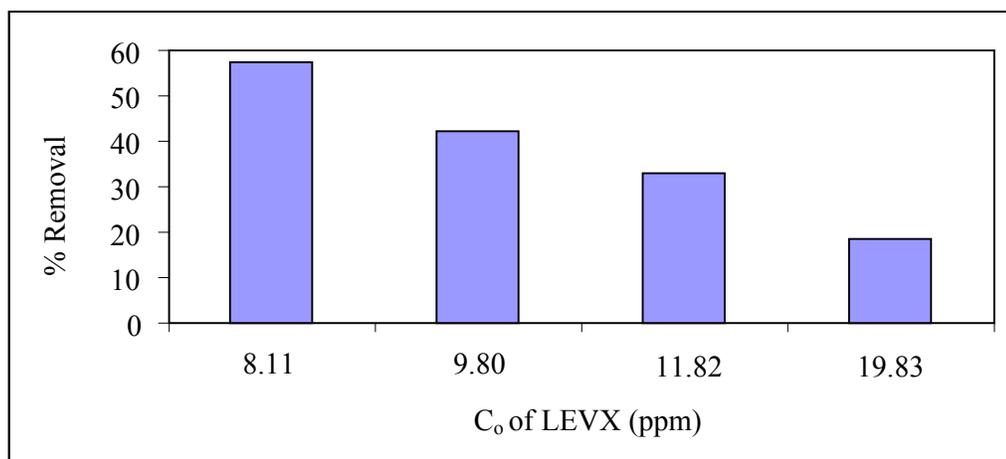


Figure 3.4.4: The % removal of LEVX on charcoal versus initial concentration of LEVX

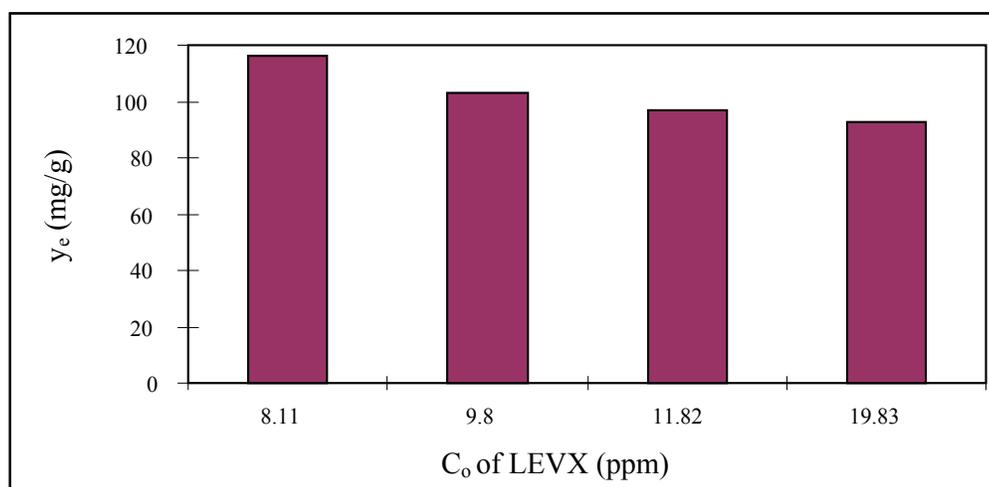


Figure 3.4.5: The Amount adsorbed of LEVX on charcoal (y_e) versus initial concentration of LEVX

3.4.1.d Effect of Charcoal Weight on Adsorption of LEVX

The % removal and amount adsorbed of LEVX by charcoal were calculated for constant initial concentration of LEVX solution with at pH=4 versus different weights of charcoal (adsorbent) to the time of equilibrium (20 min) at constant temperature = $20 \pm 1C^\circ$, values in table (3.4.4).

Table (3.4.4): Values of C_o , C_e , y_e and % removal of LEVX vs. weight of charcoal.

C_o (ppm)	C_e (ppm)	X (mg)	y_e (mg/g)	%Removal of y_e	Weight of charcoal (g)
11.36	9.503	0.186	92.85	16.26	0.002
11.36	8.026	0.333	83.35	29.35	0.004
11.36	6.963	0.440	73.38	38.71	0.006
11.36	6.283	0.508	63.46	44.69	0.008
11.36	5.438	0.592	59.22	52.13	0.010

The % removal of adsorbate and amount of LEVX adsorbed X increase as the amount of adsorbent increases used as shown in (Fig.3.4.6), (Fig.3.4.7). This can be attributed to greater surface area and availability of more adsorption sites, but in calculations $y_e = x/m$ decreases: X increases and m increases divide by more weight the decrease in adsorption capacity may be due to overlapping and saturation of adsorbent's sites of that result in decrease in the surface area available to GEMX, when the adsorbent amount 0.002g. Adsorption capacity was high, due to higher driving force to over come any resistance of GEMX molecules from adsorption to charcoal, because ratio of GEMX to charcoal is high.

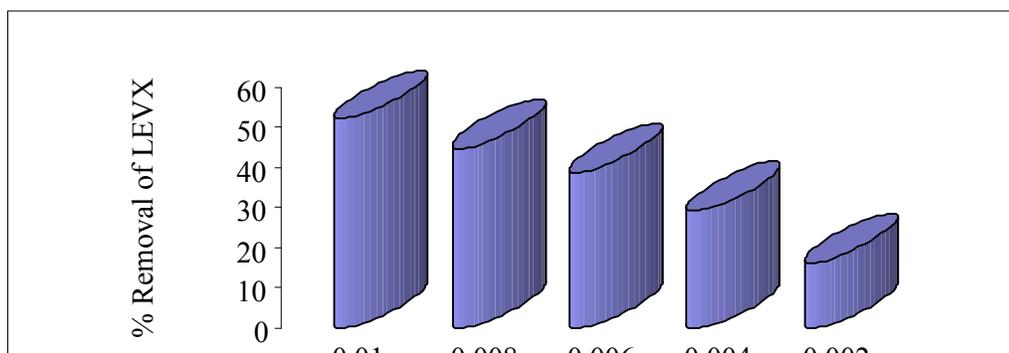


Figure 3.4.6: The % removal of LEVX vs. weight of charcoal

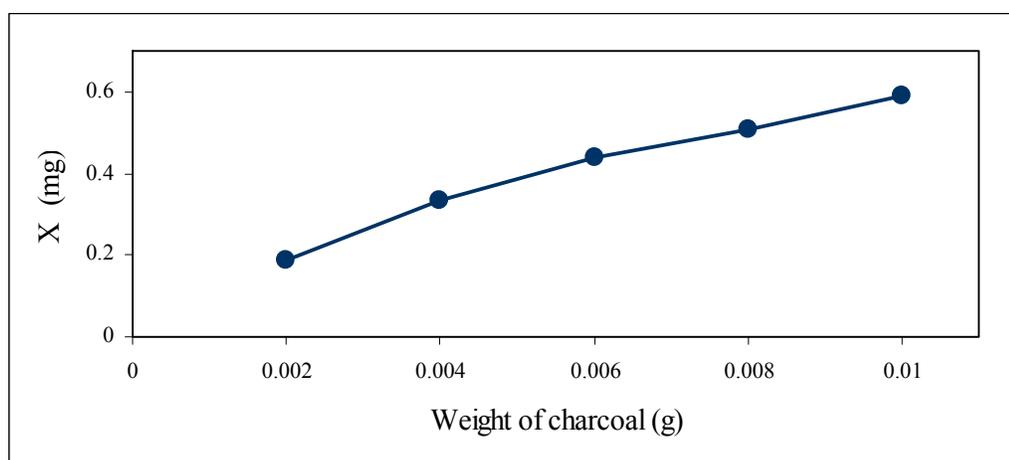


Figure 3.4.7: Amount adsorbed of LEVX versus weight of charcoal

3.4.1.e Effect of pH on Adsorption of LEVX onto Charcoal

The amount adsorbed of LEVX solutions with the same initial concentration on charcoal versus different pH values were calculated at equilibrium time (20 min) as in (Fig.3.4.8).

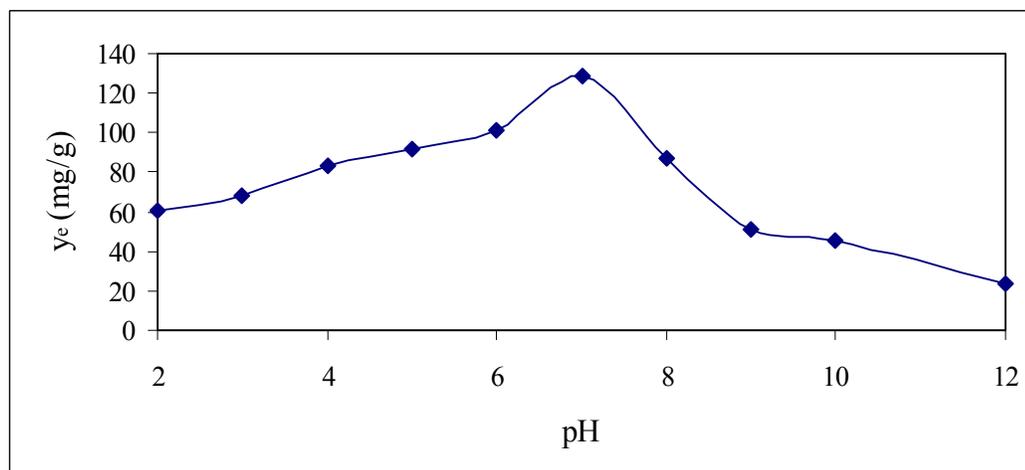


Figure 3.4.8: Amount adsorbed of LEVX on charcoal versus pH

The amount adsorbed versus pH gave more adsorption in the range of pH [5-8]. The maximum adsorption of LEVX to charcoal occurred at pH=7, near the pI of LEVX (pI of LEVX=6.77) ^[52], at this pH the carboxyl group (anionic) was half ionized (negatively charged and neutral).

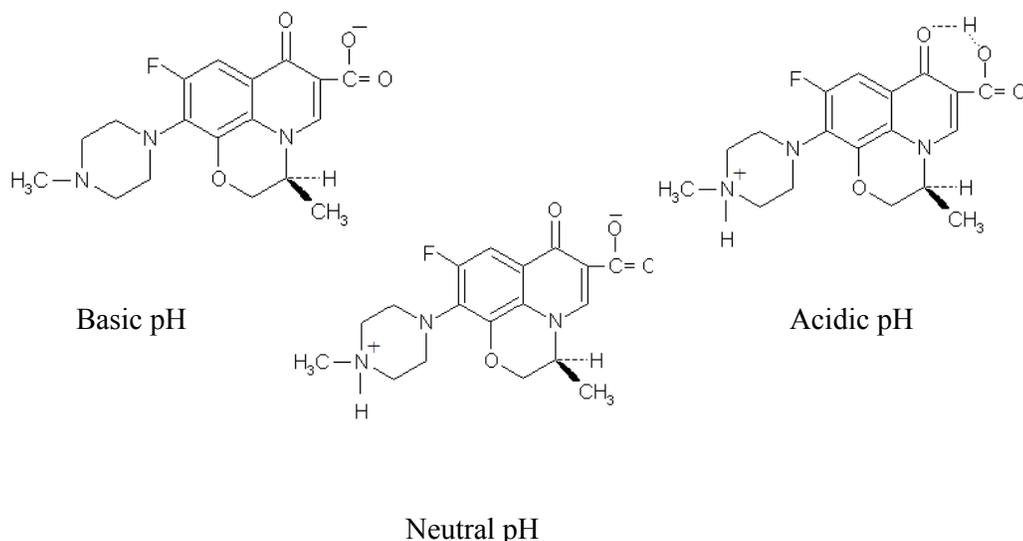


Figure 3.4.9: LEVX in solution with different pH

and piperazinyl (cationic) one, (positively charged and neutral); LEVX presents in zwitterion form. Charcoal is nonpolar adsorbent, the charge of its surface will be as the ions present on the solution, at neutral pH both H^+ and OH^- accumulates on charcoal surface resulting in most adsorption, in acidic pH range charcoal will have a net positive charge because of H^+ ions and so adsorption in acidic is more than basic, this is because of high electrostatic attraction between the positively charged surface of charcoal and negative carboxyl group of COOH at the 3-position GEMX, as the pH

increases the negative charge on the adsorbent surface will increase because OH^- ions increase thus decreases the positively charged sites of charcoal that will cause repulsion of GEMX molecules through the basic piperizino functionality at the 7-position.

3.4.1.f Adsorption of LEVX on Charcoal versus Temperature

Amount of GEMX adsorbed onto 0.01g of charcoal vs. temperature was calculated as in (Table 3.4.5).

Table 3.4.5: Effect of temperature on adsorption of LEVX on charcoal

Temperature		1/T	C_o	C_e	y_e	K_c	Ln K_c
C°	k	k^{-1}	(ppm)	(ppm)	(mg/g)	(L/g)	(L/g)
20	293	0.00341	11.17	6.79	109.50	16.127	2.78
25	298	0.00336	11.17	7.84	83.25	10.619	2.36
30	303	0.00330	11.17	8.35	70.50	8.443	2.13
35	308	0.00325	11.17	8.88	57.25	6.447	1.86
37	310	0.00323	11.17	9.47	42.50	4.488	1.50

As the temperature increased the amount of LEVX adsorbed on charcoal decreased, as shown in (Fig 3.4.10).

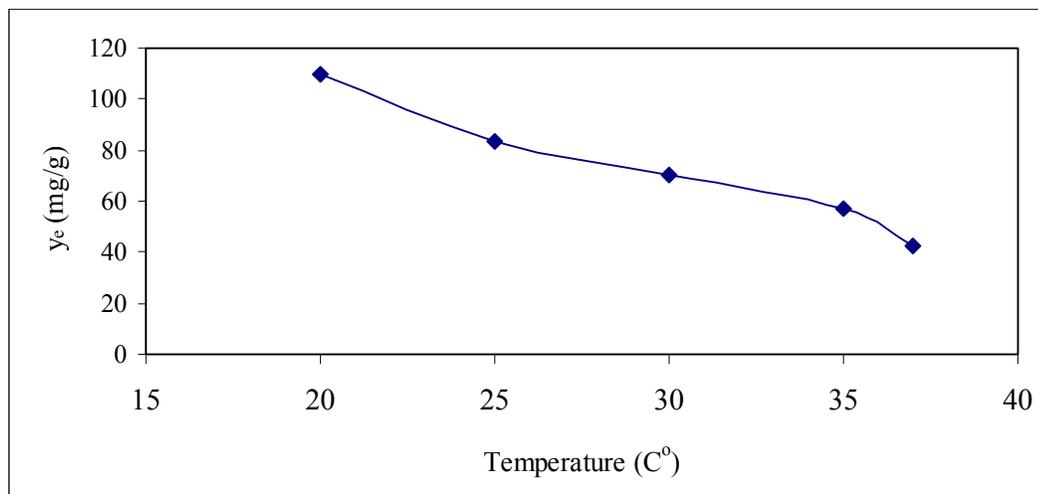


Figure 3.4.10: Amount adsorbed of LEVX on charcoal vs. temperature.

Thermodynamic parameters including: standard Gibb's free energy change (ΔG°), standard entropy change (ΔS°) and standard enthalpy change (ΔH°) were determined from the equation: $\text{Ln } K_c = (\Delta S^\circ/R) - (\Delta H^\circ/RT)$

A plot of $\text{Ln } K_c$ versus $1/T$ as in (Fig.3.4.11)

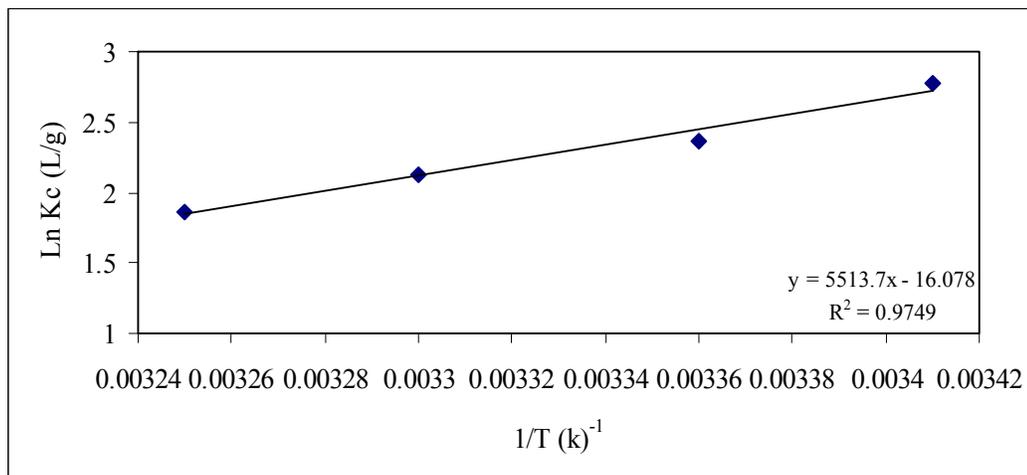


Figure 3.4.11: Standard thermodynamic equilibrium constant for LEVX on charcoal versus temperature

The calculated thermodynamic parameters are shown in (Table 3.4.6)

Table 3.4.6: Thermodynamic parameters for LEVX on charcoal

Temperature (k)	Thermodynamic parameters		
	ΔG° (kJ/mol)	ΔS° (kJ/mol)	ΔH° (kJ/mol)
293	-85.102	0.134	-45.84
298	-85.772	0.134	-45.84

303	-86.442	0.134	-45.84
308	-87.112	0.134	-45.84

The negative values of Gibb's free energy G° indicates that the feasibility of the adsorption process and spontaneous adsorption of GEMX to charcoal. The negative value of enthalpy H° shows that the adsorption process has an exothermic nature, positive value of S means that there is a decrease in the degree of freedom of the adsorbed species.

3.4.2. Adsorption of LEVX on Kaolin

3.4.2.a Adsorption of LEVX onto Kaolin: Time Dependency

Different initial concentrations of standard solution of LEVX at pH=4 adsorbed onto 0.01 ± 0.001 g kaolin at temperature equals $20 \pm 1^\circ\text{C}$, the remaining concentration with time as shown in (Table 3.4.7)

C_1 (ppm)	C_2 (ppm)	C_3 (ppm)	C_4 (ppm)	Time (min)
7.26	8.65	11.2	12.55	0
6.77	8.24	10.92	12.26	5
6.51	7.96	10.81	12.12	10
6.28	7.75	10.67	12.00	20

6.15	7.62	10.57	11.86	30
5.94	7.50	10.34	11.79	45
5.83	7.30	10.23	11.73	60

Table (3.4.7): Values of concentrations of LEVX remaining with time

The results showed that the decrease in concentration of GEMX remaining in solution was slow until equilibrium was reached after 1 hour contact between kaolin and LEVX as shown in (Fig.3.4.12)

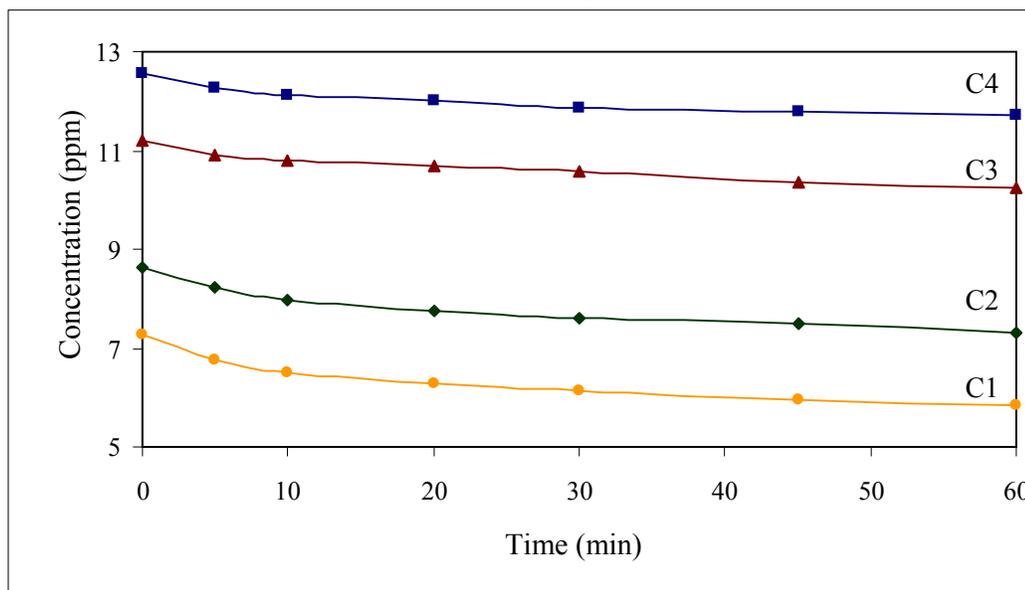


Figure (3.4.12): Adsorption of LEVX onto kaolin vs. contact time)

3.4.2.b Equilibrium Study between LEVX and Kaolin

Equilibrium concentrations and amounts adsorbed for different initial

C_o ppm	C_e ppm	y_e mg/g	$1/C_e$ ppm^{-1}	$1/y_e$ $(\text{mg/g})^{-1}$	$\text{Log } C_e$ ppm	$\text{Log } y_e$ mg/g
7.26	5.83	14.3	0.172	0.070	0.766	1.155
8.65	7.30	13.5	0.137	0.074	0.863	1.130
11.20	10.23	9.7	0.098	0.103	1.009	0.987
12.55	11.73	8.2	0.085	0.122	1.069	0.914

concentrations of LEVX at pH=4 and temperature ($20 \pm 1\text{C}^\circ$) onto kaolin as shown in (Table 3.4.8).

Table 3.4.8: Equilibrium concentrations and amounts of GEMX adsorbed onto kaolin

Two adsorption isotherms were used to study adsorption behavior of LEVX onto kaolin clearly. Langmuir isotherm was obtained from a plot of $1/y_e$ versus $1/C_e$, as in (Fig.3.4.13).

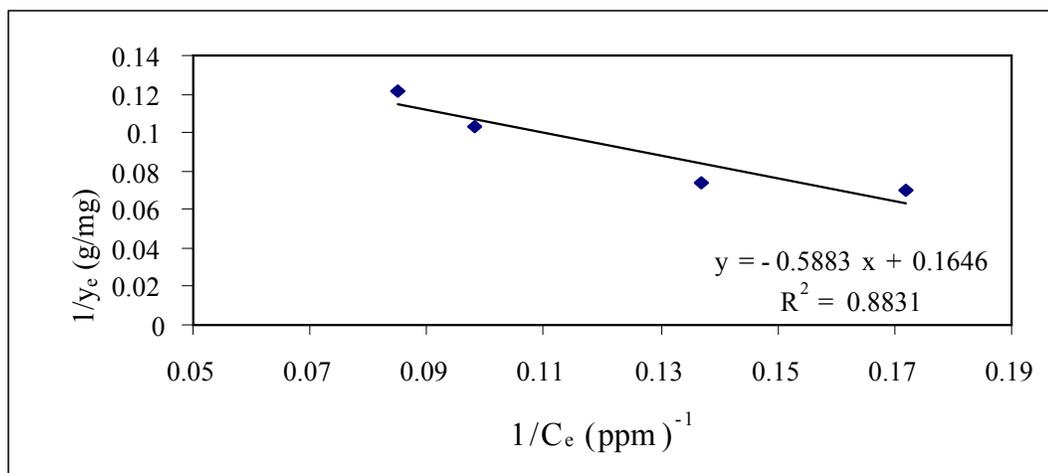


Figure 3.4.13: Langmuir isotherm for adsorption of LEVX on kaolin

Freundlich isotherm was obtained from the relation between $\text{Log } y_e$ vs. $\text{Log } C_e$ as shown in (Fig.3.4.14).

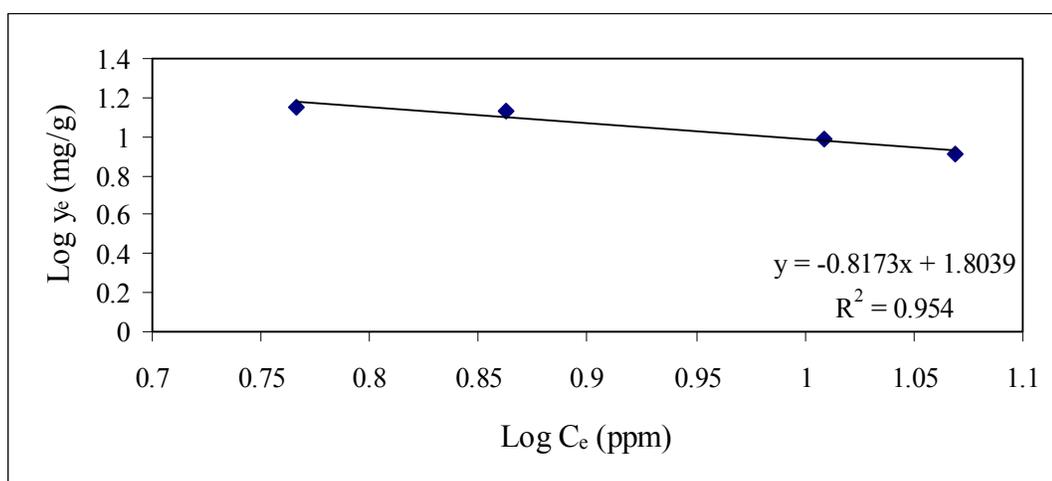


Figure 3.4.14: Freundlich isotherm for adsorption of LEVX on kaolin

The adsorption followed Freundlich isotherm better than Langmuir isotherm because R^2 in Freundlich isotherm is nearer to unity. From Freundlich isotherm $K_f = 0.26$ mg/g. The poor adsorption capacity of kaolin has been attributed to weak electrostatic attraction between LEVX and kaolin, the large particle size of kaolin and its existence as layers made the ability of adsorption so weak.

3.4.2.c Effect of Kaolin Amount on Adsorption of LEVX

Equilibrium concentrations and the amount adsorbed (X) and % removal of LEVX ($\%y_e$) of LEVX onto different weights of kaolin to the

time of equilibrium 1 hour and temperature equals $20 \pm 1C^{\circ}$, values were calculated as in (Table 3.4.9).

Table 3.4.9: Values of C_e , X, y_e and $\%y_e$ for GEMX vs. weight of kaolin

C_o (mg/L)	C_e (mg/L)	X (mg)	y_e (mg/g)	$\% y_e$ removal	m (g)
11.2	10.52	0.068	17	6.07	0.004
11.2	10.37	0.083	13.83	7.41	0.006
11.2	10.29	0.091	11.38	8.13	0.008
11.2	10.23	0.097	9.7	8.66	0.01

The % removal of of LEVX (X) adsorbed increased as the amount of kaolin adsorbent increased as shown in (Fig.3.4.15), this can be attributed to more adsorption sites are available.

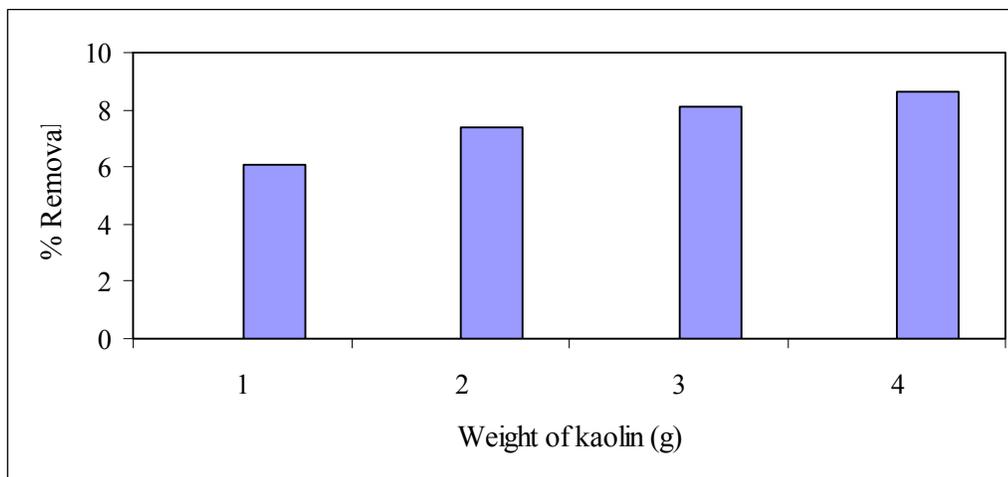


Figure 3.4.15: The % removal of LEVX on kaolin versus weight of kaolin

Y_e decreases in respect to each weight used may be due to overlapping and saturation of adsorbent's sites that result in decrease in the surface area available to LEVX as shown in (Fig.3.4.16).

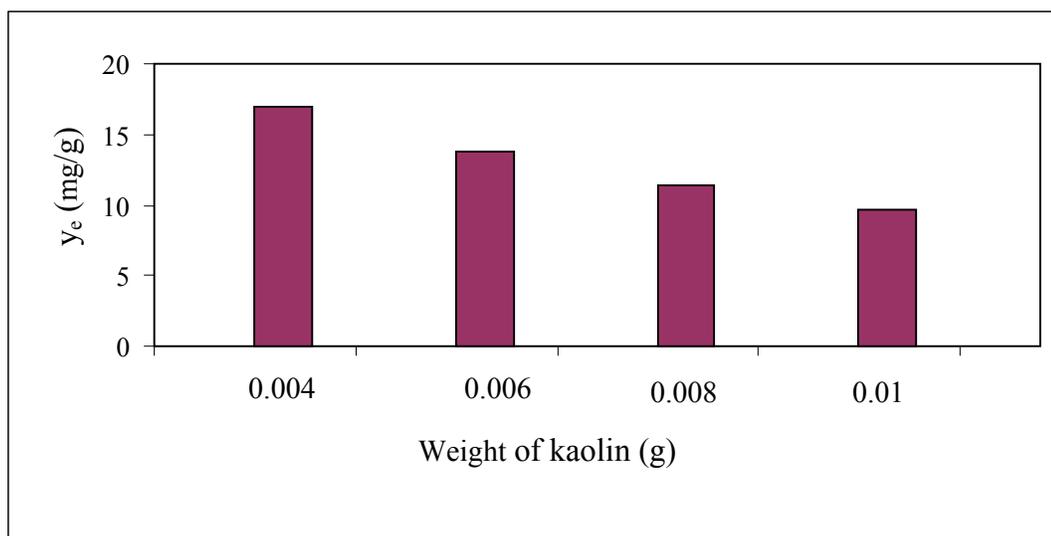


Figure 3.4.16: The amount adsorbed of LEVX onto kaolin versus weight of kaolin

When 0.006g kaolin was used adsorption was more than 0.01g kaolin, due to higher driving force to overcome any resistance of LEVX molecules from adsorption to kaolin.

The amount adsorbed of LEVX (X) increased as the amount of adsorbent used increased, as shown in (Fig.3.4.17).

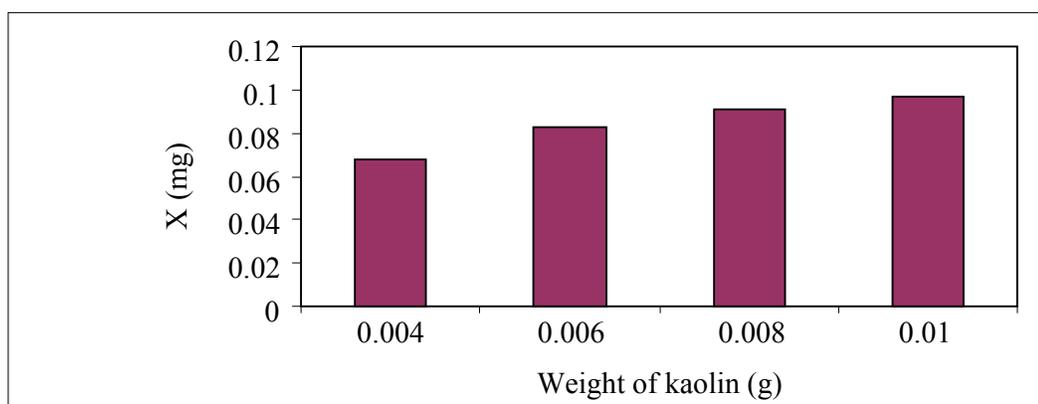


Figure 3.4.17: The amount adsorbed of LEVX versus weight of kaolin

3.4.2.d Effect of pH on adsorption of LEVX onto kaolin

The amount of LEVX solutions with the same initial concentration adsorbed (y_e) onto (0.01g) of kaolin were calculated at equilibrium time (1 hour versus different pH, as shown in (Fig.3.4.18). The results were calculated in respect to λ_{\max} at each pH. (not shown).

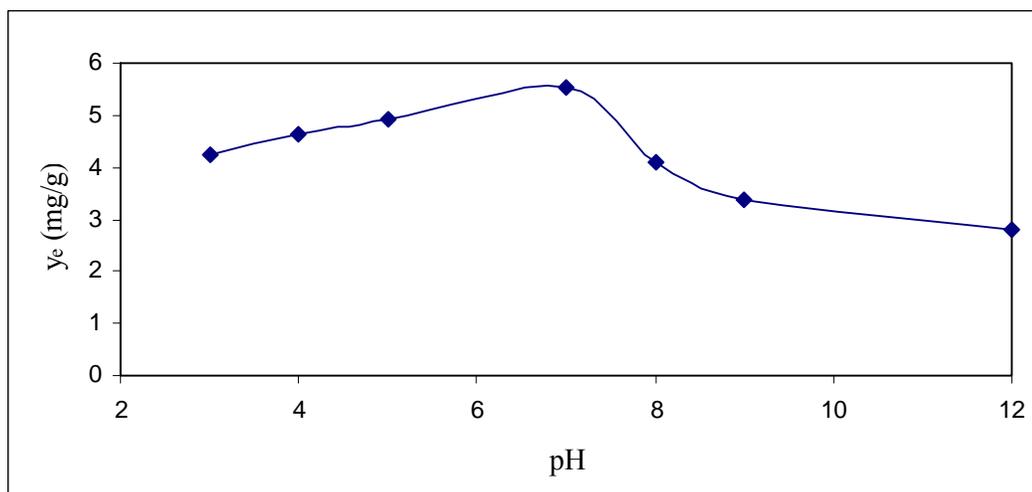


Figure 3.4.18: Amount adsorbed of LEVX on kaolin versus pH

The amount adsorbed was greater in acidic than in basic medium as in (Fig.3.4.18). LEVX has two centers a carboxyl (anionic) group at the 3-position and basic piperazinyl (cationic) group at the 7-position, 6-fluoro substituent. At pH 7: dissociation of both the 3-COOH and the basic 7-(1-

piperazino)-groups occurs leading to significant fractions of zwitterionic species as shown in (Fig. 3.4.9). The charge of the adsorbent's surface is taken in consideration kaolin particles are flat plates or disks the charge of the face of these disks is negative at all pH range and the edges of disks are positive at low pH and negative at high pH, the isoelectric point of kaolin at pH about 7, kaolin represents negative charge at entire pH range because of the high ratio of surface of face to edge. ^[55]

At acidic pH LEVX have cationic form and kaolin has a negative charge so adsorption more than basic and at pH=7 LEVX has zwitterionic form and kaolin has both negative and positive charge so adsorption quantities of LEVX on kaolin surface at pH=7 be specific and stronger than that attraction between solvent – solute leading to an increase in the quantity adsorbed. The attraction between the surface and the drug molecules at may more than basic pH where both LEVX and kaolin have negative charges that cause repulsion and less adsorption. ^[55]

3.4.2.e Adsorption of LEVX onto kaolin versus Temperature

Amount of LEVX solution of constant initial concentration at pH=4 adsorbed onto 0.01g of kaolin was investigated as a function of temperature as in (Table 3.4.10)

Table 3.4.10: Effect of temperature on adsorption of LEVX on kaolin

Temperature		1/T	C _o	C _e	y _e	K _c	Ln K _c
C ^o	k	k ⁻¹	(ppm)	(ppm)	(mg/g)	(L/g)	(L/g)
22	295	0.00339	11.3	10.34	9.6	0.928	-0.0743

25	298	0.00336	11.3	10.40	9	0.865	-0.1464
27	300	0.00333	11.3	10.47	8.3	0.793	-0.2323
30	303	0.00330	11.3	10.58	7.2	0.681	-0.3849

As the temperature increased the amount of LEVX adsorbed on kaolin decreased, as shown in (Fig 3.4.19).

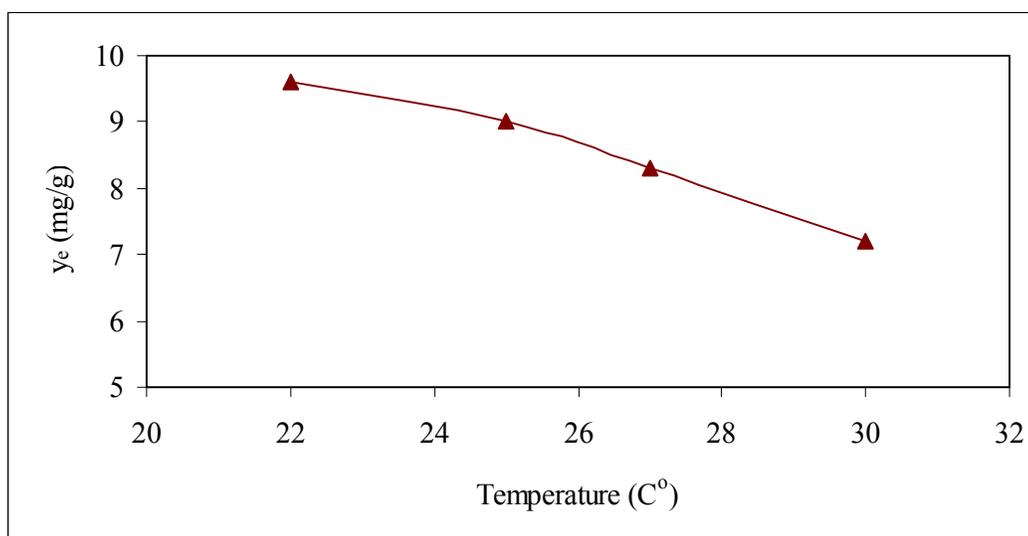


Figure 3.4.19: Amount adsorbed of LEVX on kaolin versus temperature

From equation: $\ln K_c = (\Delta S^\circ/R) - (\Delta H^\circ/RT)$

The enthalpy change (ΔH°), was obtained from the slope of a linear plot between $\ln K_c$ versus $1/T$ and the entropy change (ΔS°) was calculated from the intercept as in (Fig.3.4.20)

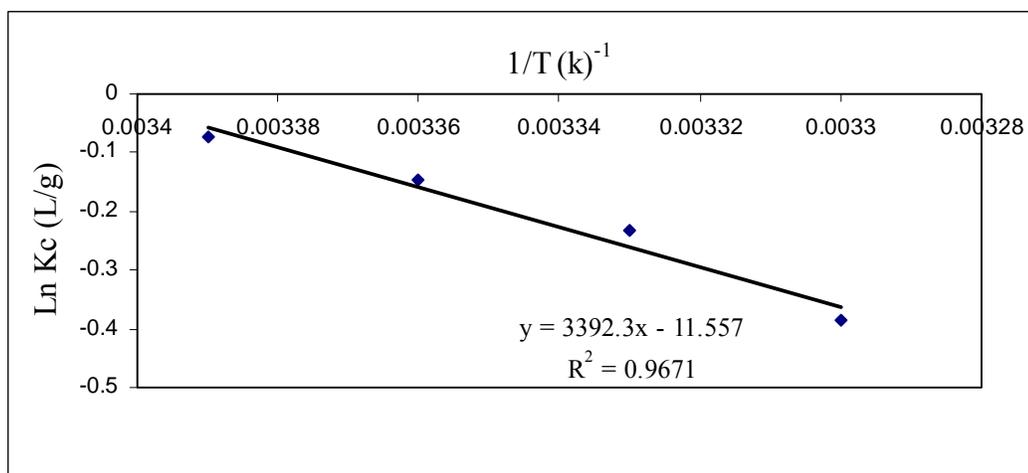


Figure 3.4.20: Standard thermodynamic equilibrium constant for LEVX on kaolin versus temperature.

Thermodynamic parameters including: standard Gibb's free energy change (ΔG°), standard entropy change (ΔS°) and standard enthalpy change (ΔH°) were calculated as shown in (Table 3.4.11)

Table 3.4.11: Thermodynamic parameters for LEVX adsorbed on kaolin

Temperature (k)	Thermodynamic parameters		
	ΔG° (kJ/mol)	ΔS° (kJ/(mol))	ΔH° (kJ/mol)
295	-56.52	0.096	-28.2
298	-56.81	0.096	-28.2
300	-57.00	0.096	-28.2
303	-57.29	0.096	-28.2

The negative values of Gibb's free energy G° indicates that adsorption of LEVX to kaolin is spontaneous, negative value of enthalpy H° shows that the adsorption process has an exothermic nature, positive value of S means that there is an increase in the degree of freedom of the adsorbed species.

**CHAPTER FOUR
RECOMMENDATIONS
AND CONCLUSIONS**

4. Recommendations and Conclusions

4.1 Conclusions

Gemifloxacin mesylate and Levofloxacin hemihydrate showed a good adsorption with charcoal but poor with kaolin and in acidic pH more than basic range. The amount of GEMX and LEVX adsorbed increased as amount of charcoal increased and as the initial concentration of drug increased, increasing the temperature caused decrease in the amount adsorbed of GEMX and LEVX. The negative values of Gibb's free energy G° indicated that the feasibility of the adsorption process and spontaneous adsorption of drugs and the negative value of enthalpy H° showed that the adsorption process had an exothermic nature, the positive value of entropy S° showed that freedom of molecules increased with increasing temperature

Because of the rapid rate of adsorption exhibited by activated charcoal for the fluoroquinolones, it could be an effective antidote for Gemifloxacin (fluoroquinolone) in cases of overdose or poisoning. No specific antidote is known for gemifloxacin. ^[56]

Activated charcoal has shown a super behaviour than kaolin in the adsorption of the Fluoroquinolones. Activated carbon is generally considered a non-toxic. Large doses are routinely given in human poisoning cases. The human dose for poisoning is 1g of activated charcoal

per kg of body weight. So examining it as an adsorbent to the fluoroquinolones is useful. Activated charcoals are widely used especially as adsorbents; it is well known that oral administration of the activated carbon has been successfully applied in the cases of overdosing.

Charcoal and Kaolin must be excluded from any pharmaceutical formulations containing GEMX or LEVX. Moreover, it could be recommended that the administration of these drugs simultaneously with any pharmaceutical product containing any of these materials should be avoided.^[58] For example kaolin is present in some medications such as antidiarrheal drugs so interaction between both fluoroquinolones and kaolin must be taken in consideration.

The amount of GEMX (mg) adsorbed per gram of alumina and silica [y_e] decreases as the amount of alumina or silica increases but to a certain limit then it remains constant. The highest adsorption of GEMX to alumina occurred at pH=6 and for silica at pH=7.

Pharmaceuticals are ubiquitous water and soil contaminants that may have subtle detrimental effects on aquatic organisms, and also possibly on human health. The risks of pharmaceuticals, or pharmaceutically active compounds, remain poorly understood. The adsorption of fluoroquinolones is pH dependant in alumina and silica and this explains the adsorption of pharmaceuticals in aquatic sources.

4.2 Recommendations

-Using the spectrophotometric method for analysis was easy, rapid, accurate and sensitive.

-Adsorption of gemifloxacin on charcoal, can considered as antidote this study opens the door to more experiments other adsorbents may be used other fluoroquinolones

-Studying the adsorption of gemifloxacin under other conditions especially that are similar to the body temperature and acidic medium of stomach.

- Levofloxacin hemihydrate are widely used as in chemotherapy so more studies will be useful especially in the human medicine so studying the adsorption of this drug with different adsorbents may be carried out. Interaction between this drug and other drugs or food may also be studied

- Other fluoroquinolones that are used in veterinary sector, such as enrofloxacin may be studied in the same way.

- Gemifloxacin mesylate is a new fluoroquinolone, not used till now in Palestine so more information about the adsorption of the drug and interaction is valuable.

- Activated charcoal and kaolin are present as medical forms, studying the interaction between them and gemifloxacin gives a guide for how they affect the bioavailability of gemifloxacin when taking simultaneously.

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Appendices

Appendix I(a):

Appendix I (b):



UQUIFA MÉXICO, S. A. DE C. V.

CERTIFICATE OF ANALYSIS

LEVOFLOXACIN HEMIHYDRATE, USP

LOT : 1059080003

	RESULTS:	SPECIFICATION:
APPEARANCE:	YELLOWISH POWDER	LIGHT YELLOWISH POWDER
IDENTIFICATION (IP):	COMPLIES	CONSISTENT TO REFERENCE SAMPLE
WATER:	2.6 %	BETWEEN 2.1 % AND 2.7 %
SPECIFIC ROTATION:	-94.9 *	-92° TO -108°
RELATED SUBSTANCES (HPLC)		
UNKNOWN IMPURITY:	0.07 %	NOT MORE THAN 0.1%
KNOWN IMPURITY:	0.09 %	NOT MORE THAN 0.15%
TOTAL IMPURITIES:	0.20 %	NOT MORE THAN 0.5%
HEAVY METALS:	< 10 ppm	NOT MORE THAN 10 ppm
SULFATED ASH:	0.03 %	NOT MORE THAN 0.1%
ASSAY (mfr.):	99.6 %	98.0 TO 102.0% ON ANHYDROUS BASIS
RESIDUAL SOLVENTS:		
ISOPROPYL ALCOHOL:	1680 ppm	NOT MORE THAN 3000 ppm
CHLOROFORM:	ND ppm	NOT MORE THAN 60 ppm
TOLUENE:	50 ppm	NOT MORE THAN 890 ppm

MANUFACTURING DATE: JUNE 05, 2008
 REANALYSIS DATE: JUNE 05, 2011

ELABORATED: 
 NAME: PEDRO CABRERA
 TITLE: QUALITY CONTROL
 DATE: NOVEMBER 27, 2008

APPROVED: 
 NAME: JOSE LUIS PRATZ
 TITLE: QUALITY CONTROLLER
 DATE: NOVEMBER 27, 2008

SUBSIDIARIA DE YULE CATTO & Co PLC

UQUIFA MEXICO S. A. DE C. V.
 Calle 37 Este No. 126 C. P. 62578 CIVAC, Jutepec, Mor. México. Tel (7) 329-50-66, Fax (7) 329-50-39

(a): Characteristics of aluminium oxide

101077 Aluminium oxide 90 active neutral (activity stage I) for column chromatography, 0.063-0.200mm (70 - 230 mesh ASTM)	
Product information	
Hill Formula	Al ₂ O ₃
HS Code	2818 20 00
EC number	215-691-6
Molar mass	101.96 g/mol
CAS number	1344-28-1
Chemical and physical data	
Solubility	(20°C) insoluble
Melting point	2050°C
Molar mass	101.96 g/mol
Density	3.94 g/cm ³ (20°C)
Bulk density	370 - 900 kg/m ³
pH value	5 - 8 (100 g/l, H ₂ O, 20°C) suspension
Boiling point	2980°C
Vapor pressure	(20°C)
Vapor pressure	(20°C)

(b): Characteristics of Activated Charcoal

Synonym:	charcoal activated
CAS Number:	7440-44-0
Linear Formula	C
Molecular Weight	12.01
vapor pressure	<0.1 mmHg (20 °C)
Properties	
Description	acid-washed with hydrochloric acid
Autoignition temp.	842°F
Resistivity	1375 $\mu\Omega$ -cm, 20°C (graphite)
mp	3550°C (lit.)
Suitability	plant cell culture tested

(c): Characteristics of Silica Gel

107730 Silica gel 60 GF ₂₅₄ for thin-layer chromatography	
Product information	
Hill Formula	O ₂ Si
Chemical formula	SiO ₂
HS Code	2811 22 00
EC number	231-545-4
Molar mass	60.08 g/mol
CAS number	7631-86-9
Chemical and physical data	
Solubility	(20°C) insoluble
Melting point	1710°C
Molar mass	60.08 g/mol
Bulk density	200 - 800 kg/m ³
pH value	7 (100 g/l, H ₂ O, 20°C) (slurry)

جامعة النجاح الوطنية

كلية الدراسات العليا

إدمصاص بعض الفلوروكوينولونات
على بعض المواد المختارة

إعداد

أريج "محمد غازي" عبد الرحمن حطاب

إشراف

د.شكري خلف

د.إبراهيم أبو شقير

قدمت هذه الأطروحة استكمالاً لمتطلبات الحصول على درجة الماجستير في الكيمياء بكلية الدراسات العليا في جامعة النجاح الوطنية في نابلس، فلسطين.

2010

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الملخص

تم دراسة إدمصاص بعض الفلوروكوينولونات (مضادات حيوية) مثل: الجيميفلوكساسين والليفوفلوكساسين على مجموعة مختارة من الممتزات هي: الفحم النشط، هلام السيليكا، الألومينا والكولين. هذه الدراسة تناولت تأثير عدة عوامل على عملية الإدمصاص مثل: - درجة الحموضة (الرقم الهيدروجيني)، وقت الاتصال بين الدواء والمادة الممتزة، تركيز الدواء، كمية المادة الممتزة ودرجة الحرارة .

تم تحديد الإدمصاص عن طريق قياس تركيز الدواء قبل وبعد الاتزان باستخدام مطياف الأشعة فوق البنفسجية والمرئية (UV-Visible Spectrophotometer) من خلال قياس الامتصاص (Absorbance) عند طول الموجة المناسبة لكل دواء، واستخدمت النتائج لتحديد منحنى الإدمصاص.

كما تمت دراسة الممتزات المناسبة لكل دواء والظروف المثالية لإدمصاصه على كل مادة، والعوامل التي تؤثر على الإدمصاص. تم تطبيق علاقات الإدمصاص (Adsorption) isotherms على النتائج، وتم حساب متغيرات ثيرموديناميكية مختلفة مثل: ΔS^0 , ΔG^0 و ΔH^0 .