An-Najah National University

Faculty of Graduate Studies

The use of Gold nanoparticles for the removal of 5-Fluorouracil from aqueous solutions

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Dedication

This thesis is dedicated to my parents for their endless love and encouragement, my uncle Walid Fayyad and his family for their support and confidence, my brothers and sisters for their continued and unfailing love, support and understanding during my pursuit of master degree. Words would never say how grateful I am to all of you. I consider myself the luckiest in the world to have such a lovely and caring family.

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To all my friends, thank you for your understanding and encouragement in my many, many moments of doubts. You make my life a wonderful experience, I cannot list all the names here but you are always on my mind.

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الإقرار

أنا الموقع أدناه مقدم الرسالة التي تحمل عنوان:

The use of Gold nanoparticles for the removal of 5-Fluorouracil from aqueous solutions

أقر بأن ما اشتملت عليه هذه الرسالة إنما هي نتاج جهدي الخاص، باستثناء ما تم الإشارة اليه حيثما ورد، وأن هذه الرسالة ككل، أو أي جزء منها لم يقدم لنيل أي درجة أو لقب علمي أو بحثي لدى أي مؤسسة تعليمية أو بحثية أخرى.

Declaration

The work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student's Name: **اسم الطالب:**

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List of Abbreviations

Symbol	Abbreviation
g	gram
mg	milligram
L	Liter
mg/L	milligram per liter
µg/l	microgram per liter
L/g	Liter per gram
J	Joule
K	Kelvin
J/K	Joule per Kelvin
KJ/mol	Kilo Joule per mole
a_s	Sips isotherm constant (L/g)
AC	Activated Carbon
A	Arrhenius factor
AOPs	Advanced oxidation processes
BCF	Bioaccumulation factor
B_s	Sips isotherm exponent
BSA	Bovine serum albumin
CI	Confidence interval
C_e	The equilibrium concentration of the adsorbate (mg/L)
C_o	The initial concentration of the adsorbate (mg/L)
dNTP	Deoxynucleotide
dUTP	Deoxyuridine triphosphate
D-R	Dubin Radushkevich
E_a	Arrhenius activation energy (kJ/mol)
EPA	Environmental protection agency
5-FU	5-Fluorouracil
FdUMP	Fluorodeoxyuridine monophosphate
FdUTP	Fluorodeoxyuridine triphosphate
FUTP	Fluorouridine triphosphate
FTIR	Fourier Transform Infrared
ΔG°	Standard Gibbs free energy change (J)
GNPs	Gold nanoparticles
ΔH°	Standard Enthalpy change (J)
HSDM	Homogeneous surface diffusion model
K_L	Langmuir isotherm constant (L/mg)
K_s	Sips isotherm model constant (L/g)
K_F	The Freundlich constant related to adsorption capacity (mg/g).
K_1	The rate constant of pseudo first-order adsorption model (min^{-1})
K_2	The rate constant of pseudo second-order adsorption model ($mg.g^{-}$

	^{1}.min^{-1})
K_{id}	The Intra-Particle diffusion rate constant (mg.g^{-1}.min$^{-1/2}$)
K_{ow}	Octanol-water partition coefficient
K_{oc}	Organic carbon partition coefficient
K_H	Henry's law constant (atm. m^3/mol)
K_d	The thermodynamic equilibrium constant (L/g)
N	The heterogeneity coefficient (g/L)
PACs	Powdered activated carbons
PI	Isoelectric point
q_e	The amount of adsorbate per unit mass of adsorbent (mg/g)
q_L	The maximum monolayer coverage capacity (mg/g)
q_t	The mass of adsorbate per unit mass of adsorbent at time t (mg/g).
R_L	Constant separation factor
R	The universal gas constant (8.314 J.mol^{-1}.K^{-1})
ΔS°	Standard Entropy change (J/K)
TS	Thymidylate synthetase
T	The absolute temperature (K)
t	Time (min)
TEM	Transmission Electron Microscopy
UV-Vis	Ultraviolet visible spectroscopy
V	The volume of the solution (L)
WWTP	Waste water treatment plant
W	Adsorbent mass (g)
Z	A constant indicates the thickness of the boundary layer (mg/g)

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Abstract

The use of cytotoxic drugs in cancer therapies is increasing annually. 5-Flourouracil (5-FU) is one of the most widely used antineoplastic drugs in the world and the threshold value toxicity of this drug is 94 ng/L (1). This research applied gold nanoparticles (GNPs) to remove 5-FU through adsorption. Concentrations were determined experimentally by UV-Vis spectroscopy. Several parameters like; contact time, temperature, pH, 5-FU initial concentration and dosage of Gold nanoparticles were tested by adsorption experiments. The equilibrium data corresponded better to Sips isotherm. The removal efficiency of 5-FU adsorbed by GNPs was more than 85% at environmental conditions (pH=[7-9], concentration of 5-FU=5mg/L, and temperature=298 K). The kinetic data showed that the adsorption followed pseudo second-order kinetic model. Thermodynamic parameters indicated that the adsorption process was exothermic and spontaneous. The activation energy value, which was 5.403 KJ/mol, implied that the adsorption between 5-FU and GNPs was physical. The use of GNPs to adsorb 5-FU was effective process since it was easy to reuse and recover GNPs using 0.1M HCL solution.

The results showed that GNPs were found to be an effective and functional adsorbent to remove 5-FU from water. It is recommended that the presence of 5-FU in our water resources should be addressed and considered to reduce it's toxic effects and different methods should be applied to remove it from water.

Chapter One

Introduction

1.1 overview

Pharmaceutical drugs are becoming a matter of concern since 1970s due to their occurrence, fate and behavior in the aquatic environment (2). These drugs, that may negatively affect the living organisms, are widely applied as human medicine for diagnosing and treating diseases. Worldwide, many medical drugs have reported in different environmental samples. In addition, pharmaceutical drugs have been detected in the environment, such as surface water, groundwater, seawater and wastewater treatment plants (3), (4).

Drugs are one of the major substances that cause pollution in the aquatic environment. Their sources are from hospital and industrial factories, leakages from waste of medical health centers, veterinary products and effluents from wastewater treatment plants (WWTPs), which may infiltrate into the soil and percolate to the ground water and other water resources.

Cytotoxic drugs can affect human health; one of these pharmaceuticals is 5-FU, which is used in the therapy treatment of various types of tumors. Today 5-FU is the most commonly used antineoplastic drug in the world (5), (6). Over 30 years ago, 5-FU was synthesized as anticancer drug. The monitoring of this medical drug and its metabolite degradation is seriously considered, because 5FU has a high toxic effect at the cellular level

especially for specific population subgroups, like pregnant women and their fetuses and the appearance of 5-FU in hospital effluents and surface water has drastically increased. In addition, 5-FU does not have the possibility to be readily adsorbed by sludge, so it is not expected to be removed in WWTP (7).

In Palestine and Jordan, Marei and Tiehm (8) studied the occurrence of pharmaceuticals in certain sites. The findings showed that some compounds such as: Ibuprofen, Diclofinac and Carbamazepine exist in considerable amount in water resources and waste water. Therefore, there is no studies about the fate and occurrence of 5-FU drug in Palestine and this is the first research to remove this drug from water in Palestine.

Several treatment processes are investigated and applied worldwide, some of these processes are advanced treatment that are required to treat the polluted water, which is subjected to toxic drugs to the extent that complies with water (9). One of these methods, adsorption by nanoparticles, holds great ability to improve treatment efficiency and to reduce the impacts of these toxic materials on the aquatic environment and the human health (10), (6).

Adsorption means the build up of adsorbate (pharmaceuticals, pesticides…etc) on the surface of an adsorbent in a fluid phase (gas or liquid), by either chemical or physical bonds (11). This process is suitable for the elimination of natural and synthetic organic pollutants at low concentrations like 5-FU from wastewater and water streams (12). In

addition, a wide range of low to medium molecular mass compounds are removed without generating by-products (13).

Many types of adsorbents are used in several separation applications. Either they came from industrial process or they have natural origin. Carbonaceous, polymeric and oxidic adsorbents are classified as engineered adsorbents. They present the highest adsorption capacities, because they are prepared and manufactured with constant properties and strict quality control. Otherwise, natural adsorbents are cost-effective and cheaper than engineered, but their characteristics are more likely to change and they show less capacity (14).

GNPs are one of the adsorbents, which are used in medical, biology and catalysis applications. They could transport and unload the pharmaceuticals, they are easy to synthesize and ready to operate and they have non-cytotoxic properties.

In this study, gold nanoparticles capped with citrate are used to adsorb 5-Fluorouracil. In addition, the parameters that affect the chemical interaction between 5-FU and GNPs have been studied such as reaction time, pH, temperature and adsorbent dosage. UV-Vis spectroscopy was used to analyze different concentrations of 5-FU during all experiments.

1.2 Research objectives

The objectives of this research are:

1) Develop a method for removal of 5-Fluorouracil drug from water using gold nanoparticles.

2) Optimize the environmental conditions for 5FU removal from water; such as pH, temperature, contact time, concentration of adsorbate and adsorbent dosage.

1.3 Research question

Will the gold nanoparticles capped with citrate be able to remove 5-FU from water?

1.4 Batch experiments

Concentrations of 5-FU drug were determined by finding out the absorbance at the characteristic wavelength using UV–visible spectrophotometer. Standard calibration charts were prepared by measuring the absorbance of different 5-FU concentrations at wavelength of 265 (Figure 1.1).

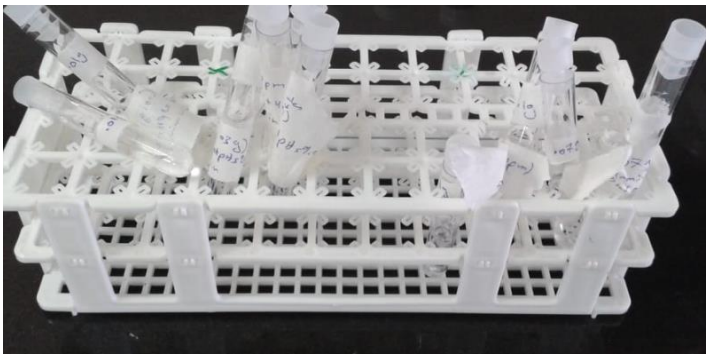


Figure1.1: batch experiment for 5-FU removal by GNPs

Chapter Two

Literature Review

2.1 Pharmaceuticals

Environmental scientists had worked and studied the risks of unknown, unrecognized or unpredicted chemical pollutants in the environment. The United State Environmental Protection Agency's (U.S.EPA) Office of research and development put a strategic plan 2000 that includes many aims. One of the top five aims is to reflect and identify the evolving threats of such chemicals (2). One large group of chemicals receive relatively slight consideration is the pharmaceuticals, which are consumed by humans and animals and could reach rivers, groundwater, lakes, soil and even drinking water. These drugs may affect the environment and cause devastating impacts (15).

The detection methods are not available for all the drugs around the world. In addition, the methods used for analysis are not standardized internationally and the detection limits could be variable according to the type of drug (16). Some medicines are more dangerous than others. This is due to their ability to influence people or wildlife. They include antibiotics, antidepressants, anti-inflammatories, analgesics and hormone replacement therapies.

Pharmaceuticals take their way into the environment through different ways. Owens found that about 30% to 90% of the active ingredient could be found in any excreted drug in an oral dose. Also many medicines are excreted to the environment and they still have active metabolites (16).

Another contribution to the environmental impact of drugs is the unsuitable disposal of them if patients does not complete their medical recipe or they want to clean out their medicine cabinet and get rids of unwanted drugs in the sink or down the toilet. In both cases, drugs will take their way to the sewage treatment plants, but these plants are not capable to eliminate such pollutants from wastewater.

Removal efficiencies of pharmaceuticals from wastewater range from 20% to more than 80% and it depends on the drug (16). In 2014, UK Water Industry Research published a report about 160 study of wastewater treatment works, showed several drugs were present in the final effluent in high concentrations enough to affect ecosystems (17). See Table 2.1.

Table 2.1: Summery of concentrations for 26 selected micro pollutants in effluents and surface waters (17)

Pharmaceutical	Effluents concentration(ng/L)	Surface waters Concentration(ng/L)
Erythromycin	130.0	3.4
Sulfamethoxazole	136.0	20.0
Iopromide	2630.0	134.0
Hydrocodone	41.0	1.6
Acetaminophen	9.5	33.0
Trimethoprim	58.0	4.0
Pentoxifylline	2.9	1.6
Naproxen	128.0	11.0
Ibuprofen	65.0	28.0
Diclofenac	40.0	3.0
Carbamazepine	226.0	25.0
Caffeine	228.0	105.0
Fluoxetine	1.7	NA

The primary cause of death in the world is cancer, after cardiovascular and infectious diseases (18). Treatment of cancer by either chemotherapy or radiation have many restrictions and side effects (19). Some factors affecting the selection of therapy are cancer type and the development stage (20). The number of people suffering from cancer are increasing daily and in the following year's there are expectations that the disease will continue to grow and spread. Cytostatic drugs are applied in chemotherapy, among several groups of pharmaceutics, and a growth in their demand is expected to increase in developed countries (21).

Cytotoxic therapy drugs have a family name known as antineoplastic, which are produced to inhibit the cells growing such as those associated with cancer tumour (22). Actually, these drugs could harm any growing eukaryotic organism (23).There are over than 50 cytotoxic compounds that

disrupt the division of cancer cells used in hospitals in developed countries. The call for therapy treatment in developed countries keeps increasing at about 10% per year according to the Department of Health (24), (25). The medical sciences ability was increased through following a trend towards more functional doses to monitor the side effects of these hazardous drugs (26), (27).

Sixteenth pharmaceutical compounds were analyzed in the water samples in palestine, namely Phenacetin, Indomethacin, Diclofinac, Ibuprofen, Fenoprofen, Ketoprofen, Gemfibrozil, Fenofibrat, Fenofibrinsaure, Bezafibrat, Clofibrinsäure, Carbamazepin, Pentoxifyllin, Naproxen, Diazepam, Etofibrat. In all of those, only Ibuprofen, Diclofinac and Carbamazepine were detected and the other are nil. From these results it was found that there is no data about the presence and behaviour of 5-FU drug in our water resources (28).

2.2 5-Fluorouracil

In the late 1950s, the antimetabolite 5-fluorouracil was present in the pharmaceutical market. It was the most anti cancer drug used in the treatment of various tumors including breast, head and neck and gastrointestinal tract cancer (5). This drug is excreted unmetabolized via urine within 24h of an approximate percentage of 2-35% (29) or 11-20% (23)from the administrated drug.

Cytotoxic drugs act in several ways, some of them by damping essential biosynthetic processes, or by being incorporated into macromolecules,

such as DNA and RNA, inhibiting their normal function. The fluoropyrimidine 5-FU does both. It is converted intracellularly into several active metabolites: fluorodeoxyuridine monophosphate (FdUMP), fluorodeoxyuridine triphosphate (FdUTP) and fluorouridine triphosphate (FUTP). These active metabolites block RNA synthesis and the action of Thymidylate Synthetase (TS) (Figure 2.1).

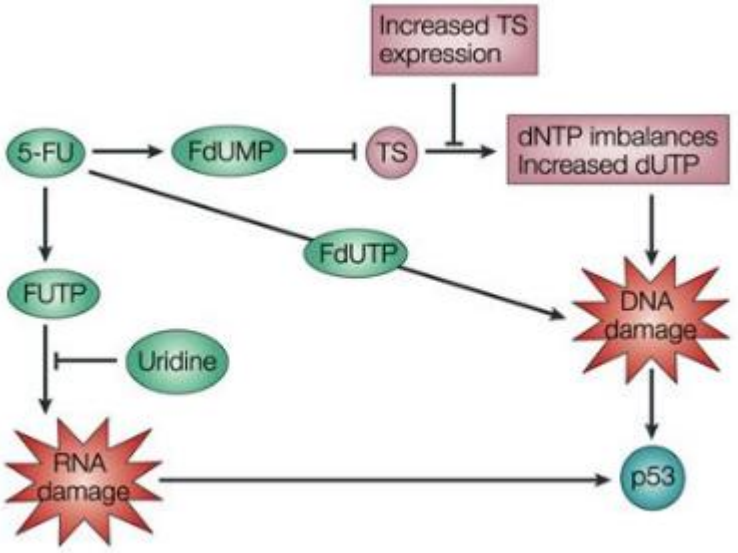


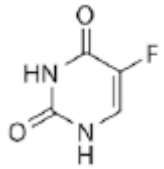
Figure 2.1: 5-FU metabolism (30)

TS is necessary for DNA replication and repair, which is interrupted by its inhibition. Also results in deoxynucleotide (dNTP) pool imbalances and increased levels of deoxyuridine triphosphate (dUTP), both of which cause DNA damage (30).

The physical and chemical properties of 5-FU were described in (Table 2.2). The boiling and melting point proved that 5-FU is a non-volatile compound, which is necessary in terms of safety, when it is operated. 5-FU is weakly vulnerable to direct photolysis under natural sunlight since it has ultraviolet absorption between 265 and 266 nm. The pKa is 8.02, which

makes 5-FU in weak acids group (31). Thus, when pH values above 8 then 5-FU molecule is mainly negatively-charged, at pH =7.4 around 25% of 5-FU is ionized, being basically neutral at pH 6 or lower (32). (Figure 2.2) shows the net charge variation of 5-FU molecule with pH.

Table 2.2: Physical-chemical properties of 5-FU (33)

Compound identification (name and structure)	**5-fluoro-1H-pyrimidine-2,4-dione** **5-Fluorouracil** 
Molecular formula	$C_4H_3FN_2O_2$
Molecular weight	**130.077 g/mol**
Volume	**95.34** $A^{\circ 3}$
Boiling and melting points	**Decomposes at 282-283℃**
Water solubility at 22℃	**1.11×** 10^4 **mg/L**
pKa	**8.02**
Vapor pressure	**2.68×** 10^{-6} **mmHg**
K_{ow}	$10^{-.89}$
K_{oc}	**8**
K_H	**1.66×** 10^{-10}**atm.** m^3/mol
BCF	**3**
Half –lives	**39.6 hr in air** **360 hr in water** **720 hr in soil** **3240 hr in sediment**
Excretion	**2-35% or 11-20%**
UV_{max}	**265-266 nm**

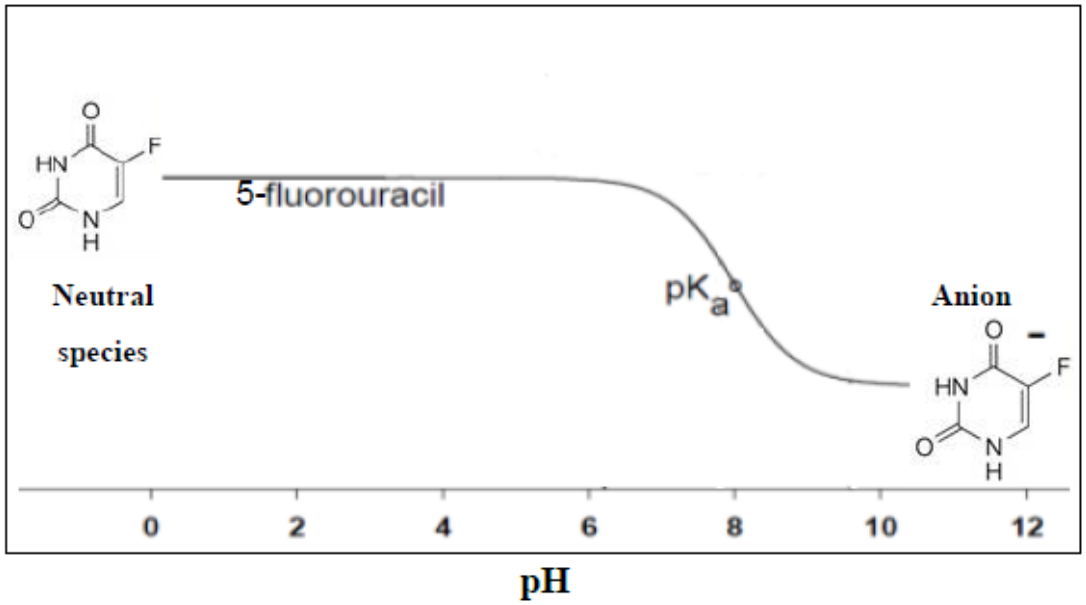


Figure 2.2: Variation in the ionization state of 5-FU molecule with pH (34)

5-Fluorouracil is primary distributed in solid and liquid phases (e.g. Biofilm, activated sludge, suspended solids, sediments and soil) since this drug has low vapor pressure(2.68×10^{-6} mmHg) and Henry's law constant (1.66×10^{-10} atm.m^3/mol). The value of octanol-water partition coefficient of 5-FU is low and it is about ($K_{ow} = 10^{-0.89}$). Therefore, this makes the drug to be low adsorbed by suspended solids in water, but still have a high mobility through soil /sediments because of its organic carbon partition coefficient ($K_{oc} = 8$).

The half-life of 5-FU is 3240, 720, 360 and 39.6 hours in sediments, soil, water and air respectively (33). This means that it is less persistent in air and more persistent in sediments. Besides these outcomes, water is the main problem, as it is the carrier medium to spread 5-FU in the environment.

5-Fluorouracil is global manufactured and consumed, being free to the environment through several waste streams (35). 5-FU concentrations in wastewaters vary from study to study, Table 2.3 showed that wastewater produced by oncological ward was found to have the highest measured of 5-FU concentration (150 μg/L). These data show that hospital effluents participate in abundant degree to the loads of these pollutants and that hospital wastewater are the main but not the only source of 5-FU in the environment in general.

Because 5-FU have hydrophilic property and does not have the possibility to be readily adsorbed to the sludge, so it is unexpected to be eliminated in convential wastewater treatment plants (WWTP) (35).

Table 2.3: 5-FU occurrence in wastewaters.

Matrix	**Concentration range (μg/L)**	**Reference**
WWTP effluent	< 0.006 - 0.015	(15)
WWTP effluent	0.0083 – 0.01	(36)
Municipal wastewater	0.0047 – 0.014	(37)
Hospital wastewater	< 0.005 - 0.027	(15)
Hospital wastewater	< 0.027	(38)
Hospital wastewater	0.027 - 124	(35)
Hospital wastewater	0.035 – 0.092	(37)
Hospital wastewater (oncological ward)	4 - 150	(7)
Hospital wastewater (oncological ward)	20 - 122	(6)

2.3 Removal processes of 5-FU

Removing micro pollutants by the application of advanced wastewater treatment processes is intensively discussed topic by (39) (40). Some of these processes are widely used in wastewater treatment such as Activated Carbone and ozonation (41). A new regulation has been promulgated by Switzerland which is the first country required to increase the removal efficiency of micro pollutants to be about 80% in the future (www.bafu.admin.ch). Some Swiss treatment plants are already developed to reach the requirements of removing micro pollutants.

Different treatment processes are considered and applied worldwide, some of these processes are advanced and tertiary treatment that are required to treat the polluted water, like membrane filtration, reverse osmosis and sand filters, but these processes are inefficient and not effective in the removal of 5-Fluorouracil as standalone treatment. So other techniques must be presented to remove it such as advanced oxidation processes (AOPs) and adsorption (9).

AOPs are practically used to eliminate substances with low biodegradability and high chemical stability as 5-FU. This process is favorable since it makes total mineralization to water, CO_2 and inorganic materials or it converts them into compounds that are more innocuous. Furthermore, AOPs can be applied in biological remediation for wastewater treatment either as a pre-treatment or as a post-treatment. Being at the same time cost efficient and extremely applicable from an economic perspective (42).

There are two classifications of AOPs: heterogeneous and homogeneous processes. The second one is divided into process that using energy and process without energy (Figure 2.3). The formation of Hydroxyl radicals is the main outcome from these applications that are very reactive to organic compounds and leads to full mineralization: (43) (44):

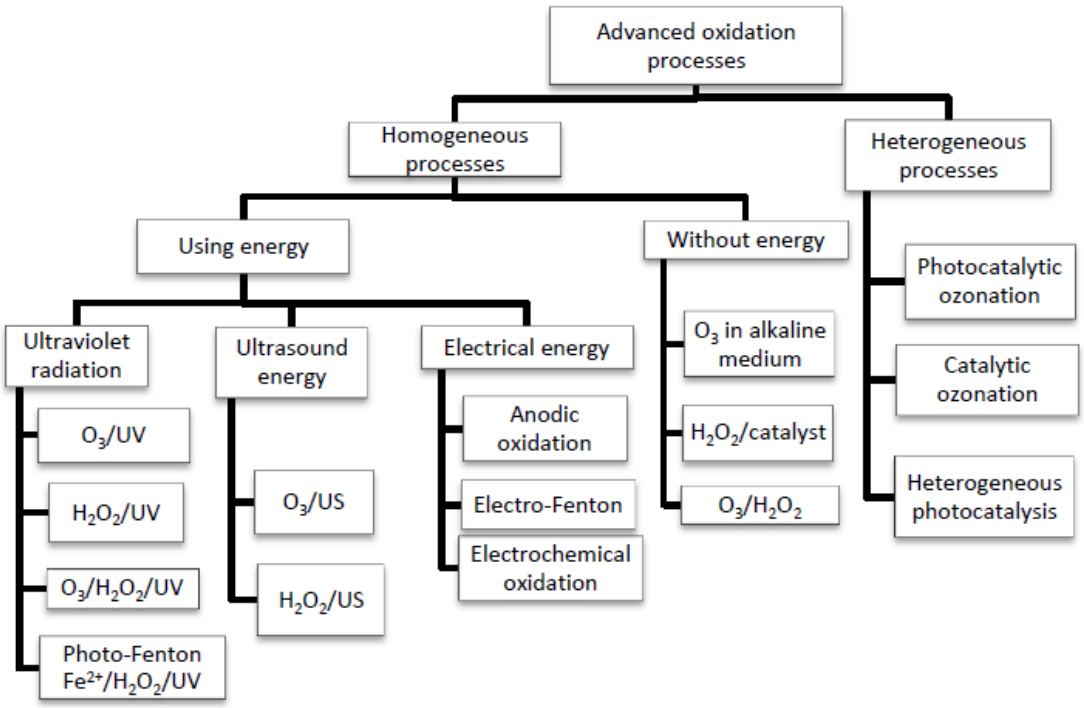


Figure 2.3: Advanced oxidation processes classification (45)

AOPs → ·OH + Pollutant → CO_2+H_2O+ inorganic ions Eq.2.1

Although AOPS are effective economic approach for the treatment of pharmaceuticals, it is expensive to use it in the removal of cytotoxic compound such as 5-FU when it is at low concentrations (46). Thus, there is a necessity to improve the removal procedures by applying combined

methodologies (e.g. adsorption + AOPs). The focus of this work will be the concentration of effluent by adsorption process to make it posteriorly degraded by AOPs.

Over the past ten years, many studies have been carried out on Pharmaceuticals decomposing using photocatalytic oxidation methods such as endocrine-disrupting compounds and anti-inflammatory agents (47) (48).Cytostatics usually lack the possibility for direct photolysis, but they may be removed during water treatment by adsorption, ozonation, advanced oxidation process or by chlorination. One of the most effective technologies is photocatalytic oxidation using TiO_2 (49), (50) . Organic compounds have been degraded by using many semiconductors, as photo catalysts (51), but TiO_2 is the most commonly used because it is inexpensive and has a higher physical and chemical stability and non-toxic compound (52).

A 5-FU was removed based on photocatalytic oxidation using different photo catalyst: Degussa P25, Aldrich TiO_2 and ZnO. Lin (1) reported that 5-FU (27.6mg/l) was nearly removed (>99.9%) within 4 h using Degussa P25 of 300mg/l. The type and properties of photo catalyst present and the compound that is required to be removed from water and air affect the performance of photocatalytic oxidation. There are two types of TiO_2 (DegussaP25, Aldrich) and ZnO that have the same band gapes (DegussaP25, Aldrich=3.0-3.2 eV; ZnO =3.2eV). Also the conduction/valence band energies are about (0.2-3.0 eV, NHE) that corresponded to wavelengths in the range of (300-388nm) (47).

Lin (1) reported that the photocatalytic oxidation of 5- fluorouracil under optimized conditions (initial concentrations of Degussa P25 and 5-fluorouracil are 20 mg/l and 200 mg/l, respectively, at pH = 5.8). (Figure2.5) shows the photocatalytic reactions including the oxidation by direct valence hole and the generation of free OH radicals.

$h_{vb}{}^{+}$+2H2O $\rightarrow$ H3O^{+} + $\cdot OH_{free}$

Eq.2.2

$e^{-}+O2^{-} \rightarrow O2^{-}$+ H2O $\rightarrow \cdot OH_{free}$ Eq. 2.3

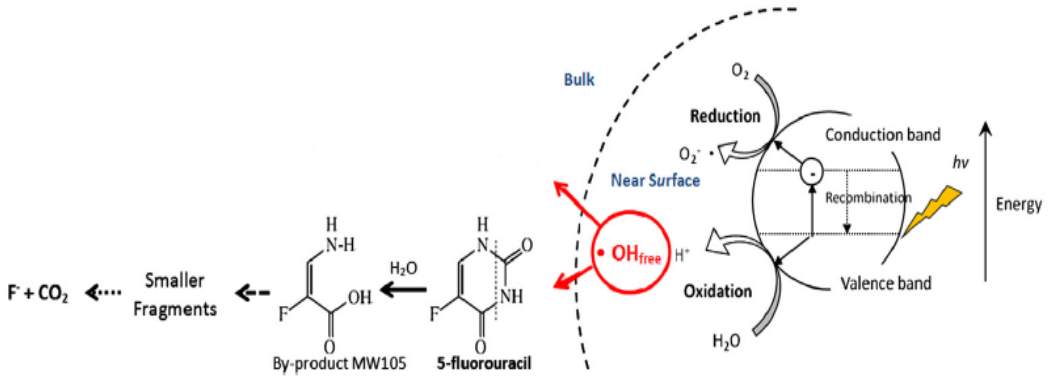


Figure2.4: Conceptual scheme of photocatalytic oxidation of 5FU, **(1)**

Table2.4: Experiential conditions (1)

concentration of 5FU (200 μg/l)	**Photo catalyst loading of (5mg/l)**	**pH**	**Reaction constant k(min/l)**	**Time of irradiation(h)**	**Efficiency**
200	Degussa P25	5.8	.0365	2	>99.99% removed
200	Aldrich TiO2	5.8	.0096	8	1.8% remained
200	ZnO	5.8	.0041	8	12.1% remained

The above Table 2.4 shows the conditions of a preliminary experiment that was executed with elementary concentration of 5FU (50 µg/l) (an environmentally relevant condition). This Degradation was described by pseudo-first order kinetics. Also this experiment showed that 5-fluorouracil did not undergo direct UV photolysis (50) and Degussa P25 which has a particle size in the range of(20-30 nm) possess a higher activity than Aldrich-TiO_2 (100-200 nm particle size), because its smaller particle size and significantly larger surface area (53).

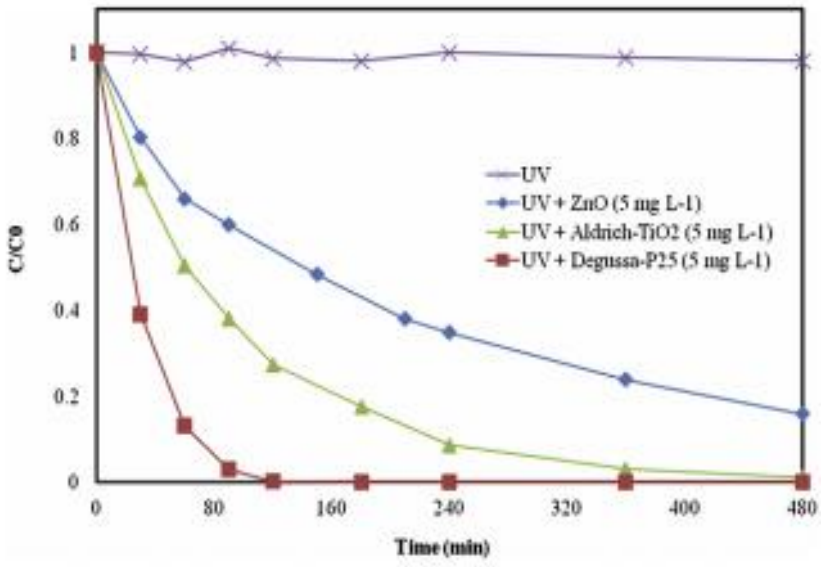


Figure2.5: The removal efficiency of 5-fluorouracil using different photo catalysts, (1)

2.4 Adsorption process

There are many advantages for the adsorption process, including high efficiency of removing organic/inorganic contaminants with low concentrations, regeneration and reuse possibility, simple procedures with reliable operational system, both continuous and batch processes are

applicable, low energy consumption and the absence of toxic byproducts (55) (56).

Two forces drive the overall process. The first one is the solubility of the solute in the adsorption solvent, which is related to the lyophobic character of the solute. So the lower the interaction between the adsorbate and the solvent where it is present, the higher the adsorption of the adsorbate on the adsorbent.

The affinity between the adsorbent and the adsorbate (pharmaceutical) is a second driven force, which comes from chemical interaction, generally termed chemical adsorption, or from van der Waals attraction, usually named physical adsorption (57).

Chemical adsorption includes the formation of chemical bonds with electrons exchange between certain surface sites and solute molecules. Generally, a single molecular layer can be adsorbed and the adsorption is irreversible and very specific. Physical adsorption is reversible and nonspecific; it does not depend on the electronic properties of the adsorbent and adsorbate. Multiple layers may be created with low adsorption energy. The solute is more strongly attached to a specific site in chemical adsorption compared to physical adsorption. Therefore, physically adsorbed molecules can transfer easily within the interface. It is usually difficult to distinguish between chemical and physical adsorption since they have different binding energies (higher energies in chemical adsorption and lower energies in physical adsorption) (58).

The effluent of wastewater treatment plant contains many micro pollutants and pharmaceuticals residue that have ecotoxicological effects. Thus, activated carbon adsorption is applied to reduce the concentrations of such pollutants in wastewater. This technique is one of few processes that effectively helps to treat the wastewater. Although AC adsorption is basically targeted at polar compounds, they are altogether removed to a certain extent which has rarely been studied before. In 2013, Kovalova (34)made a study to collect the data of batch kinetic models and adsorption isotherm with two powdered activated carbons (PACs) to evaluate the removal efficiency of the polar cytotoxic drugs 5-fluorouracil (5-Fu) and cytarabine (CytR) from WWTP effluent and ultrapure water (34).

Kovalova (34)published his study about the removing of polar micro pollutants that have octanol/water partition coefficient below (-1) like (5-FU) from wastewater by adsorbing them onto powdered activated carbon. The amount of activated Carbon that is sufficient to remove more than 90% of polar compounds are just able to remove about 50% of 5-FU. Also it was found that there is a significant effect of pH solution and ionic strength on the adsorption capacity for the charged 5-FU only. Therefore, adsorption capacities increased at weaker ionic strengths and at acidic medium. Kovalova (34) executed a study to evaluate the removal of the polar drug 5-Fluorouracil from wastewater treatment plant and ultrapure water through adsorption with two Powdered Activated Carbons (SAE and HOK). (Table 2.5) shows the characteristics and operating conditions of activated carbon.

Table 2.5: Operating conditions and characteristics of the activated carbons (34)**.**

Adsorbent	SAE Super	HOK Super
PI	9.8	10
Surface Area(m^2/g)	1300	300
Particle Size D50 (µm)	15	24
Raw material	Peat/Wood	Lignite
Matrix	WWTP effluent TOC=5mg/L	
Adsorbent(mg/L)	220	500
5-FU (mg/L)	0.2	
T(^{0}C)	20.0	
pH	7.8	

The adsorption capacity of carbons increased when having a higher surface area (e.g. SAE Super) and it was verified that the kinetic model for describing both carbons is the same, which is called Homogeneous surface diffusion model (HSDM) (Table 2.6). This model expects the diffusion of molecule to the adsorption site from the outer surface of the adsorbent particle through the pore surface. And it supposes that the interior mass transfer is controlled by surface diffusion only and the pore volume resistance is insignificant (59).

Table 2.6: Properties of adsorption of activated carbons (34).

Adsorbent (AC)	Equilibrium time (min)	Adsorption capacity (mg/g)	Kinetic Model	Isotherm Model
SAE Super	300.0	0.86	HSDM	Freundlich
HOK Super		0.38		

2.4.1 Gold nanoparticles capped with citrate

Gold is a precious metal occupies a premier position in the world economy. Over decades, it has been used in jewelry applications due to its yellow lustrous form, and in the electronics industry as a material of chemically inert contact (60). Although gold is one of the leader subject in investigation themes of science, it contributed to the renaissance and increased number of science publications in many fields especially nanoscience and nanotechnology.

Gold nanoparticles (GNPs) are presently participated in researches explosion because of their characteristics and their application capacities. These metals are the most stable and studied nanoparticles in modern science, they have attractive properties and they are produced of multiple types of materials science.

Gold nanoparticles (GNPs) have unique physical and chemical characteristics and they are easy to synthesize and ready to function. Also the core of the gold is non-toxic and inert. Therefore, it is used as a drug carrier (61). Reduction process is one of the most widely method used in GNPs synthesizes. This synthesis process can happen either by biological or chemical method. The main components in the production of GNPs are metal precursor such as chloroauric acid (HAuCl4), reducing agents as sodium citrate and sodium borohydride (62) and a stabilizer like citrate, polymers and phosphine (63). It was reported that Manson et al used sodium borohydride, sodium citrate and hydroquinone to produce (HAuCl4) acid (64).

Citrate is a common electrostatic stabilizing agent for gold nanoparticles because the particles are typically produced through a citric acid reduction reaction. Electrostatic stabilization arises from a mutual repulsion between neighboring gold nanoparticles that occurs because of the negative surface charge of the citrate layer (65).

The interaction between 5-FU and GNPs surface coated with citrate, occurred through the formation of two hydrogen bonds; one between carbonyl group in the 5-FU drug and OH in sodium citrate and the other between the NH of the drug and COO^- as shown in (Figure 2.6) (66).

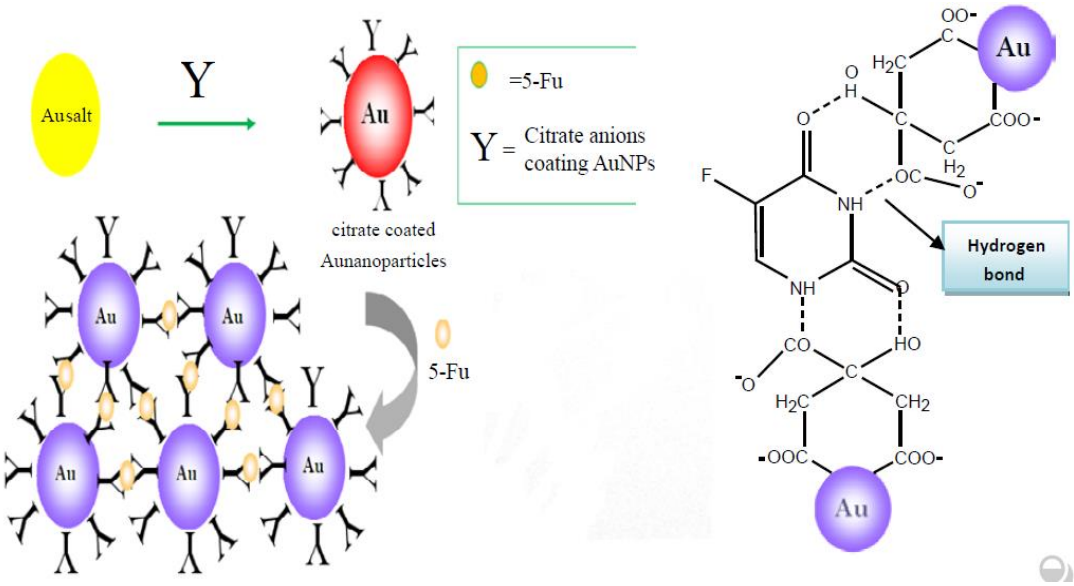


Figure 2.6: The chemical formula suggested for the interaction between 5-FU and GNPs (66)

GNPs capped with citrate are used to adsorb bovine serum albumin (BSA) molecules from aqueous solution and it has observed that the adsorption depends on many parameters such as PH, contact time, temperature and

concentration of BSA. The maximum adsorption percentage occurs at pH=8.6 and the more the initial concentration of adsorbate the more increase in adsorption percentage. Also increasing the temperature cause a decrease in the percentage and the reaction described by pseudo first-order kinetics (67).

Many studies describe the mechanism of Loading 5- Fluorouracil (5-FU) to the surface of gold nanoparticles (GNPs). This binding helps the drug to penetrate into the cell membrane and promote its activity as therapeutic drug. (66) made a research about the absorption of 5-FU into GNPs capped with citrate and it was found that the absorption band performed at longer wavelength. Also the research studied the operation factors in the system and their effects on the adsorption percentage such as, 5-FU concentration, time after mixing 5-FU with GNPs and pH.

2.4.2 Adsorption equilibrium and isotherms

Adsorption isotherm described the relationship between the adsorbate on the adsorbent surface. These isotherms are essential to discover unique adsorbents and to find the best and ideal design parameters for adsorption system. Adsorption models were produced to forecast the system performance and to make a comparison in different systems. They define the interaction between adsorbent materials and pollutants; as a result they are critical to optimize the adsorption system, the properties of the surface and adsorbent capacities. If the adsorbent and the adsorbate are being in contact for enough time, they reaches to equilibrium state where there is a

dynamic reaction between the adsorbate in the bulk solution and the solution interface. The adsorption data is described using several models such as Langmuir, Freundlich, Sips and Dubin-Radushkevich (D-R) models that are the most widely used (68).

2.4.2.1 Langmuir model

Langmuir model assumes the uptake of unimolecular thick layer of adsorbate occurs on the surface of a homogeneous adsorbent without interactions between adsorbed molecules. The mathematical form is:

$$q_e = \frac{q_L K_L C_e}{1 + K_L C_e} \qquad \text{Eq. 2.4}$$

Where q_L is the maximum monolayer coverage capacity (mg/g), C_e and K_L are the equilibrium concentration of adsorbate (mg/L) and the Langmuir adsorption equilibrium constant ((L/mg), respectively (69), q_e is the amount of pharmaceutical adsorbed per unit mass of adsorbent (mg/g) and it was calculated by using the following mass balance equation (Eq.2.5):

$$q_e = \frac{(C_o - C_e)V}{W} \qquad \text{Eq. 2.5}$$

Where C_o and C_e is the initial and equilibrium concentration of the adsorbate (mg/L) respectively, V is the volume of the solution (mL), and W is the mass of the adsorbent used (g).

$(C_o - C_e)$ represents the adsorbed amount (ppm). Langmuir parameters are found by plotting a graph of (C_e/q_e) values versus(C_e). Which are $(\frac{1}{q_L})$ as slope and $(\frac{1}{q_L K_L})$ as y-intercept (70).

One of important characteristics of Langmuir isotherm can be expressed in terms of a dimensionless separation factor (R_L)which is

$$R_L = \frac{1}{1+C_o K_L} \qquad \text{Eq. 2.6}$$

Where $C_o \; and \; K_L$ are the initial concentration of adsorbate and Langmuir constant, respectively. The value of (R_L) indicates the isotherm type to be linear if ($R_L = 1$) or unfavorable($R_L > 1$), irreversible ($R_L = 0$) and favorable ($0 < R_L < 1$).

2.4.2.2 Freundlich model

Freundlich adsorption model deals with non-ideal sorption onto surfaces including multilayer sorption. This adsorption supporting sites depends on different affinities of heterogeneous surfaces. It supposes that the binding strength decreases with increasing degree of site occupation (71). The typical form of the adsorption isotherm is:

$$q_e = K_F \; C_e^{\frac{1}{nf}} \qquad \text{Eq. 2.7}$$

Here, K_F refers to the adsorption equilibrium constant (mg/g), and n^f is the (heterogeneity coefficient) Freundlich model constant that indicates the adsorption intensity (g/l). The values of (n^f) shows the degree of nonlinearity between solution concentration and adsorption. If (n^f) is equal to unity, the adsorption is linear; and the adsorption process is chemical if the value is lower than unity or if the value is beyond unity,

adsorption is a favorable physical process (72). Freundlich parameters are found by making a plot of (Lnq_e) values versus(LnC_e). Which are ($\frac{1}{nf}$) as slope and (LnK_F) as y-intercept (70).

2.4.2.3 Sips model

Is a combination of the Langmuir and Freundlich isotherms and it is given the following general expression (73)

$$q_e = \frac{K_S {C_e}^{B_S}}{1 - a_S {C_e}^{B_S}} \qquad \text{Eq.2.8}$$

Where: Ks is Sips isotherm model constant (L/g), βs is Sips isotherm exponent, and as is Sips isotherm model constant (L/g). The linearized form is given as follows:

$$B_s lnCe = -ln\left(\frac{K_S}{q_e}\right) + lna_s \qquad \text{Eq.2.9}$$

2.4.3 Adsorption kinetics

Kinetic adsorption process is important to show the formation of adsorption bond between the adsorbate and adsorbent (74). It describes the mechanism and adsorption rate and define the time of equilibrium. Also it helps to optimize the process and identify the best operating conditions especially in full-scale batch system (75). Adsorbents have several pore structures and various surface chemistries, so these factors may control the rate of adsorption (59).

2.4.3.1 Pseudo first –order kinetics

In 1898, Lagergren proposed the first model to describe the kinetics of adsorption called pseudo-first order. This expression is applied for the liquid-solid adsorption system, the rate equation for pseudo first-order kinetic model can be written as follows for a batch system (76):

$$Ln(q_e - q_t) = Ln\, q_e - K_1 t \qquad \text{Eq. 2.10}$$

Where K_1 is the pseudo first-order rate constant of adsorption (min^{-1}). q_e and q_t are the amount of adsorbate adsorbed per unit mass of adsorbent (mg/g) at equlibrium and time t respectively. To compute the first –order rate costants ($K_1$and q_e) a graph of ln($q_e - q_t$) versus t was craeted to have linear relationship.

2.4.3.2 Pseudo second –order kinetics

Pseudo –Blanchard (77) proposed second order model for the analysis of sorption kinetics. This kinetic model suppose that the rate-determining step may be chemical adsorption, which include valence forces through exchange or sharing of electrons between the adsorbent and the adsorbate. The final integrated equation for this model is:

$$\frac{t}{q_t} = \frac{1}{K_2 q_e^2} + \frac{t}{q_e} \qquad \text{Eq. 2.11}$$

Where K_2 is the pseudo second-order rate constant of adsorption (min^{-1}). Plotting $\frac{t}{q_t}$ versus t will give a linear relationship for the second order adsorption with $\frac{1}{K_2 q_e^2}$ as y-intercept and $\frac{1}{q_e}$ as the slope of the graph (78).

2.4.3.3 Intra-particle diffusion kinetic model

Weber and Morriss described the diffusion mechanism, which is called intraparticle diffusion (79). The final equation of this adsorption kinetic model is:

$q_t = K_{id} t^{1/2} + Z$ Eq. 2.12

Where K_{id} is the intra- particle diffusion rate constant (mg/g.$min^{1/2}$), Z is a constant indicates the thickness of the boundary layer (mg/g). A plot of q_t versus $t^{1/2}$ gives a straight line of intra-particle diffusion model with Z as y-intercept and K_{id} as a slope.

2.5 Adsorption thermodynamics

Thermodynamic parameters provide useful information about the energetic changes during adsorption and it can be used to define if the process is favorable or not. These parameters include enthalpy change (ΔH), change in Gibbs free energy (ΔG) and change in entropy (ΔS) (80). The general equation that connects thermodynamic parameters is:

$\Delta G = \Delta H - T\Delta S$ Eq.2.13

Where:

ΔH: the change of the standard enthalpy (KJ/mol). The positive values of ΔH means that the adsorption process is endothermic in nature; while the negative values reveals exothermic process.

T: the absolute temperature (K).

Δ*S*: the change of the standard entropy (J/mol.K). If Δ*S* is negative, a decrease in entropy will occur and if it is positive, the entropy increases.

- Δ*G*: the change in Gibbs free energy. If Δ*G* is negative, the process is exergonic and will occur spontaneously in the forward direction to form more products. But if it is positive, the process is endergonic and not spontaneous in the forward direction. the following equation was used to calculate Δ*G*:

$$\Delta G = -R\,T\,Ln\,K_d \qquad \text{Eq.2.14}$$

Where:

K_d: is the thermodynamic equilibrium constant that equals (q_e/C_e) with a unit of mol or (L/g).

R: the universal gas constant that equals 8.314 $J.mol^{-1}.K^{-1}$.

The combination of the previous two equations will give the following equation:

$$Ln\,K_d = \frac{\Delta S}{R} - \frac{\Delta H}{RT} \qquad \text{Eq.2.15}$$

The graph of (LnK_d) versus (*1/T*) will give a straight line with (-Δ*H/R*) as slope and (Δ*S/R*) as y-intercept and it is known as Van't Hoff graph.

To determine the type of adsorption if it is chemical or physical, activation energy was calculated by equation 2.14.

$$LnK_2 = LnA - \frac{Ea}{RT} \qquad \text{Eq.2.16}$$

where E_a is the Arrhenius activation energy (kJ/mol), *R* is the gas constant (8.314 J/mol K) , *A* is the Arrhenius factor and *T* is the absolute temperature of the solution . ($-Ea/R$) is obtained as a slope of the straight line resulted from the plot of LnK_2 versus *1/T*. The physisorption processes usually have energies in the range of (5–40 kJ/mol) while higher activation energies (40–800 kJ/mol) suggest chemisorption (81).

Chapter Three

Materials and Methods

3.1 Chemicals and materials

5-Fluorouracil was purchased from sigma-Aldrich with a purity (≥ 99%). For the adsorption and kinetics tests, GNPs were used as adsorbate, which were prepared at university of Castilla-La Mancha (Spain). 5-FU solutions were prepared using Distilled water. (0.1M HCl) and (0.1M NaOH) solutions were prepared to adjust pH. Syringe filters with 0.45μm was used to ensure the accuracy of measurements.

3.2 Instrumentations

In this research, pH was determined by pH meter (model: 3510, JENWAY) with glass combination electrode (924005) and electrode holder (ATC probe (027 500)). Concentrations of 5-FU were analyzed by UV-vis spectrometry (model: UV-1800, Cat. No.: 206-25400-58, serial No.: A11635406519, SHIMADZU). Shaking water bath (Dailhan Labtech CO., LTD / Korea, serial No.: 08021904, 20 to 250 rpm digital speed control, 220V 50Hz, 1.5KW/7A) was used to control the temperature and to have a homogenous solution. The characteristics of GNPs were analyzed by IR spectrometer (Thermo Scientific Nicolet 869-142300, iD3 ZnSe ATR). The separation of 5-FU from GNPs to measure the concentrations was

done by Centurion (model: 1020D.E /UK, serial No.:7757, 230V, 120 Watt, Thermo Scientific).

3.3Preparation of gold nanoparticles

The glassware used in all experiments were soaked and cleaned in a bath of freshly prepared aqua regia, rinsed in pure water, and dried in air prior to use. GNPs capped with citrate with average size of 10.5 nm and surface area of 314 nm^2 were prepared using (Turkevich method). The first step is to prepare 1 mM of gold hyrdochlorate(HAuCl4) solution of 50 ml, and then the solution was heated under reflux to reach to the boiling point. Then 5 mL of 35 mM sodium tris- citrate was added to the mixture and the liquid is vigorously stirred .The solution was heated for another 30 min, until the color of the mixture changed to deep red which indicates the formation of GNPs. The solution was cooled to room temperature and stored at 4ºC for further use. 7.5 and 10 mL of 35 mM sodium tris-citrate were used to prepare the gold nano particles with diameters of 6.5 and 3.5, respectively (82).

3.4 Preparation of 5-Fluorouracil solutions

A stock solution of 5-Fluorouracil of 100 mg/L was prepared by dissolving 10mg of 5-FU in 100 mL of distilled water. A set of working solutions of 5-FU with different concentrations (5, 10, 20, 50 mg/L) were prepared by dilution. All solutions were stored and preserved in the refrigerator at 4℃ until their use to maintain their stability (83).

3.5 Statistical Analysis

During this research, all experimental runs were done in triplicate. Averages and standard deviations were calculated for each run. Calculations and graphical representations were done by Microsoft Excel software and Matlab program. The collected data were analyzed using ANOVA test.

3.6 Calibration curve

Calibration curve shows the relation between the concentration and absorbance and in this study, it was performed at eleven concentration levels in the range of (0.1-50 mg/L) using UV-visible Spectrophotometer (UV-1800 SHIMADZU) at 265 nm wavelength. 5Fluorouracil concentrations in the range of 0.1-50 mg/L were used to obtain a linear calibration curve with ($R^2 = 99.89\times 10^{-2}$)Figure (4.1).

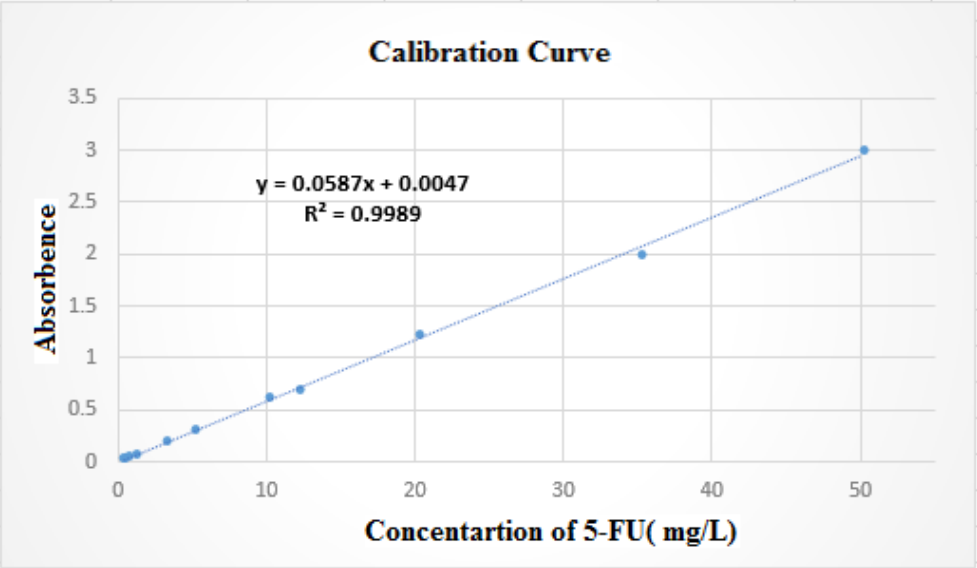


Figure 3.1: Linear calibration curve between absorbance and concentration for 5-FU concentrations in the range (0.1- 50) mg/L

3.7 Adsorption experiments

Experiments were run using different concentrations of 5-Fluorouracil in 50ml solutions by adding a specific weight of GNPs depending on the experiment. HCl (0.1M) and NaOH (0.1M) solutions were prepared to adjust the pH of solution. UV-Vis spectrophotometer at 265nm was used to determine all the adsorption measurements at various temperatures based on the adsorption parameters like contact time, adsorbent dosage, pH and adsorption kinetics, isotherm or thermodynamics. To measure the adsorbate concentration, calibration curve was performed with a linear range from (0.1-50mg/L) and all the solutions are prepared from one stock of 100 mg/L.

The percentage of removal (ε %) is the ratio of difference in initial and final concentration of 5-FU (C_0-C_f) to the initial concentration of 5-FU in the aqueous solution (C_0) and it can be calculated using Eq.3.1:

$$\varepsilon(\%) = \frac{C0-Cf}{C0} * 100\%$$

Eq.3.1

3.7.1 Effect of initial concentration of 5-FU and contact time

During batch experiments the rate at which adsorption occurs is very important for data analysis and calculations and the shaking time come from the need for the characterization of the rapidness of binding and removal of 5-FU (84).

The adsorption capacity of 5-FU on GNPs was calculated at 298K. Asample of 50 mL of 5-FU (5, 10, 20, 50 mg/L) solutions at pH= 5 was added to 100 mL beaker with 0.1 g of adsorbent and used at time range from (1 to 60 min). Then Centurion was used at 5000rpm for 5min and a thin plastic dropper carefully removed the supernatant and UV-visible spectrophotometer was used to measure the absorbance at wavelength of 265 nm.

3.7.2 Effect of pH

The pH solution strongly affects the adsorption performance, and is one of the major parameters, which should be taken in our consideration when studying ionizable compounds (e.g. 5-FU). This factor control the adsorption capacity of gold nanoparticles so to enhance the adsorption, it is necessary to ionize the adsorbate and adsorbent (85). At pH values greater than eight 5-FU have negative form so it is favored to use adsorbents of positively charged (34), (86)(Figure 2.2).

The pH range of (2-13) was applied to measure the pH effect on the adsorption process. Solutions of 0.1M NaOH and 0.1M HCl were prepared for pH adjustment. 0.1g of GNPs added to 50ml of 5-FU with initial concentration of 10 mg/L. The samples were located in shaking water bath at room temperature (T=298K) for 10 min. At the end of each time intervals and after samples were centrifuged, the adsorbent was removed and analyzed by UV-Vis at wavelength of 265 nm.

3.7.3 Effect of adsorbent dose

Many Studies demonstrated that the adsorbent dose is a parameter, which affects the adsorption capacity for a given initial concentration of the pharmaceutical. Different experiments were done with different dosage of GNPs ranging from (10-100 mg) to test the effect of adsorbent dose on the removal of 5-FU .This experiment was done using 10 mg/L solution of 5-FU and pH =10 at 298K. The samples were placed in water bath and shaken at room temperature (298K) for 10 min. The absorbance of supernatant was measured by UV-Vis.

3.7.4 Effect of temperature

Temperature is an important parameter that affecting the adsorption process. This effect is usually dictated by the energetics of the process whether it is exothermic or endothermic. The temperature effect on adsorption process was also evaluated; 0.1 g of GNPs were added to 50 mL of 5-FU solution with concentration of 10 mg/L. Each mixture was placed in a water bath and shaken at the required temperature ranging between (278-318K) for 10 min. At the end of time intervals, and after the samples were centrifuged, the adsorbent was removed and analyzed by UV-Vis.

3.8 Thermodynamics and kinetics of adsorption

Kinetic experiments were executed to understand the mechanism of 5-Fluorouracil adsorption processes over gold nanoparticles and to measure the main sorption parameters based on empirical data, which were fitted to the pseudo-first order, pseudo-second-order, and intra-particle diffusion models.

The temperature effect on adsorption equilibrium of 5-FU from water sample using gold nanoparticles was studied. Langmuir and Freundlich isotherms, which are the most widely applied isotherm, were used to analyze the equilibrium data. Adsorption equilibrium constant was obtained from Freundlich isotherm to calculate the main parameters of thermodynamic such as $\Delta H°$, $\Delta G°$, and $\Delta S°$.

Chapter Four

Results and Discussions

4.1 GNPs Characterization:

4.1.1 Fourier-transform infrared spectroscopy Characterization

GNPs capped with citrate depicted characteristic bands of citrate at 3374.17 and 1638.56cm^{-1}. A strong band at 3374.17 cm^{-1} was assigned to OH stretching and C=O stretching of carboxylate of citrate was assigned to the band at 1638.5cm^{-1} (Figure 4.1).

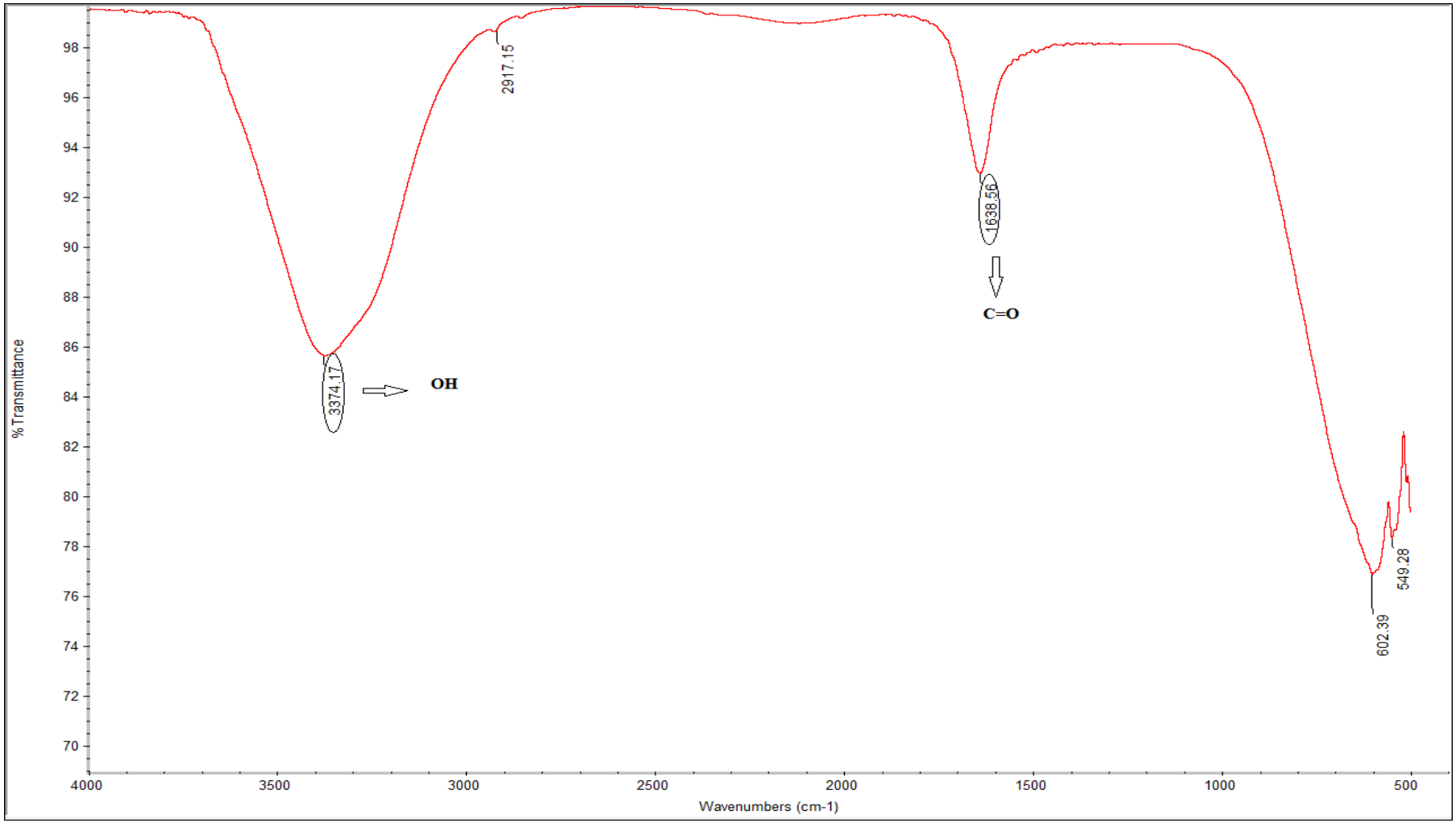


Figure 4.1: FTIR spectrum of citrate –GNPs

4.1.2 Analysis GNPs by Transmission Electron Microscopy

The size of the nanoparticles was confirmed by TEM images and the spacing between the gold nanoparticles can be observed (Figure 4.2). The average size is about 10.5 nm. The presence of particles that have a diameter greater than specified size is due to the overlapping of two or more small particles. The individual nanoparticles allow the citrate layer around the nanoparticles to be seen.

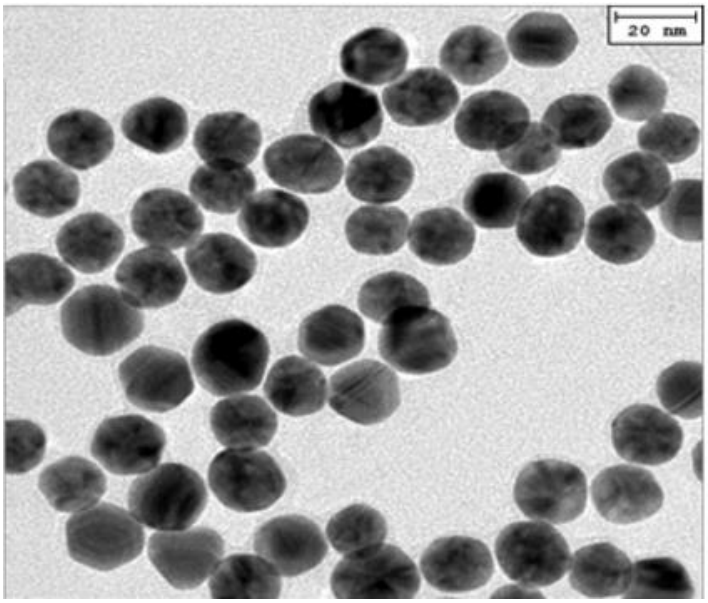


Figure 4.2: TEM image of citrate –GNPs

4.2 Investigation of adsorption parameters

There are several environmental parameters that affecting the adsorption performance such as: contact time, temperature, pH, initial concentration of adsorbate and adsorbent dosage, all of these parameters were studied in this research.

4.2.1 Effect of contact time and 5-FU concentration

The amount of 5-FU adsorbed on GNPs surfaces as a function of time (1-60min) and different initial concentrations (5, 10, 20, 50 mg/L) at pH=5 was investigated (Figure 4.3). The results show that the contact time required to reach equilibrium was less than 15min for 5-FU solutions of concentrations (5-50 mg/L). Also, increasing the time will increase the amount of the 5-Fluorouracil adsorbed by gold nanoparticles. In addition, the best adsorbed amount of 5-FU by gold nanoparticles was at 20 min for all conditions (pH, initial concentration and temperature). Then the adsorbed amount of 5-FU remained constant with the increase of the time because it reached to the equilibrium state. But 10-min period was selected for all conditions to be considered as the optimum contact time as there was a little difference in the adsorption capacity between 10 and 20 min.

In the first (1-15 min) the adsorption of 5-Fluorouracil on the Gold Nano samples were very fast and reached more than 50%. This is due to the available sites on the surfaces of gold nanoparticles and the small activation energies, which has been calculated in the section of thermodynamics. The slow subsequent step (15 - 40 min) was due to the rearrangement of 5-FU ions to find available adsorption sites on the nanoparticles.

In addition, the percentage of adsorption decreased with the increase concentration and this is because the sorption sites became saturated and its energy decreased when the concentration of 5-FU increased in the solution.

Other studies (1) described the effect of initial concentration of 5-FU on photocatalytic oxidation and found that For initial concentrations of 5-FU of 200, 20and 50 µg/L, with 20 mg/L Degussa P25 as adsorbent, 5- FU was >99.9% removed within 90, 120, and 180 min, respectively. The results indicated that 5- fluorouracil yielded the highest rate constant for an initial concentration of 200 µg/L. This result can be explained by the presence of relatively fewer contact opportunities at the two lower initial concentrations (20 and 50 µg/L).

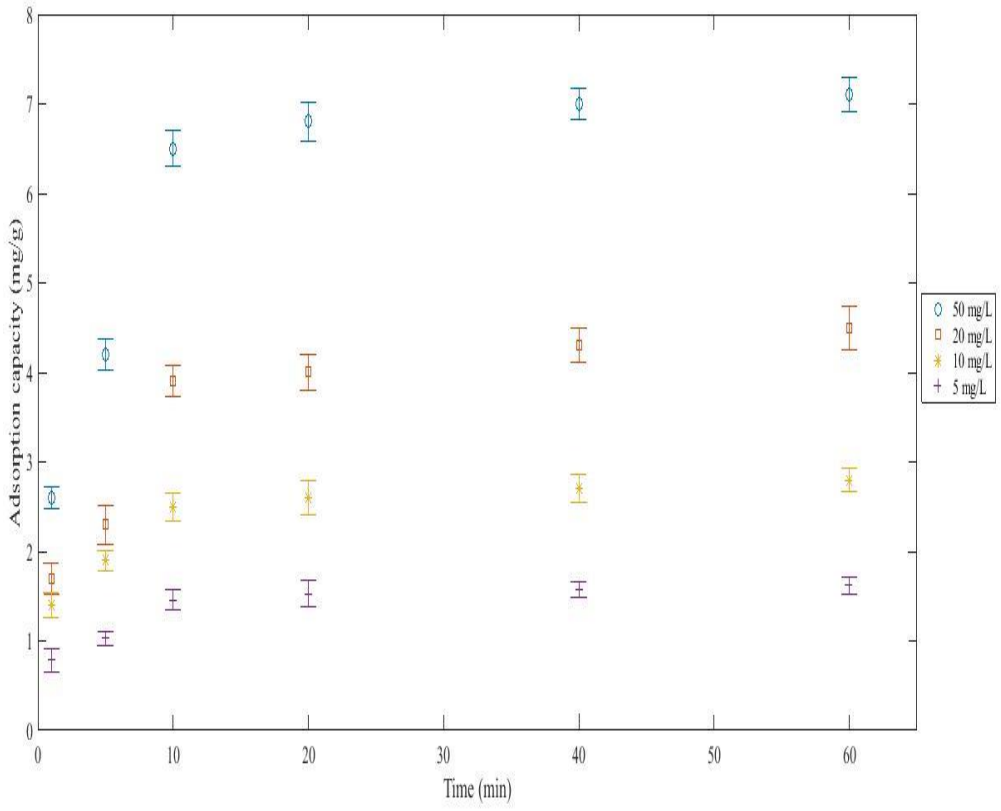


Figure 4.3: Effect of contact time and 5-FU concentration (temperature = 298K, pH= 5, solution volume= 50 mL, adsorbent dose= 0.1 g, CI=95%)

4.2.2 Effect of pH on 5-FU adsorption

The pH solution effect was studied for adsorption of 5-FU on GNPs at room temperature 298K, constant concentration of 10 mg/L, and adsorbent dosage of (0.1 g). The pH solution was adjusted in the range between 2 - 13. The pH effect on the adsorption of 5-FU onto GNPs was studied (Figure 4.4). At pH values greater than eight the adsorption efficiency of 5-FU by gold nanoparticles increased and the maximum adsorbed amount of 5-FU was at pH 10. This is because the compound is anion at High pH values and the active sites of GNPs carries positively charge, which resulted in the increase of the electrostatic force and this will attract more 5-FU anions of the solution.

Other scientists conducted a study about the removal of 5-FU using TiO_2 and the results showed that the best removal was achieved for pH 5.8. The 5-fluorouracil was >99.9% decomposed in 90 min at pH 5.8. However, residues of 19.2, 27.4, and 28.3% remained after 4 h at pH 7.8, 10.0, and 3.0. Also Kovalova (34) found in his study that the influence of the pH solution on the carbon adsorption capacity was observed only for the charged 5-Fu, with higher adsorption capacities at lower pH values.

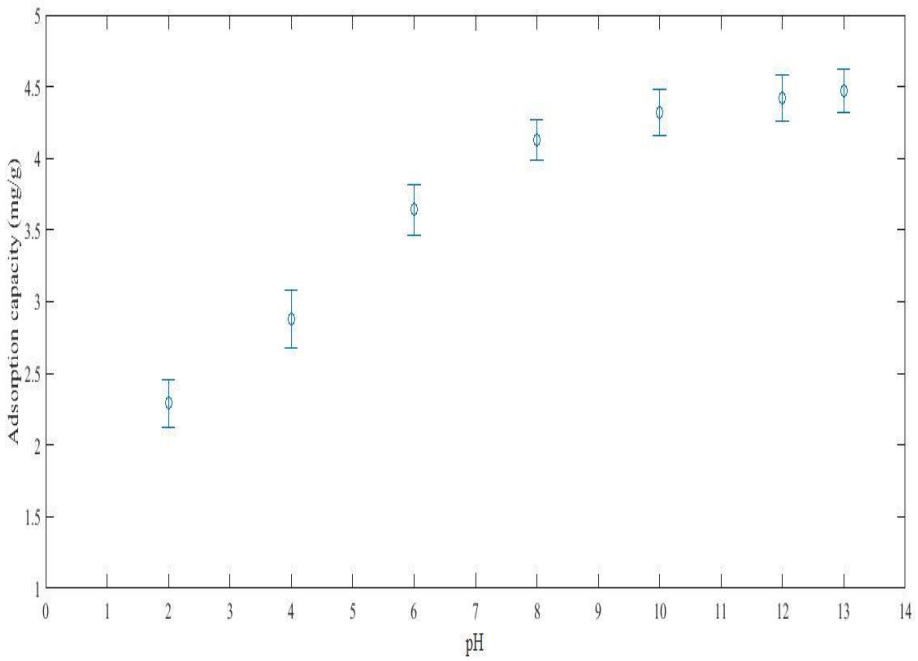


Figure 4.4: Effect of pH on 5-FU adsorption. (Co= 10 mg/L, T=298K, time= 10 min., adsorbent dose= 0.1 g, solution volume= 50 mL, CI=95%)

4.2.3 Effect of amount of adsorbent

The adsorption experiments were implemented at three different adsorbent dosage (10, 50, 70, 100 mg) at pH=10, initial concentration of 10mg/L and constant temperature=298K. Increasing the adsorbent dosage will enhance the amount of adsorbate removed and this is due to the sorption sites that are available at higher dosage values (Figure 4.5). Ultimately, at equilibrium state all active sorption sites come to be saturated and the capacity of adsorption reaches to level beyond which it decreases (87). The optimum adsorbent dosage depends on initial adsorbate concentration and Lin (1) in his research studied the effect of Degussa P25 loading (in the range of 5-100 mg/L) on the removal of 5-fluorouracil at an initial concentration of 200 µg /L. The results showed that the 5-fluorouracil was

>99.9% eliminated within 90 min at a loading of 20 mg/L of Degussa P25, while residues remained for 5, 50 and 100 mg/L of Degussa P25 (the overall degradations were 75.2%, 95.3%, and 89.4%, respectively, after a reaction time of 240 min).

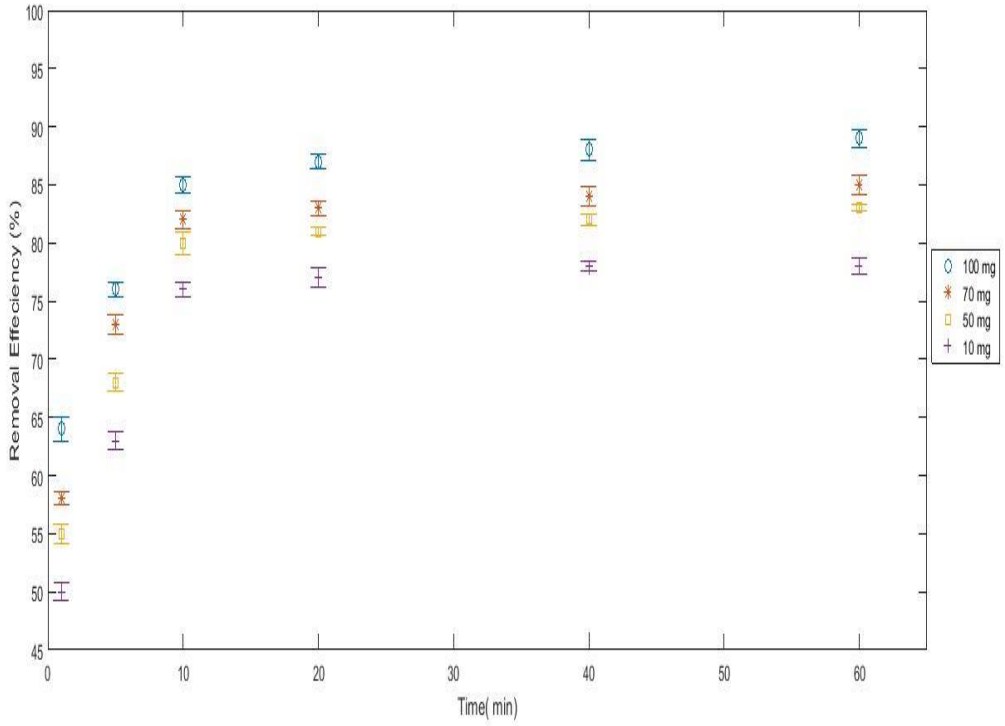


Figure 4.5: Effect of amount of adsorbent on the removal of 5-FU. (Temperature= 298K, time= 10 min., pH=10, concentration of 5-FU= 10 mg/L, solution volume= 50 mL ,CI=95%)

4.2.4 Effect of temperature on 5-FU adsorption

Temperature Experiments were done in the range of (278-318 K) at two different pH values (5 and 10). Generally the percent removal of 5-FU decreased with increasing the temperature (Figure4.6). The maximum

adsorption was achieved at 278K. This indicates that the adsorption of 5-Fluorouracil on (GNPs) follows exothermic process. The decrease of adsorption capacity of 5-FU when increasing the temperature of solution is due to that the sorption sites became less active and the kinetic energy decreased at higher temperatures therefore, there is no sufficient contact between the adsorption site and 5-FU molecules, which leads to decrease in the adsorption efficiency.

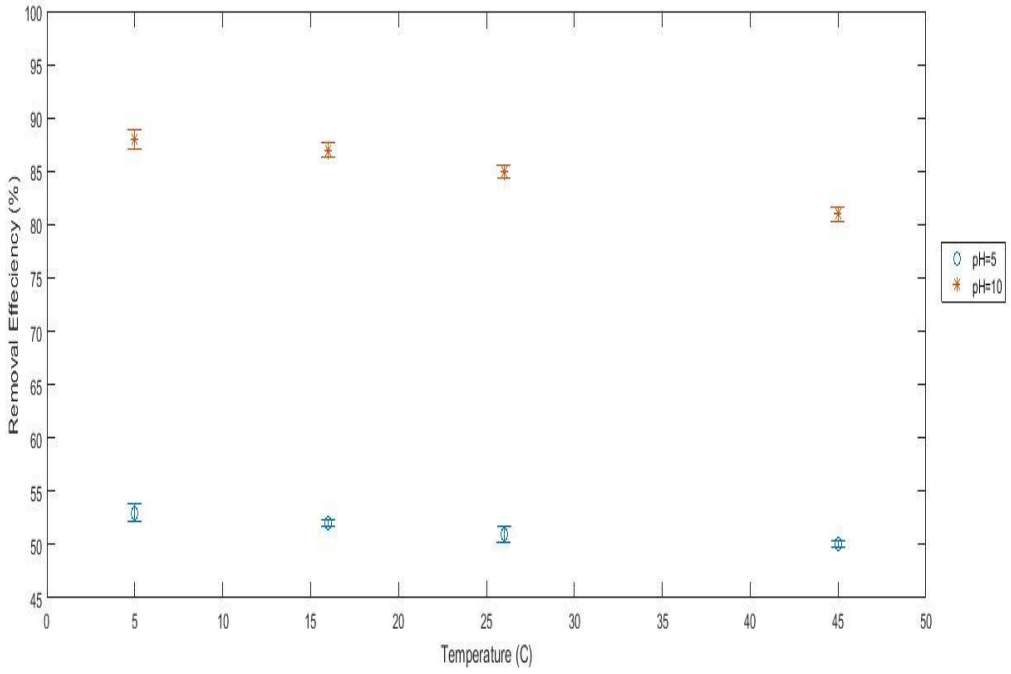


Figure 4.6: Effect of temperature on 5-FU adsorption. (Co= 10 mg/L, time= 10 min., adsorbent dose= 0.1 g, solution volume= 50 mL, CI=95%)

The same results were obtained by Kovalova (34) as his study found that a lower temperature resulted in higher adsorptive uptake of 5-Fu and CytR over a wide range of adsorbate concentrations and the effect of temperature

on adsorption can be explained by the exothermic nature of adsorption processes.

In all experiments that were run to study the effect of contact time, temperature, pH and adsorbent dosage, the coefficient of variance was mostly less than 1%. All variations were considered statistically with confidence interval (CI=95%) and the results show that the distribution of data is normal and there is no significant difference between the groups mean.

4.3 Adsorption isotherm of 5-FU

Certain parameters that describe the characterization of adsorption isotherm were calculated in this research, as it can be used to measure the maximum adsorption capacity and to study the surface properties and the adsorbent affinity (1). To have an idea about the adsorption equilibrium between the 5-FU concentration in liquid phase and the gold nanoparticles; three adsorption isotherm models were used in this study which are Freundlich, Langmuir and Sips models.

4.3.1 Langmuir Adsorption Isotherm

Langmuir model represents the adsorption on the adsorbent surface that have number of fixed active sorption sites. It assumes that each site can only hold one adsorbed molecule without interactions between molecules on different sites and these sites are energetically identical and have the same heat. In addition, it assumes that after equilibrium no further

adsorption can occurs (67). Langmuir model was represented using equation 2.4.

From (Figure 4.7) Langmuir adsorption-desorption equilibrium constant (K_L), the maximum amount adsorbed and correlation coefficient (R^2) were determined and values are shown in Table 4.1.

From Langmuir isotherm, the dimensionless constant separation factor was calculated to determine if the adsorption is favorable or not using Equation2.6.

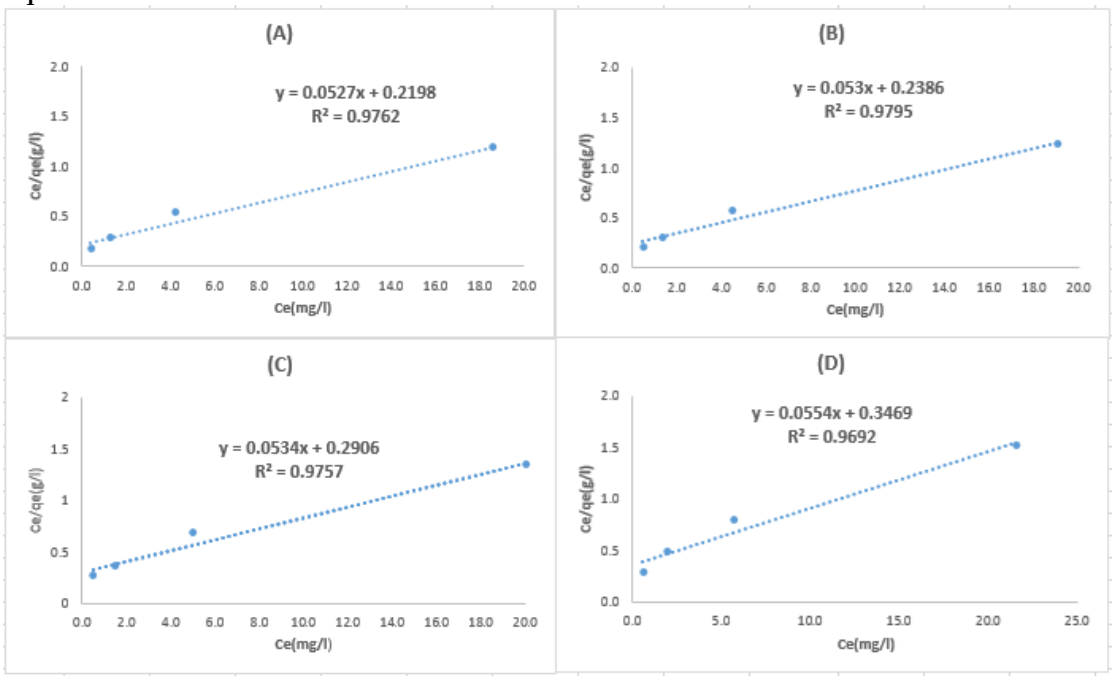


Figure 4.7: Langmuir plot for 5-FU adsorption on (GNPs). Temperature= (A) 278K, (B) 289K, (C) 298K, (D) 318K , pH= 10, time= 10 min., solution volume= 50 mL, adsorbent dose= 0.1 g.

Table 4.1: Langmuir isotherm model parameters and correlation coefficient for adsorption of 5-FU on GNPs at 278, 289, 298 and 318 K.

Model	Parameter	Temperature(K)			
		278	**289**	**298**	**318**
Langmuir isotherm	q_{max} **(mg/g)**	18.97	18.86	18.73	18.05
	K_L **(L/mg)**	0.24	0.22	0.18	0.16
	R_L	0.30	0.31	0.35	0.39
	R^2	97.62×10^{-2}	97.95×10^{-2}	97.57×10^{-2}	0.9692×10^{-2}

4.3.2 Freundlich model Isotherm

Freundlich model is the most important multisite adsorption isotherm for heterogeneous surfaces. It explains the relations between adsorbed molecules and can be applied for non-ideal sorption (88). Equation 2.7 was used to determine Freundlich parameters.

A graph of $Ln(q_e)$ against $Ln(C_e)$ was plotted to calculate Freundlich constants K_F, n and the correlation coefficient (R^2). (Figure 4.8) and (Table4.2) show the results.

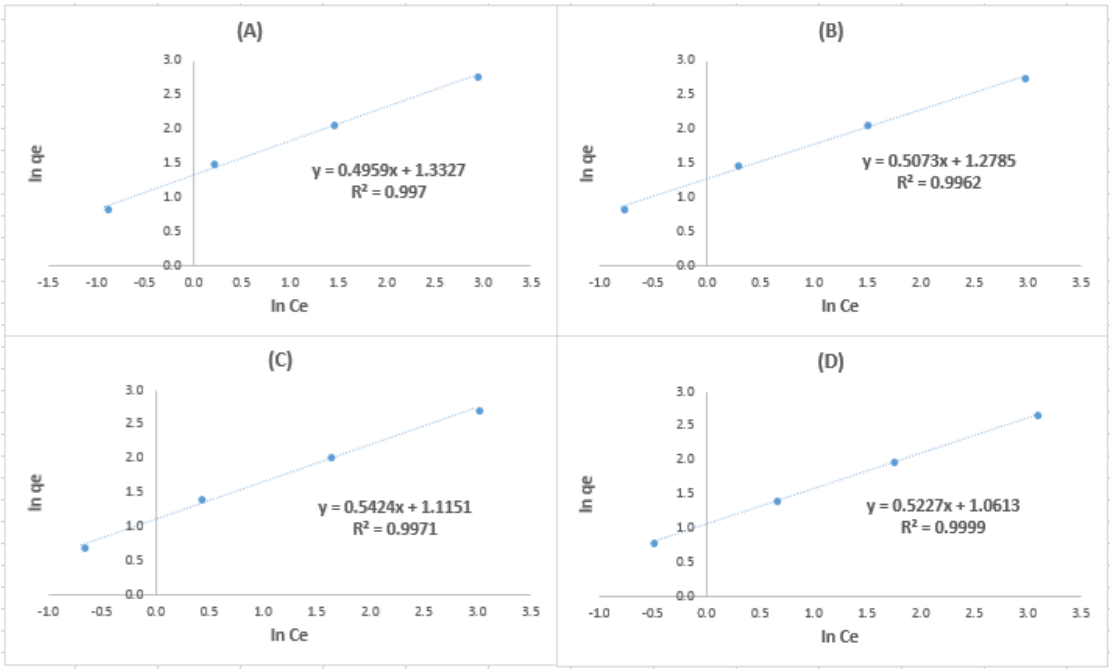


Figure 4.8: Freundlich plot for 5-FU adsorption on (GNPs). Temperature = (A) 278K, (B) 289K, (C) 298K, (D) 318K, pH= 10, time= 10 min., solution volume= 50 mL, adsorbent dose= 0.1 g.

Table 4.2: Freundlich isotherm model parameters and correlation coefficient for adsorption of 5-FU on GNPs at 278, 289, 298and 318K.

Model	Parameter	Temperature(K)			
		278	289	298	318
Freundlich isotherm	*1/n*	0.50	0.51	0.54	0.52
	(L/mg) K_F	3.79	3.59	3.05	2.89
	R^2	99.70 × 10^{-2}	99.62 × 10^{-2}	99.71× 10^{-2}	99.99× 10^{-2}

All the parameters were calculated using the required equations are listed in Table4.2. The values of correlation coefficients greater than 0.99 and the values of *1/n* (0.50-0.54) which indicates a high adsorption intensity and because $n > 1$ this may suggest that slight chemical interactions may be stablished during the adsorption process .

4.3.3 Sips isotherm model

This model is suitable for predicting adsorption on heterogeneous surfaces, thereby avoiding the limitation of increased adsorbate concentration normally associated with the Freundlich model .Therefore at low adsorbate concentration this model reduces to the Freundlich model, but at high concentration of adsorbate, it predicts the Langmuir model (monolayer adsorption) (89).

A graph of $Ln(K_s/q_e)$ against $Ln(C_e)$ was plotted to calculate Sips constants K_s, B_s, a_s and the correlation coefficient (R^2). (Figure 4.9) and (Table4.3) show the results.

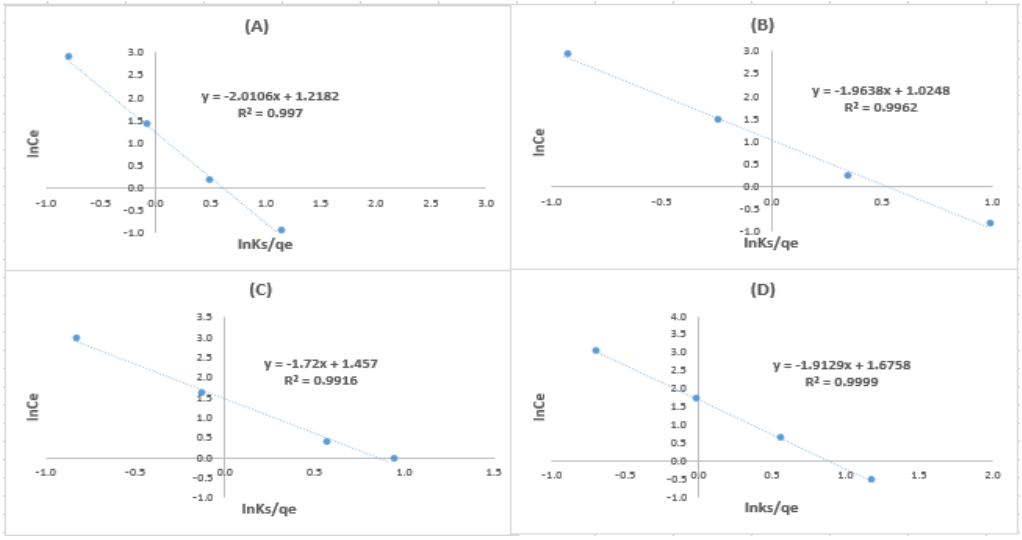


Figure 4.9: Sips plot for 5-FU adsorption on (GNPs). Temperature = (A) 278K, (B) 289, (C) 298, (D) 318K, pH= 10, time= 10 min., solution volume= 50 mL, adsorbent dose= 0.1 g.

Table 4.3: Sips isotherm model parameters and correlation coefficient for adsorption of 5-FU on GNPs at 278, 289, 298and 318K.

Model	Parameter	Temperature(K)			
		278	289	298	318
Sips isotherm	B_s	0.50	0.51	0.58	0.52
	(L/g) K_s	6.94	6.04	6.45	6.93
	a_s (L/g)	1.83	1.68	2.33	2.39
	R^2	99.7×10^{-2}	99.62×10^{-2}	99.16×10^{-2}	99.99×10^{-2}

When Bs equals unity, the Sips isotherm returns to the Langmuir isotherm and predicts homogeneous adsorption. On the other hand, deviation of Bs value from the unity indicates heterogeneous surface. Table 4.3showes that the degree of heterogeneity, Bs was less than one, which demonstrates the heterogeneity in the surface. Sorption data obtained in this study better fit the Freundlich form rather than the Langmuir form, which was also confirmed by the data in Table 4.3.

Monica Santos (57) Showed that there isn't an isotherm model which describes equilibrium data for all the carbon materials. While the adsorption of 5-FU on carbonaceous materials such as: BP2000, Merck, Vulcan XC72 and Wittco was better described by Freundlich model, the adsorption on CECA was better fitted by Langmuir and Norit by Sips.

Another study of removal of cytotoxic drugs (5-FU and CytR) from wastewater using HOK Super and SAE Super (PACs) found that the single-solute isotherm data of these compounds could be well described by the Freundlich isotherm model (34).

4.4 Adsorption kinetics of 5-FU

Different initial concentrations (5, 10, 20, 50 mg/L) were applied to conduct the kinetic studies for the adsorption of 5-FU on gold nanoparticles. The dynamic data obtained from experiments were fitted for pseudo first- order model, pseudo second order- model and the intra-particle diffusion model using equations (2.8 -2.10):

The kinetics data was analyzed for both pseudo first-order and pseudo-second order models, and it was found that the correlation coefficients (R^2) for pseudo second order was higher than pseudo-first-order and it reached more than 0.99. Also the calculated values of adsorption capacity (q_e) for pseudo-second-order were very close to the experimental values (q_e) and this means that the adsorption process of 5-Fluorouracil on the surfaces of GNPs were described by the pseudo-second-order model.

Increasing the concentration of 5-FU will decrease the values of K_1 and this is because the number of available sorption sites were reduced with the increase in concentration of 5-FU (Table 4.4). This will reduce the values of rate constant and extra time is required to reach equilibrium.

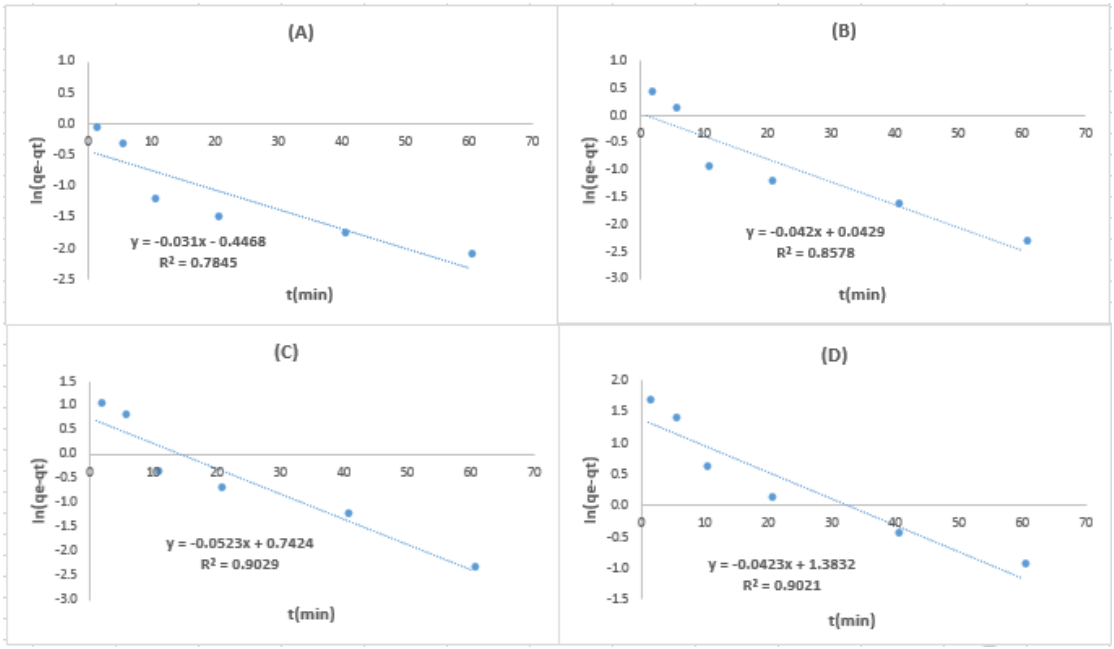


Figure 4.10: Pseudo first order sorption kinetics of 5-FU on GNPs. (Concentration= (A) 5 mg/L, (B) 10 mg/L, (C) 20 mg/L, (D) 50 mg/L, temperature = 298K, pH= 10, solution volume = 50 mL, adsorbent dose= 0.1 g

Table 4.4: Pseudo first order kinetic model parameters for 5-FU adsorption on GNPs at 298K.

C_0 (mg/L)	qe (exp) (mg/g)	Pseudo-first -order model		
		K_1 (min-1)	q_{cal} (mg/g)	R^2
5	1.75	.031	0.640	0.7845
10	2.95	.042	1.043	0.8578
20	4.60	.052	2.100	0.9029
50	8.40	.042	3.980	0.9021

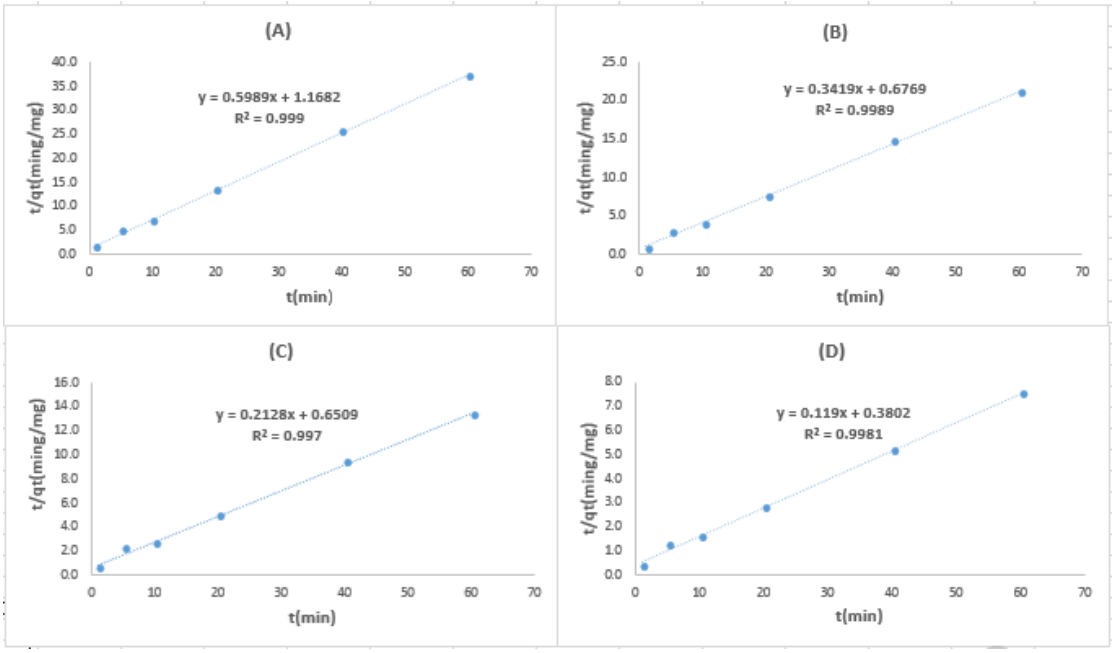


Figure 4.11: Pseudo second order sorption kinetics of 5-FU on GNPs. (Concentration= (A)5 mg/L, (B) 10 mg/L,(C) 20 mg/L, (D) 50 mg/L, temperature= 298K, pH= 10, solution volume= 50 mL, adsorbent dose= 0.1 g

Table 4.5: Pseudo second order kinetic model parameters for 5-FU adsorption on GNPs at 298K.

C_0 (mg/L)	q_e(exp) (mg/g)	Pseudo-second-order model		
		K_2 (mg. g^{-1}min^{-1})	q_{cal} (mg/g)	R^2
5	1.75	0.31	1.67	99.9×10^{-2}
10	2.95	0.17	2.93	99.89×10^{-2}
20	4.60	0.07	4.69	99.7×10^{-2}
50	8.40	0.04	8.40	99.81×10^{-2}

The mechanism behaviour of the diffusion of the adsorbed 5-FU on GNPs at various initial concentrations (5, 10, 20 and 50 mg/L) was studied based on Weber and Morris theory and by using equation5.6.

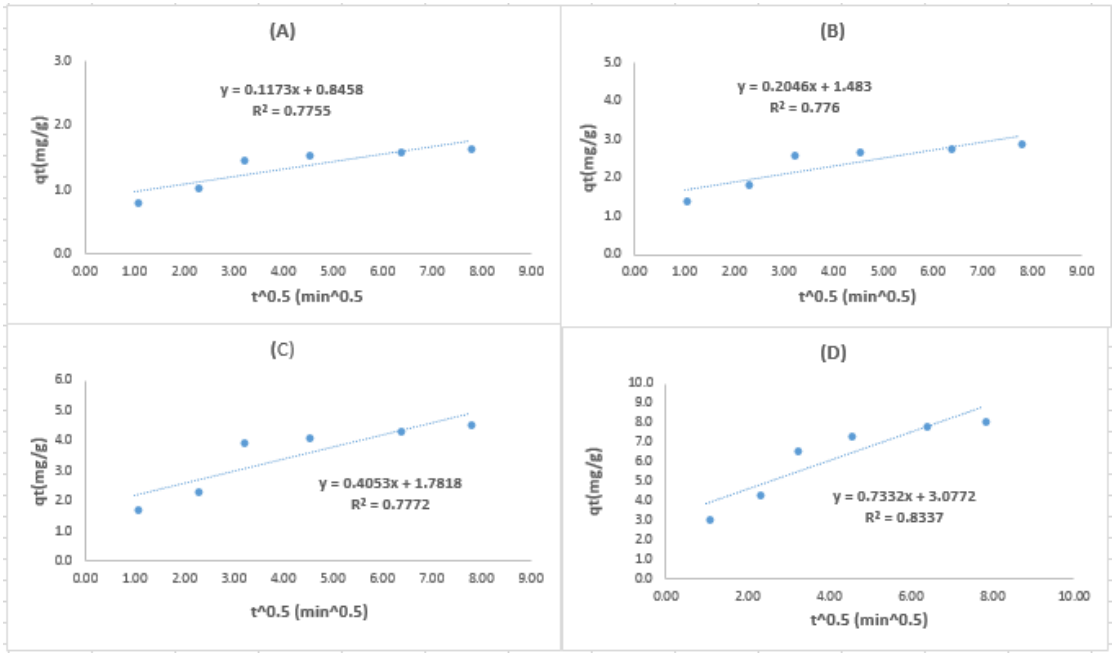


Figure 4.12: Intra-particle diffusion kinetics of 5-FU on GNPs. (Concentration= (A) 5 mg/L, (B) 10 mg/L, (C) 20 mg/L, (D) 50 mg/L, temperature = 298K , pH= 10, solution volume= 50 mL, adsorbent dose= 0.1 g

Table 4.6: Pseudo first order kinetic model parameters for 5-FU adsorption on GNPs at 298K.

C_0 (mg /L)	Intra-particle diffusion model	
	K_{id}	Z
5	0.12	0.85
10	0.20	1.48
20	0.41	1.78
50	0.73	3.08

Similar kinetic results were obtained in other studies for the adsorption of 5-FU on carbonaceous materials and it was found that it was better described by pseudo-second order model than pseudo- first order model (57). While the results of adsorption kinetic tests which were conducted

with both 5-Fu and CytR in WWTP effluent and by using SAE Super and HOK Super doses proved that The data were mathematically described by the homogeneous surface diffusion model (HSDM) (34).

4.5 Adsorption thermodynamics

Thermodynamics behaviour for the adsorption process of 5-FU molecules on gold nanoparticles surface was examined at different temperatures ranges (278–318 K), and the temperature effect on the adsorption behaviour was studied at optimal conditions (Figure 4.12).The parameters of thermodynamics were calculated by using van't Hoffs (Eq.2.15) and (Eq.2.13) (90).

In this research, the change of the standard enthalpy ΔH^0 was negative for the adsorption of 5-FU on gold nanoparticles surface. It was clear that adsorption of 5FU molecule on GNPs were exothermic, which is supported by the fact that the rate of adsorption decreases with temperature. The change of standard entropyΔS^0determines the disorderliness of adsorption at solid–liquid interface and in this research it was negative and was indicative of decreased randomness at adsorbent-adsorbate interface during the adsorption (91). AlsoΔG^0 reflects the feasibility of the adsorption. The ΔG^0 values were negative at all temperatures of the experiments, proving that the adsorption was spontaneous and thermodynamically favorable.

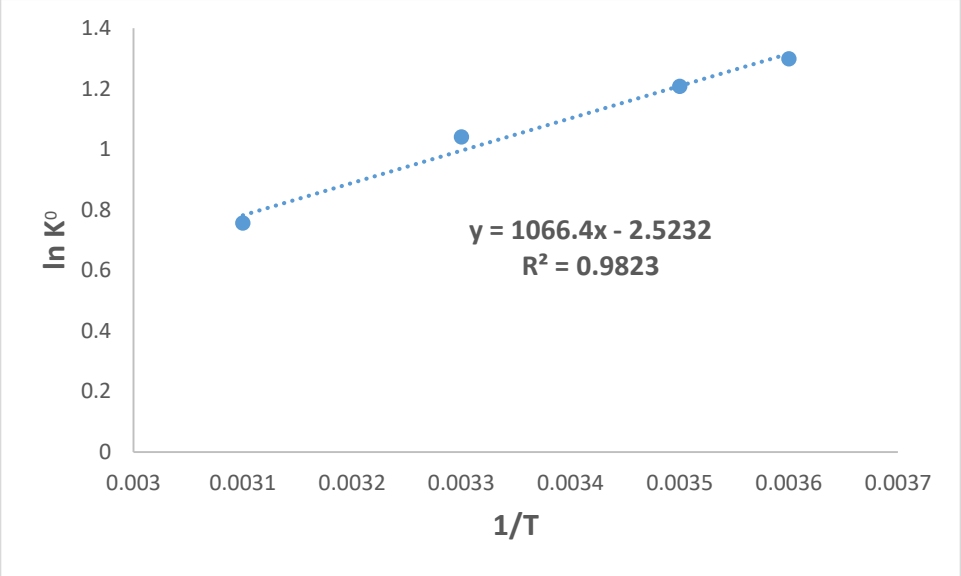


Figure 4.13: Plot of *LnK*◦ versus *1/T* for 5-FU adsorption on GNPs. (temperature= 298K, pH= 10, time= 10 min., solution volume= 50 mL, adsorbent dose= 0.1 g)

Table 4.7: Thermodynamic parameters for the adsorption of 5-FU onto GNPs (concentration = 10 ppm, pH = 10, adsorbent dose = 0.1g, t = 10 min).

Temperature (*K*)	**Δ*G*° (KJ/mol)**	**Δ*H*° (KJ/mol)**	**Δ*S*° (J/K.mol)**
278	-3037.56	-8.87	-20.98
289	-2806.78		
299	-2596.98		
318	-2198.36		

Arrhenius relationship express the pseudo-second-order rate constant of 5-FU adsorption as a function of temperature (equation 2.16).

The activation energy is 5.403 KJ/mol and this means that the adsorption of 5-FU on GNPs is physiorption (Figure 4.13).

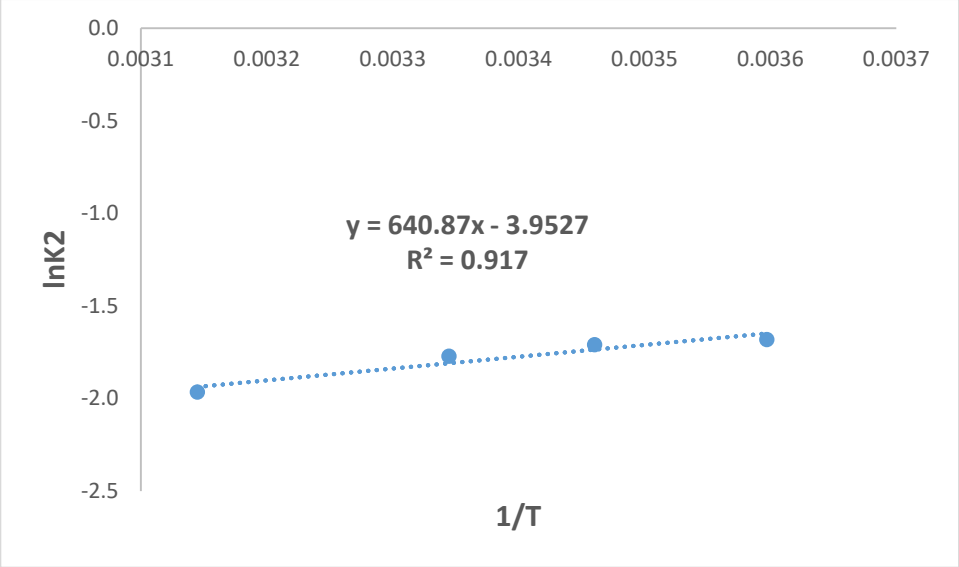


Figure 4.14: The plot of LnK_2 vs. *1/T* for the adsorption of 5-FU by GNPs surfaces using the Arrhenius equation

4.6 Recovery of 5-FU and reusability of the adsorbent

Regeneration of adsorbent is important to make the adsorption process more environmentally friendly and to reduce the cost. It helps in measuring the possibility of reuse GNPs. From thermodynamics study it was found that the adsorption between 5-FU and GNPs is govern by physiorption. And this means a weak adsorptive forces that makes the regeneration of adsorbent feasible. In addition, the pH solution affect the recovery process and it has been found that the removal efficiency increased as pH increased in the basic medium. The desorption of 5-FU can be carried out by decreasing the pH of the solution and acidic medium is more efficient for regeneration.

The GNPs can be regenerated by 0.1M of HCl, the same adsorbent was used to repeat the experiment 4 times, and the results are summarized in (Table 4.8). From the whole cycles it can be seen, there is no noticeable decrease in the sorption capacities. The desorption efficiency of 5-FU was maintained almost the same thing and this make the adsorption process of 5-FU on GNPs cost effectiveness.

Table 4.8: Percentage of 5-FU removal by the regenerated adsorbent compared with a fresh one at (temperature= 298K, pH= 10, solution volume= 50 mL, adsorbent dose= 0.1 g, contact time= 10 min, concentration= 5 mg/L)

Recycling times	**1**	**2**	**3**	**4**	**5**
GNPs (5-FU removal efficiencies, %)	**90**	**89.9**	**89.7**	**89.6**	**89.6**

Chapter Five

Conclusions and Recommendations

5.1 Conclusions

Gold nanoparticles were found to be an effective and functional adsorbent for the adsorption of 5-Fluorouracil molecules from the aqueous medium. This research studied the adsorption of 5-FU on GNPs as a function of initial 5-FU concentration, pH, temperature and adsorbent dose. It was observed that the adsorption efficiency increased when the contact time is increasing and becomes gradual after 20 min. The removal efficiency of 5-FU adsorbed by GNPs could reach to more than 85% at 298 K, pH = [7-9], concentration of 5-FU =10 mg/L and within 10 min. the maximum adsorption capacity was at pH value of 10 and it goes down when the pH of solution decreases.

The dynamical adsorption behavior of 5-FU was fitted well to pseudo second-order kinetic model. It was found that the adsorption equilibrium correlated reasonably well with the sips isotherm so at low concentrations the data was best fitted with freundlich model than Langmuir model.

The effect of temperature was studied to measure the change in thermodynamics parameters like ΔS^0, ΔG^0 and ΔH^0 , the analysis of these parameters indicated that the adsorption process was: (a) spontaneous with negative ΔG^0 and (b) mainly exothermic due to the low ΔH^0 value (-8.87KJ/mol). Negative value of ΔS^0 (-20.98 J/K.mol) showed the

decreased randomness at the solid –liquid interphase during the adsorption process. Also the activation energy value was 5.403KJ/mol which indicated that the adsorption was physiorption. GNPs were found to be easy to reuse and recover as the results showed that there was no remarkable decrease in the removal efficiency of 5-FU when regenerated adsorbent was used.

5.2 Recommendations

This work aims to remove 5-FU by adsorption. It should be reflected upon the results in order to enable further studies that lead to an efficient removal process for 5-FU from water. Recommendations for future works are:

- To use analytical method for the detection of 5-FU such as LC-MS-MS technique to monitor the concentration and occurrence of this drug in water resources.
- To study the economic feasibility of this research since this study focused only on the removal of 5-FU by GNPs.
- To study the effect of 5-FU drug on public health and environment in Palestine.
- To determine the responsibilities of ministers towards pharmaceuticals waste management in Palestine.

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جامعة النجاح الوطنية
كلية الدراسات العليا

استخدام جسيمات النانو الذهبية لإزالة 5- فلوروبوراسيل من المحاليل المائية

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أ.د. شحدة جودة

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

2018

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الملخص

يتزايد استخدام الأدوية السامة للخلايا في علاج السرطان سنوياً. 5-فلورويوراسيل هو أحد الأدوية المضادة للأورام الأكثر استخداما في العالم والقيمة السمية لهذا الدواء هي 94 نانو غرام /ل. هذا البحث استخدم جسيمات النانو الذهبية لإزالة 5-فلورويوراسيل وأجريت العديد من التجارب لدراسة سلوك امتزاز 5-فلورويوراسيل من عينات المياه من خلال التحليل الطيفي للأشعة فوق البنفسجية. تم اختبار عدة معاملات مثل: زمن التماس، ودرجة الحرارة، ودرجة الحموضة، والتركيز الأولي 5-فلورويوراسيل وكمية جسيمات النانو الذهبية المستخدمة. كانت بيانات التوازن أكثر ملائمة بواسطة نموذج sips. كانت الكفاءة لإزالة 5-فلورويوراسيل بواسطة جسيمات النانو الذهبية أكثر من 85٪ في الظروف البيئية(pH =7-9) ، تركيز 5-فلورويوراسيل =5ملغم/ل ودرجة الحرارة = 298 كلفن .تظهر البيانات الحركية أن الامتزاز يتبع النموذج الحركي الزائف من الدرجة الثانية. تشير المعلومات الديناميكية الحرارية إلى أن عملية الامتزاز كانت طاردة للحرارة وذاتية. تشير قيمة طاقة التنشيط والتي هي 5.403 كيلو جول /مول إلى أن الامتزاز بين 5فلورويوراسيل وجسيمات النانو الذهبية هو فيزيائي. ان استخدام جسيمات النانو الذهبية لامتزاز 5-فلورويوراسيل هي عملية فعالة وذلك بسب سهولة إعادة استخدام واسترداد جسيمات النانو بواسطة محلول 0.1M HCL.

أظهرت النتائج ان جسيمات النانو الذهبية هي فعالة وعملية في إزالة 5-فلورويوراسيل من الماء. يوصى بان يتم اخذ تواجد 5-فلورويوراسيل في المصادر المائية بعين الاعتبار وذلك للتقليل من اثاره السلبية ويجب تطبيق طرق مختلفة لإزالته من الماء.