DOKUZ EYLÜL UNIVERSITY
GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES

ADSORPTION OF PROMETHAZINE HYDROCHLORIDE ONTO MONTMORILLONITE K10 FROM AQUEOUS SOLUTION

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İZMİR

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ADSORPTION OF PROMETHAZINE HYDROCHLORIDE ONTO MONTMORILLONITE K10 FROM AQUEOUS SOLUTION

ABSTRACT

The sorption of promethazine hydrochloride onto montmorillonite K10 was studied under different temperatures, pH conditions, ionic strengths and contact time. Adsorption data were fitted the linearized Langmuir, Freundlich, Temkin and non-linearized Langmuir and Freundlich equation. The results show that linearized Langmuir equation gave the best fit experimental data compared to other equations. C_m (adsorption capacity) and K_f (relative sorption capacity) for the sorption of promethazine hydrochloride were evaluated from the Langmuir and Freundlich isotherms data, respectively. C_m ranged from 0.333mmol/g at 17.5°C to 0.245mmol/g at 30°C. K_f values decrease from 1.015mmol/g at 17.5°C to 0.365mmol/g at 30°C. In other words, the adsorption decreases with increase in temperature. The adsorption of promethazine hydrochloride was strongly dependent on pH and ionic strength. Equilibrium studies show that maximum adsorption was observed at pH=10.5 and adsorption capacity increased as increasing ionic strength. E (adsorption energy) values, obtained by DR isotherms demonstrated that the sorption of promethazine hydrochloride on montmorillonite K10 at 17.5°C can be explained by ion exchange. Thermodynamic parameters (ΔG, ΔH and ΔS) were computed and these parameters indicate that adsorption is exothermic, spontaneous and favourable. Adsorption kinetics reveals the adsorption process followed pseudo-second order kinetics. Thus, montmorillonite K10 can be used as excipient for promethazine hydrochloride and oral adsorbent in the case of promethazine hydrochloride poisoning.

Keywords: promethazine hydrochloride, montmorillonite K10, adsorption, excipient,

PROMETHAZİN HİDROKLORÜRÜN SULU ÇÖZELTİDEN MONTMORİLLONİT K10 ÜZERİNDEKİ ADSORPSİYONU

ÖZET

Promethazin hidroklorür'ün montmorillonite K10 üzerine sulu çözeltiden adsorpsiyonu, farklı sıcaklık, pH, iyonik şiddet ve temas süresine bağlı olarak çalışılmıştır. Adsorpsiyon verileri, Çizgisel Langmuir, Freundlich, Temkin ve Çizgisel olmayan Langmuir ve Freundlich denklemlerine uygulanmıştır. Sonuçlar, Çizgisel Langmuir denkleminin diğer denklemlere göre en iyi sonucu verdiğini göstermektedir. Promethazin hidroklorür'ün sorpsiyonu için C_m (adsorption kapasitesi) ve K_f (bağıl sorpsiyon kapasitesi) değerleri Langmuir ve Freundlich izoterm verilerinden hesaplanmıştır. C_m değeri, 17,5°C için 0,333 mmol/g'den 30°C için 0,245 mmol/g'a, K_f değeri ise 17,5°C için 1,015 mmol/g'dan 30°C için 0,365 mmol/g'a kadar azalmıştır. Sıcaklık artışıyla birlikte adsorpsiyon kapasitesinde bir düşüş gözlenmiştir. Promethazin hidroklorür'ün adsorpsiyonu pH'a ve iyonik şiddet'e önemli ölçüde bağımlıdır. Denge çalışmaları maksimum adsorpsiyonun pH=10,5'te gerçekleştiğini ve iyonik şiddetin artmasıyla adsorpsiyon kapasitesinin arttığını gösteriyor. DR izotermi yardımıyla elde edilen E (adsorpsiyon enerjisi) değerleri, adsorpsiyonun 17,5°C'de iyon değişimiyle açıklanabileceğini kanıtlıyor. Termodinamik parametreler (ΔG, ΔH ve ΔS) hesaplanmış olup bu parametreler adsorpsiyonun, ısıveren, kendiliğinden yürüyen ve tercihli olduğunu göstermektedir. Adsorpsiyon kinetiği, sürecin sahte ikinci derece kinetiğe uyduğunu açıklıyor. Sonuç olarak, montmorillonite K10 promethazin hidroklorür için bir eksipiyan ve promethazin hidroklorür zehirlenmelerinde oral adsorplayıcı olarak kullanılabilir.

Anahtar sözcükler : promethazin hidroklorür, Montmorillonit K10, adsorpsiyon, eksipiyan

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Chapter 1
INTRODUCTION

1. The Adsorption – Desorption Process

1.1 Adsorption Phenomena: General Concepts and Terminology

Adsorption is defined as the enrichment of material or increase in the density of the fluid in the vicinity of an interface with a solid (the adsorbent). The term sorption is used to embrace adsorption on the surface, absorption by penetration into the lattice of the solid and capillary condensation within the pores.

The material in the adsorbed state is called the adsorbate, in contradistinction to the adsorptive which is the general term for the material in the gas phase which is capable of being adsorbed. When adsorption occurs (or may occur) at the interface between a fluid phase and a solid, the solid is usually called the adsorbent.

Coverage is a measure of the extent of adsorption of a species onto a surface. Usually denoted by the lower case Greek "theta", q

Exposure is a measure of the amount of gas which as surface has seen; more specifically, it is the product of the pressure and time of exposure (normal unit is the Langmuir, where 1 L = 10^{-6} Torrs).

Adsorption may be classified as chemisorption (chemical adsorption) or physisorption (physical adsorption), depending on the nature of the interactive forces.

Chemisorption is adsorption in which the forces involved are valance forces of the some kind as those operating in the formation of chemical compounds.

Physisorption is adsorption in which the forces involved are intermolecular forces (van der Walls forces) of the some kind as those responsible for the imperfection of real gases and the condensation of vapors, and which do not involve a significant change in the electronic orbital patterns of the species involved. In Table 1.1 typical characteristics of adsorption processes are shown.

Table 1.1 Typical characteristics of adsorption process

Characteristics	Physical Adsorption	Chemical Adsorption
Binding force	Due to physical force of attraction, thus this process is also called as van der Waal's adsorption	Due to chemical forces or bonding, thus this process is also called as activated adsorption.
Saturation uptake	Multilayer phenomena	Single layer phenomena
Activation Energy	No activation energy involved	May be involved
Temperature Range (over which adsorption occurs)	Adsorption is appreciable at lower temperature below boiling point of adsorbate	Adsorption can take place even at higher temperature
Nature of sorbate	Amount of adsorbate removed depends more on adsorbate than on adsorbent	Depends on both adsorbent and adsorbate
Crystallographic specificity	Virtually independent of surface atomic geometry	Marked variation between crystal planes
Heat of adsorption	1 Kcal/mole	50 - 100 Kcal/mole

1.2. Factors Influencing Adsorption

1.2.1 Nature of the Adsorbent

The physicochemical nature of the adsorbent can have profound effects on both rate and capacity for adsorption. The rate of adsorption increases with increase in surface area of the adsorbent.

1.2.2 Nature of the Adsorbate

1.2.2.1 Solubility of Adsorbate

Adsorption of a solute is inversely proportional to its solubility in the solvent. The greater is the solubility, the stronger the solute-solvent bond and the small the extent of adsorption (Lundelius's rule).

In general, the solubility of any organic compound in water decreases with increasing chain length, because the compound becomes more hydrocarbon-like as the number of carbon atoms becomes greater (Traube's rule).

1.2.2.2 Molecular sizes

If the rate is controlled by intraparticle transport, the reaction generally will precede more rapidly the smaller the adsorbate molecule, within a given class of compound.

1.2.2.3 Degree of Ionization

As long as the compounds are structurally simple, adsorption is at minimum for the charged species and at a maximum for the neutral species. As compounds become more complex, the effect of ionization becomes of decreasing important.

Sorption mechanisms on clay surfaces have been studied for decades. One distinguishes between (i) inorganic cation exchange in the interlayer and on basal plane surfaces and (ii) specific pH-dependent sorption of cations and anions on clay edges. The edge sorption mechanism is a pH-dependent specific sorption on the clay edges. It has already been well established that the proton surface charge density on the clay edges depends on the physicochemical solution parameters (pH, ionic strength), which control the protonation state of the surface. In contrast, cation exchange on basal planes is related to the permanent negative charge generated in the clay structure created by isomorphic substitutions in the lattice. The density of exchange sites can be derived from the structural formula, and is compensated for by "exchangeable cations" which generally form outer sphere complexes with siloxane cavities (Tournassat et al., 2004; Sposito, 1981; Sposito, 1984).

1.2.2.4 pH

Because hydrogen and hydroxide ions are adsorbed quite strongly, the adsorption of other ions is influence by the pH of the solution. In general, adsorption of typical organic pollutant from water is increased with decreasing pH. We should also take care of the ionization equilibrium of the adsorbate.

1.2.2.5 Experimental Conditions

Temperature (Adsorption reaction are normally exothermic, thus the extent of adsorption generally increases with decreasing temperature), air flow velocity and relative humidity.

1.3 Adsorption Isotherms

Adsorption isotherm is the relation between the quantity adsorbed and the composition of the bulk phase (or the partial pressure in the gas phase) under equilibrium conditions at constant temperature.

1.3.1 Langmuir Isotherm

One of the simplest and most widely used isotherms is the Langmuir isotherm that was originally derived from adsorption kinetics by equating the rates of adsorption and desorption onto a flat surface.

The Langmuir equation is based on the following assumptions:
1- Adsorption of adsorbate molecules takes place at well-defined adsorption sites and each site can contain only one molecule.
2- The surface is homogeneous; the energy of adsorption is equal for all adsorption sites.

Whenever a gas is in contact with a solid there will be an equilibrium established between the molecules in the gas phase and the corresponding adsorbed species (molecules or atoms) which are bound to the surface of the solid.

As with all chemical equilibrium, the position of equilibrium will depend upon a number of factors:
The relative stability of the adsorbed and gas phase species involved
The temperature of the system (both the gas and surface)
The pressure of the gas above the surface

In general, factor (2) and (3) exert opposite effects on the concentration of adsorbed species. We can say that the surface coverage may be increased by raising the gas pressure but will be reduced if the surface temperature is raised.

We may derive the Langmuir isotherm by treating the adsorption process as we would any other equilibrium process - except in this case the equilibrium is between the gas phase molecules (M), together with vacant surface sites, and the species adsorbed on the surface. Thus, for a non-dissociative (molecular) adsorption process we consider the adsorption to be represented by the following chemical equation:

$$S - * + M\,(g) \rightleftharpoons S - M$$

S - *, represents a vacant surface site

In writing this equation we are making an inherent assumption that there are a fixed number of localized surface sites present on the surface.

We may now define an equilibrium constant (K) in terms of the concentrations of "reactants" and "products"

$$K = \frac{[S-M]}{[S-^{*}][M]}$$

We may also note that:

[S-M] is proportional to the surface coverage of adsorbed molecules, i.e. proportional to θ

[S -*] is proportional to the number of vacant sites, i.e. proportional to $(1-\theta)$

[M] is proportional to the pressure of gas, P

Hence, it is also possible to define another equilibrium constant, b, as given below:

$$b = \frac{\theta}{(1-\theta)P}$$

Rearrangement then gives the following expression for the surface coverage

$$\theta = \frac{bP}{1+bP}$$

This is the usual form of expressing the Langmuir Isotherm.

As with all chemical reactions, the equilibrium constant b, is both temperature-dependent and related to the Gibbs free energy and hence to the enthalpy change for the process (Seki, 2002).

The essential characteristic of the Langmuir isotherm can be expressed by a dimensionless separation factor called equilibrium parameter R_L;

$$R_L = \frac{1}{1 + bC_o}$$

C_o = initial concentration (mg/L)

b = Langmuir isotherm constant (L/mg)

Value of r<1 represents the favorable adsorption and value greater than one represents unfavorable adsorption (Acemioğlu, 2004).

1.3.2 Freundlich Isotherm

$$C_{i,s} = K_d C_{i,w}^{n}$$

$C_{i,w}$ = concentration of solute in water (mg/L)

$C_{i,s}$ = Concentration of solute in solid material (mg/kg)

K_d = Distribution constant (L/kg); n=exponential term of concentration in water. This is an empirically derived model, and has limited theoretical foundation.

The linear form of Freundlich equation is;

$$\log C_{i,s} = \log K_d + n \log C_{i,w}$$

The mechanism of sorption is mixed between fixed sites and a pseudo-partition process; many layers of fixed sites exist all with different enthalpies no mechanism can be deduced from this relation. The Fruendlich isotherm is an empirical relation.

1.3.3 DR Isotherm

Langmuir and Freundlich isotherms do not give any idea about adsorption mechanism. In order to understand the adsorption type, equilibrium data is applied to DR isotherm which has the following form:

$\ln C_{ads} = \ln C_m - \beta\varepsilon^2$

where

ε (Polanyi Potential) = [RT ln (1/Ce)] (kJ/mol)

C_m = DR monolayer capacity (mg/g)

β = DR isotherm constant related to adsorption energy (mol^2/kJ^2)

R = Gas constant (kJ/mol K) and T = temperature (K).

The mean free energy of adsorption (E), defined as the free energy change when one mole of ion is transferred from infinity in solution to the surface of the solid, was calculated from the β-value using the equation

$$E = -(-2\beta)^{-0.5}$$

It is known that magnitude of E is useful for estimating the type of adsorption and if this value is between 8 and 16 kJ/mol adsorption type can be explained by ion exchange. If the value of E is smaller than 8 kJ/mol, this shows physical adsorption due to weak van der Waals forces (Singh & Pant, 2004).

1.3.4 Temkin Isotherm

Langmuir, Freundlich and DR isotherm could not reveal the effects of indirect adsorbate/adsorbate interactions. So, Temkin suggested the following equation for describing these interactions.

$$q_e = [RT/b] \ln (A\, C_e)$$

The Temkin isotherm can be expressed in its linear form as:

$$q_e = [RT/b] \ln A + [RT/b] \ln (C_e)$$

where

$RT/b = B$

B is related to heat of adsorption. Temkin noted that the heat of adsorption of all molecules in the layer would decrease linearly with coverage due to adsorbate/adsorbate interactions (Choy et al, 1999; Allen, et al. 2004).

1.4 Adsorption Kinetics

The rate of adsorption, R_{ads}, of a molecule onto a surface can be expressed in the same manner as any kinetic expression: i.e.

$$R_{ads} = k\,C^{x}$$

where

x - kinetic order

k - rate constant

C - gas phase concentration

If the rate constant in either of the above expressions is expressed in an Arrhenius form, then we obtain kinetic equations of the form:

$$R_{ads} = AC^{x}e^{-E_a/RT}$$

where

E_a is the activation energy for adsorption,

A is the pre-exponential (frequency) factor.

The rate of adsorption is governed by

1. The rate of arrival of molecules at the surface
2. The proportion of incident molecules which undergo adsorption

We can express the rate of adsorption (per unit area of surface) as a product of the incident molecular flux, F and the sticking probability, S.

$$R_{ads} = S\,F$$

$$S = f(\theta)e^{-E_a/RT} \text{ and } F = \frac{P}{\sqrt{2\,\pi\,mkT}} \text{ Hertz-Knudsen equation}$$

where

E_a is the activation energy,

f (θ) is some, as yet undetermined, function of the existing surface coverage of adsorbed species,

P is gas pressure (Pa),

m is mass of one molecule (kg),

T is temperature (K)

Combining the equations for S and F yields the following expression for the rate of adsorption:

$R = [f(\theta)\, P/(2\pi mkT)^{1/2}]\, \exp(-E_a/RT)$

Note :

1. It should be recognized that the activation energy for adsorption may itself be dependent upon the surface coverage, i.e. $E_a = E(\theta)$.
2. If it is further assumed that the sticking probability is directly proportional to the concentration of vacant surface sites (which would be a reasonable first assumption for non-dissociative adsorption) then $f(\theta) = (1-\theta)$; where, in this instance, (θ) is the fraction of sites which are occupied (i.e. the Langmuir definition of surface coverage).

It is known that there are three consecutive steps in the adsorption of substances by a porous adsorbent. These steps can be expressed as follows

1. Film diffusion step (boundary layer).
2. Transport of the adsorbate within the pores of the adsorbent except for a small amount of adsorption which occurs on the external surface (particle diffusion)
3. Adsorption of the ingoing adsorbate on the interior surface of the adsorbent

It is generally accepted that process (3) is very rapid and does not represent the rate controlling step. (Mahramanlioglu et al, 2003).

Intraparticle diffusion is evaluated using the following equation:

$q_t = k_{int}\, t^{1/2} + C$

where

k_{int} = an intraparticle diffusion rate constant (mg/g min.$^{1/2}$).

q_t = amount adsorbed of solute per unit weight of adsorbent at any time.

C = intercept (Acemioğlu, 2004)

1.5 The Desorption Process

An adsorbed species present on a surface at low temperatures may remain almost indefinitely in that state. As the temperature of the substrate is increased, however, there will come a point at which the thermal energy of the adsorbed species is such that one of several things may occur:

1. A molecular species may decompose to yield either gas phase products or other surface species.
2. An atomic adsorbate may react with the substrate to yield a specific surface compound, or diffuse into the bulk of the underlying solid.
3. The species may desorb from the surface and return into the gas phase.

The last of these options is the desorption process. In the absence of decomposition the desorbing species will generally be the same as that originally adsorbed but this is not necessarily always the case.

Chapter 2
CLAYS

2. Introduction to clays

2.1. Description of the clay

The term “clay” is used both as a rock term and a particle-size term. When used as a rock term, clay means a natural, earthy, fine-grained material which is largely composed of a group of crystalline materials, the clay minerals.

As a particle-size term, clay is used for the category containing the smallest particles. The term is used in the U.S. and by the International Society of Soil Science for a rock or mineral particle in the soil having a diameter less than 0.002 mm (2 microns), whereas sedimentologists classify particles smaller than 0.004 mm as clay.

The terms "clay" and "clay mineral" are used in very different contexts. For example, a common interpretation of a clay substance is a material whose constituent particles are very small (i. e., "clay sized"). This is typically an engineering and sediment logical usage. Curiously, it is only very recently that clay mineralogists have agreed on meanings for the two terms at the head of this paragraph (Guggenheim & Martin, 1995). The term "clay" now refers to any material which exhibits a plastic behavior when mixed with water, while "clay mineral" refers to materials which have a layer structure or a structure substantially derived from or containing major features of such layer structures. Thus, clay minerals will be e. g., kaolinite, illite, and smectite but not, e. g., micas, talc, and pyrophyllite which occur in much larger particle sizes. A complication inherent with clays is the occurrence of materials normally considered to be amorphous or having a considerable concentration of defects, such as stacking faults. Clay minerals typically form at low temperatures (by geological standards), at low pressures (ambient or slightly

elevated) and in the presence of abundant water. Under these conditions, perfection in the organization of the crystal structure is unlikely. The details of the crystal structure of these materials are of great importance in understanding the physical and chemical properties of clays. This also is true of the highly disordered or amorphous materials where there still exists short range order.

2.1.1 General Features

2.1.1.1 Classification of Clay Minerals

I. Amorphous

- Allophane group

II. Crystalline

A. Two – layer type (sheet structure composed of units of one layer of silica tetrahedrons and one layer of alumina octahedrons)

1. Equidimensional

- Kaolinite group
- Kaolinite, nacrite, etc.

2. Elongate

- Halloysite group

B. Three- layer types (sheet structures composed of two layers of silica tetrahedrons and one central dioctahedral or trioctahedral layer)

1. Expanding lattice

a. Equidimensional

- Montmorillonite group
- Montmorillonite, saucinite, etc.
- Vermiculite

b. Elongate

- Montmorillonite group
- Nontronite, saponite, hectorite

2. Nonexpanding lattice

- Illite group

C. Regular mixed – layer types (ordered stacking of alternate layers of different types)

- Chlorite group

D. Chain structure types (hornblende – like chains of silica tetrahedrons linked together by octahedral groups of oxygen and hydroxyls containing Al and Mg atoms)

- Attapulgite
- Sepiolite
- Palygorskite

2.1.1.2 Structure of the Clay Minerals

Clays are comprised of fine-grained alumosilicates of mostly monocline or tricline symmetry which may contain sodium, calcium, potassium and other ions. The basic crystalline structure of clay minerals consists of two main structure units. The first unit is built of silica tetrahedrons. In tetrahedrons silicon atom is equidistant from four oxygens, or hydroxyl to balance the structure (As shown in Fig 2.1). Silicon atom is at the centre. Silica tetrahedral groups form hexagonal network. Silicon ion shares its charge equally between the four oxygen ions, leaving each oxygen with an excess charge of negative one. We now have the orthosilicate anion, which could at least theoretically be neutralized by four protons (hydrogen ions). This anion tends to react readily with alkali and alkali earth ions. The SiO_4^{4-} anion does have another option open to satisfy the charges

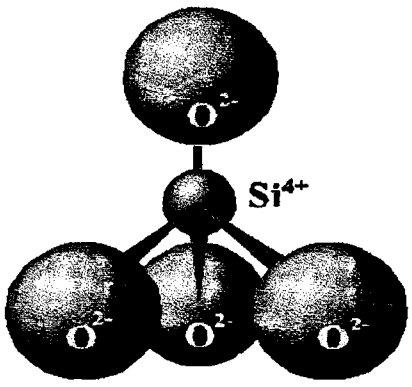


Figure 2.1 Silica tetrahedral units

The second unit is built of two sheets of closely packed oxygens or hydroxyls in which aluminum, iron, or magnesium atoms embedded magnesium, aluminum

or iron atoms in octahedral co-ordination. When magnesium is present, all the positions are filled to balance the structure (Ralph, & Grim 1968). When aluminum is present, two- thirds of the suitable positions are filled to balance the structure as shown in Fig 2.2. Within the phyllosilicate mineral structure the aluminum ion is "more comfortable" in an octahedral co-ordination. The aluminum/oxygen radius ratio is 0.41. Aluminum might be said to share +0.5 of its charge with each of the surrounding oxygen ions, leaving each oxygen ion with a negative 1.5 charge.

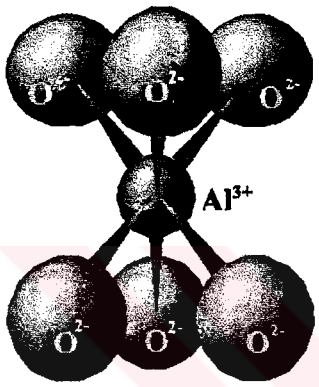


Figure 2.2 Octahedral unit

The clay crystal lattice is formed by layers of these tetrahedrons (T) and octahedrons (O). According to the succession of these layers, there are two-layer minerals whose structures are formed by a regular series of tetrahedron and octahedron layers (TOTOT....). Another possibility is the formation of three-layer minerals where one silicate layer has the structure TOT TOT TOT.

2.1.1.2 CLAY MINERAL CLASSIFICATION

Clay minerals are generally classified into three layer types based upon the number and arrangement of tetrahedral and octahedral sheets in their basic structure. These are further separated into five groups that differ with respect to their net charge (Table 2.1).

Table 2.1 Clay minerals and their net charge

Group	Layer Type	Net Negative Charge ($cmolkg^{-1}$)	Surface Area (MV)	Basal Spacing (nm)
Kaolinite	1:1	2-5	10-30	0.7
Fine-grained mica	2:1	15-40	70-100	1.0
Smectite	2:1	80-120	600-800	1.0-2.0
Vermiculite	2:1	100-180	550-700	1.0-1.5
Chlorite	2:1:1	15-40	70-100	1.4

1:1 Clay Minerals

The 1:1 layer minerals contain one tetrahedral and one octahedral sheet in their basic structural unit (Fig. 2). This two-sheet mineral type is represented by the kaolin group, with the general formula $Al_2Si_2O_5(OH)_4$. Kaolinite, the most common mineral in this group, is dioctahedral, exhibiting Al^{3+} octahedral and Si^{4+} tetrahedral coordination. The sheets are held together by van der Waals bonds between the basal oxygens of the tetrahedral sheet and the hydroxyls of the octahedral sheet. Layers are held together tightly by hydrogen bonding, which restricts expansion and limits the reactive area to external surfaces. Isomorphic substitution for Si^{4+} and Al^{3+} in this mineral is negligible. As such, soils dominated by 1:1 minerals exhibit a low capacity for adsorbing cations and have low fertility. The serpentine group, with the general formula $Mg_3Si_2O_5(OH)_4$, represents the trioctahedral version of the 1:1 layer minerals.

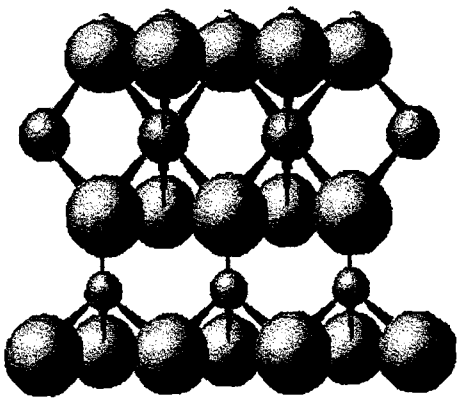


Figure 2.3 Structure of the Kaolinite

2:1 Clay Minerals

The joining of two tetrahedral sheets (one from each side) to one octahedral sheet produces a three-sheet mineral type, which is called 2:1 and is represented by the mica, smectite, and vermiculite groups. Talc [$Mg_3Si_4O_{10}(OH)_2$] and pyrophyllite [$Al_2Si_4O_{10}(OH)_2$] are typical representatives of electrically neutral 2:1 type minerals in which adjacent layers are joined to each other by van der Waals bonds (Fig. 2).

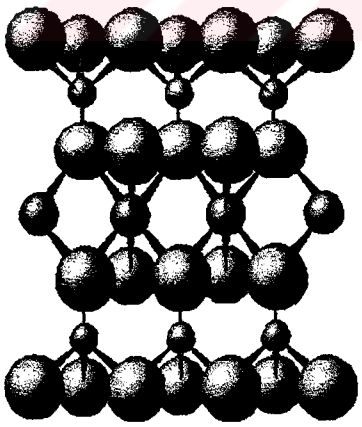


Figure 2.4 Structure of 2:1 clay minerals

Smectites generally refer to a group of expandable dioctahedral 2:1 minerals with a charge of 0.2-0.6 per formula unit. Montmorillonite, the most common member of this group, derives its charge from the octahedral substitution of Mg^{2+} for Al^{3+}.

Montmorillonite are dioctahedral smectites in which isomorphous substitution occurs. Aluminum and iron sometimes substitutes for silicon in the tetrahedral layer and iron or magnesium for aluminum in the octahedral layer (Newman, 1987). As a result of the isomorphous substitutions, crystalline order is reduced and structural imperfections arise (Ray L. Frost et al. 1996).

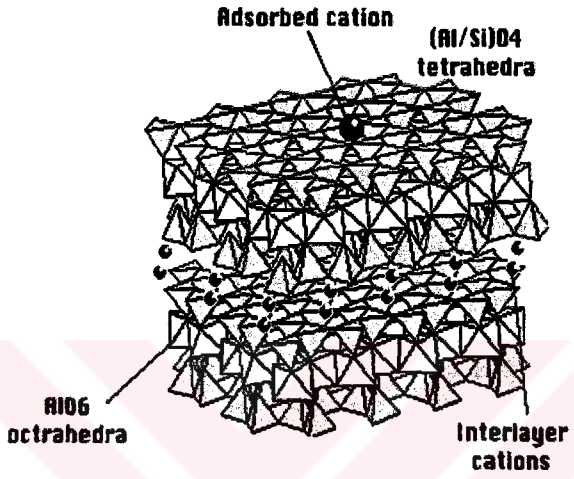


Figure 2.5 The structure of Montmorillonite

2:1:1 Clay Minerals

Chlorites are a group of minerals that exhibits a basic 2:1 layer structure similar to that described for talc or pyrophyllite, but with an interlayer brucite- or gibbsite like sheet, which forms a 2:1:1 structural arrangement. Isomorphic substitutions within the interlayer hydroxide sheet create a net positive charge that balances the negative charge arising from the 2:1 layers. A typical formula for the interlayer sheet is (MgFeAl)(OH)g; however, a variety of cation species may exist in these brucite or gibbsite-like islands that contribute to a large number of mineral species within this group. There is no water adsorption within the interlayer space; thus, chlorites are considered nonexpansive minerals.

2.2 Clay Mineral Identification and Quantification

2.2 Clay Mineral Identification and Quantification

The basic methods used for clay mineral identification and quantification involve X-ray diffraction (XRD) and thermal analyses (TA). Electron microscopy (EM) is also employed for complementary mineral characterizations.

In XRD analysis the basal spacing (or d-spacing) is measured by using Bragg's Law:

$$n\lambda = 2d \sin \theta$$

This equation allows calculating basal spacing if the wavelength, λ, of the X- rays is known, and the diffraction angle θ is known.

Table 2.2 shows the d spacing for the {001} plane as measured for various clay-type minerals. Untreated is for the minerals in their natural state, Ethylene Glycol values are obtained after treating the minerals in a solution of Ethylene Glycol, and the last column show the effect if the mineral is heated to 550°C after the Ethylene Glycol treatment.

Table 2.2 d-spacing values for various clay minerals.

d Spacing on {001} for Clay-Type Minerals (Å)			
Mineral	Untreated	Ethylene Glycol	Heated to 550°C
Kaolinite	7.1	No Change	Destroyed
Montmorillinite	14 - 15	17	9.5
Illite	10	No Change	Little Change
Chlorite	7	No Change	13.2
Mixed Layer	11	12	10

Thermal methods are based on characteristic temperature regions in which specific minerals lose their structural OH water (thermogravimetric analysis or TGA) and the enthalpy associated with the dehydroxylation reaction (differential scanning calorimetry, DSC). Mineral quantities are estimated from comparisons of the OH- or enthalpy fractions that have been measured and standard quantities of representative pure minerals.

In addition, specific surface area of powders can be determined using nitrogen (alternatively krypton) adsorption. The specific surface area plays an important role in determining soil physical and chemical properties and therefore has a great influence on processes related to soil conversation, fertility and pollution (İnel & Tümsek, 1999).

2.2.1 Cation-exchange Capacity

We can define cation exchange capacity as the total amount of positively charged cations that can exchange. The property of exchange capacity is measured in terms of miliequivalents per gram or more frequently per 100 g. Exchange capacity is determined at neutrality, that is pH 7 (Ralph E. Grim, 1968). Clay and organic matter particles act as giant anions, being covered over their surfaces with net negative charges. Cations are attracts to the surface and exchange takes place. Cation exchange capacity of some clay minerals is shown in Table 2.3

Table 2.3 CEC values of the some samples

Clay Mineral	CEC (mequivalents per 100 g, pH =7)
Kaolinite	3-15
Halloysite. $2H_2O$	5-10
Halloysite. $4H_2O$	40-50
Smectite	80-150
Illite	10-40
Vermiculite	100-150
Chlorite	10-40
Sepiolite	3-15

The cationic exchange capacity and the nature of the compensating cation play major roles in the interactions of organics with the solid surface of clays (Pusino et al., 1995; Draoui et al., 1999). Ion exchange with alkyl ammonium ions is a well-known method to make clay minerals and clays dispersible in organic solvents and to render the compatible with hydrophobic materials in compounding process (Lagaly et al., 1994).

Chapter 3
EXCIPIENTS

3. Introduction to Excipients

3.1 Description of the Excipient

The term comes from the Latin word excipiens, present participle of the verb excipere which means to receive, to gather, and to take out. This refers to one of the properties of an excipient, which is to ensure that a medicinal product has the weight, consistency and volume necessary for the correct administration of the active principle to the patient....

Excipient is any component other than active principle added intentionally to the medicinal formulation, or 'everything in the formulation except the active drug'. The interpretation of the adverb 'intentionally' brings to mind the multiple roles that an excipient must play today in a modern pharmaceutical dosage form, suitable to be administered entirely, parenterally and topically (Pifferi & Restani, 2003).

Excipients are used to fulfill many various requirements. Some of these are following;
Solvent, Emulsifier, Disintegrant, Lubricant, Thickener, Buffer, Inert bases (especially for cosmetics), Antioxidant, Diluents, Bulking agent, Coloring agent, Sweetener, Polar Gel agent, etc. (Kalinkova, 1999; Jackson et al, 2000; Pifferi & Restani, 2003)

There are a lot of excipients used in a pharmaceutical formulation. Some excipients used often in the drug formulations are as follows:

Celluloses, Pectins, β-cyclodextrins, dextrans, chitosans, calcium glycerophosphate, colloidal silica, dicalcium phosphate dihydrate, dodecyl 2-(N,N-dimethylamino) propionate, Eudragit L, methacrylic acid, polycarbophil, PEG.

3.2 Drug-excipient Interaction

Traditionally, excipients have been regarded as inert. However, numerous papers have shown that they can interact with an active medicament to affect its absorption and bioavailability (Jackson et al, 2000). And these interactions can be used in solutions of various pharmaceutical problems: the improvement of the solubility of poorly soluble drugs, increased dissolution rates, stability, increased drug release, therapeutic activity, increase of bioavailability and decrease of unwanted side effects.

Disintegration is the process whereby the dosage form breaks up into fragments and particles, exposing a large surface area of drug product to the physiological fluids and thus allowing dissolution to occur more readily. For example, cellulose derivatives (hydroxypropyl cellulose, microcrystalline cellulose, silicified cellulose, croscarmellose sodium), silica, corn starch, maltodextrin.

Lubricants tend to be hydrophobic substances that act by coating particles to prevent adhesion of the tablet to the dies and punches of the tableting machine, to aid in ejection of the tablet from the die by reducing the interparticulate friction and improving flow of the powder mixture. Lipophilic lubricants (e.g. magnesium stearate) which, when finely dispersed on the particles of the active medicament, can slow down dissolution and therefore bioavailability. Some lubricants are talc, stearic acid, privet plant wax.

In pharmaceutical formulations: acacia, xanthan gum as tablet binders and stabilizing agents; benzyl alcohol, glycerin, potassium sorbate as antimicrobial agents; beeswax, titanium dioxide, gum karaya as tablet coating agents; polysorbate 60 as emulsifying agent and gelatin as capsule and soft gel component are used.

However, if interaction between active medicament and excipient is chemical, then this can cause the degradation the active medicament. For example, hydrolysis, lipidic peroxidation, photolysis, isomerization, polymerization, epimerization, trans-esterification. In addition, interaction may occur between the carbonilic groups of a widely-used excipient like polyvinyl pyrrolidone, and pharmaceuticals containing donor groups of hydrogen, like famotidine and atenolol, thus causing problems of incompatibility.

3.3 Clay minerals as excipients

The clay minerals used as excipients are palygorskite, smectites, kaolinite and talc (Lin, et al. 2002; Viseras, & Lopez-Galindo, 1999). Kaolinite is the most common kaolin mineral and has the chemical formula $Al_2Si_2O_5(OH)_4$. This mineral is formed by weathering or hydrothermal alteration of aluminosilicate minerals. Thus, rocks rich in feldspar commonly weather to kaolinite. In order to form, ions like Na, K, Ca, Mg, and Fe must first be leached away by the weathering or alteration process. This leaching is favored by acidic conditions (low pH). Granitic rocks, because they are rich in feldspar, are a common source for kaolinite. Kaolinite, because it does not absorb water, does not expand when it comes in contact with water.

Kaolinite as excipient is used as inert bases for cosmetics. Schematic structure of it is shown in Figure 3.1.

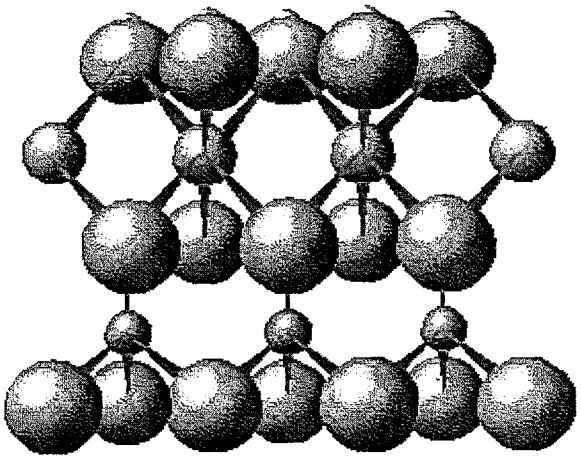


Figure 3.1 Structure of the Kaolinite

The smectite group of clays has a T-O-T structure. The most important aspect of the smectite group is the ability for H_2O molecules to be absorbed between the T-O-T sheets, causing the volume of the minerals to increase when they come in contact with water. Thus, the smectites are expanding clays. The most common smectite is Montmorillinite, with a general chemical formula:

$$(½Ca,Na)(Al,Mg,Fe)_4(Si,Al)_8O_{20}(OH)_4.nH_2O$$

Smectites as excipient are used as disintegrant, inert bases for cosmetics, emulsifying, polar gel and thickening agent (because of their colloidal characteristics).

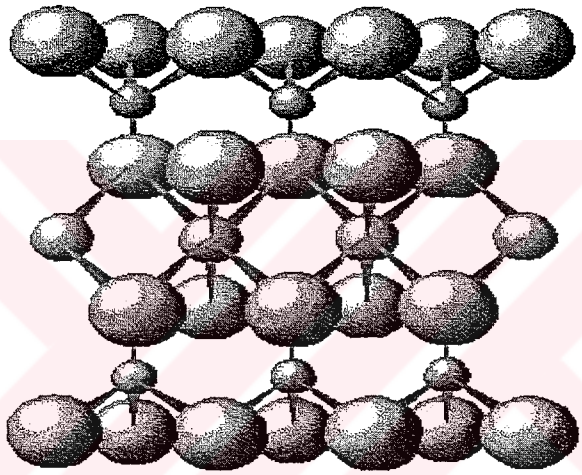


Figure 3.2 Structures of the Smectites

Palygorskite like montmorillonite belongs to a class of superfine minerals that possess developed specific surface area and cation exchange ability.

Unlike montmorillonite, crystalo-chemical structure of palygorskite causes presence of zeolite channels, i.e. vacuum in solid crystal that permits to absorb low-sized molecules of such substance as water, ammonia, etc.

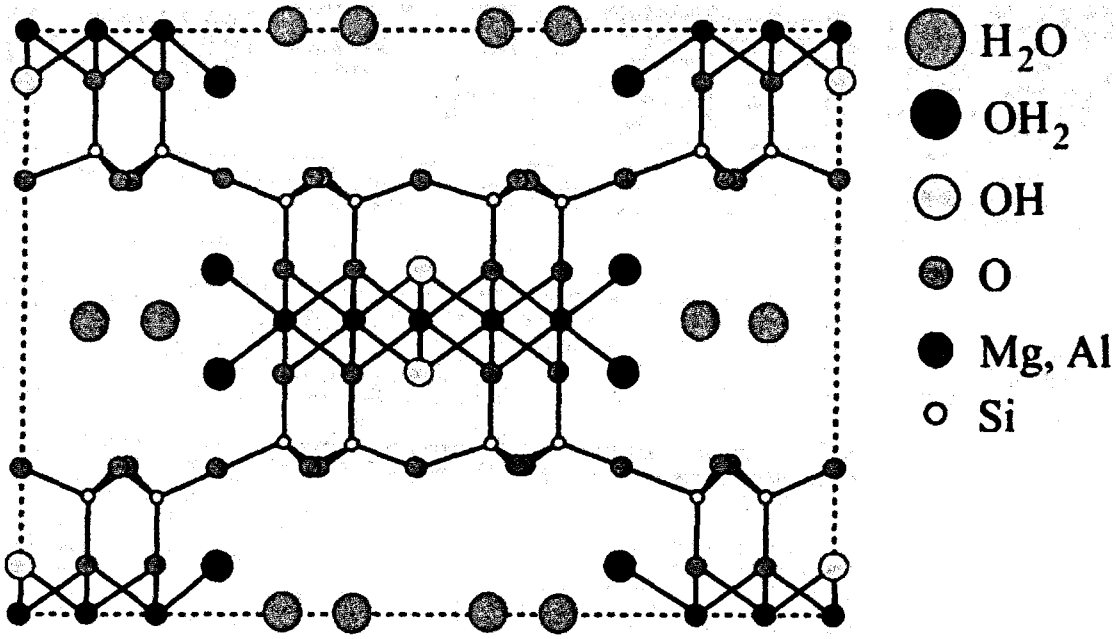


Figure 3.3 Structure of the Palygorskite

Palygorskite as excipient is used as disintegrant (due to dispersion of fibres), inert base for cosmetics, emulsifier, polar gel and thickening agent due to its colloidal characteristics.

Talc is hydrated magnesium silicate and is softest rock in the world. It generally occurs in two morphologies, either macro- or microcrystalline. Talc can have slightly differing compositions subject to the associated minerals in the ore body, but all talcs exhibit to a lesser or greater extent the following unique features: softness, hydrophobicity, platyness and organophily. These properties can be further enhanced by careful and sometimes propriety processing and bring a number of specific benefits.

Talc as excipient is used as lubricants to ease the manufacture of pills and inert bases for cosmetics (Carretero, 2002).

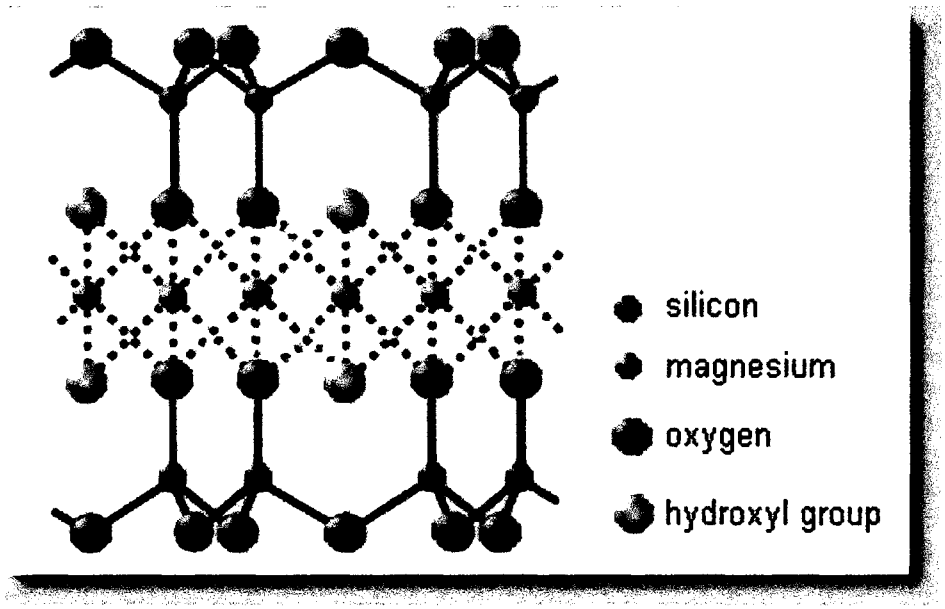


Figure 3.4 Structure of the Talc

3.3.1 The effects of the clay minerals used as excipients in the active principle

Excipients can interact with an active medicament to affect its absorption and bioavailability. When clay minerals used as excipients, this interaction can occur either in the pharmaceutical formulation itself or in the gastrointestinal tract. They change active medicament's bioavailability.

The interaction between the drug and its excipient can retard the drug's release and therefore its absorption, lowering its levels in the bloods. This effect can be beneficial for amphetamines and antibiotics but not antihistamines. Because, in amphetamines and antibiotics, slow releasing of the drug increases its therapeutic action. In addition, when used clay minerals as excipients in water-resistant sun screens (e.g. N-methyl-8-hydroxy quinoline methyl sulphate and smectite), active medicament's releasing decrease.

Interaction between a drug and clay mineral can accelerate the drug's degradation. For example, dexamethasone, an anti-inflammatory, degrades in the presence of palygorskite and sepiolite (Carretero, 2002).

Chapter 4

PROPERTIES OF PROMETHAZINE HYDROCHLORIDE

4.1. Promethazine Hydrochloride and Other Phenothiazines

Phenothiazines are an important group of neuroleptics used in the treatment of moderate and severe mental and emotional conditions. They are also known for their antiemetic effects, the potency of the effects of anesthetics, analgesics and sedatives and also as antihistamines (Whaun, et al. 1980; Quin, 1976). Some phenothiazine derivatives are Chlorpromazine, Fluphenazine, Mesoridazine, Perphenazine, Prochlorperazine, Promazine, Thioridazine, Trifluoperazine and Promethazine hydrochloride.

Promethazine hydrochloride is a phenothiazine derivative antihistamine with potent sedative properties.

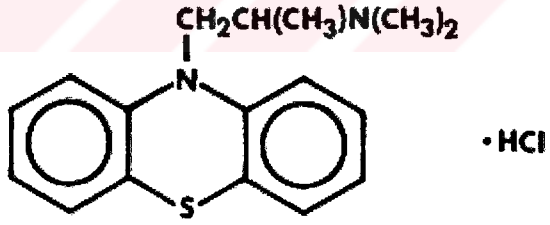


Figure 4.1 The structure of promethazine hydrochloride

Promethazine hydrochloride is a phenothiazine derivative which differs structurally from the antipsychotic phenothiazines by the presence of a branched side chain and no ring substitution.

The physical properties of Promethazine are shown in Table 4.1.

Table 4.1 Physical properties of Promethazine Hydrochloride (Woods, 1990)

Molecular Formula	$C_{17}H_{20}N_2S$, HCl
Molecular Weight	320.9 g mol^{-1}
Appearance	White or faintly yellow *
Melting Point	222 °C
Solubility	soluble in water, freely soluble in alcohol **
State/Form	Crystalline powder

* Slowly oxidizes and turns blue on prolonged exposure to air. ** Practically insoluble ether and acetone (1 in 0.6 of water; 1 in 9 of alcohol; 1 in 2 of chloroform); A 10% solution in water has a pH of 4.0 to 5.0.

4.2. The Properties of Promethazine Hydrochloride

4.2.1 Allergy

Promethazine hydrochloride is effective in treatment of various types of allergic reactions including transfusion reaction, perennial allergic rhinitis, seasonal allergic rhinitis, vasomotor rhinitis, allergic conjunctivitis, urticaria, angioedema, pruritus, and dermographism.

4.2.2 Anesthesia Adjunct

Promethazine hydrochloride is used as an anesthetic premeditation to produce sedation, reduce anxiety and also to reduce post operative nausea and vomiting. The drug is often given in conjunction with an opiate analgesic such as pethidine, particularly in obstetrics (Adams & Oswald, 1986; Uhlig et al. 1995).

4.2.3 Osteoporosis

Promethazine hydrochloride use in postmenopausal women resulted in increases in bone mineral content (BMC) (Tyan, 1993). Promethazine promoted increases in MC in postmenopausal women not taking estrogens but was most effective in women who received estrogens (Wheatley, 1964).

4.2.4 Breathlessness

Promethazine hydrochloride has been shown to have a short-term benefit in the treatment of breathlessness (Rice, et al. 1987; Lackner et al. 1994).

4.2.5 Sedation

Promethazine hydrochloride is sometimes used for its sedative effects and in some countries is marketed for this purpose, including the sedation of young children (Petrack, et al. 1996).

4.2.6 Motion Sickness

Promethazine hydrochloride is effective in the active and prophylactic treatment of motion sickness. Vomiting from other causes can be treated with higher or more frequent doses (Wood, 1981).

4.2.7 Parkinson's Disease

Used in patients with Parkinson's disease to control LEVODOPA-INDUCED DYSKINESIAS and nausea and vomiting (Tarsy et al, 1975a; Tarsy et al, 1985b).

4.2.8 Insomnia

Promethazine hydrochloride is effective in the short term treatment of insomnia (Woods, 1990).

The specific aims of this study are as below;

1- To understand the adsorption process of promethazine hydrochloride in montmorillonite K10 by using batch adsorption experiments.
2- To enhance the adsorption capacities of the clay to prepare excipient.
3- To find suitable oral adsorbent for promethazine hydrochloride poisoning.

Chapter 5
MATERIAL AND METHOD

5.1 Clay and Promethazine Hydrochloride

Montmorillonite K10 (K-Catalyst) was supplied from Fluka (Cat. No: 69866). K-10 is acid activated montmorillonite clay based on the Bavarian montmorillonite Tonsil-13. The chemical composition of montmorillonite K10 is given in Table 5.1. The sample K10 is based on calcium bentonite found in the region of Mainburg-Landshut in Germany.

N_2 adsorption-desorption isotherms at 77K were measured on SORPTOMATIC 1990 after a degassing under vacuum for 2 hours at 130°C. BET specific surface area (S_{BET}), specific pore volume (V_p), total adsorbed volume (V_T), monolayer coverage (V_m) were determined by using MILES-200 Advanced Data Processing Sorption Software Version 3.00. For the porosity analysis, the Dollimore-Heal method was used.

X-ray powder diffraction (XRD) patterns were obtained in a Seifert-XRD 3000 under 40 kV, 40 mA current intensity in the 2θ 3-10° range and using Ni-filtered Cu K_α radiation. For the range of 2θ 8-63°, a HZG4 XRD powder diffractometer was used under the same conditions. The interlayer free spacing was obtained by lowering the value of the d_{001} basal spacing with the thickness of a clay layer, 9.8 Å.

Thermogravimetric analysis(TGA) of the samples were carried out in N_2 atmosphere with a flow rate of 10 mL $min.^{-1}$ by using Shimadzu TGA 50 thermal analyser in the temperature range of 10-850°C at a heating rate of 10° $min.^{-1}$. In the TGA thermograms of montmorillonite K10, the mass loses between 20-300°C (dehydration region) was found as 10.56%, while in the region of 300-800°C

N_2 adsorption and XRD experiments were carried out in Technische Universität Chemnitz/Germany. TGA analysis was done in Dicle University, Diyarbakır/Tukey.

Table 5.1 The chemical composition of montmorillonite K10

Chemical Composition	Montmorillonit K10
SiO_2	70
Al_2O_3	14
Fe_2O_3	3.5
CaO	1.5
MgO	2.0
Na_2O	<0.5
K_2O	1.5
Ignition loss	7.0
Sulfate	---
CCl_4 Pore volume(cm^3g^{-1})	0.20-140 Å 0.35-800 Å
Hg-Porosimetry, PV Pore size (cm^3g^{-1})	0.68 100-11 0.39 1.1-0.035
Density (gL^{-1})	0.3-0.37

Table 5.2 The properties of montmorillonite K10

Sample	CEC (meq/100g clay)	Specific Surface Area, S_{BET} (m^2/g)	d_{001} Å
Montmorillonite K10	35	230	9.8

Promethazine hydrochloride (10-[2-(Dimethylamino)propyl]-phenothiazine monohydrochloride) was purchased from Aldrich Co. (Cat. No: 28, 411-4) and used as received, without any treatment or purification. Promethazine hydrochloride stock solution (1mM) was prepared by dissolving in the distilled water. Further solutions were freshly prepared from stock solution for each experimental run. Adsorption experiments were evaluated in batch equilibrium technique.

5.2 FTIR Study

FTIR spectroscopy was used to obtain the interactions between drug and clay. The FTIR spectra of drug, K10 and drug loaded K10 were obtained using KBr pellets with Perkin Elmer Spectrum BX-II FTIR spectrophotometer. Montmorillonite K10, promethazine hydrochloride and drug loaded K10 were brought to constant weight in a drying oven at 40°C for 24 h. Afterwards 100 mg of fine KBr powder was dried at 110°C and then mixed with 1 mg of samples. For pellets obtained, the infrared spectra were recorded in the range of 4000-400 cm^{-1}. The background spectrum of each KBr pellet was obtained by subtracting it from the sample spectra.

5.3 XRF and SEM Study

The elemental analysis of K10 and drug loaded was determined using X-Ray Florescence (XRF System Inc. 500 Digital Processing) attached to a scanning electron microscope (Jeol JSM 60 SEM). The surface morphologies of the K10 and drug loaded K10 were studied using a scanning electron microscope (SEM) at an accelerating voltage of 15 kV. All samples were dried and coated with gold before scanning. Photographs were taken at various magnifications (1000X and 5000X). These experiments were done in Metallurgy and Material Science Engineering Department of Dokuz Eylül University, İzmir/Turkey.

5.4. Adsorption from Solution Experiments

Adsorption isotherms were determined by using batch equilibrium method. 0.1 g of the clay, montmorillonite K10, was weighted into 50 mL of flasks filled with 25 mL aqueous solution of Promethazine Hydrochloride whose concentration was between 600 and 1100 μM. The suspensions were shaken 21 hours at room temperature and centrifuged at 3000 rpm for 15 min at the same temperature. Liquid phases were taken and equilibrium concentration was determined by calibration curves after measuring their absorbance values by using SHIMADZU UV – 1601 model UV-Vis. Spectrophotometer at 250 nm. Difference between initial concentration and equilibrium concentration is equal to portion adsorbed.

Chapter 6
RESULTS

6.1. Determination of Promethazine Hydrochloride Concentration from Calibration Curve

A stock solution (10 mM) of promethazine hydrochloride was prepared for the experiment. 0.3209 g promethazine hydrochloride was dissolved in 100 mL distilled water and calibration solutions were prepared by diluting stock solution to appropriate concentrations. The absorbance values of calibration solutions and calibration curve were shown in Table 6.1 and in Figure 6.1 respectively. The curve was plotted absorbance values of calibration solutions versus concentration.

Table 6.1 Absorbance values of promethazine hydrochloride solutions at λ =250 nm for calibration curve

Number	C x10^2 (mmol/L)	Absorbance
1	0.5	0.199
2	1.5	0.274
3	1.76	0.376
4	2	0.471
5	2.5	0.567
6	3	0.738
7	3.84	0.862
8	4	0.925

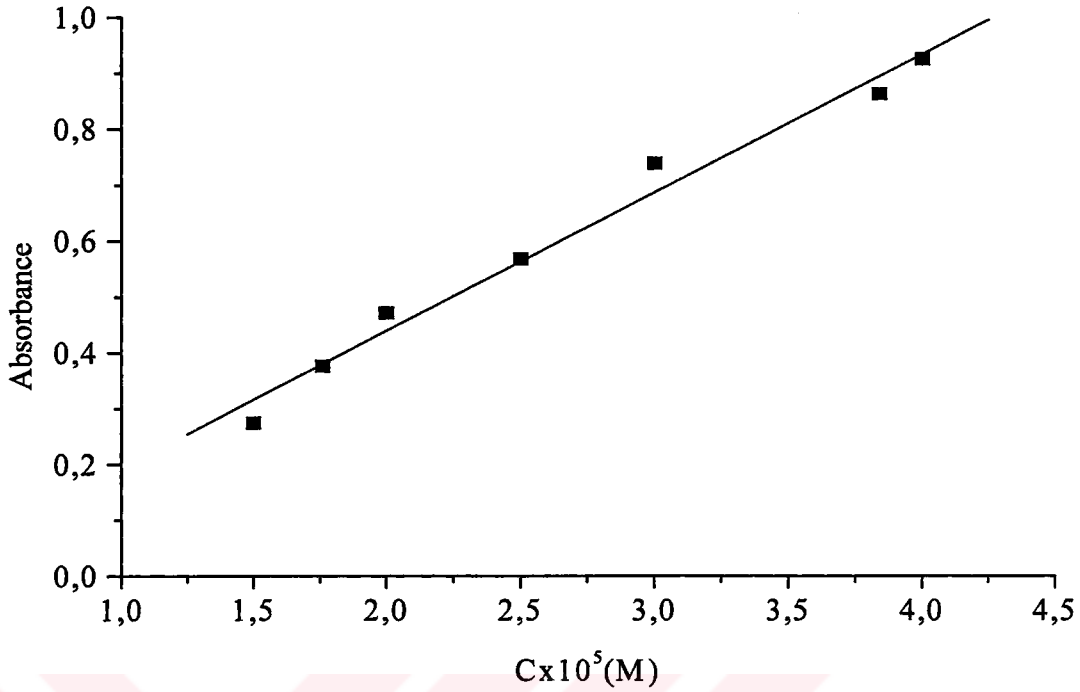


Figure 6.1 Calibration curve of promethazine hydrochloride

6.2. Adsorption of Promethazine Hydrochloride onto Montmorillonite K10

The adsorption isotherms of promethazine hydrochloride on montmorillonite K10 were determined by plotting the amount of promethazine hydrochloride adsorbed by the clay (C_s mmol/g) versus equilibrium concentration of promethazine hydrochloride (C_e mmol/L) at different temperatures. Figure 6.2 shows the promethazine hydrochloride sorption isotherms. In terms of the slope of initial portion of the curves, the shapes of these isotherms may be classified as H type at 17.5°C and 25 °C according to the Giles classification (Giles et al. 1960). It means that montmorillonite K10 have a high affinity for promethazine hydrochloride that is strongly adsorbed and no competition occurs for the sorption sites between the solvent and promethazine hydrochloride molecules at 17.5°C and 25°C. The adsorption isotherm of promethazine hydrochloride at 30°C was of L type according to Giles classification indicating that montmorillonite K10 at 30°C has a medium affinity for the promethazine hydrochloride molecules. The curves tend to constant

value of C_s and reach a plateau showing the formation of a complete monolayer of promethazine hydrochloride covering adsorbent surface. The plateaus define maximum adsorptions of 24 mmol/g, 23 mmol/g, and 20mmol/g for 30°C, 25°C, 17.5°C and respectively and each offers a surface saturation by promethazine hydrochloride molecules.

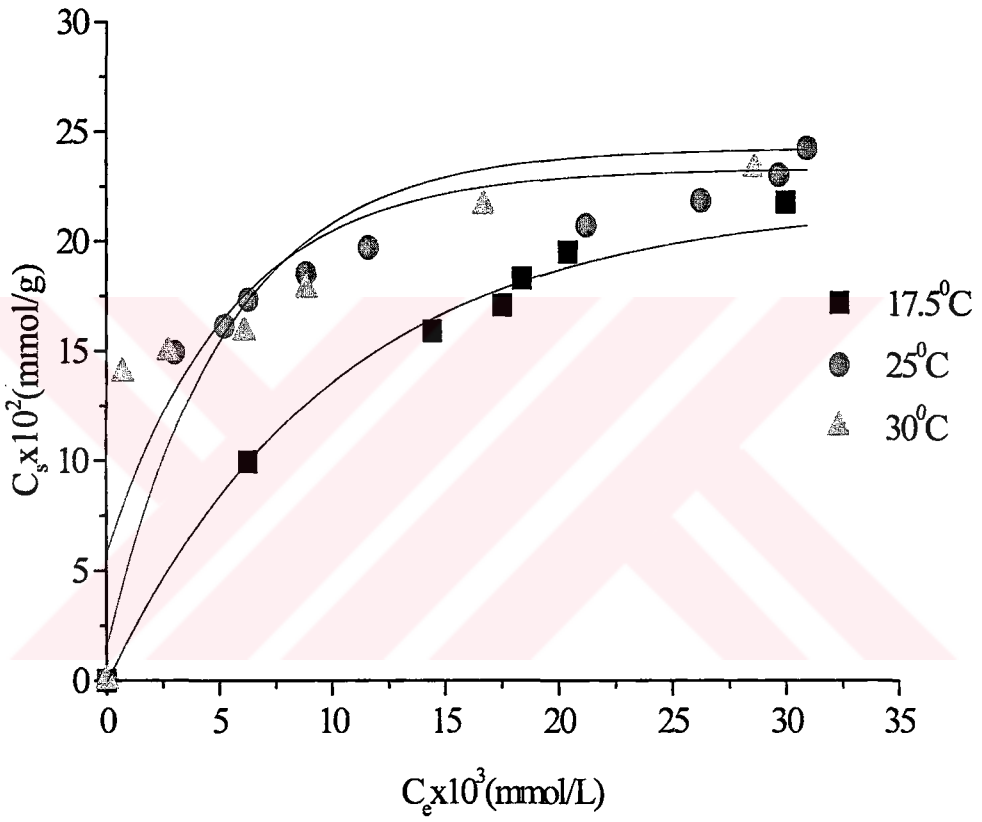


Figure 6.2 Adsorption isotherms of promethazine hydrochloride on Montmorillonite K10 at different temperatures

The fit of adsorption data to the Langmuir and Freundlich equations were investigated to find sorption capacities of the Montmorillonite K10 by using logarithmic forms as below

$C_e/C_s = 1/(C_mL) + C_e/C_m$; $\log C_s = \log K_f + n_f \log C_e$

where

C_s = the amount adsorbed of solute (mmol/g)

C_e = equilibrium concentration of solute (mmol/L)

C_m = Adsorption capacity (maximum amount that can be adsorbed by adsorbent as a monolayer (mmol/g).

L = a constant related to the adsorption energy.

K_f and n_f are known as adsorption capacity and intensity respectively (Morela & van Bladel, 1980). K_f can be considered as a measurement of the relative adsorption capacity since it is the value of C_s when C_e is the unity. (Hermosin & Cornejo, 1987; Akçay & Yurdakoç , 2000, Seki & Yurdakoc, 2002). n_f is a measurement of linearity. Figure 6.3 shows the results found by plotting C_e/C_s versus C_e for the adsorption process of promethazine hydrochloride onto Montmorillonite K10 at different temperatures.

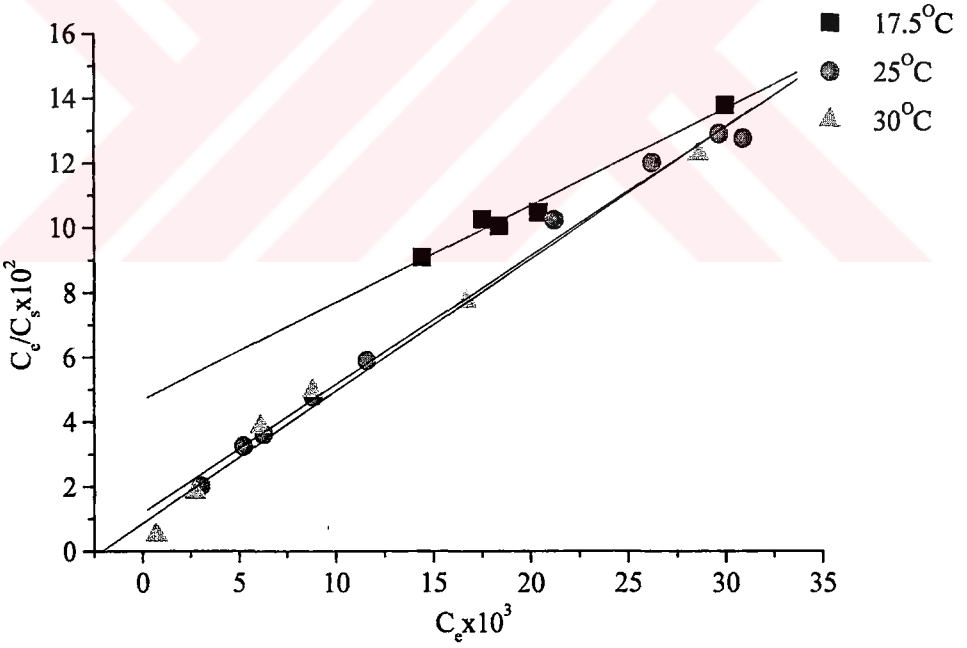


Figure 6.3 Langmuir isotherms for adsorption of promethazine hydrochloride onto K10

Langmuir equation gave a good fit for all temperatures. The correlation coefficients were in all cases greater than 0.9902 being significant at the 0.0001

probability level. C_m and L parameters were determined by using the linear regression applied to the straight lines in Figure 6.3. The sorption parameters of promethazine hydrochloride on montmorillonite K10 clay corresponding to Langmuir equation were summarised in Table 6.2. As shown in Table 6.2, C_m (maximum adsorption capacity) values are 0.333 mmol/g at 17.5°C, 0.252 mmol/g at 25°C, and 0.245 mmol/g at 30°C respectively. And the L values are from 64.098 g dm^{-3} for 17.5°C up to 469.96 g dm^{-3} for 30°C.

Table 6.2 The sorption parameters of Langmuir equation for promethazine hydrochloride on Montmorillonite K10 at different temperatures

Temperature/°C	R^2	C_m(mmol/g)	L(g dm^{-3})
17.5	0.9805	0.333	64.098
25	0.9924	0.252	337.150
30	0.9890	0.245	469.960

The applicability of original form of Langmuir equation for Promethazine hydrochloride sorption was also investigated by using computer through SigmaPlot program. The original form of Langmuir equation used in this study is as below.

$C_s = C_m L C_e / (1+LC_e)$

The nonlinear Langmuir parameters were presented in the following Table 6.3.

Table 6.3 The sorption parameters of nonlinearized Langmuir equation for adsorption of promethazine hydrochloride onto montmorillonite K10

Temperature/°C	R^2	C_m(mmol/g)	L(g dm^{-3})
17.5	0.9617	0.335	63.357
25	0.9143	0.243	422.752
30	0.5658	0.202	2134.388

As can be seen in Table 6.3, the correlation coefficients are less than 0.9617. That is to say, this method gave a poorly fit in comparison with linear form of Langmuir equation.

Dimensionless separation factor called equilibrium parameter was calculated to predict adsorption efficiency.

$$r = \frac{1}{1 + bC_o}$$

where

b = Langmuir isotherm constant ($dm^3 g^{-1}$)

C_O = initial promethazine hydrochloride concentration ($g\ dm^{-3}$)

$r < 1$ indicates the favorable adsorption and $r > 1$ indicates unfavorable adsorption (Acemioğlu, 2004).

Table 6.4 Dimensionless separation factor for adsorption of promethazine hydrochloride onto Montmorillonite K10 at different temperatures

Temperature/°C	b(L/mmol)	C_O(mmol/L)	r
17.5	64.098	0.65	0.0234
25	337.150	0.60	0.0049
30	469.960	0.56	0.0038

The values of r (dimensionless separation factor) at different temperatures are reported in Table 6.4. The value of r was found to be 0.0234 at 17.5°C, 0.0049 at 25°C and 0.0038 at 30°C. These values indicate favorable adsorption for promethazine hydrochloride.

The adsorption data were further evaluated with the logarithmic form of Freundlich equation.

$$\log C_s = \log K_f + n_f \log C_e$$

log C_s versus log C_e was plotted for promethazine hydrochloride sorption on montmorillonite K10 in the Figure 6.4. The correlation coefficients are greater than 0.972. In comparison with Langmuir equation, the fit of Freundlich equation is not as good as Langmuir equation. K_f (relative sorption capacity) and n_f (measure of the linearity of the sorption) were found by using the linear regression method applied to the straight lines in Figure 6.4.

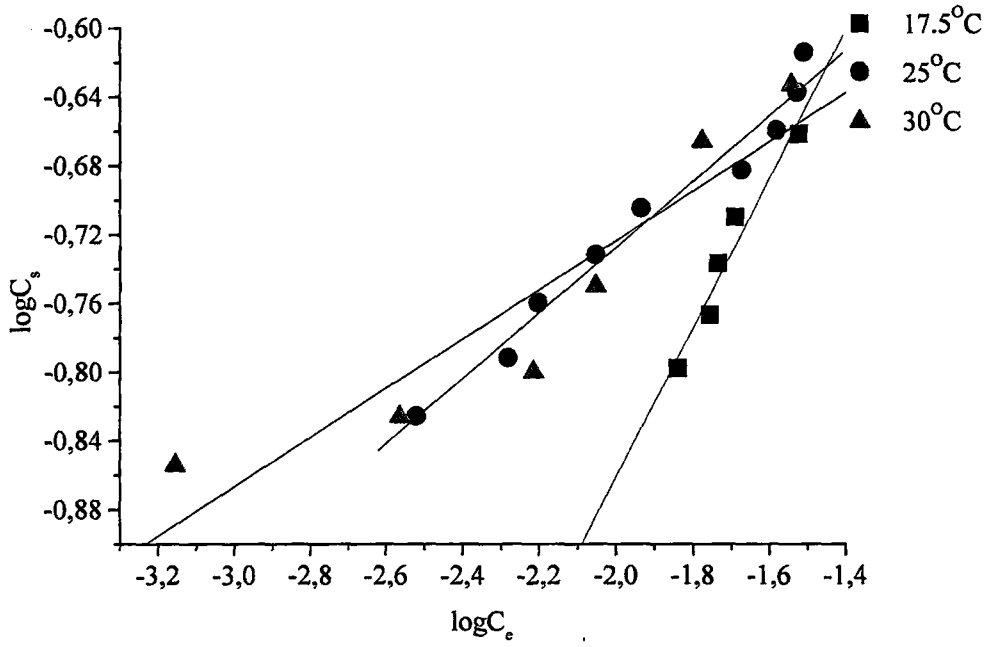


Figure 6.4 Freundlich isotherms for adsorption of promethazine hydrochloride onto K10

Freundlich constants were displayed in Table 6.5. As pointed out in Table 6.5, n_f values decrease from 0.4338 for 17.5°C to 0.1431 for 30°C. Also K_f values decrease from 1.015 mmol/g for 17.5°C to 0.365 mmol/g for 30°C. This value indicates that adsorption capacities increase when temperature decreases. It can be deduced that promethazine hydrochloride is more adsorbed at 17.5°C than 25°C and 30 °C.

Table 6.5 The sorption parameters of Freundlich equation for adsorption of promethazine hydrochloride onto montmorillonite K10 at different temperatures

Temperature/°C	R^2	K_f (mmol/g)	n_f
17.5	0.9454	1.015	0.4338
25	0.8636	0.465	0.1761
30	0.9922	0.365	0.1431

The applicability of the Freundlich equation was investigated by original form of Freundlich isotherm. Due to inherent bias resulting from linearization alternative

isotherm parameters were determined by nonlinear regression. The parameters were obtained from the linear equation fitted using SigmaPlot version 4 program as given in Table 6.6.

Table 6.6 The sorption parameters of nonlinearized Freundlich equation for adsorption of promethazine hydrochloride onto montmorillonite K10.

Temperature/°C	**R^2**	**K_f (mmol/g)**	**n_f**
17.5	0.9453	0.9644	0.4208
25	0.9659	0.4510	0.1911
30	0.8988	0.3956	0.1598

It can be said that both of these methods have a poor fit experimental data of promethazine hydrochloride adsorption. The n_f values are less than 1 in the form of nonlinear and linear Freundlich equation. If the value of n_f is equal to unity, the adsorption is linear. It indicates that adsorption sites are not homogenous in energy. According to the Tables 6.6, the values of K_f for each adsorbent raised with decreasing the temperature of the solution.

Langmuir and Freundlich isotherms do not give any idea about adsorption mechanism (Singh & Pant, 2004). So, the fit of adsorption data to the Dubinin-Radushkevich (DR) isotherm were investigated to understand the adsorption type. The well-known expression of the DR model is (Krishna, et al. 2000; and 2004);

$C_s = Q_m \exp(-\beta \varepsilon^2)$ or

$\ln C_s = \ln Q_m - \beta \varepsilon^2$

where

ε can be correlated:

$\varepsilon = RT \ln(1+1/C_e)$

β = a constant related to the adsorption energy; C_s= the amount adsorbed of solute (mmol/g); Q_m= Adsorption capacity (mmol/g); R= gas constant ($8.314.10^{-3}$ kJ mol^{-1} K^{-1}), T= absolute temperature (K).

A linear relation is obtained by plotting ln C_s against ε^2. DR isotherm constants Q_m and β were calculated from the slope and intercept of the plot at various temperatures. The slope of line yields β ($mmol^2\ kJ^{-2}$) and the intercept is equal to lnQ_m value.

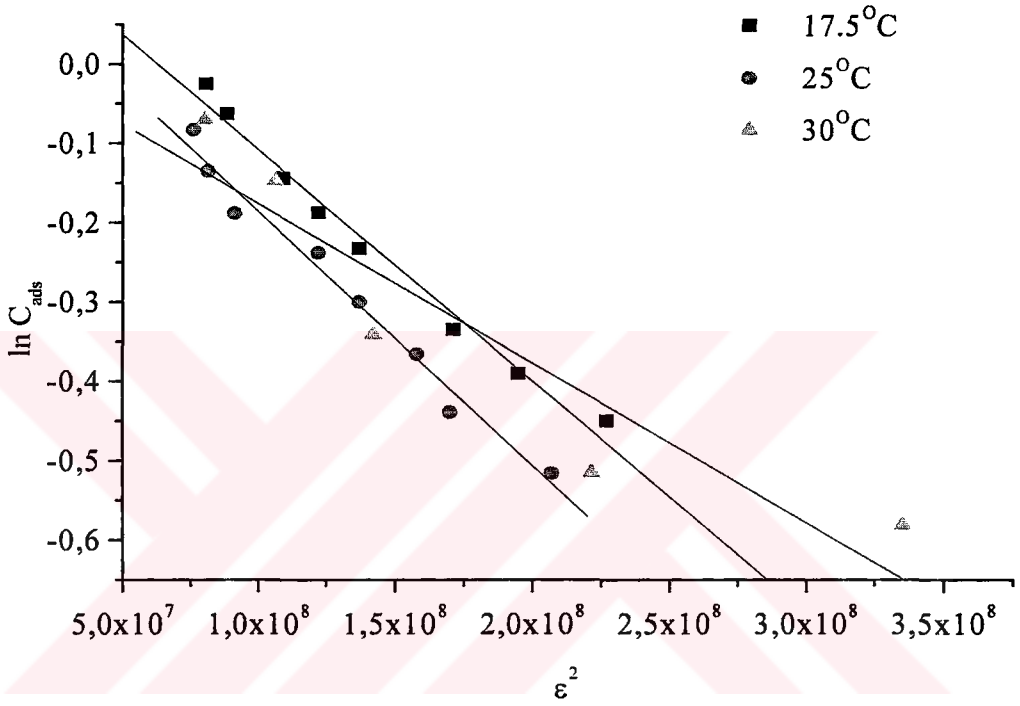


Figure 6.5 DR isotherm for adsorption of promethazine hydrochloride onto K10

The value of β is related to adsorption energy (E). E was calculated by using the following equation;

$E = -(2\beta)^{-0.5}$

The magnitude of free energy is used for estimating the type of adsorption. As E values are between 8 and 16 kJ mol^{-1}, adsorption type can be explained by ion exchange. But if this value is smaller than 8 kJ mol^{-1}, adsorption type is physical adsorption due to weak van der Waals forces. Parameters related to DR isotherm at different temperatures were summarized in Table 6.7.

Table 6.7 The sorption parameters of DR equation for Promethazine Hydrochloride on K10 at different temperatures

Temperature/°C	R^2	β (mol^2/kJ^2)	-E (kJ/mol)
17.5	0.9880	0.00396	11.237
30	0.9390	0.00139	18.966
37	0.9940	0.00115	20.851

As shown in Table 6.7, correlation factor (R) are in the range of 0.969–0.997 for montmorillonite K10 at 30°C and at 37°C respectively. E values were found to be 11.237 kJ/mol at 17.5°C; 18.966 kJ/mol at 30°C and 20.851 kJ/mol at 30°C. These values indicate that sorption of promethazine hydrochloride on montmorillonite K10 can be explained by ion exchange at 17.5°C. The adsorption capacity Q_m in DR equation was found to be 27.671 10^{-4}, 6.07 10^{-4}, 5.779 10^{-4} mmol/g, respectively. These values are less than the values of adsorption capacity obtained from Langmuir equation.

It is known that the other isotherms (Langmuir, Freundlich, DR isotherm) could not reveal the effects of indirect adsorbate/adsorbate interactions (Choy et al, 1999). In order to clarify the these interactions, equilibrium data was applied to Temkin isotherm with the following equation;

$$C_s = (RT/b) \ln (A\ C_e)$$

The Temkin isotherm can be expressed in its linear form as:

$$C_s = (RT/b) \ln A + (RT/b) \ln C_e$$

where

$$RT/b = B$$

B is related to heat of adsorption. B and A values were obtained by plotting C_s versus $\ln C_e$ at various temperatures (Figure 6.6).

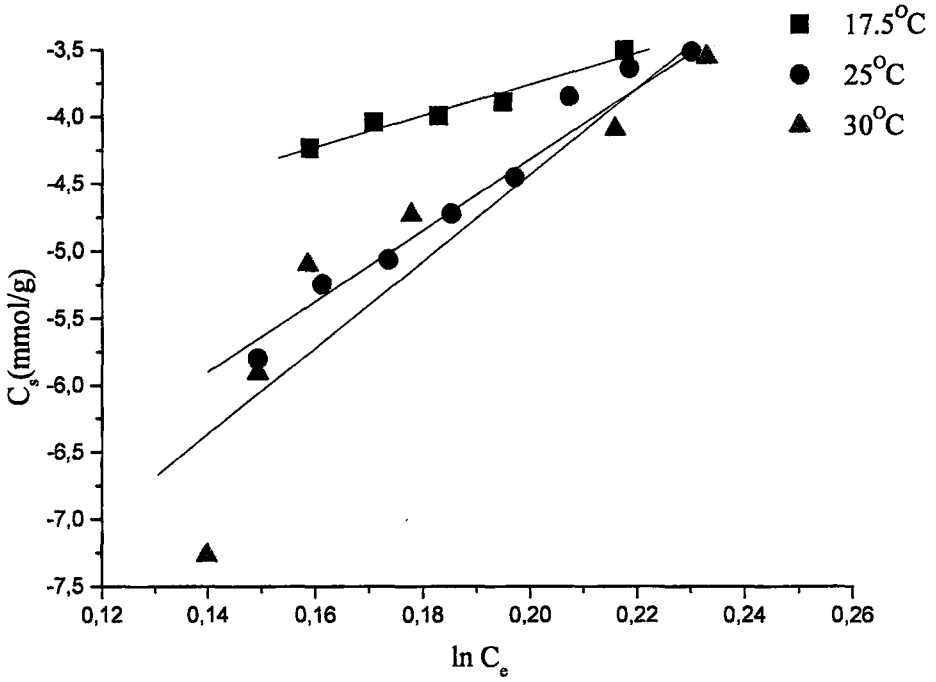


Figure 6.6 Temkin isotherms for adsorption of promethazine hydrochloride onto K10

The slope of the plots is equal to B and the intercept is equal to B lnA value. The results were presented in Table 6.8. As can be seen in Table 6.8, B values are 11.717 at 17.5°C, 26.381 at 25°C and 32.234 at 30°C and correlation factor (R) are in the range of 0.91–0.98 at 30°C and at 25°C respectively.

Table 6.8 The sorption parameters of Temkin equation for promethazine hydrochloride on montmorillonite K10 at different temperatures

Temperature/°C	B	A	R^2
17.5	11.717	0.594	0.9584
25	26.381	0.695	0.9610
30	32.234	0.714	0.8297

The results indicated that better applicability was obtained using linearized equations. A comparison of the R^2 values for the linear transform models suggested that the linearized Langmuir isotherm gave a better fit for the experimental data compared to the linearized Freundlich, DR and Temkin isotherms.

6.3 Effect of pH on Adsorption of Promethazine Hydrochloride onto K10

The pH of the aqueous solution is an important controlling parameter in the adsorption process. In order to determine the optimum pH for adsorption of promethazine hydrochloride onto montmorillonite K10, adsorption process in different hydrogen ion concentration was carried out. The pH of 10% suspension of K10 in water was 4.5. The amount of promethazine hydrochloride adsorbed by the clay (C_s mmol/g) versus equilibrium pH was plotted (Figure 6.6). It is clear that maximum adsorption was provided at pH=7.4 (at equilibrium) for initial promethazine hydrochloride concentration of 1 mM.

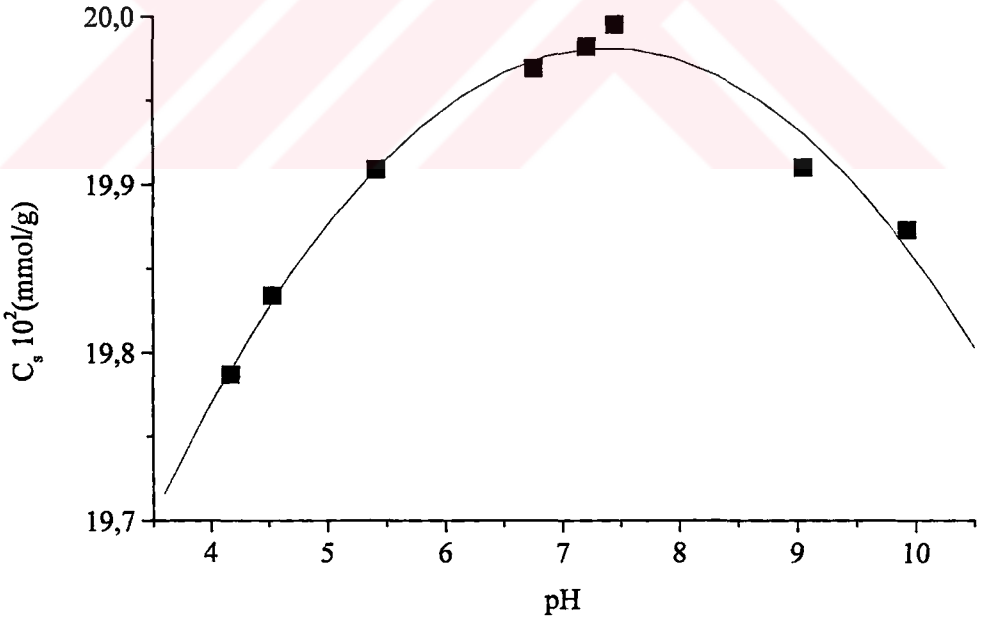
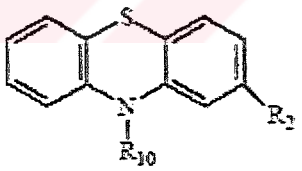
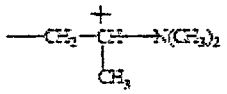


Figure 6.7 pH effects on adsorption of promethazine hydrochloride onto montmorillonite K10

It is probable that pH affects the surface charge of K10 and degree of ionization of drug and speciation of drug.olution, adsorption increased in between pH 4 to 7. But after pH=7.4, there was a decrease in the adsorption. At lower pH, more protons are available, thereby decreasing electrostatic attraction between cationic drug and positively charged sites of adsorbent. At higher pH, the surface of adsorbent becomes negatively charged. And when the concentration of OH^{-1} ion was increased, the species of neutral promethazine also increased due to increase of degree of ionization. So, no significant ionic attraction was observed.

It was well known that most drugs are weak acids or bases, and the degree of their ionization, as determined by the dissociation constant (pKa) of the drug and pH of the environment influences their solubilities. An acid with a small pKa (i.e., about 1.0) placed in an environment with a pH of 7 would be almost completely ionized and would be classified as a strong acid. In contrast, when a weak base passes from the strongly acidic environment of the stomach into the less acidic intestinal lumen, the extent of ionization decreases. The concentration of unionized species for a base with a pKa of about 4.0 is about 10 times that of the ionized species and since the neutral molecule freely diffuses through the intestinal mucosa, the drug is well absorbed.



Name	pKa	R_2	R_{10}
Promethazine	9.10	H	

6.4 Effect of Ionic Strength on Adsorption of Promethazine Hydrochloride onto K10

At different NaCl concentration, the adsorption isotherms of promethazine hydrochloride on montmorillonite K10 were determined by plotting the amount of promethazine hydrochloride adsorbed by the clay (C_s mmol/g) versus equilibrium concentration of promethazine hydrochloride (C_e mmol/L) at 25°C. Figure 6.7 shows the effect of ionic strength on adsorption of promethazine hydrochloride.

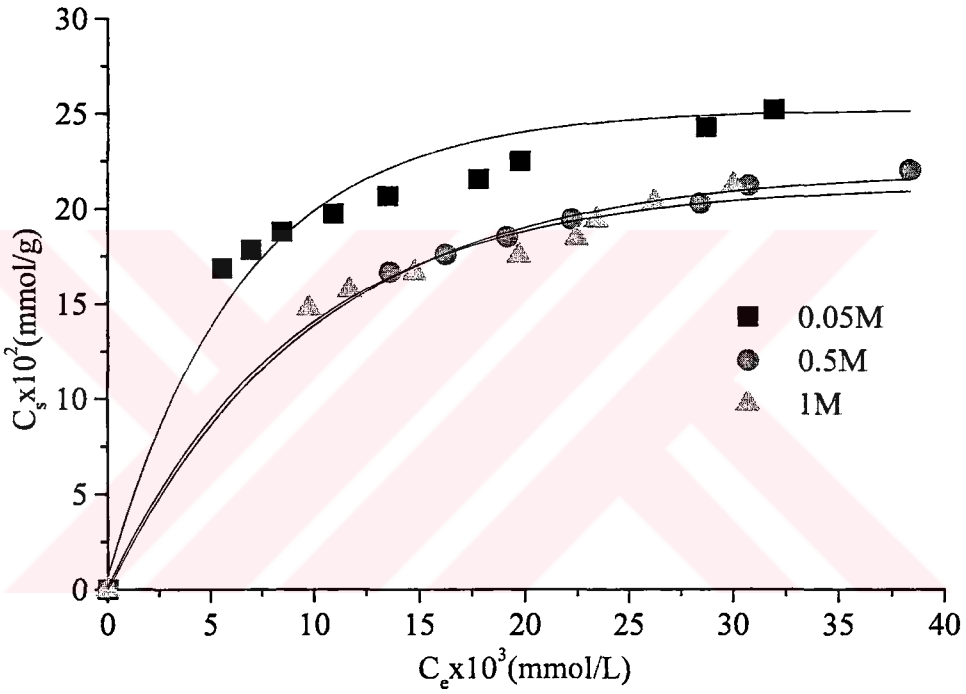


Figure 6.8 Effect of ionic strength on adsorption of promethazine hydrochloride onto K10

These isotherms may be classified as L type according to Giles classification. L type suggests medium affinity of promethazine hydrochloride on montmorillonite K10.

The equilibrium data were fitted to Langmuir equation. Figure 6.9 shows the results found by plotting C_e/C_s versus C_e for the adsorption process of promethazine hydrochloride onto K10 at different ionic strength.

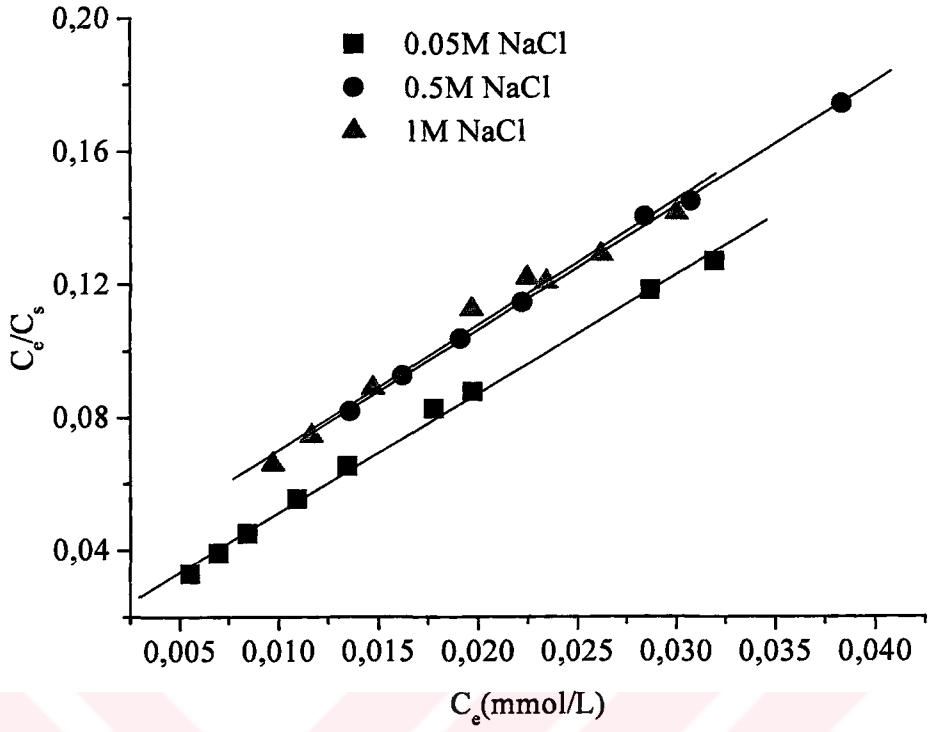


Figure 6.9 Langmuir isotherms for adsorption of promethazine hydrochloride onto montmorillonite K10 at different ionic strength

The sorption parameters of Langmuir equation were summarized in Table 6.9. As shown in Table 6.9, C_m values are 0.2796, 0.2687 and 0.2658 mmol/g for 0.05M, 0.5M and 1M NaCl concentration, respectively. L values are 231.067, 117.032 and 115.975 g/dm^3. Adsorption capacities decrease in order of $C_{m,\ 0.05M} > C_{m,\ 0.5M} > C_{m,\ 1M}$.

Table 6.9 The sorption parameters of Langmuir equation for promethazine hydrochloride on montmorillonite K10 at different ionic strength

[NaCl]/M	R^2	C_m(mmol/g)	L(g/L)
0.05	0.9962	0.2796	231.067
0.5	0.9986	0.2687	117.032
1	0.9817	0.2658	115.975

Freundlich equation was applied to quantify adsorption capacity. Figure 6.10 was obtained by plotting log C_s against log C_e at different ionic strengths.

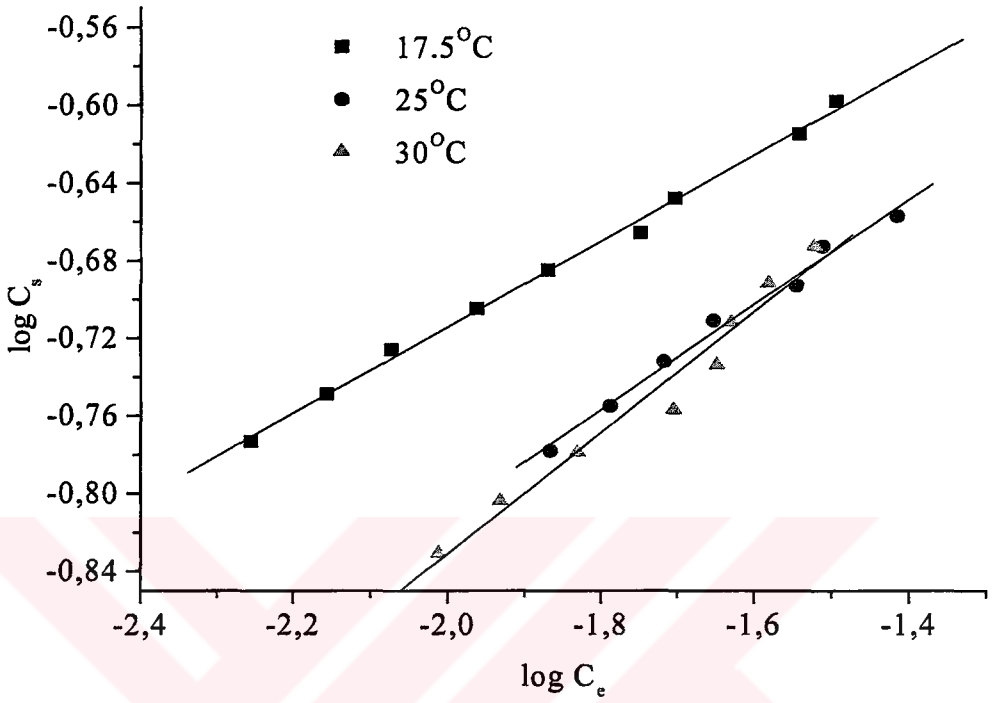


Figure 6.10 Freundlich isotherms for adsorption of promethazine hydrochloride onto montmorillonite K10 at different ionic strengths.

Parameters related to Freundlich equation were summarized in Table 6.10. As can be seen from Table 6.10, n_f values decrease from 0.3117 for 1M NaCl to 0.2219 for 0.05M NaCl. K_f values also decrease from 0.62 mmol/g for 1M NaCl to 0.536 mmol/g for 0.05M NaCl. This value indicates that relative sorption capacities increase as ionic strength increase.

Table 6.10 The sorption parameters of Freundlich equation for promethazine hydrochloride on Montmorillonite K10 at different ionic strengths

[NaCl] /M	R^2	K_f (mmol/g)	n_f
0.05	0.9964	0.536	0.2219
0.5	0.9886	0.538	0.2707
1	0.9677	0.620	0.3117

6.5 Adsorption Kinetics

In order to understand the adsorption process better, three kinetic models such as pseudo-first-order, pseudo-second-order and intraparticle diffusion were used (Özcan & Özcan, 2004; Chang et al, 2004; Tsai et al. 2004). The adsorption rate constant (k_{ad}) for adsorption of promethazine hydrochloride was calculated using Pseudo-first and second order equation:

$1/q_t = (k_1/q_1)(1/t) + 1/q_1$ Pseudo-first order

$t/q_t = 1/k_2.q_2^2 + (1/q_2).t$ Pseudo-second order

where

q_t = the amount of promethazine hydrochloride adsorbed on montmorillonite K10 at time t (mg g^{-1}),

q_1 = the maximum adsorption capacity for pseudo-first order adsorption (mg g^{-1}),

k_1 = the rate constant of pseudo-first order adsorption (min^{-1}),

q_2 = the maximum adsorption capacity for pseudo-second order adsorption (mg g^{-1}),

k_2 = the second order rate constant for the adsorption process (g.mg^{-1} min^{-1})

The plot of 1/qt versus 1/t was plotted for promethazine hydrochloride at different temperatures. Correlation coefficients (R^2) for the pseudo-first order adsorption was found to be 0.9164, 0.6483 and 0.8534 at 17.5°C, 25°C and 30°C, respectively. The plots were not given owing to their low correlation coefficients.

Figure 6.11 shows the results found by plotting t/q_t versus t for the pseudo-second order adsorption.

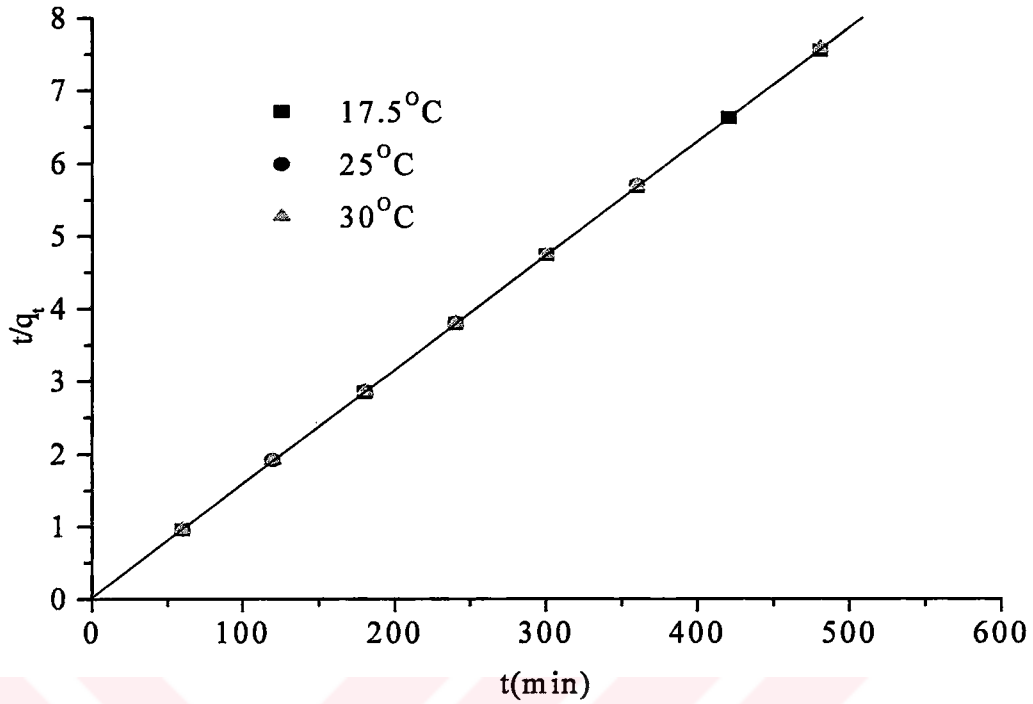


Figure 6.11 Pseudo-second order plot for adsorption of promethazine hydrochloride on K10 at different temperatures.

Correlation coefficients for pseudo-second-order kinetic (R^2) values are obtained to be 1 at each temperature. As conclusion, R values are greater than the pseudo-first-order model. The parameters of k_2 and q_2 for the adsorption of promethazine hydrochloride onto montmorillonite K10 were obtained from the slopes and intercepts of the pseudo-second-order plots respectively. The data were given in Table 6.11.

Table 6.11 The pseudo-second order parameters for promethazine hydrochloride at different temperatures.

Temperature/°C	R^2	k_2 (g mg^{-1} min^{-1})	q_2
17.5	1	0.01050	63.694
25	1	0.01208	63.371
30	1	0.01226	63.532

The rate constant for the intraparticle diffusion was obtained using the equation

$q = K_p t^{1/2} + C$

where

K_p = intraparticle diffusion rate constant (mg g^{-1} $h^{-1/2}$),

q = amount adsorbed of solute

C = intercept which gives information about boundary layer thickness.

When the plots do not pass through the origin, this is indicative of some degree of boundary layer control. If the intraparticle diffusion is involved in adsorption process, a plot of $t^{1/2}$ versus q_t would result in a linear relationship, and the particle diffusion would be controlling step if this line passed through the origin. When the plot does not pass through the origin, this imply that intraparticle diffusion is not the only rate controlling step but also other processes may control the rate of adsorption. This further may be indicative of some degree of boundary layer control. In this study, it is probable that the intraparticle diffusion is not the rate controlling step. Other process may control the rate of adsorption (Mahramanlioglu, 2003).

Figure 6.12 shows the results found by plotting q_t versus $t^{1/2}$ for the intraparticle diffusion model given in equation above. The slope of the plot is equal to K_p and its intercept value is equal to C. The correlation coefficients are greater than 0.9655 as indicated in Table 6.12. These values indicate that the adsorption complies with an intraparticle diffusion mechanism. The linear portions of curves do not pass through the origin. This demonstrates that mechanism of promethazine hydrochloride adsorption onto montmorillonite K10 is complex.

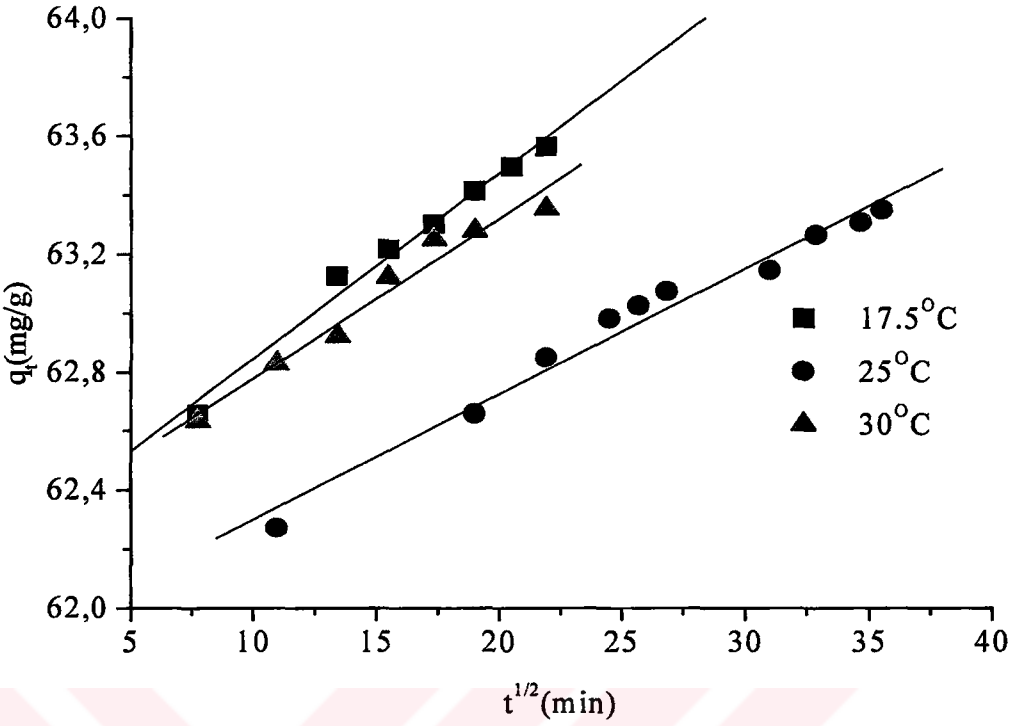


Figure 6.12 Intraparticle diffusion plot for promethazine hydrochloride onto montmorillonite K10

The intraparticle diffusion parameters were summarized in Table 6.12. As can be seen from Table 6.12, K_p values are 0.0554, 0.0708 and 0.0542mg g^{-1} $h^{-1/2}$ at 17.5°C, 25°C and 30°C, respectively. C values are 62.3539, 61.8674 and 62.2356 mg g^{-1}, respectively.

Table 6.12 Intraparticle diffusion parameters at different temperatures.

Temperatures/°C	R^2	K_p	C
17.5	0.9962	0.0554	62.3539
25	0.9974	0.0708	61.8674
30	0.9655	0.0542	62.2356

6.6 Adsorption Thermodynamics

In order to understand the effect of temperature better, it is important to know the change of thermodynamic parameters such as standard Gibbs free energy change, ΔG, standard enthalpy, ΔH, and standard entropy, ΔS. The Gibb's free energy change of adsorption is calculated from the following equation (Özcan et al, 2004):

$\Delta G^O = -RT \ln K_d$

where

K_d = The equilibrium partition constant

R = gas constant (8.314 J mol $^{-1}$ K $^{-1}$)

T = absolute temperature (K)

For each temperature, the same C_e value was selected (17.51 10^{-3}) and from this value, C_s value was calculated by using Freundlich equation. K_d was estimated using the following equation;

$K_d = C_s/C_e$

where

C_e = equilibrium concentration

C_s = the amount of adsorbed

Table 6.13 The K_d values for adsorption of promethazine hydrochloride onto montmorillonite K10 at different temperatures

Temperature/°C	C_s	K_d
17.5	0.176	10.026
25	0.228	13.021
30	0.205	11.708

Standard enthalpy, ΔH^O, and standard entropy, ΔS^O was calculated by using van't Hoff equation:

$\log K_d = \Delta H^O/2.303\ RT + \Delta S^O/2.303\ R$

The curve was plotted log K_d versus (1/T) (Figure 6.13). The slope of van't Hoff plot is equal to $\Delta H^O/2.303$ R and the intercept is equal to $\Delta S^O/2.303$ R. These thermodynamic parameters were given in Table 6.7

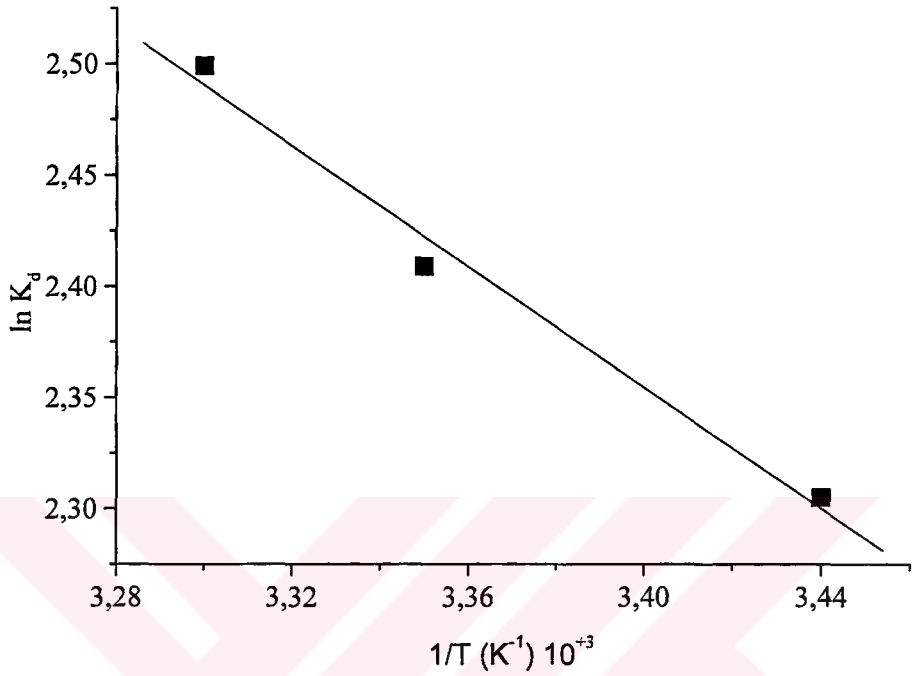


Figure 6.13 Thermodynamic plots for adsorption of promethazine hydrochloride onto K10

Table 6.14 The thermodynamic parameters for adsorption of promethazine hydrochloride onto montmorillonite K10 at different temperatures

Temperature/°C	ΔH^O (kJ/mol)	ΔS^O (kJ/mol)	ΔG^O (kJ/mol)
17.5	-11.293	0.058	-28.151
25	"	"	-28.586
30	"	"	-28.876

The negative value of ΔG^O indicates that the adsorption of promethazine hydrochloride onto montmorillonite K10 is spontaneous. ΔH^O was found to be -11.293 kJ/mol. This value confirms exothermic nature of adsorption. ΔS^O was calculated as 0.058 kJ/mol. The positive ΔS^O value indicates the increased

randomness at the solid/solution interface during the adsorption promethazine hydrochloride on K10.

According to Arrhenius, for most reaction the increase in rate with increasing temperature is non-linear. Arrhenius equation is as below

$k = A\, e^{-Ea/RT}$ or

$\ln k = \ln A - E_a/RT$

where

k = rate constant,

E_a = activation energy,

R = gas constant (8.314 J/mol K),

T = absolute temperature (K)

The curve was plotted $\ln k_2$ versus (1/T) (Figure 6.14). The slope of Arrhenius plot is equal to $-E_a/R$ and the intercept is equal to ln A.

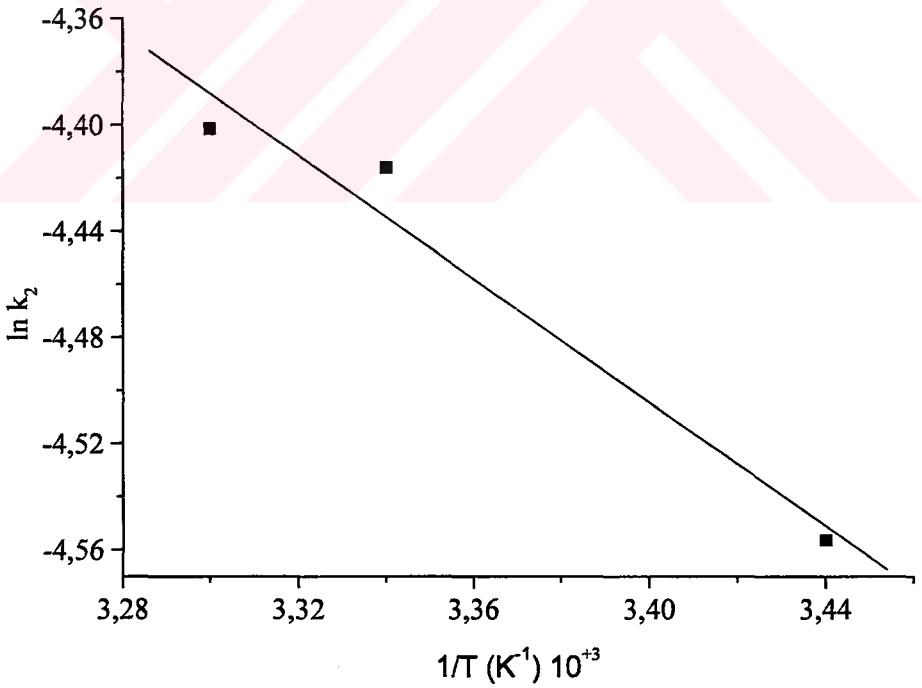


Figure 6.14 Arrhenius plot for adsorption of promethazine hydrochloride onto montmorillonite K10

The E_a and A values for adsorption of promethazine hydrochloride onto montmorillonite K10 were found to be -9.401 kJ/mol and 0.518, respectively with a correlation coefficient of R=0.9828. The E_a value indicates that process is a physical adsorption.

6.7 The Effect of Contact time on Adsorption of Promethazine Hydrochloride onto Montmorillonite K10

In order to determine the optimum contact time for adsorption of promethazine hydrochloride onto montmorillonite K10, the equilibrium concentrations were measured at definite times. The curve was plotted the amount adsorbed of promethazine hydrochloride (C_s, mmol/L) measured in the definite time intervals versus time.

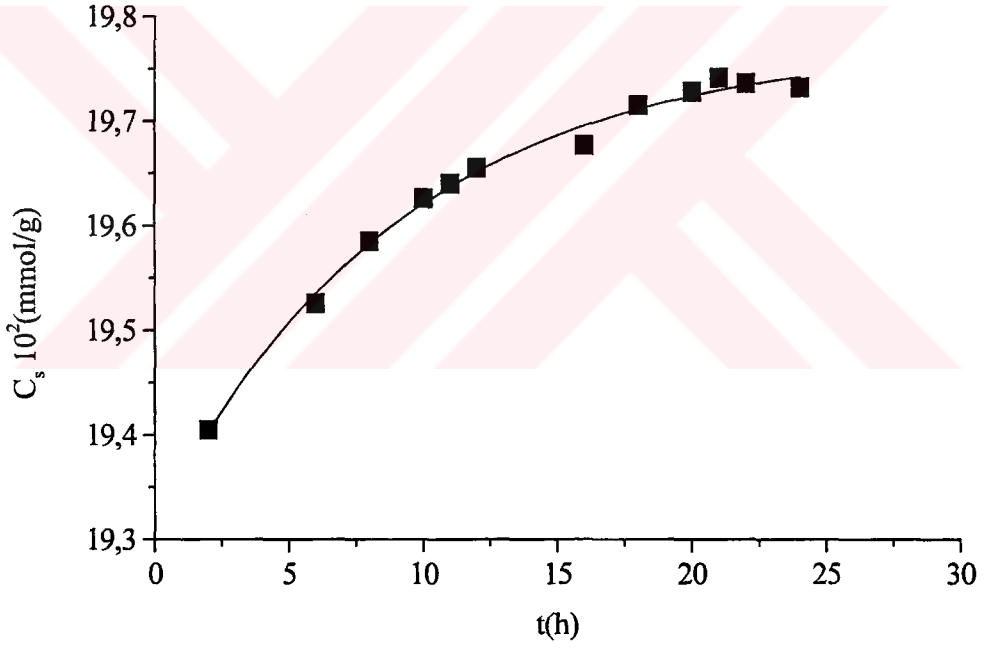


Figure 6.15 Effect of contact time on adsorption of promethazine hydrochloride on K10

As can be seen from Figure 6.15, when the contact time was increased, the amount of adsorption was also increased. The maximum adsorption time of promethazine hydrochloride onto montmorillonite K10 was found to be 21h. After this time, increase in the adsorption was not observed.

6.8 FTIR Analysis

Infrared absorption frequencies of acid-treated montmorillonite were investigated and the assignments of the bands were given in Table 6.15(Ravichandran, 1997).

Table 6.15 FTIR absorption frequencies of acid-treated montmorillonite

Assignment	**Wavenumber(cm^{-1})**
ν(Si-O)	1100sh; 1040vs,b ; 985sh
ν(Si-O), ν(Al-O)	810sh
ν(Al-O), ν(Si-O)	720w
ν(Al-O-Si)	680m; 650sh
ν(Mg-O)	530m
ν(Si-O)	460s

Key: sh=shoulder; vs=very strong; b=broad; w=weak; s=strong; m=medium

The absorption bands in the region of 3750 to 3500 cm^{-1} have been assigned to the surface structural hydroxyl groups of the layered aluminosilicates as well as of adsorbed water. The IR absorption bands in the 1150 to 400 cm^{-1} region are relatively more informative about the structural characteristics of clay minerals and are attributed to lattice vibration (Farmer, 1974).

From FTIR results (Figure 6.16), it was determined that weak interactions occurred between promethazine hydrochloride and montmorillonite K10 clay. There were not numerous variations in the spectra of the montmorillonite K10 clay after promethazine hydrochloride adsorption due to weak adsorption of promethazine hydrochloride. Therefore, the observed spectra mainly reflect the original spectra of adsorbents.

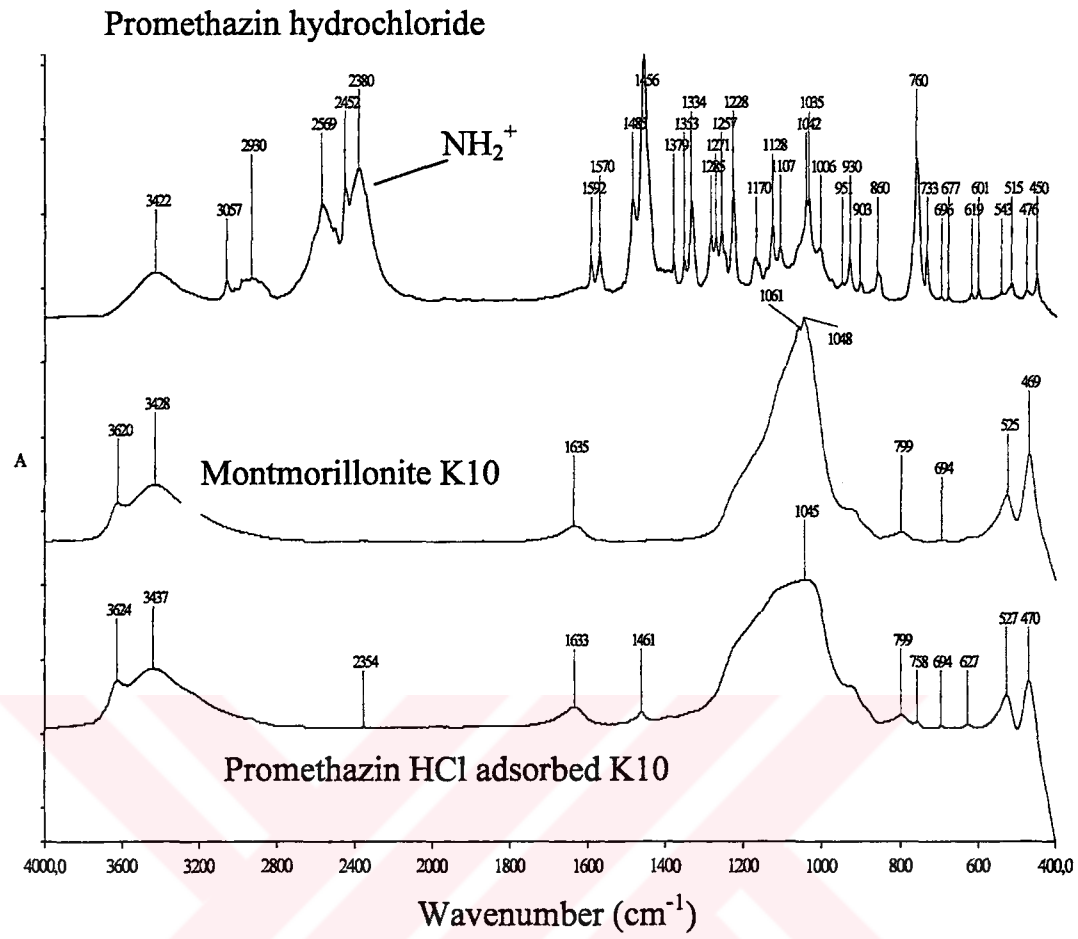


Figure 6.16 FTIR spectrum of promethazine hydrochloride, montmorillonite K10 and promethazine hydrochloride adsorbed K10

As can be seen in the spectra of montmorillonite K10 (Figure 6.16), there is an absorption band at 3620cm^{-1}. This band is typical for smectites with high amount of Al in the octahedra (Madejova, 2003). This complies with the chemical composition of the clay and SEM analysis. A band at 3428 cm^{-1} in the spectra of the fine clay shows H-O-H hydrogen bonded water. Promethazine hydrochloride treated montmorillonite K10 displays two bands at 3624 $cm^{-1}$and 3437 cm^{-1}. Intensities of these bands do not change as compared with the range of 3428-3620 cm^{-1} of spectrum of the clay. Hydrogen bond may occur between hydroxyl group of bounded water and promethazine hydrochloride species. The small band at 1635 cm^{-1} corresponds to the HOH deformation vibration. After promethazine hydrochloride treatment, OH deformation band shifted to 1633 cm^{-1} in the spectra of promethazine

hydrochloride treated montmorillonite K10. The intense silicates (Si-O vibrations within the layer) in the spectra of montmorillonite K10 are located at 1061 cm^{-1}. In addition, the bands at 525 and 469 cm^{-1} indicate Si-O-Al (octahedral Al) and Si-O-Si bending vibrations, respectively (Sohn, 2000; Madejova, 2003). As shown in the spectra of promethazine hydrochloride treated montmorillonite K10, a small shift was observed in these bands. The bands between 800-600 cm^{-1} may be attributed to Si-O-Si symmetric stretching. There are not so much shifts in these bands after promethazine hydrochloride treatment. A band at 2380 cm^{-1} in the spectra of promethazine hydrochloride indicates the N-H stretching vibrations in the quaternary ammonium group of the molecule. After the adsorption onto montmorillonite K10, this band shifted drastically to 2354 cm^{-1} and can not be seen easily. In contrast, the bands characteristic of skeletal vibrations of the aromatic ring, below 1600 cm^{-1}, shifted only slightly (Fejer et al, 2001).

6.9 SEM Analysis

Scanning Electron Microscopy (SEM) was used to examine the surface of montmorillonite K10 and promethazine hydrochloride adsorbed montmorillonite K10. SEM study was done to understand the morphology of the particles. Figure 6.17, 6.18, 6.19, 6.21, 6.23 and 6.24 show the SEM images of the pure montmorillonite K10 and promethazine hydrochloride adsorbed montmorillonite K10. The chemical analysis of selected area in the SEM images was measured by XRF and the results were shown in Table 6.16, 6.17 and 6.18. In addition, spectrum analysis of selected area in the SEM images was given in Figure 6.20, 6.22 and 6.25.

SEM images illustrate that promethazine hydrochloride are well dispersed on the montmorillonite K10. Chemical analysis of the white and dark grains in the clay-drug complex measured by XRF shows that percentage of Al of the dark grain are greater than that of white grain. This demonstrates that the area of white grains can be generally considered as the sorption sites for promethazine hydrochloride. This idea can be supported by the results of percentage of Si in white grains. However dark grains contain high level of percentage of Si and Al.

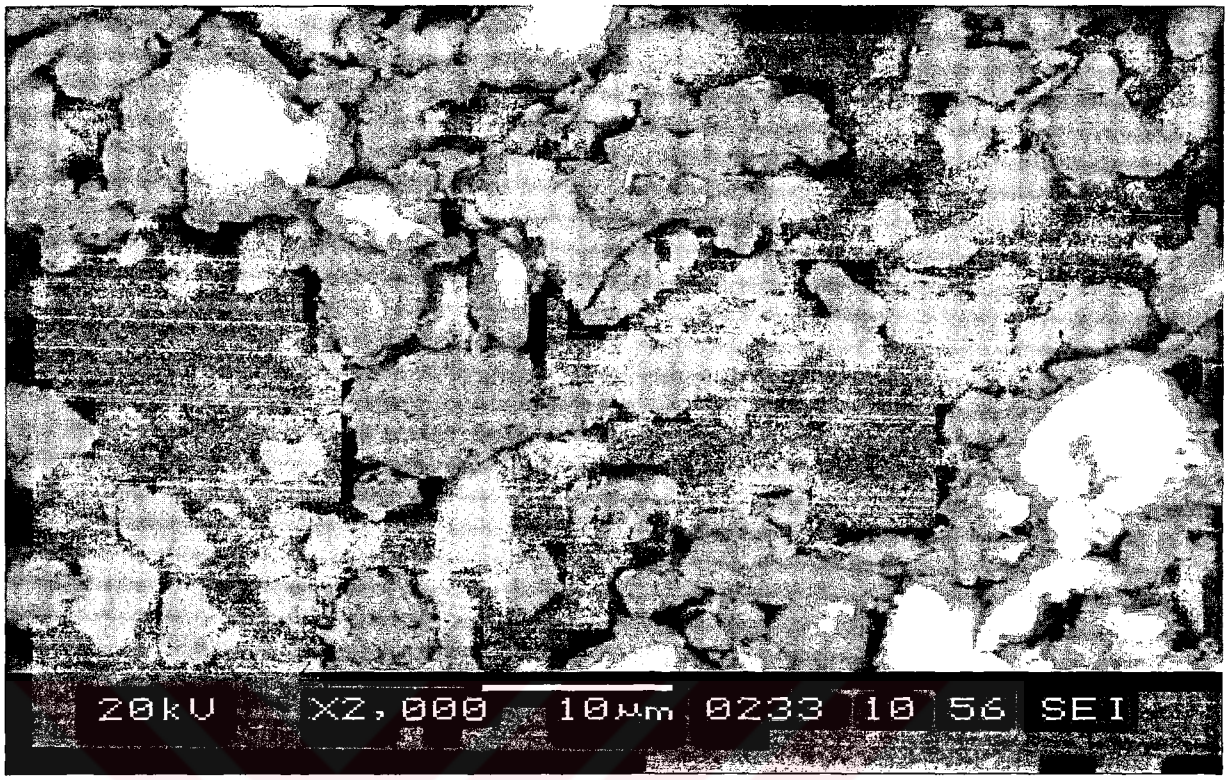


Figure 6.17 SEM images of montmorillonite K10

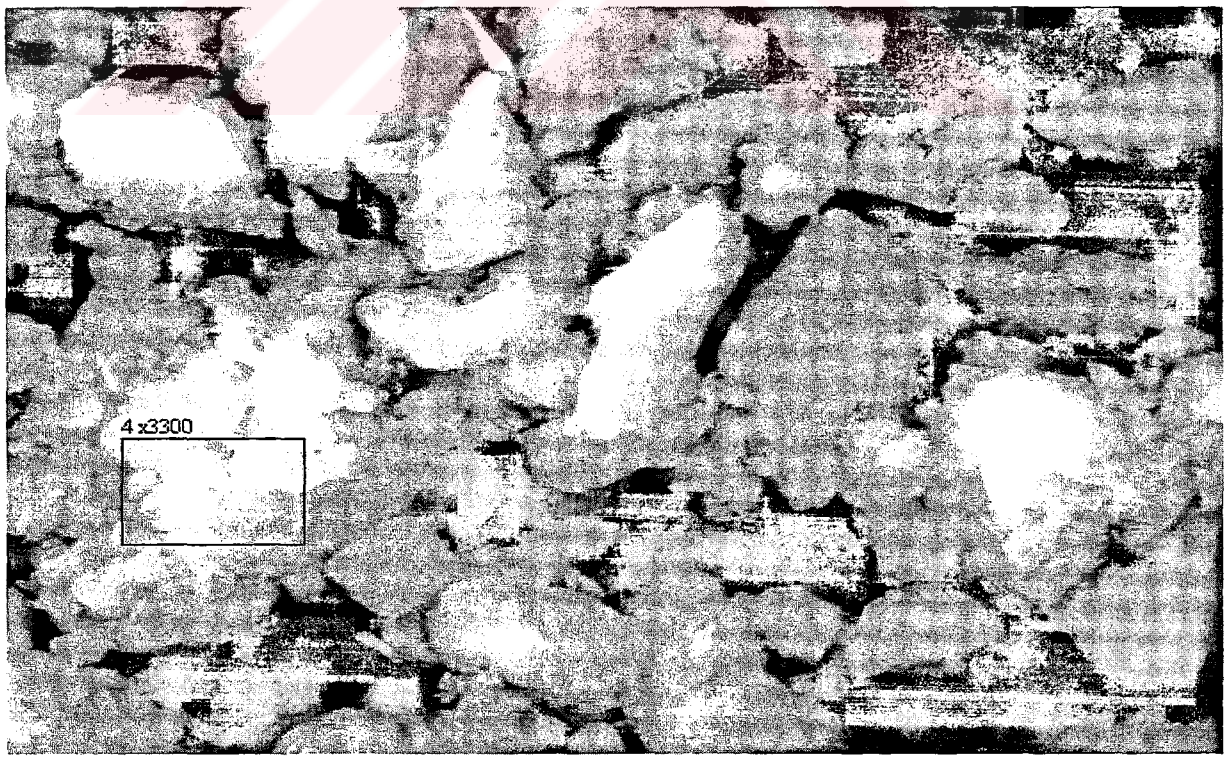


Figure 6.18 SEM images of montmorillonite K10

Table 6.16 Chemical analysis of selected areas of montmorillonite K10 by XRF

Component	Conc.				
C	19.865	wt.%			
O	36.517	wt.%			
Mg	0.876	wt.%			
Al	5.773	wt.%			
Si	34.470	wt.%			
K	0.321	wt.%			
Fe	1.532	wt.%			
Cu	0.646	wt.%			
	100.000	wt.%	Total		

Elt.	Line	Intensity (c/s)	Error 2-sig	Conc		
C	Ka	2.88	0.339	19.865	wt.%	
O	Ka	65.41	1.618	36.517	wt.%	
Mg	Ka	15.10	0.777	0.876	wt.%	
Al	Ka	116.55	2.159	5.773	wt.%	
Si	Ka	710.03	5.329	34.470	wt.%	
K	Ka	5.18	0.455	0.321	wt.%	
Fe	Ka	11.95	0.691	1.532	wt.%	
Cu	Ka	2.92	0.342	0.646	wt.%	
				100.000	wt.%	Total

kV	20.0
Takeoff Angle	35.0°

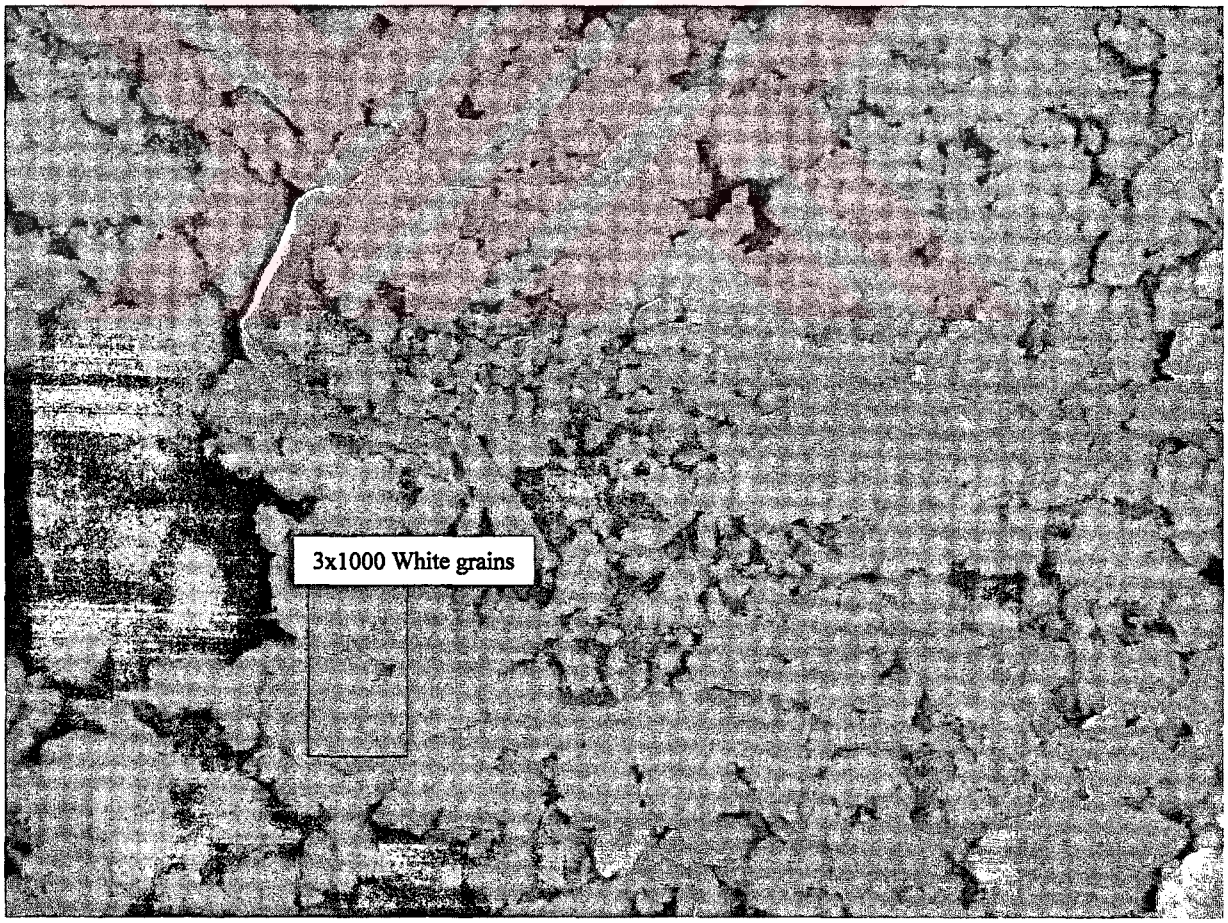


Figure 6.19 SEM images of clay-drug complex

Table 6.17 Chemical analysis of selected areas of clay-drug complex by XRF

Component	Conc.		
C	19.128	wt.%	
O	38.496	wt.%	
Mg	0.821	wt.%	
Al	6.153	wt.%	
Si	31.544	wt.%	
S	0.613	wt.%	
K	0.770	wt.%	
Fe	2.474	wt.%	
	100.000	wt.%	Total

Elt.	Line	Intensity (c/s)	Error 2-sig	Conc	
C	Ka	1.92	0.277	19.128	wt.
O	Ka	47.94	1.385	38.496	wt.
Mg	Ka	9.46	0.615	0.821	wt.
Al	Ka	83.34	1.826	6.153	wt.
Si	Ka	436.37	4.178	31.544	wt.
S	Ka	6.42	0.507	0.613	wt.
K	Ka	8.49	0.583	0.770	wt.
Fe	Ka	13.07	0.723	2.474	wt.
				100.000	wt.

kV	20.0
Takeoff Angle	35.0°

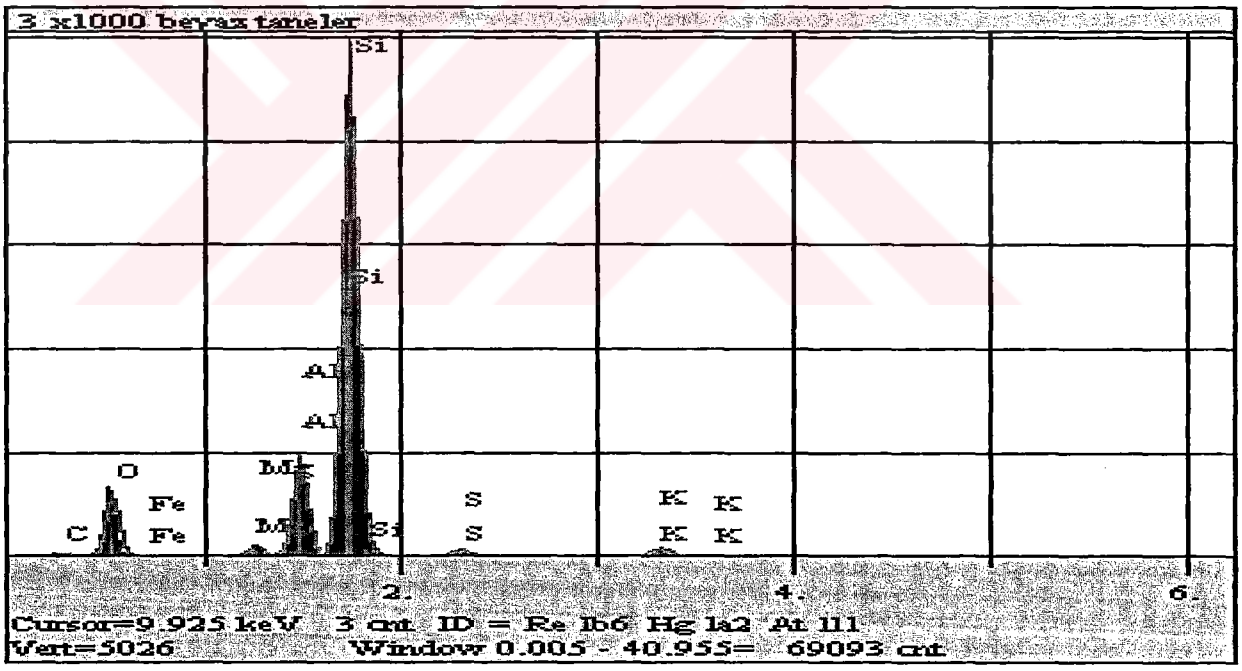


Figure 6.20 Spectrum analysis of selected area of clay-drug analysis

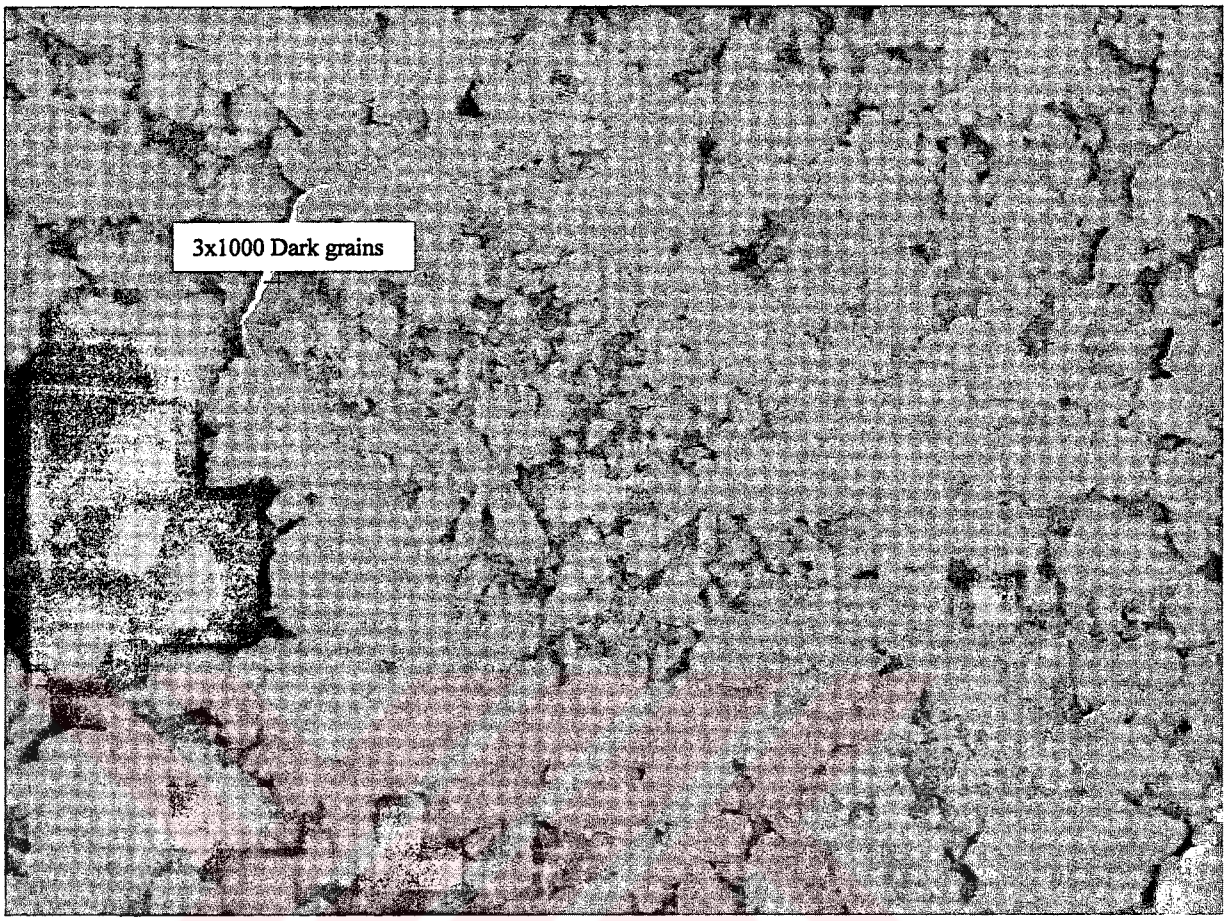


Figure 6.21 SEM image of clay-drug complex

Table 6. 18 Chemical analysis of selected area of clay-drug complex by XRF

Component	Conc.		
Mg	0.543	wt.%	
Al	18.713	wt.%	
Si	51.666	wt.%	
K	10.877	wt.%	
Fe	7.161	wt.%	
O	11.039	wt.%	
	100.000	wt.%	Total

Elt.	Line	Intensity (c/s)	Error 2-sig	Conc		
O	Ka	3.74	0.426	11.039	wt.%	
Mg	Ka	2.40	0.505	0.543	wt.%	
Al	Ka	94.04	1.998	18.713	wt.%	
Si	Ka	216.69	2.979	51.666	wt.%	
K	Ka	37.54	1.388	10.877	wt.%	
Fe	Ka	12.63	0.897	7.161	wt.%	
				100.000	wt.%	Tc

kV	20.0
Takeoff Angle	35.0°
Elapsed Livetime	100.0

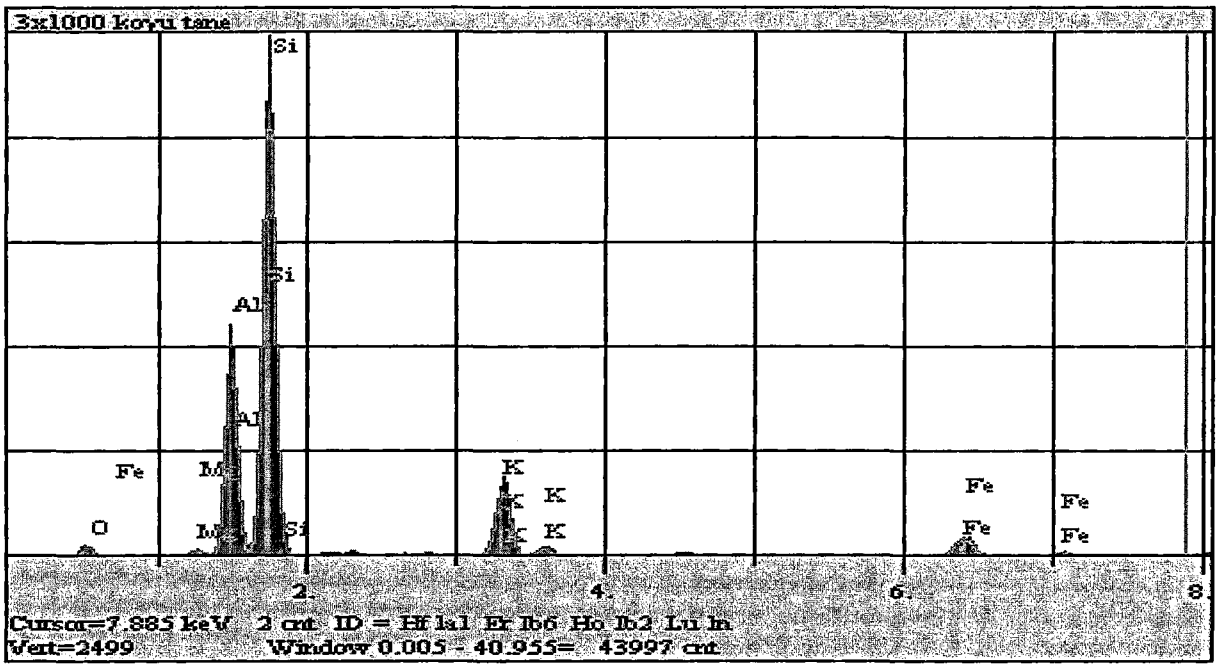


Figure 6.22 Spectrum analysis of selected area of clay-drug complex by XRF

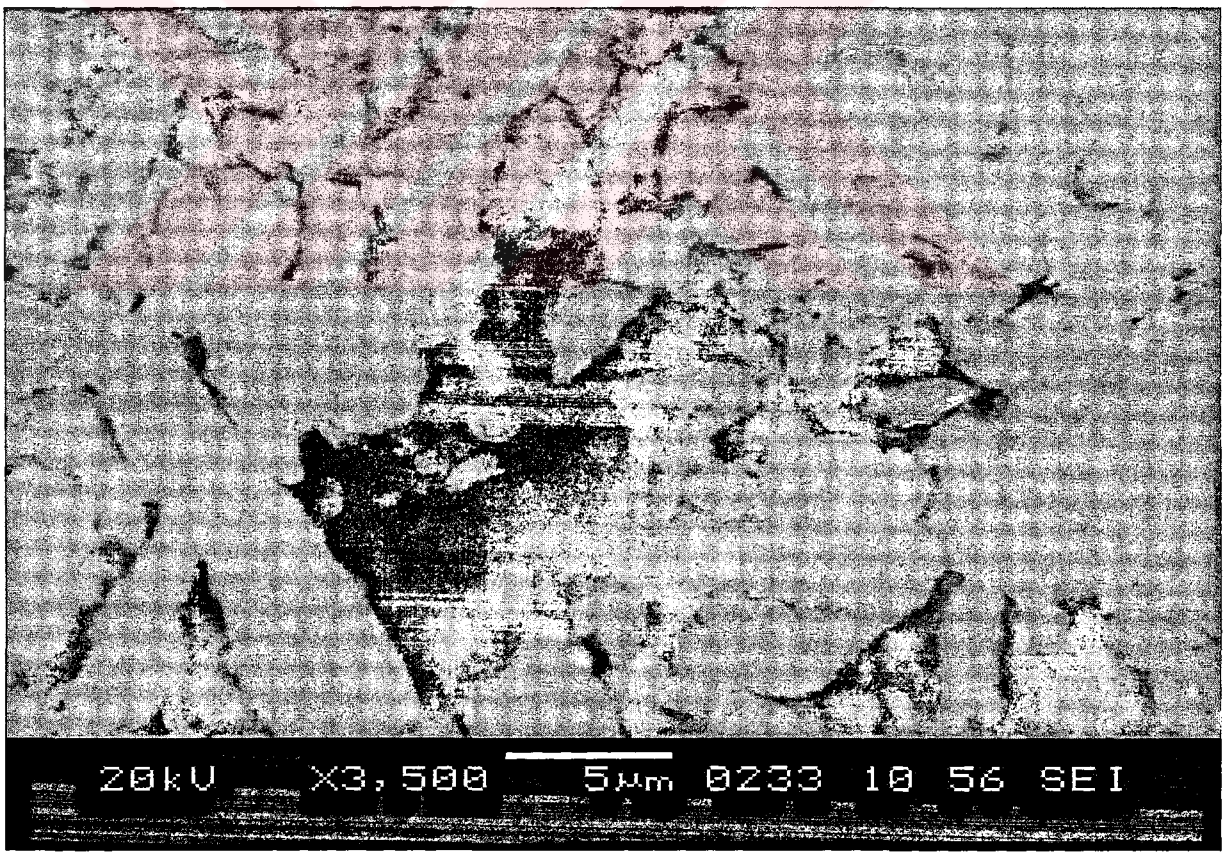


Figure 6.23 SEM image of clay-drug complex

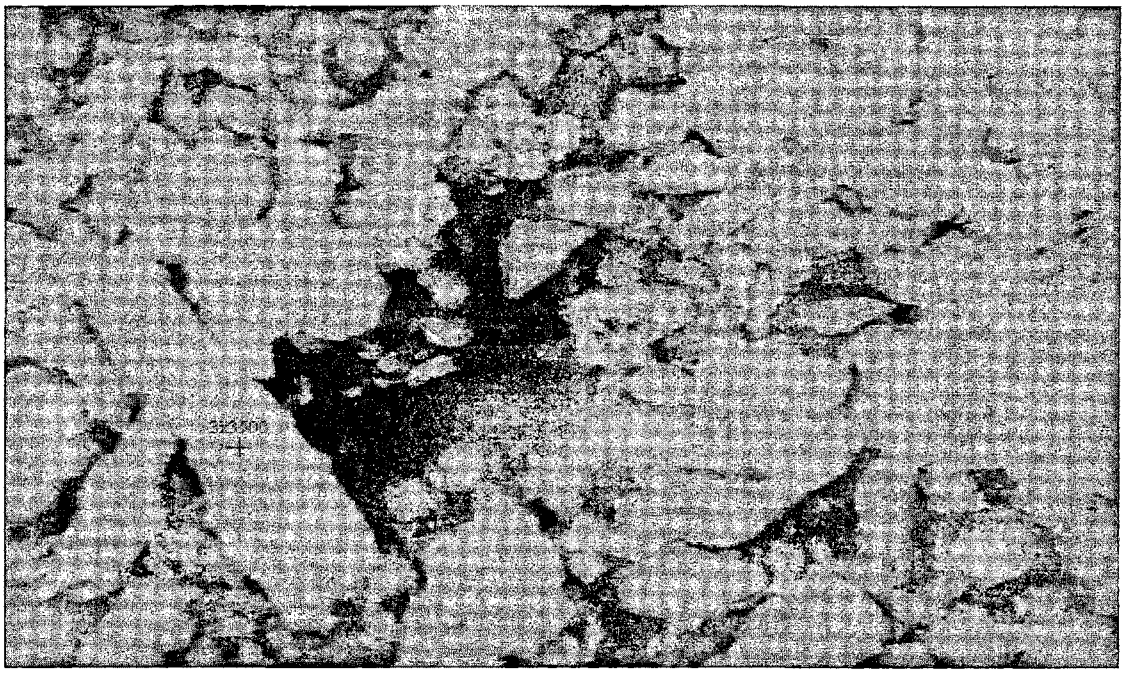


Figure 6.24 SEM image of clay-drug complex

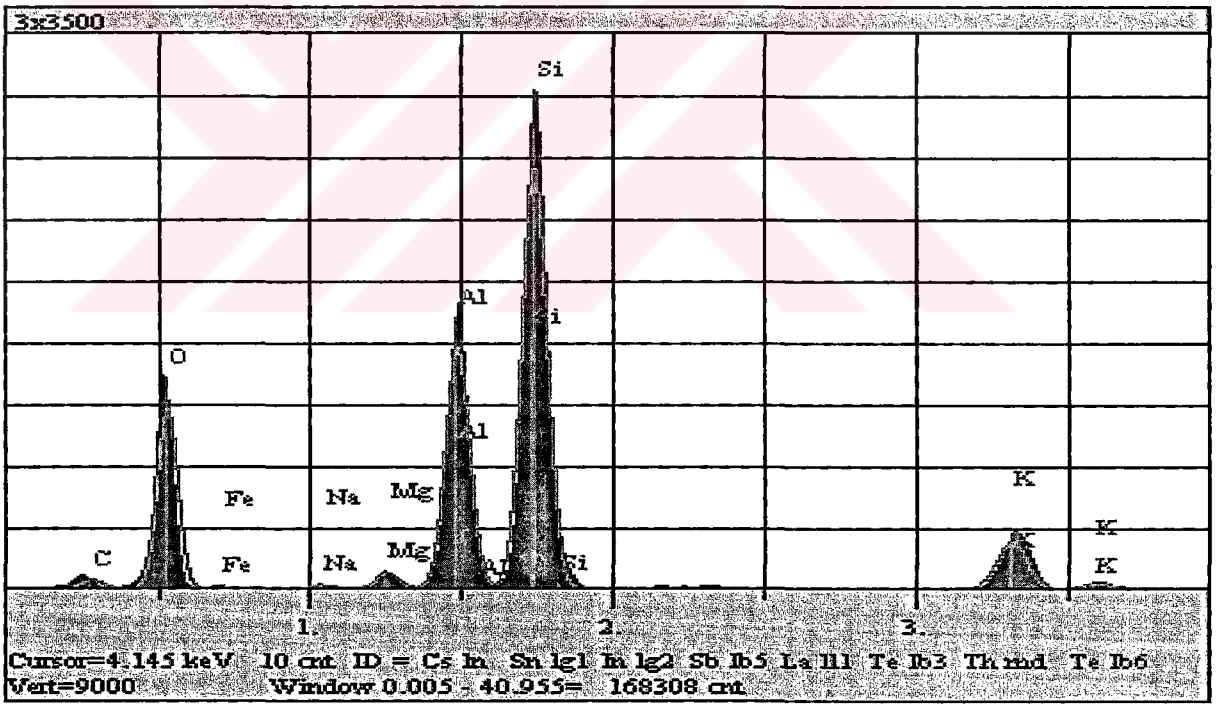


Figure 6.25 Spectrum analysis of selected area of clay-drug complex by XRF.

CONCLUSIONS

The data related to adsorption of promethazine hydrochloride onto montmorillonite K10 at various temperatures were given in Tables 6.2, 6.3, 6.4, 6.5, 6.6, 6.7 and 6.8. These data demonstrated that the amount of promethazine hydrochloride adsorbed is increasing with decrease in temperature. The isotherms were of H type at 17.5°C and 25°C but it was of L type at 30°C in terms of Giles classification. It means that montmorillonite K10 have a high affinity for promethazine hydrochloride that is strongly adsorbed and no competition occurs for the sorption sites between the solvent and promethazine hydrochloride molecules at 17.5°C and 25°C.

The equilibrium data were analyzed in each temperature using linearized Langmuir, Freundlich, DR and Temkin and nonlinearized Langmuir and Freundlich isotherms. The parameters for each isotherm were found and the correlation coefficients were computed. The linearized Langmuir isotherm gave the best correlation for each temperature (R^2>0.9805). According to linearized Langmuir isotherm, C_m (maximum adsorption capacity) values increased as temperature decreased. As shown in Table 6.4, r (dimensionless separation factor) for each temperature was found less than 1. This shows that the process is favorable.

In order to be able to explain adsorption type, the data were applied to DR isotherm. As pointed out in Table 6.7, E values were found to be 11.237, 18.966 and 20.851kJ/mol at 17.5°C, 25°C and 30°C, respectively. The results suggest that adsorption of promethazine hydrochloride onto montmorillonite K10 can be explained by ion exchange. In addition, Q_m (adsorption capacity) values calculated from DR isotherm were found less than the adsorption capacity values calculated from the Langmuir equation.

The effect of ionic strength on adsorption of promethazine hydrochloride by montmorillonite K10 was also examined. As the ionic strength is increased by adding NaCl from 0.05M to 1M, the amount of promethazine hydrochloride adsorbed is decreased in terms of value of C_m (relative sorption capacity).

The effect of pH on adsorption was also investigated. As can be seen in Figure 6.7 and from the experimental data indicated that the amount adsorbed increased as pH increased until pH 7.4 (at equilibrium). After this value, adsorption decreased. The pH value of 7.4 can be considered as the optimum pH value for the sorption of promethazine hydrochloride on K10.

The kinetic of the adsorption of promethazine hydrochloride on montmorillonite K10 was studied. The adsorption data were applied to pseudo-first-order and pseudo-second-order equation. As shown in Table 6.11, the pseudo-second order equation gave the best correlation coefficient. That is to say, the adsorption process followed a pseudo second order kinetics. The value of k_2 (the second order rate constant) was calculated to be 0.0105, 0.01208 and 0.01226 g mg^{-1} min^{-1}at 17.5°C, 25°C and 30°C, respectively. In addition, in order to test the possibility of transport from solution to the pores of the adsorbent, the intraparticle diffusion parameters were calculated. It was shown that the plots do not pass the origin. This illustrated that mechanism of adsorption of promethazine hydrochloride onto montmorillonite K10 is complex.

In order to understand the effect of temperature on the adsorption, thermodynamic parameters were calculated. As can be seen in Table 6.14, the thermodynamic evaluation of the adsorption process gave $\Delta G^O < 0$, $\Delta H^O < 0$ and $\Delta S^O > 0$. The negative values of ΔG^O (free energy) indicate that the adsorption is spontaneous. ΔH^O (enthalpy of adsorption) is exothermic. The magnitude shows the physical adsorption. Since ΔH^O is less than 10 kcal/mol, it can be defined a physical process. Activation energy, E_a was calculated as -9.401 kJ/mol. This value also indicates a physical adsorption.

At the same time, FTIR results show that weak interactions occur between promethazine hydrochloride and montmorillonite K10 clay (Figure 6.16). That is to say, the results conform to that of thermodynamic parameters.

The morphologies of the clay and clay-drug complex were examined by SEM and samples were characterized by XRF. SEM images illustrated that promethazine hydrochloride are well dispersed on the montmorillonite K10. XRF results show that drug is adsorbed onto white grains seen in the SEM images.

It can be concluded that Montmorillonite K10 is suitable for the adsorption of promethazine hydrochloride from aqueous solution. Montmorillonite K10 may be used as adsorbent for promethazine hydrochloride poisonings. On the other hand, it can be proposed that desorption or release of this drug from the clay sample after adsorption should be studied in further research works.

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