DOKUZ EYLÜL UNIVERSITY
GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES

ADSORPTION OF TRIMETHOPRIM FROM AQUEOUS SOLUTION ONTO CLAYS

by
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August, 2005
İZMİR

ADSORPTION OF TRIMETHOPRIM FROM AQUEOUS SOLUTION ONTO CLAYS

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M. Sc. THESIS EXAMINATION RESULT FORM

We have read the thesis entitled **"ADSORPTION OF TRIMETHOPRIM FROM AQUEOUS SOLUTION ONTO CALYS "** completed by **ZEHRA BEKÇİ** under supervision of **Prof. Dr. Kadir YURDAKOÇ** and we certify that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Science.

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ADSORPTION OF TRIMETHOPRIM FROM AQUEOUS SOLUTION ONTO CLAYS

ABSTRACT

The adsorption of trimethoprim (TMP) onto montmorillonite KSF from aqueous solution was studied in a batch system as a function of temperature, ionic strength, pH conditions and contact time. Linear form of Langmuir, Freundlich and Dubinin-Radushkevich (DR) adsorption isotherms are applied to evaluate adsorption data. Langmuir adsorption isotherm gave a better fit than the Freundlich model based on the correlation coefficients (R^2) values. By using Langmuir equation, maximum adsorption capacities (C_m) of montmorillonite KSF were obtained as 0,4461 $mmolg^{-1}$ at 29.5°C, 0.1686 $mmolg^{-1}$ at 37.5°C and 0.1400 $mmolg^{-1}$ at 45°C respectively. Freundlich K_f (adsorption capacity) values decrease from 0.8241$mmolg^{-1}$ at 29.5°C to 0.2318 $mmolg^{-1}$ at 45°C. As a result, adsorption of trimethoprim decreases by increasing temperature. All E (sorption energy) values obtained from DR adsorption isotherm were between 8 and 16 $kJmol^{-1}$, for that reason these E values indicate that sorption of trimethoprim onto montmorillonite KSF can be explained by ion exchange mechanism at 29.5; 37.5; 45°C and energy values are close to physical adsorption type. The adsorption capacities (X_m) of DR isotherm at 29.5; 37.5; 45°C were 2.504 10^{-3}, 2.41 10^{-3}, 1.0876 10^{-3} $molg^{-1}$, respectively. It supports that adsorption decreases when temperature increases.

The adsorptive removal of drug from aqueous solution is pH and ionic intensity dependent. The maximum adsorption at equilibrium was observed at pH=5.04 by plotting the amount of trimethoprim adsorbed by KSF (Cs $mmolg^{-1}$) versus equilibrium pH. Adsorption of trimethoprim onto montmorillonite KSF at different ionic strengths indicates that adsorption decreases when the ionic strength of the medium increases owing to the competition to negatively charged clay surface between the protonated form of trimethoprim and Na^+ ions.

Several kinetic models including the pseudo-first-order-equation, pseudo-second-order equation, and intraparticle diffusion model were applied to find out adsorption mechanism. The adsorption system obeys the pseudo-second-order kinetic model by taking into account of the correlation coefficients and the intraparticle diffusion is not the only rate-controlling step.

Thermodynamic parameters; $\Delta H°$, $\Delta S°$ and $\Delta G°$ were estimated and these parameters show that occurred adsorption is exothermic, favorable and spontaneous. Activation energy value (E_a) is between 5-40 $kJmol^{-1}$ values and it indicates that physical adsorption mechanism is occurred. For all, it can be easily understood that montmorillonite KSF can be used to remove trimethoprim from wastewater and as a drug carrier for trimethoprim.

Keywords: adsorption, trimethoprim, montmorillonite KSF, clay, adsorption isotherms

TRİMETHOPRİMİN SULU ÇÖZELTİDEN KİLLER ÜZERİNE ADSORPSİYONU

ÖZ

Trimethoprimin (TMP) montmorillonit KSF üzerine sulu çözeltiden adsorpsiyonu kesikli sistemde sıcaklık, iyonik şiddet, pH ve denge zamanının bir fonksiyonu olarak çalışıldı. Langmuir, Freundlich ve Dubinin-Radushkevich (DR) adsorpsiyon izotermlerinin lineer formları adsorpsiyon verilerini değerlendirmek için kullanıldı. Langmuir adsorpsiyon izotermi korelasyon katsayılarına (R^2) göre, Freundlich modelinden daha iyi uyum göstermektedir. Langmuir eşitliğini kullanarak, montmorillonit KSF için maksimum adsorpsiyon kapasiteleri (C_m) 29.5°C'de 0.4461 $mmolg^{-1}$, 37.5°C'de 0.1686 $mmolg^{-1}$ ve 45°C'de 0.1400 $mmolg^{-1}$ olarak elde edildi. Freundlich K_f (adsorpsiyon kapasitesi) değerleri ise 0.8241 $mmolg^{-1}$'den 0.2318 $mmolg^{-1}$'e sıcaklık 29.5°C'den 45°C'e artarken düşmektedir. Sonuç olarak, trimethoprimin adsorpsiyonu sıcaklık artışı ile düşmektedir. DR adsorpsiyon izoterminden elde edilen tüm E (sorpsiyon enerjisi) değerleri 8 ile 16 $kJmol^{-1}$ değerleri arasında yer alması trimethoprimin montmorillonit KSF üzerine 29.5; 37.5; 45°C'deki adsorpsiyonlarının iyon değişim mekanizması ile gerçekleştiğini göstermektedir ve enerji değerleri fiziksel adsorpsiyonu simgeleyen 8 $kJmol^{-1}$değerine yakındır. 29.5; 37.5; 45°C'de DR izoterminden elde edilen X_m (adsorpsiyon kapasitesi) değerleri sırasıyla $2.504\ 10^{-3}$, $2.41\ 10^{-3}$, $1.0876\ 10^{-3}$ $molg^{-1}$'dır. Bu değerler adsorpsiyonun sıcaklık artışı ile azaldığını da desteklemektedir.

Sulu çözeltiden ilacın adsorpsiyon ile uzaklaştırılması pH ve iyon şiddetine bağlıdır. Dengede maksimum adsorpsiyon, denge pH'ına karşı KSF tarafından adsorplanan trimethoprim miktarını (C_s $mmolg^{-1}$) grafiğe geçirilerek pH=5.04'de gözlenmiştir. Trimethoprimin farklı iyon şiddetlerinde montmorillonite KSF üzerine adsorpsiyonu protonlanmış trimethoprim ile ortamdaki Na^+ iyonlarının negatif yüklü kil yüzeyine olan yarışı nedeniyle ortamın iyon şiddeti arttıkça adsorpsiyonun düştüğünü göstermektedir.

Adsorpsiyon mekanizmasını bulmak için sahte-birinci-mertebeden tepkime kinetiğini, sahte- ikinci-mertebeden tepkime kinetiğini ve intraparticle difüzyon modelini içeren birkaç kinetik model uygulanmıştır. Adsorpsiyon sistemi korelasyon katsayılarını dikkate alarak sahte- ikinci-mertebeden tepkime kinetiğine uymaktadır ve intraparticle difüzyon modeli hızı kontrol eden tek basamak değildir.

Termodinamik parametreleri; $\Delta H°$, $\Delta S°$ ve $\Delta G°$, hesaplanmış olup bu parametreler gerçekleşen adsorpsiyonun ısıveren, tercihli ve kendiliğinden yürüyen olduğunu göstermektedir. Aktivasyon enerjisi (E_a), 5-40 $kJmol^{-1}$ arasında yer alması fiziksel adsorpsiyonun gerçekleştiğini göstermektedir. Tüm bunlardan, montmorillonit KSF atık sulardan trimethoprimin uzaklaştırılmasında kullanabileceği gibi trimethoprim için iyi bir ilaç taşıyıcı olabileceği anlaşılmaktadır.

Anahtar sözcükler : adsorpsiyon, trimethoprim, kil, montmorillonit KSF, adsorpsiyon izotermleri

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CHAPTER ONE
INTRODUCTION

1. The Adsorption – Desorption Process

1.1 Introduction to Adsorption Phenomena

The use of solids for removing substances from either gaseous or liquid solutions has been widely used since biblical times. This process, known as *adsorption,* involves nothing more than the preferential partitioning of substances from the gaseous or liquid phase onto the surface of a solid substrate. (Marczewski, 2002). Simply adsorption is defined as the accumulation of matter at the solid-liquid interface (Rytwo, 2004). From the early days of using bone char for decolorization of sugar solutions and other foods, to the later implementation of activated carbon for removing nerve gases from the battlefield, to today's thousands of applications, the adsorption phenomenon has become a useful tool for purification and separation (Marczewski, 2002).

Adsorption phenomena are operative in most natural physical, biological, and chemical system, and adsorption operations employing solids such as activated carbon and synthetic resins are used widely in industrial applications and for purification of waters and wastewaters. (Marczewski, 2002).

The interface of two different phases is always anisotropic. That is, in the interface the molecular interactions in one side differ from interactions in the other side. If the molecules in a phase are mobile (e.g., gas – solid or liquid – solid interfaces), then these different molecular interactions cause a concentration difference between the interface and bulk phase of mobile molecules. This type of change in concentration taking place in the interface is called *adsorption*. This is the reason why the interface is often referred to as the adsorption space or adsorbed phase. If the mobile molecules can penetrate into the bulk of the other phase, then this process is called *absorption*. It is sometimes

difficult or impossible to distinguish between adsorption and absorption; it is then convenient to use the wider term *sorption*. The name of the phase with localized (non-mobile) molecules is the *adsorbent*, and the mobile molecules bound on the adsorbent surface called *adsorbate*. The phase with mobile molecules before the adsorption, i.e., the phase that is capable of being adsorbed is named adsorptive. So the whole process of adsorption can be expressed with the following simple and symbolic relationship (Adamczyk, 2002).

Adsorbent + Adsorptive ⟶ Adsorbate

(Toth, 2002).

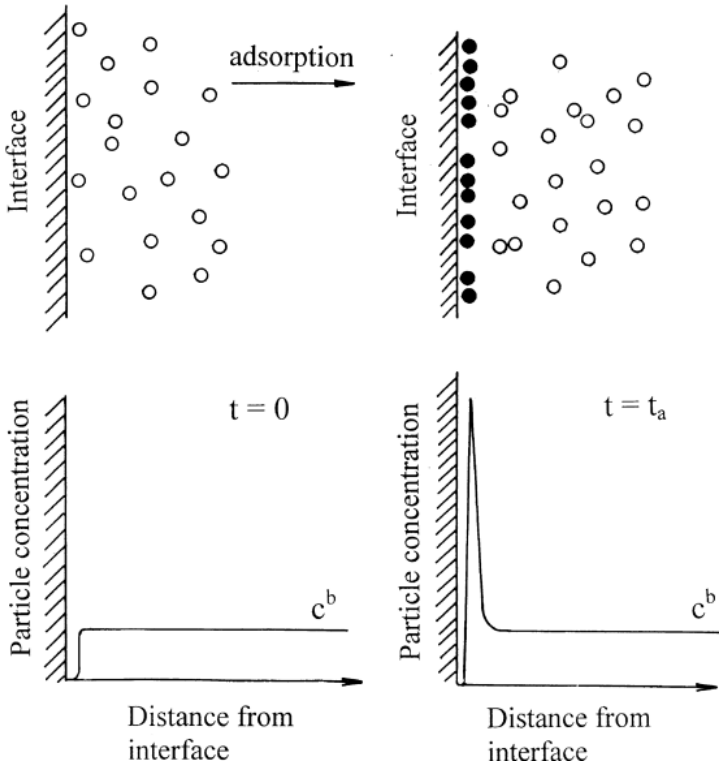


Figure 1.1 Schematic representation of particle adsorption at solid / liquid interfaces.

The solid adsorbents are often characterized by their specific surface area (a_s) and pore size distribution. The value of as refers to unit mass (m) of adsorbent:

$$a_S = \frac{A_s}{m}$$

the pore size distribution provides information on the size and amount of pores present in the solid adsorbent: Macropores are pores with widths exceeding about 50 nm. Mesopores are pores widths between 2 nm and 50 nm. Micropores are pores with widths not exceeding about 2 nm (Toth, 2002).

A large specific surface area is preferable for providing large adsorption capacity, but the creation of a large internal surface area in a limited volume inevitably gives rise to large numbers of small sized pores between adsorption surfaces. The size of the micropores determines the accessibility of adsorbate molecules to the internal adsorption surface, so the pore size of the micropores is another important property for characterizing adsorptivity of adsorbents. Especially materials such as zeolite and carbon molecular sieves can be specifically engineered with precise pore size distributions and hence turned for a particular separation (Marczewski, 2002).

Surface polarity corresponds to affinity with polar substances such as water or alcohols. Polar adsorbents are thus called “hydrophilic” and aluminosilicates such as zeolites, porous alumina, silica gel or silica-alumina are examples of adsorbents of this type. On the other hand, nonpolar adsorbents are generally “hydrophobic”. Carbonaceous adsorbents, polymer adsorbents and silicate are typical nonpolar adsorbents. These adsorbents have more affinity with oil or hydrocarbons than water (Marczewski, 2002).

The average thickness of the adsorbate is often expressed with names mono- and multilayer adsorption. In monolayer adsorption, all the adsorbed molecules are in

contact with the surface of the adsorbent. In the multilayer adsorption, the adsorption space accommodates more than one layer or molecules so that not all adsorbed molecules are in direct contact with the molecules of the adsorbent. (Toth, 2002).

Coverage is a measure of the extent of adsorption of a species onto a surface. Usually denoted by the lower case Greek "theta", q (Gereli, 2005).

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) (Gereli,G., 2005).

1.2 Adsorption Processes

There is two type of adsorption, the first type is known as physisorption (physical adsorption) and the second one is called as chemisorption (chemical adsorption).

Adsorption in which the forces involved are intermolecular forces (van der Waals forces) of the same kind as those responsible for the imperfection of real gases and the condensation vapors, and which do not involve a significant change in the electronic orbital patterns of the species involved. The term van der Waals adsorption is synonymous with physical adsorption (IUPAC Compendium of Chemical Terminology 2nd Edition, 1997).

The only bonding is by weak van der Waals – type forces. There is no significant redistribution of electron density in either the molecule or at the substrate surface.

A chemical bond, involving substantial rearrangement of electron density, is formed between the adsorbate and substrate. The nature of this bond may lie anywhere between the extremes of virtually complete ionic at complete covalent character. This is called as chemical adsorption (Blatt, 1980, Hillier, 1995, & Velde, 1995).

Table 1.1 Typical characteristics of adsorption process

Properties	Chemisorption	Physisorption
Binding force	Due to chemical forces or bonding, thus this process is also called as activated adsorption.	Due to physical force of attraction, thus this process is also called as Van der Waals adsorption.
Saturation uptake	Single layer phenomena	Multilayer phenomena
Activation energy	May be involved.	No activation energy involved.
Temperature range (over which adsorption occurs)	Adsorption can take place even at higher temperatures. When temperature increases adsorption increases.	Adsorption is appreciable at lower temperature below boiling of adsorbate. When temperature increases adsorption decreases
Nature of adsorption	Often dissociative may be irreversible	Non- dissociative. Reversible
Crystallographic specificity	Marked variation between crystal planes	Virtually independent of surface atomic geometry
Heat of adsorption	50-100 kCal/mole	1 kCal/mole
Kinetics of adsorption	Very variable-often an activated process.	Fast- since it is a non–activated process

The problem of distinguishing between chemisorption and physisorption is basically the same as that of distinguishing between chemical and physical interaction in general.

Changes in the electronic state may be detectable by suitable means (e.g. UV, infrared or microwave spectroscopy, electrical conductivity, magnetic susceptibility).

1.3 Factors Influencing Adsorption

1.3.1 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.

1.3.2 Nature of the Adsorbate

1.3.2.1 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).

On the other hand, 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).

1.3.2.2 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.

1.3.2.3 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, Greneche, tisserand, & Charlet, 2004; Sposito, 1981; Sposito, 1984).

1.3.2.4 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.

1.3.2.5 Experimental Conditions

Temperature (Adsorption reaction are normally exothermic, thus the extent of adsorption generally increases with decreasing temperature), air flow velocity and relative humidity (Gereli, 2005).

1.4 Adsorption Isotherms

An adsorption isotherm for a single gaseous adsorptive on a solid is the function which relates at constant temperature the amount of substance adsorbed at equilibrium to the pressure (concentration) of the adsorptive in the gas phase (IUPAC Compendium of Chemical Terminology 2nd Edition, 1997).

The successful representation of the dynamic adsorptive separation of the solute from solution onto an adsorbent depends upon a good description of the equilibrium separation between the two phases. Adsorption equilibrium is established when the

amount of solute being adsorbed onto adsorbent is equal to the amount being desorbed. At this point, the equilibrium solution concentrations remain constant. By plotting solid phase concentration against liquid phase concentration graphically, it is possible to depict the equilibrium adsorption isotherm. There are many theories relating to adsorption equilibrium.

1.4.1 Langmuir Isotherm

The Langmuir isotherm theory assumes monolayer coverage of adsorbate over a homogenous adsorbent surface (Langmuir, 1918). Langmuir isotherm 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:

1. The relative stability of the adsorbed and gas phase species involved
2. The temperature of the system (both the gas and surface)
3. 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-θ)

[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.

Graphically, a plateau characterizes the Langmuir isotherm. Therefore, at equilibrium, a saturation point is reached where no further adsorption can occur. Sorption is assumed to take place at specific homogeneous sites within the adsorbent. Once a molecule occupies a site, no further adsorption can take place at that site. In Eq. (1), K_L and a_L are the Langmuir isotherm constants; C_e and C_s are the liquid phase concentration and solid phase concentration of adsorbate at equilibrium.

$$C_s = \frac{K_L}{1 + a_L C_e} C_e \tag{1}$$

The Langmuir constants, K_L and a_L are evaluated through linearization of Eq. (1):

$$\frac{C_e}{C_s} = \frac{1}{K_L} + \frac{a_L}{K_L} C_e \tag{2}$$

Hence by plotting C_e / C_s against C_e it is possible to obtain the value of K_L from the intercept which is $(1/K_L)$ and the value of a_L from the slope, which is (a_L/K_L). The theoretical monolayer capacity is C_m and is numerically equal to (K_L/a_L). So Eq. (2) is rearranged as the below.

$$\frac{C_e}{C_s} = \frac{1}{C_m\, a_L} + \frac{C_e}{C_m} \tag{3}$$

The Langmuir equation is applicable to homogeneous sorption where the sorption of each molecule has equal sorption activation energy. The equation is thermodynamically

consistent and follows Henry's Law at low concentrations. As C_e becomes lower, $a_L C_e$ is much less than unity and $C_s = K_L C_e$, that is, analogous to Henry's Law (Allen, Gan, Matthews, & Johnson, 2003).

To determine if the adsorption process is favorable or unfavorable, for the Langmuir type adsorption process, the isotherm shape can be classified by a term 'R_L', a dimensionless constant separation factor, which is defined as below (Arslanoğlu, Kar, & Arslan, 2005).

$$R_L = 1/[\,1 + a_L A_0] \quad (4)$$

where R_L is a dimensionless separation factor. A_0 is initial absorbance and a_L Langmuir constant.

The shapes of the isotherms for $0 < R_L < 1$, $R_L > 1$, $R_L = 1$ and $R_L = 0$ are favorable, unfavorable, linear and irreversible, respectively (Weber, & Chakkravorti, 1974).

1.4.2 Freundlich isotherm

The Empirical Freundlich expression (Eq. (5)) is an exponential equation and therefore, assumes that as the adsorbate concentration increases so too does the concentration of adsorbate on the adsorbent surface. Theoretically, using this expression, an infinite amount of adsorption can occur (Freundlich, 1906).

Freundlich equation is based on a monolayer adsorption by the adsorbent with a heterogeneous energy distribution of active sites (Aksu & Kabasakal, 2004)

$$C_s = K_f C_e^{\,nf} \quad (5)$$

In this equation K_f and n_f are the Freundlich constants characteristic on the system. K_f and n_f are indicators of adsorption capacity and heterogeneity factor, respectively.

The Freundlich equation aggress well with the Langmuir expression, it does not reduce to the linear isotherm (Henry's Law) at low surface coverage and provides no information on the monolayer adsorption capacity (Allen et. al, 2003).

Both these theories suffer from the disadvantage that equilibrium data over a wide concentration range cannot be fitted with a single set of constants (McKay, Bino, & Altemeni, 1980).

To determine the constants K_f and n_f , the linear form of the equation shown below may be used to produce a graph of $\ln C_s$ against $\ln C_e$ (Allen et. al, 2003).

$$\ln C_s = \ln K_f + n_f \ln C_e \quad (6)$$

1.4.3 Dubinin – Radushkevich (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 following linear form of DR isotherm:

$$\ln C_{sorb} = \ln X_m - \beta\varepsilon^2 \quad (7)$$

where C_{sorb} is the amount of ions sorbed onto the adsorbent ($molg^{-1}$), X_m represents DR monolayer capacity of the sorbent ($molg^{-1}$), β a constant related to sorption energy (mol^2/kJ^2) and ε Polanyi sorption potential, the amount of energy required to pull a sorbed molecule from its sorption site to infinity which is equal to:

$$\varepsilon = RT \ln (1+1/C_e) \quad (8)$$

where R is the gas constant in $kJmol^{-1}K^{-1}$; T is the temperature in Kelvin and C_e is the equilibrium concentration in solution ($mol\ dm^{-3}$). The Polanyi adsorption theory postulates fixed volume of sorption site close to sorbent surface and existence of

sorption potential over these sites. The sorption potential is related to an excess of sorption energy over the condensation energy and is independent of temperature. The plot of $\ln C_{sorb}$ versus ε^2 follows linearity. The value of X_m is determined from the intercept and the value of β is derived from the slope. The sorption energy, E for ions onto adsorbent calculated using the expression:

$$E = -(2\beta)^{-1/2} \quad (9)$$

is the range of 8-16 $kJmol^{-1}$ designated for ion exchange mechanism (Malik, Hasany, & Subhani, 2005). If the value of E is smaller than 8 $kJmol^{-1}$, this shows physical adsorption due to weak van der Waals forces (Singh & Pant, 2004).

1.5 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.

$$R_{ads} = k\, C^{x} \quad (10)$$

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:

$$R_{ads} = AC^{x} e^{-E_a / RT} \quad (11)$$

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

Ea 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:

$$R = [f(\theta)\,P/(2\pi mkT)^{1/2}]\exp(-E_a/RT) \qquad (12)$$

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, Kirbaslar, & Kizilcikli, 2003).

Intraparticle diffusion is evaluated using the following equation:

$$q_t = k_{int}\, t^{1/2} + C \qquad (13)$$

where

k_{int} = an intraparticle diffusion rate constant (mg/gmin.$^{1/2}$).
q_t = amount adsorbed of solute per unit weight of adsorbent at any time (mg/g).
C = intercept (Acemioğlu, 2004).

1.6 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 (Gereli, 2005).

1.7 Adsorption of Drugs

The drug adsorption process and its influence on the drug product properties are importance for the application of the new drug products. To identify the adsorption mechanism, firstly, adsorption isotherms will be presented and treated to calculate the affinity constant and the maximal amount of drug adsorbed.

Indeed, modern active ingredients are rarely administered alone but are combined most often with inert substances called excipients. Drug dosage forms may vary from simple solutions to very complex delivery systems. The complexity of the dosage form is not intentional but is determined by the properties and the quality of the final dosage form that are required to be achieved. For example, excipients are added to the drug substance to improve its flow ability, compressibility, solubility, and stability; to mask an unpleasant taste; to aid in disintegration after administration; or to act as a sustained-release system or a drug carrier for drug targeting. The interaction of the excipients with the drug substance will therefore influence the pharmacodynamic properties and the therapeutic efficacy of the drug substance. Indeed, although drugs differ in their chemical structure and therapeutic application, there are some general principles that are shared by all drug products and that govern the efficacy of a drug.

In order for a drug to act, it must be absorbed (i.e., it must reach the bloodstream), be transported to the appropriate organ or tissue, and be bound to its specific receptor. This process requires that the drug be transported from the site of administration to the site of action in a diluted and uncombined form or in combination with a specific compound in connection with the energy-yielding membrane transport process. It becomes therefore obvious that, in both cases, the adsorption of a drug to an excipient will dramatically influence the above-mentioned processes. In addition, it may strongly affect the accuracy of analytical testing of the drug product (content, dissolution time, and so on). Care must therefore be taken in the selection of the excipients, and characterization of

these interactions must be performed to ensure that the formulation will give the required bioavailability and therapeutic efficacy. Moreover, this careful study is a prerequisite to achieve batch uniformity and reproducibility, which are some of the qualities expected from modern pharmaceuticals.

The potential source of a drug substance-excipient interaction must be carefully investigated during the early phase of the development of a new drug product. These possible interactions have to be considered as well as other physicochemical properties of the drug substance such as crystal size and shape, polymorphism, solubility and stability profiles, partitioning effect, and dissolution behavior. Considering now the history of a drug from its synthesis to its administration, critical steps in which drug adsorption may occur can be identified and seem to be similar for solid and liquid dosage forms. Finally, the drug substance may be intentionally adsorbed onto a drug carrier to form either a sustained-release or a targeting system.

An acid with a small pK_a (i.e., about 1.0) placed in an environment with a pH=7 would be completely ionized and would be classified as a strong acid. In contrast, the extent of ionization decreases when a weak base passes from the strongly acidic environment of the stomach into the less acidic intestinal lumen. The concentration of unionized species for a base with a pK_a 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.

The degree of adsorption of the drugs can be explained by the mechanism involved. Different types of bonds are involved in the formation of complexes with organic compounds: ionic bounds with cations, ion-dipole bonds involving interlayer cations, hydrogen bonds, van der Waals forces, π bonds and, in some cases, covalent bonds.

Porubcan, Watters, & McFarland, 1978 have demonstrated the ‘physical’ adsorption of digoxin: at physiological pH, this interaction is sensitive to dilution and independent of pH. Similarly, with anionic compounds, there is a surface interaction involving physical mechanisms. In neutral medium the appearance of a negative charge can lead to detrimental interactions, through electrostatic repulsion between drugs and the negatively charged surface of the layers. In the case of cationic and amphoteric compounds, a twin mechanism has been forwarded by Porubcan et al. (1978), involving ‘physical’ adsorption common to all organic compounds, and a chemical interaction (cation exchange). Cation exchange is pH-dependent. In acid medium, the drugs were mainly present in ionized form (positively charged) and were strongly adsorbed. The nonionized form became predominant and the drug was released when the pH increased, (Gereli, 2005).

In between pH=3 and pH=7, the composition of clay is not modified and exchanges are indepented of pH (Gereli, 2005).

CHAPTER TWO
CLAYS

2. Introduction to Clays

2.1 Definition of Clay

We share the surface of the earth with sediments, sedimentary rocks, and soils and our lives benefit greatly from the existence of these fine–grained materials. The clay minerals from something like one third of the sediments (clay rich muds and silts), sedimentary rocks (principally shale) and soils (Giese, & Oss, 2002).

The most of us the word "clay" usually means a fine – grained material which when mixed with water becomes extremely plastic and mouldable (Wilson, 1987). By plasticity is meant the property of the moistened material to be deformed shape being retained when the deforming pressure is removed (Grim, 1978). The plasticity is a result of complex interactions between the water and the surfaces of the constituents of clay principally the clay minerals (Giese et. al, 2002).

The term "clay" is often (e.g. in soil mechanics) used in the restricted sense of a particle size classification term for the natural constituents of soils and sediments. In this usage, clays describe a chemically very heterogeneous and structurally complex assemblage of colloidal particles, having a diameter less than 0.002 mm (2 microns) (Giese et. al, 2002).

Alkalies such as sodium, lithium and potassium and alkaline earths such as magnesium, calcium and barium are often present in the molecular structure of clays and have a significant effect in the physical and chemical properties.

Clays occurring in nature rarely comprise pure, single clay minerals. They usually contain a variety of non- clay impurities such as quartz, calcite, mica, feldspar and pyrite, among others.

The utility of clay minerals is strongly linked to their interfacial properties, (especially with water) (Giese et. al, 2002). For that reason clays have a much wider impact on our lives than many of us commonly realize (Wilson, 1987).

2.2 Classification of The Clay Minerals

"Clay minerals" refers collectively to the group of fine- grained hydrous silicates of aluminum (and also to some extent of magnesium or iron). When examined under the scanning electron microscope, these minerals are seen to consist of readily identifiable particles, which can have a variety of geometric shapes. Despite this variety of morphology, clays are closely interrelated in terms of their basic crystal structures, and also in the characteristic physical and chemical properties resulting from their crystal chemistry (Wilson, 1987).

The Grim's classification of the clay minerals which based distinctions on the shape of the clay minerals and the expandable or nonexpendable character of the 2:1 and 1:1 layer silicates is given below.

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 (Grim, & Güven, 1978)

2.3 Structure of The Clay Minerals

Most clay minerals involve two basic types of units in their atomic structure. The manner in which these units are combined and the type of exchangeable atoms that are present will play a very significant role in the type of clay mineral that forms.

The first unit is built of silica tetrahorns. The tetrahedral sheet is composed of silicon bounded to four oxygen atoms. Each unit consists of a central four-coordinated atom (e.g. Si) surrounded by four oxygen atoms that, in turn, are linked with other nearby atoms (e.g. Si), thereby serving as inter-unit linkages to hold the sheet together (Juma, 1998).

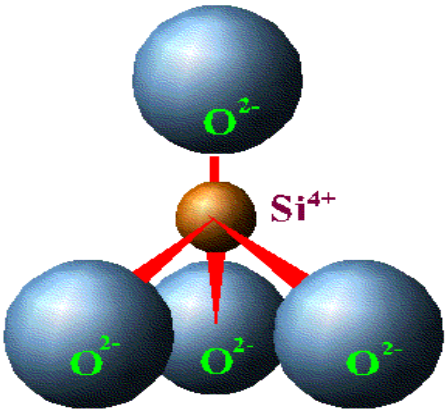


Figure 2.1 Silica tetrahedral units

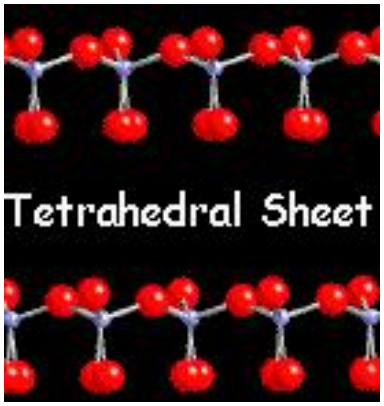


Figure 2.2 Tetrahedral Sheet

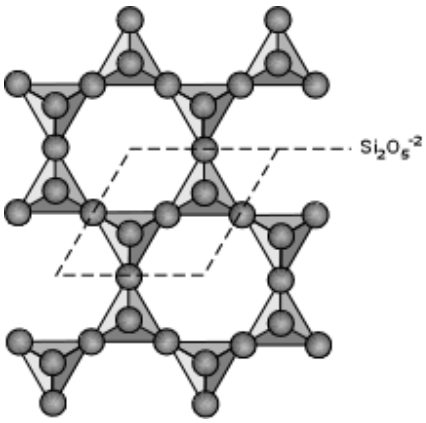


Figure 2.3 A basic structural unit of $Si_2O_5^{2-}$

The second unit consist of octahedrals. An octahedral sheet, consisting of two layers of oxygen atoms or hydroxyl groups, between which aluminium, magnesium iron are bonded in six – fold coordination. If the layer contains mainly trivalent aluminium ions which occupy two thirds of the available octahedral interstices, this is known as a gibbsite type or dioctahedral layer. Conversely, if the layer contains mainly divalent

magnesium ions, this will occupy all of the octahedral sites, and the layer is called a brucite – like or trioctahedral layer (Wilson, 1987).

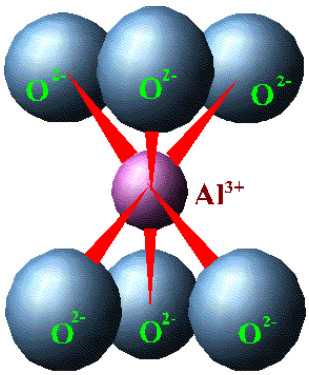


Figure 2.4 Octahedral unit

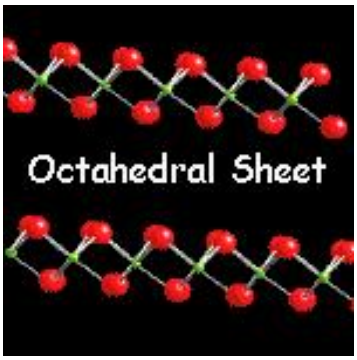


Figure 2.5 Octahedral sheet

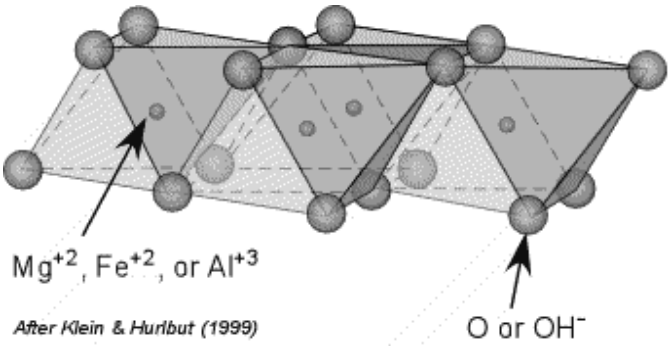


Figure 2.6 Octahedral sheet

The structural units of clays therefore consist of either alternating tetrahedral (T) and octahedral sheets (O) (OT or 1:1 structure), as in the kaolinite group of clay minerals; tetrahedral sheets (TOT or 2:1 structure), as in illite and the smectite clay minerals, of which the most common member is montmorillonite; or an arrangement in which the layer TOT units alternate with a brucite layer (2:1:1 structure) as in chlorite. The basic structural arrangements of the more common clay minerals are illustrated schematically in figure 2.7 (Wilson, 1987).

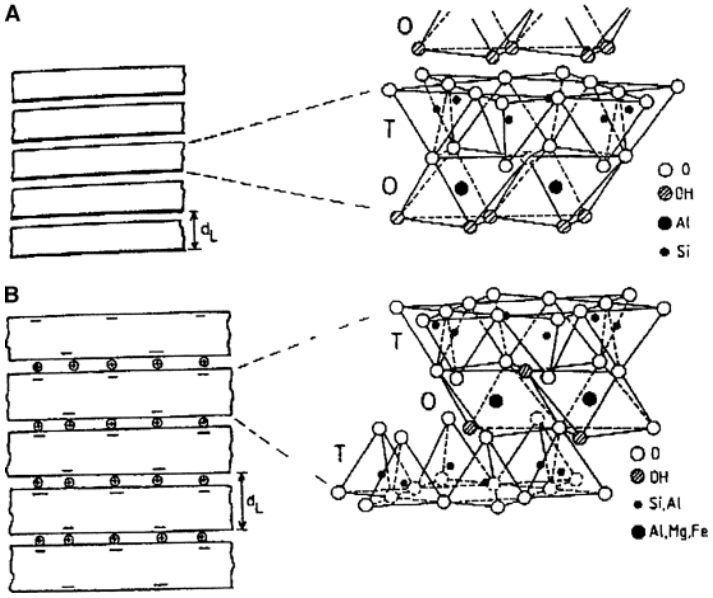


Figure 2.7 Layer structures of two-layer minerals (1:1 clay minerals) (A) and of three-layer minerals (2:1 clay minerals) (B); T, O=tetraeder and octaeder layers, respectively; d_L=layer distance.

Table 2.1 Clay minerals and their net charge

Group	Layer Type	Net Negative Charge ($cmolkg^{-1}$)	Surface Area (m^2/g)	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

Kaolinites are composed of one tetrahedral sheet linked to an octahedral sheet, therefore they are classified as 1: 1 type layer silicates (White, 1987). Kaolinite is non-expanding clay mineral and different layer are held together by hydrogen bonding which occurs between the plane of basal oxygen atoms within a tetrahedral sheet and the plane of hydroxyl group within the octahedral layer. The formula for kaolinite is $(Si_4)^{IV}(Al_4)^{VI}O_{10}(OH)_8$ which indicates that there is no substitution of Si^{4+} with Al^{3+} in the tetrahedral layer and no substitution of Al^{3+} with Mg^{2+}, Zn^{2+}, Fe^{2+}, Ca^{2+}, Na^{+}, or K^{+} in the octahedral layer. In order to calculate the net charge of kaolinite one has to remember that the charge of Si is +4, Al is +3, oxygen is -2 and OH is -1. Thus net layer charge of kaolinite is:

= [4(+4)] + [4(+3)] + [10(-2)] + [8(-1)]
= 28 - 28
= 0

In nature, kaolinite has a small net negative change because the clay crystals have broken edges.

Diagrammatic Representation of Kaolinite

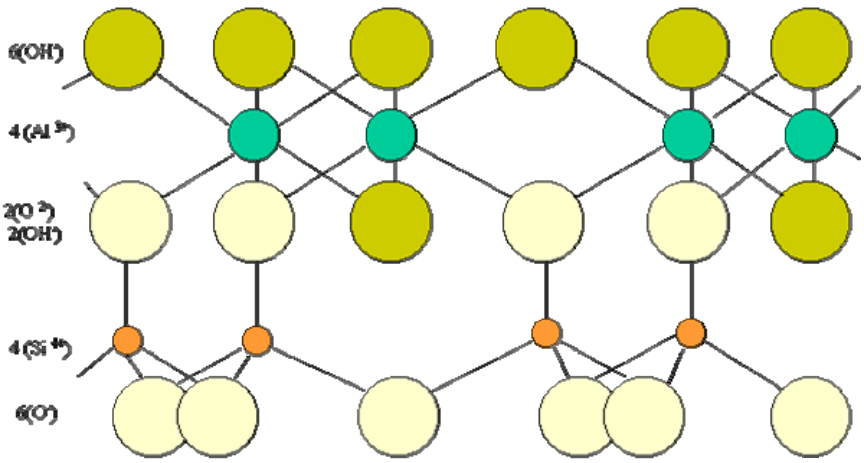


Figure 2.8 The structure of kaolinite

Smectite minerals have three layers with the aluminum atoms lying between two layers of silicon atoms in a 2:1 structure, sharing the valencies of their oxygen atoms (Juma, 1998).

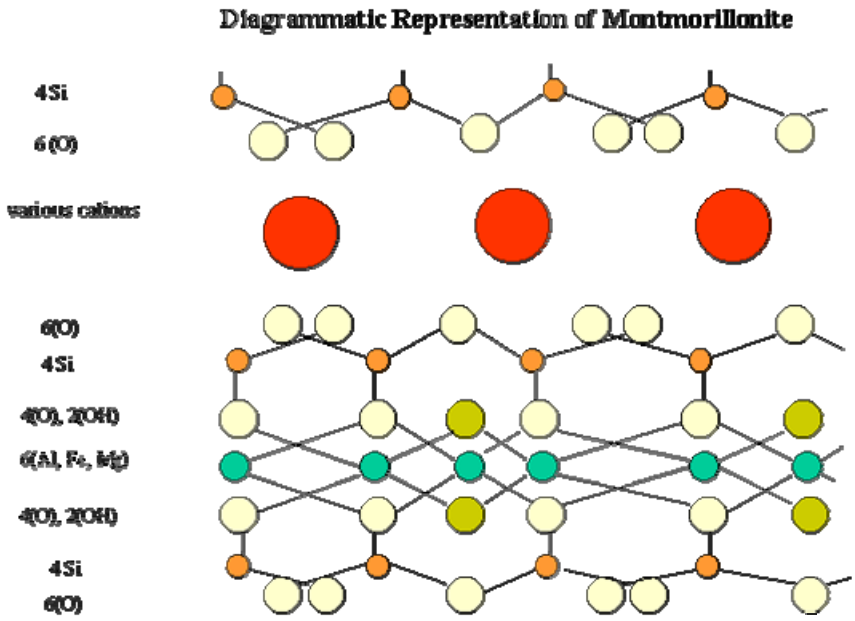


Figure 2.9 Structure of montmorillonite (smectite) (Juma, 1998).

This group is composed of several minerals including pyrophyllite, talc, vermiculite, sauconite, saponite, nontronite and montmorillonite. They differ mostly in chemical content. Montmorillonite, a type of smectite is expanding clay mineral and different layers are held together by bonding between divalent cations and water with basal oxygen atoms of the tetrahedral sheets. The formula for montmorillonite is $(Si_{7.8}Al_{0.2})(Al_{3.4}Mg_{0.6})O_{20}(OH)_4$. The formula indicates that there is substitution for Si^{4+} by Al^{3+} in the tetrahedral layer and for Al^{3+} by Mg^{2+} in octahedral layer (Juma, 1998).

These substitutions lead to net negative charges on the clay structure which must be satisfied by the presence of charge-balancing cations somewhere else in the structure. The interlayer is hydrated, which allows cations to move freely in and out of the

structure. Because the interlayer is open and hydrated, cations may be present within the interlayer to balance negative charges on the sheets themselves. These cations between the layers are part of the cation exchange capacity of the soil. Smectites will have a CEC of around 80 to 150 meq/100 g. (Juma, 1998). Also, the amount of water present in the interlayer of montmorillonite results in swelling under wet conditions and shrinking in dry conditions (Juma, 1998).

In contrast to montmorillonite, illite is a 2:1 clay mineral with potassium (K) in the interlayer that restricts shrinking and swelling (Juma, 1998).

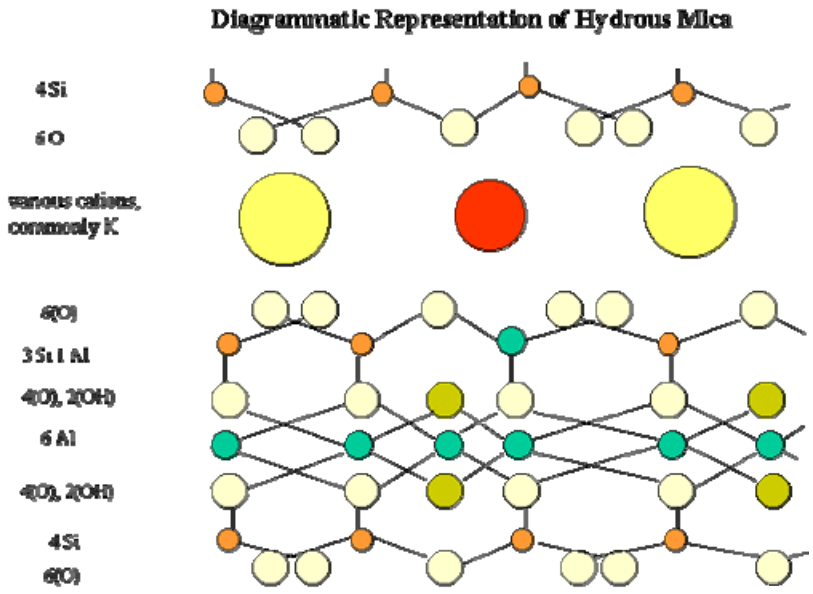


Figure 2.10 Structure of mica, illite (Juma, 1998).

The general formula for the illites is:

$K_yAl_4(Si_{8-y},Al_y)O_{20}(OH)_4$

usually with $1 < y < 1.5$, but always with $y < 2$ (Stephen, 2001). Potassium ions bind to the oxygen plane of the basal tetrahedral layers of adjacent units (Juma, 1998).

Because of possible charge imbalance, Ca and Mg can also sometimes substitute for K. The K, Ca, or Mg interlayer cations prevent the entrance of H_2O into the structure. Thus, the illite clays are non-expanding clays (Stephen, 2001).

Vermuculites have a 2: 1 structure of primary mica minerals. Vermiculites contain either Al^{3+} or Mg^{2+} and Fe^{2+} as normal octahedral ions, and tetrahedral sheets in which Al^{3+} occurs as a substituted ion in place of some of the Si^{4+}. Vermiculite differs from the micas in that it contains hydrated cations rather than unhydrated K^{+} in the interlayer space. The weak bonding afforded by these ions allows vermiculite to expand on wetting. Expansion is less than in montmorillonite, however. Unlike montmorillonite and kaolonite, vermiculite does not form by crystallization from solution, but instead it is formed by alteration, or the selective replacement of ions in a structure without destroying the structure (e.g. micas are altered to vermiculites) (White, 1987).

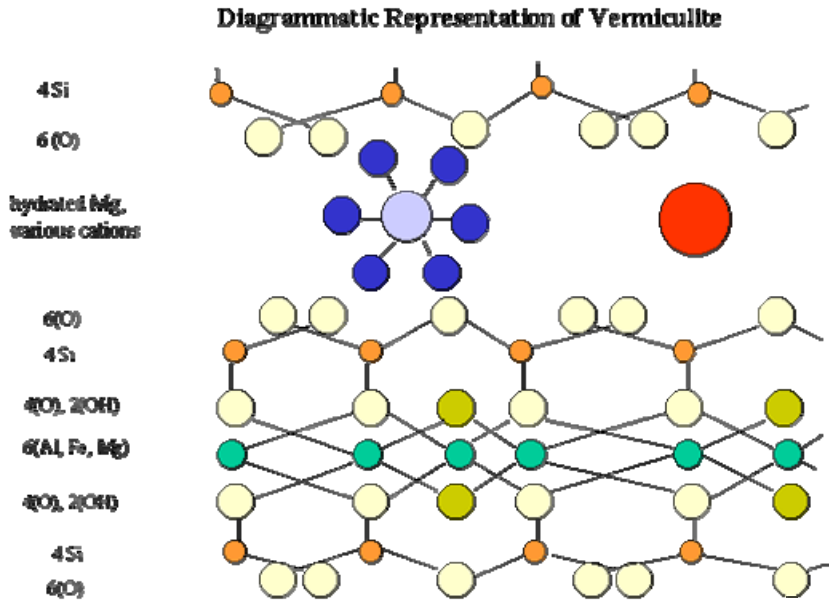


Figure 2.11 General structure of Vermiculite

Chlorites are composed a group which embraces a range of minerals that have certain outstanding characteristics in common. All have a basic 2: 1 layer structure, and they are

non-expanding. Chlorites differ from other 2: 1 layer minerals in one unique respect, i.e., they contain a stable, positively charged octahedral sheet rather than adsorbed cations in the interlayer space. The octahedral sheet consists of two layers of OH^- ions that enclose either Mg^{2+}, Fe^{2+}, or Al^{3+} as the central octahedral cations and leads to a positive charge of the sheet. By virtue of its positive charge, the interlayer sheet neutralizes the negative charge of the 2: 1 sheets. Because chlorite contains two octahedral sheets, it is called a 2: 1: 1 layer mineral. Sometimes, octahedral materials in chlorite neither totally fill the interlayer space between sheets nor completely neutralize the negative charge of the sheets. This unsatisfied charge is neutralized by various cations adsorbed to the particle surfaces from the solution phase. The thickness of the chlorite layer is 1.4 nm (White, 1987).

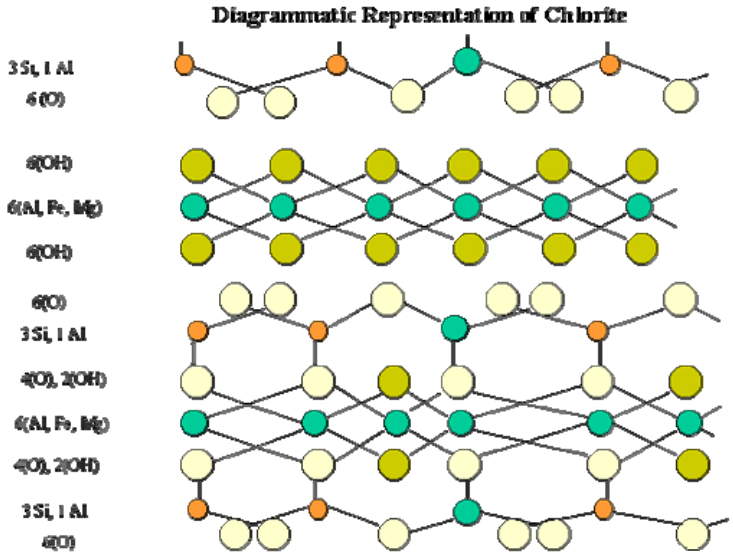


Figure 2.12 General structure Chlorite (White, 1987).

Allophanes are poorly categorized substances, which are sometimes regarded as clay minerals and at other times considered among hydroxides. It is for sure that they are poorly structured, i.e., amorphous in character and they consist of silica and hydrous oxides. They are abundant in soils derived from volcanic ash deposits. The structural

formula of Allophane can be written as $Si_3Al_4O_{12}*nH_2O$. Another similar silicate is Imogolite which is $Si_2Al_4O_{10}*5H_2O$ (White, 1987).

2. 4 Formation and Occurrence of Clays

Clays and clay minerals occur under a fairly limited range of geologic conditions. (Juma, 1998) The rock cycle or sedimentary cycle is shown in simplified form in figure 2.13. particles formed in the weathering environment may be transported by erosion and the action of rivers to the sedimentary environment. Upon burial and consequent increases in pressure and temperature, sediments undergo a complex series of chemical and biological changes, referred to as diagenesis. To some extent, similar reactions can occur at shallower depths in hydrothermal settings. At a later stage, very deep burial, or the intrusion of igneous rocks, causes metamorphic alteration of sedimentary rocks, or eventual melting to give igneous rocks.

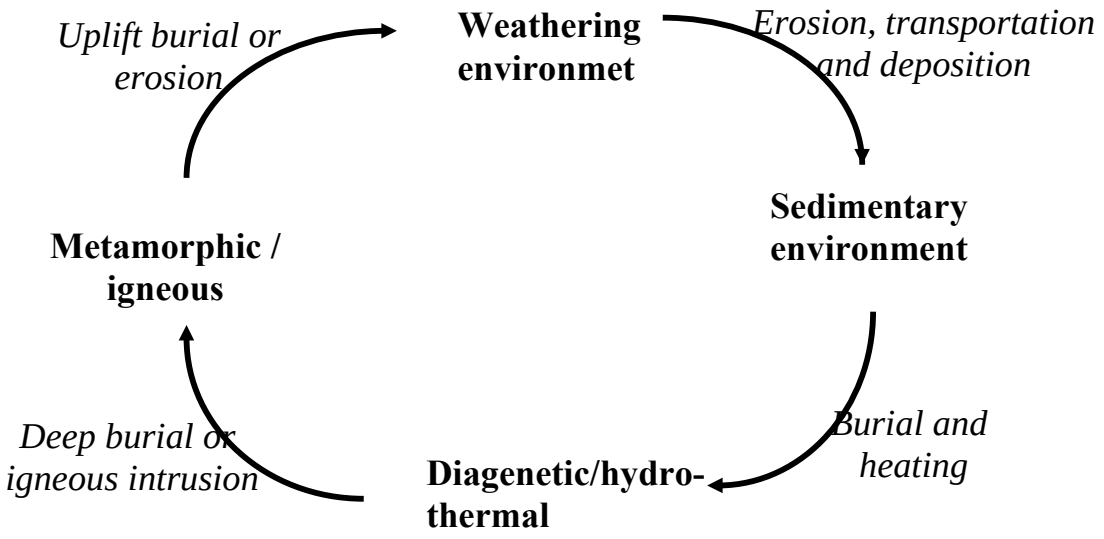


Figure 2.13 Simplified illustration of rock cycle (Srodon, & Eberl, 1984).

After subsequent uplift to the surface, the entire process begins again. It is obvious that clays which formed in one environment can be "inherited" by another environment, so that their present location does not imply local formation (Wilson, 1987).

All of the environments may cause the formation of clay minerals from preexisting minerals. Extensive alteration of rocks to clay minerals can produce relatively pure clay deposits that are of economic interest. For example, bentonites (primarily montmorillonite) used for drilling muds and clays used in ceramics.

2.5 Uses of Clay

Clays play a very important role in many industries. Their use depends upon their physical and chemical properties. Their important uses are listed as below;

In the paper industry as a coating and filling agent,
In foundries, as binding agent in the preparation of moulding sands for metallurgical casting.
In oil well drilling, as constituent of drilling fluids, either in the form of Na-Montmorillonite (aqueous fluids) or as an organophilic clay (in water - in- oil emulsion –based fluids),
In civil engineering, to hinder the movement of water or chemical wastes; for excavation support; for lubrication of cables or pipes, and as a waterproofing agent,
As a backfill in radioactive waste repositories,
As an adsorbent: in industry for the removal of oil and grease from floors; domestically, in pet litter. It is also used for decolorizing vegetables oils, clarifying wine, and in water filtration and purification,
In the manufacture of bricks, tiles and other building materials,
Organophilic forms of smectites are used in the manufacture of inks cosmetics and polishes; to control the gelling properties of lubricating greases, and to add thioxotropic (Shear thinning) properties to fibreglass resins. (Wilson, 1987),

In pharmacology, as a drug carrier.

2.6 Properties of Clays

2.6.1 Ion Exchange

One of the fundamental properties of clays is the electrical charge on their unit particles which means that clays will sorb cations and / or anions that neutralize the layer charge, but which are exchangeable. This means that they can readily be replaced by other anions or cations when brought into contact with these ions in aqueous solution (Wilson, 1987) except under extremely acidic conditions, the layer charge is predominantly negative, a fact which may be verified by investigating the electrochemical properties of clay. This means that clays tend to sorb cations, and are said to have a certain cation exchange capacity, or CEC, which can expressed as a certain number of chemical equivalents per unit weight of dry clay (normally quoted in milliequivalents per hundred grams). It has been suggested that broken bonds at particle edges may also contribute to exchange capacity. However, there is considerable evidence to suggest that, except under fairly alkaline conditions, the charges due to edge effects are positive, leading to anion rather than cation adsorption at these sites. There are two possible mechanisms for creation of positive edge charges:

(i) Protonation of exposed Al-OH groups or

(ii) The dissolution of some of the clay at pH < 4 followed by edge- adsorption of aluminum ions. Whichever mechanism is dominant, the existence of positive edge charges explains many of the colloidal properties of clay dispersions.

The negatively charged clay surfaces do not have an equal affinity for all cations, but in fact exhibit a selectivity which depends upon such factors as the ionic charge, size and state of hydration of the cations. In general, cation-exchange selectivity increases with ionic radius. Thus, the order of increasing affinity for the alkali-metal ions are Li, Na, K,

Rb, and Cs, and for the alkaline-earth ions Mg, Ca, Sr, Ba. The both series, increasing adsorption selectivity of corresponds with decreasing polarizability and energy of hydration in aqueous solution, i.e. the cations which hold on to their hydration shells most firmly are the least strongly adsorbed by clays. The relative adsorption selectivity of monovalent and bivalent ions varies somewhat with clay type and layer charge. Bivalent ions and polyvalent ions are in general quite strongly adsorbed. Also some monovalent ions, e.g. ammonium or the organic alkylammonium ions, are very strongly adsorbed and permit only limited swelling on account of their large sizes and relatively low hydration energies (Stephen, 2001). Often, the clay mineral has to be modified by ion exchange with organic cations when used as absorbent for a pesticide and drugs (El-Nahhal, Nir, Polubesova, & Rubin, 1999, Bojamueller, Nenemann,& Lagally, 2000).

2.6.2 Cation- Exchange Capacity (CEC)

The CEC is the abbreviation for the cation exchange capacity of the soil. Any element with a positive charge is called a cation and in this case, it refers to the basic cations, calcium (Ca^{2+}), magnesium (Mg^{2+}), potassium (K^{+}) and sodium (Na^{+}) the acidic cations, hydrogen (H^{+}) and aluminium (Al^{3+}). The amount of these positively charged cations a clay can hold is described as the CEC. In other word, 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 (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 2.2

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, Gelsomino, & Gessa, 1995, Draoui, Denoyel, Chgoura, & Rouquerol, 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 (Bergaya, & Lagaly, 2000).

Table 2.2 CEC values of the some samples

Clay Mineral	CEC (milliequivalents 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

2.7 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:

$$n\lambda = 2d \sin \theta \qquad (1)$$

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

The table 2.3 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 (the principal ingredient in anti-freeze), and the last column show the effect if the mineral is heated to 550^{o}C after the Ethylene Glycol treatment.

Table 2.3 d-spacing values for various clay minerals.

d Spacing on {001} for Clay-Type Minerals (Å)			
Mineral	Untreated	Ethylene Glycol	Heated to 550^{o}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 or 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).

CHAPTER THREE
CLAY AND HEALTH

3.1 Clay is Alive

The universe is made up of living and nonliving systems. For example, the plant is a living system and follows the pattern of living, reproducing, and growing, giving witness to the cycle of life and death. On the other hand, rocks fall into the category of nonliving systems. A rock will do only one thing: decompose, or fall apart into simpler and simpler elements. If we were to place a couple of tablespoons of clay in a jar of water and return one million years later, we would find that the clay we would come back to is not the same one we had left behind. It changed to another mineral. For example, under certain conditions volcanic ash will turn to smectite. And smectite, in turn, will change to kaolinite, certain conditions permitting. Thus, the elements are kept in continuous motion, charged by an unseen life force. This is the definition of an active clay mineral. Being active, it changes, grows, and re-configures itself (California Earth Minerals, 2001-2002).

That the clay is alive gives some idea about the uses of clay minerals. In the past few years, due to the increasing success of natural remedies the use of clay material for cosmetic and medical purposes has increased (Mascolo, Summa, & Tateo, 1999).

3.2 Effect of Clay Minerals Upon Human Health

3.2.1 *Historical Use of Clay in Treatment*

The use of minerals for medicinal purposes is almost as old as mankind itself. Minerals have been used for curative ends since Prehistory (Carretero, 2002). They were

used to cure wounds, soothe irritations, as a method of cleansing the skin, etc. The use Nubian earth as an anti-inflammatory or the use of mud materials for mummification of cadavers can be cited as examples. In the Ancient Greek period, mud materials (Lemnas Earth) were used as antiseptic cataplasms to cure skin afflictions, as a cure for snake bites. Cleopatra, Queen of Egypt, used muds from the Dead Sea for cosmetics purposes and Marca Polo describes how in his travels he saw Muslim pilgrims cure fevers by the ingestion of "pink earth". "De Materia Medica" which dates from Roman times, 60BC describes the use of clays, especially for stomach and intestinal ailments. During the Middle Ages Avicena and Averroes in the 9th and 10th Centuries classified and encouraged the use of medicinal muds, and Galeno, Arabic doctor, used clays for the malaria. During the Renaissance Pharmacopoeia appeared. First mineralogical classifications were made. The development of Crystallography and Mineralogy in the 18th and early 19th Centuries was of great importance in increasing the knowledge of the raw mineral materials used in pharmacy and cosmetics (Carretero, 2002). At present, clay minerals are used for many fields as curing agents.

3.2.2 The Use of Clay Mineral in Pharmaceutical Formulations

Silica, talc and other phyllosilicates such as kaolinite, smectites and fibrous clays are among the most widely used minerals in composition of medicines (Viseras, Meeten and Lopez- Galindo, 2001). All clays will adsorb; however, the smectite group is the only one capable of absorption. Most clays sold in the health food industry belong to the smectite category (California Earth Minerals, 2001 – 2003).

Clay minerals used in the composition of medicines can either be used as they are or after divers chemical treatments intended to bring out one particular quality. The special characteristics of the clays make them ideal for use as pharmaceutical excipients, or as

active ingredients, finding application in several OTC pharmaceutical products as a result of their antacid and antidiarrhoeal properties (Viseras, Meeten, & Lopez- Galindo, 2001). The other reason for using clays in composing medicines is that the clay minerals have chemical inertness and low or null toxicity for the patient (Carretero, 2002).

Palygorskite and kaolinite are used as gastrointestinal protector because of their high specific area and sorption capacity. These minerals adhered to the gastric and intestinal mucous membrane protects them and can absorb toxins, bacteria and even viruses. Unfortunately they also eliminate enzymes and other necessary nutritive elements, which make their prolonged use inadvisable (Carretero, 2002).

Laxatives encouraged defecation can act by osmosis, by irritating the small bowel or the colon rectum. Additionally, the clay minerals used, sodium smectites, act by osmosis (Carretero, 2002).

Clay minerals used in the formulation of the antidiarrhoeaics. Most pharmaceutical formulations against diarrhea work by reducing the quantity of liquid that reaches the colon-rectum from the small bowel. In this case, it is advisable that absorbent minerals be used to eliminate the excess water in faces and excess gases in the digestive tract. Also, clay minerals are utilized for protecting skin and cosmetic purposes.

Kaolinite, talc and smectites are substances capable of adhering to the skin forming a film which protects it mechanically against external physical or chemical agents (Carretero, 2002). Because of all these reasons, these clay minerals used for composing powders, creams and ointments to protect the skin. These minerals have capacity to

adsorb dissolve and suspended substances, such as greases, toxins, and even bacteria, and viruses.

The use of palygorskite as a dermatological protector is not advisable and they practically do not appear in any pharmaceutical formulation due to the present existing doubts concerning their possible carcinogenic effect if inhaled, although some author s maintain that these minerals are neither toxic nor dangerous (Carretero, 2002).

Clay minerals are used as active principles in cosmetics, in face masks, due to their high absorbency level of substances such as greases, toxins, etc. Therefore, they are recommended for inflammatory processes such as boils, acne, ulcers, etc. They are also used in creams, powders, emulsions, etc., as antiperspirants and to give the skin opacity, remove shine and cover blemishes. Clay minerals such as kaolinite, smectites, talc and palygorskite are used, although use of the last two is recommended only in liquid preparations (creams, emulsions, etc.) (Carretero, 2002).

Foremost among the uses of clay minerals for health is that the clay minerals are used as excipients. Excipients are used for three purposes in formulation of pharmaceutical products. First one is improving its organoleptic characteristics such as taste, smell and colour, or its physical – chemical properties such as viscosity. The second one is facilitating the pharmaceutical formulation's preparation, and the last one is promoting the pharmaceutical formulation's disintegration when it is orally administered in the form of pills, capsules, etc. (Carretero, 2002).

The clay minerals used as excipients are palygorskite, smectites, kaolinite and talc. These minerals are used as: (a) lubricants to ease the manufacture of pills (talc) , (b)

agents to aid disintegration, due to their ability to increase in volume in the presence of water (smectites), or the dispersion of fibres (palygorskite), which favour the liberation of the drug of the pharmaceutical formulation when it arrives in the stomach, (c) inert bases for cosmetics (palygorskite, kaolinite, smectites, talc), and (d) as emulsifying, polar gel and thickening agents because of their colloidal characteristics (palygorskite, smectites) and to avoid the segregation of the pharmaceutical formulation's components and the formation of a sediment which is difficult to redistribute (Carretero, 2002).

It is important that clay minerals used as excipients effect the active principle of drug. For that reason, the bioavailability study of drug interacted with clay minerals are done. Clay minerals used as excipients can have an influence on two highly important aspects in the drug's bioavailability: its liberation and its stability.

The first aspect is too significant for many studies. The interaction between the drug and its excipient can retard the drug's release and therefore its absorption, lowering its levels in the blood. If we control desorption of the drug, it will give a positive effect upon its therapeutic action of the drugs (amphetamines and antibiotics).

Various uses of clay minerals are discussed but this is not enough to tell all uses. Sepiolite and smectites have the ability to form complexes with organic compounds which absorb ultra-violet radiation thus enabling them to be used in sun screens with protection factors. Also clay minerals effect the degradation of drugs. If a drug which degrades in the presence of protons coincides in the stomach with a clay mineral, it will degrade more rapidly than if the mineral were not there. (Carretero, 2002).

In spas and aesthetic medicine, geotherapy, pelotherapy and paramuds are used due to their absorption/adsorption capacity, their cation exchange capacity, plastic properties, rheology, grain size and cooling index. They are used in spas to treat dermatological diseases and to alleviate the pain of chronic rheumatic inflammations. In

aesthetic medicine, they are mainly used to clean and moisturize the skin and to combat compact lipodystrophies, acne and cellulite (Carretero, 2002).

All of these indicate that clay is alive and take part in our lives as a helper (server).

CHAPTER FOUR
TRIMETHOPRIM

4. Uses of Trimethoprim

4.1 Actions of Trimethoprim

Trimethoprim reversibly inhibits bacterial dihydrofolate reductase (DHFR), an enzyme active in the folate metabolic pathway converting dihydrofolate to tetrahydrofolate. Depending on the experimental conditions the effect may be bactericidal or bacteriostatic.

Trimethoprim binds to plasmodial DHFR but less tightly than to the bacterial enzyme. Its affinity for mammalian DHFR is some 50,000 times less than for the corresponding bacterial enzyme.

The majority of common pathogenic bacteria are sensitive *in vitro* to trimethoprim at concentrations well below those reached in blood, tissue fluids and urine after the administration of recommended doses. These organisms include:

Gram Negative;

Escherichia coli; Haemophilus influenzae*;* Proteus mirabilis*;* Salmonella spp. (including S. typhi and S. paratyphi); Shigella spp.;Vibrio cholerae.

Gram Positive;

Listeria monocytogenes; Staphylococcus aureus; Staphylococcus epidermidis and saprophyticus*;* Streptococcus faecalis*;* Streptococcus pyogenes; Streptococcus viridans.

Variable Sensitivity;

Klebsiella / Enterobacter spp.; Proteus spp. (indole positive); Providencia spp.; Serratia marcescens; Streptococcus pneumoniae; Yersinia spp.

Relatively Insensitive;

Brucella spp.; Clostridium spp.; Neisseria spp.

Organisms which are insensitive include;

Bacteroides spp.; Lactobacillus spp.; Mycobacteria; Mycoplasmas; Pseudomonas spp.; Ureaplasma urealyticum.

Satisfactory sensitivity testing is achieved only with recommended media free from inhibitory substances especially thymidine and thymine (http://www.inhousepharmacy-europe.com/infections/triprim-information.html).

Trimethoprim is used for the treatment and prevention of urinary tract infections, traveler's diarrhea, respiratory and middle ear infections, and, when combined with either sulfamethoxazole or dapsone, for prevention and treatment of Pneumocystis infections.

4.2 Bacteria and Folic Acid and DNA Syntheses

Dihdrofolate reductase (DHFR) is one of the most studied enzymes with respect to drug design due to its central role in the synthesis of DNA. The discovery of the sulfonamides and the later elucidation of their mode of antibacterial action foreshadowed the design of a range of chemotherapeutic agents specific to bacterial as opposed to eukaryotic enzymes for antibiotic use. This area of research entered a new phase of development with the discovery by Hitchings (Then, 1993) of the diaminopyrimidines,

including trimethoprim (TMP). These are a group of potent antibiotics that exhibit a high degree of specificity for bacterial dihydrofolate reductase due to structural differences between the bacterial and mammalian enzymes (Hitchings, 1989). Humans are unable to make folic acid, a precursor of purine synthesis. We require an exogenous supply of this metabolite obtained from our diet. Many bacteria are, however, able to generate folic acid from *para*-amino benzoic acid (PABA) and this pathway provides a target for synthetic antimicrobial agents like the **sulphonamides** and **trimethoprim**. **Sulphonamides** act by inhibition of dihydropteroate synthetase because it acts as a structural analogue of the normal substrate, PABA. Trimethoprim inhibits dihydrofolate reductase, the next step in the folic acid biosynthetic pathway (http://www.bmb.leeds.ac.uk/mbiology/ug/ugteach/dental/tutorials/antibiotics/dna.html).

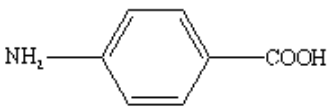


Figure 4.1 Chemical structure of *para*-aminobenzoic acid

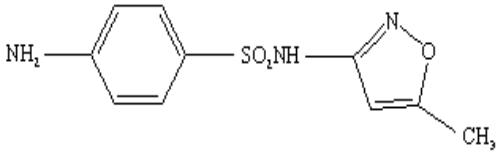


Figure 4.2 Chemical structure of sulphamethoxazole**,** a sulphonamide

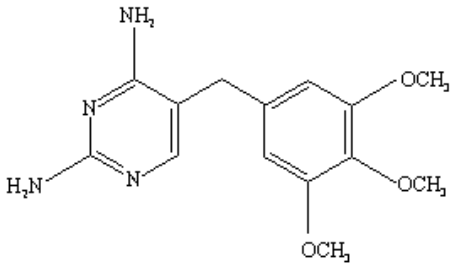


Figure 4.3 Chemical structure of trimethoprim

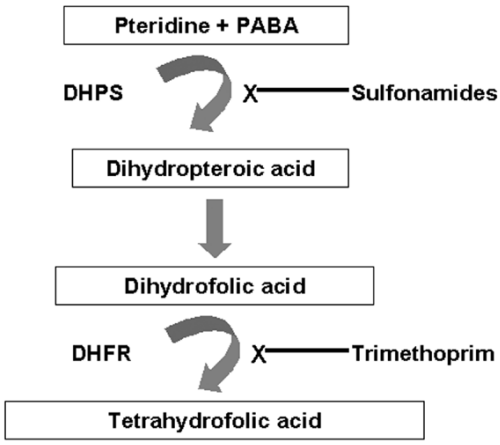


Figure 4.4 Inhibition of folate synthesis by sulfonamides and trimethoprim. PABA, paraaminobenzoic acid; DHPS, dihydropteroate synthase; DHFR, dihydrofolate reductase.

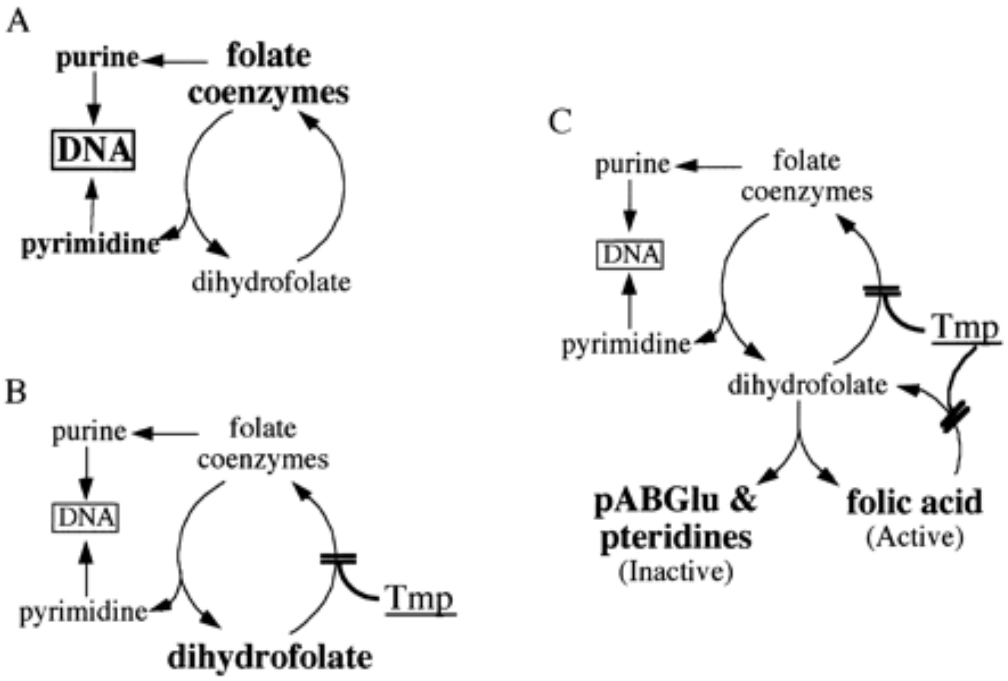


Figure 4.5 Schematic representation of the one-carbon cycle showing *A)* normal function, *B)* conventional model of trimethoprim action showing accumulation of dihydrofolate, and *C)* mode of action of trimethoprim suggested by the current results whereby the accumulating DHF is either oxidized to folic acid or is catabolized to pABGlu and pteridines**. (**Quinlivan, Mcpartlin, Weir , & Scott, 2000**)**

Folate coenzymes are required for the transfer of one-carbon units in the biosynthesis of purines and pyrimidines, in amino acid interconversions, and for the provision of methyl groups. The critical function of dihydrofolate reductase (DHFR) in restoring tetrahydrofolate (THF) concentrations (Fig.4.1A) after thymidylate biosynthesis established the basis for antifolate drug therapy not only in infection, but also in cancer, inflammatory, and autoimmune conditions (Brumfitt, & Miller 1980). Though the consequences of THF depletion (Fig.4.5B) include the cessation in biosynthesis of purines and protein, the metabolic block of greatest severity in animals and bacteria is thought to be the interruption of thymidylate synthesis, so-called 'thymineless death' (Blakley, 1969).

The 2, 4-diaminopyrimidine derivative TMP is the preferred inhibitor of bacterial dihydrofolate reductase in clinical and veterinary use. This is because of its broad spectrum of antibacterial effects, its high degree of selectivity for the bacterial enzyme, and its suitable pharmacodynamic and pharmacokinetic properties (Bushby, & Hitchings, 1968). In combination with a sulfonamide such as sulfamethoxazole, which inhibits folate biosynthesis, the antibacterial spectrum of TMP was extended, greater potency was achievable with lower doses resulting in fewer side effects, and bactericidal power was increased compared to the more bacteriostatic activity of the single components. With or without a sulfonamide, however, a feature of antifolate action is the cessation of nucleotide biosynthesis coincident with disruption of folate metabolism (Quinlivan, McPartlin, Weir, & Scott, 2000).

4.3 Pharmacokinetics of Trimethoprim

After oral administration trimethoprim is rapidly and nearly completely absorbed. The presence of food does not appear to delay absorption. Peak levels in the blood occur between one and four hours after ingestion and the level attained is dose related.

Effective levels persist in the blood for up to 24 hours after a therapeutic dose. Steady state levels in adults are reached after dosing for 2 to 3 days.

Trimethoprim is a weak base with a pKa of 7.3. It is lipophilic. Tissue levels of trimethoprim are generally higher than corresponding plasma levels, the lungs and kidneys showing especially high concentrations. Trimethoprim concentrations exceed those in plasma in the case of bile, prostatic fluid and tissue, saliva, sputum and vaginal secretions. Levels in the aqueous humor, breast milk, cerebrospinal fluid, middle ear fluid, synovial fluid and tissue (interstitial) fluid are adequate for antibacterial activity. Trimethoprim passes into amniotic fluid and fetal tissues reaching concentrations approximating those of maternal serum.

Approximately 50% of trimethoprim in the plasma is protein bound. The half life in man is in the range 8.6 to 17 hours in the presence of normal renal function. It is increased by a factor of 1.5 to 3 when the creatinine clearance is less than 10 ml/minute. There appears to be no significant difference in the elderly compared with young patients.

The principal route of excretion of trimethoprim is renal and approximately 50% of the dose is excreted in the urine within 24 hours as unchanged medicine. Several metabolites have been identified in urine. Urinary concentrations of trimethoprim vary widely. Within 2 hours of any therapeutic dose the concentrations achieved are greatly in excess of the minimum inhibitory concentration (MIC) of most pathogenic bacteria responsible for urinary tract infections. High concentrations usually persist in the urine for 24 hours or more after a single dose. Even in patients undergoing chronic haemodialysis levels of trimethoprim achieved in the urine exceed the MIC for most of the urinary tract pathogens.

4.4 Chemical and Physical Properties of Trimethoprim

Table 4.1 Physical properties of Trimethoprim

Empirical Formula	$C_{14}H_{18}N_4O_3$
Molecular Weight	290.32 $gmol^{-1}$
Appearance	White to yellowish powder
Melting Point	199 - 203 °C
Solubility	Insoluble in water, freely soluble in alcohol
State/Form	Crystalline powder
Stability	Stable under ordinary conditions
Particle size	80 - 100 (mesh)
Storage	Sealed, in dark place

The chemical designation of trimethoprim is 5-[(3, 4, 5-trimethoxyphenyl) methyl]-2, 4-pyrimidine diamine. It is a white to yellowish compound with bitter taste.

Goal of the study is composed various parts. Firstly, this study is carried out for the purpose of removing trimethoprim in wastewater treatment plants and in any where that drug effluents are present via the adsorption behavior of the clay minerals. For this reason batch adsorption experiments are made to clarify the adsorption process of trimethoprim onto montmorillonite KSF. Secondly, because the clay minerals are used as drug carrier, the adsorption capacities of KSF were find to prepare excipients. Lastly, in trimethoprim poisoning, to find a suitable adsorbent is one of the aims of this theses.

CHAPTER FIVE
MATERIAL AND METHOD

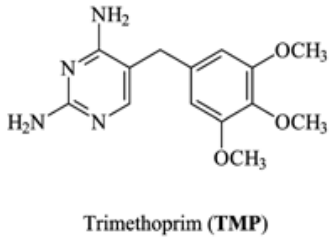
5.1 Clay and Trimethoprim

Montmorillonit KSF is a commercial product of Fluka (Cat. No. 69906) and was utilized for adsorption experiments as an adsorbent. The properties of KSF were summarized in Table 5.1.

Table 5.1 Chemical composition of montmorillonite KSF

Component	%
SiO_2	55.0
Al_2O_3	18.0
Fe_2O_3	4.0
MgO	3.0
CaO	3.0
Na_2O	<0.5
K_2O	1.5
Sulphate	5.0
Ignition Loss	10.0

Trimethoprim (Sigma Cat. No. T 7883) was purchased from Merck and used without further purification and treatment. Its structural formula is shown in Figure 5.1. In the preparation of drug solution, distilled water and ethanol was used.



Trimethoprim (**TMP**)

Figure 5.1 Structural formula of trimethoprim

5.2 FTIR Study

FTIR spectroscopy was used to obtain the information about the interactions between drug and clay sample. Trimethophorim, KSF and trimethoprim loaded KSF were brought to constant weight in a drying oven at 50 ºC for 24 h. The samples were kept in the desiccators. 100 mg of fine KBr powder was dried at 110 ºC and mixed with 1 mg of samples. For pellets, the infrared spectra in the range 4000-400 cm^{-1} were recorded on a Perkin Elmer FTIR spectrophotometer (Spectrum BX-II). The background spectrum of each KBr pellet was obtained by subtracting it from the sample spectra.

5.3 SEM Measurements

Scanning electron microscopy, SEM was carried out in a Jeol JSM 60 SEM attached an X-ray energy dispersive spectrometer, EDS. The surface morphologies of KSF, trimethoprim loaded KSF were studied using a scanning electron microscope at an accelerating voltage of 20 kV. The samples that were used were dried and coated with gold before scanning. For SEM, photographs were taken at different magnifications (between 1000X and 5000X).

5.4 Adsorption from Solution Experiments: Determination of Equilibrium Concentration

Adsorption isotherms were determined by using batch equilibrium method. For batch adsorption experiments, 0.1 g of KSF was added into 25 mL of trimethoprim solution. Concentrations of Trimethoprim in aqueous solutions were between 20 and 240 μM. The solutions were shaken at 150 rpm in a temperature controlled shaking water bath (Memmert) for 7 h to reach equilibrium under experimental conditions. After 7 h, the samples were taken and centrifuged at 5000 rpm for 15 min. Liquid phases were taken and equilibrium concentration of drug in resultant solution was determined using Shimadzu UV-Visible 1601 model Spectrophotometer at λ_{max}=271 nm. The amount of

trimethoprim adsorbed on KSF montmorillonite was calculated by difference of initial concentration and the equilibrium concentration of trimethoprim. The same procedures were performed at solution temperatures of 17 ºC and 45 ºC to find thermodynamic parameters. The ionic strengths were adjusted to 0.1, 0.05 and 0.01 using 1 M NaCl solutions. Experiments were also carried out at various time intervals to determine kinetic parameters.

In this study, adsorption of trimethoprim (TMP) onto montmorillonite KSF has been studied. The Langmuir, Freundlich and DR equations were used to fit the equilibrium isotherm. The kinetic and thermodynamic parameters were calculated to find out adsorption rate constants and adsorption mechanism. These results will be useful for further applications in removing antibiotics from wastewaters and to prepare drug carriers.

CHAPTER SIX
RESULTS

6.1 Determination of Trimethoprim Concentration from Calibration Curve

1 mM stock solution of trimethoprim was prepared by dissolving 0.02903 g trimethoprim in a 100 mL solution which was prepared by using 40% ethanol and 60% distilled water to enhance the solubility of the drug. Calibration solutions at appropriate concentrations were prepared by diluting stock solution, and flasks containing the drugs were wrapped with aluminum foil since trimethoprim is photosensitive. The absorbance values of calibration solutions and calibration curve of trimethoprim were shown in Table 6.1 and Figure 6.1, respectively. The absorbencies of calibration solutions were measured at 288.5 nm wavelength using quartz cells. Absorbance values of calibration solutions were plotted versus concentration.

Table 6.1 Absorbance values of trimethoprim solutions at λ =288.5 nm for calibration curve

Number	C x10^5 / mol L^{-1}	Absorbance
1	1	0.085
2	2	0.136
3	3	0.201
4	4	0.262
5	5	0.327
6	6	0.393
7	7	0.453
8	8	0.525
9	9	0.589
10	12	0.822
11	13	0.864
12	14	0.939

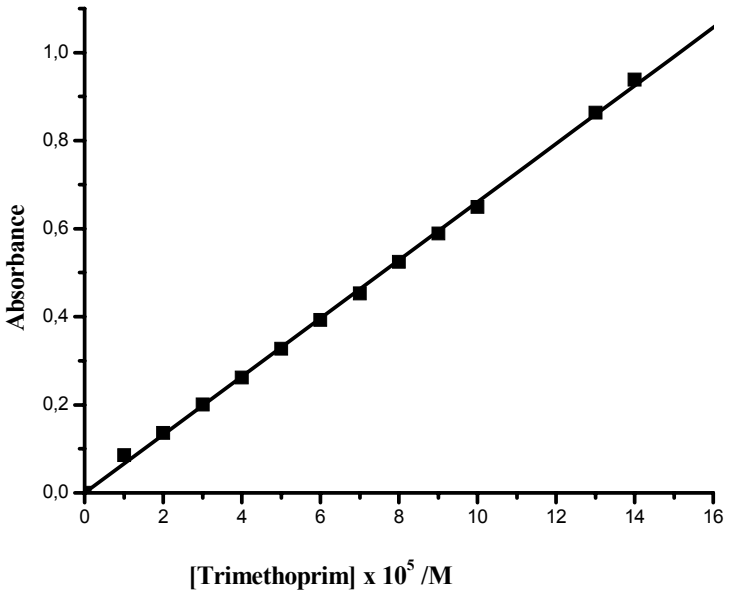


Figure 6.1 Calibration curve of trimethoprim

6.2 The Effect of Contact Time on Adsorption of Trimethoprim onto Montmorllonite KSF

To determine the optimum contact time for adsorption of trimethoprim onto montmorillonit KSF, the equilibrium concentrations were measured at certain times and the amounts of trimethoprim adsorbed were estimated by the equilibrium concentrations which were obtained in a day. Than the curve that indicated the effect of contact time on adsorption was plotted the amount of trimethoprim adsorbed (C_s, mmol L^{-1}) measured in the certain (definite) time intervals versus time. Initial work over 24 hours period indicated that equilibrium is established in 7h. It can be seen from Figure 6.2, when the contact time was increased; the amount of trimethoprim adsorbed was also increased.

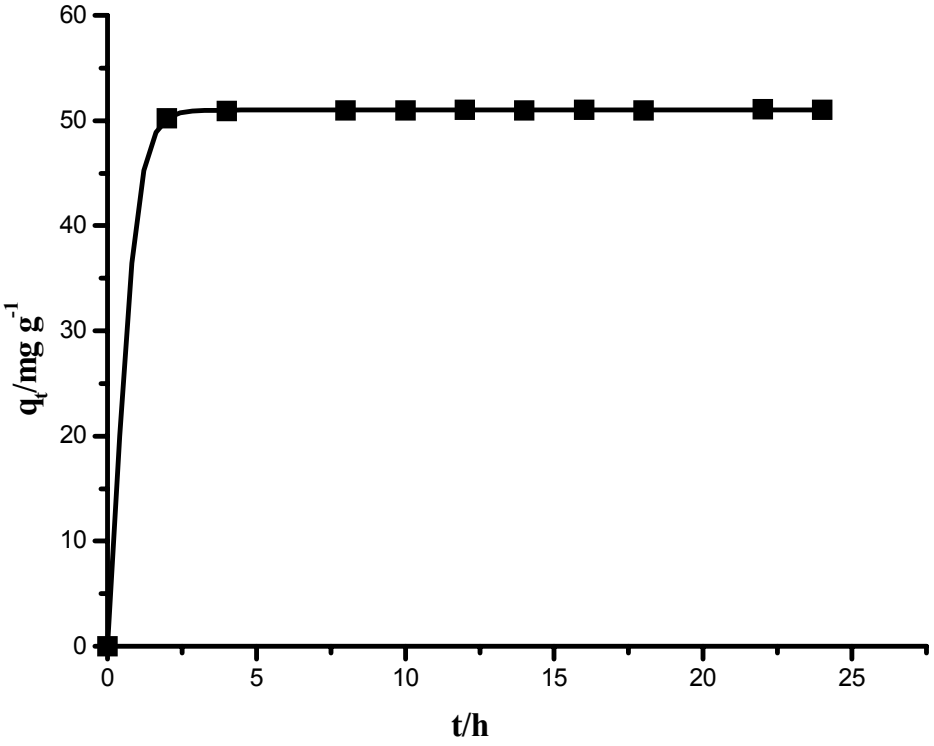


Figure 6.2 Effect of contact time of trimethoprim adsorption onto montmorillonite KSF

6.3 Adsorption of Trimethoprim onto Montmorillonite KSF

Spectrophotometric method was used to determine the concentrations of trimethoprim after adsorption. A set of samples for the drug–KSF suspensions was prepared with different concentrations. The stoppered flasks containing the clay-drug suspensions are agitated in a shaker (Memmert) with shaking speed 150 rpm. A portion of the supernatant layer was taken, centrifuged for 10-15 min and concentrations of the drug after equilibrium was determined spectrophotometrically. The data obtained was used to form adsorption isotherm of trimethoprim on KSF.

The adsorption isotherms of trimethoprim on montmorillonite KSF clay were determined by plotting the amount of trimethoprim adsorbed by KSF (C_s $mmolg^{-1}$) versus equilibrium concentration of trimethoprim (C_e $mmolL^{-1}$). Figure 6.3 shows the trimethoprim sorption isotherms at 29.5; 37.5 and 45 °C. In terms of the slope of initial portion of the curves, the shapes of these isotherms correspond to L type according to the Giles classification (Giles, McEwan, Nakhwa, & Smith, 1960). The L curve indicates that there is no strong competition from the solvent for sites on the surface. Another possibility is that, if the adsorbate has linear or planar molecules, the major axis is parallel to surface. In that study, it can be easily said that montmorillonite KSF has a medium affinity for the trimethoprim molecules. The curves tend to constant value of C_s and reach a plateau showing the formation of a complete monolayer of trimethoprim covering adsorbent surface. The plateaus define maximum adsorptions of 25 10^{-2} $mmolg^{-1}$; 8.6 10^{-2} $mmolg^{-1}$ and 8.2 10^{-2} $mmolg^{-1}$ for 29.5°C; 37.5°C, 45°C respectively and each offers a surface saturation by trimethoprim molecules. The amounts of trimethoprim adsorbed by montmorillonite KSF decrease by increasing temperature.

$$29.5°C > 37.5°C > 45°C$$

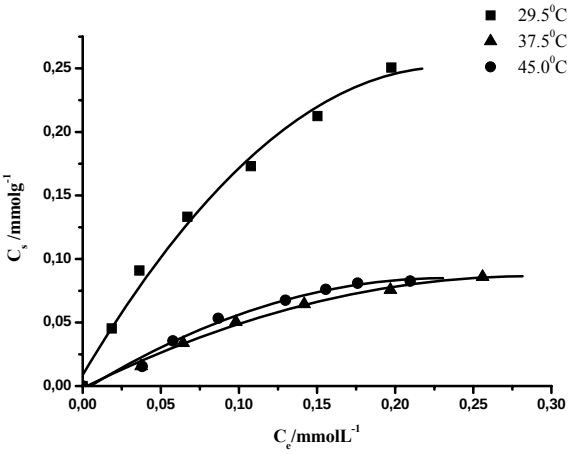


Figure 6.3 Adsorption isotherms of TMP on KSF at different temperatures

Langmuir(1) and Freundlich equations (2) are applied to evaluate the adsorption data. In order to find sorption capacities of the montmorillonite KSF, the linear forms of these equations are used.

$$C_e/C_s = 1/(C_mL) + C_e/C_m \quad (1)$$

$$\ln C_s = \ln K_f + n_f \ln C_e \quad (2)$$

where

C_e = the liquid phase concentration of adsorbate at equilibrium ($mmolL^{-1}$),

C_s = the solid phase concentration of adsorbate at equilibrium ($mmolg^{-1}$),

C_m = the maximum adsorption capacity (maximum amount that can be adsorbed by adsorbent as a monolayer ($mmolg^{-1}$),

L = Langmuir constant regarding the adsorption energy,

K_f = adsorption capacity

n_f = heterogeneity factor (adsorption intensity) (a measurement of linearity).

C_m and L parameters are obtained by plotting C_e/C_s versus C_e for the adsorption process of trimethopim onto montmorillonite KSF at different temperatures (Fig. 6.4). The sorption parameters of trimethoprim on montmorilklonite KSF corresponding to Langmuir equation were summarized in Table 6.2. C_m (maximum adsorption capacity) values are 0.4461 $mmolg^{-1}$ at 29.5°C, 0.1686 $mmolg^{-1}$ at 37.5°C and 0.1400 $mmolg^{-1}$ at 45°C respectively. In addition, L values are 5.838 gdm^{-3} at 29.5°C ; 4.166 gdm^3 at 37.5°C and 7.291 gdm^{-3} at 45°C.

It can be added that although the adsorption of trimethoprim onto KSF can be fitted by Langmuir, the assumptions of these isotherms may not be purely satisfied (Seki, 2002). One should keep in mind that the isotherm shapes themselves can never prove the adsorption mechanism for adsorption; they can only provide a reasonable mechanism for adsorption. It can be added that adsorption mechanism must be proved by molecular

spectroscopy, the other isotherm equation such as Dubinin Radushkevich (DR) equation and thermodynamic parameters (http://www.dekker.com/servlet/product/productid/E-ESCS/toc).

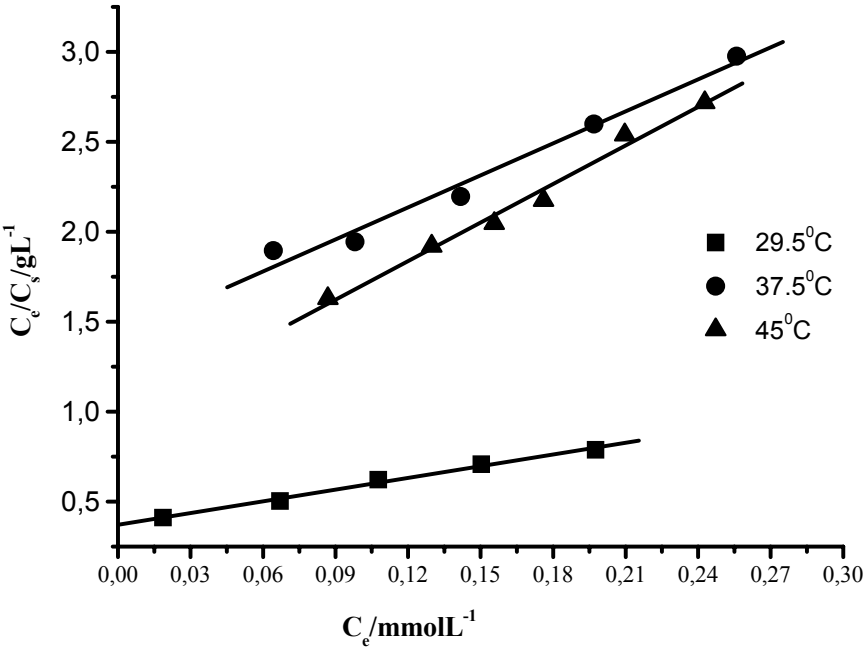


Figure 6.4 Langmuir isotherms for adsorption of trimethoprim onto KSF at different temperatures.

Table 6.2 The sorption parameters of Langmuir equation for trimethoprim onto KSF at different temperatures

Temperature/°C	R^2	$C_m/mmolg^{-1}$	L/gdm^{-3}
29.5	0.9920	0.4461	5.8380
37.5	0.9790	0.1686	4.1665
45.0	0.9864	0.1400	7.2910

To determine the adsorption process is favorable or unfavorable, for the Langmuir type adsorption process, the isotherm shape can be classified by a term 'R_L' a dimensionless constant separation factor, which is defined as below;

$R_L = 1 / (1 + a_L C_0)$ (3)

where

a_L = Langmuir isotherm constant (L/mmol),

C_0 = initial trimethoprim concentration (mmol L^{-1})

The shapes of the isotherms for $0 < R_L < 1$, $R_L > 1$, $R_L = 1$ and $R_L = 0$ are favourable, linear and irreversible, respectively (Weber& Chakkravorti, 1974).

Table 6.3 Dimensionless seperation factor for adsorption of trimethoprim onto montmorillonite KSF at different temperatures.

Temperature/°C	**a_L/ L/mmol**	**C_O/mmol/L**	**R_L**
29.5	5.8383	0.20	0.4613
37.5	4.1665	0.20	0.5455
45.0	7.2910	0.20	0.3138

The values of R_L (Dimensionless separation factor) at different temperatures are reported in Table 6.3. The values of R_L were between 0 and 1. These values indicate that favorable adsorption for trimethoprim occurred.

In order to determine the constants K_f (relative sorption capacity) and n_f, (measure of the linearity of the sorption) the linear form of the equation shown below may be used to produce a graph of $\ln C_s$ against $\ln C_e$.

$\ln C_s = \ln K_f + n_f \ln C_e$ (4)

A graph indicating adsorption of trimethoprim onto montmorillonite KSF which is formed by plotting $\ln C_s$ versus $\ln C_e$ is shown in the Figure 6.5. The correlation

coefficients are greater than 0.9498. Based on R^2 values, the fit of Freundlich equation is not good as Langmuir equation.

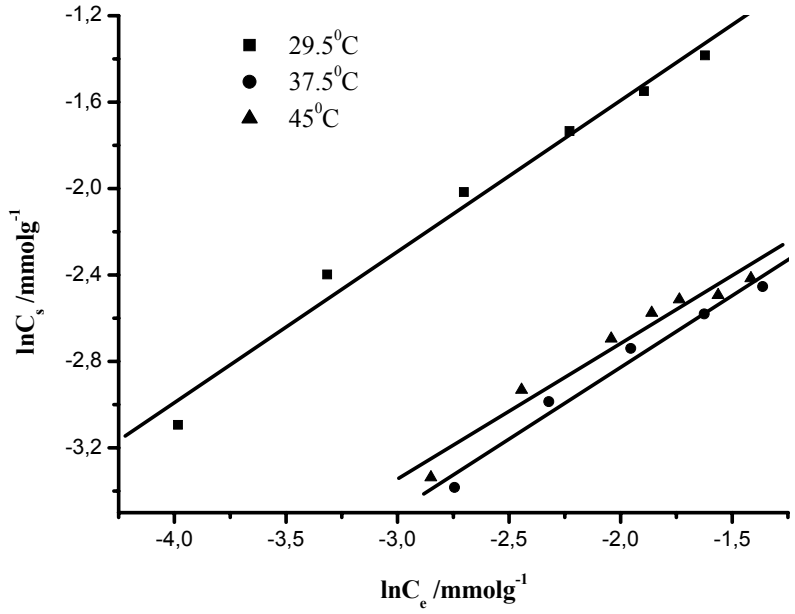


Figure 6.5 Freundlich isotherms for adsorption of trimethoprim onto KSF at different temperatures.

Table 6.4 The sorption parameters of Freundlich equation for adsorption of trimethoprim onto montmorillonite KSF at different temperatures

Temperature/°C	R^2	K_f/mmol g^{-1}	n_f
29.5	0.9826	0.8241	0.6995
37.5	0.9498	0.3191	0.8612
45.0	0.9605	0.2318	0.6275

Freundlich constants were shown in Table 6.4. As can be seen from Table 6.4, K_f values decrease by increasing temperature. This result indicates that adsorption capacities of

KSF increase when temperature decreases. It can be easily understood that trimethoprim is more adsorbed at 29.5°C than 37.5°C and 45°C. It can be said that the values of n_f are smaller than 1, reflecting the favorable adsorption (Ghiaci, Abbaspur, Kra, & Seyedeyn, 2004).

Both these theories suffer from the disadvantage that equilibrium data over a wide concentration range can not be fitted with a single set of constants (Mc Kay et.al, 1986). The n_f values are less than 1 in the form of linear Freundlich equation. n_f is indicator of heterogeneity factor. If the value of n_f is equal to unity, the adsorption is linear. It indicates that adsorption sites are not homogeneous in energy.

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

$$C_s = X_m e^{-\beta\varepsilon^2} \quad \text{or} \tag{5}$$

$$\ln C_s = \ln X_m - \beta\varepsilon^2 \tag{6}$$

where

ε can be correlated :

$$\varepsilon = RT \ln (1+1/C_e) \tag{7}$$

C_s = The amount adsorbed of solute ($molg^{-1}$)

X_m = The maximum adsorption capacity of the sorbent ($molg^{-1}$).

β = a constant related to the sorption energy (mol^2/kJ^2).

R = gas constant ($8.314\ 10^{-3}$ kJ mol^{-1} K^{-1}).

T = Temperature in Kelvin.

C_e = the equilibrium concentration in solution (mol dm^{-3}).

The plot of $\ln C_s$ versus ε^2 follows linearity. The value of X_m is determined from the intercept and the value of β is derived from the slope. The figure of DR isotherm for adsorption of trimethoprim onto montmorillonite KSF at different temperatures is shown at below.

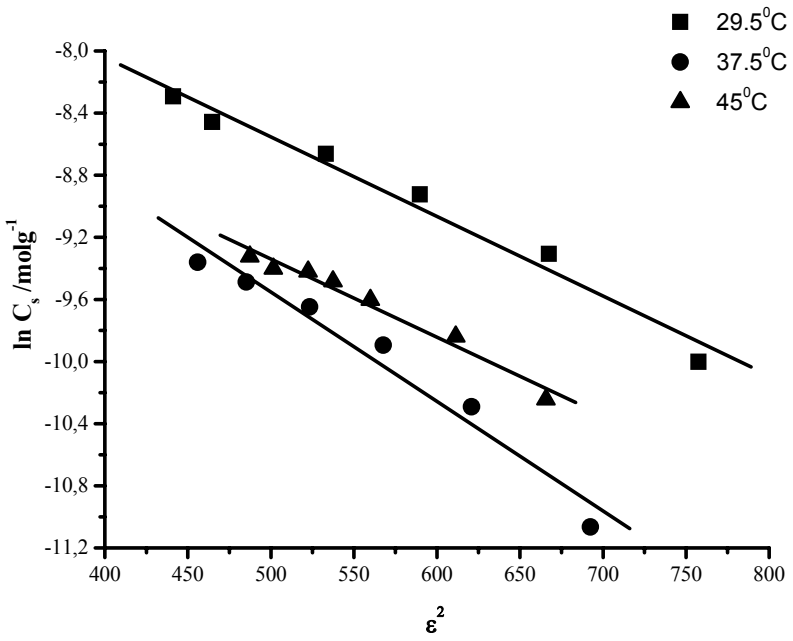


Figure 6.6 DR isotherms for adsorption of trimethoprim onto montmorillonite KSF at different temperatures

The sorption energy, E for ions onto adsorbent calculated using the expression:

$$E = -(2\beta)^{-1/2} \quad (8)$$

is the range of 8-16 $kJmol^{-1}$ designated for ion exchange mechanism. If sorption energy is smaller than $8kJmol^{-1}$, adsorption type is physical adsorption due to weak van der Waals forces. Parameters related to DR isotherm at different temperatures were summarized in Table 6.5 (Mahramanlıoğlu et. al,2003).

As seen in Table 6.5, correlation factors (R^2) in the range of 0.9622 – 0.9758 for montmorillonite KSF at 37.5°C and at 29.5°C, respectively. All E values were between

8 and 16 kJmol^{-1}, for that reason these E values indicate that sorption of trimethoprim on montmorillonite KSF can be explained by ion exchange mechanism at 29.5; 37.5; 45°C. The adsorption capacities (X_m) at 29.5; 37.5; 45°C which were obtained by using DR equation were 2.504 10^{-3}, 2.41 10^{-3}, 1.0876 10^{-3} molg^{-1}, respectively.

Table 6.5 The sorption parameters of DR equation for trimethoprim on montmorillonite KSF at different temperatures

Temperature/ °C	**R^2**	**x_m/molg^{-1}**	**β/mol^2/kJ^2**	**-E/ kJ mol^{-1}**
29.5	0.9758	0.00250	0.00513	9.872
37.5	0.9622	0.00241	0.00705	8.422
45.0	0.9710	0.00109	0.00503	9.970

The correlation factors (R^2) indicated that better applicability was obtained using linearized Langmuir, DR and Freundlich isotherms, respectively.

6.4 Effect of pH on Adsorption of Trimethoprim onto Montmorillonite KSF

The pH of solution is one of the most important parameters affecting the adsorption process. To determine the optimum pH for adsorption of trimethoprim onto montmorillonite KSF, adsorption process in different hydrogen ion concentration was carried out. The pH of % 10 suspensions of KSF in a solution which composed of %40 ethanol and %60 H_2O was 3.31.

To indicate pH effects on adsorption, the amount of trimethoprim adsorbed by the clay (C_s mmolg^{-1}) versus equilibrium pH was plotted. That is shown in Figure 6.7. It is obvious that maximum adsorption at equilibrium was provided at pH 5.04 for initial trimethoprim concentration of 0.4 10^{-3} M at 27°C.

It is probable that pH affects the surface charge of KSF and degree of ionization of drug and speciation of drug solution, adsorption increased in between pH=2.5 and pH=5.04.

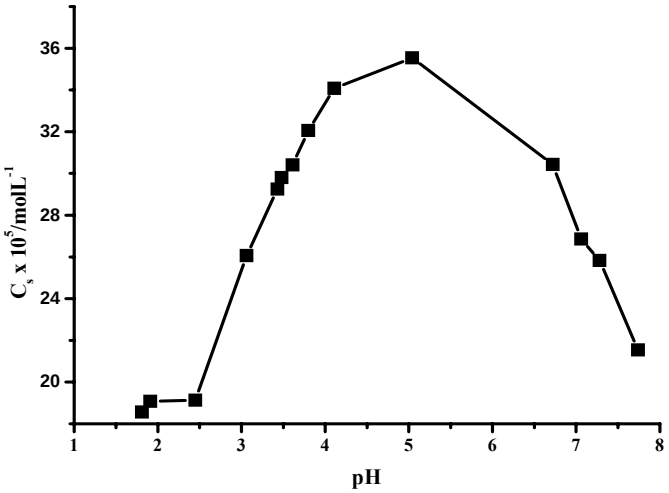


Figure 6.7 pH effects on adsorption of trimethoprim onto montmorillonite KSF

The amount adsorbed of trimethoprim by montmorillonite KSF at pH 5.04 is much larger than the other pH conditions. Adsorption increased from pH= 2.5 to 5.04. There was a decrease in the range of the pH=5.04 to 8. At low pH conditions, all of the trimethoprim which has a pK_a value of 7.3 is in the protonated form of the drug is strongly adsorbed to the negatively charged sites of montmorillonite surface, by cation-exchange process, therefore, the drug is weakly adsorbed in the stomach which has a low pH value and also at nearly pH=7.5, the drug is in neutral form. For that reason no significant ionic attraction was observed and the adsorption mechanism of trimethoprim to montmorillonite KSF at basic conditions is physical one, and is a weak one, this will allow the release of the drug in the intestines.

It was well known that most drugs are weak acids or bases; trimethoprim is a weak base with a pK_a value of 7.3. The most basic site at the heterocyclic ring of trimethoprim shown in Figure 6.8 is N_1. The protonation of trimethoprim is represented in Figure 6.8.

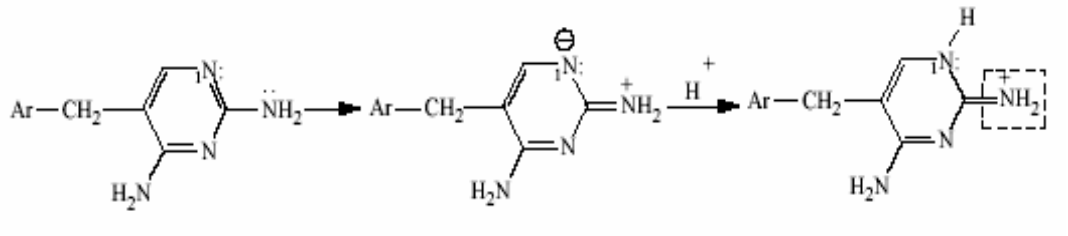


Figure 6.8 The protonation of trimethoprim

$$BH^+ \leftrightarrow B: + H^+$$

B: represents the trimethoprim and BH^+ is the conjugate acid. At stomach pH, practically the entire drug is in the protonated form. As seen in Figure 6.7, at pH=5.04, maximum adsorption is observed.

In the duodenum, neutral, acidic and basic compounds are eventually released: clay only delays gastrointestinal absorption, as demonstrated by McGinity in the case of amphetamine.

6.5 Effect of Ionic Strength on Adsorption of Trimethoprim onto Montmorillonite KSF

Ionic strength is the most important variable in drug-clay interaction. In the present study, ionic strength of the medium exhibited some effect on adsorption of trimethoprim onto montmorillonite KSF.

At different NaCl concentration, the adsorption isotherms of trimethoprim onto montmorillonite KSF were determined by plotting the amount of trimethoprim adsorbed by the clay (C_s mmolg^{-1}) versus equilibrium concentration of trimethoprim (C_e mmolL^{-1}) at 26°C. Figure 6.9 shows the effect of ionic strength on adsorption of trimethoprim.

The isotherms plotted may be classified as L type according to Giles classification. L type suggests medium affinity of trimethoprim on montmorillonite KSF.

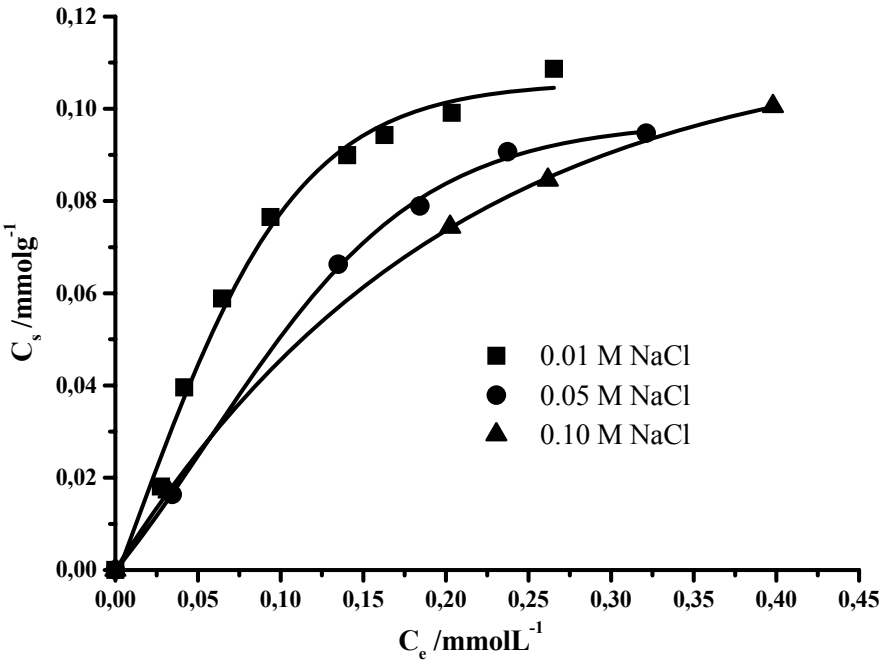


Figure 6.9 Effect of ionic strength on adsorption of trimethoprim onto montmorillonite KSF

The equilibrium data were filled to Langmuir equation. In Figure 6.10, the Langmuir isotherm for adsorption of trimethoprim onto KSF is shown. This graph is obtained by plotting C_e/C_s versus C_e for the adsorption process of trimethoprim onto KSF at different ionic strength.

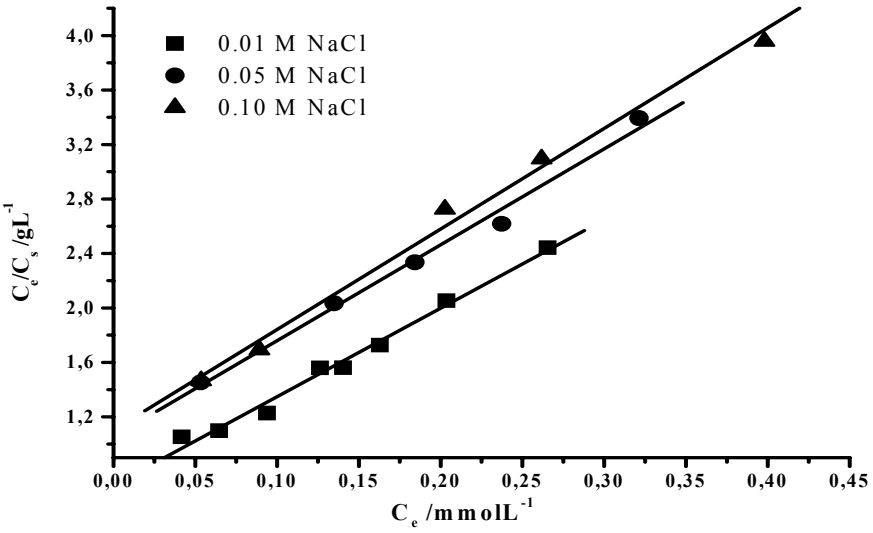


Figure 6.10 Langmuir isotherms for adsorption of trimethoprim onto montmorillonite KSF at different ionic strength.

The sorption parameters obtained from Langmuir equation were summarized in Table 6.6. As can be seen from Table 6.6, the amounts of trimethoprim adsorbed on montmorillonite were decreased with increased concentration of NaCl in medium. This result was supported by the investigation of M. A. Qtaitat, who studied the interaction of trimethoprim – montmorillonite. As the ionic strength is increased from 0.01 to 0.1 by addition of NaCl, the amount of drug adsorbed is decreased. This probably due to the competition between the protonated form of the drug molecules and Na ions to negatively charged surface of the clay, thus, adsorption is decreased. It is well understood from the C_m (adsorption capacities) values. By increasing ionic strength, C_m values are decreasing from 0.1538 mmolg^{-1}to 0.1354 mmolg^{-1}.

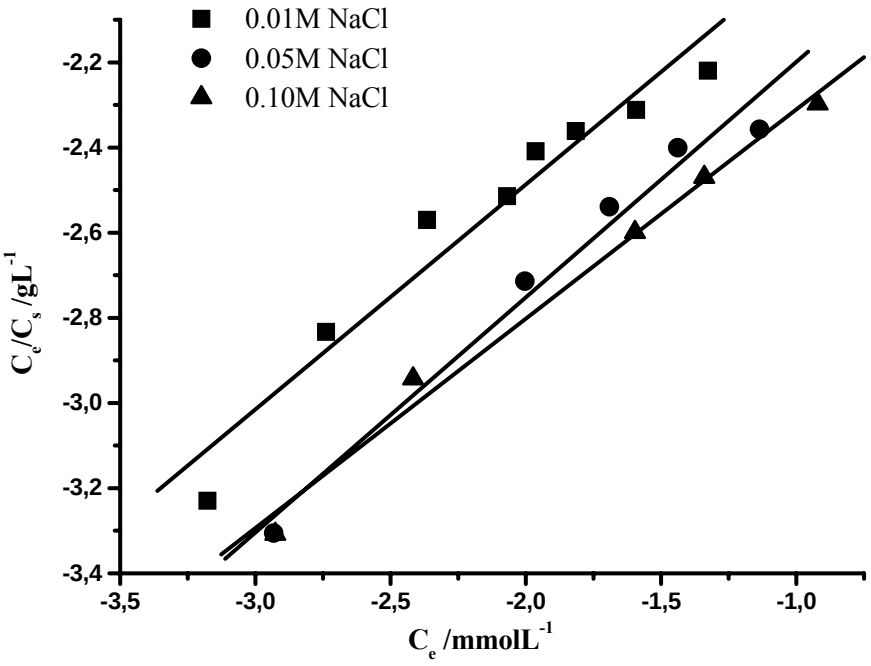


Figure 6.11 Freundlich isotherms for adsorption of trimethoprim onto montmorillonite KSF at different ionic strengths

Table 6.6 The sorption parameters of Langmuir equation for trimethoprim onto montmorillonite KSF at different ionic strengths

[NaCl]/M	R^2	C_m/mmolg^{-1}	L/gL^{-1}
0.01	0.9873	0.1538	9.3284
0.05	0.9907	0.1419	6.6808
0.10	0.9924	0.1354	6.6991

That adsorption is decreased when the ionic strength is increased is understood and supported by Freundlich and DR equations, too. Freundlich equation was applied to quantify adsorption capacity. Figure 6.11 was obtained by plotting $\ln C_s$ against $\ln C_e$ at different ionic strengths.

Parameters related to Freundlich equation and DR equations were summarized in Table 6.7 and Table 6.8, respectively. As can be seen from Table 6.7, K_f values decrease from 0.2393 $mmolg^{-1}$ for 0.01M NaCl to 0.1622 $mmolg^{-1}$ for 0.1M NaCl. This result demonstrates that relative sorption capacities decrease by increasing ionic strength.

Table 6.7 The sorption parameters of Freundlich equation for trimethoprim onto montmorillonite KSF at different ionic strengths.

[NaCl]/M	**R^2**	**K_f/$mmolg^{-1}$**	**n_f**
0.01	0.9446	0.2393	0.5283
0.05	0.9773	0.1928	0.5527
0.10	0.9887	0.1622	0.4916

The DR graph is drawn by plotting $\ln C_s$ versus ε^2. X_m (maximum sorption capacity of the sorbent) and β (a constant related to the sorption energy) values are obtained by means of this graph. The figure of DR isotherm for adsorption of trimethoprim onto montmorillonite KSF at different ionic strength is shown in below.

Table 6.8 The sorption parameters of DR equation for trimethoprim onto montmorillonite KSF at different ionic strengths

[NaCl]/M	**R^2**	**X_m/$molg^{-1}$**	**β/mol^2/kJ^2**	**-E/$kJmol^{-1}$**
0.01	0.9570	8.3630	0.00469	10.3252
0.05	0.9846	7.4888	0.00499	10.0100
0.10	0.9928	5.5980	0.00450	10.5409

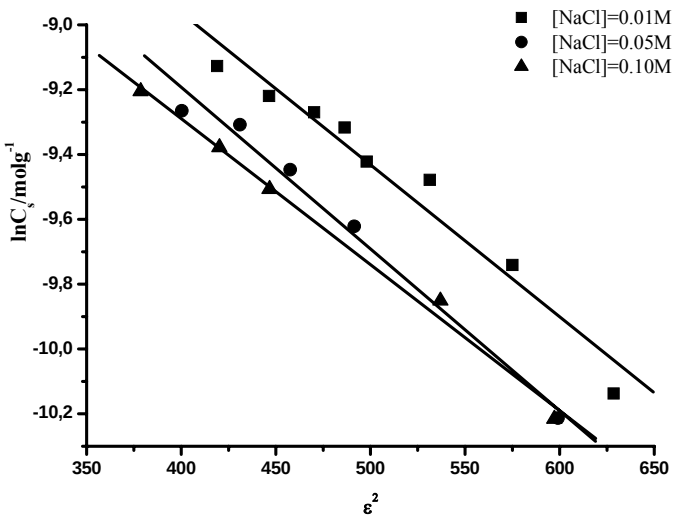


Figure 6.12 DR isotherms for adsorption of trimethoprim onto montmorillonite KSF at different ionic strengths

6.6 Adsorption Kinetics

In order to optimize the design of an adsorption system of trimethoprim onto montmorillonite KSF, it is important to establish the most appropriate correlations for the equilibrium data for each system. In this respect, several kinetic models including the pseudo-first-order equation, pseudo-second-order equation, and intraparticle diffusion model were applied to find out adsorption mechanism.

$1/q_t = (k_1/q_1)(1/t) + 1/q_1$ Pseudo-first-order (9)

$t/q_t = 1/k_2.q_2^2 + (1/q_2).t$ Pseudo-second-order (10)

$q_t = k_p\, t^{0,5} + C$ (11)

where

q_t is the amount of trimethoprim adsorbed (mgg^{-1}) on montmorillonite KSF at various time t ,

q_1 is the maximum adsorption capacity (mgg^{-1}) for the pseudo-first order adsorption ,

k_1 is the pseudo-first-order rate constant for the adsorption process (min^{-1}),

q_2 is the maximum adsorption capacity (mgg^{-1})for the pseudo-second-order adsorption,

k_2 is the rate constant of pseudo-second-order for the adsorption ($g\ mg^{-1}min^{-1}$),

C is the intercept for the intraparticle diffusion model (mgg^{-1}),

k_p is the intraparticle diffusion rate constant ($mg\ g^{-1}\ min^{-0,5}$).

The straight-line plots of $1/q_t$ versus 1/t for the pseudo-first-order reaction and t/q_t vs (versus) t for the second-order reaction for the adsorption of trimethoprim onto montmorillonite KSF have also been tested to obtain the rate parameters. The k_1, k_2, q_1, q_2 and correlation coefficients R_1^2 and R_2^2 of trimethoprim under different conditions were calculated from these plots and are given in Table 6.9 and 6.10 (Özcan, & Özcan, 2004).

Table 6.9 The pseudo-first-order parameters for trimethoprim at different temperatures.

Temperature/°C	**R^2**	**k_1/min^{-1}**	**$q_1\ (mgg^{-1})$**
22.5	0.9594	18.0244	27.4273
37.5	0.8452	13.1717	24.0848
50.0	0.9802	16.9935	22.4719

Table 6.10 The pseudo-second-order parameters for trimethoprim at different temperatures.

Temperature/°C	R^2	k_2/g $mg^{-1}min^{-1}$	q_2 (mgg^{-1})
22.5	0.9981	0.004060	26.4061
37.5	0.9985	0.006179	23.6967
50.0	0.9997	0.011367	21.7155

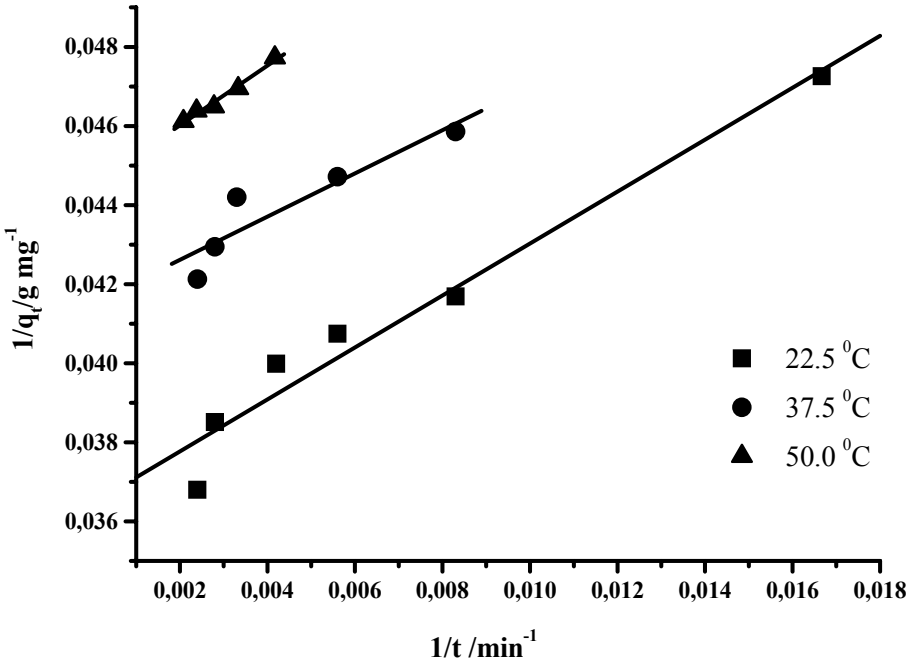


Figure 6.13 Pseudo-first-order plot for adsorption of trimethoprim onto montmorillonite KSF at different temperatures

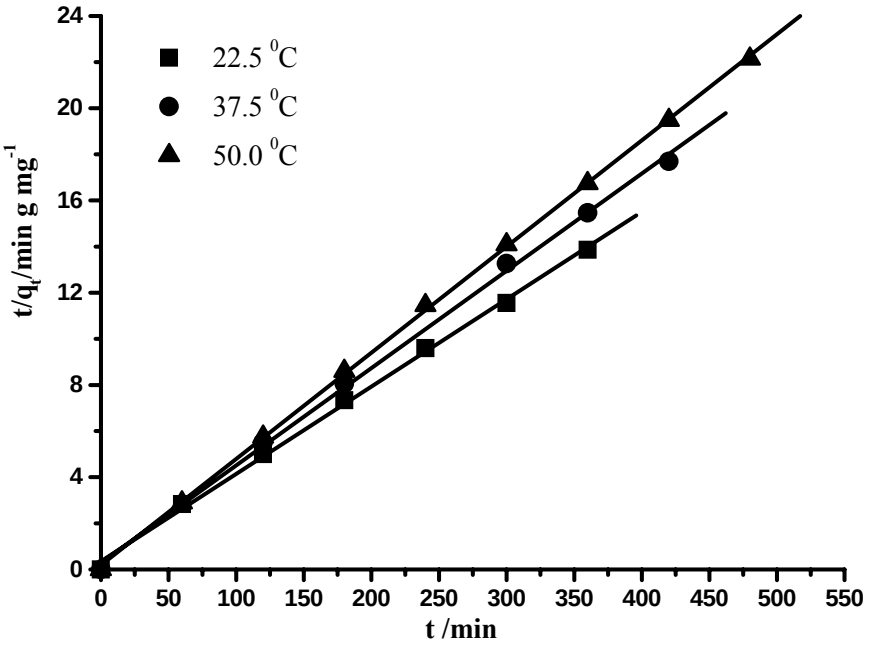


Figure 6.14 Pseudo-second-order plots for adsorption of trimethoprim onto montmorillonite KSF at different temperatures

As can be seen from Table 6.9 and 6.10, the correlation coefficients (R_1^2) for pseudo-first-order kinetic model are between 0.8452 and 0.9802 and the correlation coefficients (R_2^2) for pseudo-second-order kinetic model are between 0.9981 and 0.9997. These results show that the adsorption system obeys the pseudo-second-order kinetic model.

Adsorption kinetics are usually controlled by different mechanisms, of which the most limiting are the diffusion mechanisms, including the initial curved portion, attributed to rapid external diffusion or boundary layer diffusion and surface adsorption, and the linear portion, a gradual adsorption stage due to intraparticle diffusion starts to decrease due to the low concentration in solution as well as fever available adsorption sites.

The rate-limiting step may be due to intraparticle diffusion. The rate constant for the intraparticle diffusion was obtained using the (11) equation.

C gives an idea about the boundary layer thickness. If the intraparticle diffusion is involved in the adsorption process, then a plot of the square root of time ($t^{1/2}$) versus the uptake (q_t) would result in a linear relationship and the particle diffusion would be the controlling step if this line passed through the origin.

When the plots do not pass through the origin, this is indicative of some degree of boundary layer control and the further show that the intraparticle diffusion is not the only rate-controlling step, but also other processes may control the rate of adsorption, all of which may be operating simultaneously.

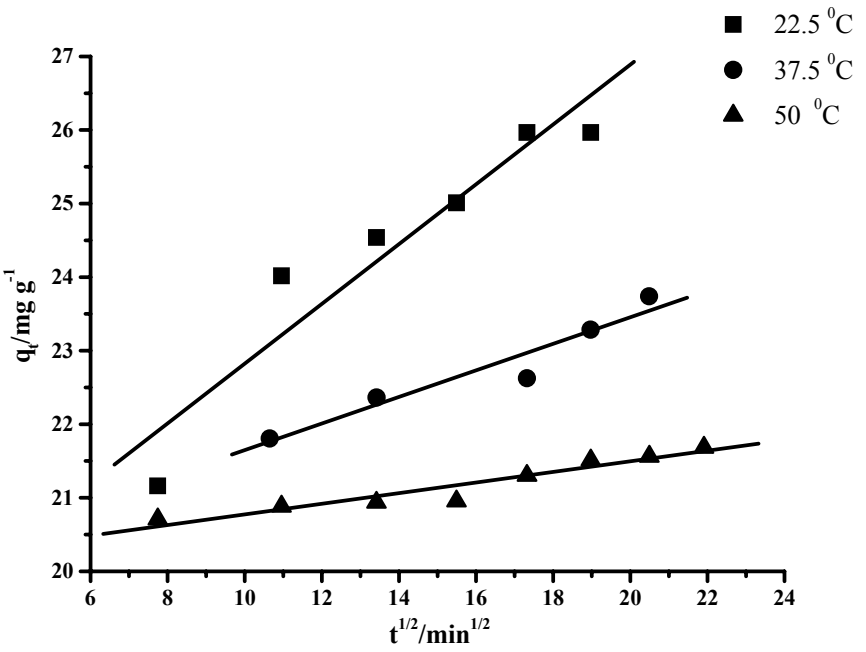


Figure 6.15 Intraparticle diffusion plot for trimethoprim onto montmorillonite KSF at different temperatures

The slope of the linear portion from Figure 6.15 can be used to derive values for the rate parameter, k_p, for the intraparticle diffusion, given in Table 6.11.

Table 6.11 Intraparticle diffusion parameters for trimethoprim onto montmorillonite KSF at different temperatures.

Temperatures/°C	**R^2**	**k_p /mg $g^{-1}min^{-1/2}$**	**C/mg g^{-1}**
22.5	0.8997	0.4064	18.7597
37.5	0.9270	0.1807	19.8410
50.0	0.9185	0.0723	20.0508

From Table 6.11, it is understood that the intraparticle diffusion is not the rate controlling step. Other process may control the rate of adsorption (Mahramanlioglu, et. al, 2003). The correlation coefficients (R_p^2) for the intraparticle diffusion model are between 0.8997 and 0.9270. The linear portions of curves do not pass through the origin. This indicates that the intraparticle diffusion is not the only rate-controlling step and adsorption mechanism of trimethoprim onto montmorillonite KSF is complex. The larger the intercept (C value), the greater is the boundary layer effect. C values are 18.7597, 19.8410, 20.0508 mgg^{-1} at 22.5, 37.5 and 50°C, respectively. As can be seen from Table 6.9 and 6.10, the values of the sorption capacity at equilibrium q_1 and q_2 are decreased from 27.4273 mg g^{-1} to 22.4719 mg g^{-1} and from 26.4061 mg g^{-1} to 21.7155 mg g^{-1}, respectively when the temperature is increased from 22.5°C to 50°C. This suggests that a low temperature favors drug carrier by adsorption onto KSF.the values of the rate constant, k_2 were found to increase from 0.003676 $gmg^{-1}min^{-1}$ to 0.011367 $gmg^{-1}min^{-1}$ for the sorption of trimethoprim for an increase in the solution temperature from 22.5°C to 50°C (Özcan, et. al, 2004).

6.7 Thermodynamic Parameters of Adsorption

The thermodynamic parameters of the adsorption process are obtained from experiments at various temperatures. It is essential to clarify the change of

thermodynamic parameters. Gibbs free energy change, ΔG, standard enthalpy, ΔH, and standard entropy, ΔS are estimated by applying thermodynamic equations. The Gibbs free energy change of adsorption is estimated from the following equation (Özcan, et. al, 2004).

$$\Delta G^\circ = -RT \ln K_d \quad (12)$$

where

K_d = The equilibrium constant at temperature T,

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

T = absolute temperature (K).

For each temperature, the same t value was selected (240 min) and from this value, firstly q_t then C_s and C_e values were calculated by using Pseudo-second-order equation. K_d was estimated using the following equation;

$$K_d = C_s / C_e \quad (13)$$

where

C_e = equilibrium concentration

C_s = the amount of adsorbed

Table 6.12 The equilibrium constant (K_d) for adsorption of trimethoprim onto montmorillonite KSF at different temperatures in 4 hours

Temperature/°C	**C_s X10^4 /molL^{-1}**	**C_e X10^4/molL^{-1}**	**K_d**	**lnK_d**	**1/T/K^{-1}**
22.5	3.5021	1.4979	2.3380	0.8493	0.00338
37.5	3.1746	1.8255	1.7391	0.5533	0.00322
50.0	2.9423	2.0577	1.4299	0.3576	0.00310

To determine the values of ΔH° and ΔS°, the van't Hoff equation is used;

$$\ln K_d = (\Delta S°/R) - (\Delta H°/RT) \quad (14)$$

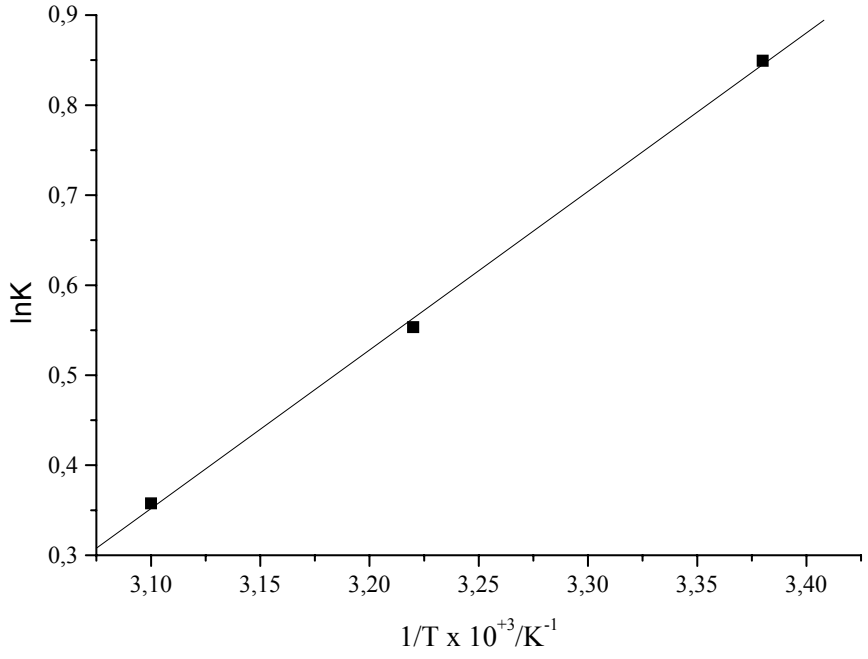


Figure 6.16 van't Hoff of $\ln K_d$ vs 1/T for adsorption of trimethoprim onto montmorillonite KSF

$\Delta H°$ and $\Delta S°$ can be obtained from the slope and intercept of a van't Hoff plot of ln K_d versus 1/T (Aksu, & Kabasakal, 2004).

Thermodynamic parameters calculated with the second-order rate constant are presented in Table 6.13.

Table 6.13 Thermodynamic parameters for adsorption of trimethoprim onto montmorillonite KSF

Temperature/°C	**$\Delta H°$/kJ mol^{-1}**	**$\Delta S°$/J mol^{-1}K^{-1}**	**$\Delta G°$/kJ mol^{-1}**
22.5	-14.2330	-41.1450	-2.0866
37.5			-1.4284
50.0			-0.9602

The Gibbs free energy demonstrates a spontaneous and favorable adsorption process. The higher negative value reflects a more energetically favorable adsorption (Aksu, et al, 2004). The Gibbs free energy value at 22.5°C is the highest negative value than the values of other temperatures. For that reason more energetically favourable adsorption is occurred at 22.5°C.

As shown in Table 6.13, the values of ΔH° and ΔS° were negative for the adsorption of trimethoprim onto montmorillonite KSF. The negative value of ΔH° indicates that the adsorption process is exothermic in nature and the negative value of ΔS° showed the decrease in degree of freedom or decrease the disorder of adsorption process. The negative value of ΔS° suggests decreased ramdomness at solid/ solution interface and no significant changes occur in the internal structure of the adsorbent through the adsorption of trimethoprim onto montmorillonite KSF (Özcan, et. al, 2004).

The activation energy, Ea, was obtained from an Arrhenius plot. Arrhenius equation is shown below;

$$k_2 = A\, e^{-Ea/RT} \quad \text{or} \qquad (15)$$

$$\ln k_2 = \ln A - E_a/RT \qquad (16)$$

where

k_2 = rate constant of pseudo-second-order adsorption ($gmg^{-1}min^{-1}$),

A = The Arrhenius factor,

R = gas constant (8.314 $Jmol^{-1}\ K^{-1}$),

T = absolute temperature (K).

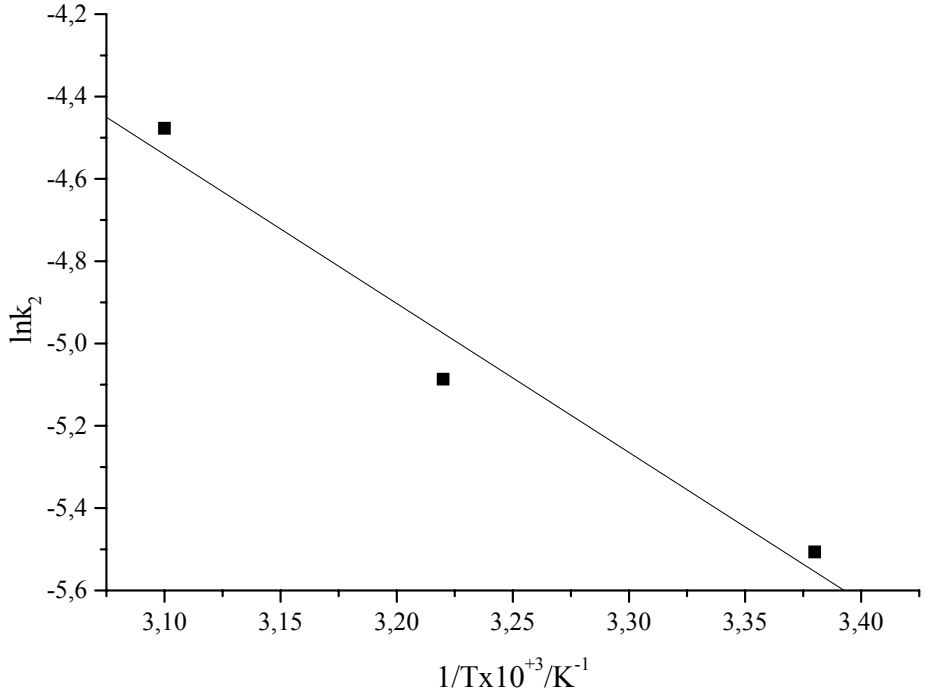


Figure 6.17 The Arrhenius plot for the adsorption of trimethoprim onto montmorillonite KSF

The plot of lnk_2 versus 1/T for the adsorption of trimethoprim onto montmorillonite KSF were applied to obtain the activation energy, E_a from the slope.

Adsorption energy obtained is 29.2807 $kJmol^{-1}$ with the correlation coefficient (R^2) 0.9666. This activation energy value is between 5-40 $kJmol^{-1}$values. Since it is low, it is understood that the physical adsorption mechanism is occurred. It can be easly said that the positive value of Ea represent the nature of physical adsorption of trimethoprim onto montmorillonite KSF, there is an energy barrier in the adsorption process.

6.8 SEM Analysis

The surface morphologies of clay and TMP loaded clay which examined scanning electron microscopy (SEM) were presented in Figure 6.18a and Figure 6.19a respectively.

The chemical content of the clay and TMP loaded clay were obtained using semi quantitative EDS data, which was given in Figure 6.18b and Figure 6.19b, respectively.

In Figure 6.18a, silicate layers with different sizes can be seen and disperse in various direction. It can be added that the distribution of silicate particles are heterogeneous. From EDS analysis of clay sample, it was determined that SiO_2 is the basic constituent of clay with the content of 60.109 %.

After loading, in the photograph of TMP loaded clay, small white grains can be seen. This can be due to fact that drug particles were accumulated on the surface of clay sample.

It can be deduced from the EDS analysis of TMP loaded clay that constituent of SiO_2 was decreased to 42.063 % after loading of TMP. However the content of carbon in drug loaded clay was increased to 19.714 % due to adsorption of TMP on clay. This result confirmed the previous findings obtained from SEM photograph.

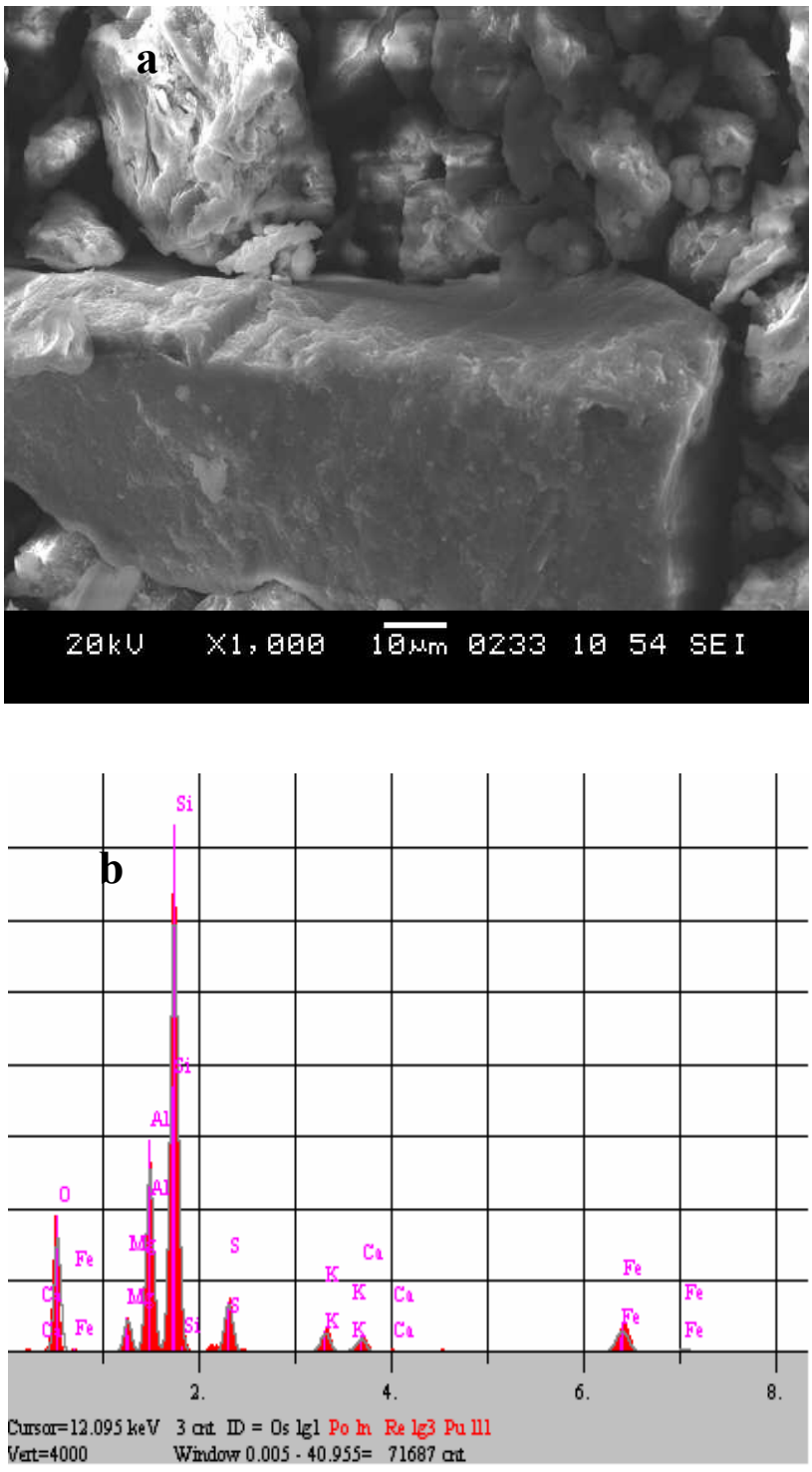


Figure 6.18 SEM Micrographs of a) KSF (x1000) b) EDS analysis of KSF.

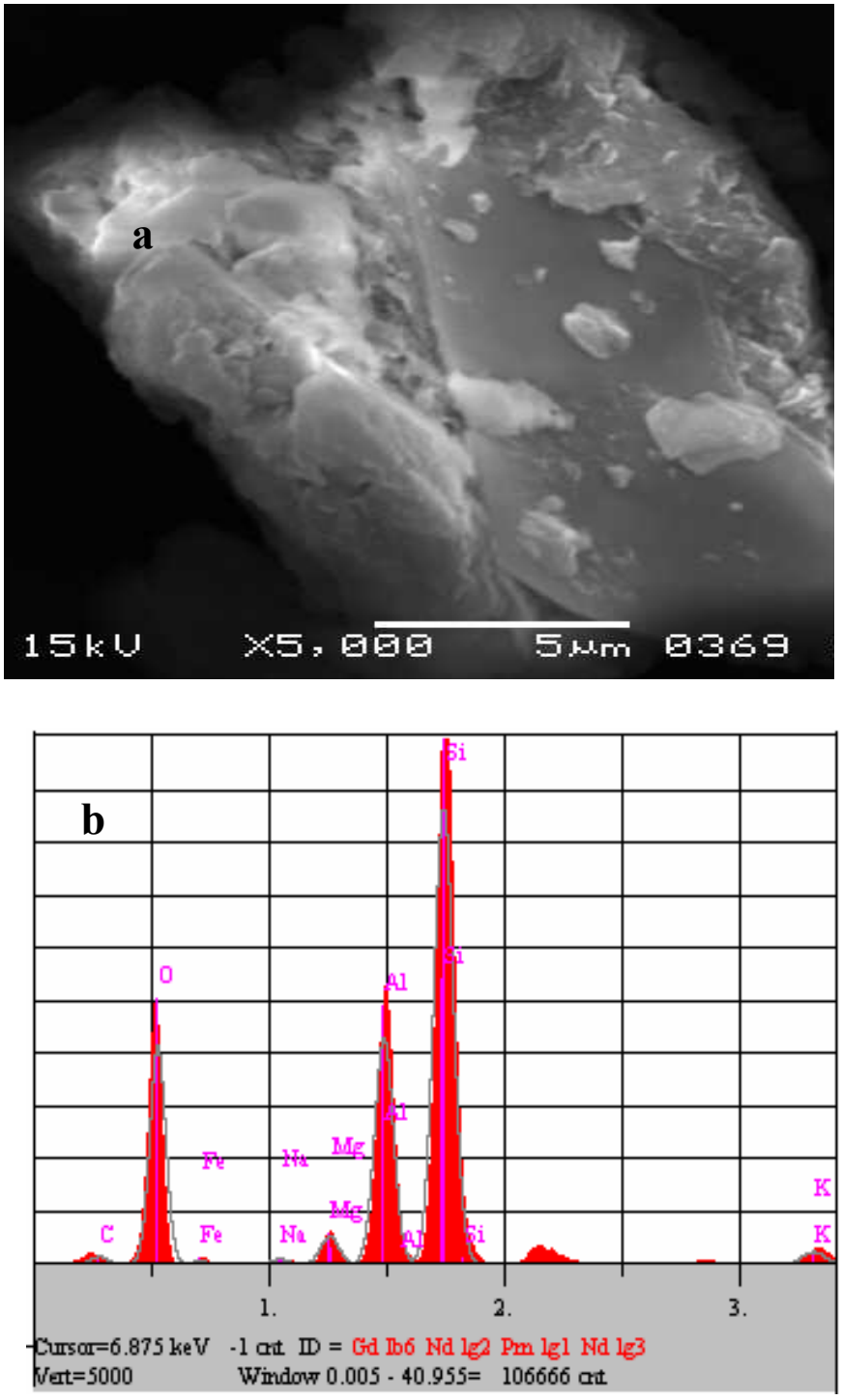


Figure 6.19 SEM Micrographs of a) TMP adsorbed KSF (x5000) b) EDS analysis of TMP adsorbed KSF.

6.9 FTIR Study of TMP adsorption

Figure 6.21 displays the FTIR spectra of TMP, TMP-KSF and KSF. As illustrated in Figure; the absorption band located at 1633 cm^{-1} in the spectrum of KSF is assigned to deformation mode of water. After adsorption of TMP, this band shifted to 1627 cm^{-1}. This small change may be indication of hydrogen bonding between water bonded to the clay and TMP. In the spectrum of TMP, the bands near 1593 and 1565 cm^{-1} can be evaluated as NH_2 deformation bands. Presumably, these bands can not be seen easily due to combination of these bands with water deformation bands. In the spectra of KSF, the bands detected at 529 and 479 cm^{-1} can be identified as Si-O-Al and Si-O-Si bending vibrations respectively. After adsorption of TMP, small shifts were observed in these peaks. In the spectrum of KSF, a strong peak at 1045 cm^{-1} corresponds to Si-OH stretching vibration. When we compare two spectra (KSF and KSF-TMP), it is seen that, intensity of Si-OH stretching band is increased significantly. It may be due to difference in the environment. The band at 1686 cm^{-1} in the spectrum of TMP, was shifted to 1666 cm^{-1} in the spectrum of TMP-KSF which can be attributed to the stretching vibration of $C=NH_2$. The most basic site at the heterocyclic ring of TMP is N_1 where protonation occurs. As can be seen from Scheme 1, $C= NH_2$ group which is the positively charged moiety of TMP interact with the negatively site of KSF as a consequence of ion-exchange between TMP and positively charged ions existing on clay surface. As a result of interaction, stretching vibration of $C=NH_2$ at 1686 cm^{-1} shifted to 1666 cm^{-1}. These results offer the ion-exchange mechanism for TMP adsorption onto KSF, which is supported by DR isotherm.

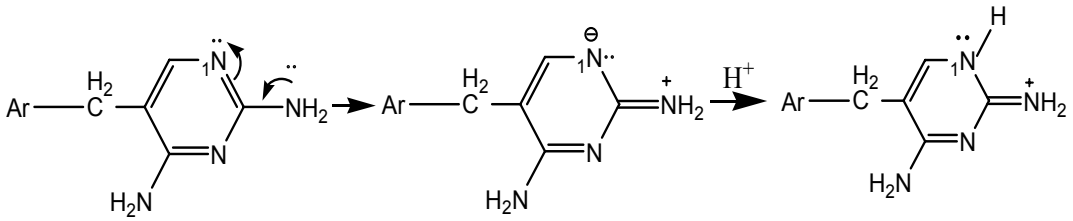


Figure 6.20 Protonation of TMP

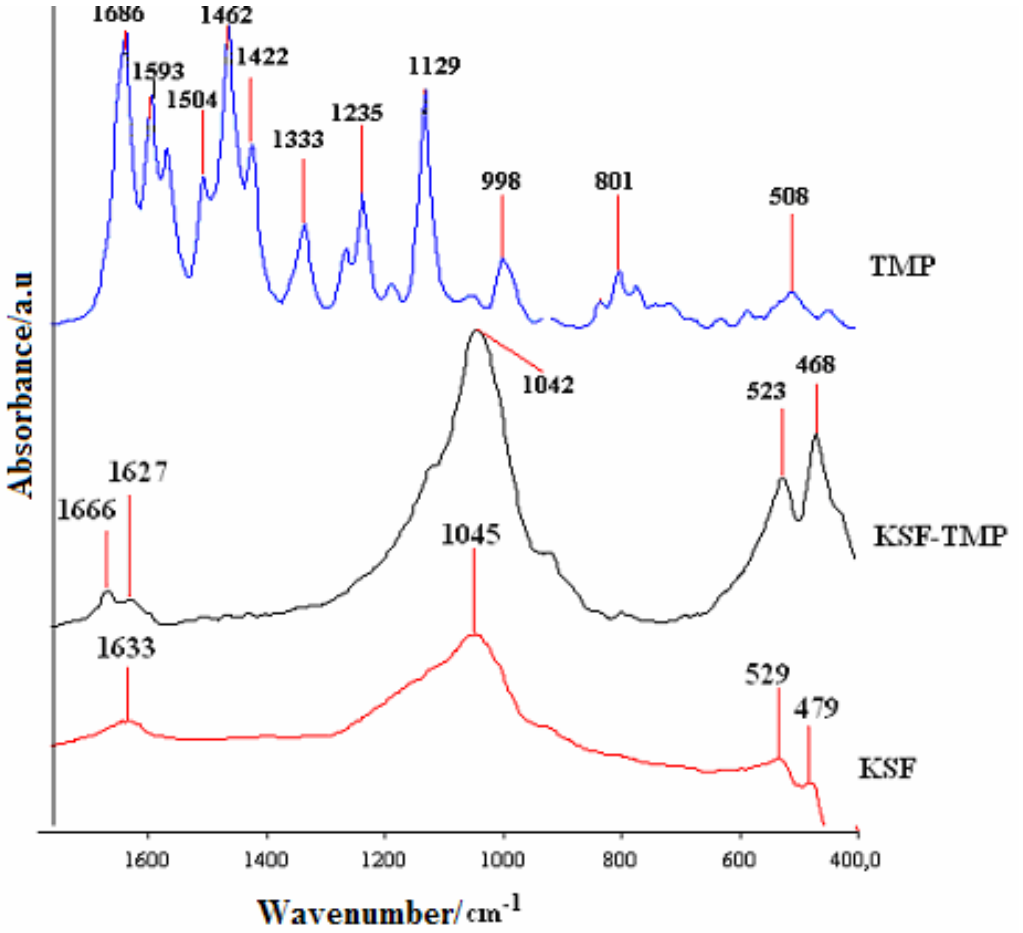


Figure 6.21 FTIR Spectrum of KSF, KSF-TMP and TMP

CHAPTER SEVEN
CONCLUSION

7. Conclusion

The adsorption of trimethoprim (TMP) onto montmorillonite KSF from aqueous solution was studied in a batch system as a function of temperature, ionic strength, pH conditions and contact time. The optimum contact time for adsorption of trimethoprim onto montmorillonit KSF was found as 7 hours by plotting the amount of trimethoprim adsorbed (C_s,mmol L^{-1}) measured in the certain time intervals versus time (see Fig. 6.2). The shapes of the adsorption isotherms of trimethoprim on montmorillonite KSF correspond to L type according to the Giles classification as shown in Fig.6.3. The L curve indicates that there is no strong competition from the solvent for sites on the surface. Another possibility is that, if the adsorbate has linear or planar molecules, the major axis is parallel to surface. In that study, it can be easily said that montmorillonite KSF has a medium affinity for the trimethoprim molecules. As far as the adsorption isotherms concerned, the amounts of trimethoprim adsorbed by montmorillonite KSF decreased with the increase in temperature.

Linear form of Langmuir, Freundlich and Dubinin-Radushkevich (DR) adsorption isotherms are applied to evaluate adsorption data. Additionally to clarify adsorption type, DR equation was utilized. As can be seen Table 6.2 and 6.3, Langmuir adsorption isotherm gave a better fit than the Freundlich model based on the correlation coefficients (R^2) values. By using Langmuir equation, maximum adsorption capacities (C_m) of montmorillonite KSF were obtained as 0.4461 $mmolg^{-1}$ at 29.5°C, 0.1686 $mmolg^{-1}$ at 37.5°C and 0.1400 $mmolg^{-1}$ at 45°C respectively. Freundlich K_f (adsorption capacity) values decrease from 0.8241$mmolg^{-1}$ at 29.5°C to 0.2318$mmolg^{-1}$ at 45°C. As a result, adsorption of trimethoprim decreases by increasing temperature. Favorable adsorption for trimethoprim was occurred since the values of R_L (dimensionless separation factor) were between 0-1 and Freundlich n_f (heterogeneity factor) values were smaller than 1.

The values of R_L (Dimensionless separation factor) and n_f values at different temperatures are reported in Table 6.3 and Table 6.4.

DR isotherm parameters at 29.5; 37.5 and 45.0 °C were summarized in Table 6.7. As seen from Table 6.7, E values are in the range of 8.422-9.970 $kJmol^{-1}$. All E (sorption energy) values obtained from DR adsorption isotherm were between 8 and 16 $kJmol^{-1}$, for that reason these E values indicated that sorption of trimethoprim onto montmorillonite KSF can be explained by ion exchange mechanism at 29.5; 37.5; 45°C and energy values are close to physical adsorption type. The adsorption capacities (X_m) of DR isotherm at 29.5; 37.5; 45°C were 2.504 10^{-3}, 2.41 10^{-3}, 1.0876 10^{-3} $molg^{-1}$, respectively. It supports that adsorption decreases when temperature increases.

The adsorptive removal of drug from aqueous solution is pH and ionic intensity dependent. The maximum adsorption at equilibrium was observed at pH=5.04 by plotting the amount of trimethoprim adsorbed by KSF (C_s $mmolg^{-1}$) versus equilibrium pH (see Fig.6.7). Montmorillonite KSF is acid activated clay that has a pH value of 3.31 in a aqueous solution and trimethoprim is a weak base with a pK_a value of 7.3. At low pH conditions, all of the trimethoprim is in the protonated form. At lower pH, adsorption is high via the attraction between the negatively charged surface of clay and protonated form of the drug. On the other hand, adsorption at basic pH decreases because no significant ionic attraction was observed and the weak physical adsorption is occurred. In the equilibrium pH range 5.04 - 8, lower adsorption of trimethoprim is due to the presence of excess hydroxyl ions come from water and ethanol competition with the trimethoprim for the adsorption sites. At basic conditions, this will allow the release of the drug in the intestines.

Ionic strength of the medium exhibited some effect on adsorption of trimethoprim onto montmorillonite KSF. The sorption parameters obtained from Langmuir, Freundlich and DR isotherm equations were summarized in Table 6.6, 6.7 and 6.8. As seen in Table 6.6, 6.7 and 6.8, the amounts of trimethoprim adsorbed on montmorillonite

were decreased with increased concentration of NaCl in medium. The addition of salt cause competition between the protonated form of the drug molecules and Na^+ ions to negatively charged surface of the clay by cation-exchange mechanism in acidic condition. C_m (adsorption capacity for Langmuir isotherm), K_f (adsorption capacity for Freundlich isotherm) and X_m (maximum sorption capacity of the sorbent for DR isotherm) values are decreasing from 0.1538 $mmolg^{-1}$ to 0.1354 $mmolg^{-1}$; from 0.2393$mmolg^{-1}$ to 0.1622 $mmolg^{-1}$ and from 0.8363 $mmolg^{-1}$ to 0.5980 $mmolg^{-1}$, respectively.

Several kinetic models including the pseudo-first-order equation, pseudo-second-order equation, and intraparticle diffusion model were applied to find out adsorption mechanism. As can be seen from Table 6.9 and 6.10, the correlation coefficients (R_1^2) for pseudo-first-order kinetic model are between 0.8452 and 0.9802 and the correlation coefficients (R_2^2) for pseudo-second-order kinetic model are between 0.9981 and 0.9997. These results show that the adsorption system obeys the pseudo-second-order kinetic model. If the intraparticle diffusion is involved in the adsorption process, then a plot of the square root of time ($t^{1/2}$) vs the uptake (q_t) would result in a linear relationship and the particle diffusion would be the controlling step if this line passed through the origin. When the plots do not pass through the origin, this is indicative of some degree of boundary layer control and the further show that the intraparticle diffusion is not the only rate-controlling step, but also other processes may control the rate of adsorption, all of which may be operating simultaneously. The linear portions of intraparticle diffusion curves do not pass through the origin. This indicates that the intraparticle diffusion is not the only rate-controlling step and adsorption mechanism of trimethoprim onto montmorillonite KSF is complex. The larger the intercept (C value), the greater is the boundary layer effect. C values are 18.7597, 19.8410, 20.0508 mgg^{-1} at 22.5; 37.5 and 50°C, respectively. As can be seen from Table 6.9 and 6.10, the values of the sorption capacity at equilibrium q_1 and q_2 are decreased from 27.4273 mg g^{-1} to 22.4719 mg g^{-1} and from 26.4061 mg g^{-1} to 21.7155 mg g^{-1}, respectively when the temperature is increased from 22.5°C to 50°C. This suggests that a low temperature favors drug carrier

by adsorption onto KSF. The values of the rate constant, k_2 were found to increase from 0.003676 $gmg^{-1}min^{-1}$ to 0.011367 $gmg^{-1}min^{-1}$ for the sorption of trimethoprim for an increase in the solution temperature from 22.5°C to 50°C.

The values of ΔH and ΔS were negative for the adsorption of trimethoprim onto montmorillonite KSF. The negative value of ΔH indicates that the adsorption process is exothermic in nature and the negative value of ΔS showed the decrease in degree of freedom or decrease the disorder of adsorption process and also being negative value of ΔG demonstrates a spontaneous and favorable adsorption process. Activation energy value (E_a) is between 5-40 $kJmol^{-1}$ values and it shows physical adsorption mechanism is occurred.

From EDS analysis of clay sample, it is determined that SiO_2 is the basic constituent of clay with the content of 60.109 %. After loading, in the photograph of TMP loaded clay, small white grains can be seen. This can be due to fact that drug particles were accumulated on the surface of clay sample.

As can be seen from Figure 6.20 and 6.21, C= NH_2 group which is the positively charged moiety of TMP interact with the negatively site of KSF as a consequence of ion-exchange between TMP and positively charged ions existing on clay surface. As a result of interaction, stretching vibration of C=NH_2 at 1686 cm^{-1} shifted to 1666 cm^{-1}. These results offer the ion-exchange mechanism for TMP adsorption onto KSF, which is supported by DR isotherm.

For all, it can be easily understood that montmorillonite KSF can be used to remove trimethoprim from wastewater and as a drug carrier for trimethoprim.

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