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Adsorption of Promethazine hydrochloride with KSF Montmorillonite

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Abstract Adsorption of Promethazine hydrochloride (PHCl) onto KSF Montmorillonite from aqueous solution has been investigated. Experiments were conducted at various pH values, ionic backgrounds and solution temperatures. The pseudo-second-order equation successfully predicted the adsorption among the tried kinetics models (pseudo-first-order, pseudo-second-order and intraparticle diffusion). Langmuir, Freundlich and DR adsorption models were used to describe equilibrium isotherms and the isotherm constants were obtained. The increase in solution temperature caused a decrease in the adsorption capacity values found from Freundlich and DR isotherm. The adsorption type can be explained by combined ion exchange and physisorption. Thermodynamic parameters of adsorption of Promethazine hydrochloride (PHCl) onto KSF were also evaluated. The surface morphologies of KSF and PHCl loaded KSF were examined using a scanning electron microscope (SEM). FTIR measurements of samples were also conducted.

Keywords KSF · drug · kinetic · thermodynamic parameters

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1 Introduction

Silica and some phyllosilicates such as talc, kaolinite, smectites and fibrous clays are among the most widely used minerals in the composition of medicines (Viseras and Lopez Galindo, 1999; Galan et al., 1985). Montmorillonite is one of the clay minerals and consists of hydrated aluminum silicates with fine grains and large spaces between the layers (Lin et al., 2002). Montmorillonite is characterized by both its high adsorptive capacity and surface area (Qtaitat, 2004; Babar et al., 1999). Montmorillonite is also considered as a bioinert, therefore from the pharmaceutical point of view, it is important to find out, whether the co-administration with conventional drugs is possible. The use of clay minerals in pharmaceutical formulations is as active principle or excipient. When clay minerals are used as excipient there might be an interaction between the drug and the mineral which influences the bioavailability of the active principle, both in its liberation process and its stability (Carretero, 2002).

Promethazine hydrochloride is one of the most potent and widely prescribed antihistaminic drugs for the prevention and treatment of nausea, vomiting, motion sickness, etc. Presently, it is available in tablets, syrup, and injectable and suppository dosage forms (Babar et al., 1999). The solubility of promethazine hydrochloride a cationic drug is high in water.

The interactions between cationic drugs and montmorillonite prolong the release of a cationic drug (Fejer et al., 2001). This has led us to ascertaining the

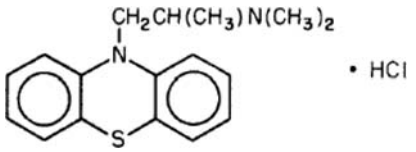

Fig. 1 The structure formula of promethazine hydrochloride

interactions between Promethazine hydrochloride and KSF montmorillonite. Taking into account the above facts, kinetic, thermodynamic and equilibrium parameters of adsorption process were also obtained and surface characterization was examined in details. Optimum conditions (for the range investigated) such as pH, temperature and ionic strength were also studied. The results obtained in this study may give some information in further understanding for the effective administration of PHCl that contain KSF montmorillonite as drug carrier.

2 Experimental

2.1 Adsorption studies

Promethazine hydrochloride (PHCl) stock solution (1 mM) was prepared by dissolving it in distilled water. Further working solutions were freshly prepared from stock solution for each experimental run. The structure formula of PHCl is given in Figure 1.

KSF montmorillonite was supplied from Fluka (Fluka No: 69866). The sample KSF is based on calcium-bentonite which is obtained in the region of Mainburg-Landshut in Germany. The chemical composition of KSF is presented in Table 1.

KSF montmorillonite was oven-dried at 378 K for 2 h, and then stored in a desiccators for further works.

Table 1 Chemical composition of KSF

Component	Percentage by weight
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

Adsorption experiments were performed in a batch equilibrium technique. 0.1 g of KSF were weighed and mixed with 25 mL aqueous solution of PHCl at various initial concentrations in a series of reagent flasks at a constant speed 150 rpm in an isothermal mechanical shaker (MEMMERT). Samples were subjected to shaking for 8 h to reach equilibrium. Samples were withdrawn after 8 h and centrifuged at 4000 rpm for 15 min. The supernatant was decanted and the equilibrium concentration of each solution was measured by spectrophotometer (Shimadzu UV-Vis 1601 model) at the λ_{max} value 250 nm. The amount of adsorbed PHCl onto KSF was determined by the difference between the initial and equilibrium concentrations of drug solution.

Similar experiments were carried out by varying temperature (17, 25 and 37°C), solution pH and ionic strength. In pH experiments, the solution pH was adjusted by adding either a small amount of HCl or NaOH solution. The ionic strength was adjusted to 0.1, 0.05 and 0.01 using 1 M NaCl solution.

2.2 FTIR measurements

In order to determine complementary evidence for the adsorption of PHCl onto KSF montmorillonite, FTIR measurements were conducted. FTIR spectra of pellets were recorded in the region of 400–4000 cm^{-1}. The FTIR spectra of PHCl, KSF and PHCl loaded KSF were found using KBR pellets with Perkin Elmer FTIR spectrophotometer (Spectrum BX-II). The samples were brought to constant weights in a drying oven at 35°C for 24 h. Appropriate amounts of fine KBr powder was dried at 110°C for 2 h and mixed with 1 mg of sample. The background spectrum of each KBr pellet was found by subtracting it from the sample spectra.

2.3 SEM analysis

The elemental composition of KSF and PHCl loaded KSF was obtained by using X-Ray Florescence (XRF system Inc 500 Digital Processing) attached to a scanning electron microscope (Jeol JSM 60 SEM). The surface morphologies of KSF and PHCl loaded KSF were studied using a scanning electron microscope at an accelerating voltage of 20 kV. All samples were dried and coated with gold before scanning to increase conductivity. SEM photographs were taken at different magnifications (in the range of 1000X and 5000X).

2.4 Validity of models

In order to quantitatively compare the applicability of the models, a normalized standard deviation Δq is calculated by using the following equation (Karaca et al., 2004);

$$\Delta q = 100x\sqrt{\frac{\sum[(q_{t,\exp} - q_{t,cal})/q_{t,\exp}]^2}{n-1}} \quad (1)$$

Where the subscripts cal and exp are the calculated and experimental data and n, is the number of data points.

3 Results and discussion

3.1 Adsorption isotherms

Equilibrium data of PHCl onto KSF at various temperatures were shown in Fig. 2. As can be seen from Fig. 2, KSF has an adsorption capacity ranging from 0.20 to 0.25 mmol/g when the solution temperature is between 290 and 310 K. This can be considered as monolayer capacities that are increased with increasing solution temperature. It is probable that the mobility of drug, PHCl increases with increasing temperature for monolayer capacity.

It has been also discussed that any increase in temperature may produce a swelling effect within the layers of montmorillonite penetrating the large drug molecule further (Gündoğan et al., 2004). As was known, montmorillonite has an expanding lattice. In our work, for investigation of adsorption of PHCl onto KSF, the adsorption equilibrium data were fitted using Langmuir and Freundlich models, which correspond to homogenous and heterogeneous adsorbent surfaces respectively. The equations can be expressed as follows;

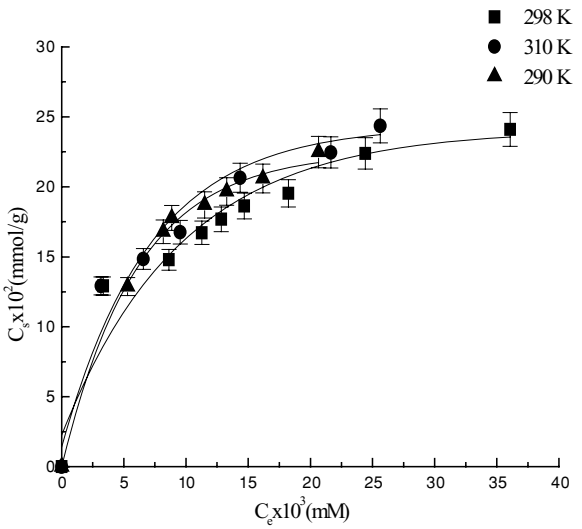

Fig. 2 Adsorption of PHCl onto KSF at different temperatures

$$C_s = \frac{C_m L C_e}{1 + LC_e} \quad (2)$$

$$C_s = K_f C_e^{nf} \quad (3)$$

K_f (mmol g^{-1}) and n_f are considered as relative adsorption capacity and adsorption intensity respectively. The values of C_m and L are the Langmuir constants representing monolayer adsorption capacity (mmol/g) and energy of adsorption respectively. The constants in the equations can be easily found by linearizing the above equations as follows:

$$\frac{C_e}{C_s} = \frac{1}{C_m L} + \frac{C_e}{C_m} \quad (4)$$

$$\ln C_s = \ln K_f + n_f \ln C_e \quad (5)$$

The values of C_m and L were computed from the slope and intercept of the linear plot of C_e/C_s versus C_e and are presented in Table 2.

As can be seen in Table 2, both adsorption isotherms can well predict the adsorption of PHCl onto KSF with high correlation coefficients. Based on Δq values for PHCl adsorption onto KSF, linear form of Langmuir isotherms seems to produce a better fit in comparison with linear form of Freundlich isotherm at 290 and 298 K. The Langmuir equation is applicable to homogenous sorption, where the sorption of each molecule has equal sorption activation energy (Allen et al., 2004). However, based on Δq values, linear form of Freundlich isotherms appears to produce a better fit than Langmuir model at 310 K. It can be added that although the adsorption of PHCl onto KSF can be fitted by Langmuir or Freundlich isotherm, the assumptions of these isotherms may not be purely satisfied. According to Freundlich equation, K_f values are 0.75, 0.78 and 1.00 mmol/g for 310, 298 and 290 K respectively. The relative adsorption capacity values were increased with increasing of temperature. It can be said that the values of n_f are smaller than 1, reflecting the favorable adsorption. For fixed values of K_f and C_e, the smaller

Table 2 Isotherm constants for PHCL adsorption onto KSF at various temperature

	290 K	298 K	310 K
Linear form of Langmuir			
C_m (mmol g^{-1})	0.29	0.30	0.29
L (dm^3 mmol^{-1})	161.2	108.4	182.4
R	0.997	0.991	0.992
Δq (%)	2.99	3.07	9.74
Linear form of Freundlich			
K_f (mmol g^{-1})	1.00	0.78	0.75
n_f	0.38	0.34	0.31
R	0.972	0.990	0.987
Δq (%)	4.71	6.89	3.88
DR			
X_m (mol g^{-1})	1.62×10^{-3}	1.28×10^{-3}	1.07×10^{-3}
k (mol^2 J^{-2})	60.2	62.2	63.0
R	0.975	0.992	0.984
E (kJ mol^{-1})	−9.337	−14.00	−15.69
Δq (%) 7 3.97	2.11	4.85	
Tempkin Isotherm			
A	1530	2864	2631
B (dm^3 g^{-1})	0.066	0.050	0.056
R	0.987	0.964	0.977
Δq (%)	3.48	6.34	6.12

value of n_f, the stronger is the affinity. If n_f value is smaller than 1, it indicates that increased adsorption modifies the sorbent in a way that increases the sorption capacity, as if forming new adsorption sites (Ghiachi et al., 2004).

Dubinin-Radusckevich (DR) isotherm has been used to describe the sorption of PHCl onto KSF. The DR equation has the following form (Qadeer et al., 1995),

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

where X_m is DR monolayer capacity (mg g^{-1}), k is a constant related to adsorption energy; C_s is the amount of drug adsorbed per unit weight of adsorbent (mg g^{-1}) and ε is the Polanyi Potential, which can be expressed as

$$\varepsilon = RT \ln\left(1 + \frac{1}{C_e}\right) \tag{7}$$

Where C_e is the equilibrium concentration of drug in aqueous solution (mol L^{-1}), R is the gas constant and T is the temperature (K). When the plots of $\ln C_s$ against ε^2 at different temperatures were employed, the plot of the line yields k and the intercept gives the adsorption capacity, X_m.

The constant k is used to calculate the mean free energy E (kJ mol^{-1}) of sorption per molecule of the sorbate when it is transferred to the surface of the solid from infinity in the solution. The equation can be given as follow:

$$E = -(2k)^{-0.5} \tag{8}$$

The calculated values were presented in Table 2. As can be seen from Table 2, X_m values increased from 1.07×10^{-3} to 1.62×10^{-3} mg g^{-1} with decrease in temperature from 310 to 290 K. The magnitude of E gives information about the type of adsorption. If this value is between 8 and 16 kJ mol^{-1}, adsorption type can be explained by ion-exchange (Mahramanlioğlu et al., 2002). As was seen from Table 2 that E values were found to be −9.33, −14.00 and −15.69 kJ mol^{-1} for 290, 298 and 310 K respectively. With an increase of the temperature from 290 to 310 K, the mean free energy values also increase. According to DR equation, adsorption capacity values were equal to 1.62×10^{-3}, 1.28×10^{-3} and 1.07×10^{-3} mol/g for 290, 298 and 310 K respectively. It can be derived that the adsorption capacity values of DR isotherm raised as the solution temperature decreased. These findings are also consistent with K_f values obtained from Freundlich equation.

In comparison with C_m monolayer capacity values obtained from Langmuir equation similar results were not observed.

The adsorption data was also applied to The Tempkin isotherm. Temkin and Pyzhev considered the effects of some indirect adsorbate/adsorbate interactions on adsorption isotherms and suggested that because of these interactions the heat of adsorption of all the molecules in the layer would decrease linearly with coverage. The linear form of Temkin isotherm can be given as below;

$$C_s = B \ln A + B \ln C_e \tag{9}$$

and

$$B = RT/b \tag{10}$$

where T is the absolute temperature (K) and R is gas constant. A is the Tempkin isotherm constant. The constant b is related to the heat of adsorption (Akkaya and Ozer, 2005). The results were given in Table 2. Tempkin isotherm constant A increased with increasing temperature from 290 to 298 K and decreased in the range 298–310 K.

3.2 Adsorption kinetics

The mass transfers of adsorption often involve many controlling mechanism of which the individual contribution may not be clearly recognized, at the same time during the course to approach adsorption equilibrium (Chang et al., 2004). In this respect, for simplicity, several kinetic models such as pseudo-first-order kinetic model, pseudo-first-order model and intraparticle diffusion model were used to describe the adsorption kinetic by means of lumped analysis of kinetics data.

3.2.1 Pseudo-first-order model

Pseudo-first-order equation can be expressed as below;

$$\frac{1}{q_t} = \left(\frac{k_1}{q_1}\right)\left(\frac{1}{t}\right) + \frac{1}{q_1} \tag{11}$$

Where k_1 is the pseudo-first-order rate constant (min^{-1}), q_t is the amount of drug adsorbed (mg g^{-1}) at different times t, q_1 is the maximum adsorption capacity (mg g^{-1}) for pseudo-first-order adsorption (Özcan and Özcan, 2004). Plots of $1/q_t$ versus $1/t$ for the adsorption onto KSF were employed to generate the intercept values of $1/q_1$ and the slope of k_1/q_1. The values of k_1, q_1 and the correlation coefficients were given in Table 3.

3.2.2 Pseudo-second-order-model

The pseudo-second-order kinetic equation is as follows;

$$\frac{t}{q_t} = \left(\frac{1}{k_2 q_2^2}\right) + \frac{t}{q_2} \tag{12}$$

Table 3 Kinetic parameters for the adsorption of PHCL onto KSF at various temperatures

	290 K	298 K	310 K
Pseudo-First-Order			
k_1 (min^{-1})	0.89	3.11	1.04
q_1 (mg g^{-1})	17.12	63.90	63.83
R_1	0.947	0.959	0.973
Δq (%)	0.35	1.71	0.10
Pseudo-Second-Order			
k_2 ($\text{g mg}^{-1}\,\text{min}^{-1}$)	4.30×10^{-3}	5.70×10^{-3}	12.90×10^{-3}
q_2 (mg g^{-1})	63.21	63.90	63.86
R_2	0.999	1	1
Δq (%)	0.34	0.42	0.07
Intraparticle			
K_p ($\text{mg g}^{-1}\,\text{min}^{-1/2}$)	0.13	0.06	0.03
C (mg g^{-1})	60.17	62.19	62.97
R_p	0.960	0.895	0.964
Δq (%)	0.21	0.52	0.07

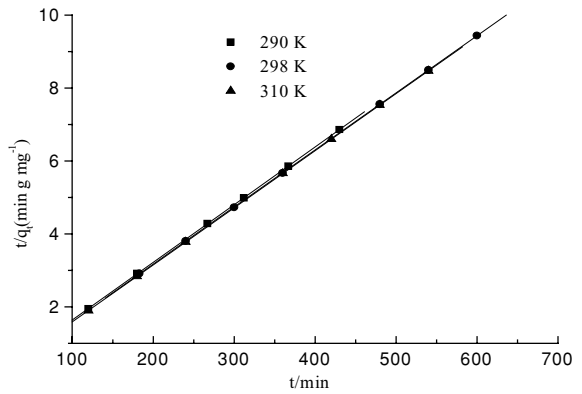

Fig. 3 Second-order-plot for the adsorption of PHCl onto KSF at various temperatures

Where q_t is described earlier, k_2 is the pseudo-second-order rate constant; q_2 is the maximum adsorption capacity (mg g^{-1}) for the second order adsorption process (Karaca et al., 2004). The plots of t/q_t versus t for PHCl adsorption onto KSF were drawn at various solution temperatures and given in Fig. 3. From the slope and intercept values, q_2 and k_2 values were calculated and the results were given in Table 3.

3.2.3 Intraparticle diffusion model

For the intraparticle diffusion model, the following expression was used as

$$q_t = K_p t^{1/2} + C \tag{13}$$

where K_p is the intraparticle diffusion rate constant (mg g^{-1} min$^{-1/2}$), C is the intercept. When q_t is plotted against $1/T$, a straight line with slope K_p and intercept. The values of the intercept give an idea about the boundary layer thickness = larger the intercept, the greater is the boundary layer effect (Özcan and Özcan, 2004). It was also observed that intercept values increased as the solution temperature increased. Presumably, it may be said that at higher temperatures, the boundary layer effect is the greater. The same result is reported in Özcan & Özcan's report (Özcan and Özcan, 2004). Intraparticle diffusion plots do not pass through the origin. This may be indicative of some degree of boundary layer control. This also implies that the intraparticle diffusion does not only contribute to the rate determining step, but also other process may control the rate of adsorption simultaneously. The K_p values are calculated to be as 0.13, 0.06, 0.03 mg g^{-1} h$^{-1/2}$. This confirms that adsorption is also governed by the diffusion within pores of the adsorbent.

When the values of normalized standard deviations of pseudo-first-order and pseudo-second-order model were compared, the latter is better than the previous one. It can be reached that adsorption system obeys the second order kinetic model. Besides, based on R values for PHCl sorption, the pseudo-second-order model seems to produce a better model in comparison with the pseudo-first-order model. As given in Table 3, the maximum adsorption capacity values for pseudo-second-order kinetic model was not affected by temperature drastically. However an increase in temperature increases the rate constant of pseudo-second-order-adsorption from 4.30×10^{-3} to 12.90×10^{-3} (g mg^{-1} min^{-1}).

3.3 Thermodynamic parameters

In order to find the activation energy values of adsorption process, the Arrhenius equation was used in the following:

$$\ln k = \ln A - \frac{E_a}{RT} \tag{14}$$

Where E_a (the minimum energy that requires for the reaction to proceed) is the activation energy of sorption process, A is the Arrhenius constant, T is the solution temperature, k, is the rate constant for the second order kinetics. The activation energy (E_a) and Arrhenius plot (A) were estimated from the slope and intercept of the plot of $\ln k$ versus $1/T$ (Fig. 4).

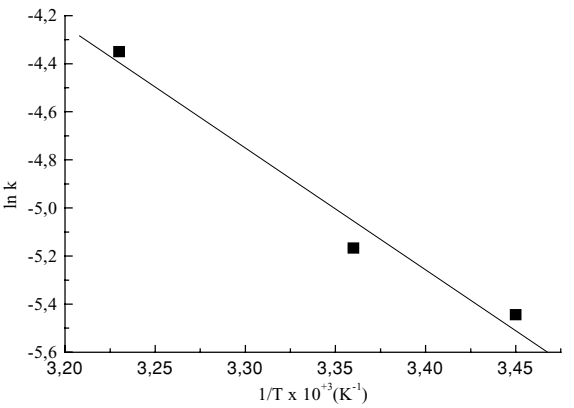

Fig. 4 Arrhenius plot for PHCl adsorption onto KSF

Table 4 Thermodynamic parameters for PHCl adsorption on KSF

T/K	K_c	ΔG°/kJ mol^{-1}	ΔS°/kJ mol^{-1} K^{-1}	ΔH°/kJ mol^{-1}
290	6.280	−4.429	0.187	49.743
298	11.592	−6.070		
310	23.856	−8.175		

K_c Equilibrium constant.
ΔG° Standard free energy.
ΔS° Standard entropy change.
ΔH° Standard enthalpy change.

The results were given in Table 4. The magnitude of activation energy gives information about the type of adsorption. The physisorption process usually has energies in the range of 5–40 kJ mol^{-1}, while higher activation energies (40–800 kJ mol^{-1}) suggest chemisorptions (Nollet et al., 2003). The value of E_a was found to be 41.7 kJ mol^{-1}. However, it is difficult to be sure of that the type of adsorption is considered as chemisorption, since the activation energy value obtained from experimental study is only slightly larger than 40 kJ mol^{-1}. Presumably, it indicates an ion-exchange process for PHCl adsorption onto KSF. This conclusion was also supported by DR isotherm.

In order to understand better the effect of temperature on the adsorption, it is important to study the thermodynamic parameters such as standard Gibbs free energy change, (ΔG°), standard enthalpy change ΔH°, and standard entropy change, ΔS°.

The Gibbs free energy of adsorption was estimated from the following equation

$$\Delta G^\circ = -RT \ln K_c \tag{15}$$

Standard entropy change ΔS° and standard enthalpy change, ΔH°, of adsorption process can be found from van't Hoff equation as shown below

$$\ln K_c = -\Delta H^\circ_{ads}/RT + \Delta S^\circ/R \tag{16}$$

Where R is the gas constant, K_c is adsorption equilibrium constant computed using the following equation

$$K_c = C_s/C_e \tag{17}$$

where C_s is the amount of adsorbed by adsorbent, and C_e is the equilibrium concentration of drug in the solution. The plot of ln K_c versus $1/T$ should be linear. ΔH° and ΔS° were computed from the slope and intercept of van't Hoff plots of ln K_c versus $1/T$.

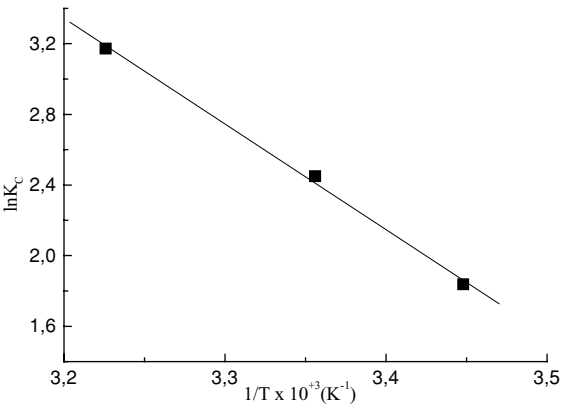

Fig. 5 van't Hoff plot for the adsorption of PHCl onto KSF

The results were given in Table 4. The van't Hoff plot for adsorption of PHCl onto KSF was presented in Fig. 5.

The magnitude of the change in free energy can be used to determine the type of adsorption. In this study, ΔG° values were found to be −4.429, −6.070 and −8.175 kJ mol^{-1}, indicating physisorption is between −20 and 0 kJ/mol; chemisorption has a range of −80 to −400 kJ mol^{-1} (Yu et al., 2001). It is seen that the temperature increased from 290 to 310 K, ΔG° is increased from −4.429 to −8.175 kJ mol^{-1}. It can be concluded that physisorption contributes to the adsorption mechanism. The negative values of ΔG° at different temperatures indicate the spontaneous nature of the sorption process.

The positive values of the standard enthalpy change ΔH°, 49.743 kJ mol^{-1}, imply that the interaction between drug molecules and KSF is endothermic in nature. If heat of an adsorption process is < 40 kJ mol^{-1}, it is physical process, and at the same time, the activation energy of a physical process is also generally low (Mc Bride, 1994). The positive values of the standard enthalpy change may be an indication of the occurrence of monolayer adsorption. This result is supported by

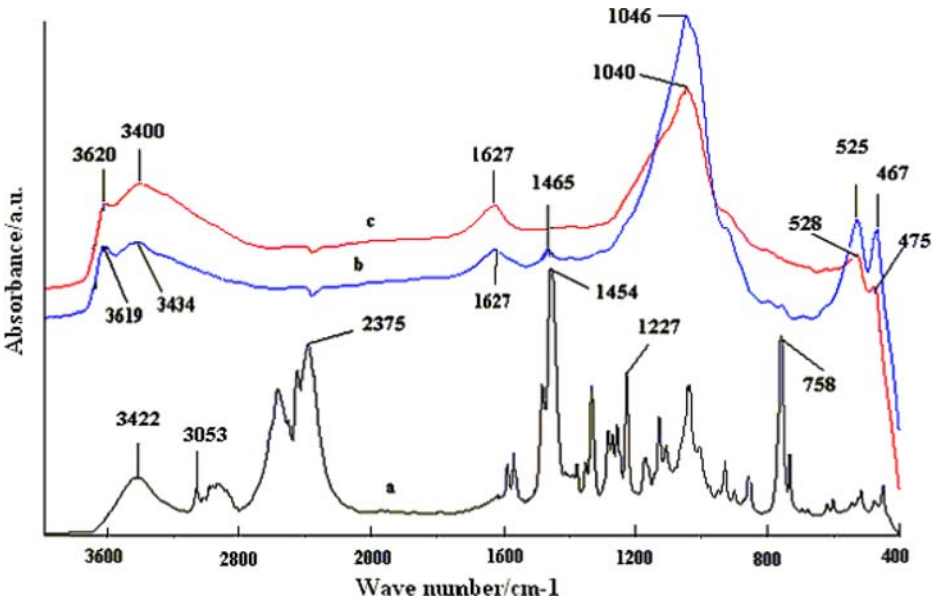

Fig. 6 FTIR specra of PHCl (a), adsorbed onto KSF (b), KSF (c)

its best Langmuir fit. ΔH° values for PHCl adsorption onto KSF are greater than this value may show ion-exchange adsorption mechanism. It is probable that the activation energy of chemical process is high. This result is consistent with previous findings that define the adsorption as ion-exchange mechanism.

Positive value of ΔS° corresponds to an increase in degree of freedom of the adsorbed drug molecules. Also, the positive value of ΔS° above indicates that some structural changes may have taken place as a result of interactions of drug molecules with active groups in the clay surface (Yadava et al., 1991).

3.4 FTIR measurements

FTIR was applied to identify the surface groups that are responsible for drug adsorption. Fig. 6 illustrates the spectra of PHCl, KSF and PHCl loaded KSF. In the spectrum of KSF, the absorption bands at 3620 cm^{-1} is typical for smectites with high amount of Al in the octahedral (Madejova, 2003). The bands at 1633 and 481 cm^{-1} are assigned to the stretching vibrations of clay Si-O within the layer. As can be seen from Fig., the intensity of the band at 481 cm^{-1} increased after adsorption with PHCl. The stretching absorption band of Al-O-Si seemed at 531 cm^{-1} is diminished after adsorption with PHCl. A band at 3400 cm^{-1} in the spectra of KSF is due to stretching vibrations of the OH groups and shifted to 3428 cm^{-1} in the spectrum of PHCl loaded KSF. The band at 1633 cm^{-1} also corresponds to the OH deformation of water.

As shown in Fig. 6, N-H stretching vibrations in the quaternary ammonium group of the molecule appear at 2380 cm^{-1}. After PHCl treatment, this band can not be seen easily. Furthermore, the band located at 1456 cm^{-1} in the spectrum of PHCl can be suggested as skeletal vibrations of the aromatic ring. The most important difference between two spectra (KSF and PHCl loaded KSF) is the band at 1468 cm^{-1}, which can be attributed to substituted aryl compound. This may also be acceptable evidence that PHCl is not only attached on the surface of KSF, but also may form chemical bonds with some groups such as Si-O within montmorillonite.

3.5 Effect of ionic strength

The adsorption of PHCl onto KSF may be affected by the presence of inorganic salt. In order to investigate the effect of ionic strength, various amounts of NaCl concentrations were used. In our study, the adsorbed amounts of NaCl were determined under 0.01, 0.1 and 0.5 M NaCl. It can be reached that increasing concentration of NaCl increased the adsorbed amounts of PHCl, which justify that inorganic salts is one of

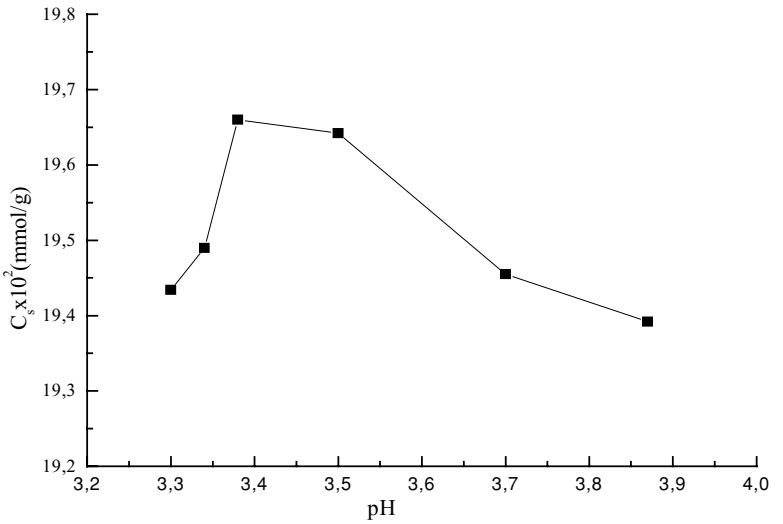

Fig. 7 The effect of pH on the adsorption of PHCl onto KSF

the main factor affecting adsorption process. The reason why the adsorption is increased with increasing of ionic strength may be that ionization of salt in aqueous solution binds water molecules and competition occurs at low level between drug molecules and water molecules for sorption sites.

3.6 Effect of pH

It is known that the pH is one of the most important factors which affect the sorption process. Some experiments were performed to find the optimum pH on the PHCl adsorption onto KSF for initial PHCl concentration of 0.8 mM using different initial pH values changing from 2 to 10. The amount of PHCl adsorbed was plotted against the equilibrium pH values. As was shown in Fig. 7, the optimum pH value is about 3.4. Since KSF is an acidic adsorbent, the equilibrium pH values are quite low. It can be realized that the amount of PHCl adsorbed increased until the pH value of 3.4. The pHs beyond that value, a decrease was observed. It is clear that adsorption process is dependent on the pH of the solution. In the equilibrium pH range studied, PHCl becomes positively charged due to acidic media. Beyond the pH of 3.4, a decrease in adsorption takes place owing to decrease of degree of ion-exchange between cationic drug and H^+ protons which exist on the KSF surface. Because at low pH values, silanol groups on the clay surface becomes more protonated. Moreover, according to the findings from DR isotherm and thermodynamic studies, the dominant adsorption type controlling adsorption was ion-exchange.

3.7 SEM analysis

The morphologies of KSF clay and PHCl loaded KSF was examined by scanning electron microscopy (SEM). It is easy to see the layered crystalline microstructure of KSF. The silicate particles disperse in various directions and appear to be flexible. As can be seen from Fig. 8, the length and thickness of the layers have different dimensions and can not be considered as homogenous.

The chemical content of the clay was determined using the semiquantitative EDS data (Fig. 8g, h and data was given below Fig. 8), which showed that the natural clay is composed of MgO, Al_2O_3, SiO_2, K_2O, CaO, and Fe_2O_3. After adsorption of PHCl onto KSF, some white grains appear on the surface of the layer structure of KSF. White grains may contain a big amount of drug molecules. This idea can be supported by EDS analysis of point A (white grains) and point B (dark part) shown in the micrographs of e. The EDS analysis of point A (white grains) and point B (dark place) was presented in Fig. 8. According to Fig. 8b, the percentage of C atom in point A and point B was found to be 28.98 and 17.98% respectively. This may indicate that the percentage of drug particles in white grains is quite high. The reason of high level of C atom in point B may be due to deposition of the powder samples on a carbon film for SEM analysis.

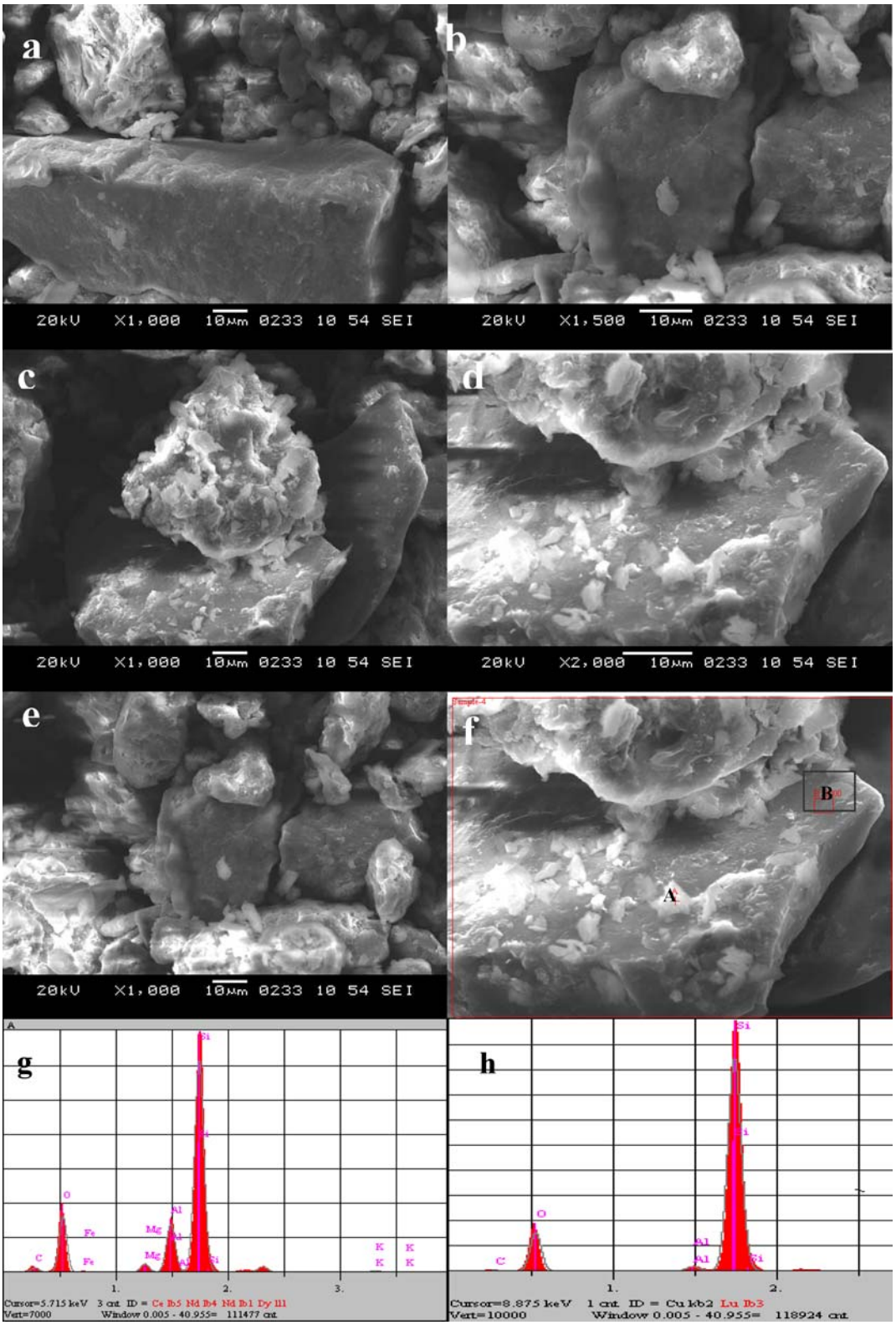

Fig. 8 SEM Micrographs of a) KSF (×1000) b) KSF (×1500) c) PHCl loaded KSF (×1000) d) PHCl loaded KSF (×1500) e) PHCl loaded KSF (×1000) f) PHCl loaded KSF (×2000) g) EDS analysis of point A h) EDS analysis of point B

4 Conclusion

The result showed that adsorption of PHCl onto KSF is particularly sensitive to pH, ionic strength, and temperature of the solution. The adsorption of PHCl onto KSF at pH 3.4 and high ionic strength was greater. Presumably, this may allow the release of Promethazine hydrochloride in intestinal medium due to distance between the pH values of maximum adsorption occurred and intestinal juice.

With respect to the suitability of pseudo-second-order and pseudo-first-order kinetic models for adsorption of PHCl onto KSF, it has been determined that adsorption kinetics of model drug PHCl obeys pseudo-second-order kinetics which belongs to better normalized standard deviation. Nonetheless it is probable that sorption of PHCl can not be only described by kinetic model and it is a complex process. This was likely combined control of pseudo-second-order kinetic model and intraparticle diffusion. Langmuir, Freundlich and Dubinin Raduschkevich equations were used to describe adsorption of drug onto KSF. The equations were in good agreement with experimental results. However it can be said that Langmuir model provides the best correlation with the data according to correlation coefficients. From the thermodynamic studies, it is determined that physical adsorption may also be possible for adsorption mechanism. The activation energy of sorption and the mean energy of adsorption E determined in the D-R equation support the ion-exchange mechanism as a dominant adsorption type. It can be concluded that adsorption process was administrated combined control of ion exchange and physisorption. The adsorption process was spontaneous and a positive value of standard enthalpy change shows the endothermic nature of adsorption process.

From the experiments conducted, it can be inferred that KSF may be used in the adsorption of PHCl. Moreover it is probable that releasing of PHCl from KSF in intestinal juice may also be possible.

Nomenclature

C_e	equilibrium concentration (mmol L^{-1})
C_s	the amount of sorbed (mmol g^{-1})
C_m	monolayer coverage (mmol g^{-1})
L	a constant (Langmuir)
K_f	relative adsorption capacity (mmol/g)
n_f	a constant (Freundlich)
X_m	the adsorption capacity (mol/g)
k	a constant (Dubinin Radushkevich)
E	the mean free energy change of adsorption (kJ mol^{-1})
A	Tempkin isotherm constant
B	Tempkin isotherm energy constant (dm^3 g^{-1})
b	Tempkin isotherm energy constant (J mol^{-1})
ΔG°	standard free energy change (kJ mol^{-1})
ΔH°	standard enthalpy change (kJ mol^{-1})
E_a	the activation energy of sorption process, (kJ mol^{-1})
ΔS°	standard entropy change (kJ mol^{-1} K^{-1})
K_c	the equilibrium constant
R	gas constant (J mol^{-1} K^{-1})
T	temperature (K)
k_1	the pseudo-first-order rate constant (min^{-1})
q_t	the amount of drug adsorbed at different times t (mg g^{-1})
q_1	the maximum adsorption capacity for pseudo-first-order adsorption, (mg g^{-1})
k_2	the pseudo-second-order rate constant, (g mg^{-1} min^{-1})
q_2	the maximum adsorption capacity for the second order adsorption process, (mg g^{-1})
K_p	the intraparticle diffusion rate constant, (mg g^{-1} $min^{-1/2}$)

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