Rev. Cubana Quím.
Vol. 28, no. 2, mayo-agosto, 2016, págs. 625-644, e-ISSN: 2224-5421

Termodinámica del proceso de adsorción in vitro de teofilina en carbón activado a partir de fluido gástrico simulado

Thermodynamic process of theophylline adsorption in vitro on to activated carbon in simulated gastric fluid

Dr. C. Carlos A. Rey-Mafull, Dr. C. Julio César-Llópiz, Dr. C. Dachamir Hotza, MSc. Raquel García-Gallardo
mafull@imre.oc.uh.cu

Instituto de Ciencia y Tecnología de Materiales (IMRE-UH)

Recibido: 28 de septiembre de 2015 Aprobado: 25 de enero de 2015

Resumen

Se estudia la adsorción in vitro de teofilina en carbones activados (NB, NE, BDH, Ch3J, Merck, Panreac, ML y M) en FGS a pH 1.2 4 h y temperaturas entre 300 - 317 K usando baño termostatado con agitación. Los datos experimentales fueron analizados con: Langmuir I y II, DR, Halsey, Freundlich, Harkins-Jura, Temkin and BET. Las muestras se caracterizaron por pH_{zpc} y N2 77 K. El modelo Langmuir TI fue el que tuvo mejor ajuste por regresión: lineal (R^2=098) y no lineal (R^2=0.95, RAMSE=43). El modelo asume adsorción en monocapa e interacciones específicas. La adsorción ocurre por quimisorción y exotérmicamente (ΔH = -36,81-88,70 kJ/mol) con q_m (316-587 mg/g). $\Delta G < 0$ explica el carácter espontáneo del proceso, siendo favorecido a bajas temperaturas. La $\Delta S < 0$ representa una disminución en los grados de libertad del sistema, adoptando una configuración molecular muy parecida al del estado disuelto.

Palabras clave: carbón activado, teofilina, parámetros termodinámicos, isotermas de adsorción.

Abstract

The *in vitro* adsorption of theophylline onto seven selected materials (NB, NE, BDH, Ch3J, Merck, Panreac, ML) was studied in simulated gastric fluid at pH 1.2 and 4 h by using shaker water bath within a temperature range 300 to 317 K in batch experiments. The experimental adsorption was fitted by eight isotherms models: Langmuir Type I and II, DR, Halsey, Freundlich, Harkins-Jura, Temkin and BET. Materials were characterized by $pH_{zpc,}$ and N_2 77 K. The best linear (R^2=098) and non linear (R^2=0.95, RAMSE=43) fittings of isotherms models were obtained with Langnuir TI which assumes monolayer adsorption and specific interactions. The theophylline adsorption was controlled by chemisorptions and exothermically process (ΔH = -36.81-88.70 kJ/mol) with maximal capacity, q_m (316-587 mg/g). The $\Delta G<0$ indicate the spontaneous character and more favourable at lower temperature. $\Delta S<0$ suggests a decrease in the order of the adsorbed system with losses of freedom willingly.

Keywords: activated carbon, theophylline, thermodynamic parameters, adsorption isotherms.

Introduction

Many legal and illegal drugs are frequently taken in excess, which can constitute a relevant health problem. Because of its large specific surface area and high degree of surface activity, activated carbon is remarkably efficient in the removal of many toxic compounds. It can have a variety of surface properties to meet the requirements of different applications. In pharmaceutical applications, it has been used as a very effective adsorbent for the treatment of drug overdose. Most uses and applications of activated carbon are based upon its structural properties and surface chemistry [1–7].

Theophylline (3,7-dihydro-1,3- dimethyl-1H-purine-2,6-dione) was employed as adsorbate in this experiment. Theophylline is a xanthine bronchodilator and a muscle relaxant, used in the treatment of both chronic and acute asthmatic attacks. Due to its low therapeutic index, careful control of its release from dosage forms has to be ensured, because high doses of theophylline may produce toxic effects (tachycardia, fever and convulsions). It is also a good hydrogen bonding acceptor according to its structure [6, 7].

The surfaces of activated carbon are heterogeneous and it has no regular atomic structure. The chemical nature of activated carbon combined with a high surface area, porosity distribution and superficial chemistry makes it an ideal medium for the adsorption of organic chemicals. The surface of the ACs has a certain amount of hydroxyls groups, which are good hydrogen bonding donors. Depending on the chemical structure of a molecule and the surface structure of an activated carbon, a molecule may interact with the particular polar functional group on the surface (specific interaction) [8, 9].

The interactions with the surface functional groups are specific and are accompanied by relatively high changes (negative) in enthalpy. The interactions with the basal carbon planes (non specific interaction) and the enthalpy changes are relatively small (negative or positive). The specific interaction between a drug and the surface can result from hydrogen bonding, dipole–dipole, dipole-induced dipole or ion–ion interactions (ionized drug with the ionized surface). The non-specific interaction could result from London dispersion forces or hydrophobic bonding [10–14].

The study of thermodynamic parameters involved in the process of adsorption may help to clarify and highlight which could be the mechanisms involved in this interaction surface. The quantitative contribution of these values will provide the necessary information that will allow direct studies of materials more efficient and effective for removing pharmaceutical compounds of high toxic level. Thus the other purpose of this paper is to evaluate the effect of surface of different AC on the adsorption of theophylline. In the present study, the adsorption isotherms of theophylline from SGF were measured by carrying out static adsorption experiments on all samples. The results were interpreted by eight isotherms models: Langmuir Type I and II, Dubinin - Radushkevich, Halsey, Freundlich, Harkins-Jura, Temkin and BET, and thermodynamics parameters by *Van't Hoff* plotted [12-14].

Material and methods

Activated carbon

The activated carbon employed here was the industrial grade to application in medical pharmaceutical and biotechnological field. All materials studied are industrially produced and purchased in the market. NB (Germany), NE (Holland), P (Spain), Merck (Germany), BDH (UK), Ch3J (China), ML (purified-Cuba) and M (not purified-Cuba).

The activated carbon M (not purified) was supplied by the Plant Production Baracoa Activated Carbon and treatment subsequently by acid/base process (ML). The particle

size of all samples is 100 % < 250 microns. All materials meet the requirements of USP 30 except M [12, 13].

Simulated gastric fluid (SGF)

The SGF was prepared according to the USP 30-NF 25, [15] was prepared with the active ingredient of theophylline as described: 2 g of NaCl were dissolved in 7 mL of concentrated HCl, enrazing to 1 L with distilled water free of CO_2 by adjusting the pH of the solution to 1,2. The drugs concentration used was 73,5 mg/L. The calibration curve in SGF was performed using a spectrophotometer UV/VIS [Ultrospec 2100 pro from Amersham Biosciences]. The optical density of all samples was determined with maximum absorbance at λ_{max} = 270 in the zone of Lambert Beer transmittance. The calibration curve was adjusted using the linear regression analysis or least squares quadratic, $R^2 > 99$. Each experiment was performed by triplicate.

Equilibrium adsorption experiments and analytical method

During adsorption process the amount of carbon used varied in the range of 0,06 g and was added to small vials, 6 mL, previously prepared with the drugs dissolved in SGF would be kept under constant stirring of 150 r.p.m for 4 h at different temperature 300, 306, 310 and 317 K. Once this time ending the samples were filtered to separate the solid phase and the liquid extract 5 ml solution for reading in the UV/VIS [Ultrospec pro from Amersham Biosciences]. Sampling was filtrated by removing 5 mL aliquots ending the experimental. Experimental solutions at desired concentrations were obtained by dilution of the stock solution with SGF readjusted to pH 1.2. Previously established linear Beer-Lambert relationships were used in the concentration analysis. For the solutions with higher concentrations, dilution was required to operate the analysis in the Beer-Lambert region. Percentage absorbance readings are taken from the calibration curve which determines the equilibrium concentration corresponding to each of the points of the isotherm. The amount of adsorption at equilibrium, q_e [mg/g], was

calculated by $q_e = \frac{(C_0 - C_e)V}{M}$, where [mg/mL] initial concentration [t = 0] and C_e [mg/ mL] equilibrium [t=4 h], V [L] is the volume of the solution and M [g] is the weight of carbon.

Specific surface area

Adsorption isotherms of N_2 (77 K) were obtained on a Quantachrome Autosorb surface analyzer system. The Brunauer, Emmett and Teller (BET) isotherm, equation (1), is the most usual standard procedure used when characterizing an activated carbon. The relative pressure $\left(\frac{P}{P_0}\right)$ range recommended in order obtaining the best straight line that is 0,05 to 0,3. To obtain the characteristic parameters of equation 2, it is necessary to plot $\left(\frac{P}{P_0}\right)$ vs. $\frac{\left(\frac{P}{P_0}\right)}{V_0\left(1-\frac{P}{P_0}\right)}$ terms, where P (mm Hg) is the applied pressure, P_o (mmHg) vapor pressure of N_2 at 77 K, V_o (cm^3/g) volume of adsorbed gas, V_m (cm^3) volume of gas adsorbed monolayer and C constant. [12, 13, 16, 17]

$$\frac{\left(\frac{P}{P_o}\right)}{V_o\left(1-\frac{P}{P_o}\right)} = \frac{1}{(V_m C)} + \frac{C-1}{V_m C}\left(\frac{P}{P_o}\right) \qquad (1)$$

Point of zero charge (pH_{zpc})

Z potential measurements were performed on a Malvern Instrument. The method involves dispersing the powdered solid in water at different pH and subjecting the suspension to an electric field. The point of zero charge corresponds to the pH value at which the particle does not migrate in the presence of an electric field. The different samples were dispersed ultrasonically during two intervals of 15 s to ensure dispersion

of these in the solution before analysis. All materials have a particle size of 100 % <250 microns.

Adsorption isotherms models

An equilibrium isotherm expresses the relation between the amounts of adsorbate removed from solution at equilibrium by unit of mass of adsorbent at constant temperature. Equilibrium data of the teophylline adsorption were processing by eight "two-parameter isotherms" including: Langmuir Tipo I and II, Freundlich, Dubinin - Radushkevich (DR), Temkin, BET, Halsey, and Harkins - Jura. The linear expressions of those isotherm equations and the way to obtain the isotherm parameters are given in table 1. The method of least squares was used for obtaining the trend lines and the characteristic parameters were determined from the respective linear form. Best fit among the isotherm models is assessed by the linear coefficient of determination (R^2). To non linear fitted isotherms of experimental data and models calculated was recorded for the higher R^2 value and the lower root mean square error (RMSE) test measures the difference between the experimental and model data were considered too. The mathematical form of this test statistic can be expressed as equation (2) [18–24].

$$\mathrm{RMSE} = \sqrt{\left(\frac{1}{n-p}\right)\sum_{1}^{n}\left(q_{e,\exp} - q_{e,calc}\right)^2} \qquad (2)$$

where

n is a number of data points; p, number of models parameters, $q_{e\ exp}$. experimental adsorption values (mg/g); $q_{e\ calc}$. calculated adsorption values (mg/g).

TABLE 1. ISOTHERMS AND THEIR LINEARIZED EXPRESSIONS

Isotherms	Non linear models	Linear models	plots
Langmuir	$q_e = q_m\left[\frac{K_L C_e}{1+K_L C_e}\right]$ $\Delta G = -RT\ln[K_L]$	TI $C_e/q_e = \left[\frac{1}{K_{LI} q_m}\right] + \left[\frac{C_e}{q_m}\right]$ TII $\frac{1}{q_e} = \left[\frac{1}{K_{LII} q_m}\right]\left[\frac{1}{C_e}\right] + \frac{1}{q_m}$	$\frac{C_e}{q_e}$ vs C_e $\frac{1}{q_e}$ vs $\frac{1}{C_e}$
Freundlich	$q_e = K_F C_e^{1/n}$	$\ln q_e = \ln K_F + n^{-1}\ln C_e$	$\ln q_e$ vs $\ln C_e$
D-R	$q_e = q_{max}\exp^{-D\varepsilon^2}$ $\varepsilon = RT\ln\left[1+\left(\frac{1}{C_e}\right)\right]$	$\ln q_e = \ln q_{max} - D\varepsilon^2$ $E = [2D]^{-0.5}$	$\ln q_e$ vs ε^2
Temkin	$q_e = \frac{RT}{b}\ln[K_{TK} C_e]$	$q_e = B\ln K_{TK} + B\ln C_e$ $B = \frac{RT}{b}$	q_e vs $\ln C_e$
BET	$q_e = \frac{\left(\frac{C_e}{C_0 - C_e}\right)}{\frac{1}{Kq_m} + \left(\frac{K-1}{Kq_m}\right) * \frac{C_e}{C_0}}$	$\frac{C_e}{q_e(C_0 - C_e)} = \frac{1}{q_m K} + \frac{K}{q_m C_e}$	$\frac{\left(\frac{C_e}{C_0 - C_e}\right)}{q_e}$ vs $\frac{C_e}{C_0}$
Harkins-Jura	$q_e = \left[\frac{A}{B - \log C_e}\right]^{1/2}$	$\frac{1}{q_e^2} = \frac{B}{A} - \frac{\log C_e}{A}$	$\frac{1}{q_e^2}$ vs $\log C_e$
Halsey	$q_e = \exp^{\left(\frac{\ln K_H - \ln C_e}{n}\right)}$	$\ln q_e = \frac{1}{n}\ln K_H - \frac{1}{n}\ln C_e$	$\ln q_e$ vs $\ln C_e$

Thermodynamic parameters of adsorption

The change in Gibbs free energy of the sorption process, ΔG^0_{ads}, equation 3, is related to the sorption equilibrium constant K_{ads} by the classical *Van`t Hoff* equation, equation 4: [18–19]

$$\Delta G^0_{ads} = -RT \ln K_{ads} \qquad (3)$$

Since $\Delta G^0_{ads} = \Delta H^0 - T\Delta S^0$, one gets where K_{ads} is obtained from the following relationships using the experimental data, equation 4, 5 and 6:

$$\ln K_{ads} = -\frac{\Delta H^0}{RT} + \frac{\Delta S^0}{R} \qquad (4)$$

$$K_{ads} = \left[\left(\frac{C_0 - C_e}{C_e}\right)\right]\left[\frac{V\rho}{w}\right] = \frac{q_e\rho}{C_e} \qquad (5)$$

$$\ln\left[\frac{q_e}{C_e}\right] = -\frac{\Delta H^0}{RT} + \frac{\Delta S^0}{R} \qquad (6)$$

where

ρ is the density of the solution (1 g/L), ΔG^0 the free energy change (kJ/mol), ΔH^0 the standard enthalpy change (kJ/mol), T the absolute temperature (K), K_{ads} is the equilibrium constant of interaction between the adsorbate and the ACs surface and R is the universal gas constant (8.31 J/mol K) and ΔS^0 the entropy of the system. The ΔH^0 can thus be determined from the slope of the *Van`t Hoff* plot ln (q_e/C_e) vs 1/T and the intercept represent the entropy variation ΔS^0.

Results and Discussion

Specific surface pore size and micropore volume of activated carbon

The values obtained after evaluating Eq. BET in its linear form are reported, table 2 and pores distribution, figure 1. Surface areas are in a normal range for this type of material. We distinguish 3 groups of surface areas corresponding to: a very high surface area of 1400 m^2/g (NB), a second value of surface area of 720 m^2/g (ML) and a third group with very close together and around 540 m^2/g (Ch3J, M and Panreac). With regard to surface area ratios established between these materials, with reference to the value of surface area of NB, and following the same order: 1 (NB), 1.64 (NE), 1.98 (ML) and 2.19 (Merck), 2.63 (BDH), 2.65 (Ch3J), 2.65 (M), 2.65 (P), respectively. These commercial materials are obtained by different activation processes and initial raw materials. The pore volume and sizes were calculated by: MP (Micropore method) and DFT (density functional theory).

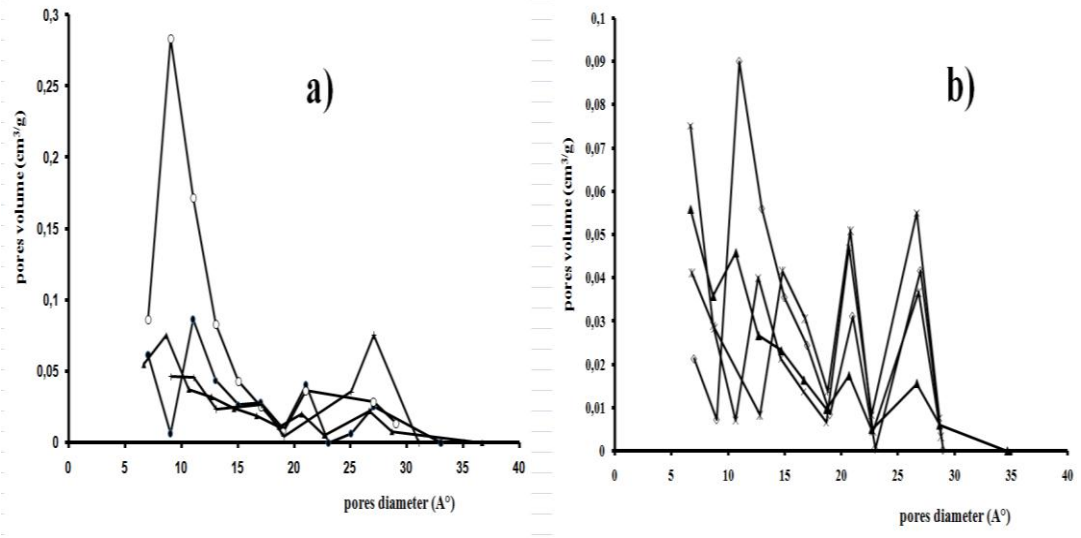

Figure 1. Distribution of pores (MP method) by N_2 adsorption at 77 K a) NB (o) NE (●) ML (Δ) BDH (+) b) Merck (x) Ch3J (◊) P (*) M (▲)

TABLE 2. SURFACE AREA OF AC (N_2 AT 77 K) OBTAINED FROM MODEL BET, TOTAL PORE VOLUME AND AVERAGE PORE SIZE OBTAINED FROM: TDF: DENSITY FUNCTIONAL THEORY[1] AND MP, MICROPORES METHOD[2]

Activated carbon	Surface area (m^2/g)	Micropores volume[1] (cm^3/g)	Average pore size[2] (Å)
NB	1 430	0,77	7,51
NE	869	0,37	7,60
ML	721	0,31	7,85
M	539	0,24	7,50
BDH	543	0,24	7,54
Ch3J	540	0,30	7,50
Merck	614	0,29	7,51
P	539	0,26	7,51

Potentiometric properties (pH_{zpc})

The pH_{pzc} is an important feature of any activated carbon, which is already, indicated the surface charge of this material in solution. The concentrations of H^+ and OH^- adsorbed on the surface are equal in pH_{pzc} and therefore, the surface charge is neutral. The electrokinetic properties of solids is a direct consequence of superficial chemical environment thus depending on the surface chemistry of the solid material to be placed

in an aqueous dispersion in order to retain certain adsorbates from the aqueous medium, present a given surface charge at the interface solid/liquid, which may be on average negative, positive or neutral. If the solid surface is on average positively charged dissolved species will negatively charged migrate towards a higher affinity for the solid surface and to be adsorbed. From the data obtained was the pH_{pzc}: NB (2,67), ML (6,25), M (4,55), Merck (5,55), BDH (2,53) and Panreac (2,65) respectively. The pH of the system which are used for these AC ranging from 1,2 to 7. The pH_{pzc} values in all cases analyzed are more than pH 1,2, so that the surface will have a net positive charge. Otherwise the surface of these activated carbons will turn negative.

Theophylline adsorption

As we know, theophylline is a pharmaceutical material used as a muscle relaxant and vasodilator, and is also a good hydrogen bond acceptor structure as shown in fig. 2, primarily interacting with phenolic hydroxyl groups, which are good hydrogen bond donors to which appear on the AC surface.

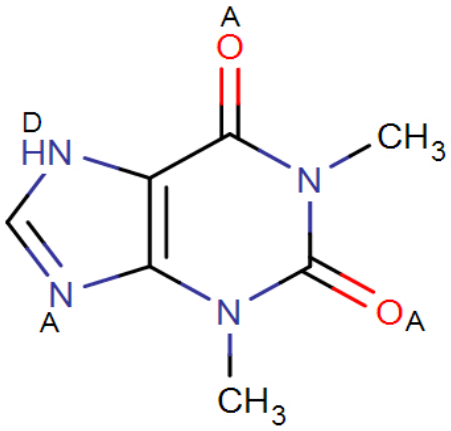

Figure 2. Molecular structure of theophylline ($C_7H_8N_4O_2$): A (aceptor) and D (donor)

The values obtained from the theophylline adsorption study are shown in figures 3-4 and tables 3-4.

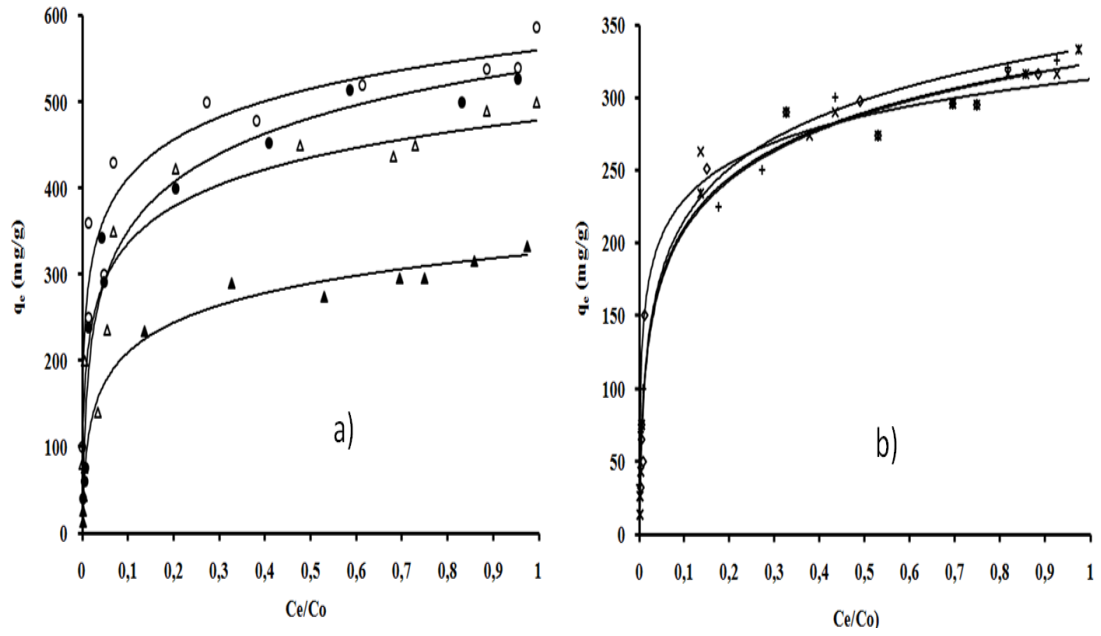

Figure 3. Experimental data of adsorption isotherms profile of theophylline in SGF: a) NB (o) NE (●) M (▲) ML (Δ) b) Merck (x) BDH (+) Ch3J (◊) P (*)

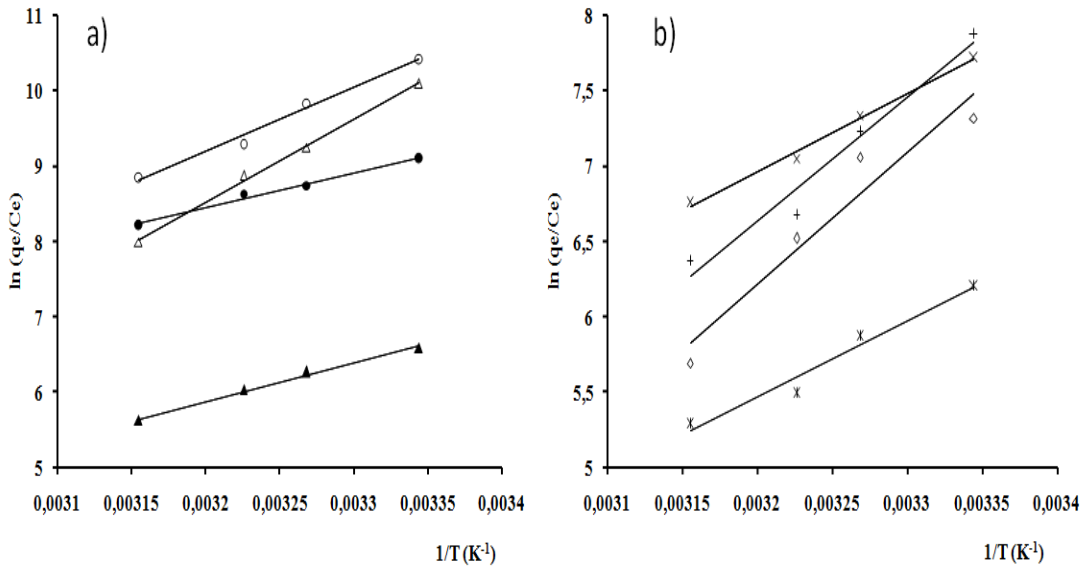

Figure 4. Van`t Hoff plot of adsorption equilibrium constant $K_{ads.}$ for adsorption of theophylline onto: a) NB (o) NE (●) M (▲) ML (Δ) b) Merck (x) BDH (+) Ch3J (◊) P (*)

Theophylline is a weak acid so that it shows very little dissociation solution, its pK_a = 8.79 > pH = 1.2. This low dissociation means that the predominant species in solution is a molecular species which is unlikely to occurred dissociation of the molecule. The solubility of theophylline is not affected across a wide pH range (1-7). Yang, W. [21]

did not encounter decreasing the adsorption of organic aerogels theophylline AC and the effect of pH variation. Bailey, DN [25], did not find the pH range no significant effect for the different drugs, including theophylline in AC. Is also common in both studies that theophylline at acid pH and well adsorbed too. Although recognizing the effect of temperature, which in our case is not a problem because our system operates at a constant temperature, so that competitively, solubility and adsorption in the system will not have competition [26].

The adjustment of each adsorption isotherm model was evaluated as shown in table 3. The model that best fits the experimental data is the Langmuir TI. We believe that the results obtained theophylline adsorption can be explained by a single model. For this reason it is accepted that the monolayer formation process adsorption means with high levels of total energy involved $\Delta H > -20.9$ kJ/mol, table 4.

Navarrete, *et al*, [26, 27] explain the phenomenon of adsorption, through two stages: stage one monolayer responsive to the Langmuir model and involves enthalpies of the order of up -26,3 and -42,4 kJ/mol and the other multi-layer formation process (oligomerization) involves enthalpies of up to -19,1 and -15,3 kJ/mol. They employed a model mixed Langmuir-Freundlich. In this work the model employed are not mixed. If we pick up the values of ΔH^0 obtained by Navarrete. [26, 27] we can see that they are in the same order as those calculated in this study. For example: -26,3 (to stage one) + -15,3 (second stages) = - 41,6 kJ/mol and -42,4 (to stage one) + -19,1 (second stages) = - 61,5 kJ/mol for AC with surface areas of 757 and 1085 m^2/g, respectively. In this case, the ΔH^0 total adsorption process as a single value and are in the range of -36,81 to 88,70, table 4. By the thermodynamic values reached (figure 4, table 4), in the theophylline adsorption process can be characterized by: $\Delta H < 0$, $\Delta G < 0$ and $\Delta S < 0$. The process was controlled by quase chemical and exothermically conditions (ΔH

= -36.81-88.70 kJ/mol). When the magnitude of the ΔH values lies in the range of 2.1 to 20.9 and 80 to 200 kJ/mol, for physical and chemical adsorption respectively. [28, 29] The negative value of ΔG indicates the feasibility and spontaneity of the adsorption process. The variation of $\Delta S < 0$ suggests an increase in the order of the adsorbed system on the surface of the AC, and a decrease in the system of freedom willingly.

Regarding the dimensions the size of theophylline molecule is not a barrier to transport by diffusion through the micropores of AC. Whereas the diameter of theophylline molecule is about 5.9 Å and that the size requirements to avoid steric effects during diffusion through the pores should range between 1.2 -1.7 of the diameter adsorbed molecule which corresponds to 7.08 -10.3 Å pore diameters of the AC. Pores not find the access limitation in this respect for all AC and pore size sufficient to adsorbed the theophylline molecule, figure 1. [21–23]

The experimental values q_m obtained in this study are of the order reported in the literature for this type of drug. Yang, W. [21] (pH = 1.2) reported from 83.9 to 208 mg/g. Navarrete, R *et al.* [26,27] reported values of 331-341 mg/g and Myotoku, M *et al.*, [30] reported 264.2 mg/g.

The effectiveness of the degree of compaction of the molecule of theophylline on the surface of the activated carbon is related to the optimal distribution of the sites of adsorption to the maximum extent of packaging of this molecule. To calculate the molecular cross sectional area of theophylline ($Å^2$) the following equation 7 was employed:

$$A_o = {A_{SP} MW} \Big/ {N_0 K} \qquad (7)$$

Where: A_{sp} (m^2/g) is the specific surface area of the activated carbon, obtained from BET analysis of N_2 vapour adsorption data, MW is the molecular weight of

theophylline, K is the number of moles of theophylline adsorbed per gram of adsorbent at maximum surface coverage, and N_0 is the Avogadro's number.

The determination of the area of the molecule of theophylline shows a better orientation on the surface of activated carbon, in an order of priority NE > BDH > NB. The cause could be a better distribution of the active sites of adsorption, in both textural and functional plane respectively. The calculation of the area which occupies the theophylline molecule on AC (table 5) are well represented by the models of LTI and LTII with relative error -6% and 0.13% respectively.

To determine whether or not significant differences (α = 95%) in theophylline adsorption capacity $q_{e\ experimental}$ (table 6) among all materials studied were made multiple range analysis tests. The method is based on calculating the shortest Fisher significant difference (LSD). This test confirms that significant differences were not found between the experimental values of AC/ML compared to other international standards; however not with AC/NB and AC/NE. This corroborates that the AC/ML could be considered a competitive material in terms of theophylline adsorption capacity. All adsorption capacity values obtained for the materials studied are very good and competitive, including those reported in the literature.[7, 21, 26, 27, 30]

TABLE 3. CHARACTERISTIC PARAMETERS OF MODELS

		Activated carbon								
Models	**Parameters**	**ML**	**NB**	**NE**	**P**	**M**	**BDH**	**Merck**	**Ch3J**	**Average**
DR	D	$1x10^{-4}$	$8x10^{-5}$	$1,5x10^{-4}$	$2x10^{-5}$	$2x10^{-4}$	$1x10^{-4}$	$17x10^{-5}$	$12x10^{-5}$	
	E	71	79	58	51	50	71	54	65	
	q_m	992	1086	1901	1339	1224	665	1212	821	
linear model	R^2	0,86	0,87	0,87	0,91	0,88	0,96	0,92	0,88	0,89
q_{exp}/q_{calc}	R^2	0,89	0,887	0,88	0,90	0,91	0,98	0,92	0,91	0,91
q_{exp}/q_{calc} (non linear)	RAMSE	57	62	93	45	65	18	44	37	53
LTI	q_m	500	565	529	347	326	330	338	312,5	
	K_{LI}	333	443	386	96	307	303	296	320	
linear model	R^2	0,99	0,99	0,99	0,94	0,99	0,99	0,99	0,99	**0,98**
q_{exp}/q_{calc}	R^2	0,88	0,89	0,97	0,97	0,98	0,95	0,98	0,96	**0,95**
q_{exp}/q_{calc} (non linear)	RAMSE	84	74	40	30	19	40	23	31	**43**
LTII	q_m	500	588	435	333	303	200	500	335	
	K_{LII}	$8x10^{-7}$	$6x10^{-7}$	$3x10^{-6}$	$7x10^{-6}$	$6x10^{-7}$	$2x10^{-7}$	$6x10^{-6}$	$4x10^{-6}$	
linear model	R^2	0,96	0,95	0,95	0,99	0,97	0,82	0,97	0,98	0,95
q_{exp}/q_{calc}	R^2	0,91	0,78	0,97	0,94	0,94	0,48	0,98	0,96	0,87
q_{exp}/q_{calc} (non linear)	RAMSE	273	124	64	49	94	112	139	37	112
Freundlich	K_F	982	1075	1808	1380	1094	665	639	796	
	n	4,02	4,65	2,60	2,05	2,31	4,10	4,10	3,25	
linear model	R^2	0,86	0,86	0,86	066	0,92	0,95	0,96	0,87	0,87
q_{exp}/q_{calc}	R^2	0,89	0,88	0,71	0,73	0,78	0,98	0,78	0,73	0,81
q_{exp}/q_{calc} (non linear)	RAMSE	64	64	384	213	241	20	39	254	160
Halsey (pend -)	K_H	$10,4x10^{11}$	$125x10^{12}$	$30,4x10^{7}$	$6,4x10^{5}$	$11,2x10^{12}$	$112x10^{11}$	$2,6x10^{7}$	$12x10^{8}$	
	n	4,02	4,65	2,60	2.07	4,65	4,65	2,29	3,25	
linear model	R^2	0,86	0,86	0,85	0,66	0,86	0,86	0,86	0,87	0,84
q_{exp}/q_{calc}	R^2	0,76	0,90	0,88	0,63	0,98	0,12	0,98	0,43	0,71
q_{exp}/q_{calc} (non linear)	RAMSE	4824	3938	27976	13451	2300	670	4656	3823	7704,75
Temkin	K_{TK}	29156	78108	10127	4602	9020	83577	2647	21547	
	B	62	65	81	53	50	36	51	45	
	b	41	40	32	48	52	72	50	57	
linear model	R^2	0,88	0,93	0,96	0,92	0,93	0,93	0,93	0,95	0,94
q_{exp}/q_{calc}	R^2	0,88	0,93	0,96	0,92	0,93	0,93	0,95	0,95	0,94
q_{exp}/q_{calc} (non linear)	RAMSE	53	46	40	39	13	30	56	31	39
H-J	A	$25x10^{3}$	$50x10^{3}$	$6,7x10^{3}$	$0,8x10^{3}$	$8,3x10^{3}$	$6,7x10^{3}$	$1x10^{3}$	$9,1x10^{3}$	
	F	1,25	1,50	1,60	1,50	1,25	1,47	1,44	1	
linear model	R^2	0,65	0,59	0,58	0,49	0,81	0,63	0,39	0,60	0,64
q_{exp}/q_{calc}	R^2	0,89	0,89	0,93	0,93	0,81	0,82	0,63	0,91	0,85
q_{exp}/q_{calc} (non linear)	RAMSE	316	359	364	210	209	221	225	194	262
BET	q_m	24	25	18	29	10	25	15,5	59	
	A	10	154	56	12	26	154	32	17	
linear model	R^2	0,44	0,57	0,62	0,63	0,50	0,57	0,72	0,74	0,60
q_{exp}/q_{calc}	R^2	0,14	0,24	0,23	0,21	0,20	0,11	0,35	0,31	0,22
q_{exp}/q_{calc} (non linear)	RAMSE	1297	438	404	233	276	1372	265	261	568

TABLE 4. THERMODYNAMICS PARAMETERS OF THEOPHYLLINE ADSORPTION ONTO ACS IN SGF

Activated carbon	Thermodynamics parameters				
	ΔH^0 (kJ/mol)	ΔS (J/k mol)	$T\Delta S^0$ (J/mol)	ΔG^0 (kJ/mol)	R^2
			43 643	-25.26	
NB	-68.91	-136	44 664	-24.39	0,98

			45 248	-23.35	
			46 270	-22.75	
			6 420	-19.07	
ML	-88.70	-215	6 578	-17.92	0,99
			6 667	-16.77	
			68 069	-16.37	
			29 087	-15.98	
M	-45.31	-97,3	29 768	-15.54	0,99
			30 157	-15.15	
			30 838	-14.46	
			47 082	-24.44	
BDH	-66.05	-157	48 184	-22.92	0,96
			48 814	-22.31	
			49 916	-20.53	
			22 131	-18.70	
Merck	-74.05	-74	22 649	-18.18	0,99
			22 946	-17.70	
			23 464	-17.37	
			64 205	-15.0	
Panreac	-40.57	-85,4	65 708	-14.57	0,93
			66 567	-13.81	
			68 070	-13.61	
			52 701	-17.73	
Ch3J	-70.84	-176	53 934	-17.50	0.91
			54 639	-16.37	
			55 873	-14.62	
			14 749	-22.06	
NE	-36.81	-49.3	15 095	-21.69	0.98
			15 292	-21.69	
			15 637	-21.13	

TABLE 5. ESTIMATED CALCULATION OF THE VALUE OF SPECIFIC SURFACE AREA FOR THEOPHYLLINE MOLECULE TAKING AS REFERENCE THE VALUE 55.6 Å²

Models	Activated carbon									
	ML	NB	NE	P	M	BDH	Merck	Ch3J	Average Å²	% relative error
DR	21.75	39.44	13.68	12.05	13.18	24.43	15.16	19.68	19.92	64
LTI	43.15	75.74	100.40	46.48	49.47	49.24	54.36	51.63	58.81	**-6**
LTII	43.15	72.77	59.78	48.43	53.23	81.24	36.75	48.52	55.49	0.13
Average Å²	36	63	58	35	37	52	35	40		
% relative error	35	13	4	37	33	6	37	28		

TABLE 6. MULTIPLE RANGE TESTS

Statistic parameters	Activated carbon							
	ML	NB	NE	P	M	BDH	Merck	Ch3J
Homogeneous groups	X	X	X	X	X	XX	X	X
Contrast	---	---	---	NB/P NE/P ML/P	NB/M NE/M ML/M	NB/BDH NE/BDH ML/BDH	NB/Merck NE/Merck ML/Merck	NB/Ch3J NE/Ch3J ML/Ch3J
Coeff. of variation. (%)	36	44	4	66	62	58	64	55
Average $q_{e\ exp.}$(mg/g)	341	418	326	191	200	214	206	199
$q_{m\ exp.}$ (mg/g)	500	587	527	300	333	336	357	316
St. error	45	45	53	37	39	35	41	33

Conclusion

The best linear (R^2=098) ***and*** non linear (R^2=0.95, RAMSE=43) ***fittings*** of ***isotherms models*** were obtained with Langmuir TI ***which assumes monolayer adsorption and specific interactions of theophylline in FGS and was found to be applicable for ACs. By the thermodynamics values reached in the theophylline adsorption process can be characterized by: ΔH < 0, ΔG < 0 and ΔS < 0. The process was controlled by quase chemical and*** exothermically conditions (ΔH = ***-36.81-88.70 kJ/mol). The negative value of ΔG indicates the feasibility and spontaneity of the adsorption process. The***

variation of ΔS < 0 suggests an increase in the order of the adsorbed system on the surface of the ACs, and a decrease in the system of freedom willingly. The calculation of the area which occupies the theophylline molecule on ACs is well represented by the models of LTI and LTII with relative error -6% and 0.13% respectively. In consequence, these materials may be suggested as antidote for theophylline.

Gratitude

The authors thanks to Programa de Estudantes-Convênio de Pós-Graduação (PEC/PG), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (Capes), Brazil Referencias.

Bibliographic references

1. QIANG, G., WURSTER, E., "Specific and non-specific interactions of procaine with activated carbon surfaces", *J. of Colloid Interf. Sci.*, 2011, 58(3), 541-546.

2. AMERICAN ACADEMY OF CLINICAL TOXICOLOGY AND EUROPEAN ASSOCIATION OF POISONS CENTRES AND CLINICAL TOXICOLOGISTS, "Position Statement and Practice Guidelines on the Use of Multi-Dose Activated Charcoal in the Treatment of Acute Poisoning", *Clin. Toxicol.*, 1999, 37(6), 731–751.

3. AMERICAN ACADEMY OF CLINICAL TOXICOLOGY AND EUROPEAN ASSOCIATION OF POISONS CENTRES AND CLINICAL TOXICOLOGISTS, "Position Paper: Single-Dose Activated Charcoal", *Clin. Toxicol.*, 2005, 43(2), 61–87.

4. SOTELO LUIS, J. *et al*.,"Competitive adsorption studies of caffeine and diclofenac aqueous solutions by activated carbon", *Chem. Eng. J.*, 2014, 240(2), 443–453.

5. NAM WOO, S. *et al*., "Adsorption characteristics of selected hydrophilic and hydrophobicmicropollutants in water using activated carbon", *J. Hazardous Mater.*, 2014, 270(3), 144–152.

6. HAMZAH, M. M., "An in vitro adsorption study of theophylline on some drugs and excipients"**,** *J. Pharm. Research*., 2010, 3(1), 49-52.

7. YANG, W., WU, D., FU, ·R., "Adsorption of theophylline from aqueous solution on organic aerogels and carbon aerogels", *J. Porous Mater.*, 2009, 16(2), 507–512.

8. BANDOSZ, J. T., "Activated Carbon Surfaces in Environmental Remediation", first edition, New York: Elsevier, 2006, 571 p., ISBN-13: 978-0-12-370536-5

9. VESNA, R., VLADISLAV, R., MARIJA, K., OTMAN, O., ALINE, A., "The adsorption of pharmaceutically active compounds from aqueous solutions onto activated carbons", *J. Hazard Mater.*, 2014, 282(1), 43 – 54.

10. HADI, M., SAMARGHANDI, R., MCKAY, G., "Equilibrium two-parameter isotherms of acid dyes sorption by activate carbons: Study of residual errors", *Chem. Eng. J.*, 2010, 160(2), 408 – 416.

11. AZMIER, M., KHABIBOR, N., "Equilibrium, kinetics and thermodynamic of Remazol Brilliant Orange 3R dye adsorption on coffee husk-based activated carbon", *Chem. Eng. J*, 2011, 170(1), 154 – 161.

12. MAFULL REY, C. A. *et al.*, "Comparative study of the adsorption of acetaminophen on activated carbons in simulated gastric fluid", *Springer Plus.* 2014, 3(48), 1-12.

13. MAFULL REY, C.A. *et al.* "Thermodynamic Parameters of Adsorption from Systems Activated Carbon Chlordiazepoxide and Activated Carbon-Diazepam", *Rev. Cubana de Química*, 2013, 25(2), 235-249.

14. GHAEDI, M., ANSARI, A., SAHRAEI, R., "ZnS:Cu nanoparticles loaded on activated carbon as novel adsorbent for kinetic, thermodynamic and isotherm studies of Reactive Orange 12 and Direct yellow 12 adsorption" , *Spectrochim. Acta Part A*, 2013, 114(2), 687– 694.

15. UNITED STATED PHARMACOPEIA, USP, USP30-NF25, Activated Charcoal, p. 1701.

16. MORENO, C., CARRASCO, M., LÓPEZ, R., ALVAREZ, M., " Chemical and physical activation of olive-mill waste water to produce activated carbons", *Carbon*, 2001, 39(9), 1415 - 1420.

17. SMÍŠEK, M., CERNÝ, S., *Active Carbon, Manufacture, Properties and Applications*, Amsterdam: Elsevier Publishing Co., 1970. 479 p.

18. KUMAR, A., PRASAD, B., MISHRA, I., "Isotherm and kinetics study for acrylic acid removal using powdered activated carbon", *J. Hazard Mater*., 2010, 176(1-3), 774 – 783.

19. KUMAR, A., PRASAD, B., MISHRA, I., "Adsorptive removal of acrylonitrile by commercial grade activated carbon: Kinetics, equilibrium and thermodynamics", *J. Hazard Mater*, 2008, 152(2), 589 – 600.

20. HADI, M., SAMARGHANDI, R., MCKAY, G., *"*Equilibrium two-parameter isotherms of acid dyes sorption by activate carbons: Study of residual errors", *Chemical Eng. J.*, 2010, 160(2), 408 - 416.

21. YANG, W., WU, D., FU, R., *"*Adsorption of theophylline from aqueous solution on organic aerogels and carbon aerogels*", J Porous Mater*, 2009, 16(5), 507-512.

22. QUESADA, I., JULCOUR, C., JAVIER, J. ANNE, WILHELM, A. DELMAS, H., "Comparative adsorption of levodopa from aqueous solution on different activated carbons", *Chem Eng J*., 2009, 152(1), 183-188.

23. RICHARD, D., DELGADO, M., SCHWEICH, D., *"*Adsorption of complex phenolic compounds on active charcoal: Adsorption capacity and isotherms", *Chem Eng J.*, 2009, 148(1), 1-7.

24. LIU, Q. S., ZHENG, T., WANG, P., JIANG, J. P., LI, N., *"*Adsorption isotherm, kinetic and mechanism studies of some substituted phenols on activated carbon fibers", *Chem Eng J*., 2010, 157(2-3), 348-356.

25. BAILEY, D. N., BRIGGS, J. R., *"*The effect of ethanol and pH on the adsorption of drugs from simulated gastric fluid onto activated charcoal", *Ther. Drug Monit*, 2003, 25(3), 310 - 313.

26. NAVARRETE, R. A. *et al.*, "Interactions of xanthines with activated carbon I. Kinetics of the adsorption process", *Appl. Surf. Sc*., 2006, 252(3), 6022–6025.

27. NAVARRETE, R. A. *et al.*, "Interactions of xanthines with activated carbón II. The adsorption equilibrium", *Appl. Surf. Sc*., 2006, 252(5), 5056–6000.

28. SHIN, S., JANG, H., YOON, I., *"*A study on the effect of heat treatment on functional groups of pitch based activated carbon fiber using FTIR" , *Carbon*, 1997, 35(12), 17-39.

29. INDRA, D. *et al.*, *"Removal* of congo red from aqueous solution by bagasse fly ash and activated carbon: Kinetic study and equilibrium isotherm analyses", *Chemosphere*, 2005, 61(4), 492–501.

30. MYOTOKU, M., SUYAMA, T., HAJI, H., "Examination of Utility Kremezin as an Antidote for Acute Drug Poisoningt"*, Jpn. J. Hosp. Pharm.*, 1995, 21(6), 483-487.