Model Selection for the Adsorption of Phenobarbital by Activated Charcoal

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Activated charcoal is known to adsorb a wide variety of substances from solution, and several equations have been used to fit the resulting adsorption data. The determination of the correct model to fit phenobarbital adsorption onto activated charcoal was made using a calorimetric method. The differential heats of displacement of water by phenobarbital for four activated charcoals were determined and found to be linearly related to the amount of phenobarbital adsorbed. The activated charcoals studied had statistically similar heats of displacement. The linear relationship between heat evolved and the amount of phenobarbital adsorbed is consistent with the assumptions implicit in the Langmuir model.

KEY WORDS: phenobarbital; adsorption; activated charcoal; Langmuir; Freundlich; heat of displacement.

INTRODUCTION

Although the Langmuir model has most frequently been used to describe adsorption of solutes from solution, recent articles in the literature (1,2) have proposed the Freundlich equation to be more appropriate for the characterization of solute adsorption by activated charcoals. Additionally, other authors have fit data involving charcoal to an empirical second-order polynomial equation (3), a three-parameter equation (4), a power equation (5), and a modified Freundlich equation (2,6). Generally, the selection of any one particular treatment has been based upon the correlation coefficient obtained from the fitted equation, and not on the fundamental physicochemical properties that should govern the system. The Langmuir and Freundlich treatments differ fundamentally with respect to the requirements placed upon the differential heat of adsorption as a function of the extent of adsorbent surface coverage. These heat of adsorption requirements can be used, for any adsorbate/adsorbent system, to determine which treatment is more appropriate for describing solute adsorption from solution.

In this study, the aforementioned approach was used to determine the most appropriate way to characterize the adsorption of phenobarbital by four activated charcoals. Such a determination is essential to ongoing *in vivo* studies in which adsorbent effectiveness in phenobarbital detoxification is being related to the surface characteristics of the adsorbents.

MATERIALS AND METHODS

Simulated intestinal fluid, U.S.P. (without pancreatin; SIF), was prepared according to the *United States Pharmacopoeia, Volume XXI.*

Approximately 913 mg of phenobarbital, free acid, was dissolved in sufficient SIF to provide a final volume of 1000 ml. Eight different aliquots were diluted to 100 ml, using the same batch of SIF as was used to prepare the phenobarbital stock solution, and heated in a water bath at 37°C.

All charcoal samples were vacuum-dried (100°C, 25 μm Hg) for 24 hr prior to use. The charcoals differed greatly in surface area as can be seen in Table I. Surface areas were determined by BET analysis of nitrogen vapor adsorption isotherms, at relative pressures of 0.05 to 0.25, using a Quantasorb instrument (Quantachrome Corp., Syosset, NY). A Tronac Model 450 isoperibol calorimeter (Tronac Inc., Orem, UT) was used to measure the heats of displacement and heats of solution. The calorimeter was interfaced to an Apple IIE computer through an ADALAB analog-to-digital converter and accompanying signal amplifier. The bath temperature was maintained at 37 ± 0.0004°C and the stirrer was operated at 600 rpm. The water-bath temperature was measured using an NBS (National Bureau of Standards)-certified thermometer.

Twenty-five (25.0) ± 0.2 mg of activated charcoal was placed in a cylindrical stainless-steel ampoule which had thin glass endplates (7). The charcoal samples were then wetted with SIF. The ampoule was sealed and mounted in the ampoule breaking/stirring device. Fifty milliliters of the appropriate phenobarbital solution was placed in the reaction vessel (a Dewar flask). An initial system heat capacity was determined, the sample run was made, and then a final heat capacity was determined. Since the initial and final heat capacities should be essentially equal (no chemical reaction was occurring), the average value of the two heat capacities was employed in the calculation of the phenobarbital integral heat of displacement. The sample run was initiated by breaking the two glass endplates of the sample ampoule and was concluded when the rate of temperature change in the reaction vessel had returned to its baseline value. The stirrer was stopped after the final heat capacity determination and the charcoal was allowed to settle for 15 min. A 1.0-ml aliquot of the supernatant was removed from the Dewar flask and ultrafiltered. A 150-μl aliquot of the ultrafiltrate was removed and diluted to 5 ml with 0.1 *N* NaOH. This solution was analyzed for phenobarbital concentration spectrophotometrically at 254 nm. These paired calorimetric and spectrophotometric determinations were done in duplicate. Figure 1 shows a typical adsorption isotherm. The Langmuir and Freundlich constants, as determined by nonlinear regression analysis, are listed in Table II.

The integral heat of solution was determined in a similar manner. An appropriate amount of phenobarbital was placed in the sample ampoule, described above, which was then sealed and mounted in the ampoule breaking/stirring device. Fifty milliliters of SIF was placed in the reaction vessel and the integral heat of solution determined as previously described. Calorimetric determinations of the integral heats of solution were done in triplicate.

The four activated charcoals studied were SuperChar (Gulf Bio-Systems, Inc., Dallas, TX), Darco KB-B (Ameri-

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Table I. Activated Charcoal Surface Areas as Determined by BET Analysis of Nitrogen Vapor Adsorption Isotherms

Charcoal sample	Surface area (m^2/g) ± SD
SuperChar	2900 ± 170
Darco KB-B	1490 ± 20
Norit B Supra	1510 ± 30
Norit, U.S.P. XX	940 ± 60

can Norit Company, Inc., Jacksonville, FL), Norit, U.S.P. XX (American Norit Company, Inc., Jacksonville, FL), and Norit B Supra (American Norit Company, Inc., Jacksonville, FL).

RESULTS AND DISCUSSION

The selection of the appropriate model to describe the physical adsorption of phenobarbital by activated charcoal should be based upon the assumptions of the model and the physicochemical behavior of the system. While statistical evaluations of the fits of models to the data are useful, both previous (8) and current (Table II) work on this system have indicated that differences in the correlation coefficients are small. Furthermore, if decisions are based upon correlation coefficients alone, Table II indicates that different charcoals require different models. Although this situation is possible, it would seem that a more fundamental test of the model applicability should be employed.

The Langmuir model is given by the relationship

$$\frac{n_2^s}{m} = \frac{k_1 k_2 C_{eq}}{1 + k_1 C_{eq}} \qquad (1)$$

where n_2^s is the amount of solute adsorbed, m is the mass of adsorbent, C_{eq} is the concentration of unadsorbed solute at equilibrium, k_1 is the affinity constant, and k_2 is the capacity of an adsorbent for a given material. This model assumes that the differential heat of adsorption is independent of surface coverage, all the sites available for adsorption are energetically equivalent, the adsorbed phase is confined to a monolayer, there are no lateral interactions between adsorbate molecules, the adsorbate solution is very dilute, and there is no mixed film formation at maximum solute adsorption (9). If the integral heat of adsorption is linearly related to the amount of solute adsorbed, the Langmuir model is the appropriate model to fit the data.

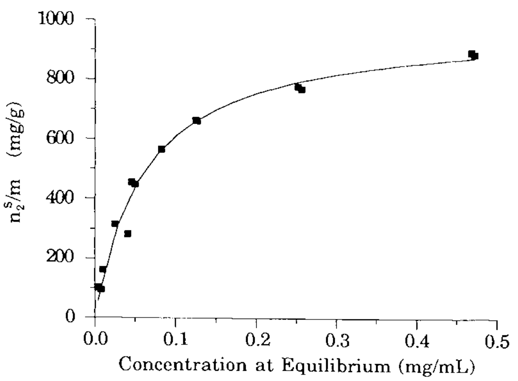

Fig. 1. Nonlinear regression plot of the Langmuir adsorption isotherm for SuperChar activated charcoal.

Table II. Model Parameters Obtained by Nonlinear Regression[a]

System	Langmuir equation	Freundlich equation
Darco KB-B, SIF, $n = 2^b$		
k_1 (ml/mg)	8.0	$P = 0.371$
k_2 (mg/g)	383	K (mg/g) = 396
r	0.962	0.990
θ^c	19–93	
SuperChar, SIF, $n = 2$		
k_1 (ml/mg)	16.4	$P = 0.371$
k_2 (mg/g)	980	K (mg/g) = 1255
r	0.991	0.970
θ	10–91	
Norit B Supra, SIF, $n = 2$		
k_1 (ml/mg)	45.7	$P = 0.239$
k_2 (mg/g)	483	K (mg/g) = 666
r	0.947	0.997
θ	22–96	
Norit, U.S.P. XX, SIF, $n = 2$		
k_1 (ml/mg)	82.7	$P = 0.232$
k_2 (mg/g)	184	K (mg/g) = 277
r	0.971	0.989
θ	47–98	

[a] Data obtained by UV analysis of the calorimeter cell contents at the end of each calorimetric determination.

[b] n is the number of runs, with each run consisting of eight points.

[c] Percentage of surface coverage by phenobarbital.

The Freundlich equation is given by the relationship

$$\frac{n_2^s}{m} = K C_{eq}^P \qquad (2)$$

where K is a constant related to the capacity of the adsorbent for the adsorbate and P is a constant related to the affinity of the adsorbent for the adsorbate. The Freundlich equation was first employed in a purely empirical manner (10). This equation can, however, be derived with the assumption that variation in the amount adsorbed with change in surface coverage is entirely due to change in the differential heat of adsorption (9). On that basis, the Freundlich equation is herein referred to as a model. If the integral heat of adsorption varies as a power function with the amount of solute adsorbed, the Freundlich model is the appropriate model to fit the data.

In general, the differential heat of adsorption can be expressed as

$$\overline{Q}_2 = \left(\frac{\partial Q_2}{\partial n_2^s}\right)_{T,P,\Sigma,n_1^s} \qquad (3)$$

where $\overline{Q}_2$ is the differential heat of adsorption of phenobarbital, Q_2 is the integral heat of adsorption of phenobarbital, n_2^s is the number of moles of phenobarbital adsorbed, Σ is the surface area of the solid/liquid interface, and n_1^s is the number of moles of water adsorbed (11). This expression cannot be employed directly in the calorimetric experiment. If clean, dry, activated charcoal is immersed in a phenobarbital solution, there are thermal effects arising from the adsorption of phenobarbital (exothermic), the adsorption of water (exothermic), and the dilution of the bulk phenobarbital solution (endothermic). Water and phenobarbital will have different heats of adsorption and the relative amounts of the two components adsorbed will vary continuously as solution concentration is increased. To simplify the experiment, the activated charcoal was prewet with SIF prior to ampoule closure. During the phenobarbital adsorption process that occurred after ampoule breakage, some of the water adsorbed on the charcoal surface was displaced by the adsorbing phenobarbital molecules. The thermal processes occurring in the calorimeter cell were the endothermic desorption of water molecules, the exothermic adsorption of phenobarbital, and the endothermic dilution of the bulk phenobarbital solution. The net effect of the first two processes is referred to as the heat of displacement. It can be seen that this term will be a constant fraction of the integral heat of adsorption if it is assumed that a molecule of phenobarbital always displaces the same number of water molecules on the adsorbent surface. Therefore, the integral heat of displacement was used to evaluate the manner in which the integral heat of adsorption varied with the amount of phenobarbital adsorbed.

Accurate determination of either the integral or the differential heats of displacement requires that the thermal effect due to dilution of the bulk phenobarbital solution, as a result of the adsorption process, be accounted for. This thermal effect arises from differences in the differential heat of solution at different phenobarbital concentrations. The expression for the corrected integral heat of displacement is (12,13)

$$Q_{D2} = Q_{DM} - n_f \left[\left(\frac{\partial Q_s}{\partial n_2^s} \right)_{n_f} - \left(\frac{\partial Q_s}{\partial n_2^s} \right)_{n_b} \right] \tag{4}$$

where Q_{D2} is the corrected integral heat of displacement, Q_{DM} is the measured heat of displacement, n_b and n_f are the number of moles of phenobarbital in the bulk solution at the beginning and the end of the adsorption process, and $(\partial Q_s/\partial n_2^s)_{n_b}$ and $(\partial Q_s/\partial n_2^s)_{n_f}$, respectively, are the differential heats of solution of phenobarbital at n_b and n_f (constant volume).

Figure 2 shows the plot of the integral heat of solution versus the amount of phenobarbital dissolved (constant volume). The concentration range selected for the dissolution studies was chosen to encompass all phenobarbital concentrations observed in the adsorption studies. Figure 2 thus includes both the lowest C_{eq} value and the highest initial concentration. Not surprisingly, for the dilute phenobarbital concentrations employed, the plot is linear. The heat of dilution correction term in Eq. (4), $n_f\ [(\partial Q_s/\partial n_2^s)_{n_f} - (\partial Q_s/\partial n_2^s)_{n_b}]$, thus becomes zero.

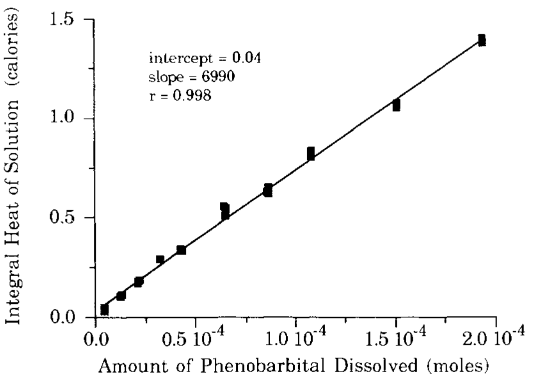

Fig. 2. Plot of the integral heat of solution versus the moles of phenobarbital dissolved. Ten concentrations were used and determinations were made in triplicate.

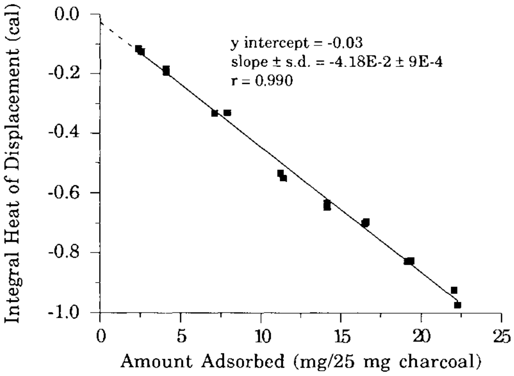

Fig. 3. Plot of the integral heat of displacement versus the amount of phenobarbital adsorbed for SuperChar activated charcoal.

The differential heat of displacement, $\overline{Q}_{D2}$, measured calorimetrically, was determined as follows:

$$\overline{Q}_{D2} = \frac{\Delta Q_{D2}}{\Delta n_2^s} \tag{5}$$

where Q_{D2}, the integral heat of displacement, was obtained from the calorimetric results and n_2^s, the amount of phenobarbital adsorbed, was obtained from the spectrophotometric results. A plot of the integral heat of displacement versus the amount of phenobarbital adsorbed is totally independent of any model-specific assumptions when determined in this manner. Such a plot will reflect the number of adsorption sites and the energies of those sites. In order to profile the entire surface properly, the amount of phenobarbital adsorbed should range from that required to cover a very small fraction of the surface to that required for complete surface coverage. Practically, how low the experimental surface coverage can be will be limited by the sensitivity of the calorimeter, the energy of interaction and the surface area of the material. The requirement of a broad range of surface

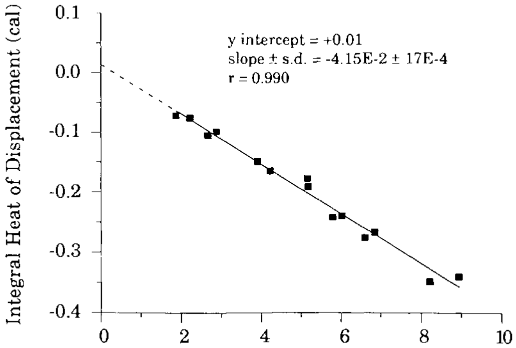

Fig. 4. Plot of the integral heat of displacement versus the amount of phenobarbital adsorbed for Darco KB-B activated charcoal.

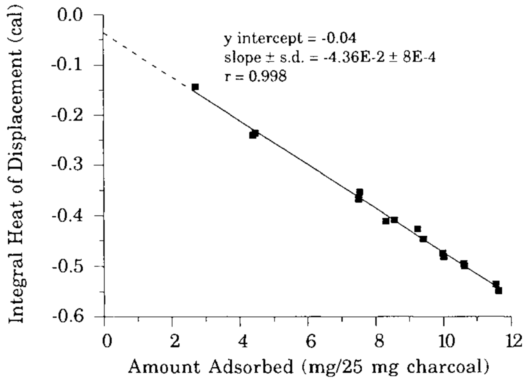

Fig. 5. Plot of the integral heat of displacement versus the amount of phenobarbital adsorbed for Norit B Supra activated charcoal.

coverages was met for all activated charcoals except Norit, U.S.P. XX, which is a relatively low surface area activated charcoal.

Figures 3–6 show that the integral heats of displacement are linearly related to the amounts of phenobarbital adsorbed. This indicates that, for all four activated charcoals, the differential heats of adsorption remain constant, a critical assumption of the Langmuir model. The linear relationship also implies that all the sites available for adsorption are energetically equivalent (11,14), a second necessary assumption for the Langmuir model to be valid. The latter conclusion seems somewhat unusual based on what is known about typical activated charcoal surfaces (15). Apparently, the interactions between phenobarbital and the various oxygen-containing sites on the surface are not different enough to be manifested in a systematic way. Finally, plot linearity indicates that there is no change in the orientation of the phenobarbital molecules on the surface at high surface coverages.

The maximum difference in $\overline{Q}_{D2}$ between the four activated charcoals was found to be 8% (Table III). The unlikely possibility that these values were significantly different was addressed by the comparison of the slopes in Figs. 3–6, since $\overline{Q}_{D2}$ values were calculated from these slopes. It can be seen from the standard deviations of the slopes that measurement precision was quite good. Parallelism of the four regression lines was tested using SAS (Statistical Analysis System Institute, Inc., Cary, NC). The slopes could not be shown to be statistically different even at confidence levels as low as 50%.

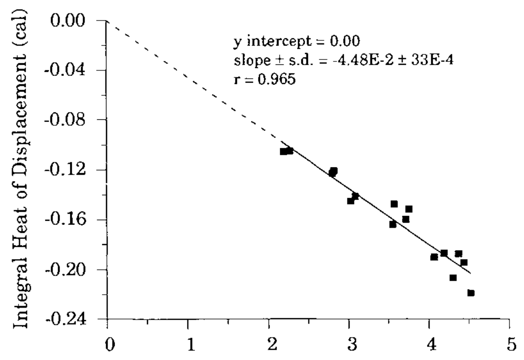

Fig. 6. Plot of the integral heat of displacement versus the amount of phenobarbital adsorbed for Norit, U.S.P. XX activated charcoal.

Table III. Differential Heats of Displacement for the Replacement of Water by Phenobarbital on the Charcoal Surface (Medium Is Simulated Intestinal Fluid, U.S.P.)

System	Heat of displacement, $\overline{Q}_2$ (kcal/mol of phenobarbital adsorbed)
Darco KB-B	−9.6
SuperChar	−9.7
Norit B Supra	−10.1
Norit, U.S.P. XX	−10.4

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