AAPS PharmSciTech

AAPS PharmSciTech, 2000; 1(3) article 25
(http://pharmscitech.com/)

Prediction of Adsorption from Multicomponent Solutions by Activated Carbon Using Single-Solute Parameters

Submitted: May 30, 2000; Accepted: August 28, 2000

Dale Eric Wurster,[1,2] Khouloud A. Alkhamis,[1,3] and Lloyd E. Matheson[1]

[1]College of Pharmacy, University of Iowa, Iowa City, IA 52242
[2]Obermann Center for Advanced Studies, University of Iowa, Iowa City, IA 52242
[3]Current address: Jordan University of Science and Technology, Irbid, Jordan

ABSTRACT The adsorption of 3 barbiturates—phenobarbital, mephobarbital, and primidone— from simulated intestinal fluid (SIF), without pancreatin, by activated carbon was studied using the rotating bottle method. The concentrations of each drug remaining in solution at equilibrium were determined with the aid of a high-performance liquid chromatography (HPLC) system employing a reversed-phase column. The competitive Langmuir-like model, the modified competitive Langmuir-like model, and the LeVan-Vermeulen model were each fit to the data. Excellent agreement was obtained between the experimental and predicted data using the modified competitive Langmuir-like model and the LeVan-Vermeulen model. The agreement obtained from the original competitive Langmuir-like model was less satisfactory. These observations are not surprising because the competitive Langmuir-like model assumes that the capacities of the adsorbates are equal, while the other 2 models take into account the differences in the capacities of the components.

The results of these studies indicate that the adsorbates employed are competing for the same binding sites on the activated carbon surface. The results also demonstrate that it is possible to accurately predict multicomponent adsorption isotherms using only single-solute isotherm parameters. Such prediction is likely to be useful for improving in vivo/in vitro correlations.

KEYWORDS: Multicomponent Adsorption, Activated Carbon, Barbiturate, Adsorption Prediction

INTRODUCTION

Prediction of multicomponent adsorption equilibria using single-component isotherm information is still one of the most challenging problems in the adsorption field. In acute overdoses, adsorption rarely involves a single component. Hence, adsorption system design must be capable of addressing multicomponent equilibrium data.

Adsorption of barbituric acid derivatives by activated carbon has been studied extensively [1-4]. Most of these studies dealt with single-solute adsorption. However, because adsorption rarely involves a single component in acute overdoses, design of test adsorption systems should be based on studying multicomponent equilibria. Compared with single-component isotherms, obtaining multicomponent isotherms is tedious. As a result, many models have been employed to predict multicomponent isotherms from single-component equilibrium data. However, many of these models were either too simplified to

***)Corresponding authors:** Dale Eric Wurster, Ph.D., College of Pharmacy and Obermann Center for Advanced Studies, University of Iowa, Iowa City, IA 52242; telephone: (319) 335-8825; facsimile: (319) 353-5594; e-mail: dale-e-wurster@uiowa.edu

Khouloud A. Alkhamis, Ph.D. , College of Pharmacy, University of Iowa, Iowa City, IA 52242; *Current address:* Jordan University of Science and Technology, Irbid, Jordan; telephone: 011-962-2-7095111-23437; facsimile: 011-962-2-295019; e-mail: khou@just.edu.jo

describe the complexity of a multicomponent isotherm or too mathematically complicated to be used in practice.

The purpose of this investigation is to present several methods used to predict multicomponent equilibrium adsorption data and apply these methods to 2-component combinations of 3 barbiturates, namely, phenobarbital, mephobarbital, and primidone.

Selection of Barbituric Acid Derivatives

Phenobarbital, mephobarbital, and primidone vary systematically in their structures. Phenobarbital, mephobarbital, and primidone all have one ethyl group and one phenyl group on C_5 of the barbituric acid ring (Figure 1).

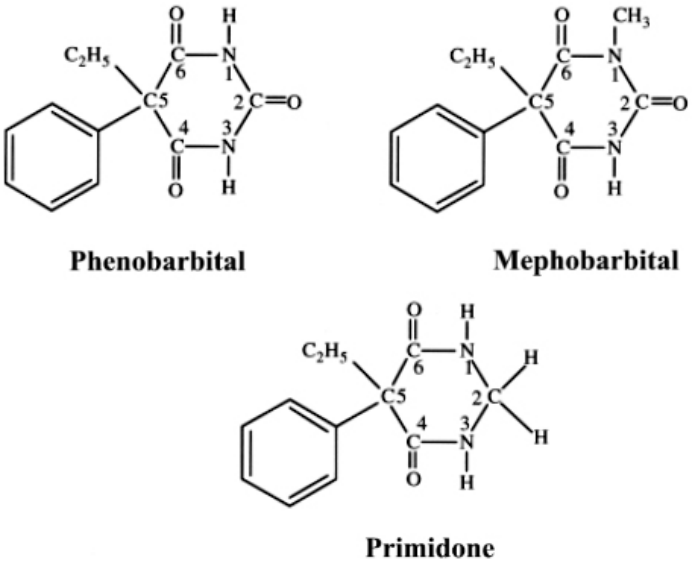


Figure 1. Chemical structures of the barbituric acid derivatives employed in this work.

The difference between phenobarbital and mephobarbital is that the latter has an additional methyl group on nitrogen N_1. Compared with phenobarbital, primidone lacks the oxygen on carbon C_2 [5]. Based on the overall similarity of the structures, it is expected that these compounds will interact with the same binding sites. These studies are likely to be valuable in understanding the specificity of physical interactions.

Theoretical Section

Selection of the appropriate model to describe the physical adsorption process should be based on the assumptions of the model and the physicochemical behavior of the system. The modeling of multicomponent adsorption isotherms requires an accurate understanding of the competitive equilibria involved between the mixed components and the adsorption sites. Numerous, and often complicated, models have attempted to give a mathematical description of the phenomena. In addition to the difficulty in understanding the different mechanisms, the ability to experimentally obtain the numerical parameters for these theoretical models is also difficult. From all of the proposed models described in the literature, several models have been selected for additional evaluation. This selection was based on the theoretical development of their equations and also on their general acceptance.

Competitive Langmuir-like Model

The extension of the basic Langmuir model [6] to the description of competitive adsorption phenomena was first proposed by Schwab [7], Butler and Ockrent [8], and Markham and Benton [9]. This model is based on the same assumptions as was the original Langmuir-like model. The fraction of the surface covered, θ , is given by:

$$\theta_1 = \frac{AC_{eq_1}}{1 + AC_{eq_1} + BC_{eq_2}} \qquad (1)$$

and

$$\theta_2 = \frac{BC_{eq_2}}{1 + BC_{eq_2} + AC_{eq_1}} \qquad (2)$$

where θ is the fraction of the surface covered, C_{eq} is the concentration of the component in solution (unadsorbed) at equilibrium, and A and B are the affinity constants of components 1 and 2, respectively.

Young and Crowell [10] noted that the competitive Langmuir-like equation can be used for aqueous and gaseous systems in which the capacities are not equal.

The observation that capacities might differ, even for similar size adsorbates, on the same activated carbon is common. Broughton [11] observed that the extension of the Langmuir-like theory to adsorption from binary adsorbate systems is thermodynamically consistent only for the special case where the capacities of the 2 components are equal. If the Langmuir-like model for competitive adsorption satisfactorily predicts the extent of adsorption from a bisolute system when the capacities are not equal, it is probably because there is competition for all available sites [12]. The difference in the capacity values in this case would be caused by a difference in surface area covered by one adsorbate as compared with the competing adsorbate. However, a slight difference in molecular size or orientation on the surface could result in the surfaces within small pores being available only to one adsorbate. If adsorption of either component of a bisolute system occurs on sites that are inaccessible to one of the species, the Langmuir-like model for competitive adsorption is not expected to yield accurate results.

Modified Competitive Langmuir-like Model

The original competitive Langmuir-like model was improved by Jain and Snoeyink [12], whose modification was based on the hypothesis that adsorption without competition occurs on some sites when the capacities are not equal. Further, it was assumed that the number of sites for noncompetitive adsorption would be proportional to the difference between the maximum loadings of the species, in other words, $(X_{m,1} - X_{m,2})$, where $X_{m,1} > X_{m,2}$. On this basis, the following equations were described:

$$X_1 = \frac{(X_{m,1} - X_{m,2})AC_{eq1}}{1 + AC_{eq1}} + \frac{X_{m,2}AC_{eq1}}{1 + AC_{eq1} + BC_{eq2}} \quad (3)$$

$$X_2 = \frac{X_{m,2}BC_{eq2}}{1 + AC_{eq1} + BC_{eq2}} \quad (4)$$

where X_1 and X_2 are the amounts of solutes 1 and 2 adsorbed per unit weight, or per unit surface area, of adsorbent at equilibrium concentrations C_{eq1} and C_{eq2}, respectively; and A and B are the affinity constants of components 1 and 2, respectively, that are derived from single-solute systems. The first term on the right side of equation 3 is the Langmuir-like expression for the amount of species 1 that adsorbs without competition. The second term, based on the Langmuir-like model for competitive adsorption, represents the amount of species 1 adsorbed on the surface in competition with species 2.

Ideal Adsorbed Solution (IAS) Model

The IAS model was first developed by Myers and Prausnitz [13] for gaseous mixtures. It was then extended to liquid– solid equilibria and applied by Radke and Prausnitz [14], Jossens et al. [15], Fritz and Merk [16], and Fritz and Schluender [17]. This theory is based on the thermodynamic equivalence of the spreading pressure of each solute at equilibrium. The spreading pressure of a solute, π_i, is defined as the difference between the interfacial tension of the pure solvent– solid interface and that of the solution– solid interface for that solute. It is mathematically given by the equation:

$$\pi_i = \frac{RT}{S} \int_0^{C^*_{eqi}} \frac{X_i}{C_{eq\,i}} \, dC_{eqi} \quad (5)$$

Here, C_{eqi} and X_i are the corresponding solution-phase and solid-phase equilibrium concentrations and amounts of species i in the multicomponent system. C^*_{eqi} is the equilibrium concentration of species i in a single-solute system, which gives the same spreading pressure as that of the mixture. S is the surface area of the activated carbon, R is the ideal gas constant, and T is the absolute temperature. In single-component systems, C_{eqi} and X_i are mathematically related through the single-solute adsorption isotherms, such as the simple Langmuir-like or Freundlich adsorption equations. In general, this can be stated as:

$$X_i = f(C_{eq_i}) \quad (6)$$

If x^S_i is allowed to represent the mole fraction of species i in the adsorbed phase, the following 3 equations can be readily established [14]:

$$C_{eq_i} = C^*_{eqi} \bullet x^s_i \quad (7)$$

$$\sum_{i=1}^{n} x_i^s = 1 \qquad (8)$$

$$X_i = X_T \bullet x_i^s \qquad (9)$$

where X_T is the total quantity of material adsorbed from the mixture. The quantity X_T can be calculated from:

$$\frac{1}{X_T} = \sum_{i=1}^{n} \frac{x_i^s}{X_{i*}} \qquad (10)$$

At equilibrium, the spreading pressure for each component in the mixture should be equal, and the previous equations can be solved once the initial conditions are specified [18].

The results of this theory may be very satisfactory in certain cases, but, as emphasized by Mckay and Al Duri [19], the mathematical complexity of the procedure, especially for more than 2 component mixtures, has restricted its use.

LeVan-Vermeulen Model

The competitive Langmuir-like model has been corrected for its thermodynamic inconsistency by LeVan and Vermeulen [20]. IAS theory is employed in this correction. This model predicts the equilibrium relationships of solute mixtures only from data derived from single adsorption isotherms and is perhaps the simplest isotherm derived from IAS theory.

The first-order Taylor series approximation of the LeVan-Vermeulen equation is the competitive Langmuir-like model, if the capacities are the same for both of the 2 components. If the capacities are different for the 2 components, the LeVan-Vermeulen model is represented by a Taylor series that converges very rapidly and can be limited in most practical cases to its first 2 or 3 terms. The third-order Taylor series approximation of the isotherm for component 1 can be written as:

$$X_1 = \frac{\overline{X_m} AC_{eq_1}}{1 + AC_{eq_1} + BC_{eq_2}} + \Delta_{L2} \cdot (1 + \Delta_{L3}) \qquad (11)$$

where $\overline{X_m}$ is a weighted monolayer capacity. $\overline{X_m}$ equals:

$$\overline{X_m} = \frac{X_{m,1} AC_{eq_1} + X_{m,2} BC_{eq_2}}{AC_{eq_1} + BC_{eq_2}} + 2\frac{(X_{m,1} - X_{m,2})^2}{X_{m,1} + X_{m,2}} \frac{AC_{eq_1} BC_{eq_2}}{(AC_{eq_1} + BC_{eq_2})^2} \left[\left(\frac{1}{AC_{eq_1} + BC_{eq_2}} + \frac{1}{2}\right)\ln(1 + AC_{eq_1} + BC_{eq_2}) - 1\right] \qquad (12)$$

where $X_{m,1}$ and $X_{m,2}$ are the capacity constants for component 1 and component 2, respectively. Furthermore,

$$\Delta_{L2} = (X_{m,1} - X_{m,2}) \frac{AC_{eq_1} BC_{eq_2}}{(AC_{eq_1} + BC_{eq_2})^2} \ln(1 + AC_{eq_1} + BC_{eq_2}) \qquad (13)$$

$$\Delta_{L3} = \frac{X_{m,1} - X_{m,2}}{X_{m,1} + X_{m,2}} \frac{1}{AC_{eq_1} + BC_{eq_2}} \left[\frac{(BC_{eq_2})^2 + (2BC_{eq_2}) - (4AC_{eq_1}) - (AC_{eq_1})^2}{AC_{eq_1} + BC_{eq_2}} \ln(1 + AC_{eq_1} + BC_{eq_2}) + \frac{3(AC_{eq_1})^2 + 4AC_{eq_1} + AC_{eq_1} BC_{eq_2} - 2BC_{eq_2} - 2(BC_{eq_2})^2}{1 + AC_{eq_1} + BC_{eq_2}}\right] \qquad (14)$$

The isotherm for component 2 can be obtained by interchanging the component subscripts in equations 11, 13, and 14.

The LeVan-Vermeulen model for bisolute systems was further extended to any number of adsorbates by Frey and Rodrigues [21]. This model applies when the single-component isotherms correspond closely to Langmuir-like isotherms and when the maximum adsorption capacities for the various adsorbates are not too dissimilar.

MATERIALS AND METHODS

Preparation of the Activated Carbon

A small amount of activated carbon, SuperChar® (lot G812R, Gulf Bio-Systems, Inc, Dallas, TX) was spread evenly in a petri dish and placed in a vacuum oven. The vacuum setup consisted of a NAPCO vacuum oven (Model 5831, Precision Scientific, Chicago, IL), a Welch Duo-Seal vacuum pump (Model 1402, Sargent-

Welch Scientific Co, Skokie, IL), and a Mcleod vacuum gauge (Kontes, Morton Grove, IL). The activated carbon was dried at 100° C and 25 μmHg for 24 hours before use. Upon removal from the vacuum oven, the sample was placed in a vacuum desiccator and allowed to come to room temperature. The sample was then immediately used for the experiment.

Surface Area Determination

Surface area was determined by BET (Brunauer, Emmett, and Teller) analysis of nitrogen vapor adsorption isotherms, at relative pressures of 0.025–0.20, using a Quantasorb instrument (Quantachrome Corp, Boynton Beach, FL).

Adsorption from Solution by the Rotating Bottle Method

General Procedure

Simulated intestinal fluid (SIF) without pancreatin was prepared according to the *United States Pharmacopeia*, volume XXIII (p.2053, Rockville, MD: The United States Pharmacopeial Convention; 1994). SIF consisted of 6.8 g of potassium phosphate monobasic (enzyme grade, Fisher Scientific, Fair Lawn, NJ, lot numbers 955698 and 962007), ~190 mL of 0.2N NaOH (Fisher Scientific, Fair Lawn, NJ, lot 946154), and sufficient water to make 1000 mL (pH adjusted to 7.5 ± 0.1 with 0.2N NaOH).

The stock drug solution was prepared by dissolving the adsorbate in 500 mL of SIF. Aliquots were then removed from this stock solution and diluted to 100 mL using the same batch of SIF that was used to prepare the stock solution. Five-milliliter aliquots were removed from each of these latter dilutions and were then used as standards for further analysis. Ten samples of the activated carbon (approximately 5 mg each) were individually weighed in glass weighing funnels. Each sample, including the glass weighing funnel, was placed in an individual screw-top bottle, and the appropriate adsorbate solution was added. Two layers of Teflon tape were placed over the top of the bottle to prevent leakage and to avoid direct contact of the suspension with the cap. The screw cap was then put on the bottle. The filled bottles were rotated in a Vanderkamp Sustained Release Apparatus (Model W-115 water bath, Model 103906 motor, Van-Kel Industries, Inc, Edison, NJ) equipped with a heating circulator (Model 1120, VWR Scientific, St Paul, MN) at 25 rpm for 45 minutes (37° C). Rotation of the bottles was then stopped with the bottles in an upright position in the water bath, and the activated carbon was allowed to settle to the bottom of the bottles (2 hours at 37° C). An aliquot of the supernatant in each bottle was removed for subsequent analysis. These adsorption studies were performed in triplicate.

Procedure for Mephobarbital Phenobarbital Adsorption Studies

Mephobarbital (Sigma Chemical Co, St Louis, MO, lot 97F-0466) and phenobarbital (Sigma Chemical Co., St Louis, MO, lot 76H0293) stock solutions were prepared separately, using the same batch of SIF. Nine different aliquots of mephobarbital stock solution were prepared (0.003– 0.05 mg/mL) so as to contain 6, 9, 12, 18, or 24 mg of phenobarbital stock solution and were diluted to 100 mL using the same batch of SIF. After this point, the general procedure described above was followed.

High-Performance Liquid Chromatography Analysis of Mephobarbital Phenobarbital Solutions

The mephobarbital and phenobarbital concentrations, both before the addition of activated carbon and after the attainment of equilibrium, were determined at 250 nm using a reversed-phase high-performance liquid chromatography (HPLC) system that included a liquid pump (Model LC-6A), integrator (Model CR601), variable wavelength UV detector (Model SP06), auto injector (Model SIL-6B), and system controller (Model SCL-6B) (all Shimadzu Scientific Instruments, Columbia, MD). The assay conditions were mobile phase, 50:50 0.05 mol phosphate buffer (pH 3.0):Methanol; flow rate, 1.0 mL/min; column, μBondapak™ (Waters, Milford, MA) C18, 3.9 x 300 mm, 10 μ particle size; injection volume, 20– 50 μL. The wavelength of analysis (250 nm) was chosen so

that mephobarbital and phenobarbital could be analyzed simultaneously in 1 chromatographic run. Initial concentrations were used to construct a standard curve for each experiment, and quantitation was performed by peak area integration.

Procedure for Primidone Phenobarbital Adsorption Studies

Primidone (Sigma Chemical Company, St Louis, MO, lot 48F0043) and phenobarbital stock solutions were prepared separately. Nine different aliquots of primidone stock solution were prepared (0.008– 0.29 mg/mL) so as to each contain either 6, 9, 12, 18, or 24 mg of phenobarbital stock solution and then diluted to 100 mL using the same batch of SIF. After this point, the general procedure described above was followed.

HPLC Analysis of Primidone Phenobarbital Solutions

The primidone and phenobarbital concentrations were determined with the aid of a reversed-phase HPLC system, using a Waters μBondapak C18 column. The wavelength for the detection of both primidone and phenobarbital was 250 nm. The sensitivity of the detector was set at 0.01 AUFS (absorbance units full scale). The HPLC system was the same as described previously. The HPLC assay conditions were also the same except for the mobile phase ratio (60% phosphate buffer, pH 3: 40% methanol).

Adsorption Procedure for Data in the High Surface Coverage Region

The ability to conduct adsorption experiments can be severely limited if the compound has poor solubility. This limitation can be due to inaccuracies in the weighing of very small amounts of the activated carbon. Because it was necessary to obtain data in the region of high surface coverage, the following specialized procedure was used. Nine samples of the activated carbon (approximately 1 mg each) were individually weighed in aluminum pans using a microbalance (Model M3P-000V001, Sartorius GmbH, Göttingen, Germany). Each sample, including the aluminum pan, was placed in an individual screw-top bottle, and the appropriate adsorbate solution was then added. After this point, the general procedure described above was followed.

RESULTS AND DISCUSSION

Surface Area of the Activated Carbon

SuperChar was found to have a specific surface area of 3000 ± 30 m^2/g. This value is quite close to the value obtained by a previous investigator [4].

Single Solute Adsorption

The Langmuir-like model for competitive adsorption, the modified Langmuir-like model for competitive adsorption, and the LeVan-Vermeulen model all require the use of the Langmuir-like parameters for single-solute systems. Accordingly, it was necessary to determine single-solute adsorption isotherms for the adsorbates used in this study, namely, mephobarbital, phenobarbital, and primidone.

The Langmuir-like model was selected to fit the data. This selection was based on the results of the heat of displacement studies obtained by previous investigators. Burke et al. [22]. observed a linear relationship between the integral heat of displacement and the amount of phenobarbital adsorbed by activated carbon. Huang [3] observed a similar relationship between the integral heats of displacement and the amounts of mephobarbital and primidone adsorbed by the activated carbon.

These studies showed that the differential heats of displacement were independent of surface coverage and that the phenobarbital, mephobarbital, and primidone binding sites were energetically equivalent. This indicated that the Langmuir-like model was the correct model to fit the adsorption data for the adsorbates used in this study.

The nonlinear equilibrium adsorption isotherms are presented in Figures 2-4. The parameters of the Langmuir-like equation and the capacity and affinity constants are presented in Table 1.

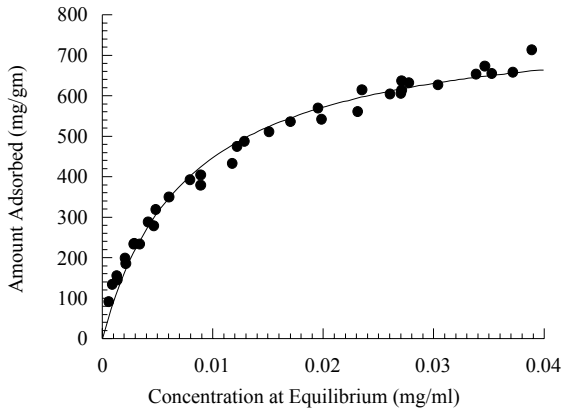


Figure 2. Nonlinear Langmuir-like plot for mephobarbital adsorption by activated carbon.

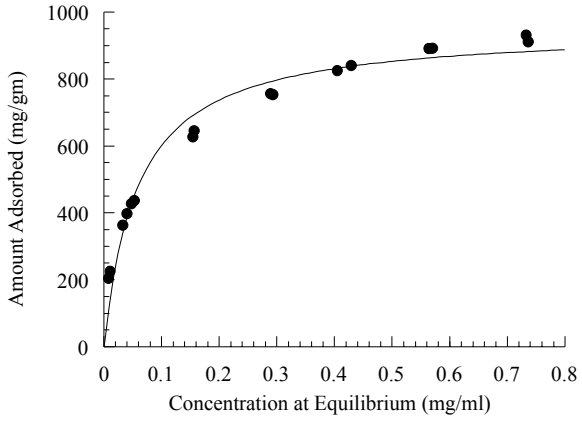


Figure 3. Nonlinear Langmuir-like plot for phenobarbital adsorption by activated carbon.

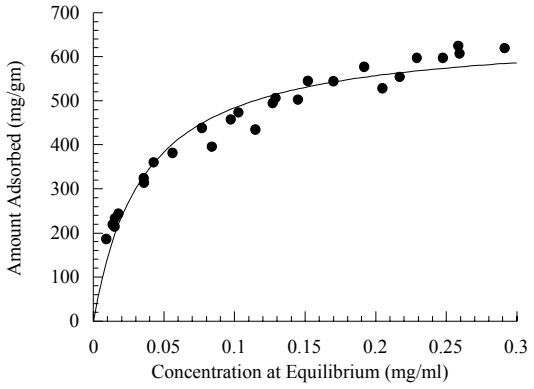


Figure 4. Nonlinear Langmuir-like plot for primidone adsorption by activated carbon.

Table 1. Adsorption Parameters Obtained from Curve-Fitting of the Nonlinear Langmuir-like Equation to Mephobarbital, Phenobarbital, and Primidone Data

	Mephobarbital	Phenobarbital	Primidone
Capacity Constant (μmol/g) 95% Confidence Level (mg/g) 95% Confidence Level	3220 (3090– 3350) 792 (760– 824)	4100 (3870– 4340) 952 (898–1010)	3010 (2840– 3170) 656 (619– 691)
Affinity Constant (mL/mg) 95% Confidence Level	129 (113– 145)	17 (13– 21)	28 (22–34)
r^2 (Coef. of Det.)	.984	.970	.950

The capacity (952 mg/g) and affinity constants (17.1 mL/mg) obtained for phenobarbital adsorption by SuperChar agree with the values obtained by Burke [4]. That investigator, using the same batch of SuperChar, obtained a capacity of 980 mg/g and an affinity of 16.4 mL/mg.

Statistical analyses were performed to compare the model parameters of mephobarbital, phenobarbital, and primidone. The results, at the 95% confidence level, showed that SuperChar had the greatest capacity for phenobarbital. The capacities for mephobarbital and primidone were statistically equal ($P > 0.05$). The difference in capacities between phenobarbital and mephobarbital indicates that mephobarbital occupies a larger area on the activated carbon surface and that a certain number of binding sites are not accessible to mephobarbital. Presumably, this is due to steric factors. The difference in capacities between phenobarbital and primidone suggests that the carbonyl group at position C_2 is likely to be involved in the binding of phenobarbital, while the carbonyl group at either position C_4 or C_6 must be involved in the binding of primidone. These conclusions are also based on previous work [3,4,23], which indicated that barbiturates are likely to interact with the hydroxyl groups on the carbon surface by hydrogen bonding.

The results, at the 95% confidence level, also showed that the affinity constants are statistically different. SuperChar has the highest affinity for mephobarbital (*P*

< 0.05). The affinity constant of primidone is significantly higher than that of phenobarbital (P < 0.05). This order of affinities is expected because the solubilities of these drugs are in the following order: mephobarbital < primidone < phenobarbital [24]. In general, higher solubility results in lower adsorption affinity. This generalization assumes that the adsorption mechanism remains the same.

Multisolute Adsorption

The experimental data for the adsorption studies of 2 bisolute systems (mephobarbital– phenobarbital and primidone– phenobarbital) are presented in Figures 5 and 6. The results clearly show that by increasing the initial concentration of phenobarbital, the extents of mephobarbital and primidone adsorption decrease. These results indicate that these adsorbates are competing for the same binding sites on the activated carbon.

The competitive Langmuir-like model and the modified competitive Langmuir-like model were both applied to these 2 bisolute systems. Correlations between the experimental and the calculated amounts of mephobarbital, phenobarbital, and primidone adsorbed by the activated carbon are presented in Figures 7-12. The parameters of the Langmuir-like equation for single-solute systems were used in these calculations. Excellent agreement was obtained between the experimental and the calculated data using the modified competitive Langmuir-like model.

Figures 7, 9, 10, and 12 show that the intercepts are close to 0, while the slopes are close to 1. Thus, the modified competitive Langmuir-like model can successfully predict the extent of adsorption for each component of both of the 2 bisolute systems used in this study from single-component parameters.

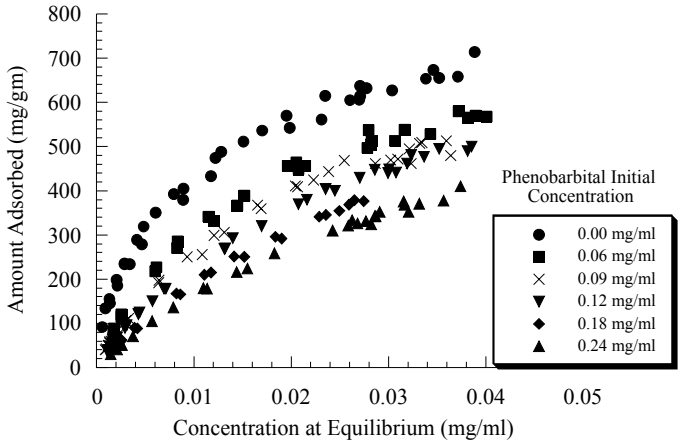


Figure 5. Adsorption of mephobarbital by activated carbon using different initial concentrations of phenobarbital.

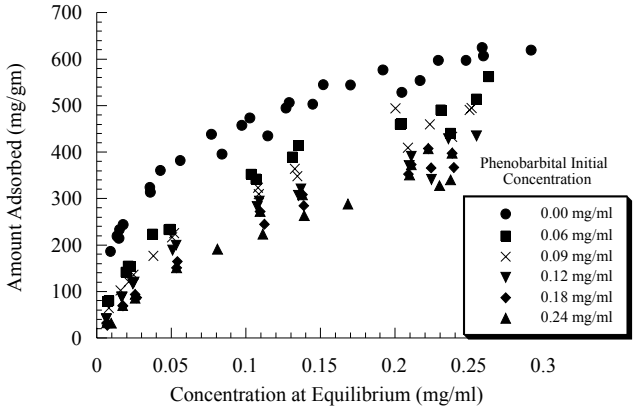


Figure 6. Adsorption of primidone by activated carbon using different initial concentrations of phenobarbital.

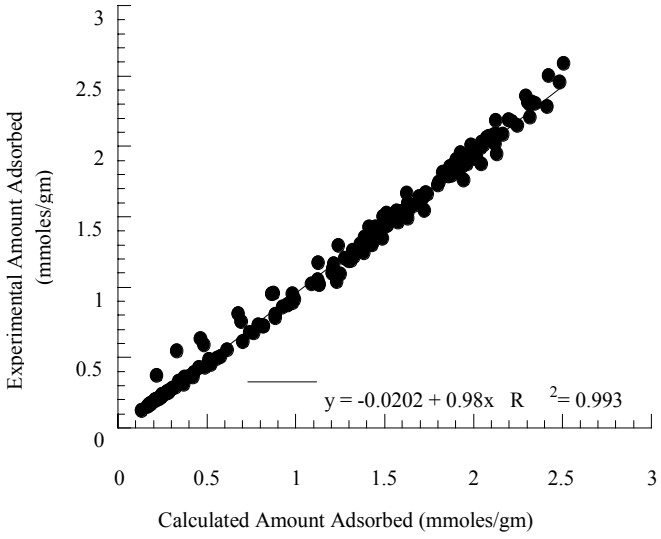


Figure 7. Correlation of experimental and calculated adsorption data for mephobarbital (bisolute system) by activated carbon. Calculated data are from the competitive Langmuir-like equation and the modified competitive Langmuir-like equation. (Same equation as for the lower capacity component.)

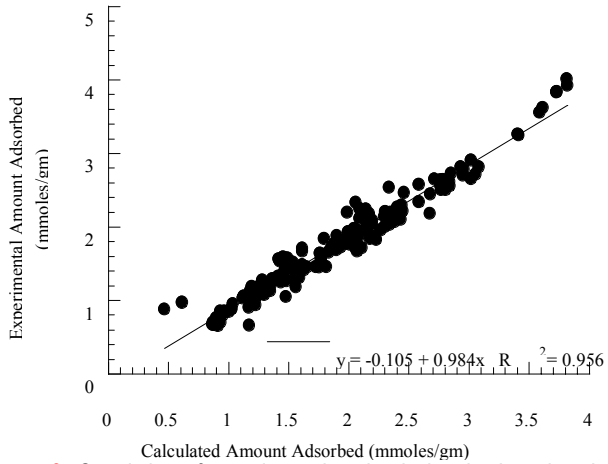


Figure 8. Correlation of experimental and calculated adsorption data for phenobarbital (phenobarbital- mephobarbital experiment) by activated carbon. Calculated data are from the competitive Langmuir-like equation.

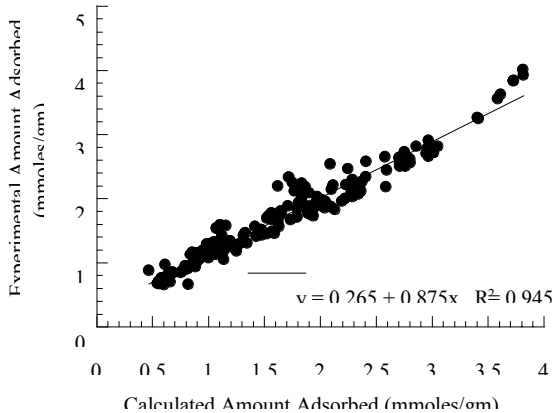


Figure 9. Correlation of experimental and calculated adsorption data for phenobarbital (phenobarbital- mephobarbital experiment) by activated carbon. Calculated data are from the modified competitive Langmuir-like equation.

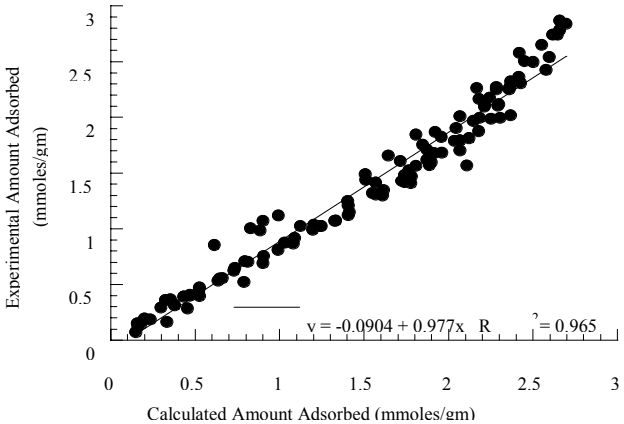


Figure 10. Correlation of experimental and calculated adsorption data for primidone (bisolute system) by activated carbon. Calculated data are from the competitive Langmuir-like equation and the modified competitive Langmuir-like equation. (Same equation as for the lower capacity component.)

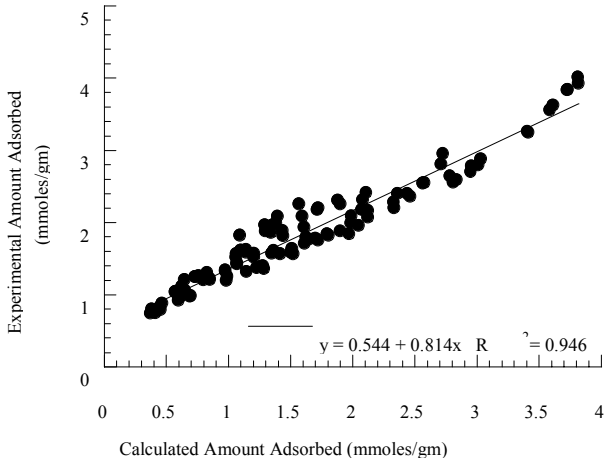


Figure 11. Correlation of experimental and calculated adsorption data for phenobarbital (phenobarbital primidone experiment) by activated carbon. Calculated data are from the competitive Langmuir-like equation.

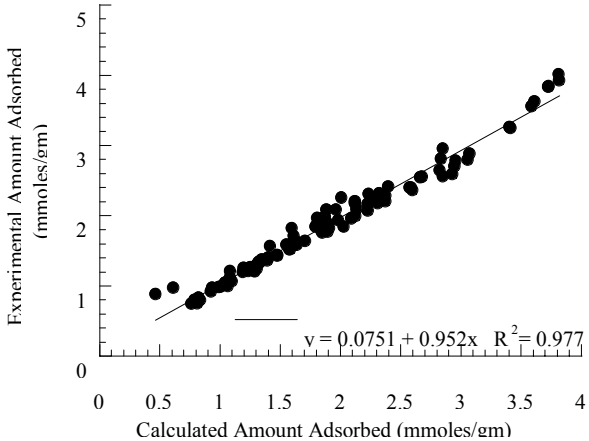


Figure 12. Correlation of experimental and calculated adsorption data for phenobarbital (phenobarbital primidone experiment) by activated carbon. Calculated data are from the modified competitive Langmuir-like equation.

Excellent agreement between the experimental and the calculated data was also observed for mephobarbital and primidone using the original competitive Langmuir-like model (Figures 7 and 10). The prediction of the extent of phenobarbital adsorption was less satisfactory (Figures 8 and 11). The original competitive Langmuir-like model underestimated the extent of phenobarbital adsorption. This result is not surprising and has already been pointed out by other investigators [25]. The competitive Langmuir-like model is thermodynamically consistent only in the special case where the capacities of the adsorbates are equal. The assumption of identical capacities for compounds of different molecular sizes is unrealistic because each molecule occupies an area on the activated carbon surface that is dependent on its exact size, its substitution pattern, its

3-dimensional conformation, and other steric factors.The LeVan-Vermeulen model was next applied to the experimental data. Excellent agreement was observed between the experimental data and the calculated data using the single-solute parameters of the Langmuir-like equation (Figures 13-16).

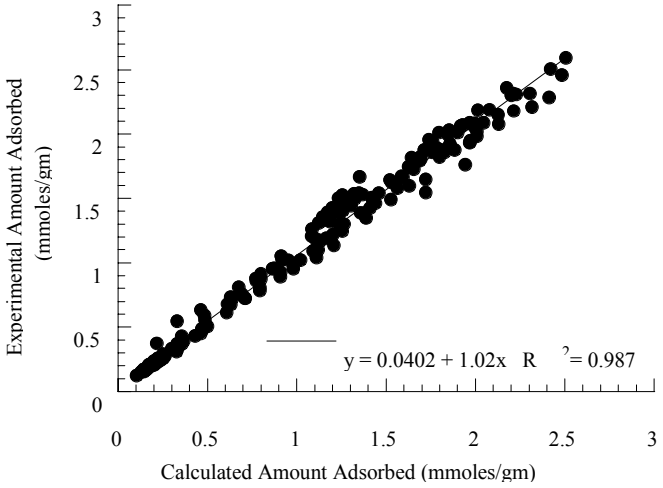


Figure 13. Correlation of experimental and calculated adsorption data for mephobarbital (bisolute system) by activated carbon. Calculated data are from the LeVan-Vermeulen equation.

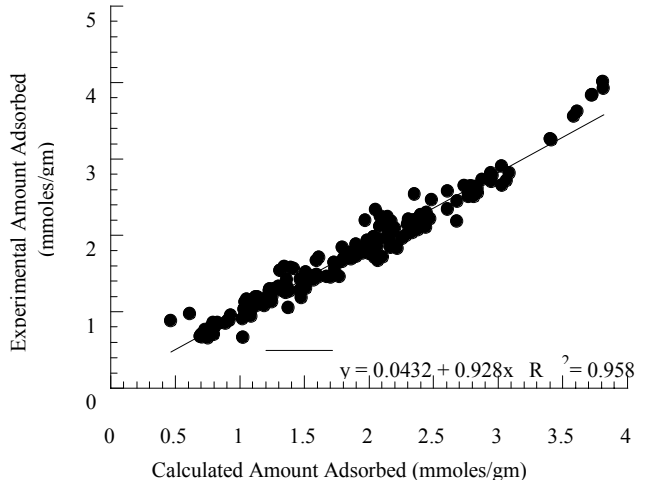


Figure 14. Correlation of experimental and calculated adsorption data for phenobarbital (phenobarbital mephobarbital experiment) by activated carbon. Calculated data are from the LeVan-Vermeulen equation.

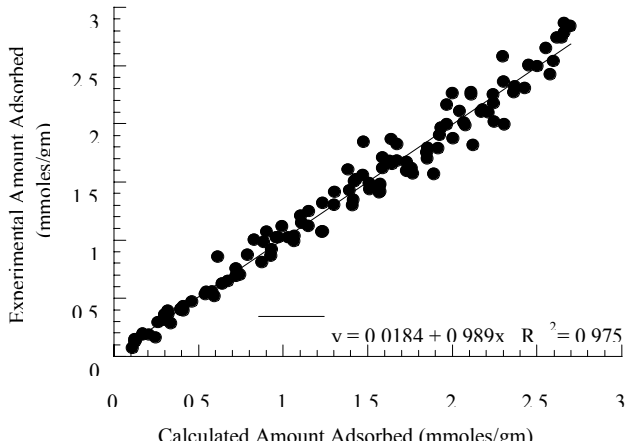


Figure 15. Correlation of experimental and calculated adsorption data for primidone (bisolute system) by activated carbon. Calculated data are from the LeVan-Vermeulen equation.

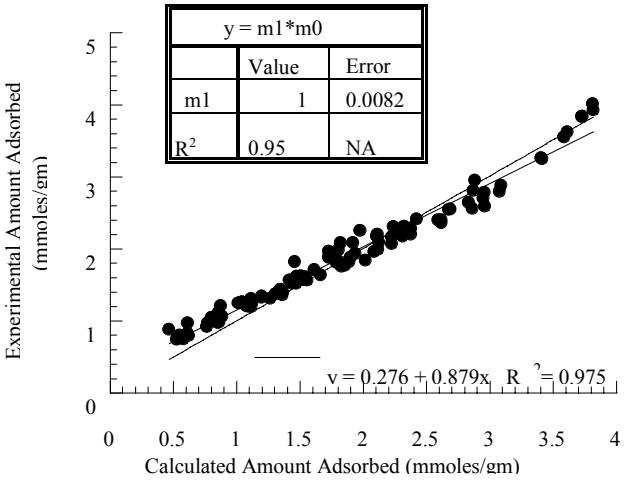


Figure 16. Correlation of experimental and calculated adsorption data for phenobarbital (phenobarbital primidone experiment) by activated carbon. Calculated data are from the LeVan-Vermeulen equation.

Because the LeVan-Vermeulen model uses conventional thermodynamic principles, such as the Gibbs adsorption relationship, and takes into account the difference in the capacities of the adsorbates, this was the expected result. However, prediction of phenobarbital adsorption in Figure 16 was less satisfactory when the intercept was not forced to 0 because the y-intercept was larger than desirable. It is not clear whether the intercept in this case has meaning or not because the r values for the 2 plots are not much different (Figure 16).

Nonlinear curve fitting of the experimental data using

the competitive Langmuir-like model and the modified competitive Langmuir-like model was also performed. This required the use of 2 independent variables. This task can be considered to be a multivariant, nonlinear programming problem. To reduce the standard errors of the estimated regression coefficients, the nonlinear regression analysis of the models was performed using the whole set of single and competitive data. The analysis was performed using the SAS computer program package (Version 6.12, SAS Institute, Inc, Cary, NC). The results of the regression analyses are presented in Tables 2-7. At the 95% confidence level, the parameters (capacities and affinities) obtained using the modified competitive Langmuir-like model were not significantly different from those determined for single-component adsorption. These results indicate that when the adsorbates are competing for the same binding sites, the modified competitive Langmuir-like model can successfully predict the multicomponent adsorption isotherms using only single-component parameters.

Table 2. Competitive Langmuir-like Isotherm Parameters for Mephobarbital

Methods: Gauss-Newton and Marquardt; Program: SAS				
Parameter	Estimate	Standard Error	95% Confidence Interval	
			Lower	Upper
Mephobarbital Capacity (μmol/g)	3240	34.1	3180	3310
Mephobarbital Affinity (mL/mg)	123	3.6	116	130
Phenobarbital Affinity (mL/mg)	17.4	0.4	16.5	18.3

Table 3. Competitive Langmuir-like Isotherm Parameters for Phenobarbital (Mephobarbital-Phenobarbital)

Methods: Gauss-Newton and Marquardt; Program: SAS				
Parameter	Estimate	Standard Error	95% Confidence Interval	
			Lower	Upper
Mephobarbital Affinity (mL/mg)	74.5	3.8	67.0	82.0
Phenobarbital Affinity (mL/mg)	13.1	0.6	11.9	14.3
Phenobarbital Capacity (μmol/g)	4130	67.2	4000	4270

Table 4. Modified Competitive Langmuir-like Isotherm Parameters for Phenobarbital (Mephobarbital Phenobarbital)

Methods: Gauss-Newton and Marquardt; Program: SAS				
Parameter	Estimate	Standard Error	95% Confidence Interval	
			Lower	Upper
Mephobarbital Capacity (μmol/g)	3290	186	2930	3660
Mephobarbital Affinity (mL/mg)	124	17.8	89.0	159
Phenobarbital Capacity (μmol/g)	4180	66.3	4040	4310
Phenobarbital Affinity (mL/mg)	13.3	0.6	12.1	14.5

Table 5. Competitive Langmuir-like Isotherm Parameters for Primidone

Methods: Gauss-Newton and Marquardt; Program: SAS				
Parameter	Estimate	Std. Error	95% Confidence Interval	
			Lower	Upper
Primidone Capacity (μmol/g)	3030	46.9	2930	3120
Primidone Affinity (mL/mg)	27.0	1.7	23.7	30.3
Phenobarbital Affinity (mL/mg)	23.3	1.4	20.5	26.1

Table 6. Competitive Langmuir-like Isotherm Parameters for Phenobarbital (Primidone-Phenobarbital)

Methods: Gauss-Newton and Marquardt; Program: SAS				
Parameter	Estimate	Stdandard Error	95% Confidence Interval	
			Lower	Upper
Primidone Affinity (μmol/g)	10.9	0.6	9.7	12.1
Phenobarbital Affinity (mL/g)	13.8	0.6	12.5	15.0
Phenobarbital Capacity (μmol/g)	4100	58.7	3980	4210

Table 7. Modified Competitive Langmuir-like Isotherm Parameters for Phenobarbital (Primidone-Phenobarbital)

Methods: Gauss-Newton and Marquardt; Program: SAS				
Parameter	Estimate	Standard Error	95% Confidence Interval	
			Lower	Upper
Primidone Capacity (μmol/g)	2860	121	2620	3100
Primidone Affinity (mL/mg)	26.2	3.3	19.7	32.8
Phenobarbital Capacity (μmol/g)	4130	51.2	4030	4230
Phenobarbital Affinity (mL/mg)	14.6	0.6	13.4	15.8

The agreement between the parameters obtained for phenobarbital using the original competitive Langmuir-like model and the single-solute adsorption parameters was less satisfactory. This result was expected because the model assumes that the capacities of the adsorbates are equal.

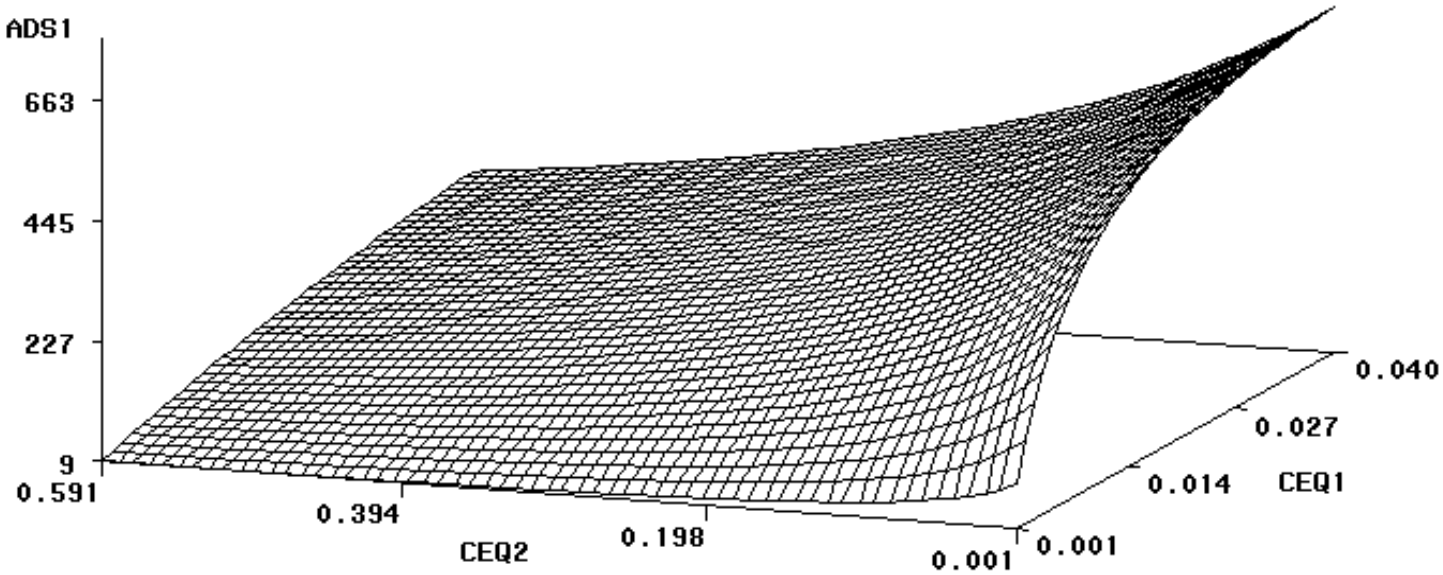
Figure 17 shows a typical 3-dimensional isotherm: C_{eq1},C_{eq2}, and Ads_1. This response surface plot was generated using SAS from the adsorption parameters previously obtained. The plot shows that by increasing the concentration at equilibrium of mephobarbital, the amount of mephobarbital adsorbed by activated carbon increases. An increase in the equilibrium concentration of phenobarbital results in a decrease in the amount of mephobarbital adsorbed.

Figure 17. Three-dimensional graph for mephobarbital adsorption by activated carbon in the presence of phenobarbital (competitive Langmuir-like and modified competitive Langmuir-like models). CEQ1 refers to the concentration of mephobarbital at equilibrium; CEQ2 refers to the concentration of phenobarbital at equilibrium; ADS1 refers to the amount of mephobarbital adsorbed by activated carbon.

CONCLUSIONS

This work has attempted to establish a comparison between the different multicomponent adsorption models. This comparison is based on the physicochemical principles and on the assumptions of each model. The competitive Langmuir-like model can successfully predict multicomponent adsorption under the following conditions. First, the competing adsorbates must obey the assumptions of the Langmuir-like equation for single solutes. Second, the capacities of the adsorbates must be equal. Third, the adsorbates must be competing for the same binding sites.

The competitive Langmuir-like model can be considered to be the simplest model for prediction of multicomponent adsorption. This model has no restrictions regarding the number of adsorbates that can be used. However, the major disadvantage of employing the competitive Langmuir-like model is the assumption of equal capacities for different adsorbates. This assumption is unrealistic because each molecule will occupy a certain area on the adsorbent that is related to the adsorbate's structure, 3-dimensional conformation, and other steric factors.



The modified competitive Langmuir-like model can successfully predict multicomponent adsorption under the following conditions. First, the competing adsorbates must obey the assumptions of the Langmuir-like equation for single solutes. Second, the adsorbates must be competing for the same binding sites. The modified competitive Langmuir-like model does not assume equal capacities for different adsorbates. This model can successfully predict multicomponent adsorption using single-solute parameters, even if the difference in the adsorbate capacities is quite large. This is true as long as the difference in capacities is based on steric factors and/or size factors and not on totally different binding sites. However, the main disadvantage of this model is that it is applicable only to bisolute systems.

The LeVan-Vermeulen model uses the IAS theory to derive binary Langmuir-like and Freundlich isotherms. This was accomplished for cases of moderate numerical difference between the parameters appearing in the single-component equations [20]. IAS theory, like the Langmuir-like model, is based on the concept of ideal behavior of the bulk phase and the adsorbed phase. IAS theory is also based on the premises that the adsorbent is inert and that it possesses a specific surface area that is identical for all adsorbates.[14] This latter assumption would not be valid, for example, for a molecular sieve adsorbent wherein the area available for adsorption depends on the size of the adsorbate molecule.[13] Similarly, the assumptions of IAS theory will not be valid for a heterogeneous surface when the different adsorbates interact with different surface functional groups (the effective specific surface area is not identical for all adsorbates).

Therefore, although it is mathematically complicated, it is reasonable to use IAS theory for prediction of multicomponent adsorption on homogeneous surfaces. It is not, however, consistent to use the IAS theory to derive a binary Freundlich isotherm because the Freundlich model is derived with the assumption of a continuously varying heat of adsorption.[26]

The LeVan-Vermeulen model takes into account the difference in the capacities between the adsorbates by using a weighted monolayer capacity. This is achieved by using the first 2 terms or the first 3 terms of a Taylor series. However, if the difference in the capacities between the adsorbates is quite large, it is expected that the LeVan-Vermeulen equation, which is limited to a 3-term Taylor series, will not be able to predict multicomponent adsorption as efficiently as the modified competitive Langmuir-like model.

Based on the previous discussion and the experimental comparisons between the different models, the following conclusion has been reached. Although the experimental results indicated that the modified competitive Langmuir-like model and the LeVan-Vermeulen model could both successfully predict multicomponent adsorption for the barbituric acid derivatives, the modified competitive Langmuir-like model is preferred.

Finally, the results obtained demonstrate that the adsorbates used in this study are competing for the same binding sites. This was expected, given the drugs' structural similarities, and this expectation was one of the reasons that these drugs were selected for this comparison of models.

ACKNOWLEDGEMENTS

The facilities provided by the Obermann Center for Advanced Studies at The University of Iowa contributed significantly to the completion of this work, which is gratefully acknowledged.

REFERENCES

1. Andersen AH. Experimental studies on the pharmacology of activated charcoal. III. Adsorption from gastro-intestinal contents. *Acta Pharmacol*. 1948;4:275-284.

2. Nogami H, Nagai T, Uchida H. Physico-chemical approach to biopharmaceutical phenomena. V. Relationship between the adsorption by carbon black from aqueous solution and the biopharmaceutical data of barbituric acid

derivatives. *Chem Pharm Bull*. 1969;17:176-180.

3. Huang L-F. [Ph.D. thesis]. *Determination of the Heats of Displacement for Various Barbituric Acid Derivatives on Two Activated Charcoals*. Iowa City, IA: University of Iowa; 1993.

4. Burke GM. [Ph.D. thesis]. *Adsorptivity and Surface Characterization of Activated Charcoals.* Iowa City, IA: University of Iowa; 1991.

5. *The Merck Index.* 12th ed. Whitehouse Station, NJ: Merck and Co., Inc.,; 1996.

6. Langmuir, I. The adsorption of gases on plane surfaces of glass, mica and platinum. *J Am Chem Soc*. 1918;40:1361-1403.

7. Schwab GM. *Theoretische und experimentelle Fortschritte auf dem Gebiete der heterogenen Gasreaktionen. Ergebnisse der Exakten Naturwissenschaften*. Vol. 7. Berlin: Springer;1928:276-341.

8. Butler JAV, Ockrent C. Studies in electrocapillarity. III. *J Phys Chem*. 1930;34:2841-2859.

9. Markham EC, Benton AF. The adsorption of gas mixtures by silica. *J Am Chem Soc*. 1931;53:497-506.

10. Young DM, Crowell AD. In: *The Adsorption of Gas Mixtures*. Washington, DC: Butterworths, Inc.;1962:373-377.

11. Broughton DB. Adsorption isotherms for binary gas mixtures. *Ind Eng Chem*. 1948:40(8):1506-1508.

12. Jain JS, Snoeyink VL. Adsorption from bisolute systems on active carbon. *J WPCF*. 1973;45(12):2463-2479.

13. Myers AL, Prausnitz JM. Thermodynamics of mixed-gas adsorption. *AICHE J*. 1965;11(1):121-126.

14. Radke CJ, Prausnitz JM. Thermodynamics of multi-solute adsorption from dilute liquid solutions. *AICHE J*. 1972;18(4):761-768.

15. Jossens L, Prausnitz JM, Fritz W, Schlunder EU, Myers AL. Thermodynamics of multisolute adsorption from dilute aqueous solutions. *Chem Eng Sci*. 1978;33:1097-1106.

16. Fritz W, Merk W, Schlünder EU, Sontheimer H. In: Suffet IH, McGuire MJ, eds. *Activated Carbon Adsorption of Organics from the Aqueous Phase*. Vol. 1. Ann Arbor, MI: Ann Arbor Science Publishers, Inc.; 1980:193-195.

17. Fritz W, Schlünder EU. Competitive adsorption of two dissolved organics onto activated carbon-I. *Chem Engin Sci*. 1981;36:721-730

18. Singer PC, Yen C-Y. In: Suffet IH, McGuire MJ, eds. *Activated Carbon Adsorption of Organics from the Aqueous Phase.* Vol. 1. Ann Arbor, MI: Ann Arbor Science Publishers, Inc.;1980:167-189.

19. Mckay G, Al Duri B. Prediction of multicomponent adsorption equilibrium data using empirical correlations. *Chem Eng J.* 1989;41:9-23.

20. LeVan MD, Vermeulen T. Binary Langmuir-like and Freundlich isotherms for ideal adsorbed solutions. *J Phys Chem*. 1981;85:3247-3250.

21. Frey D, Rodrigues AE. Explicit calculation of multicomponent equilibria for ideal adsorbed solutions. *AICHE J*. 1994;40(1):182-186.

22. Burke GM, Wurster DE, Buraphacheep V, Berg MJ, Veng-Pedersen P, Schottelius DD. Model selection for the adsorption of phenobarbital by activated charcoal. *Pharm Res*. 1991;8(2):228-231.

23. Burke GM, Wurster DE, Berg MJ, Veng-Pedersen P, Schottelius DD. Surface characterization of activated charcoal by x-ray photoelectron spectroscopy (XPS): Correlation with phenobarbital adsorption data. *Pharm Res*. 1992;9(1):126-130.

24. Alkhamis KA. [Ph.D. thesis]. *Prediction of the Adsorption Isotherm Parameters of Various Barbituric Acid Derivatives and Diazepam by Activated Carbon.* Iowa City, IA: University of Iowa; 1997.

25. Bellot JC, Condoret JS. Selection of competitive adsorption model for modelling displacement chromatography. *J Chromatogr*. 1993;657:305-326.

26. Adamson AW. Solid Liquid Interface In: *Physical Chemistry of Surfaces*. 5th ed. New York: John Wiley and Sons; 1990:425.