Chemical Engineering Science 64 (2009) 1480 – 1487

Contents lists available at ScienceDirect

Chemical Engineering Science

journal homepage: www.elsevier.com/locate/ces

Thermodynamics of water interactions with human stratum corneum. II. Interpretation via the Guggenheim–Anderson–deBoer isotherm

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ARTICLE INFO

Article history:
Received 24 June 2008
Received in revised form 22 October 2008
Accepted 11 November 2008
Available online 27 November 2008

Keywords:
Adsorption isotherm
Entropy of sorption
Heat of sorption
Isothermal calorimetry
Sorption isotherm
Stratum corneum

ABSTRACT

Studies of adsorption on biologically derived materials typically include direct measurement of either the adsorption isotherm or the heat of adsorption, but not both. Simultaneous measurement of adsorption and heat of adsorption should provide a more reliable description of the material under study. In this context, an analysis of the thermodynamics of water sorption is presented and a multilayer heat of sorption equation is derived within the framework of the Guggenheim–Anderson–deBoer (GAB) model. This model is applied to the previously published data for water vapor sorption and heat of water vapor sorption on stratum corneum (SC) over a range of relative humidities. The GAB models effectively characterize both heat evolution and equilibrium mass uptake over a broad water activity range. The thermodynamic results suggest significant restructuring of the SC during the sorption process; the sorption data alone are not sufficient to identify this effect. The results of this study emphasize first, the importance of incorporating a multilayer approach with variable energies of interaction in modeling of water uptake by SC and second, the utility of correlating sorption and calorimetric data simultaneously.

1. Introduction

Water adsorption and the thermodynamics of water adsorption play a key role in the processing of many biologically derived materials. For example, there has long been interest in the interaction of water with wool and hair keratins, due to the importance of these materials in textiles and personal care applications (Cassie, 1945; D'Arcy and Watt, 1970; Downes and Mackay, 1958; Li and Holcombe, 1992; Li and Luo, 1999; Morrison and Hanlan, 1957; Watt, 1960, 1964, 1980). Similarly, there is significant interest in the interaction of water with foodstuffs (Fasina et al., 1997; Marcos et al., 1997; Quirijns et al., 2005a,b; Velazquez et al., 2003). Adsorption properties are typically quantified through the adsorption isotherm and through energetic effects (both enthalpic and entropic). These energetic effects are often useful in understanding the fundamental phenomena underlying macroscopic effects, and are needed for tight optimization of large-scale processing operations that require controlling moisture levels or drying.

Direct measurements of the heat of adsorption are rarely accompanied by simultaneous determination of the adsorption isotherm. It is quite common to quantify the energetic effects of sorption using the isosteric heat of adsorption (Sircar, 2007), by measuring adsorption isotherms at several temperatures and applying the Clausius–Clapeyron equation to calculate the enthalpy of adsorption. For biologically derived materials, this approach is often complicated by the conformational and structural changes induced by water adsorption and temperature changes. The simultaneous measurement of the adsorption isotherm and the heat of adsorption overcomes this difficulty, as well as the limitations of the use of the Clausius–Clapeyron equation (Yadav et al., 2007).

In this context, the human stratum corneum (SC) is useful as a model system to study water interactions with biologically derived materials. The SC is a major barrier to the absorption into the circulation of most substances that are deposited on the skin surface. This barrier is essential to maintain physical and chemical equilibria with the environment. Since the SC is the rate-limiting diffusional barrier for most compounds, excised SC or skin sections containing SC are often used in determinations of the rate and extent of dermal absorption. Studies of water sorption (Anderson et al., 1973a,b; Blank, 1952; El-Shimi and Princen, 1978a; El-Shimi et al., 1975; Kasting and Barai, 2003; Leveque et al., 1987; Spencer et al., 1975; Yadav et al., 2007) and diffusion (Blank et al., 1984; Bouwstra et al., 1991; Bull, 1944; El-Shimi and Princen, 1978b; Kasting et al., 2003; Potts et al., 1991; Stockdale, 1978) in the SC have been published by various groups. The equilibrium sorption of water on SC follows a type II or type III isotherm, with a small amount of water sorbed at

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0009-2509/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.ces.2008.11.015

lower relative humidity (RH), and a relatively large amount of water sorbed at higher RH (Anderson et al., 1973a,b; Blank, 1952; El-Shimi and Princen, 1978a; El-Shimi et al., 1975; Kasting and Barai, 2003; Leveque et al., 1987; Spencer et al., 1975).

Kasting and Barai (2003) interpreted water vapor sorption data on SC from six laboratories using the Brunauer–Emmett–Teller (BET), D'Arcy–Watt, and Frenkel–Halsey–Hill (FHH) isotherms. The BET isotherm was modified to account for the finite water sorption observed when the gas phase was saturated with water vapor; otherwise, the BET isotherm describes the water sorption isotherm of human SC only below a water activity of 0.5 (Blank, 1952). A modified version of the FHH model (Kasting and Barai, 2003) and D'Arcy–Watt model (El-Shimi and Princen, 1978a; Kasting and Barai, 2003) successfully described the water sorption isotherm of human SC. The D'Arcy–Watt model has up to five parameters, and considers vapor-phase interactions with heterogeneous sorbents (D'Arcy and Watt, 1970; El-Shimi and Princen, 1978a; Kasting and Barai, 2003; Watt, 1980), while the FHH model includes long-range interactions between the sorbate and the sorbent, and assumes that the potential energy of the sorbate–sorbent interaction varies as the inverse n th power of the separation distance. The value of n varies between 2 and 3 for many systems (Adamson, 1976; Kasting and Barai, 2003). The parameters used in these models are linked to energetic interactions, but they have been determined in the cited studies purely by fitting the water sorption isotherms.

The results obtained by Kasting and Barai (2003) highlight two key aspects of the process by which water adsorbs onto SC. First, sorption clearly involves primary sorption of water onto active sites within the SC and subsequent adsorption of less tightly bound water in secondary layers. Second, the properties of the water bound in the secondary layers are influenced significantly by the presence of the SC. This second result invalidates one of the assumptions involved in the derivation of the BET isotherm, that the properties of water in the secondary layers are equivalent to the properties of liquid water. These results are consistent, however, with the assumptions used to develop the Guggenheim–Anderson–deBoer (GAB) isotherm, which is an extension of the Langmuir and BET adsorption models (Fasina et al., 1997; Marcos et al., 1997; Pradas et al., 2004; Pudipeddi et al., 1996; Quirijns et al., 2005a,b; Velazquez et al., 2003). In addition, the parameters of the GAB isotherm have clear thermodynamic interpretations that can be used to understand more completely the sorption process.

The present study couples the energetics of water interactions with SC with the sorption isotherm to provide insight into the sorption process; this is perhaps the first study reporting the simultaneous analysis of sorption and calorimetry data using the GAB isotherm. A multilayer heat of sorption equation is derived for the GAB model; this equation is then used in conjunction with the GAB water vapor sorption equation to obtain model coefficients. This model is used to characterize water uptake and heat of sorption on SC measured by isothermal microcalorimetry (Yadav et al., 2007). These results are used to infer structural changes during the sorption process (Kasting and Barai, 2003). The broader implications of the approach presented here are also discussed.

2. GAB adsorption isotherm and thermodynamics

2.1. Adsorption isotherm

The GAB isotherm is an extension of the Langmuir and BET adsorption models (Fasina et al., 1997; Marcos et al., 1997; Pradas et al., 2004; Pudipeddi et al., 1996; Quirijns et al., 2005a,b; Velazquez et al., 2003). It is based on the assumption of multilayer physical adsorption onto an adsorbent surface with active sites that are identical, distinguishable, and independent (Fasina et al., 1997; Marcos et al., 1997; Quirijns et al., 2005a,b; Velazquez et al., 2003). The isotherm does not account for lateral interactions between molecules (Quirijns et al., 2005a,b). The development of the isotherm traditionally accounts for three types of adsorbed molecules: molecules adsorbed directly on the adsorbent surface, which are strongly influenced by interactions with the surface; molecules adsorbed in the next several layers (the *multilayer*), which are influenced less significantly by interactions with the adsorbent surface; and layers beyond the multilayer, which have properties identical to those of the adsorbate in bulk liquid form.

Based on these assumptions, the traditional form of the GAB sorption isotherm is obtained (Marcos et al., 1997; Pradas et al., 2004; Velazquez et al., 2003) as

$$\theta = \frac{Ckx}{(1-kx)(1-(1-C)kx)} \tag{1}$$

Eq. (1) relates the fractional coverage, θ, to the adsorbate activity, x, through the parameters, C and k. The natures of the parameters C and k, which are related to the thermodynamics of the adsorption process, are discussed in detail below. The fractional coverage is defined as

$$\theta = \frac{n}{n_m} \tag{2}$$

where n represents the moles adsorbed and n_m represents the moles adsorbed at monolayer coverage (one adsorbate molecule per adsorption site).

Pradas et al. (2004) developed Eq. (1) using a classical thermodynamic argument, modeling the adsorption process as a set of reactions in which i adsorbate molecules (B) associate with one adsorption site ($X0$) to form the complex XiB:

$$X0 + iB \quad \leftrightarrow \quad XiB \tag{3}$$

At equilibrium, the chemical potentials are related by

$$\mu_{XiB} = \mu_{X0} + i\mu_B \tag{4}$$

The chemical potential of the unassociated sites can be expressed as

$$\mu_{X0} = \mu^0_{X0} + RT \ln\theta_0 \tag{5}$$

where

$$\theta_i = \frac{n_i}{n_m} \tag{6}$$

n_i is the number of complexes XiB, R is the gas law constant, T is the absolute temperature, and the superscript 0 denotes a property at standard state; n_0 is number of unoccupied adsorption sites. The chemical potential of the unassociated adsorbate can be written as

$$\mu_B = \mu^0_B + RT \ln x \tag{7}$$

The chemical potential of complex XiB can be expressed as the sum of contributions from the first adsorbed layer and the multilayer:

$$\mu_{XiB} = \mu^0_{XB} + (i-1)\mu^*_B + RT\ln\theta_i \tag{8}$$

where the superscript * indicates a property of the multilayer.

The GAB isotherm, Eq. (1), follows directly from these assumptions (Pradas et al., 2004); the following relationships are also obtained:

$$\theta_i = C\theta_0(kx)^i \tag{9}$$

$$C = \exp\left(\frac{\mu^*_B - \mu^0_{XB}}{RT}\right) \tag{10}$$

$$k = \exp\left(\frac{\mu_B^0 - \mu_B^*}{RT}\right) \tag{11}$$

The parameters n_m, C, and k can be evaluated from the adsorption isotherm (n as a function of x); however, a single adsorption isotherm is not sufficient to identify the relative importance of entropic and enthalpic contributions to the adsorption process. Thus, additional data are required to isolate the entropic and enthalpic contributions.

2.2. Calorimetric heat of adsorption

Calorimetry can be used to obtain the heats of adsorption as a function of adsorbate activity. For the adsorption process described by Eq. (3), it is convenient to express enthalpic effects in terms of the enthalpy of adsorption of the first adsorbed layer, H_1, and the enthalpy of adsorption to the multilayer, H_m. These enthalpies are defined in terms of the molar enthalpy of the adsorbate in the gas phase, H_G, and the partial molar enthalpies in the adsorbed layers:

$$H_1 \equiv H_{XB}^0 - H_G \tag{12}$$

$$H_m \equiv H_B^* - H_G \tag{13}$$

Superscripts and subscripts for the enthalpy follow the same conventions used for chemical potentials. H_1 and H_m are defined in a manner that is independent of choice of standard state, and are negative when adsorption is exothermic. The integral calorimetric heat of adsorption, Q, can be calculated from the adsorption isotherm and the enthalpies of adsorption defined above; the development follows that presented by Pudipeddi et al. (1996) for adsorption processes following the BET isotherm. Q is defined as positive when the adsorption process is exothermic.

The heat Q_i evolved by the formation of all complexes XiB can be written as

$$-Q_i = n_i(H_1 + (i-1)H_m) \tag{14}$$

Eq. (14) can be combined with Eq. (9) and rearranged to provide the result

$$-Q = -\sum_{i=1}^{\infty} Q_i = n_m C\theta_0 \left\{(H_1 - H_m)\sum_{i=1}^{\infty}(kx)^i + H_m\sum_{i=1}^{\infty} i(kx)^i\right\} \tag{15}$$

The series in Eq. (15) are convergent if $kx < 1$, in which case

$$-Q = \frac{n_m C\theta_0(kx)}{(1-kx)^2}\{H_1 + (H_m - H_1)(kx)\} \tag{16}$$

The fraction of sites unoccupied can be calculated from C, k, and x, assuming $kx < 1$:

$$\theta_0 = 1 - \sum_{i=1}^{\infty}\theta_i = 1 - \sum_{i=1}^{\infty} C\theta_0(kx)^i = \frac{1-kx}{1-(1-C)kx} \tag{17}$$

Combining Eqs. (1), (16), and (17),

$$-Q = n[H_1 + (H_m - H_1)(kx)] \tag{18}$$

which can be arranged to a form more convenient for regression:

$$-\frac{Q}{n} = H_1 + (H_m - H_1)(kx) \tag{19}$$

Eqs. (1) and (19) provide a form through which isotherm and calorimetric data can be correlated to determine values for H_1 and H_m.

2.3. Isolation of enthalpic and entropic effects

The parameters C and k can provide insight into the adsorption process if the entropic and enthalpic contributions to these factors can be established. The molar enthalpies of adsorption H_1 and H_m are related to the more fundamental enthalpies H_B^0, H_B^*, and H_{XB}^0. The standard-state enthalpy of the adsorbate can be included in the expressions for H_m and H_1:

$$H_m \equiv H_B^* - H_G = (H_B^* - H_B^0) - (H_G - H_B^0) \tag{20}$$

$$H_1 \equiv H_{XB}^0 - H_G = (H_{XB}^0 - H_B^0) - (H_G - H_B^0) \tag{21}$$

Taking the standard state as liquid adsorbate at the conditions of the adsorption experiment, the difference $-(H_G - H_B^0)$ is the latent heat of condensation, H_L. As a consequence,

$$H_B^* - H_B^0 = H_m - H_L \tag{22}$$

$$H_{XB}^0 - H_B^0 = H_1 - H_L \tag{23}$$

Noting the definition of chemical potential, inserting these results into Eqs. (20) and (21) and rearranging recovers the standard expressions for C and k (Pradas et al., 2004):

$$C = \exp\left(\frac{S_{XB}^0 - S_B^*}{R}\right)\exp\left(\frac{H_m - H_1}{RT}\right) = C_0\exp\left(\frac{H_m - H_1}{RT}\right) \tag{24}$$

$$k = \exp\left(\frac{S_B^* - S_B^0}{R}\right)\exp\left(\frac{H_L - H_m}{RT}\right) = k_0\exp\left(\frac{H_L - H_m}{RT}\right) \tag{25}$$

Superscripts and subscripts for the entropy follow the same conventions used for chemical potentials and enthalpies. Eqs. (24) and (25) illustrate the entropic nature of the pre-exponential factors C_0 and k_0. Further, the partial molar entropies of the adsorbate on the surface and in the multilayer can be calculated directly from C, k, and the molar enthalpies of adsorption:

$$S_B^* - S_B^0 = \left(\frac{H_m - H_L}{T}\right) + R\ln k \tag{26}$$

$$S_{XB}^0 - S_B^0 = \left(\frac{H_1 - H_L}{T}\right) + R\ln Ck \tag{27}$$

2.4. Comparison with BET adsorption isotherm and thermodynamics

The critical difference between the assumptions of the GAB model and those of the BET model concern the properties of the material adsorbed in the secondary layers. In the BET model, the properties in the secondary layers are taken to be the same as those of the adsorbate in bulk liquid form. Since the bulk liquid is the reference state for thermodynamic properties, the assumptions of the BET model imply:

$$\mu_B^* = \mu_B^0 \tag{28}$$

As a consequence, $k = 1$ for the BET model, and the standard expression for the BET adsorption isotherm follows directly:

$$\theta = \frac{Cx}{(1-x)(1-(1-C)x)} \tag{29}$$

The corresponding expression for Q is

$$-\frac{Q}{n} = H_1 + (H_1 - H_L)x \tag{30}$$

As noted above, the GAB isotherm predicts finite adsorption as $x \to 1$, while the BET isotherm, Eq. (29), predicts unlimited adsorption as $x \to 1$. Both models predict that the average calorimetric heat, Q/n, will be linear with x, and that limit of Q/n as $x \to 0$ will be $-H_1$. Thus, this correlation provides an estimate of the enthalpy of adsorption for the first adsorbed layer regardless of the relative validities of the GAB and BET assumptions.

2.5. Differential enthalpy of adsorption

Eq. (18) expresses the measured integral heat of adsorption in terms of the gas-phase adsorbate activity and the parameters of the GAB model. In many practical applications, the differential enthalpy of adsorption, $\overline{\Delta H}$, is also of interest. This differential enthalpy can be calculated by differentiating Eq. (18) with respect to the number of moles adsorbed:

$$\overline{\Delta H} = -\frac{dQ}{dn} = H_1 + (H_m - H_1)(kx)\frac{1 + r(1-\theta)}{1 - r\theta} \tag{31}$$

The parameter r is defined as

$$r = \frac{1 - kx}{1 + kx} \tag{32}$$

Eq. (31) allows calculation of the differential enthalpy of adsorption based on knowledge of the GAB parameters; in the absence of such a relationship, the differential enthalpy must be estimated by numerical differentiation of experimental results. (The definition of $\overline{\Delta H}$ used here is slightly different from the definition used in the investigators' previous work, in which a correction was included to account for the latent heat of condensation.)

3. Application to water sorption on human SC

3.1. Experimental details

The above results were applied to the data previously published by Yadav et al. (2007). Human SC obtained from cadavers (back and thigh) was prepared by the heat separation technique followed by trypsinization (Kligman and Christophers, 1963). SC samples (10–15 mg) were dried under vacuum, mounted on a wire screen and placed in a specially modified C80-D isothermal calorimeter; the experimental setup has been described in detail elsewhere (Yadav et al., 2007). The sample was then exposed to air of known RH and the heat released was measured. After each heat flow measurement, the sample was weighed to determine the water uptake. The sample was subsequently dried to a constant weight prior to re-exposure to air at a different RH. The water sorption and heat of sorption results are shown in Fig. 1. Two samples were obtained for each location for each donor, so that a total of eight SC samples were used; the results presented here are the average of the values obtained for replicate samples.

3.2. Data analysis

Initially, estimates of H_1, H_m, n_m, C, and k were determined for each sample individually (Yadav et al., 2007) by fitting Eqs. (1) and (19) to the experimental data for n and Q/n by simultaneous nonlinear least-squares regression using a program written in SigmaPlot® (Systat Software, San Jose, CA). The regression minimized was the residual sum of squared deviations (SSQ), defined as

$$SSQ = \sum_{i=1}^{N} \left\{ [n_i(obs) - n_i(fit)]^2 + \left[\left(\frac{Q}{n}\right)_i (obs) - \left(\frac{Q}{n}\right)_i (fit) \right]^2 \right\} \tag{33}$$

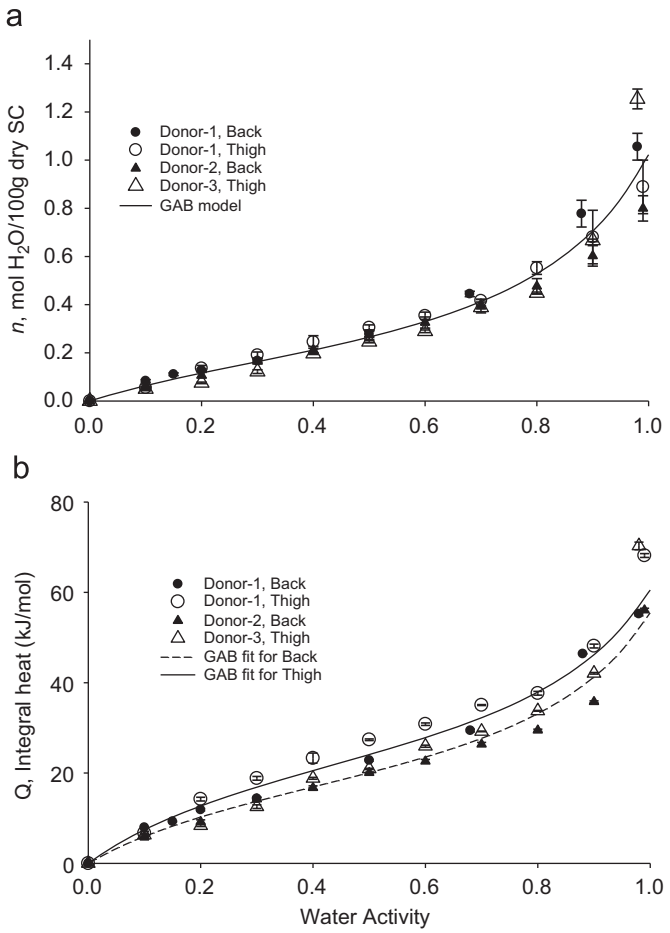

Fig. 1. Experimental data for (a) water sorption and (b) heat of sorption on human SC at 32 °C correlated using the GAB model, Eqs. (1) and (19).

Regression results are presented in Table 1. The value of H_L was 43.7 kJ/mol (interpolated at 32 °C using data from Smith et al., 1996).

The regression resulted in correlation coefficients ranging from 0.982 to 0.989, indicating that the GAB model provides a good representation of the data. The results presented in Table 1 indicate (1) that H_m is not statistically distinguishable from H_L (−43.67 kJ/mol) (with p values ranging from 0.46 to 0.98), (2) that the values of C, k, and n_m do not, within the precision of the parameter estimates, differ among the sample types, and (3) that H_1 for back SC is lower than for thigh SC. These results suggest that complete data set can be described using single values of C, k, and n_m, $H_L = H_m$, and separate values of H_1 for back and thigh data.

A second set of correlations was completed with pooled data. n_m, C, and k were estimated using nonlinear least-squares regression based on Eq. (1); again, a program written in SigmaPlot® was used. Results of this procedure are presented in Table 2; this regression was used to generate the curves in Fig. 1. Estimates of H_1 for back and thigh data were determined from regression of Q/n as a function of x using Eq. (19); results of this regression are presented in Table 2 and are shown graphically in Fig. 2. The correlation coefficient for the fit to Eq. (1) was 0.987, comparable to the correlation coefficients obtained when data for the various sample types were correlated independently. Final values of the regression parameters were independent of initial estimates.

Table 1
GAB model (Eqs. (1) and (19)) parameters describing water sorption and heat of water sorption on individual samples of human SC using data from (Yadav et al., 2007); parameters were obtained using *simultaneous* regression of sorption and calorimetric data for individual samples.

		Donor 1 back	Donor 1 thigh	Donor 2 back	Donor 3 thigh
C	Dimensionless	6.3 ± 1.4	3.0 ± 0.8	3.6 ± 2.0	3.2 ± 0.7
n_m	mol H_2O/100 g dry SC	0.20 ± 0.02	0.31 ± 0.11	0.26 ± 0.15	0.18 ± 0.02
k	Dimensionless	0.85 ± 0.04	0.70 ± 0.13	0.72 ± 0.25	0.87 ± 0.03
H_1	kJ/mol H_2O	-97 ± 4	-119 ± 19	-94 ± 5	-126 ± 19
H_m	kJ/mol H_2O	-46 ± 8	-44 ± 20	-48 ± 9	-46 ± 17
r^2	Dimensionless	0.986	0.989	0.982	0.987

Values shown are least-squares fit ± 95% confidence interval.

Table 2
GAB model (Eqs. (1) and (19)) parameters describing water sorption and heat of water sorption on human SC using *pooled* data from (Yadav et al., 2007); C, n_m, and k obtained by regression of pooled sorption data; H_1 obtained by linear regression of Q/n vs. x with data pooled by location (back or thigh); and H_m set to latent heat of condensation.

C	Dimensionless	4.39 ± 0.01
n_m	mol H_2O/100 g dry SC	0.21 ± 0.01
k	Dimensionless	0.80 ± 0.01
H_1 (back)	kJ/mol H_2O	-97.1 ± 1.2
H_1 (thigh)	kJ/mol H_2O	-122.3 ± 1.4
H_m	kJ/mol H_2O	-43.67
r^2	Dimensionless	0.987

Values shown are least-squares fit ± 95% confidence interval.

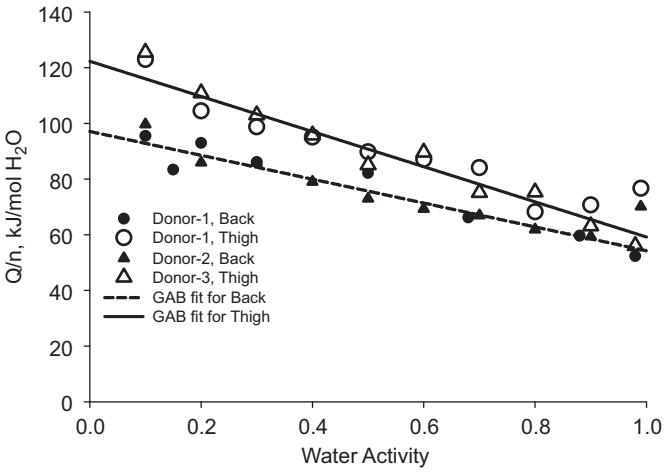

Fig. 2. Correlation of average calorimetric heat of water vapor sorption on human SC at 32 °C with water activity.

4. Discussion

4.1. Physical interpretation of GAB results

In the past, numerous studies have been conducted to describe water sorption on various keratins (Anderson et al., 1973a,b; Blank, 1952; Cassie, 1945; D'Arcy and Watt, 1970; Downes and Mackay, 1958; El-Shimi and Princen, 1978a; El-Shimi et al., 1975; Kasting and Barai, 2003; Leveque et al., 1987; Li and Holcombe, 1992; Li and Luo, 1999; Morrison and Hanlan, 1957; Spencer et al., 1975; Watt, 1960, 1964, 1980). Many of these reports have focused on wool and hair keratins, due to their importance in textiles and personal care (Cassie, 1945; D'Arcy and Watt, 1970; Li and Holcombe, 1992; Li and Luo, 1999; Morrison and Hanlan, 1957; Watt, 1960, 1964, 1980). However, with the exception of Leveque's calorimetric study (Leveque et al., 1987), the current literature on human SC provides little information about the energetics of SC–water interaction. This report combines mass uptake and energetics data to describe human SC–water interactions.

The monolayer water content, n_m, for human SC obtained from mass uptake measurements in the calorimeter at 32 °C was 0.038 g H_2O/g dry SC (0.21 mol H_2O/100 g dry SC in Table 1). These values are in excellent agreement with the value 0.039 g H_2O/g dry SC reported by Kasting and Barai (2003) based on a GAB analysis of gravimetric measurements at 20 °C. The water sorption observed at high water activity in this study is much less than that for the studies summarized by Kasting and Barai (2003), with the exception of the work of El-Shimi and Princen (1978b). Using a vapor phase sorption method, these investigators determined several isotherms with saturated water sorptions comparable to those observed in this study. Kasting and Barai (2003) incorrectly interpreted these values as weight fractions. The reason for the low water sorption in the present study, and that of El-Shimi and Princen, is not entirely clear.

Although the analysis presented here suggests that 0.038 g H_2O/g dry SC is tightly adsorbed to SC lipids and keratins, it is not correct to think about this water up to this hydration stage being "bound" and the remainder being "free". As discussed elsewhere (Kasting and Barai, 2003; Yadav et al., 2007) the monolayer water content, n_m, obtained from isotherm analysis of SC water sorption data is much less than the amount of bound water as determined by other techniques. Spectroscopic (Hansen and Yellin, 1972; Foreman, 1976) and calorimetric (Walkley, 1972) characterization of partially hydrated SC has shown that 0.33–0.5 g H_2O/g dry SC becomes associated with the tissue based on narrowing of infrared and nuclear magnetic resonance line widths and the lack of a melting endotherm at 0 °C. This is approximately 10 times the GAB monolayer value. A partial explanation for this difference may be found in the fact that keratin fibers uncoil as they hydrate and expose more primary binding sites, a phenomenon that has been recognized for many years (Cassie, 1945; Blank, 1952). In contrast, the GAB model describes an immobile substrate with a fixed number of binding sites. One may infer from this comparison that the primary binding sites that unfurl as the SC swells have a weaker enthalpic interaction with water than do the primary sites in very dry SC; otherwise, greater cumulative heats of sorption would be measured and a higher value of n_m obtained. It is also evident that the entropic interactions between SC keratin fibers and the GAB multilayer water surrounding them are sufficient to prevent the water from freezing (cf. Walkley, 1972).

The pre-exponential factors C_0 and k_0, defined by Eqs. (24) and (25) are expressions of entropic effects in the adsorption process. Adamson postulated a value of C_0 close to unity for the BET model (Adamson, 1976). However, Pradas et al. (2004) criticized the subsequent practice of approximating this parameter as one and showed for a water-synthetic polymer (poly 2-hydroxyethyl acrylate) system that C_0 has values in the range 0.1–0.5, depending on the temperature (280–340 K). A value of C_0 less than one is expected if the mobility of molecules within the first adsorbed layer is restricted (Pradas et al., 2004). Hill (1948) showed that the reduction of the value of C_0 (therein called R) expected for the loss of translational degrees of freedom by diatomic molecules is only a factor of 5. Based

Table 3
Water entropies estimated using the GAB model for water sorption on human SC.

	S (J/mol K)	
	Back	Thigh
Gas phase (S_G)	143	
Saturated liquid (S_B)	0	
Multilayer (S_B^*)	−2	
Fictitious solid state	−11	
First sorbed layer (S_{XB}^0)	−245	−161

The entropy of solid water at experimental conditions was estimated by dividing the heat of fusion by the experimental temperature. Entropies are referenced to saturated water at the experimental temperature, 32 °C.

on the results presented in Table 2, $C_0 = 3.1 \times 10^{-9}$ from SC from the back and 1.4×10^{-13} for SC from the thigh. C_0 values almost as low have been estimated for other natural materials. For example, Turhan and Gunasekaran (2002) report C_0 values of 7.7×10^{-5} for fuzzy cottonseed and 2.2×10^{-4} for starch-coated cottonseed. However, the values of C_0 obtained in this study are too low to explain based simply on loss of translational freedom.

The low values of C_0 must be attributable to entropic effects. Eqs. (26) and (27) can be used to calculate the partial molar entropies S_{XB}^0 and S_B^* relative to that of the standard state entropy of water. Results of these calculations are presented in Table 3; the entropy of water vapor and a fictitious frozen state at the experimental temperature are shown for comparison. As expected based on the value of k_0, the partial molar entropy of water adsorbed in the multilayer is less than the molar entropy of liquid water but greater than that of a fictitious frozen state. The partial molar entropy of water in the first adsorbed layer is remarkable inasmuch as it is less than that of a fictitious frozen state in which water has extremely limited mobility and a low-entropy crystalline structure. Thus, the low molar entropy associated with the first adsorbed layer suggests that water adsorption to this layer results not only in reduced mobility for the adsorbed water, but also in significant restructuring of the SC itself. This result is supported by ATR–FTIR results published elsewhere by the authors (Yadav et al., 2009) that indicate significant protein conformation changes occur during water adsorption in human SC. This restructuring of the SC is not evident from the isotherm data alone. It is the combination of isotherm data with the energetics of the adsorption process that allows identification of this effect.

The functional consequences of the primary water binding enthalpy (H_1) differences between back skin and thigh skin noted in this study are uncertain. Broad body surfaces are considered by most to have comparable permeability to both water and organic solutes, although there is some basis for thinking trunk skin is more permeable than arm/leg skin for the latter (Scheuplein, 1978). However, this difference is not consistently observed. For example, application of testosterone patches to abdomen, back, thigh and upper arm in a clinical study involving 34 hypogonadal men resulted in comparable testosterone blood levels in all four groups (Physician's Desk Reference, 2002). It seems more likely that the H_1 enthalpy difference may be a factor in water holding capacity of the skin, which is very important to skin moisturization, skin barrier homeostasis and, ultimately, to skin health (Imokawa et al., 1989; Rawlings and Matts, 2005). However, the factors affecting these phenomena are complex and include SC lipid content, natural moisturizing factor levels and environmental factors in addition to possible enthalpic effects (Harding, 2004). Since skin health is of great concern to a broad audience, it may be that enthalpy measurements and analysis thereof, such as the work described here, can play a role in sorting out the complex factors affecting this condition.

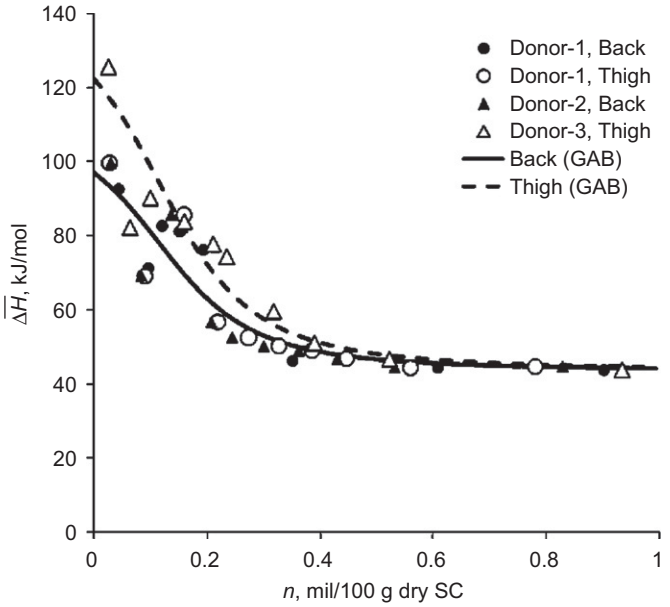

Fig. 3. Differential enthalpy of water sorption on human SC as a function of water sorption; data points obtained by numerical differential of calorimetric and adsorption results (Yadav et al., 2007); curves obtained using Eq. (31) and parameter values from Table 2.

4.2. Broader implications

The discussion above demonstrates the use of correlated sorption and calorimetry results to provide a physical interpretation of the observed water sorption behavior of human SC. This interpretation is critical to understanding permeation through skin and the impact of pharmaceutical and cosmetic materials on skin. However, the methodology presented and applied in this work has broader implications in chemical engineering applications, especially applications involving the processing of biologically derived materials. For example, many adsorption and desorption processes are not isothermal, making the temperature dependence of isotherm parameters a matter of practical importance. The GAB isotherm provides an explicit form for the temperature dependence of C and k through Eqs. (24) and (25). If isotherms are measured at several temperatures, the isotherm data can be correlated at each temperature using Eq. (1) to provide values of C and k. Eqs. (24) and (25) can then be used to determine the enthalpic and entropic contributions to the parameters in the GAB model. Quirijns et al. (2005a,b) have applied this approach, for example. This approach requires sorption data obtained over a range of temperature, and assumes implicitly that there is no change in the material under study throughout the temperature range; this assumption can be questionable for biologically derived materials. The methodology used in the present study can be used to circumvent this problem, since the entropic and enthalpic contributions to the adsorption isotherm can be obtained at a single temperature using independent calorimetric results. Changes in these contributions would be indicative of changes in the material under study.

In addition, there are often significant heat effects associated with adsorption and desorption processes, and optimization of these processes requires a reliable quantitative relationship between sorption and heat loads. As noted above, it is common to quantify the heat effect associated with a sorption process using the isosteric heat of sorption calculated using the Clausius–Clapeyron equation (Sircar, 2007). The authors (Yadav et al., 2007) have reviewed the limitations of applying this practice to biologically derived materials such as SC;

these limitations were one of the original motivations for calorimetric studies of SC.

When calorimetric results are available, it is no longer necessary to resort to use of the Clausius–Clapeyron equation to determine the differential enthalpy of adsorption, $\overline{\Delta H}$. In principle, the calorimetric and sorption data can be differentiated numerically to determine $\overline{\Delta H}$; however, calculation of $\overline{\Delta H}$ by numerical differentiation of experimental results is quite susceptible to experimental errors. The GAB isotherm provides an alternate approach. Experimental results can be correlated directly, after which Eq. (32) can be used calculate $\overline{\Delta H}$. The results of this procedure are exemplified in Fig. 3. In this figure, the data points are obtained by numerical differentiation of the sorption and calorimetric data, while the curves were generated using Eq. (32) and the parameter values presented in Table 2. There is reasonably good agreement between differential enthalpies determined by numerical differentiation of the experimental results and differential enthalpies determined using the GAB model.

5. Conclusions

This study presents a multilayer heat of sorption equation developed within the framework of the GAB model. This equation has been applied to a model system, adsorption of water on human stratum corneum at 32 °C. The GAB model effectively described major features of the experimental sorption and heat of sorption data for this system, even at high activities where the BET model fails. In conjunction with coordinated sorption and calorimetric data, the model can be used to isolate enthalpic and entropic effects during the sorption process. For the samples studied here, the calorimetric results indicate significant restructuring of the SC occurs during water sorption. The model can be applied to a broader range of biologically derived materials to obtain the differential heat of adsorption without numerical differentiation of experimental results. The analysis presented also illustrates the utility of simultaneous correlation of sorption and calorimetric data to provide a more complete picture of the sorption process.

Notation

C	parameter in GAB and BET isotherms, dimensionless
C_0	pre-exponential factor in C, dimensionless
H	enthalpy
H_1	enthalpy of adsorption from gas to first surface layer, J/mol
H_L	latent heat of condensation, J/mol
H_m	enthalpy of adsorption from gas to multilayer, J/mol
$\overline{\Delta H}$	differential enthalpy of adsorption, J/mol
k	parameter in GAB isotherms, dimensionless
k_0	pre-exponential factor in k, dimensionless
n	moles sorbed, mol/g sorbent
n_i	moles sorbed in layers 1 through i, mol/g sorbent
Q	calorimetric heat of adsorption, J
Q_i	calorimetric heat of adsorption of layers 1 through i, J
R	gas law constant, J/mol K
S	entropy, J/mol K
T	temperature, K
x	sorbate gas-phase activity, dimensionless

Greek letters

θ	fractional coverage of surface, dimensionless
θ_i	fractional coverage of surface layer i, dimensionless
μ	chemical potential, J/mol

Subscripts

m	monolayer coverage
$X0$	free surface binding site
XB	surface binding site with single molecule of bound sorbate
G	gas phase

Superscripts

^{0}	standard state
*	thermodynamic property in multilayer

Acknowledgments

The authors gratefully acknowledge fellowships from A. William Forbriger, Rindsberg and partial support from NIOSH/CDC Grant R01 OHO7529.

References

Adamson, A.W., 1976. Physical Chemistry of Surfaces. Wiley, New York.
Anderson, R.L., Cassidy, J.M., Hansen, J.R., Yellin, W., 1973a. The effect of in vivo occlusion on human stratum corneum hydration–dehydration in vitro. Journal of Investigative Dermatology 61 (6), 375–379.
Anderson, R.L., Cassidy, J.M., Hansen, J.R., Yellin, W., 1973b. Hydration of stratum corneum. Biopolymers 12, 2789–2802.
Blank, I.H., 1952. Factors which influence the water content of the stratum corneum. Journal of Investigative Dermatology 18, 433–440.
Blank, I.H., Moloney, J., Emslie, A.G., Simon, I., Apt, C., 1984. The diffusion of water across the stratum corneum as a function of its water content. Journal of Investigative Dermatology 82, 183–194.
Bouwstra, J.A., de Vries, M.A., Gooris, G.S., Bras, W., Brussee, J., Ponec, M., 1991. Thermodynamic and structural aspects of the skin barrier. Journal of Controlled Release 15, 209–220.
Bull, H.B., 1944. Adsorption of water by proteins. Journal of the American Chemical Society 66, 1499–1507.
Cassie, A.B.D., 1945. Absorption of water by wool. Transactions of the Faraday Society 41, 458–464.
D'Arcy, R.L., Watt, I.C., 1970. Analysis of sorption isotherm of non-homogeneous sorbents. Transactions of the Faraday Society 66, 1236–1245.
Downes, J.G., Mackay, B.H., 1958. Sorption kinetics of water vapor in wool fibers. Journal of Polymer Science 28, 45–57.
El-Shimi, A.F., Princen, H.M., 1978a. Diffusion characteristics of water vapor in some keratins. Colloid and Polymer Science 256, 209–217.
El-Shimi, A.F., Princen, H.M., 1978b. Water vapor sorption and desorption behavior of some keratins. Colloid and Polymer Science 256, 105–114.
El-Shimi, A.F., Princen, H.M., Risi, D.R., 1975. Water vapor sorption, desorption, and diffusion in excised skin: Part I. Technique. In: Baier, R.E. (Ed.), Applied Chemistry at Protein Interfaces. American Chemical Society, Washington.
Fasina, O., Sokhansanj, S., Tyler, R., 1997. Thermodynamics of moisture sorption in alfalfa pellets. Drying Technology 15, 1553–1570.
Foreman, M.I., 1976. A proton magnetic resonance study of water in human stratum corneum. Biochemica Biophysica Acta 437, 599.
Hansen, J.R., Yellin, W., 1972. NMR and infrared spectroscopy studies of stratum corneum hydration. In: Jellinek, H.H.G. (Ed.), Water Structure at the Water–Polymer Interface. Plenum Press, New York, pp. 19–28.
Harding, C.R., 2004. The stratum corneum: structure and function in health and disease. Dermatologic Therapy 17 (Suppl. 1), 6–15.
Hill, T.L., 1948. Statistical mechanics of multimolecular adsorption. IV. The statistical analog of the BET constant a_1b_2/b_1a_2. Hindered rotation of a symmetrical diatomic molecule near a surface. Journal of Chemical Physics 16, 181–189.
Imokawa, G., Akasaki, S., Minematsu, Y., Kawai, M., 1989. Importance of intercellular lipids in water-retention properties of the stratum corneum: induction and recovery study of surfactant dry skin. Archives of Dermatological Research 281, 45–51.
Kasting, G.B., Barai, N.D., 2003. Equilibrium water sorption in human stratum corneum. Journal of Pharmaceutical Sciences 92, 1624–1631.
Kasting, G.B., Barai, N.D., Wang, T.-F., Nitsche, J.M., 2003. Mobility of water in human stratum corneum. Journal of Pharmaceutical Sciences 92, 2326–2340.
Kligman, A.M., Christophers, E., 1963. Preparation of isolated sheets of human stratum corneum. Archives of Dermatology 88, 702–705.
Leveque, J.L., Escoubez, M., Rasseneur, L., 1987. Water–keratin interactions in human stratum corneum. Bioengineering and the Skin 3, 227–242.
Li, Y., Holcombe, B.V., 1992. A two stage sorption model of the coupled diffusion of moisture and heat in wool fabrics. Textile Research Journal 62, 211–217.
Li, Y., Luo, Z., 1999. An improved simulation of the coupled diffusion of moisture and heat in wool fabric. Textile Research Journal 69, 760–768.
Marcos, B., Esteban, M.A., Lopez, P., Alcala, M., Gomez, R., Espejo, J., Marcos, A.Z., 1997. Monolayer values at 30 °C of various spices as computed by BET and GAB models. Zeitschrift fur Lebensmittel—Untersuchung und—Forschung 204, 109–112.

Morrison, J.L., Hanlan, J.F., 1957. Swelling of fibrous proteins. Nature 179, 528–529.
Potts, R.O., Golden, G.M., Francoeur, M.L., Mak, V.H.W., Guy, R.H., 1991. Mechanism and enhancement of solute transport across the stratum corneum. Journal of Controlled Release 15, 249–260.
Pradas, M.M., Sanchez, M.S., Ferrer, G.G., Ribelles, J.L.G., 2004. Thermodynamics and statistical mechanics of multilayer adsorption. Journal of Chemical Physics 121, 8524–8531.
Pudipeddi, M., Sokoloski, T.D., Duddu, S.P., Carstensen, J.T., 1996. Quantitative characterization of adsorption isotherms using isothermal microcalorimetry. Journal of Pharmaceutical Sciences 85, 381–386.
Quirijns, E.J., Bvan Boxtel, A.J., van Loon, W.K.P., van Straten, G., 2005a. An improved experimental and regression methodology for sorption isotherms. Journal of the Science of Food and Agriculture 85, 175–185.
Quirijns, E.J., van Boxtel, A.J.B., van Loon, W.K.P., Van Straten, G., 2005b. Sorption isotherms, GAB parameters and isosteric heat of sorption. Journal of the Science of Food and Agriculture 85, 1805–1814.
Rawlings, A.V., Matts, P.J., 2005. Stratum corneum moisturization at the molecular level: an update in relation to the dry skin cycle. Journal of Investigative Dermatology 124, 1099–1110.
Scheuplein, R.J., 1978. Skin permeation. In: Jarrett, A. (Ed.), The Physiology and Pathophysiology of the Skin. Academic Press, New York, p. 1740.
Sifton, D.W. (Ed.), 2002. Physician's Desk Reference, 56th ed. Medical Economics Company, Montvale, NJ, p. 3378.
Sircar, S., 2007. Recent developments in macroscopic measurement of multicomponent gas adsorption equilibria, kinetics, and heats. Industrial and Engineering Chemistry Research 46, 2917–2927.
Smith, J.M., Van Ness, H.C., Abbott, M.M., 1996. Introduction to Chemical Engineering Thermodynamics. McGraw-Hill, pp. 668–673.
Spencer, T.S., Linamen, C.E., Akers, W.A., Jones, H.F., 1975. Temperature dependence of water content of stratum corneum. British Journal of Dermatology 93, 159–164.
Stockdale, M., 1978. Water diffusion coefficients versus water activity in stratum corneum: a correlation and its implications. Journal of the Society of Cosmetic Chemists 29, 625–639.
Turhan, M., Gunasekaran, S., 2002. Water vapour adsorption properties of fuzzy and starch-coated cottonseeds. Biosystems Engineering 83, 175–184.
Velazquez, G., Herrera-Gomez, A., Martin-Polo, M.O., 2003. Theoretical determination of first adsorbed layer of water in methylcellulose. Journal of Food Engineering 59, 45–50.
Walkley, K., 1972. Bound water in stratium corneum measured by differential scanning calorimetry. Journal of Investigative Dermatology 5, 225–227.
Watt, I.C., 1960. Kinetic study of the wool-water system. Part II: the mechanisms of two-stage absorption. Textile Research Journal 30, 644–653.
Watt, I.C., 1964. Sorption of organic vapors by wool keratin. Journal of Applied Polymer Science 8, 1737–1750.
Watt, I.C., 1980. Sorption of water vapor by keratin. Journal of Macromolecular Science—Reviews of Macromolecular Chemistry C18, 169–245.
Yadav, S., Pinto, N.G., Kasting, G.B., 2007. Thermodynamics of water interaction with human stratum corneum. I. Measurement by isothermal flow calorimetry. Journal of Pharmaceutical Science 96, 1585–1597.
Yadav, S., Wickett, R.R., Pinto, N.G., Kasting, G.B., Thiel, S.W., 2009. Comparative thermodynamic and spectroscopic properties of water interaction with human stratum corneum. Skin Research and Technology, in press.