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RESEARCH PAPER

Hot-Melt Coating: Water Sorption Behavior of Excipient Films

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ABSTRACT

Hot-melt coating allows encapsulation of water-labile, drug-laden substrates to form a barrier that resists moisture ingress. To understand the interaction of water with excipients that can form moisture-protective coatings, sorption behavior of films of lipidic (glyceryl behenate) and polymeric (polyvinyl alcohol) coating excipients was investigated. A simple and rapid method using a new, fully automated instrumental technique to investigate the sorption/desorption behavior of excipient films is reported. Further, the influence of temperature and film thickness on the sorption behavior of films is examined. Both excipient films displayed sorption isotherms that were classified as type III and demonstrated hysteresis during desorption. The sorption data for both films did not follow the Langmuir model, and the BET model could only be used restrictively. The GAB model fitted the sorption data at all conditions and over the entire range of water activity studied. The ability of the Young and Nelson model to explain the hysteresis behavior, from analytical and mechanistic perspectives, is evaluated. Temperature and film thickness were found to profoundly influence the nature of moisture interaction and distribution of moisture in the excipient films. An Arrhenius-type relationship was observed between equilibrium moisture content of excipient films and temperature at constant water activity.

KEY WORDS: Dynamic vapor sorption; GAB model; Hot melt coating; Moisture barrier films; Water-solid interaction; Young and Nelson model.

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INTRODUCTION

Development of hot-melt coating methods for retardation of drug-release applications has been recently reviewed (1). Typically, lipidic/waxy excipients with low melting points (<373 K) are sprayed in their molten state to form a uniformly continuous film that acts as the rate-controlling membrane for drug release. This coating approach may also be used to achieve protection for substrates of moisture-labile active ingredients by appropriately modifying the film thickness. The hydrophobic wax coating presents a barrier for moisture ingress into the drug-laden substrate. Hence, a clear understanding of the water sorption/desorption behavior of such excipient films is necessary (2–6). From experience, glyceryl behenate (GB) was found to be a suitable excipient for hot-melt applications and was included in this study. For comparison, a novel formulation of polyvinyl alcohol (PVA) being commercially promoted as a moisture-protective aqueous film-coating excipient was used. GB is a low-molecular-weight waxy excipient, whereas PVA is a high-molecular-weight polymeric excipient.

Dynamic vapor sorption technique (DVST) is a fully automated gravimetric sorption system used to rapidly measure uptake and loss of moisture. This is done by flowing a carrier gas (nitrogen) at a specified relative humidity (RH) over the material specimen suspended from an ultrasensitive microbalance capable of measuring changes in mass lower than 1 part in 10 million. A schematic of the DVST apparatus is shown in Figure 1. Compared with traditional experimental approaches utilizing saturated salt solutions, DVST offers fast equilibration times, high precision/sensitivity in mass determination and temperature control, small sample size requirement, and full automation to facilitate convenient and accurate moisture sorption/desorption investigations.

The purpose of this investigation was to study the sorption/desorption behavior of the excipient films and the nature of their interaction with water. It is intended to investigate the moisture distribution and how it is influenced by temperature and film thickness. Evaluation of the utility of DVST in studying the sorption/desorption phenomenon of excipient films was also of great interest.

MATERIALS AND METHODS

GB (Compritol 888 ATO, lot A17008) and PVA (Opadry AMB OY-B-28920, lot 5066503) were obtained from Gattefossé, Saint Priest, France, and Colorcon, West Point, PA, respectively. Films of GB were cast by melting 5 g of material (melting point ≈ 342 K) in a flat, circular aluminum pan (diameter $= 9.53 \times 10^{-2}$ m and height $= 9.53 \times 10^{-3}$ m) normally used for loss on drying determinations (Mettler, Hightstown, NJ) and allowing the molten wax to cool over the area of the pan to form a uniform film. Films thus obtained had a mean thickness of 6.73×10^{-4} m ($n = 10; \mathrm{SD} = 2.54 \times 10^{-5}$ m). For the PVA films, a 20% w/w dispersion of the polymer in deionized water was first prepared. This dispersion was then poured on the aluminum pan to deliver 5 g of solids and dried in an oven at 333 K for 12 hr. PVA films had a mean thickness of 8.94×10^{-4} m ($n = 10; \mathrm{SD} = 2.03 \times 10^{-4}$ m). To obtain

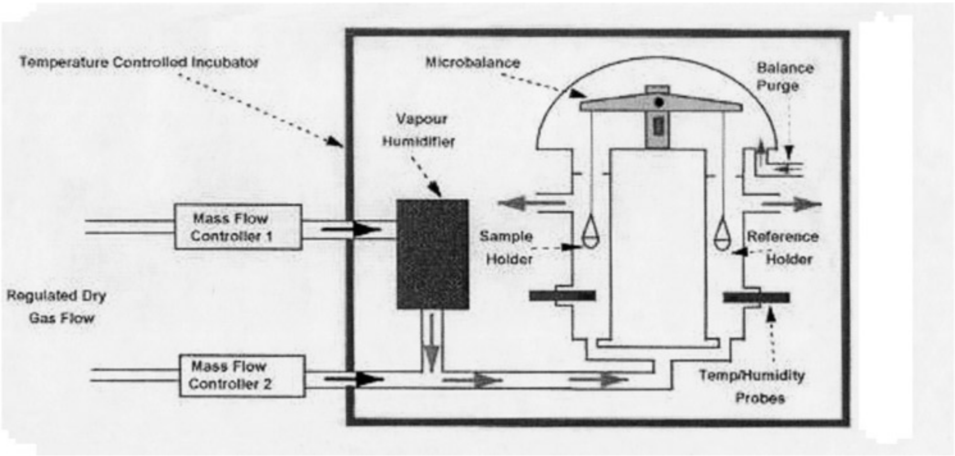

Figure 1. Schematic representation of the DVST apparatus.

films of greater thickness, the above procedure was repeated with twice the amount (i.e., 10 g) of solid contents for both excipients. The thicker films had a mean thickness of 1.42×10^{-3} m ($n = 10$; SD $= 3.39 \times 10^{-5}$ m) and 1.35×10^{-3} m ($n = 10$; SD $= 8.13 \times 10^{-5}$ m) for GB and PVA, respectively. No plasticizers were added to maintain purity of excipients in films. A DVST method using DVS-2000 with DVS analysis suite, Version 3.3 Standard (Surface Measurement Systems Limited, N.A., Coopersburg, PA) was defined to establish water activity (a_w) of 0.00, 0.17, 0.34, 0.51, 0.68, and 0.85. The ultrasensitive balance was calibrated before use and whenever temperature was changed, the humidity probes were calibrated to cover the range of operation as specified by the manufacturer. One full cycle facilitated determination of sorption and desorption portions of the isotherm.

RESULTS AND DISCUSSION

Construction of Isotherms

Films of GB were brittle and hard, whereas PVA films were flexible and soft. Rectangular specimens of the prepared films were cut using a blade for sorption analysis. Usually, DVST uses glass pans to hold the sample. However, to achieve exposure of the entire surface area of the film, the film specimen was inserted in a metallic paper clip and suspended from the balance instead of using glass pans. The method exposed the film sample to each programmed water activity for a minimum of 2 hr. After the initial 2 hr, the condition for reaching equilibrium was defined as the percent of change in mass per minute [dm/dt(%/min), i.e., slope of sample mass versus time plot] computed over any continuous 10 min duration should fall below a user-specified threshold value. The USP suggests that for equilibrium moisture determinations, weighing should be performed every hour until consecutive readings record a mass change of less than 0.25% (approximately 0.0042%/min). Threshold values of 0.002%/min and 0.004%/min were used for GB and PVA films, respectively. GB film samples weighed approximately 0.150 g and that of PVA weighed approximately 0.050 g. The film sample weight and threshold values for equilibration were determined based on preliminary experiments to optimize run time. The isotherms thus constructed by plotting equilibrium moisture content (EMC or V in gram of water/gram of film) against water activity for GB and PVA films at T = 293, 303, and 313 K are shown in Figures 2 and 3, respectively. The shape of isotherms suggests that they are type III isotherms as per Martin (7). Martin stated that type III isotherms are relatively uncommon and result when heat of adsorption in the first layer is less than the latent heat of condensation in the successive layers and the value of BET constant (C_{BET}) is less than 2.

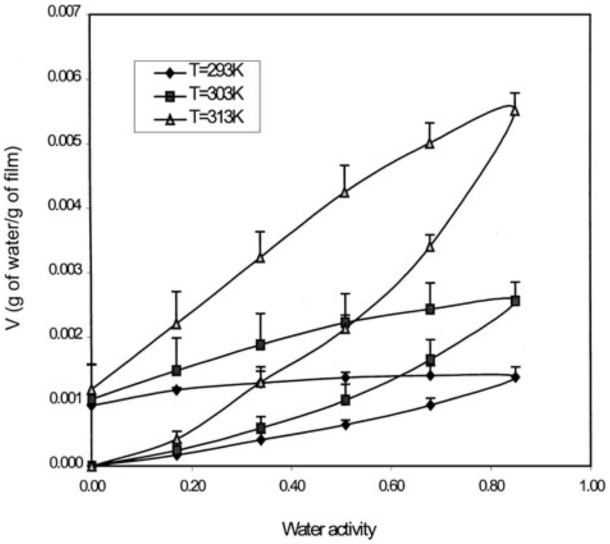

Figure 2. Sorption isotherms for GB film at various temperatures. Values of equilibrium moisture content (V) are mean of $n = 3$.

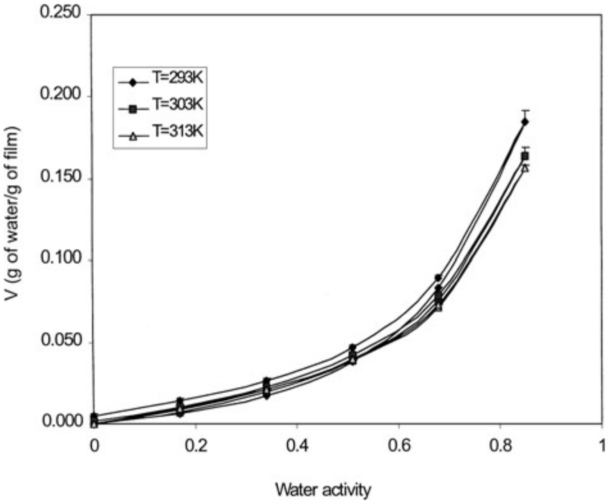

Figure 3. Sorption isotherms for PVA film at various temperatures. Values of equilibrium moisture content (V) are mean of $n = 3$.

Effect of Temperature

From Figures 2 and 3, it is evident that for GB films, increasing temperature leads to increasing area owing to hysteresis and higher EMC. Contrarily, PVA films displayed decreasing area owing to hysteresis and lower EMC with increasing temperature. Plots of logarithm of EMC against reciprocal temperature at various levels of water activity (shown in Figure 4) were found to be linear for GB and PVA films, suggesting an Arrhenius-type relationship. A relationship of the type, $V = A(\exp(E_{sorp}/RT))$, at constant water activity, where V is the EMC at a specified water activity, A is a proportionality constant, R is the universal gas constant, and T is absolute temperature, is valid for $0.17 \leq a_w \leq 0.85$. The Arrhenius-type relation suggests that the slope should perhaps be construed as a measure of the energy (E_{sorp}) associated with the sorption/desorption of moisture in the solid as temperature varies at constant water activity. When slopes obtained by linear regression from these plots were graphed against water activity, again a linear relationship was observed for both excipients (shown in Figure 5). Hence, a relationship of the form, $E_{sorp,aw} = M_E(a_w) + E_{sorp,0}$, may be defined for $0.17 \leq a_w \leq 0.85$ and $293 \leq T(\text{in K}) \leq 313$. Here, $E_{sorp,aw}$ is energy of sorption/desorption at a water activity a_w, $E_{sorp,0}$ is the same at $a_w = 0$, and M_E is the change in $E_{sorp,aw}$ from $E_{sorp,0}$ computed per unit change in a_w. It is possible that there may be binding of water molecules to the electronegative oxygen atom in the terminal carboxylic group of GB via hydrogen bonding. Further, as temperature increases and is closer to the melting temperature of the wax, the intermolecular distances increase, leading to greater number of carboxylic groups becoming available for bonding the water molecules. This hypothesis is consistent with the observation of increasing EMC with increasing temperature for GB film. Also, as more water molecules complete bonding with increasing water activity, the E_{sorp} decreases steadily in a linear manner as observed in Figure 5.

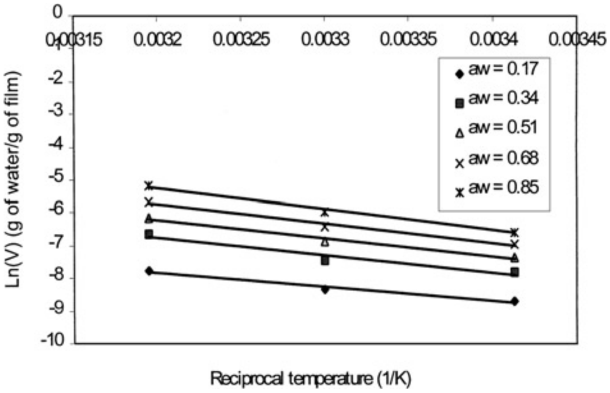

Figure 4. Arrhenius plots of mean equilibrium moisture content (V and $n = 3$) at constant water activity for GB film. Solid lines are best-fit lines from linear regression.

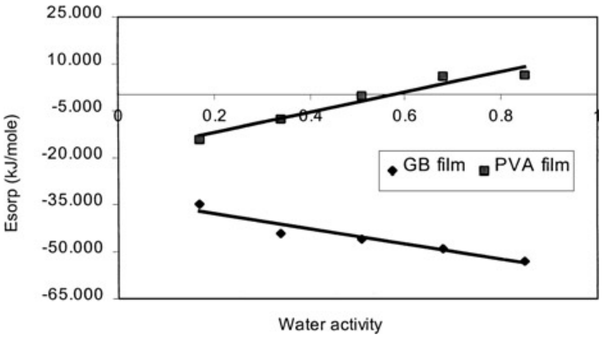

Figure 5. Variation in energy of sorption (E_{sorp}) for GB and PVA films. Solid lines are best-fit lines from linear regression.

Estimation of Microrate Constants

Langmuir described k_1 and k_2 as the microrate constants governing the sorption and desorption processes, respectively, in studying sorption over solids (7). Using the film sample mass data recorded every minute by DVST, we estimated the microrate constants for sorption and desorption for both excipient films. The method of estimation was to calculate the slope of the tangent at the very initial portion of the mass versus time plot at constant water activity. It was assumed that the very initial data during wetting or drying phases result owing only to sorption and desorption, respectively. The estimated values of k_1 and k_2 for GB and PVA films at T = 293, 303, and 313 K have been tabulated in Tables 1 and 2.

From the tables, it can be inferred that the estimated values of k_1 and k_2 for PVA relative to GB are greater by an order of approximately 10. This is a natural implication of their chemical nature, because GB is very hydrophobic (stemming from the long aliphatic chains attached to the glyceryl backbone) relative to PVA. The data for PVA film follow an orderly pattern and is more precise compared with the GB film. This may be attributable to the wide variation in GB data resulting from very small changes in weight during sorption or desorption potentially owing to its high hydrophobicity. The estimates for both microrate constants increase with increasing water activity and temperature for the PVA film. The same cannot be stated with certainty for GB film because of the

Table 1.

Estimates of Microrate Constants for Sorption (k_1) and Desorption (k_2) Processes Assuming Langmuir Behavior for GB Film at T = 293, 303, and 313 K

Water Activity	T = 293 K Mean (n = 3)	SD	T = 303 K Mean (n = 3)	SD	T = 313 K Mean (n = 3)	SD
Sorption Microrate Constant ($k_1 \times 10^6$ in g/min)						
0.17	1.33	0.58	2.67	1.15	2.00	1.00
0.34	2.67	1.15	1.67	0.58	5.67	4.51
0.51	2.33	0.58	3.00	1.00	4.00	1.00
0.68	3.33	1.15	3.33	1.53	5.67	4.04
0.85	4.00	2.65	5.00	1.00	5.67	1.53
Desorption Microrate Constant ($k_2 \times 10^6$ in g/min)						
0.17	4.33	3.21	2.67	1.53	4.00	1.00
0.34	2.33	1.53	2.67	0.58	6.67	4.93
0.51	1.67	0.58	4.33	1.15	5.00	4.58
0.68	2.33	0.58	7.00	0.00	7.67	4.04

wide spread of data. For the isotherms shown in Figures 2 and 3, the Langmuir model could not be used to explain the data for both excipients at any temperature. The reasons are obvious because the Langmuir model is based on a simple set of assumptions that are rarely valid in actual experimentation. Further, it is incorrect to calculate desorption microrate constants as described above when the data recorded demonstrate hysteresis. The purpose of these computations was to perform a cursory examination of the nature of microrate constants. Hence, it is important that the estimated microrate constants reported here be understood only within a limited scope.

BET and GAB Analysis

The BET model was used to analyze the isotherms in Figures 2 and 3. The BET model could be used satisfactorily to fit sorption data for GB film at T = 293 and 303 K and PVA film at T = 293 and 313 K, where $0.17 \leq a_w \leq 0.51$ only. Data for PVA and GB films at other temperatures did not follow the BET model. The values of BET constant (C_{BET}), monolayer value (V_m), and the constant heat due to site interaction (H_s) thus computed for the GB and PVA films have been tabulated in Table 3. As noted by Martin, the BET constants in most cases were found to be less than 2. The BET model, although more

Table 2.

Estimates of Microrate Constants for Sorption (k_1) and Desorption (k_2) Processes Assuming Langmuir Behavior for PVA Film at T = 293, 303, and 313 K

Water Activity	T = 293 K Mean (n = 3)	SD	T = 303 K Mean (n = 3)	SD	T = 313 K Mean (n = 3)	SD
Sorption Microrate Constant ($k_1 \times 10^6$ in g/min)						
0.17	13.3	5.77	20.0	0.00	26.7	5.77
0.34	16.7	5.77	26.7	5.77	33.3	5.77
0.51	26.7	5.77	40.0	0.00	50.0	0.00
0.68	46.7	5.77	66.7	5.77	86.7	5.77
0.85	66.7	5.77	100	0.00	100	0.00
Desorption Microrate Constant ($k_2 \times 10^6$ in g/min)						
0.17	20.0	0.00	30.0	0.00	40.0	0.00
0.34	36.7	5.77	46.7	5.77	60.0	0.00
0.51	63.3	11.5	83.3	5.77	100.0	0.00
0.68	80.0	10.0	100.0	0.00	200.0	0.00

Table 3.

Results of BET and GAB Model Fits for GB and PVA Films at Varying Temperatures

T (K)	Slope	Intercept	C_{BET}	V_m (g of water/g of film)	H_s (J/mole)
BET Data for GB Films					
293	1244.2	955.63	2.302	4.546×10^{-4}	2031.05
303	491.15	752.93	1.652	8.038×10^{-4}	1264.62
BET Data for PVA Films					
293	−19.14	36.94	0.482	5.618×10^{-2}	−1778.52
313	11.24	21.11	1.532	3.092×10^{-2}	1110.07
303 (th)	−764.35	846.61	0.099	1.187×10^{-2}	−5818.44

T (K)	K	C_{GAB}	V_m (g of water/g of film)	$H_l - H_m$ (J/mole)	$H_L - H_m$ (J/mole)
GAB Data for GB Films					
293	0.8361	1.948	6×10^{-4}	1624.39	−436.08
303	0.7655	1.087	15×10^{-4}	210.16	−673.20
313	0.8974	0.767	30×10^{-4}	−691.35	−281.72
303 (th)	0.9834	0.535	10×10^{-4}	−1575.75	−42.17
GAB Data for PVA Films					
293	0.9291	0.365	0.080	−2455.23	−179.15
303	0.8567	0.501	0.080	−1741.17	−389.64
313	0.9570	1.430	0.034	930.26	−114.38
303 (th)	1.0850	0.238	0.005	−3612.09	205.52

(th) Indicates films of greater thickness, and BET results are valid for $0.17 \leq a_w \leq 0.51$.

effective than the Langmuir model, also makes assumptions such as the heat of sorption for first layer being constant and equal to the total heat of vaporization plus a constant heat owing to site interaction that are not entirely true and, hence, its applicability is limited (3).

The GAB model is an extended BET model as per the modifications developed by Guggenheim et al. (8). The GAB equation is:

$$V = [C_{GAB} \cdot K \cdot V_m \cdot a_w][(1 - K \cdot a_w)/(1 - K \cdot a_w + C_{GAB} \cdot K \cdot a_w)]$$

where C_{GAB} and K are parameters related to the heat of sorption and other variables were defined earlier. In contrast to the BET model, the GAB model involves the additional parameter K and takes into account a layer or layers of sorbed vapor, which may be taken up with a degree of binding intermediate to those of the monolayer and the bulk water taken up in a nonspecific manner. The parameters K and C_{GAB} may be determined as, $K = B_l \cdot \exp[(H_L - H_m)/RT]$ and $C_{GAB} = D \cdot \exp[(H_l - H_m)/RT]$, where B_l and D are constants, H_L is the heat of condensation, H_m is the heat of sorption of water sorbed in the intermediate layer, and H_l is the heat of sorption of water in the first sorbed monolayer. The GAB model was used successfully to describe the sorption data for both excipient films at all temperatures and over the entire range of water activity. As per the GAB equation, reciprocal of EMC was plotted against water activity, and the parameters K, C_{GAB} and V_m were estimated using nonlinear regression analysis (SigmaPlot 4.0 for Windows, SPSS, Inc., Chicago). A typical example showing the ability of the GAB model to fit data over the entire range of water activity is shown in Figure 6. The resulting parameters from nonlinear regression have been tabulated in Table 3.

There seems to be reasonable agreement between the monolayer values (V_m) estimated from the GAB and BET models for GB and PVA thin films, with the GAB values being greater. A similar observation was made while studying the interaction of water with celluloses, but that report stated that the BET monolayer values as being greater (9). The monolayer values for PVA film relative to GB film are significantly greater. This may be attributable to the polymeric nature of PVA, wherein water acts as a plasticizer to open up the long chains that make up the structural matrix and hence exposes all the interior sites for sorption. The monolayer values for GB film increase with increasing temperature, whereas for PVA film the values decrease with increasing temperature. Assuming B_l and

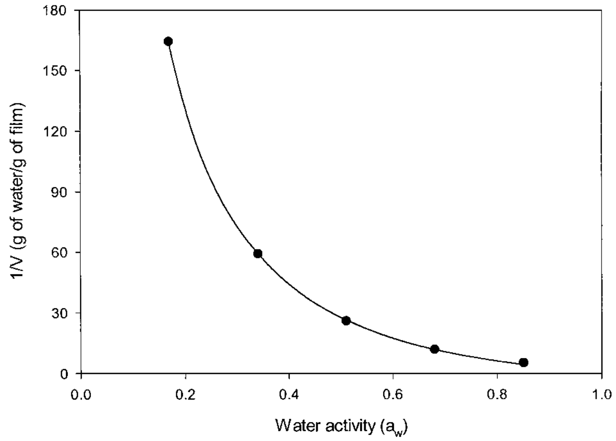

Figure 6. Fit of sorption data using the GAB model for PVA film at T = 293 K. ● Indicates actual data, and — represents the fitted data obtained by nonlinear regression. 1/V is the reciprocal of mean equilibrium moisture content ($n = 3$).

D to be unity, the values for $(H_L - H_m)$ and $(H_l - H_m)$ were computed and are included in Table 3. From Table 3, the heat of sorption of water in the first sorbed monolayer (H_l) is less than the heat of sorption of water sorbed in the intermediate layers (H_m), in most cases leading to the observation of type III isotherms (7).

Analysis of Hysteresis

Although numerous theories have been proposed to clarify the phenomenon of hysteresis, none has offered a comprehensive explanation (3,10–12). One popular model used extensively to analyze hysteresis is the Young and Nelson model (YNM) (13,14). The YNM was developed to describe the equilibrium sorption and desorption behavior of biological materials such as starch. They distinguish three forms of moisture: a bound or adsorbed monolayer on the surface, normally condensed or external water, and absorbed or internal moisture. The mathematical equations describing the YNM are:

$$\theta = a_w/(a_w + (1 - a_w)E) \tag{1}$$

$$\varphi = a_w(\theta) \tag{2}$$

$$\begin{aligned}\beta = &-(a_w \cdot E)/(E - ((E-1)\cdot a_w)) \\ &+ (E^2/(E-1))\ln(E - ((E-1)\cdot a_w)/E) \\ &- (E+1)\ln(1 - a_w)\end{aligned} \tag{3}$$

$$M_s = A(\theta + \beta) + B\varphi \tag{4}$$

$$M_d = A(\theta + \beta) + B\theta\, a_{w\,max} \tag{5}$$

where θ is the fraction of surface covered by a monomolecular layer, φ is the fraction of surface covered by a layer of water two or more molecules thick and β is the total amount of adsorbed moisture in a multilayer, M_s and M_d are the moisture contents of the material during sorption and desorption conditions, and $a_{w\,max}$ is the maximum water activity condition. A, B, and E are parameters unique to each material.

$$E = \exp[-(q_l - q_L)/kT]$$

$$A = (\rho_w V_m)/W'_m$$

$$B = (\rho_w V_a)/W'_m$$

where q_l is the heat of adsorption of water bound to the surface, q_L is the normal heat of condensation of water, k is the Boltzmann's constant, T is absolute temperature, V_m and V_a are volumes of adsorbed and absorbed moisture, respectively, ρ_w is the density of water, and W'_m is the mass of the dry material. Finally, $A \cdot \theta$ is the amount of monolayer moisture, $A \cdot (\theta + \beta)$ is the externally adsorbed moisture, and $B \cdot \varphi$ is the amount of internally absorbed moisture during the sorption cycle.

Equations 1–5 were used to test fit the sorption/ desorption results obtained in this study for both excipient films under various conditions. A segmented nonlinear regression procedure was developed to simultaneously fit the sorption and desorption data to YNM equations using SAS statistical software (Version 6.12, SAS Institute Inc., Cary, NC) and obtain best estimates of the parameters A, B, and E. In all cases, excellent fit to actual data was observed, and a typical example comparing actual and YNM predicted data is shown in Figure 7. The estimated

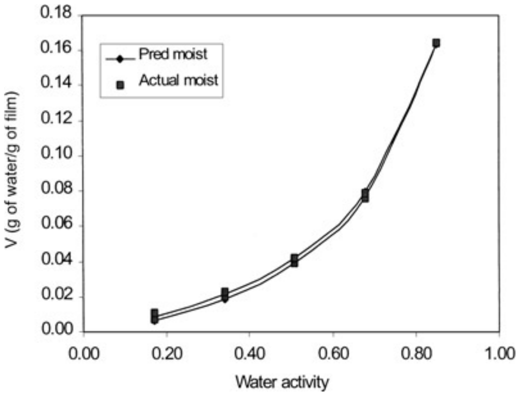

Figure 7. Comparative sorption isotherms of actual and predicted data obtained using the Young and Nelson model for PVA film at T = 303 K. V is mean equilibrium moisture content ($n = 3$).

Table 4.

Estimates of Young and Nelson Model Parameters A, B, and E Used to Describe Hysteresis in Sorption Data at Various Temperatures for GB and PVA Films

Excipient Film	T (K)	A	B	E	$q_L - q_1$ (J/mole)
GB	293	$<10^{-11}$	1.58×10^{-3}	0.0341	−8230.23
GB	303	$<10^{-11}$	2.94×10^{-3}	0.1685	−4486.30
GB	313	$<10^{-11}$	6.65×10^{-3}	0.3749	−2553.18
GB (thick)	303	0.00	2.184×10^{-3}	0.0294	−8884.41
PVA	293	49.59×10^{-3}	98.17×10^{-3}	2.696	2416.04
PVA	303	53.04×10^{-3}	26.96×10^{-3}	1.908	1627.56
PVA	313	54.03×10^{-3}	5.84×10^{-3}	1.696	1374.76
PVA (thick)	303	0.00	110.1×10^{-3}	4.049	3522.94

parameters for both excipient films at various temperatures have been tabulated in Table 4.

The parameter A for GB film at all conditions was practically zero, indicating that all the moisture adsorbed exists as absorbed moisture in the internal structure of the material. Because YNM was developed for biological materials, moisture absorbed in the internal structure would mean that the moisture had crossed the exterior cell wall and entered the interior of the cell. Such an explanation would not fit the present situation because of the nonbiological nature of the excipients. Hence, the absorbed moisture should perhaps be understood as water molecules that have formed some kind of a chemical bond with the adsorbate molecules (chemisorption). On examination of the molecular structure of GB, it is very likely that such bonding occurs as an irreversible hydrogen bond as discussed above. Similarly, the hydroxyl groups in PVA can also form hydrogen bonds with water molecules (15). For the PVA film, the parameter A remains fairly constant with temperature, indicating a constant monolayer value. However, the parameter B for both GB and PVA films was found to vary with temperature; a relationship similar to that discussed above between ln(V) and 1/T was also seen between ln(B) and 1/T for both excipient films. This could be a result of the forming or breaking of hydrogen bonds between water and the adsorbate in an Arrhenius-type manner with varying temperature.

It must be emphasized that although YNM offers a reasonable analytical solution to the hysteresis phenomenon, it does not provide a mechanistic solution attributable to the assumptions that form its basis. Further, the interpretation of “internally absorbed” moisture for nonbiological materials is unclear. It should be applied cautiously, and the physical significance of the parameters (A, B, and E) must be carefully considered.

Effect of Film Thickness

Comparative sorption isotherms for thick and thin films of GB and PVA at T = 303 K are presented in Figures 8 and 9, respectively. For the thick GB film, the EMC during the sorption portion are lower relative to the thin film. However, at the end of desorption, the amount of moisture being retained remains approximately the same. The GAB model could again be used to describe the entire data for thick films of both excipients, and results are shown in Table 3. The PVA thick film demonstrated very different behavior compared with the thin film. The PVA thick film

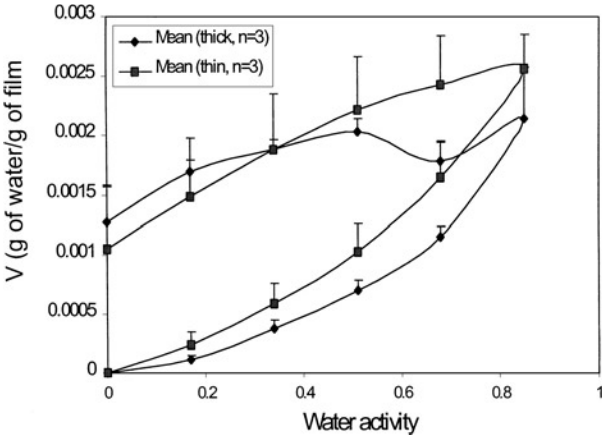

Figure 8. Comparative sorption isotherms for GB films of varying thicknesses at T = 303 K. V is mean equilibrium moisture content ($n = 3$).

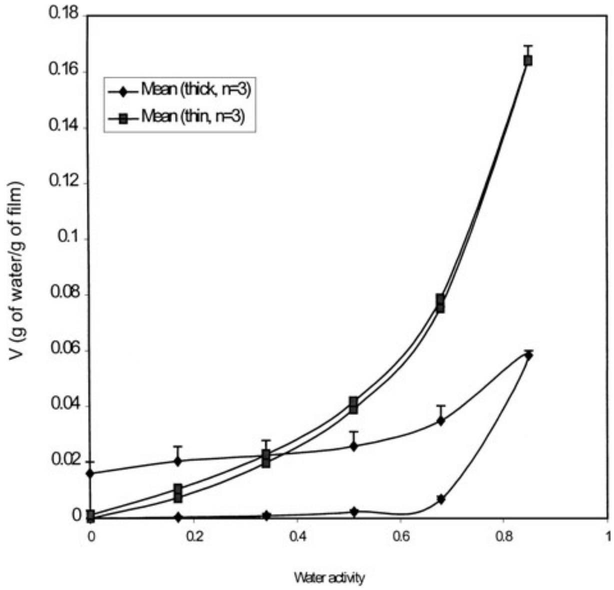

Figure 9. Comparative sorption isotherms for PVA films of varying thicknesses at T = 303 K. V is mean equilibrium moisture content ($n = 3$).

takes up moisture only at very high water activities and retains considerably greater moisture at end of drying. Interestingly, for the thick films of both excipients, the parameter A from YNM analysis is zero (results tabulated in Table 4), indicating that the retained moisture exists only in the absorbed state. This could result either because of chemisorption as noted above or because of the different nature of internal microporous structure of the thick film leading to larger amounts of moisture condensing in the pores in an irreversible manner. In a typical coating process, the particle size of the substrates is heterogeneous and so is the coating film thicknesses on each substrate. If films of varying thicknesses retain different amounts of moisture, the process variables should be closely controlled to achieve as uniform a coating thickness as possible for satisfactory product performance. This is of vital importance for sustained-release and moisture-protective coating applications because the residual moisture in the coating film may migrate into the core and interact with the active ingredient in an adverse manner during storage.

CONCLUSIONS

DVST is an extremely useful tool to develop simple, fast, and convenient methods for investigation of sorption and desorption behavior of excipient films. It was found that a model assuming the existence of water in three different states, one tightly bound layer, additional less tightly bound layers, and bulk water in a nonspecific manner, is most successful in describing the sorption isotherms for PVA and GB films under all conditions of study. The hysteresis demonstrated by both excipients could be modeled accurately using the YNM, although physical interpretation of model parameters was not definite. It is hypothesized that water molecules may form an irreversible hydrogen bond with the carboxylic and hydroxyl groups in GB and PVA films, respectively, leading to water retention by the films.

Although the models described here were successful in analytically fitting experimental data, it is necessary to perform a complete thermodynamic analysis of the water-film interaction to clarify the sorption process at a molecular level (15,16). The results pertaining to fits of theoretical models, along with the underlying thermodynamics of sorption/desorption processes, will better facilitate comprehension of the interaction of water with excipient films. A relationship similar to the Clausius-Clayperon equation was observed between the EMC of films and temperature at constant water activity (3). Also, it was found that the amount of moisture retained by the film is influenced by the film thickness for the PVA film.

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