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Report

The Relationship Between the Glass Transition Temperature and Water Vapor Absorption by Poly(vinylpyrrolidone)

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Water associated with amorphous solids is known to affect significantly the physical and chemical properties of dosage form ingredients. An analysis of water vapor absorption isotherms of poly(vinylpyrrolidone) measured in this and other laboratories, over the range −40 to 60°C, along with the measurement of the glass transition temperature of poly(vinylpyrrolidone) as a function of water content is reported. It is observed that the amount of water vapor absorbed at a particular relative humidity increases with decreasing temperature, along with a significant change in the shape of the isotherm. It is also shown that at any temperature the state of the solid changes from a highly viscous glass to a much less viscous rubber in the region where absorbed water appears to enter into a "solvent-like" state. Further, the apparent "tightly bound" state, observed at low relative humidities, appears to exist when the polymer enters into a very viscous glassy state. It is concluded that the apparent states of water and polymer are interrelated in a dynamic manner and, therefore, that they cannot be uncoupled by simple thermodynamic analyses based only on a water-binding model.

KEY WORDS: poly(vinylpyrrolidone); glass transition temperature; water vapor absorption; amorphous polymer.

INTRODUCTION

Polar polymers such as proteins, starches, celluloses, and a variety of water soluble systems are often used as excipients in pharmaceutical dosage forms. Such polymers can take up and retain large amounts of water in their amorphous portions when exposed to water vapor at various relative humidities (1). Since such absorbed water can influence the physical or chemical properties of the polymer and other excipients present, it is important to understand the underlying mechanisms involved in water–polymer interactions.

In the pharmaceutical literature to date, emphasis has been placed on the state of water molecules associated with the polymer and the relative ability of this water to influence the properties of materials mixed with the polymer, for example, chemical stability (2). A number of studies have used techniques, such as NMR and dielectric measurements, which appear to estimate the molecular mobility of water (3,4). From these studies it has been concluded generally that a certain proportion of water molecules may be "tightly bound" to the solid, while the amounts absorbed in excess of this value are more "solvent-like," approaching the properties of bulk water (5). Analyses of water vapor absorption isotherms for such systems have generally shown that the data can be fit, to varying degrees, to the BET (6) equation for gas adsorption or to other forms related to it (7). In the BET equation

$$W = \frac{W_m C_B}{[1 - p/p_0]\,[1 - (p/p_0) + C_B(p/p_0)]} \tag{1}$$

where W is the mass of gas adsorbed per mass of dry solid at a relative pressure of p/p_0, W_m is the mass of gas corresponding to monolayer coverage or when possible binding sites are saturated, and C_B is a constant which reflects the overall free energy of adsorption.

Although there is no theoretical reason to expect water vapor absorption into an amorphous solid to fit a gas adsorption model, there is evidence to suggest that the point on the isotherm corresponding to a water content of W_m may be related to the point below which water appears to be "tightly bound"; at W_m certain effects of water on solids change significantly, e.g., changes in solid mechanical properties (8,9). There is also evidence to suggest that, for any solid at some water content that is a definitive multiple of W_m, a second critical point is present in the isotherm. In the case of starch this point corresponds to a water content of about three times W_m (5), whereas for microcrystalline cellulose it is about five times W_m (10). It is at this point where water appears to take on its "solvent-like" character and, again, where certain effects of water on solids, for example, chemical instability, appear to occur (11).

That the changes in properties of water and solid may be related in a more complex manner can be expected when one recalls that water absorbed into an amorphous solid can act as a plasticizer, and therefore, that it can lower the glass

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transition temperature, T_g, of the polymer (12). Since the viscoelastic properties of amorphous solids will differ significantly below and above the glass transition temperature, it is clearly possible, as recently suggested by Levine and Slade (12), that the change in apparent states of absorbed water in such polymers may actually arise from a change in the physical state of the polymer as plasticization occurs. Thus, what has been referred to as the "tightly bound" state of water may simply arise from an immobility created by the high viscosity of the glassy state. Likewise, the "solvent-like" state of water at higher water contents may reflect the much less viscous rubbery state of the polymer above T_g. This also suggests that the state of the polymer above and below its T_g, as reflected in its viscoelasticity, actually may contribute significantly to the amount of water absorbed at a particular relative pressure, as well as to the shape of the isotherm.

In this report an analysis of water vapor absorption isotherms for poly(vinylpyrrolidone) measured in this and another laboratory (13) over the range of −40 to 60°C is presented, along with the measurement of the glass transition temperature of poly(vinylpyrrolidone) as a function of water content. The aim of this study is to test more quantitatively the hypothesis that water vapor absorption by amorphous solids as a function of relative pressure is determined by both the chemical affinity of water for the polymer and the role of water as a plasticizer. Furthermore, we wish to see whether the latter might be the major determinant of the apparent state of water in these solids and of the critical points where water appears to influence the properties of these solids.

MATERIALS AND METHODS

Materials

Poly(vinylpyrrolidone) (PVP K-30) was obtained from the General Aniline and Film Corporation. A solution of poly(vinylpyrrolidone) was dialyzed to remove residual contaminants from the polymerization process and any low molecular weight fractions present. The solution was lyophilized and the resulting average molecular weight from intrinsic viscosity determination was 40,000, which agreed with the manufacturer's reported value.

Sodium hydroxide, potassium acetate, magnesium chloride, sodium nitrite, sodium chloride, and potassium chloride were obtained from Columbus Chemical Industries, Inc. Lithium, chloride and potassium carbonate were obtained from the J. T. Baker Chemical Company. Magnesium nitrate and sodium bromide were obtained from Mallinckrodt, Inc. Potassium iodide and potassium nitrate were obtained from MCB Manufacturing Chemists, Inc.

Isotherm Determination

The relative pressure was controlled using a series of 7 to 10 desiccators prepared with various saturated salt solutions. The relative humidity values were taken from the literature (14–16) and are listed in Table I. Poly(vinylpyrrolidone) samples were dried *in vacuo* at 90°C for 12 hr, weighed, and placed in desiccators in triplicate. The samples were weighed weekly to monitor water vapor uptake. The samples were assumed to be at equilibrium when the sample weight change from the previous measurement was no more than 5 mg/g. Since the samples stored at higher relative humidities and temperatures took approximately 5 weeks to reach equilibrium, for convenience and consistency, all samples were stored in the desiccators for 5 weeks. Isotherms were determined at 30, 40, 50, and 60°C.

Table I. Relative Humidities of Saturated Salt Solutions Used in this Study

Saturated salt solution	p/p_0			
	30°C	40°C	50°C	60°C
Sodium hydroxide	0.076	0.063	0.049	0.036
Lithium chloride	0.113	0.112	0.111	0.110
Potassium acetate	0.215	0.216	0.215	a[a]
Magnesium chloride	0.324	0.316	0.305	0.293
Potassium carbonate	0.432	a	a	a
Magnesium nitrate	a	0.484	0.455	a
Sodium bromide	0.560	a	a	0.497
Sodium nitrite	a	a	0.600	a
Potassium iodide	0.679	a	a	0.631
Sodium chloride	0.751	0.747	0.744	0.745
Potassium chloride	0.836	0.823	0.812	a
Potassium nitrate	0.923	a	a	a

[a] Indicates that literature value was not available or solution was not used at that temperature.

Measurement of Glass Transition Temperature

Differential scanning calorimetry was performed on the poly(vinylpyrrolidone) samples previously equilibrated with water vapor using a Perkin-Elmer DSC-II. Helium was used to purge the DSC cell, and the instrument was cooled using a liquid nitrogen reservoir. Sample weights ranged from 5 to 15 mg, and the samples were hermetically sealed in coated aluminum sample pans to prevent moisture loss during heating. Samples were heated at a rate of 20 K/min. The first sample run typically showed an endotherm at the glass transition that did not appear in subsequent runs. The T_g values were determined in duplicate from the second run.

RESULTS AND DISCUSSION

Figure 1 depicts the amount of water absorbed into poly(vinylpyrrolidone) as a function of relative pressure for four representative temperatures, over the range −40 to 60°C, using data from −40 to 22°C obtained by MacKenzie and Rasmussen (13) for the same grade of poly(vinylpyrrolidone). By extending their data up to 60°C we hoped to be in a better position to see any effects brought about as the polymer was plasticized from its glassy to rubbery states.

From Fig. 1 we see, as might be expected, that the process appears exothermic, that is, the amount of absorption at a particular relative pressure decreases with increasing temperature. In contrast with what might be observed with a simple dissolution process, however, note that the various curves representing the higher temperatures tend to take on a more sigmoidal shape, with a more significant increase in absorption at higher relative pressures.

Figure 2 depicts a plot of the glass transition tempera-

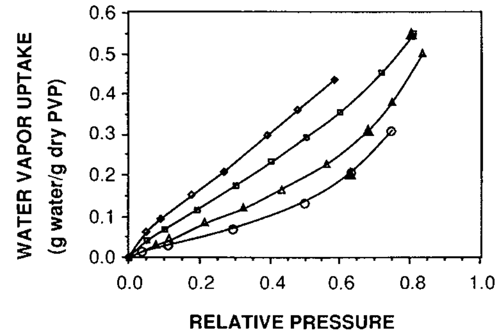

Fig. 1. Water vapor absorption isotherms for poly(vinylpyrrolidone) at four representative temperatures. Temperature of isotherm determination, *T:* 60°C (○); 30°C (△); −20°C (□); −40°C (◇). Data at −20 and −40°C were taken from the literature (13). Filled triangles represent the calculated water content necessary to depress T_g to T (see text for explanation).

Table II. Analysis of Absorption Isotherm Data for Water–Poly(vinylpyrrolidone) at Various Temperatures[a]

T (°C)	T (K)	W_m (g/g)	$W(T_g = T)$ (g/g)	$W(T_g = T)/W_m$
60	333	0.082	0.205	2.5
50	323	0.094	0.238	2.5
40	313	0.100	0.274	2.7
30	303	0.119	0.313	2.6
22	295	0.128	0.343	2.7
2	275	0.144	0.435	3.0
−10	263	0.148	0.496	3.1
−30	243	0.209	0.610	2.9
−40	233	0.221	0.674	3.0

[a] Data at 30°C and higher were obtained in this study, and the remaining low-temperature data were taken from the literature (13).

ture of poly(vinylpyrrolidone) *versus* water content. These results are in excellent agreement with those of Tan and Challa (17) but higher than those reported earlier by others (12,13,18). Tan and Challa had shown that earlier results were most likely lower primarily because of inadequate attention to the initial drying of the sample. This was confirmed by preliminary experiments in this study. The rate of heating and the methods used may also be factors. Note that the rate of change in the glass transition temperature is very significant over the range of 0 to 2.5% water, that is, the glass transition temperature is depressed by 48°. A further increase in water content results in a more gradual change in the glass transition temperature until ultimately it is depressed by 150° at 44% water.

Table II lists values of $W(T_g = T)$, the amount of water absorbed at each temperature, T, which would reduce the glass transition temperature of poly(vinylpyrrolidone) to T, calculated using data from Fig. 2. At levels of water absorption below $W(T_g = T)$ the polymer is in the glassy state, and at higher levels of absorption the polymer is in a rubbery state, characterized by a decreasing viscosity (19). Points representing $W(T_g = T)$ at each temperature are superimposed on the isotherms shown in Fig. 1. At low temperatures $W(T_g = T)$ has not yet been reached and the shape of the isotherm is devoid of the upward shift in absorption values which gives water vapor absorption isotherms of hydrophilic polymers their usual sigmoidal shape. At higher temperatures, as seen in Fig. 1, the upward inflection appears to occur in the vicinity of $W(T_g = T)$. This is also true for the other temperatures (data not shown). Thus, in those cases where the upward shift occurs, sufficient water appears to have been taken up to cause the value of T_g to be less than T and hence to cause the polymer to assume a more rubbery state.

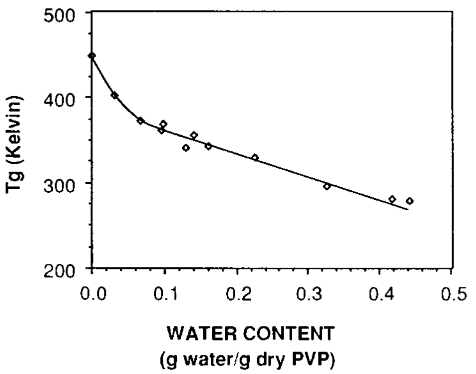

Fig. 2. Glass transition temperature (T_g) of poly(vinylpyrrolidone) (PVP) as a function of water content.

In effect, therefore, the plasticizing effects of water appear to produce a morphological change in the polymer which now allows a disproportionally greater amount of water to be absorbed, despite the more unfavorable thermodynamics at higher temperatures. An analysis performed with water vapor absorption data and glass transition temperatures from the literature for cellulose (20,21) and the protein, elastin (22,23), also shows that the upward inflection in the isotherm is most likely associated with the glass-to-rubber transition due to the absorbed water (data analysis not shown). Hence, it appears that the "solvent-like" state of water in polymers is actually a complex combination of water and polymer existing together in a rubbery polymer state.

Table II also lists values of W_m generated from fitting the data in Fig. 1 to Eq. (1). The values of W_m decrease almost threefold over the range of −40 to 60°C. Also listed in Table II are the ratios of $W(T_g = T)$ to W_m at the various temperatures. Here, we may note that this ratio is relatively constant at all temperatures, giving a value of approximately 3.0. The change in W_m with temperature appears to indicate that W_m does not represent the absolute maximum number of binding sites available on the polymer for directly "bound" water. If this was so, we might have expected a decreased affinity of water for poly(vinylpyrrolidone), but the maximum number of binding sites, reflected in W_m, would be expected to remain constant. It appears instead, in view of the constant ratio of $W(T_g = T)$ to W_m, that W_m is related to $W(T_g = T)$ and that it may also be reflecting the changing morphology of the solid as water is absorbed, perhaps in the form of a secondary solid-state transition, as is often seen with amorphous polymers in the glassy state. Analysis of DSC scans in the region of W_m, within the limits of detection, did not reveal evidence of a solid-state transition. Consequently, we are now studying this issue more closely using dynamic mechanical analysis.

From this study, therefore, it is concluded that the interpretation of absorption isotherms for water and amorphous polymers, like poly(vinylpyrrolidone), in terms of "tightly bound" and "solvent-like" states of water is misleading and inadequate in providing a basis for understanding the molecular processes involved during water vapor absorption. It is further concluded that the apparent states of water and polymer are interrelated in a dynamic and complex manner and that they cannot be uncoupled by a simple thermodynamic analysis which addresses the problem only in terms of tightly bound and solvent-like water. Rather, it is necessary to carry out studies which examine systems in the context of a multicomponent system.

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