Influence of Moisture Adsorption on Volume Shrinkage and Diametral Tensile Strength of Sucrose Tablets

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Changes in the size and tensile strength of tablets were investigated after storage at several levels of relative humidity (R.H.). Sucrose has a critical relative humidity (CRH) of 84.0%. The diameter and thickness of the tablets decreased with storage at increasing R.H., and then suddenly increased above the CRH. The relationship between the rates of the volume change and moisture adsorption was linear ($R^2 = 0.963$).

The diametral tensile strength increased with storage at 84% R.H., above which it decreased. This was due to the increase in the radii of curvature of the water films and smoothing of the particulate surface by dissolution of surface asperities. It was therefore assumed that slippage and transfer of particles easily occurs between contacting surfaces.

Diametral tensile strength increased with increasing water evaporation.

Keywords sucrose; moisture content; volume change; shrinkage; adhesive force; diametral tensile strength

Moisture adsorption plays an important role in the physical and chemical stability of excipients and polymers for solid dosage forms of drugs such as capsules and tablets. This makes knowledge of moisture adsorption kinetics, including the rate of moisture uptake, the equilibrium moisture content, and hygroscopicity valuable. In solid dosage forms and excipients, moisture adsorption phenomena can provide useful information for the selection of excipients such as disintegrating agents, direct compression carriers, binders and coating agents, as well as for humidity control during production and storage.

The amount of moisture adsorbed by drugs and excipients at various temperatures and relative humidity (R.H.) influences the flow, compression characteristics, and the hardness of granules and tablets. In addition, moisture transmission through polymers and free films may be useful for characterizing effects on the dissolution and the transport of drugs from the dosage forms.

We have been investigating the moisture adsorption and volume expansion of tablets made of compacted excipients[2)] and found that the rates of adsorption and expansion increased with increase in water vapor pressure, and at lower temperatures.

In this study, we investigated the effects of moisture adsorption on the volume shrinkage and diametral tensile strength of sucrose tablets, and also examined the relationship between them at a particular R.H.

Experimental

Materials Table I lists the physical characteristics of the samples. Sucrose was obtained as a commercial sample (Wako Pure Chemical Industrial Ltd.), crushed with a sample mill (Fuji Powdal, model KIIW-1) and then passed through a 44—74 μm sieve. The samples were stored in a desiccator with silica gel.

TABLE I. Physicochemical Properties of Sucrose

Molecular weight	342.3
Specific gravity	1.59
Melting point	190.0 °C
Solubility	199.5 g/100 ml water
	0.003 g/100 ml ethanol

These data are from the respective manufacturer.

Preparation of Tablets Samples were compressed using a universal tension and compression tester (Minebea, model TCM 5000C). Sucrose was compressed under 50 kg/cm² pressure and flat tablets with a 1.6 cm diameter were obtained.

Moisture Adsorption Measurement Tablets were placed in a desiccator in a constant temperature incubator at 25 °C and left for various periods. The R.H. in the desiccator was manipulated using saturated solutions of inorganic salts. Upon their removal from the desiccator, the moisture content of samples was determined by the Karl Fisher method (Kyoto Electronics Industrial Co., Ltd. model MKA-3).

Measurement of Change in the Dimension of Tablets Due to Moisture Adsorption Dimensional changes in the diameter and thickness of tablets were measured with a micrometer at 25 °C and 68% R.H. after storage at various levels of R.H.

Measurement of Diametral Tensile Strength The diametral tensile strength of tablets was measured using a diametral compression test as described elsewhere.[3)] The test consisted of applying a load diametrically, measuring the maximum load P when the tablet fractured and calculating the diametral tensile strength, σ, using the following equation[4,5)]:

$$\sigma = 2P/\pi Dt \quad (1)$$

where D is the diameter of the tablet and t is the tablet thickness.

Results

Rate of Moisture Adsorption Figure 1 shows the

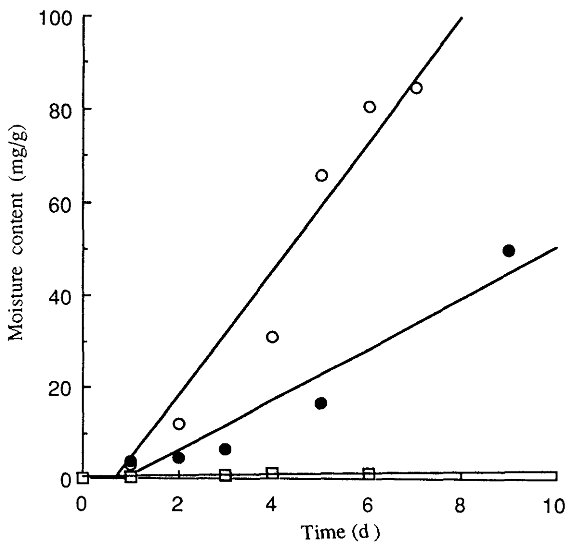

Fig. 1. Adsorption Isotherms of Water Vapor on Sucrose
□, R.H. = 84%; ●, R.H. = 88%; ○, R.H. = 92%.

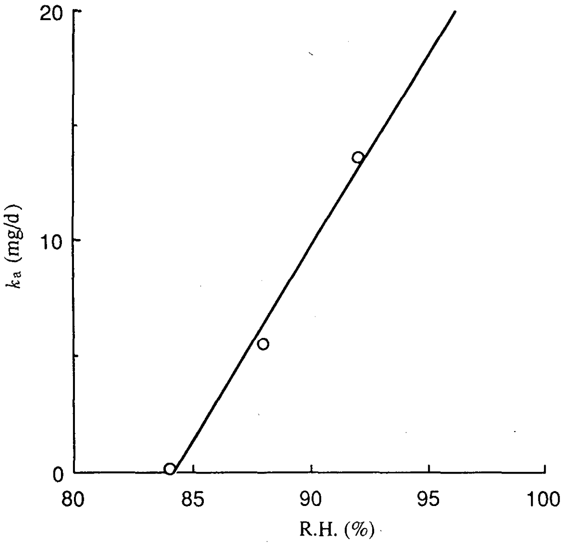

Fig. 2. Relationship between R.H. and the Rate of Moisture Adsorption

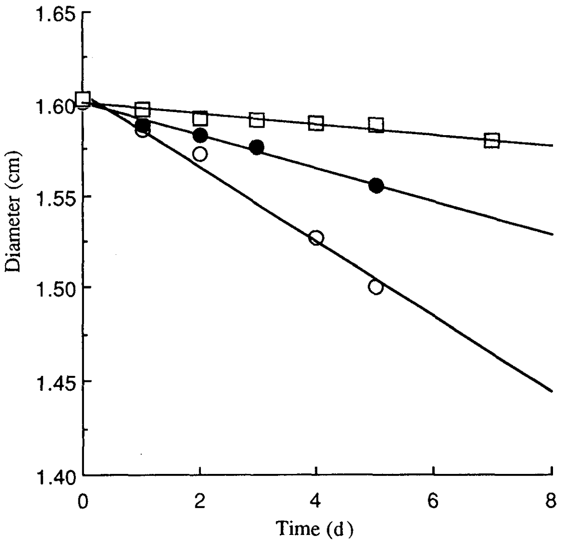

Fig. 3. Changes in Tablet Diameter with Time as a Function of R.H.
□, R.H. = 84%; ●, R.H. = 88%; ○, R.H. = 92%.

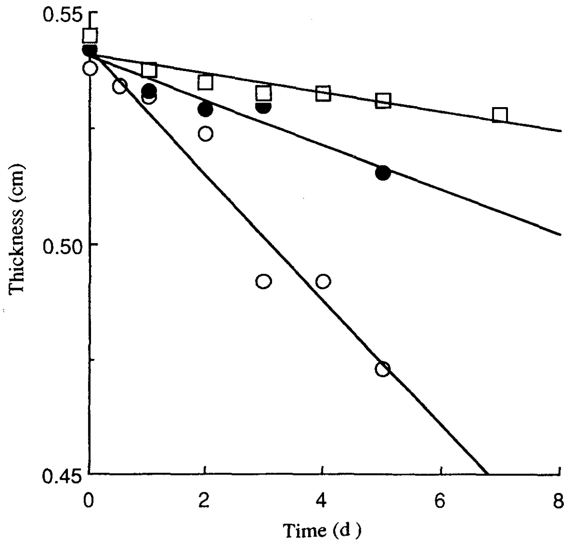

Fig. 4. Changes in Tablet Thickness with Time as a Function of R.H.
□, R.H. = 84%; ●, R.H. = 88%; ○, R.H. = 92%.

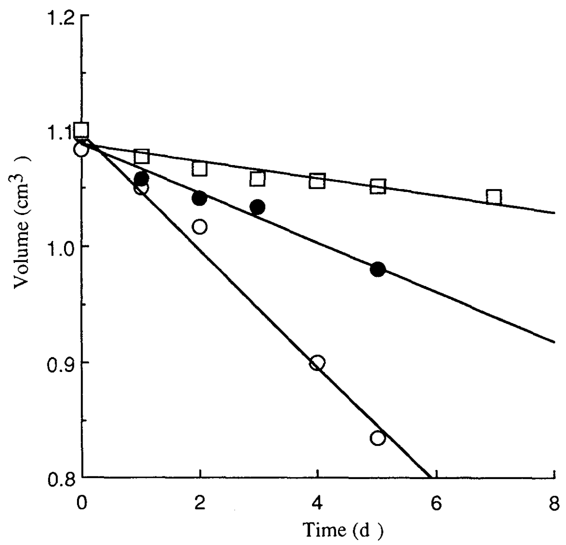

Fig. 5. Changes in Tablet Volume with Time as a Function of R.H.
□, R.H. = 84%; ●, R.H. = 88%; ○, R.H. = 92%.

moisture adsorption for sucrose at various levels of R. H. The points shown are the average values of five measurements. The rate of moisture adsorption increased with increasing water vapor pressure over time. However, at R.H. of 84%, the moisture content of sucrose was fairly constant.

The rate of moisture adsorption was calculated from these results and plotted against the R. H. as shown in Fig. 2. The critical relative humidity (CRH) of sucrose obtained by extrapolating the rate of moisture adsorption to zero was 84.17%. This was in close agreement with that previously reported (84.0%).[6]

Effect of Moisture Adsorption on Tablet Dimensions Figure 3 shows the effect of R.H. on the diameter of tablets as a function of storage. The diameter of tablets decreased linearly over time, and decreased even further with increasing R.H.

Figure 4 shows the effects of R.H. and storage on tablet thickness. The thickness decreased with time, and the degree of increase in R.H.

The volume change with time and R.H. is shown in Fig. 5. These results are similar to those shown in Figs. 3 and 4.

Water vapor changes during storage result in caking and shrinkage of water soluble materials. Kanazawa and Chikazawa[7] reported that micro-caking occurs as a result of a solid phase reaction due to moisture adsorption at 40% R.H.

In general, shrinkage is represented by the following equation for sintering[8]:

$$\Delta l/l_0 = k_1 t^{2/5} \tag{2}$$

$$\Delta l = l_0 - l$$

$$k_1 = [(20\gamma\delta^3/\sqrt{2})(Dv/\gamma^3 \boldsymbol{B}T)]^{2/5} \tag{3}$$

where l_0 is the initial length, l is the length at time t, Dv is the self diffusion coefficient, γ is the surface tension, δ is the internal molecular distance, $\boldsymbol{B}$ is the Boltzmann constant and T is the temperature.

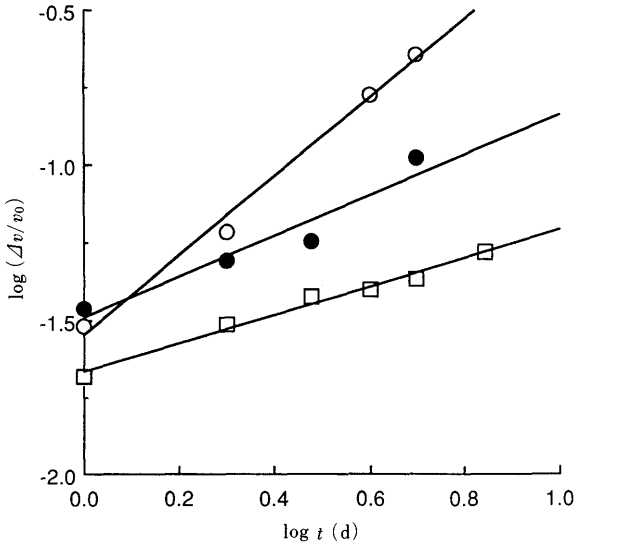

Fig. 6. Relationship between the Logarithm of Volume Shrinkage and that of Time as a Function of R.H.

□, R.H. = 84%; ●, R.H. = 88%; ○, R.H. = 92%.

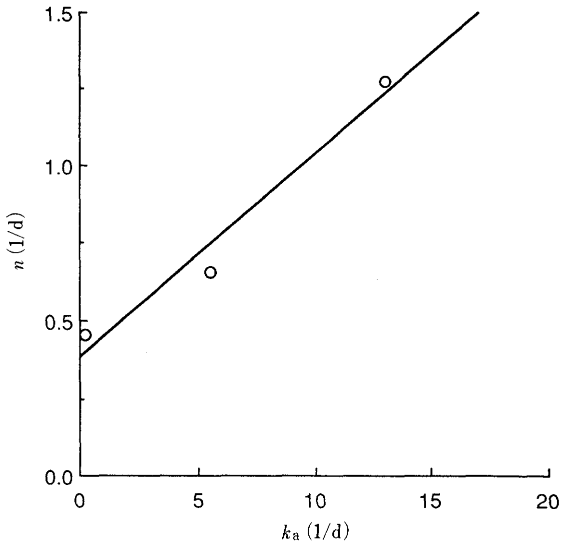

Fig. 7. Relationship between the Moisture Adsorption Rate Constant (k_a) and the Rate of Volume Shrinkage (n)

Additionally, volume shrinkage is represented by the following equation[9]:

$$\Delta v/v_0 = k_2 t^{4/5} \quad (4)$$

$$\Delta v = v_0 - v$$

$$k_2 = (3c/8)[(80\gamma\delta^3 Dv)/(BT\gamma^3)]^{4/5} \quad (5)$$

where v_0 is the initial particle volume, v is the particle volume at time t, and c is the coordination number.

The change in the ratio of volume shrinkage at constant humidity is shown in Fig. 6. This was plotted as the logarithm of volume shrinkage, $\Delta v/v_0$ against the logarithm of time, t. These plots show a good linear relationship ($R^2 = 0.928 - 0.992$) for storage at each R.H. We suggest the following equation for caking:

$$\Delta v/v_0 = kt^n \quad (5)$$

where k is a constant and is initially zero, and n is the volume shrinkage rate constant.

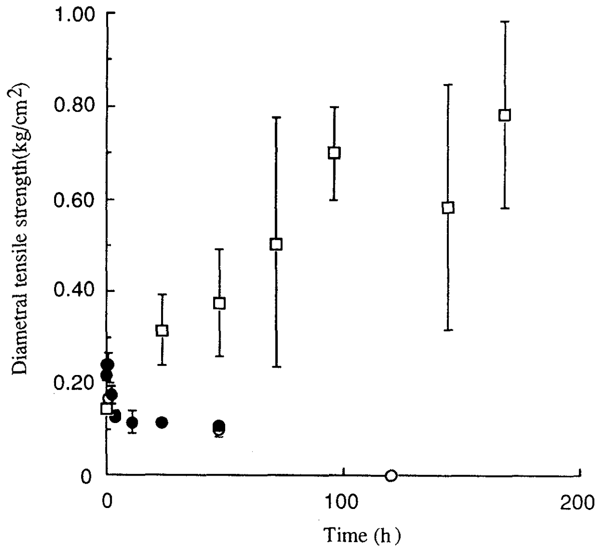

Fig. 8. Changes of Diametral Tensile Strength with Time as a Function of R.H.

□, R.H. = 84%; ●, R.H. = 88%; ○, R.H. = 92%.

TABLE II. Changes in Diametral Tensile Strength with Drying

Stored temp. (°C)	Stored R.H. (%)	Stored time (d)	Moisture content (mg/g)	Strength (kg/cm^2)
	Moisture adsorption			
25	88.0	5	16.8	0.19
25	88.0	5	16.8	0.19
25	84.0	8	1.0—1.5	1.60
25	84.0	8	1.0—1.5	1.60
	Drying			
25	84.0	1	3.92	1.50
25	75.0	1	0.77	15.8
25	75.0	1	—	3.8
25	75.0	3	—	7.8

We examined the effect of the moisture adsorption rate constant, k_a, on the volume shrinkage rate constant, n. Figure 7 was plotted using the moisture adsorption rate constant, k_a, as the abscissa, against the volume shrinkage rate constant, n, as the ordinate. These results were essentially a straight line, indicating that the volume shrinkage of sucrose is affected by moisture adsorption.

Changes in Diametral Tensile Strength with Moisture Adsorption Figure 8 shows the effect of R.H. on the diametral tensile strength of tablets as a function of time in storage. When the R.H. was above the CRH, the diametral tensile strength decreased with storage time, and finally deliquesced.

The diametral tensile strength of samples remarkably increased with storage time at the initial stage of moisture adsorption and reached equilibrium.

Changes in Diametral Tensile Strength with Drying Table II shows the conditions under which caking occurs, the diametral tensile strength of tablets and the amounts of moisture that evaporated during the drying process. The diametral tensile strength increased as the amount of evaporated water increased.

Although it is generally thought that moisture adsorption causes hydroscopic substances to cake, moisture evaporation from humidified powders due to certain environmental changes also seems to be necessary for caking, as Moss and others[10] have pointed out.

Discussion

The moisture-induced changes in the diametral tensile strength and tablet size may be interpreted as follows.

According to Rumpf,[11] the tensile strength T, of a compacted powder layer is due to the adhesive force A acting at the coordination points. Assuming that the particles forming the compacted powder layer are homogeneous in size and spherical, the tensile strength can be expressed by the following equation:

$$T=[(1-\varepsilon)/\pi]c(A/d^2) \tag{6}$$

where ε is the porosity, c is the average coordination number assumed by Rumpf to be $c\varepsilon=\pi$ and d is the average particle diameter.

In this study, we assumed that the adhesive force, A was the result of the presence of a liquid of solid bridge between two homogeneous particles. We calculated the adhesion force, A when stored under dry and at 84% R.H. conditions.

In dry storage:

$$A=T[\varepsilon/(1-\varepsilon)]d^2=3.83\times10^{-3}\,\boldsymbol{g}$$

where T is 147.2 $\boldsymbol{g}$/cm^2, ε is 0.428 and d is 59 μm.

Storage under 84% R.H.:

$$A=17.8\times10^{-3}\,\boldsymbol{g}$$

The adhesive force between particles (A) stored in a 84% R.H. was thus much higher than that of particles under dry storage. Furthermore, we calculated the dimensionless adhesive force, Fh using the following equation[12]:

$$Fh=A/(\gamma d) \tag{7}$$

where γ is the surface tension.

For dry storage:

$$Fh=8.84$$

For storage under 84% R.H.:

$$Fh=41.1$$

The dimensionless adhesive force, Fh when stored under conditions of 84% R.H., increased five times over that stored under dry conditions. Accordingly, the degree of the liquid bridge and volume shrinkage are small at a R.H. of up to 84%, but the adhesive force between the particles has a high value. Also, the diametral tensile strength increased with the increase in contact area. We concluded that slippage and transfer of particles easily occurs between the contact surfaces due to the rapid increase in number of molecular layers. This is a result of the extensive capillary condensation that occurs on the surface, and between the points of contact on the particles and smoothing of the surface by dissolution of surface asperities. The tablet size remarkably decreased as the moisture content increased with air humidified above the CRH. However, the frictional resistance between particles and the diametral tensile strength decreased owing to lubrication by water. The theoretical prediction of the adhesion force in the pendular state made by Fisher[13] and Haines[14] indicates that the adhesion should decrease with increasing moisture contents.

The increased diametral tensile strength after drying is due to a solid bridge being formed by dissolving solids stored in a R.H. above the CRH.

References and Notes

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