Accelerated Moisture Sorption Measurements by DVS Microsample Analysis

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This application note describes the approach to reduce analysis times by up to ten times by utilising the very high sensitivity of the ultra-balance employed in the DVS instrument.

Introduction

A key requirement in the development of new pharmaceutical products is the screening of large numbers of candidate substances for potentially undesirable physical properties such as moisture sorption/stability. Dynamic Vapour Sorption (DVS) automated moisture sorption analysers are now widely used throughout the industry to do this, thus reducing the typical analysis times from weeks/months with static sorption methods to hours/days. Modern pharmaceutical development is driven by the need to discover new active substances and bring them to the market as quickly as possible. Therefore there is an increasing demand for even faster methods of screening the large number of candidate substances generated by the latest pharmaceutical discovery processes.

Moisture Sorption Kinetics

The moisture sorption kinetics of a solid material (how quickly moisture is taken up), are dominated by two key factors:

(1) Mass transport in the gas phase – how quickly moisture (at a particular %RH) is supplied to the sample.

(2) Diffusion into the sample – this may be a combination of diffusion through a powder bed and/or diffusion into individual particles.

In the DVS the first factor is already optimised by having a dynamic flow of 200sccm of humidified gas over the sample, ensuring quick delivery of moisture to the surface of the sample. The second factor is primarily a function of the total sample mass and the average particle size of the sample as shown in Figure 1.
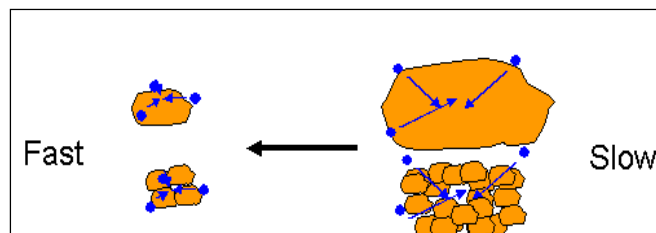

Figure 1. The effect of particle and sample size on moisture diffusion kinetics.

In a typical DVS experiment 10-30mg of particulate sample is used either in a bowl shaped sample holder or a flat-bottomed holder. In the ideal case, to optimise the sample diffusion kinetics and mass transport to the sample, it should be thinly spread over as large a surface area with as little sample as possible, illustrated in Figure 2.
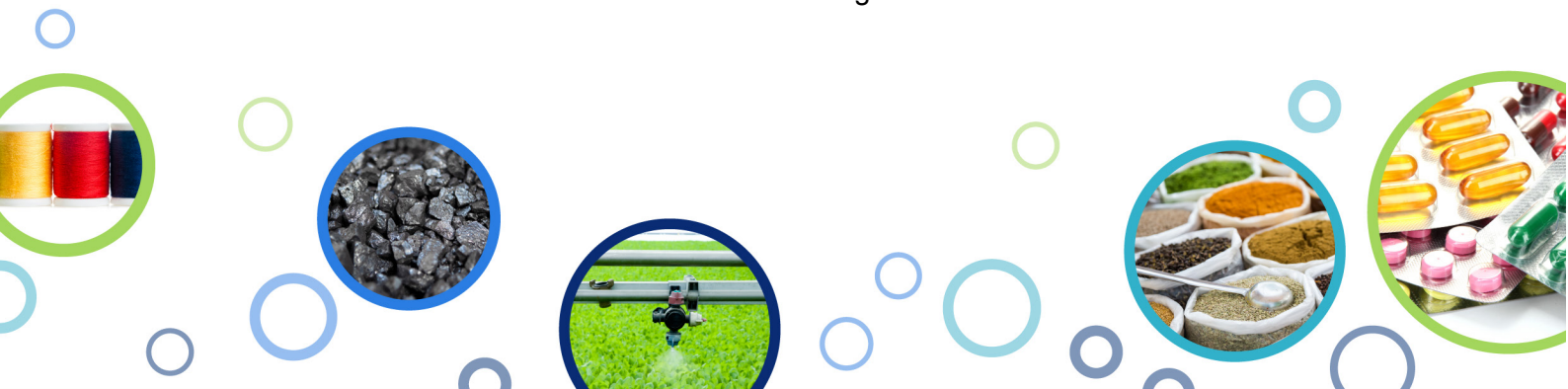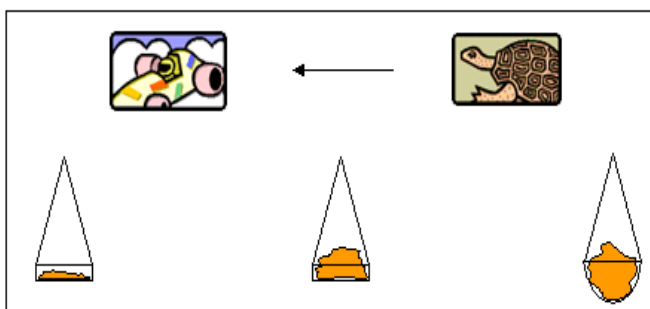
Figure 2. The effect of sample geometry and holder on moisture diffusion kinetics.

For such small sample sizes the kinetics will then largely be dominated by the relative hygrospicity of the sample being studied. The ultimate sample size will therefore be dictated by both the sensitivity and long-term stability of the ultra-balance utilised in the sorption analyser. For samples less than 1mg in mass, which we shall refer to herein as 'microsamples', it is calculated that a sub-μg sensitivity and a base line stability better than 10μg is desirable for screening of moisture uptakes of greater than 1% by weight.

Method

All experiments were carried out on a DVS automated moisture sorption analyser. This system utilises a SMS UltraBalance with a sensitivity of 0.1 μg and typical baseline stabilities of 2.5-5.0 μg per day. The symmetrical design of the sorption analyser coupled with a single isothermal temperature zone, ensures that optimum balance performance is achieved. Measurements were made on a sample of Polyvinylpyrrolidone K 25 (PVP av. molecular weight 25,000) with sample masses of 26.5939mg and 0.5123mg on two separate instruments over the 0-90% RH range at 25°C. An additional step of 95% RH was measured for the microsample to demonstrate the effect on kinetics at high humidities. The microsample was spread evenly over the bottom of a shallow convex sample holder, the larger sample was placed in the deeper bowl shaped cup to accommodate all of the powder. One should note that when

working with microsamples it is vitally important to ensure the cleanliness of the sample holders since any residual hygroscopic substances from previous analyses may have a significant impact upon the results.
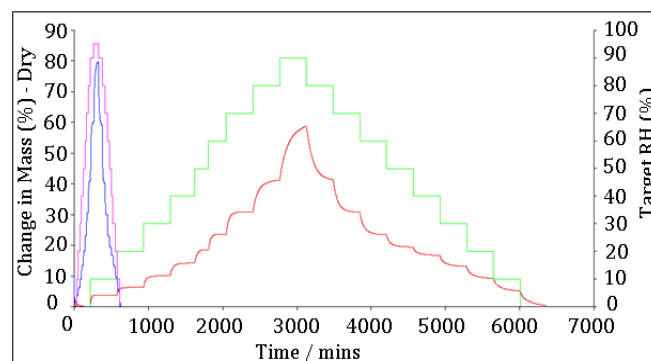
Results

Figure 3. The kinetics of moisture sorption for a microsample(blue) and normal sample(red) of PVP measured by DVS.

The kinetics of moisture sorption for the two samples of PVP are shown in Figure 3. The data clearly demonstrate the effect of sample size is very dramatic to the overall speed of analysis. In this case an increase in analysis time of approximately 10 times is observed for a corresponding decrease in sample mass of approximately 50 times.

Table 1. Comparison of equilibrium percentage moisture contents during sorption and desorption for the normal and micro PVP samples measured by DVS.

Target RH%	Sorption Normal PVP	Sorption Micro PVP	Desorption Normal PVP	Desorption Micro PVP
0.0	0.00	0.00	0.37	-0.64
10.0	3.74	3.71	5.14	4.69
20.0	6.44	6.28	9.23	8.89
30.0	10.21	9.15	13.08	12.88
40.0	14.25	13.63	16.67	16.42
50.0	18.59	18.24	19.41	19.20
60.0	23.62	23.30	23.44	22.82
70.0	30.89	30.56	30.80	29.88
80.0	41.10	41.06	41.39	40.16
90.0	58.84	60.03	58.84	59.22
95.0		79.49		79.49

Table 1 shows a comparison of the equilibrium moisture contents calculated from the moisture sorption profiles in Figure 3. The data clearly show that there is very good agreement between the sorption and desorption data for the two samples, in particular in the low % uptake region which is critical for screening purposes. Note, at 90% RH the sorption data for the normal PVP sample had not reached equilibrium within the experimental parameters chosen.

Conclusion

This short study demonstrates how a DVS moisture sorption analyser can be successfully used to study the moisture sorption of microsamples (<1.000 mg) leading to a dramatic reduction in the analysis time required for each sample. This is achieved by using the unrivalled sensitivity and stability of the DVS ultra-balance, combined with appropriate preparation of the microsample and sample holder.