Surface Measurement Systems
World Leader in Sorption Science

DVS Application Note 40

Using the DVS to Study the Water Sorption Properties of Multi-Component Systems

Dan Burnett, Armando R. Garcia and Frank Thielmann, Surface Measurement Systems Ltd.

Dynamic Vapour Sorption (DVS) was used to measure the water sorption isotherms of two pharmaceutical formulations and were compared to the moisture isotherms of the individual components. The first formulation was granules consisting of microcrystalline cellulose, hydroxypropylcellulose (HPC), and Lovastatin. The second mixture consisted of co-lyophilised bovine serum albumin (BSA) and mannitol.

Introduction

The interactions between drugs and excipients have a significant impact on product stability and performance. For instance, high molecular weight excipients can be added to stabilize amorphous actives. Drug-carrier interactions can determine drug release profiles. Additionally, drug-binder interactions can determine ultimate granule and tablet strength. Therefore, understanding the interactions between components in pharmaceutical materials can be paramount in developing successful formulations.

The water vapour sorption properties of pharmaceutical materials such as excipients, binders, and drug formulations are recognised as critical factors in determining their storage, stability, processing and application performance [1]. In this study, DVS is used to determine if the moisture sorption properties of the individual components will match those of a pharmaceutical formulation. If they differ, then the paths used to create the formulation much change the water vapour sorption properties of the components. Similar experiments were done by Crowley and Zografi [2] where they compared the water sorption properties of amorphous drug/polyvinylpyrrolidone dispersions with those of the individual components.

Theory

An isotherm describes the equilibrium vapour uptake as a function of vapour partial pressure. In order to compare the water sorption properties of a mixture to the individual components, moisture isotherms must be collected on each component of the mixture, separately. Then, the mixture isotherm can be compared to an isotherm comprised of the weighted averages of the individual components. This is illustrated in Equation (1) below:

$$W_{Mixture} = (W_a m_a) + (W_b m_b) + (W_c m_c) + \ \ldots \quad (1)$$

where *W* is the percentage weight gain at a particular vapour partial pressure, *m* is the mass fraction, and the subscripts *a, b, c,* etc. represent the individual components of the mixture. If the percentage weight gains are measured at the same water vapour partial pressures for the mixture and individual components, then the mixture isotherm can be compared to mass fraction-weighted isotherms of the individual

components. The above methodology could be applied to any mixture and any vapour isotherm.

Method

Dynamic vapour sorption (DVS) is a well-established method for the determination of vapour sorption isotherms. The DVS instrument used for these studies measures the uptake and loss of vapour gravimetrically using a SMS ultra-balance with a mass resolution of ±0.1 µg. The high mass resolution and excellent baseline stability allow the instrument to measure the adsorption and desorption of very small amounts of probe molecule. The vapour partial pressure around the sample is controlled by mixing saturated and dry carrier gas streams using electronic mass flow controllers. The temperature is maintained constant ±0.1 °C, by enclosing the entire system in a temperature-controlled incubator. Water vapour isotherms were collected on all samples over a wide humidity range at 25.0 °C.

The first mixture studied were granules consisting of hydroxypropylcellulose (HPC), Lovastatin, and microcrystalline cellulose (MCC). A dry blend of MCC and Lovastatin were granulated in a HPC binder solution. The final granule composition was 4.1% HPC, 5.1% Lovastatin, and 90.8% MCC.

The second mixture studied was a co-lyophilised mixture of bovine serum albumin (BSA) and mannitol. The mannitol-BSA sample was obtained by freezing 3ml volumes of formulation within 10ml vials to a temperature of -50 °C. Freeze drying was conducted with a shelf temperature of –30 °C for a period of 24 hours with a constant 200 µbar vacuum before secondary heating at 20 °C for 9 hours (50 µbar). The final concentration of BSA in the dried material was 20% w/w.

Results

Figure 1 displays the water sorption isotherms for the individual components of the HPC/MCC/Lovastatin mixture. The percent change in mass (referenced to the dry mass) is plotted on the y-axis, while the target relative humidity is plotted on the x-axis. The Lovastatin material (blue trace in Figure 1) is very hydrophobic, as indicated by the minimal percentage change in mass between 0 and 95% RH. HPC (red trace) and MCC (green trace) are significantly more hydrophilic.

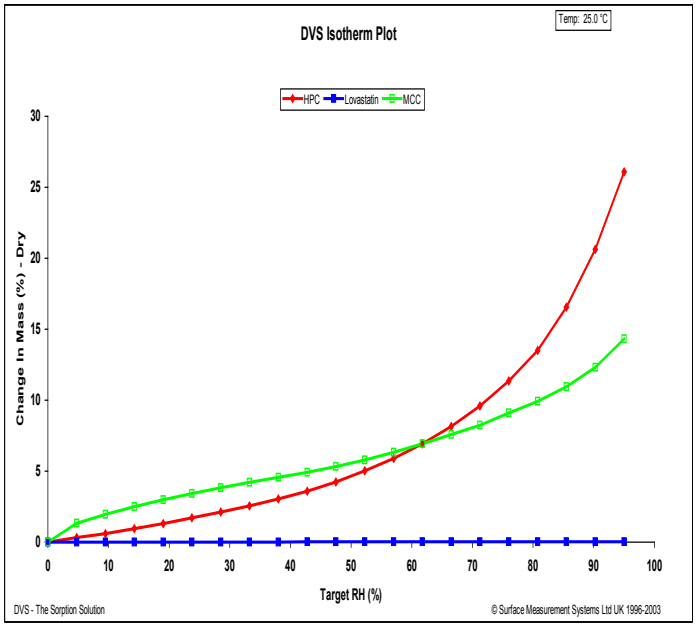

Figure 1. Water sorption isotherms for HPC (red), MCC (green), and Lovastatin (blue) 25.0 °C.

Figure 2 displays the water sorption isotherms for the actual granules (blue) and the theoretical isotherm based on the mass-fraction weighted isotherm (red) from the individual component isotherms. Clearly, there is very little difference between the measured isotherm and predicted isotherm, indicating interactions between the components do not significantly alter the moisture sorption properties of the individual components. The minor deviations between the actual and theoretical isotherms are considered to be within the error margins of the experiments or due to the inaccuracies in the % composition of the formulation.

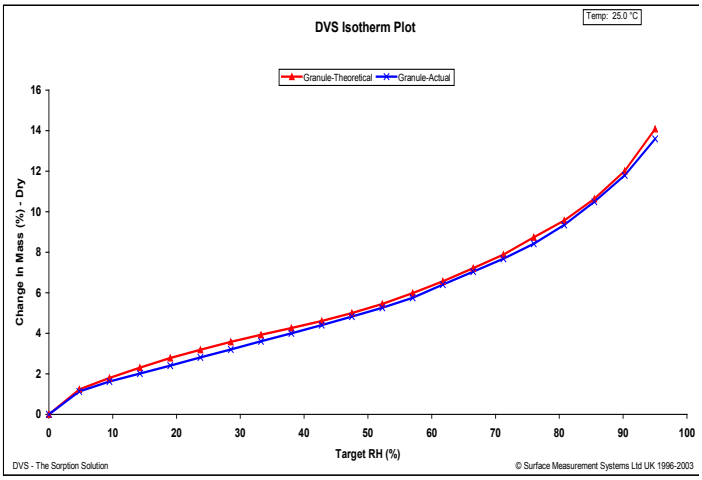

Figure 2. Theoretical (red) and actual (blue) water sorption isotherms for the granule sample measured at 25 °C.

The moisture sorption isotherms for pure freeze-dried BSA (red) and mannitol (blue) are displayed in Figure 3. These materials were lyophilised under the same conditions as the BSA-mannitol mixture.

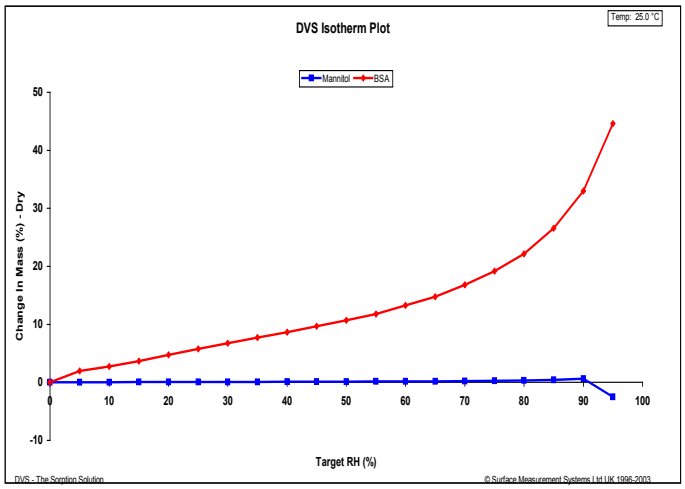

Figure 3. Water sorption isotherms for freeze-dried BSA (red) and mannitol (blue) at 25.0 °C.

The mannitol material is considerably less hydrophilic compared to the BSA sample. The mannitol isotherm shows a drop in mass for the 95% RH step, due to sample crystallization. The moisture sorption kinetics (data not shown) show typical behaviour for a moisture-induced crystallisation event. The crystalline phase will often have a much lower capacity and/or affinity for water vapour, resulting in a net mass loss at a critical relative humidity. For this sample, mannitol crystallizes at 95% RH and 25 °C.

Measured (red) and theoretical (blue) moisture sorption isotherms for an 80% mannitol 20% BSA co-lyophilised powder are displayed in Figure 4. The predicted isotherm is based on the weight-fraction averaged values from the individual component isotherms.

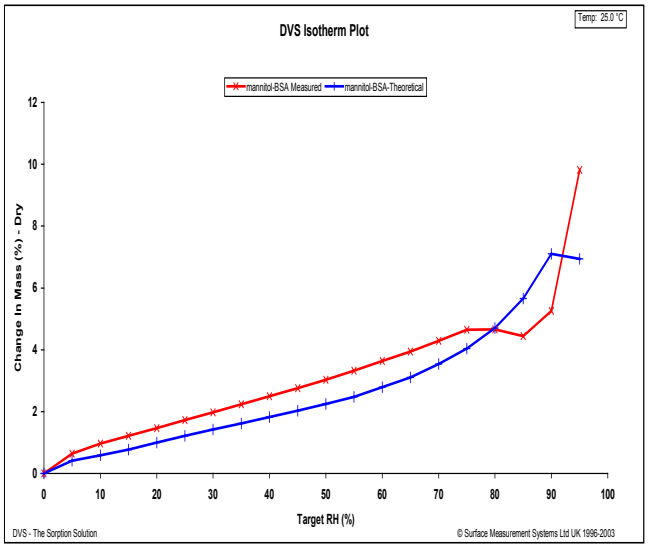

Figure 4. Measured (red) and theoretical (blue) isotherms on for the mannitol-BSA sample at 25 °C.

There is clearly a difference between the measured isotherm and theoretical isotherm for this mannitol-BSA sample. The predicted isotherm exhibits a significantly lower water sorption capacity below 80% RH, compared to the actual isotherm. Also, the co-lyophilised BSA-mannitol sample shows an amorphous to crystalline transformation at 75% RH, as indicated by the decrease in vapour sorption capacity. For the individual mannitol component, this transformation does not occur until the 95% RH step. Therefore, when co-lyophilised, the BSA material acts as a plasticizing agent for mannitol. There are significant interactions between the mannitol and BSA such that their sorption isotherms are not additive. This is in sharp contrast to the HPC/MCC/Lovastatin granules where the predicted isotherm exactly matched the actual isotherm.

Conclusion

Water sorption isotherms were collected for two pharmaceutical formulations and compared to theoretical isotherms comprised of the weight-fraction averages of the individual components. For HPC/MCC/Lovastatin granules produced via wet granulation, there was no difference between the measured and predicted isotherms. In contrast, for co-lyophilised BSA/mannitol, there were significant differences between the measured and predicted isotherms. Therefore, co-lyophilisation notably altered the water sorption properties of the individual components. Similar methodology could be applied to any solid formulation to study how the production route affects the moisture sorption properties of the mixture/blend.

References

[1] York, P., Int. J. Pharm. 14 (1983) 1-28.
[2] Crowley, K.J. and Zografi, G., J. Pharm. Sci. 91 (2002) 2150-2165.

Head Office:
Surface Measurement Systems, Ltd
5 Wharfside, Rosemont Road
LondonHA0 4PE, UK
Tel: +44 (0)20 8795 9400
Fax: +44 (0)20 8795 9401
Email: science@surfacemeasurementsystems.com

United States Office:
Surface Measurement Systems, Ltd, NA
2125 28th Street SW, Suite I
Allentown PA, 18103, USA
Tel: +1 610 798 8299
Fax: +1 610 798 0334