DVS
Application
Note 26

# Isotherm Types and Adsorption Mechanisms of Solvents on Pharmaceutical Excipients

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***The interaction of organic solvents and water with pharmaceutical powders is highly important for the understanding of solvent-based processes, e.g. wet-granulation, crystallization, drying or prediction of product stability and shelf life. For these reasons information about the adsorption mechanism of these solvents on powder surfaces is required. This information can often be obtained from the shape of the vapour sorption isotherm.***

## Introduction

Sorption isotherms describe the amount of vapour adsorbed or desorbed at different equilibrium concentrations (partial pressures) in the gas phase. The shape of a sorption isotherm depends on the interaction between the vapour molecules and the solid sample and allows for conclusions regarding the sorption mechanism. For this reason it is not surprising that vapours of different nature can show different isotherm shapes when adsorbing on the same material. This has implications on all processes where solvents are involved, such as wet-granulation, crystallisation or drying.

In the current paper differences in adsorption behaviour between solvents shall be demonstrated by the adsorption of water and a series of alcohols on a crystalline α-lactose monohydrate sample. The resulting adsorption isotherms will be fitted with different adsorption models and conclusions about the adsorption mechanism will be drawn.

## Theory

The isotherm shapes are usually described by the BDDT classification [1]. This system distinguishes five different types of sorption isotherms (type I – V) which was later extended by an additional type VI. They are shown in Figure 1.

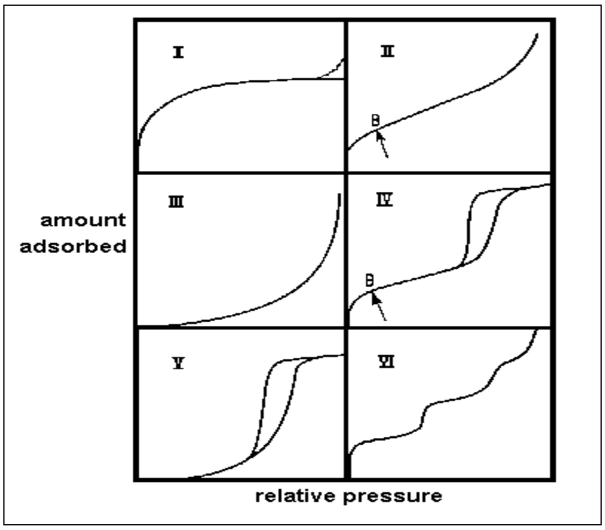


*Figure 1. Isotherm types according to the BDDT classification.*

However, type VI isotherms have no relevance for vapour sorption at ambient conditions and type I isotherms are rarely observed unless the material

is strongly microporous or chemisorption occurs. For this reason they will not be discussed in this paper. One can clearly identify two sets of isotherms. One set, consiting out of type II and IV shows a significant uptake at low partial pressures followed by small adsorption at intermediate vapour concentration and again a high uptake at elevated partial pressures. The other set comprises type III and V isotherms with a characterisatic low uptake at low concentration and a strong increase in adsorption at higher vapour concentration.

These differences in the adsorption and desorption behaviour are due to differences in the sorption enthalpy of solvents [2]. This is illustrated in Figure 2.

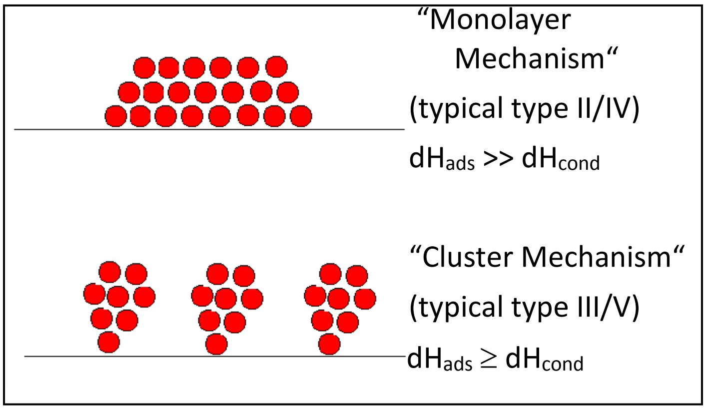


*Figure 2. Sorption mechanisms of solvents on solid surfaces.*

If the vapour molecule has a strong interaction with the solid surface (equivalent to a high heat of sorption) in relation to the interaction between two vapour molecules (equivalent to a high heat of condensation) the vapour adsorbs on the surface as a monolayer in the ideal case of a perfectly homogeneous surface. After completion of the monolayer multilayer formation occurs which can be described as a condensation of vapour molecules on the initial monolayer. This is a typical behaviour for molecules with low polarity such as alkanes or nitrogen. It is for this reason that those molecules can be used for the determination of the specific surface area according to the BET theory. A more detailed description of the BET method can be found in Application Note 18 [3].

The opposite case is when the vapour has an interaction with the surface which is energetically similar or just slightly higher than the interaction with another vapour molecule (meaning the heat of sorption is similar to the heat of condensation). This causes only very few molecules to adsorb at low concentration (they prefer to interact loosely in the vapour phase) followed by condensation at higher partial pressures on the few initially adsorbed molecules. Such effect can be described as cluster formation since there is no monolayer formation occurring.

In reality these two mechanisms and the corresponding isotherm shapes are extremes and usually occur in combination due to the heterogeneous nature of true surfaces. However, it is extremely useful to understand the fundamental mechanisms which drive adsorption on solid surfaces.

## Method

All experiments were performed on a DVS automated gravimetric vapour sorption analyser (Surface Measurement Systems Ltd., London, UK). The DVS measures the uptake and loss of vapour gravimetrically using a SMS UltraBalance with a mass resolution of ±0.1 µg. The relative concentration around the sample was controlled by mixing saturated and dry carrier gas streams using mass flow controllers. The measurement temperature was maintained constant at 25.0 °C, ±0.1 °C, by enclosing the entire system in a temperature-controlled incubator.

A mass of 20 mg for the water experiments (and around 100 mg for the alcohol measurements) was loaded into a sample cup and placed in the system. Prior to being exposed to any vapour the samples were equilibrated for a short time at 0% p/po to remove any surface water present and establish a dry, baseline mass. Next, the samples were exposed to the following concentration profile: 0 to 10% in 1% steps, 20% to 90% in 10% steps, 95% and the same for desorption. At each stage, the sample mass was allowed to reach equilibrium before the partial pressure was increased or decreased. From the complete sorption and desorption profile an isotherm was calculated using the DVS Advanced Analysis Suite v3.6.

The α-lactose monohydrate sample was obtained from Acros and recrystallised by exposing it to a high humidity atmosphere. This procedure was applied to ensure that any contribution of the amorphous phase was eliminated. Alcohols used in this study were methanol, ethanol, 1-propanol and 1-butanol, all supplied by Aldrich. Deionised water was supplied by Fisher.

## Results

Figure 3 displays adsorption and desorption isotherms for two cycles of water at 25 °C. There is good agreement between the adsorption and desorption branch suggesting that there is no significant hysteresis. The second cycle is almost identical to the first confrming that there are no irreversible effects involved.

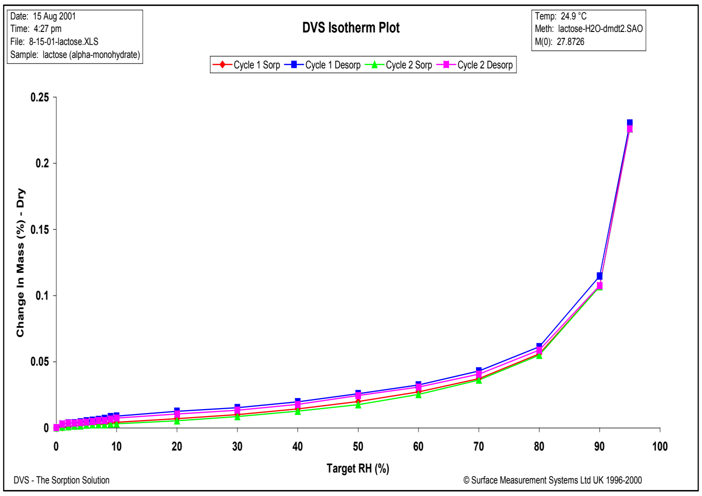


*Figure 3. Water sorption isotherms on the lactose sample at 25.0 °C.*

Figure 4 shows a comparison of the alcohol isotherms. Only adsorption isotherms from the first cycle are shown since there was no hysteresis and no significant difference between the first and second cycle. The first cycle water adsorption isotherm was also included for comparison at the same uptake levels.

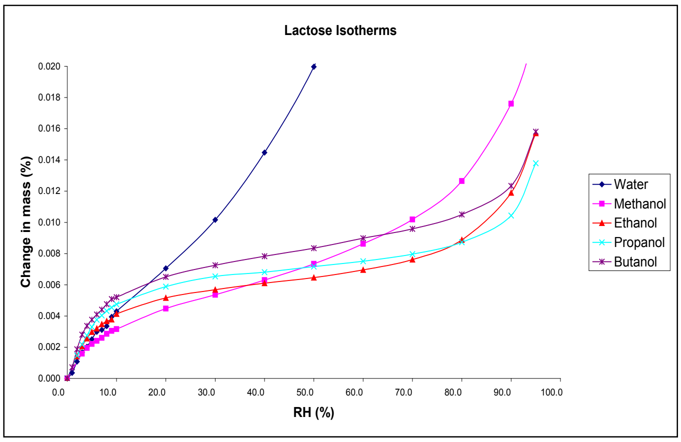


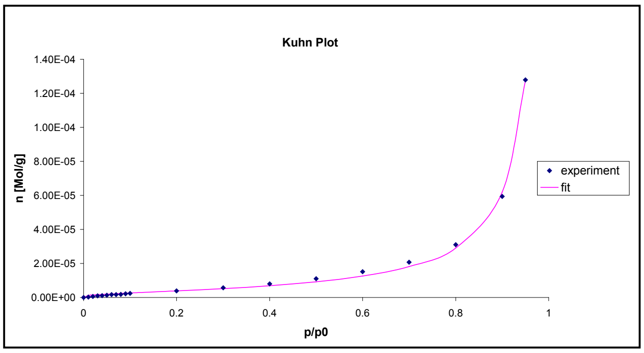
*Figure 4. Adsorption isotherms for methanol, ethanol, 1-propanol and 1-butanol on the lactose sample at 25.0 °C (with water isotherm for comparison).*

While water sorption isotherms in Figure 3 clearly suggest an adsorption mechanism dominated by type III behaviour Figure 4 indicates that there is a change in the mechanism to type II with decreasing polarity of the alcohol.

Water often tends to exhibit type III behaviour when adsorbed on low energy surfaces due to its strong intermolecular hydrogen bonding. For this reason it is not recommended to use water as a probe molecule in a BET surface determination. Alcohols show a mixed isotherm type due to their polar contribution (from the OH-group) and their non-polar alkane chain. The bigger the chain length the less polar the alcohol. It is for this reason that butanol is close to a typical type II adsorption isotherm.

In order to support the conclusions drawn above, the isotherms have been fitted to a range of vapour sorption models using the SMS Isotherm Suite v1.1. This software contains a wide range of theoretical and semi-empirical equations to fit sorption isotherms. The software also allows the choice of the best fit from a ranking of the fit coefficients.

Amongst the various models applied the results of the Kuhn equation should be examined closer for this application. The Kuhn equation is based on the assumption of a different adsorption potential for each surface site, combined with cluster formation on each site as the partial pressure increases [4]. This mechanism corresponds to type III behaviour. For this reason it is not surprising that the equation is found to be the best fit for the water sorption isotherm but poorly fits the alcohol isotherms. This reflects the significant change from a strong type III to a mixed type II/III behaviour for the alcohols. These findings are illustrated in Figure 5 for water (left) and 1-butanol (right)



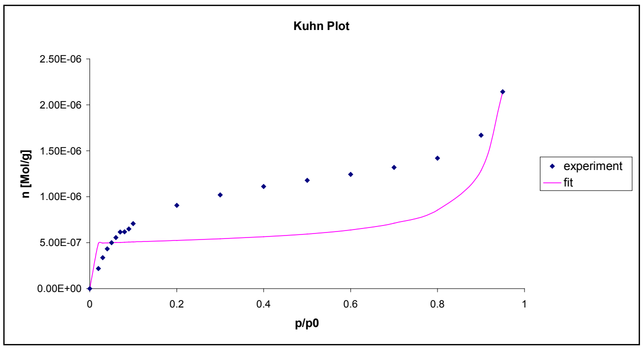


*Figure 5. Adsorption isotherms for water and 1-butanol on lactose sample at 25.0 °C with fit from the Kuhn model*

## Conclusion

This method provides reliable, accurate and independent validation of RH generation and measurement in DVS water sorption instrumentation.

## References

[1]Brunauer, S, Deming, L., Deming, W. and Teller, E., J. Amer. Chem. Soc. 62 (1940), 1732
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[3]Williams, D. and Levoguer, C., Application Note 18, SMS London 1998
[4]Kuhn, I., J. Coll. Interf. Sci. 23 (1967), 563