Dynamic water vapor sorption analysis for the determination of amorphous lactose

– White Paper 20-01

Introduction

Ingredients, such as sugars, can be present in an amorphous or a crystalline state. The amorphous state is either specifically adjusted to benefit from the special product structures and properties, or it is caused process-related, e.g. during spray- and freeze drying, grinding, compaction, extrusion, evaporation or baking [1].

A characteristic of amorphous products is their hygroscopicity. The associated high water-binding capacity leads to a reduction of the product viscosity and to an increased mobility of the molecules. By exceeding a critical moisture content uncontrolled recrystallization is favored. In consequence, product changes such as caking, reduced solubility, increase of Maillard reactions and fat oxidation as well as a rougher mouthfeel affect the physical and chemical stability, the acceptance and the quality of the product [2,3].

In this context, milk-based powders are often critical. Commonly, these powders are produced by spray- or drum drying. Thereby, water is quickly removed and at least a part of the lactose is converted into an amorphous state [2].

Due to the versatile use of lactose-, milk- and whey powder this is important in both the food- and pharmaceutical sectors.

To estimate the stability of such products and formulations, the knowledge about the amorphous content and the recrystallization kinetics is crucial.

In literature, several methods have been described to determine the amorphous content of powdered products. However, the detection limits of these methods are often limited to amorphous contents above 10 % for X-ray diffraction and Differential Scanning Calorimetry [1] or 1 % for FT-Raman spectroscopy [4], NIR-spectroscopy [5] and solution calorimetry [9].

Lower detection limits could be achieved using isothermal microcalorimetry (0.2 %) [7,8] and solid-state NMR (0.5 %) [8].

Besides these methods gravimetric dynamic water vapor sorption (DVS) was successfully applied for determining amorphous contents [3,9,10].

Compared to the above-mentioned methods, DVS is an easy and sensitive method with a detection limit down to 0.1 % [11].

Principle of the method

The DVS method to determine amorphous contents is based on the idea that amorphous powders have a higher affinity to adsorb water than crystalline materials. However, water acts as a plasticizer and lowers the glass transition temperature of the product. In Fig. 1 the moisture sorption isotherms of amorphous and crystalline lactose are shown in comparison.

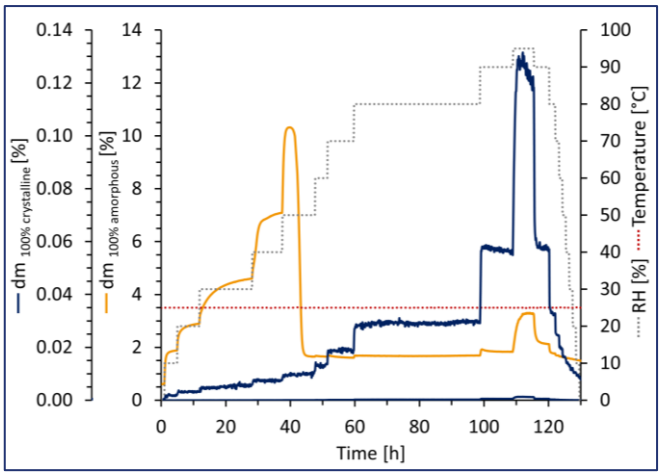

Fig. 1: Sorption kinetics of amorphous and crystalline lactose. Decrease of mass at a RH of > 40 % (amorphous lactose) is attributed to the onset of crystallization.

If a critical moisture of 40 % RH is exceeded, the amorphous lactose sample starts to crystallize. The lower water binding ability of the crystalline form causes the release of water and thus a decrease in mass.

In comparison, crystalline lactose shows a strong mass increase only at relative humidities above 90 % which can be explained by an incipient dissolution (Fig. 1).

To determine the amorphous content of a powder sample by DVS analysis, several methods have been described in literature. The basic idea is to obtain a calibration curve by measuring the sorption behavior of powder mixtures with different ratios of amorphous to crystalline. Saleki-Gerhard et al. [1] correlated the equilibrium moisture uptake at different relative humidities to the amorphous content of the mixture.

Buckton and Darcy [12] performed several adsorption/desorption cycles and calculated the area between the first and the subsequent cycles to draw conclusions on the crystallization kinetics and the amorphous content of the sample.

The method described by Mackin et al. [7] is based on calculating the differences in relative mass changes before and after crystallization of the sample.

A further method was recently proposed by Vollenbroek et al. [11]. This approach uses the BET-model (Eq. 1) to calculate the moisture content which corresponds to a monomolecular coverage of the material.

$$X = \frac{X_m \cdot C \cdot a_w}{(1 - a_w) \cdot (1 + (C - 1) \cdot a_w)} \qquad \text{Eq. 1}$$

In contrast to crystalline materials, the process of moisture uptake into amorphous powders can be described more by absorption than by adsorption [13].

Moisture uptake at the beginning is described as a kind of dissolution process of the adsorbate into the amorphous material associated with a fill up of the void volume of the micropores within the amorphous material. For validity of the BET equation the adsorbate volume measured at full saturation of the micropores is assumed to be equal to the volume of the monomolecular layer [13].

Analysis

Analyses were performed in the multisampling water vapor sorption analyzer SPS11-10µ. The device is characterized by its high robustness together with a high sensitivity and reproducibility of the induced mass changes of the sample.

Amorphous lactose was obtained by freeze-drying. Crystalline lactose (Lactohale 100) was obtained from DFE pharma. For calibration, mixtures with amorphous contents ranging from 0-100% amorphous lactose were prepared.

The instrument settings were adjusted to a min. and max. time per cycle of 60 min and 48 h. The default weight limit was set to a mass change of 25 %. Equilibrium conditions were specified according to the resolution limit of the balance (10 µg). Samples were measured every 7 min. The temperature was set to 25 °C and the adsorption/desorption behavior was recorded at relative humidities from 0-95-0 %. A second similar cycle was run subsequently to verify complete crystallization (Fig. 2).

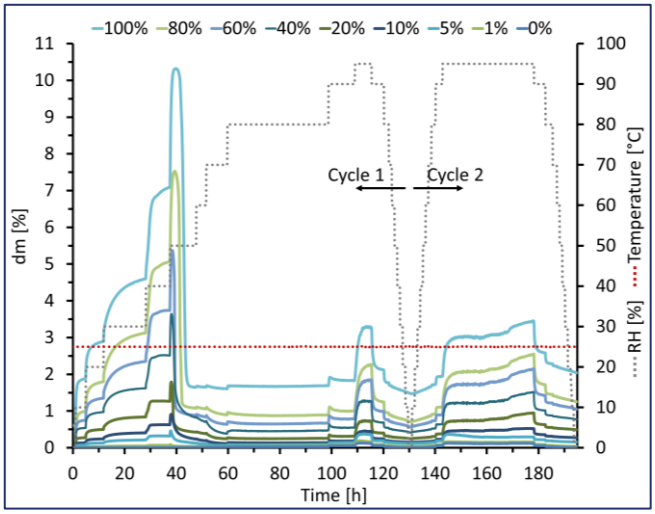

Fig. 2: Sorption kinetics of amorphous/crystalline lactose mixtures before (cycle 1) and after (cycle 2) crystallization.

Moisture sorption and mass loss increases with the amorphous content. The mass increase at 95 % RH

(cycle 1 and 2) is due to beginning dissolution processes.

In the second cycle no crystallization peak could be detected. This indicates a complete crystallization of the amorphous lactose.Determination of amorphous contents

As shown in Fig. 2 the moisture uptake varies depending on the amorphous content. As proposed by Vollenbroek et al. [11], the BET constant Xm which corresponds to the moisture content at complete monomolecular saturation of the sample can be used to describe this dependency (Eq. 1).

For calibration, the BET constants C, which describes the specific, temperature-dependent sorption enthalpy of the monolayer molecules, and Xm were determined by fitting the data to the BET model using the method of least squares in the aw-range from 0-0.3.

Fig. 3 shows the measured isotherms and the corresponding BET fits of a 100 % crystalline and amorphous lactose sample exemplary.

Correlation coefficients of the fit were always above 0.998. Sorption isotherms of the amorphous/crystalline mixtures have been corrected for the moisture adsorption of the 100 % crystalline sample. Corresponding BET constants are summarized in Tab. 1.

A calibration curve was obtained by plotting the monomolecular moisture content X_m over the amorphous content of the mixture (Fig. 4). The linear dependency over the whole range (0-100 %) was found to fit the dependency of these two parameters (Eq. 2) .

$$y = 0.0673 \cdot x - 0.0956 \qquad R^2 = 0.9983 \qquad \text{Eq. 1}$$

The constant C decreased with increasing amorphous content according to a power law function. However, the correlation was less pronounced (R^2=0.8945).

Table 1: BET constants depending on the amorphous lactose content of the mixtures.

Amorphous content [%]	0	1	5	10	20	40	60	80	100
X_m	0.01	0.05	0.29	0.60	1.25	2.35	3.93	5.32	6.70
C	4.87	3.35	2.31	2.00	1.99	2.10	1.63	1.59	1.61

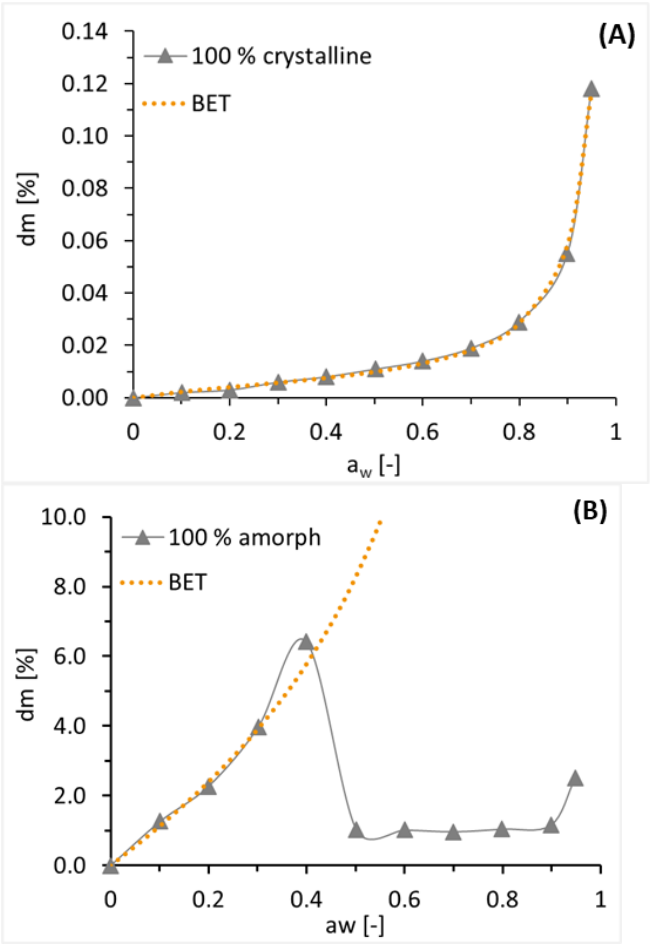

Fig. 3: Experimental data and BET prediction of the sorption isotherms of crystalline **(A)** and amorphous **(B)** lactose.

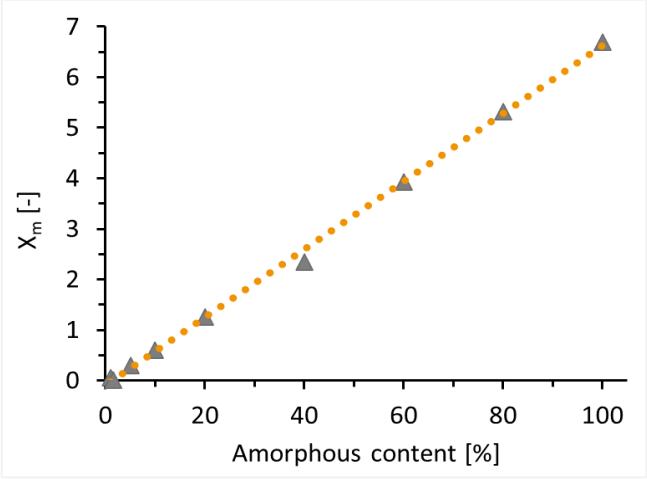

Fig. 4: Calculated moisture content of the monolayer (X_m) dependent on the amorphous lactose content in the mixture.

Conclusion

It could be shown that amorphous contents can be determined by dynamic water vapor sorption analysis. The use of the automated multisampling SPS-device allows both a simple and highly sensitive method for a precise determination of amorphous fractions in powdered materials.

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