Amorphous lactose in pharmaceuticals

– Application Note 20-05

Introduction

Lactose is widely used in the pharmaceutical industry, e.g. as filler, binder, carrier substrate or diluent in tablets, capsules or dry powder inhalators [1,2].

Lactose can be present in a crystalline or an amorphous state. The amorphous state is often caused process-related during spray- and freeze drying, grinding, compaction, extrusion or evaporation [1,3]. While crystalline lactose is characterized by a regular arrangement of the molecules, the amorphous state commonly does not show any regular structures. Another characteristic of amorphous lactose is its hygroscopicity, which is associated with a high water-binding capacity. This promotes uncontrolled crystallization, combined with the release of crystallization water, if a critical moisture content is exceeded [4].

For that reason, even low amorphous amounts can have negative effects on the product quality with regard to handling, dosage and drug efficacy [2,5]. This makes both the determination and the adjustment of the amorphous fraction an important task, e.g. for the specific adaption of process parameters or to assess the stability of lactose-containing products within the scope of quality assurance.

Principle of the method

The DVS method is based on the higher moisture sorption affinity of amorphous compared to crystalline materials. In addition, water vapor sorption induces crystallization of the amorphous parts. Both kinetics of water vapor sorption and crystallization events can be followed by DVS experiments.

For quantitative determination of the amorphous content by DVS, several methods have been described in literature [2,3,5,6].

The basic idea is to obtain a calibration curve by measuring the sorption behavior of powder mixtures with different ratios of amorphous to crystalline.

Results

Kinetics of moisture sorption of various amorphous/crystalline lactose mixtures are shown in Fig. 1. If a critical moisture of 40 % RH is exceeded, the amorphous lactose starts to crystallize. The lower water binding ability of the crystals causes the release of water and thus a decrease in mass. In comparison, crystalline lactose shows a mass increase only above 90 % RH which can be explained by an incipient dissolution (Fig. 1).

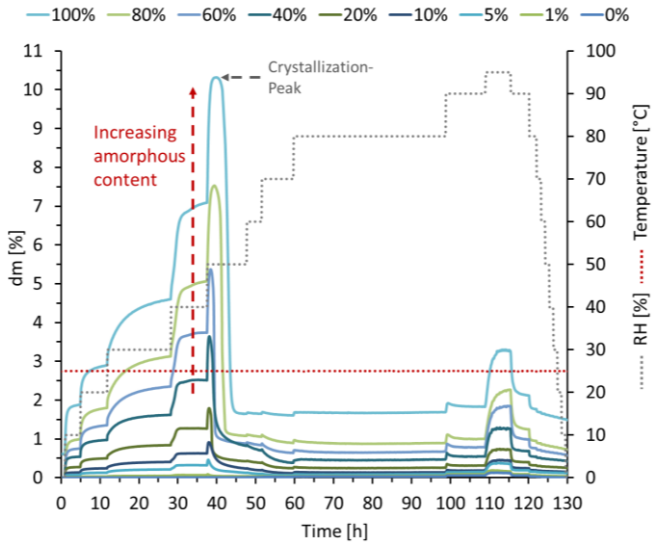

Fig. 1: Sorption kinetics of amorphous/crystalline lactose mixtures.

From the results shown in Fig. 1, a calibration curve was obtained by plotting the monomolecular moisture content X_m over the amorphous content of the mixture as proposed by Vollenbroek *et al.* [2]. A linear relationship over the entire range (0-100 %) with a correlation coefficient of $R^2 = 0.9983$ was obtained (Fig. 2).

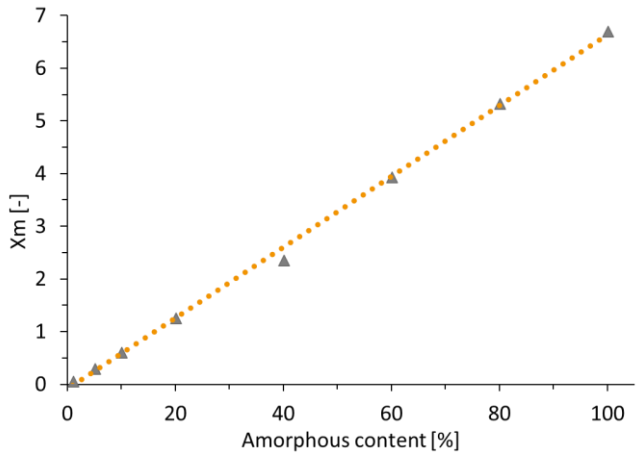

Fig. 2. Calculated moisture content of the monolayer (X_m) dependent on the amorphous lactose content in the mixture

Conclusion

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.

With the help of the obtained calibration, the amorphous portion in unknown lactose powders can be determined on basis of their water vapor sorption behavior.

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References

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