THE USE OF SOLUTION CALORIMETRY IN ASSESSING PARTIALLY AMORPHOUS DRY POWDER INHALATION CARRIERS

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Delivery to the lungs of poorly flowing micronised drug is known to be problematic. The majority of commercially available dry powder inhalers incorporate an inert carrier particle, such as crystalline lactose monohydrate. In this study, we have attempted to change the carrier particle characteristics in order to improve the segregation of the drug particle from the carrier surface during inhalation. This was achieved by the addition of amorphous lactose fines to the carrier, followed by controlled crystallization using defined relative humidity and airflow conditions. This resulted in a partially crystalline carrier that exhibited different characteristics according to the degree of crystallinity.

Solution calorimetry was used to assess the small degree of crystallinity of the lactose prior to mixing with salbutamol sulphate, a common drug used in the treatment of asthma. Drug deposition analysis showed that small variations in crystallinty of the carrier lead to significant variations in the carrier morphology. More importantly, when assessed using a twin stage impinger, the efficiency by which salbutamol was liberated from the carrier surface was seen to significantly improve for a given amorphous content. For example, a carrier with 6% amorphous content is able to deliver 39% of the emitted drug dose as respirable. However, the fine particle fraction of drug delivered by 4.5% or 7% amorphous carriers is less than half that of the 6% amorphous carrier.

Variations in crystallinity are known to significantly alter physical and chemical properties of pharmaceutical powders [1,2]. Here, we have demonstrated how it can be controlled to produce better performing partially amorphous inhalation carriers.

References

[1] G. Buckton and P. Darcy, Int. J. Pharm. 179 (1999) 141-158.

[2] B. Hancock and G. Zografi, J. Pharm. Sci. 86 (1997) 1-12.