**Introduction**

With several patent expirations of innovator dry powder inhaler (DPI) products looming, the major challenge for generic entry is demonstrating bioequivalence (BE) with respect to the reference product. Demonstrating BE of locally acting drugs is challenging, because they do not rely on systemic circulation for targeting the therapeutic site of action.

The US FDA has conceived a concept for demonstrating BE of topical products, which is called Q3-equivalence. This term describes structural similarity between test and reference DPI products and refers to the arrangement of matter and state of aggregation of the product. However, demonstrating Q3-equivalence between test and reference DPI products is challenging due to the complexity of DPI dosage forms.

**Methods**

Seretide™ Accuhaler™ and Advair Diskus® were sourced from a wholesale pharmacy. These batches were investigated in terms of the dissolution of the Fluticasone Propionate (FP) in each product and the agglomerate structure using the Morphology-Directed Raman Spectroscopy (MDRS) method.

**Results**

**Unidose Collection System**

The aerosol collection system was specifically engineered to address the fundamental challenges of current in vitro dissolution testing of orally inhaled drug products[1].

**Dissolution Analysis**

The dissolution of the FP component of the aerosolised ISM dose of Seretide and Advair is shown in Fig. 3. These data suggest that the dissolution rate of FP in Seretide was slower than that of FP in Advair.

These data suggest that differences in the in vitro dissolution of the aerosolised dose of both products may be related to differences in the physicochemical properties of the API/excipient ingredients in the formulation, manufacturing variables between sites and shipping and storage.

Differences in the dissolution rate of FP in both products, suggests that the drug-drug and drug-lactose interactions within the formulated powder may influence in the dissolution kinetics of FP. It is well known for solid oral dosage forms that increased dispersion of a low soluble drug within a soluble matrix upon blending can significantly increase the dissolution of sparingly soluble drugs. To understand this behaviour in more detail, MDRS studies of the ISM dose of Seretide and Advair were also investigated.

**Conclusion**

We have shown that the dissolution kinetics of FP are slower in Seretide than in the Advair DPI drug product.

Moreover, through the application of MDRS we have been able to link these differences to the extent of agglomeration of the FP to other components of the formulation, which may help to increase the materials dissolution kinetics.

Hence, our proposed approach of combining orthogonal analytical techniques such as MDRS and UniDose-enabled dissolution testing of DPI formulations may help to deconvolute the microstructure of the aerosolised dose, which may provide a systematic approach to quantify and compare the microstructure of DPI formulation systems. This may therefore enable the demonstration of Q3-equivalence of DPI formulations.

**References**


---

*Correspondence: Gonçalo Farias (g.farias@bath.ac.uk)