

Novel TDM strategy; Inhaled breath as an alternative matrix in TDM for inhalation medicine

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Background: Inhalation therapy is the first choice for the treatment of respiratory diseases. However, the lung deposition of inhalants is widely variable depending on the patient's respiratory function and inhalation pattern, leading to individual variability in therapeutic efficacy. Nonetheless, the clinical utility of TDM for inhalant concentration in blood samples remains controversial¹⁾. Therefore, an alternative sampling strategy for lung inhalant deposition monitoring is desired. In the present study, the photo reflection method (PRM) for detection of drug particles in inhaled breath was evaluated to assess the relationship between the particle emission signals and lung deposition profiles.

Methods: The lung deposition of the inhaled drug from Symbicort[®] Turbuhaler[®] was evaluated using a twin-stage liquid impinger (TSLI), an *in vitro* aerodynamic particle size analyzer. Four different inhalation patterns were defined based on the flow increase rate (4.9–9.8 L/s²) and peak flow rate (30 L/min and 60 L/min). The inhalation flow rate and particle emission profile were measured using an inhalation flow meter and a PRM drug release detector, respectively. The inhalation performance was characterized by output efficiency (OE, %) and stage 2 deposition of TSLI (an index of the deagglomeration efficiency, St2, %). The OE×St2 is defined as the amount delivered to the lungs.

Results: The particle emissions generated by four different inhalation patterns were completed within 0.4 seconds after the start of inhalation and were observed as sharper and larger peaks under conditions of a higher flow increase rate. The OE×St2 ranged from 4.9% to 39.7%, depending on the inhalation patterns. There were significant correlations between the OE or OE×St2 and the photo reflection signal (p<0.001).

Conclusions: Inline particle emission monitoring in inhaled breath as an alternative matrix could be a useful non-invasive real-time monitoring tool for dry powder inhalers.

Reference: 1) Hira D, et al., *J Allergy Clin Immunol Pract.* 9(12):4507 (2021).

Key Words (up to 6 max.) Dry powder inhaler; real-time monitoring; alternative matrix; non-invasive; photo reflection method

Abstract Categories: Alternative Matrices in TDM and CT