A Comparison of Aerosol Deposition Prediction by Administration in Different Phases of the Respiratory Cycle

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INTRODUCTION

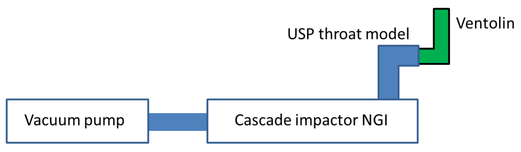
The purpose of this study was to compare performance of administration of the pMDI during different phases of the respiratory cycle to predict particle deposition in the respiratory tract.

METHODS

- In this study, a measurement of the particle size of salbutamol was performed using a pMDI (Ventolin alone, pMDI) with or without a VHC (pMDI+VHC). We tested two VHC with Ventolin: a cylindrical VHC1 (Aerochamber Plus,Trudell Medical International, London, Ontario, Canada) and an ovoid VHC2 (Itinhaler, Protec'Som Laboratory, Valognes, France).

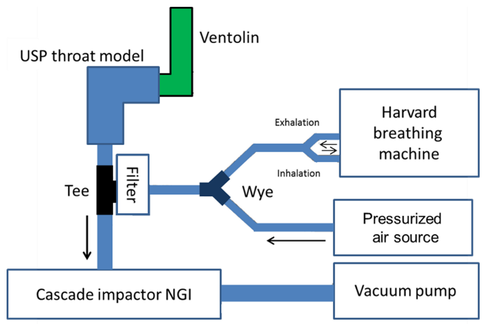
- Two methods of measurements of the particle size distribution were used.
- Prior to the experiment, pMDI was primed with 10 actuations. The VHC was connected to the NGI via the USP induction port (Copley Scientific, Nottingham, UK). The pMDI was shaken during 5 s then discharged into the throat.

First method



This method, according to the European Pharmacopoeia, used a constant flow rate (30 L/min).

Second method



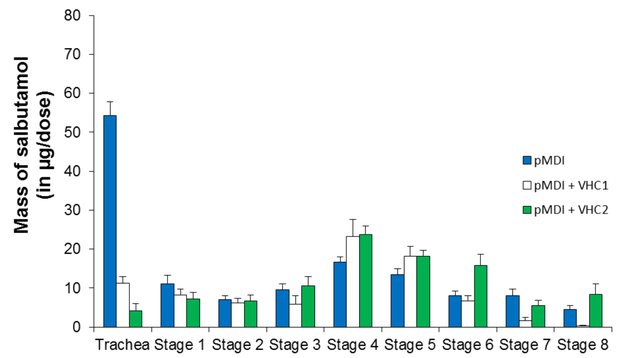
This method used a Harvard Apparatus Dual Phase Control respiratory pump (Harvard Apparatus, Les Ulis, France) modeling the respiratory cycles of a patient. This method simulated breathing with inspiratory and expiratory phases.

- The salbutamol concentration was assay by spectrophotometry at 240 nm (Lightwave II, Biochrom, UK). For each condition, the 6 replicate measures were performed.

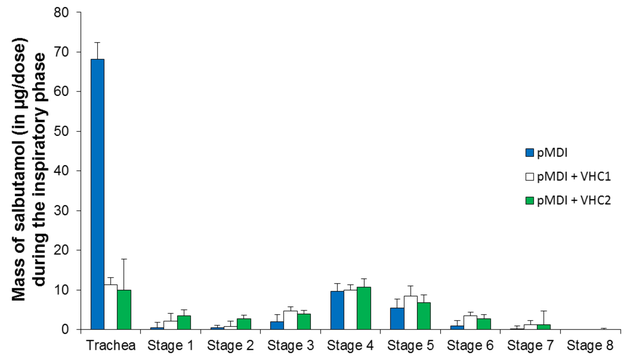
RESULTS

- Results demonstrate a lower amount of salbutamol mass deposited into the USP induction port with the method of the European Pharmacopoeia compared to the method modeling the respiratory cycles. In fact, with pMDI, 51 ± 4% of the emitted dose was deposited into the USP induction port with the European Pharmacopoeia method compared to 79 ± 3% with the method modeling the respiratory cycle during the inspiratory phase.
- In addition, with pMDI+VHC1, 12 ± 2% of the emitted dose was deposited into the USP induction with the European Pharmacopoeia method compared to 25 ± 8% with the method modeling the respiratory cycle during the inspiratory phase.
- Finally, with pMDI + VHC2, 4 ± 2% of the emitted dose was deposited into the USP induction with the European Pharmacopoeia method compared to 23 ± 4% with the method modeling the respiratory cycle during the inspiratory phase.
- Using the breath simulator method, the delivered aerosol was higher when the actuation of the canister was actuated during the inspiratory phase compared to the expiratory phase

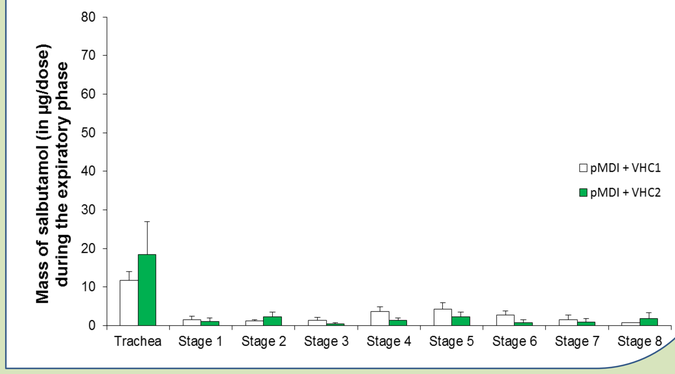
A) Mass of salbutamol (in µg per dose) deposited in the NGI in accordance with European Pharmacopoeia method.



B) Mass of salbutamol (in µg per dose) deposited in the NGI with pMDI actuation in the respiratory cycles during the inspiratory phase.



C) Mass of salbutamol (in µg per dose) deposited in the NGI with pMDI actuation in the respiratory cycles during the expiratory phase



	European Pharmacopoeia method			Method modeling the respiratory cycles (inspiratory phase)			Method modeling the respiratory cycles (expiratory phase)	
	pMDI	pMDI +VHC 1	pMDI +VHC 2	pMDI	pMDI +VHC 1	pMDI +VHC 2	pMDI +VHC 1	pMDI +VHC 2
FPD	42±10	56±6	73±11	18±4	27±7	25±2	14±3	8±2

In addition, the particle size distributions were different when the canisters were actuated during the inspiratory phase compared to the expiratory phase (Figure 2B and 2C). During the inspiratory phase, the fine particle dose was higher with pMDI + VHC1 and pMDI + VHC2 compared to the expiratory phase (Table 1). These results suggest that the timing of the actuation in the inspiratory cycle with a VHC has a high influence on the aerosol deposition in the lungs.

CONCLUSIONS

Measurements of the particle size distribution depend on the method used. The measurement method using a breath simulator allows the influence of timing of actuation in the inspiratory cycle on aerosol deposition prediction. A scintigraphic imaging study will be required to determine the most appropriate method to predict lung deposition.