Comparison of Aerosol Characteristics from Two HFA Pressurized Metered Dose Inhaler Formulations using Anti-Static Valved Holding Chambers

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Introduction

The valved holding chamber (VHC) has been developed for use with a pressurized metered dose inhaler (pMDI) to optimize aerosol delivery to respiratory patients. Conventional VHCs require washing before use to reduce the static charge build-up on the inner surface of the VHC which may reduce the dose available for inhalation. [1] The OptiChamber Diamond (Diamond; Philips Respironics) and AeroChamber Plus Z-Stat (Z-Stat; Monaghan Medical Corp., Plattsburgh, NY) VHCs are compact, anti-static VHCs designed to provide effective aerosol delivery.

The Diamond VHC is transparent, allowing the user to observe aerosol within the chamber, and can be used with either a mouthpiece or a specifically designed detachable facemask.

Standardized analysis of the data obtained from the Next Generation Impactor (NGI) is important to obtaining accurate, reproducible particle size results. Without standardized analysis it would be difficult to assess aerosol performance when comparing different devices or formulations.

This study compared the aerosol characteristics of two hydrofluoroalkane (HFA; also known as hydrofluorocarbon HFC) formulations commonly used for the treatment of asthma, albuterol sulfate HFA (salbutamol sulphate) and fluticasone propionate HFA, using a preproduction Diamond VHC and a Z-Stat VHC. The test was performed using an NGI and CITDAS V3.10 to generate the aerosol characteristics data.

Method

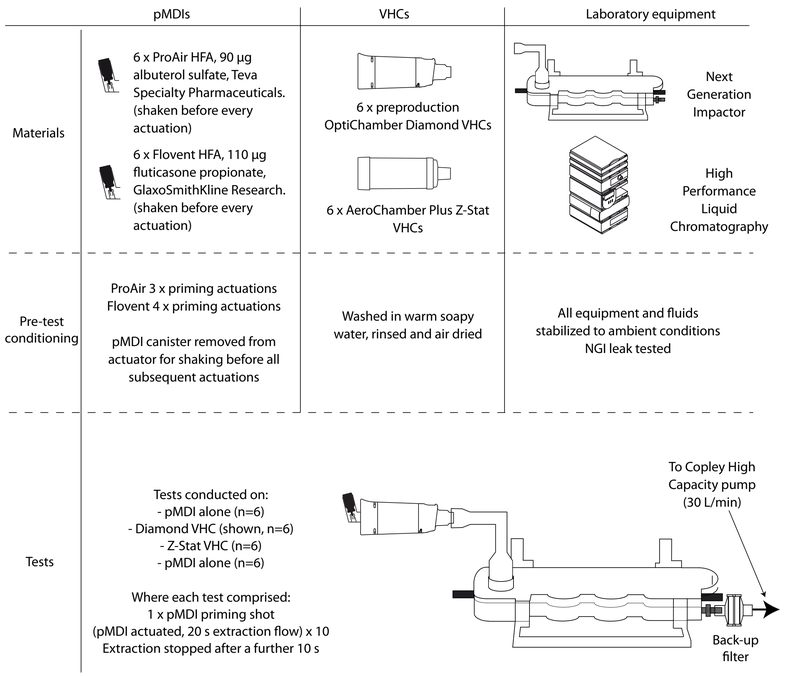

Figure 1. Experimental test method

After each test, the induction port, back-up filter, NGI cups and VHCs were processed using 10% Acetonitrile solution for tests with albuterol sulfate pMDIs and HPLC assay diluent for the tests with fluticasone propionate pMDIs. CITDAS V3.10 was used to generate the aerosol characteristics data. The mean Emitted Dose (drug entering NGI), Fine Particle Dose (amount of drug in NGI ≤ 4.7 µm), Fine Particle Fraction (percentage of emitted dose in particles ≤ 4.7 µm), and Mass Median Aerodynamic Diameter (MMAD) were calculated. The equipment was washed and dried after each drug/VHC test.

Results

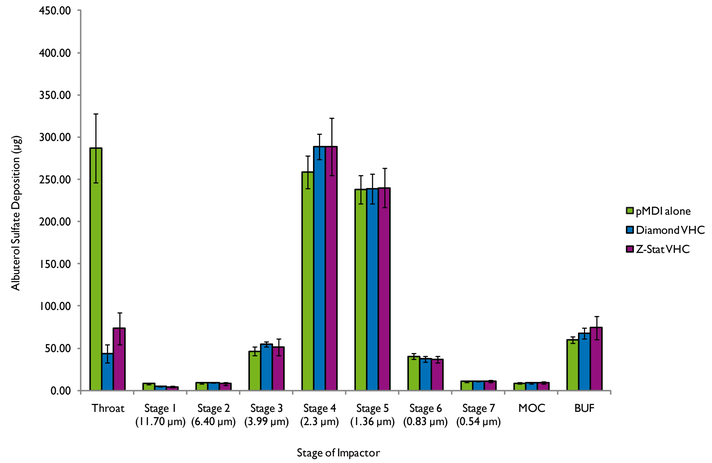

Figure 2. The deposition of albuterol sulfate in the different stages of the test set up and NGI stages including the micro-orifice collector (MOC) and back-up filter (BUF). Error bars represent standard deviation about the mean (n=12 for pMDI alone, n=6 for VHCs).

Figure 2 shows that the particle size distributions of albuterol sulfate from the three devices were generally similar, but the amount of albuterol sulfate aerosol deposited in the throat of the impactor was much greater for pMDI alone compared with the two VHCs.

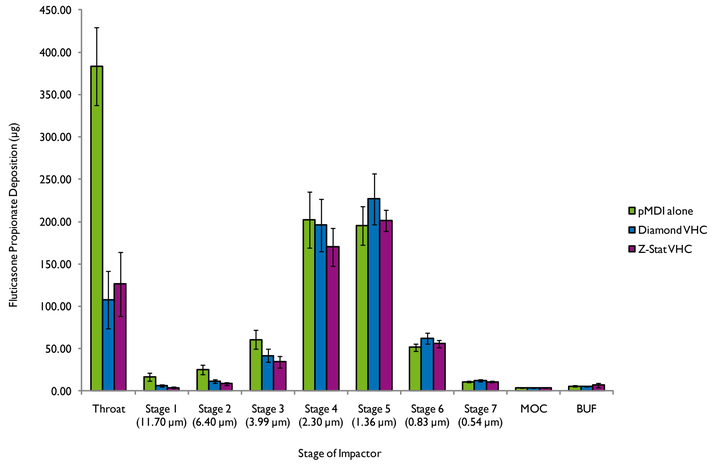

Figure 3. Deposition of fluticasone propionate in the different stages of the test set up and NGI stages including the micro-orifice collector (MOC) and back-up filter (BUF). Error bars represent standard deviation about the mean (n=12 for pMDI alone, n=6 for VHCs).

Figure 3 shows that the particle size distributions of fluticasone propionate from the three devices were also generally similar, but from the pMDI alone resulted in a very high deposition of drug in the throat of the impactor. Comparison of Figures 2 and 3 shows that the distribution of particles within the impactor was similar for the two drug formulations, but the amount of albuterol sulfate that was deposited on the back-up filter was proportionally larger than the proportion of fluticasone propionate deposited on the back-up filter.

Table 1. Aerosol characteristics of each drug with the pMDI alone, Diamond VHC, and Z-Stat VHC. Data presented as test means with standard deviations (SD).

	Emitted Dose (µg)		Fine Particle Fraction (%)		Fine Particle Dose (µg)	
Drug	Albuterol sulfate	Fluticasone propionate	Albuterol sulfate	Fluticasone propionate	Albuterol sulfate	Fluticasone propionate
pMDI alone	90.68 (1.28)	94.92 (6.80)	63.73 (4.22)	51.47 (4.47)	57.80 (4.04)	48.92 (6.12)
Diamond VHC	69.70 (3.80)	66.78 (6.83)	87.80 (1.49)	77.61 (4.93)	61.20 (3.68)	51.95 (7.12)
Z-Stat VHC	72.27 (5.29)	61.54 (2.14)	84.43 (2.68)	74.36 (5.23)	61.11(6.20)	45.77 (3.75)

The aerosol characteristics are presented in Table 1 and show that the fine particle dose for the aerosol from the pMDI alone was similar to that from the VHCs despite the differences in emitted dose and fine particle fraction.

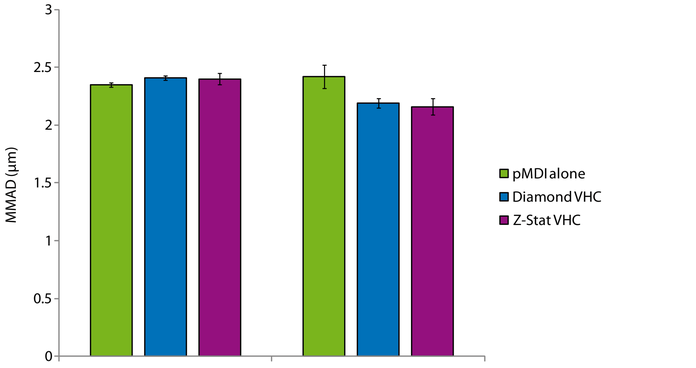

Figure 4. The MMAD of albuterol sulfate and fluticasone propionate from pMDI alone, Diamond and Z-Stat VHCs. Error bars represent standard deviation about the mean (n=12 for pMDI alone, n=6 for VHCs).

The MMAD for fluticasone propionate was higher for pMDI alone compared with VHCs.

Conclusions

- The MMAD of aerosol from the VHCs for suspension based fluticasone propionate were lower than from pMDI alone.
- The use of an anti-static VHC compared with pMDI alone had less of an effect upon the MMAD from a solution based albuterol sulfate formulation than from a suspension based fluticasone propionate formulation.
- The aerosol characteristics and particle size distributions from the two VHCs were similar.

References

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