

DRUG DELIVERY PERFORMANCE OF A DISPOSABLE PAPERBOARD HOLDING CHAMBER VERSUS TWO PLASTIC HOLDING CHAMBERS

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Introduction

Valved holding chambers (VHCs) assist many patients with the coordination of pressurized metered-dose inhaler (pMDI) medication delivery. However, when an MDI is actuated into a holding chamber, some fraction of the drug output deposits inside the device, which reduces the dose of drug delivered to the patient, and can change the particle size distribution. Some of this drug loss through plastic holding chambers can be attributed to static attraction between drug particles and the chamber walls. In this study, the MDI drug output and particle size distribution characteristics of three VHCs were compared. The three VHCs evaluated included one collapsible, disposable VHC made from non-static paperboard (LiteAire, Thayer Medical), and two VHCs made from rigid polymer (AeroChamber Plus, Monaghan Medical; and OptiChamber Advantage, Respironics).

Materials and Methods

250 µg/dose fluticasone propionate (Flixotide, GlaxoSmithKline) was used as the test MDI drug throughout this study. For particle size distribution analysis, one of each of the three VHCs (as shown in Figure 1) was attached to an Andersen cascade impactor using a 28.3 L/min vacuum. Each VHC received seven actuations of Flixotide. Drug collected on the impactor plates was eluted with 9 mL of dimethyl sulfoxide, and the resulting solutions read via UV/Vis spectroscopy at 260 nm.

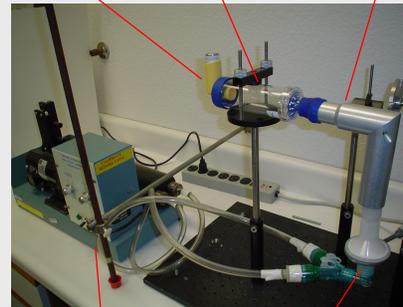


Figure 1. AeroChamber Plus, LiteAire, OptiChamber Advantage

Materials and Methods (continued)

For the drug output analysis, five of each of the VHCs (n=5) were evaluated. The testing apparatus (shown in Figure 2) consisted of a USP throat model connected to a ventilator (Harvard Apparatus) simulating tidal breathing of 750 mL at 12 breaths/min and 1:1 I:E. Each VHC received three MDI actuations, each at the beginning of an inhalation. Drug was collected on a filter downstream of the throat model, was eluted with 9 mL of dimethyl sulfoxide, and was read at 260 nm.

Metered Dose Inhaler Holding Chamber USP throat model



Breathing simulator Drug collection filter

Figure 2. Drug output testing apparatus

Results

The results are summarized in Table 1. The fluticasone propionate particle size distributions from the three VHCs (shown graphically in Figure 3) were similar, both in terms of MMAD and respirable output fraction. In terms of drug output per actuation (shown graphically in Figure 4), the output of the LiteAire ($108 \pm 9 \mu\text{g}$, 43% of 250 µg/actuation canister output) was significantly higher than the outputs of both the AeroChamber Plus ($83 \pm 18 \mu\text{g}$, 33% of canister output) and the OptiChamber ($65 \pm 19 \mu\text{g}$, 26% of canister output).

Results (continued)

Holding Chamber Comparisons	LiteAire	AeroChamber Plus	OptiChamber
Cost (\$ Aus)	\$4.50	\$20 - \$50*	\$20 - \$50*
Chamber volume (mL)	160	150	218
Mass Median Aerodynamic Diameter (MMAD) (µm)	2.9	3.0	3.2
% of drug mass in respirable range (MMAD < 4.7 µm)	85%	83%	72%
Drug mass delivered per actuation (µg)	$108 \pm 9^{\#}$	83 ± 18	65 ± 19
% of 250 µg/actuation canister output delivered by device	43% [#]	33%	26%

*Unit price from Niche Medical

†Retail price range in Australian pharmacies for AeroChamber Plus, estimate for OptiChamber

‡Significantly higher than the other two VHCs tested; p < 0.05

Table 1. Results Summary

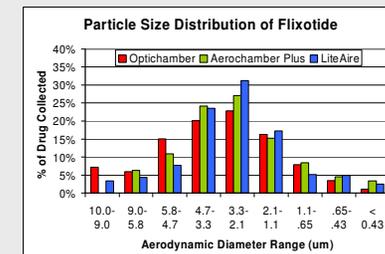


Figure 3. Particle size distributions of fluticasone propionate (Flixotide)

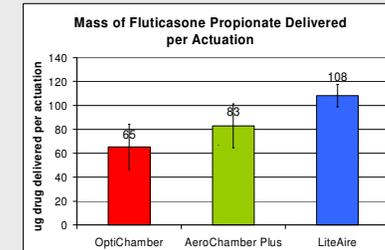


Figure 4. Mass of fluticasone propionate delivered per MDI actuation (250 µg/dose from canister alone)

Conclusions

Under the conditions tested, the paperboard LiteAire provided drug delivery performance that was statistically superior to the rigid plastic VHCs evaluated. Based on these results, the LiteAire appears to offer an effective, lower-cost alternative to plastic holding chambers, particularly for single-patient, single-use applications.