Performance Comparison of Copley and Andersen 8-Stage Cascade Impactors

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Introduction

The Andersen MARK II cascade impactor is the commonly accepted standard for characterizing size distributions of aerosol products and is listed as Apparati 1 and 3 in the *US Pharmacopoeia 25* for testing MDI and DPI products, respectively. The Mark II version of the Andersen impactor was introduced in 1977 and consists of eight multi-jet stages and a filter, vertically stacked, designed for use at a flow rate of 28.3 L/min. Several published reports have characterized the performance of the Mark II impactor. These include studies by Mitchel *et al*[1] and Vaughn[2] detailing impactor calibration and wall loss studies and reports from Stein[3,4] showing variability in results between impactors with various MDI products. This study compares Andersen-type impactors produced by both Copley Scientific Ltd., Nottingham, UK, and ThermoAndersen (formerly Graseby-Andersen), Smyrna, GA. The cascade impactors used in this study were visually inspected by microscope to compare jet characteristics for impactors of both manufacturers. Many of the jets from ThermoAndersen impactors show a small ridge of metal at the orifice exit remaining from the machining process in addition to nonsymmetrical shapes. No significant machining or orifice shape issues were observed for the Copley impactors. In addition to microscopic evaluation, impactor performance was also evaluated by testing several inhalation products using impactors from both manufacturers.

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Materials

Microscopic evaluation of both impactors was performed using an Olympus BX51 microscope (Olympus America Inc., Melville, NY) using either a 4X or 10X magnification. Photographs obtained for each jet were taken using an Olympus DP11-N digital camera (Olympus America Inc., Melville, NY) mounted above the focusing lens of the microscope.

Particle size measurements were performed in a controlled temperature and humidity environment using typical operational parameters as outlined in the *US Pharmacopoeia* for metered-dose inhalers. Three MDI products, QVAR® (40 μg), Ventolin® (90 μg) and Proventil® HFA (108 μg), were tested in order to evaluate a range of MMAD values and formulations. Each MDI unit was actuated into one Copley and one ThermoAndersen impactor to reduce the impact of can-to-can variation. Each inhaler was appropriately primed prior to testing. After introducing an appropriate number of actuations into the impactor, deposited drug mass was recovered from the impactor components and the resulting samples assayed by HPLC. Multiple experiments were performed (n=5) for each impactor using each product. During data analysis, any replicate having a recovered drug mass for significant stages exceeding the critical value of Dixon's Q test[5] at the 95% confidence level were rejected in an effort to reduce variability introduced from factors not related to impactor performance.

Results and Discussion

Based on the microscopic evaluation of the Copley and Andersen impactors, some very noticeable differences are observed. Jet entrances on the ThermoAndersen instruments are not tapered for the lower stages (only jets for Stages 0 and 1) and many jets show some metal protruding slightly into the airstream at the jet exit. In some cases the protruding metal appears to be the result of use, while in the majority of cases it is the result of the machining process. These physical characteristics may have several consequences. First, the abrupt change in the airstream for Stages 2-7 that do not have a tapered entrance to the jet leads to deposition of particles whose inertia is too large to complete the trajectory change into the jet. This phenomenon has been observed in our lab and reported elsewhere[2]. Second, the metal ledge observed at the orifice exit could act as an impaction surface, increasing loss of particles to the stage. In addition, it is possible that there may be some disruption of the air flow through the jet. These factors would likely contribute to some reduction in the efficiency of the stage.

All jet entrances on the Copley instrument have a taper that would likely reduce material losses at the entrance of the jet. The obstructions at the orifice exit were not observed for the Copley impactors.

To evaluate the effect of these microscopic observations on the size distributions obtained for an aerosol, ThermoAndersen impactors were assembled from stages with similar stage areas as the Copley impactors used in this study. A comparison of these impactors based on d_{50} values computed from the average jet diameter (as reported from measurements made by the manufacturer) is given in Table 1. Based on these d_{50} values, similar size distributions would be expected between all impactors.

Table 1:Calculated d_{50} Values for ThermoAndersen and Copley Aluminum Impactors

	Calculated d_{50} (μm)							
	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	Stage 6	Stage 7
Copley Impactor SN 3372	9.03	5.87	4.69	3.27	2.07	1.11	0.68	0.40
Copley Impactor SN 3373	9.03	5.85	4.69	3.27	2.06	1.11	0.69	0.40
Copley Impactor SN 3374	9.03	5.85	4.69	3.27	2.07	1.11	0.68	0.40
Andersen Impactor Composite A	9.03	5.88	4.69	3.27	2.06	1.11	0.68	0.40
Andersen Impactor Composite B	9.03	5.86	4.69	3.27	2.06	1.10	0.69	0.40
Andersen Impactor Composite C	9.03	5.88	4.68	3.27	2.06	1.10	0.67	0.40

Results for QVAR® show nearly indistinguishable distributions between all Copley impactors (Figure 1). This result is not surprising due to the nearly identical d_{50} values for each stage. Particle size distribution results for Ventolin® using these same impactors show some differences between impactors, probably due to greater can-to-can variation as the result of the suspension formulation with this product than to the impactors used.

The ThermoAndersen impactors show a much greater variation in particle size results for QVAR® (Figure 2) than observed for the Copley impactors. Some variation in particle size distribution may be expected due to some difference in d_{50} values, especially for stages 5 and 6 (Table 1). However, comparison of results between the Copley and ThermoAndersen impactor for the same MDI unit (Figures 3 and 4), show some anomalies in mass deposition that are not accounted for by stage area values or can variation. These differences will be discussed later. Particle size results from Ventolin® using ThermoAndersen impactors show variation similar to that observed with the Copley impactors, again probably the result of the suspension formulation. This variation between cans masks any significant differences between each manufacturer's impactors that might be present.

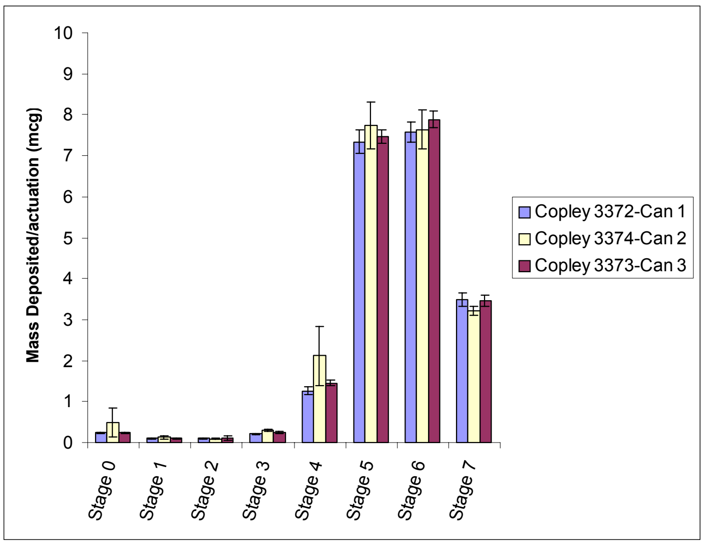

Figure 1: Size distribution obtained for QVAR using Copley impactors.

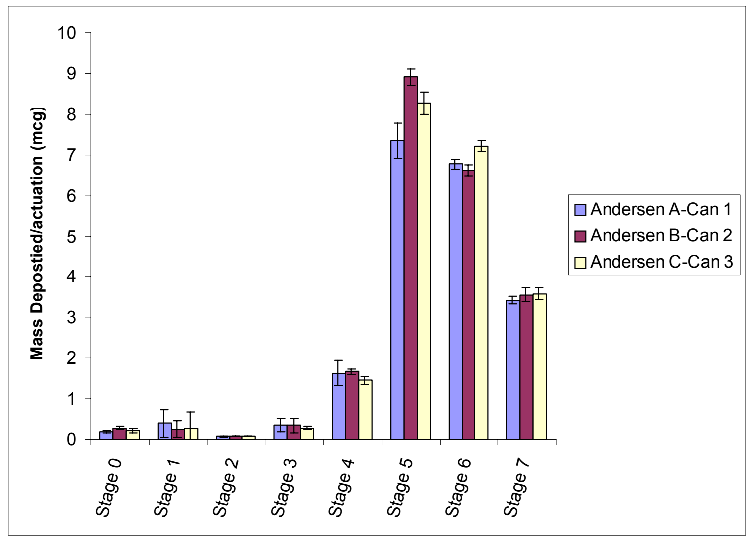

Figure 2: Size distribution obtained for QVAR using ThermoAndersen impactors.

Comparison of results for Copley and ThermoAndersen impactor used to test single MDI canisters of QVAR® show differences in mass deposition below stages 5 and 6 in several cases. For example, Figure 3 shows a larger mass of drug below stage 6 for the Copley impactor than collected for the ThermoAndersen impactor. Since both of these impactors had nearly identical d_{50} values for the lower stages (Table 1), it is possible that this anomaly is due to the loss of mass to the metal obstructions at the jet exit for the ThermoAndersen impactor. While metal protrusions are observed for many stages of the ThermoAndersen impactors, their effect on mass deposition for upper stages may be imperceptible since much less mass is collected below these stages and the overall change in jet orifice (as a percentage of jet area) is much smaller. Another anomaly between mass deposition with the Copley and ThermoAndersen impactors for the lower stages is observed in Figure 4. In this example, the differences in deposition between stages 5 and 6 may be explained by comparing the differences in the stage d_{50} values.

The larger mass deposited below stage 5 of the ThermoAndersen impactor may be the result of the smaller d_{50} value for this stage and result in a lower mass below stage 6 (which is observed). By similar analogy, mass deposition below stage 7 of the ThermoAndersen impactor would also be expected to be smaller. However, this is not observed, perhaps the result of greater variability in the actual aerodynamic particle size in the fine aerosol present.

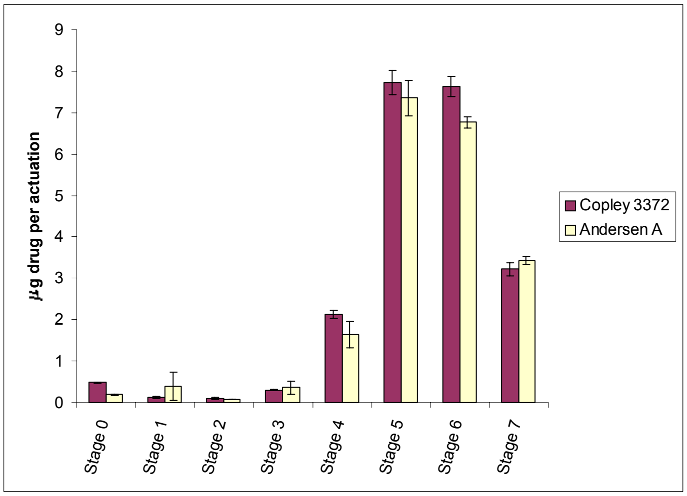

Figure 3: Comparison of Size Distribution Data Obtained for Copley and ThermoAndersen Impactor using QVAR MDI 1.

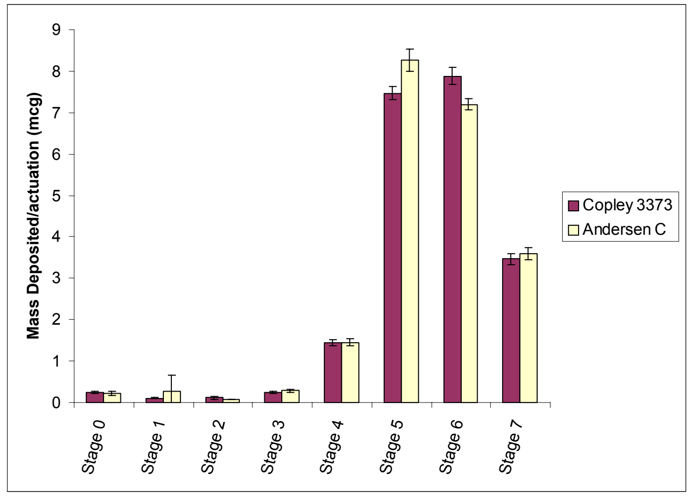

Figure 4: Comparison of Size Distribution Data Obtained for Copley and ThermoAndersen Impactor using QVAR MDI 3.

Evaluation of material losses to the stage jets for the ThermoAndersen and Copley instruments shows no significant difference in material losses for any of the products to the stages between both instruments. While every effort was made to carefully extract material from the stages, the small jet sizes for the lower stages likely reduce the efficiency of removing material from the interior of the jet. Further investigation as to material losses to the stages will be necessary.

Conclusion

Physical differences between ThermoAndersen and Copley impactors are readily observed as the Copley impactors have stage jets that are more uniform in shape and free of obstruction. The imperfections observed with the ThermoAndersen impactors appear to manifest in anomalies in the masses deposited in the lower stages as compared to the Copley instrument with nearly identical stage areas and d_{50} values. However, any differences are small and will likely be obscured when combined with variance from the product and range of stage areas obtained from multiple impactors.

References

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