Effect of Design on the Performance of a Dry Powder Inhaler Using Computational Fluid Dynamics. Part 2: Air Inlet Size

MATTHEW S. COATES,1,2 HAK-KIM CHAN,2 DAVID F. FLETCHER,1 JUDY A. RAPER1,3
1Department of Chemical Engineering, University of Sydney, Sydney, NSW 2006, Australia
2Faculty of Pharmacy, University of Sydney, Sydney, NSW 2006, Australia
3Department of Chemical Engineering, University of Missouri-Rolla, Rolla, Missouri

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ABSTRACT: This study investigates the effect of air inlet size on (i) the flowfield generated in a dry powder inhaler, and (ii) the device-specific resistance, and the subsequent effect on powder deagglomeration. Computational fluid dynamics (CFD) analysis was used to simulate the flowfield generated in an Aerolizer with different air inlet sizes at 30, 45, and 60 l/min. Dispersion performance of the modified inhalers was measured using mannitol powder and a multistage liquid impinger at the same flow rates. The air inlet size had a varying effect on powder dispersion depending on the flow rate. At low flow rates (30 and 45 l/min), reducing the air inlet size increased the inhaler dispersion performance by increasing the flow turbulence and particle impaction velocities above their critical levels for maximal powder dispersion. At 60 l/min, reducing the air inlet size reduced the inhaler dispersion performance by releasing a large amount of powder from the device before the turbulence levels and particle impaction velocities could be fully developed. The results demonstrate that the maximal inhaler dispersion performance can be predicted if details of the device flowfield are known.

INTRODUCTION

In recent years there has been a rapidly growing interest in the pharmaceutical industry to develop dry powder aerosol systems capable of producing respirable particles of defined characteristics. The performance of such aerosol delivery systems is dependent on the combination of the powder formulation and delivery device utilized.1–5 Studying the effect of design on the overall performance of a dry powder inhaler, we have shown that the structure of the inhaler grid significantly affects the amount of powder retained in the device (by controlling the degree of particle contact with the internal walls of the mouthpiece) without affecting the inhaler dispersion performance.6 The size of the inhaler air inlet controls the velocity of air entering the device, which influences both the levels of turbulence generated in the device and the intensity of particle collisions with the device walls. Coupling computational fluid dynamics (CFD) with experimental powder dispersion analysis, we have recently provided an initial quantification of the turbulence levels and average particle impaction velocities that maximized the dispersion performance of a dry powder inhaler.7 Studying the mechanisms of powder deagglomeration, Voss and Finlay8 showed that turbulence plays a significant, although not necessarily the...
dominant, role on fine particle dispersion, whereas mechanical impaction of the powder on a grid is not an effective break-up mechanism. The inhaler air inlet size also affects the specific resistance of the device, which controls the maximum attainable flow rate (PIFR), as well as the rate at which flow is developed in the device (FIR). Although numerous studies have examined the influence of inhalation characteristics on the performance of dry powder inhalers, those examining the interaction of powder during flow development are limited.

The aim of this study is to determine the effect the air inlet size has on the flowfield generated in a dry powder inhaler and how the flowfield variations affect the performance of the modified device. This extends the knowledge of which features of the device design significantly contribute to the overall inhaler performance and provides a better understanding of how the generated levels of turbulence and particle impaction velocities affect powder deagglomeration. Additionally, the effect of specific device resistance on the inhaler flow development rate, and the subsequent effect this has on the inhaler dispersion performance are discussed.

METHODS

CFD analysis, using ANSYS CFX5.7.1, was performed in conjunction with experimental powder dispersion analysis to determine how the performance of an Aerolizer® (Plastiape S.p.A., Osnago, Italy) varied when small modifications were made to the size of the inhaler air inlets. The original Aerolizer® design was studied along with designs containing air inlets of two-thirds and one-third the original area (Fig. 1). For each case, simple geometry changes were made to the original air inlet to obtain the modified design (performed by Plastiape S.p.A.). CFD analysis was performed to determine the flowfield generated in the devices at flow rates of 30, 45, and 60 l/min. The performance of the inhalers was determined experimentally using a multi-stage liquid impinger at the same flow rates (see Dispersion Methodology).

Values of the device resistance, determined from the computational results, increased from 0.072 (cmH2O)½/(l/min) for the full inlet case to 0.100 and 0.148 (cmH2O)½/(l/min) for the two-thirds and one-third inlet cases, respectively. Therefore, each test flow rate studied is realistically attainable at a maximum inspiratory effort of 80 cmH2O. Although performing the study at a series of constant flow rates has the limitation of not maintaining a constant device pressure drop at each flow, it allows the effects of flow rate to be studied.

The Aerolizer® dry powder inhaler (Plastiape S.p.A) was examined in this study as it is a readily available commercial device. To operate the Aerolizer®, the inhaler is twisted open and a drug filled capsule (size three) is placed into the device. The inhaler is then closed and the capsule pierced using a four-pin piercing mechanism. Upon inhalation, the air flow entering the inhaler through the tangential air inlets acts to rotate the capsule at high speed ejecting the drug powder into the surrounding flowfield. The deagglomerating forces provided by the device flowfield disperse the drug agglomerates to produce a fine respirable aerosol cloud. The inhaler also contains a grid, positioned at the bottom of the mouthpiece, primarily included to prevent the capsule from exiting the device.

Computational Methodology

The flowfield generated in the Aerolizer® with different air inlet sizes was obtained by solving the Reynolds Averaged Navier Stokes equations together with the Shear Stress Transport (SST) turbulence model and automatic wall functions using the commercial CFD code ANSYS CFX 5.7.1 as described in Coates et al. To benefit from the ability of the SST model to solve the turbulence equations all the way to the wall in a complex geometry requires fine computational meshes (to ensure that the near wall node is always positioned at y-plus <5). The computational mesh used throughout this study was sufficiently fine that the near wall node was always positioned at this lower limit of y-plus.

A steady-state simulation was run to solve the device flowfield using a typical timestep of between 0.0001 and 0.0005 s. The angular velocity of the capsule at each flow rate, required to model the
motion of the rotating capsule, was determined using high-speed photography. Due to the difficulty in modeling the irregular motion of the spinning capsule, a simplified model using a fixed axis of rotation and constant angular velocity was employed. The same numerical studies as reported in Coates et al. were performed to ensure that the flow turbulence properties obtained in this analysis were independent of the computational mesh chosen.

Lagrangian particle tracking was performed as a post-processing operation, in which the fate of 1000 and 5000 particles with a density of 1520 kg/m$^3$ and particle diameter of 3.2 mm (mono-disperse) were tracked through the fluid after release from the capsule and subjected to drag and turbulent dispersion forces. Due to the dilute nature of the system, one-way coupling between the solid and fluid phases was assumed and currently no particle deagglomeration was modeled. Modifications to the computational code were made to provide the speed of all particle collisions with the lower region of the device (as indicated in Fig. 2).

Validation of the CFD models used throughout this study, performed using laser doppler velocimetry (LDV) techniques by comparing the mouth-piece exit velocities obtained from the computational models with experimental data, showed that good agreement was observed between the computational and experimental results over a range of flow rates and device designs. Due to the complexity of the inhaler geometry, no experimental validation of the levels of turbulence generated in the device or the interaction of particles with individual turbulent eddies has currently been performed. Therefore, the CFD results presented in this study are intended to illustrate significant trends in the properties of the device flowfield rather than for quantitative analysis.

![CFX](image)

**Figure 2.** Schematic of the lower region of the Asthmeqer used when determining the average impaction velocity of particle collisions.

**Dispersion Methodology**

The dispersion performance of the inhalers was determined using a spray-dried mannitol powder (particle size $d_{50} = 3.2$ μm, span $([d_{90} - d_{10}]/d_{50}) = 1.3$) and a four-stage (plus filter) liquid impinger (Copley, Nottinghamshire, UK), as described by Coates et al. For each dispersion, the impinger was run at the test flow rate for a total of 4 s using a timed valve. The runs were performed in triplicate to obtain mean values. Throughout the dispersion analysis, the temperature and relative humidity of the laboratory were maintained at 21 ± 2°C and 45 ± 5%, respectively. Mannitol was assayed by high performance liquid chromatography (HPLC) (Waters, Milford, MA) using refractive index detection (Waters 410 differential refractometer). Centrifuged samples (100 μL) were injected into a C18 radial-pak column with de-ionized water as the mobile phase running at a flow rate of 1 mL/min for 10 min. A calibration curve was constructed using standard solutions of mannitol, which allowed the mass of powder deposited on each stage of the impinger and the fine particle fraction to be determined.

In this study, the fine particle fraction was defined as the mass fraction of particles smaller than 5 μm, referenced against either the total mass of powder loaded into ($\text{FPF}_{\text{Loaded}}$), or the total mass of powder emitted from ($\text{FPF}_{\text{Em}}$), the device. As the cut-off at each impinger stage varies with flow rate, interpolation of the cumulative undersize plot was used to determine the fine particle fraction. Values of the stage cut-off diameter were approximated as being inversely proportional to the square root of the air flow rate. The percentage recovery throughout the dispersion analysis was 100 ± 5%. Analysis of variance (ANOVA) tests followed by pairwise $t$-tests were carried out with a probability of less than 0.05 considered statistically significant (Minitab 13).

**RESULTS**

**Aerosol Characterization Results**

The experimental dispersions showed that at 30 l/min, reducing the air inlet size increased the performance of the inhaler (Fig. 3a and b). The $\text{FPF}_{\text{Loaded}}$ and $\text{FPF}_{\text{Em}}$ were increased from 15.0% and 40.1% for the full inlet size to 38.9% and 52.7% one-third air inlet size, respectively. Statistically significant differences in the $\text{FPF}_{\text{Loaded}}$
When the flow rate was increased to 60 l/min, reducing the size of the air inlet actually reduced the inhaler performance (Fig. 3a and b). The \( FPF_{\text{Loaded}} \) and \( FPF_{\text{Em}} \) reduced from 44.7% and 56.0% for the full inlet size to 36.2% and 49.1% one-third air inlet size, respectively. Statistically significant differences in the \( FPF_{\text{Loaded}} \) (\( p = 0.025 \)) and \( FPF_{\text{Em}} \) (\( p = 0.006 \)) were observed between each inlet case, except for the \( FPF_{\text{Em}} \) between the full and two-thirds inlet sizes (\( p = 0.122 \)) and the \( FPF_{\text{Loaded}} \) between the two-thirds and one-third inlet sizes (\( p = 0.087 \)).

A significant reduction in capsule retention was observed as the air inlet size was reduced at 30 l/min (Fig. 4a). For the full inlet, 46.6% of the loaded powder was retained in the capsule, reducing to 10.5% and 6.8% for the two-third and one-third inlet sizes, respectively. At 45 l/min, capsule retention reduced from 9.4% for the full inlet to

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**Figure 3.** (a) %FPF loaded from the dispersion results indicating that the size of the air inlet has a varying effect on the overall inhaler performance at different flow rates. (b) %FPF emitted from dispersion results indicating that the size of the air inlet has a varying effect on the inhaler dispersion performance at different flow rates (*denotes a statistically significant difference between the indicated and following result).
5.3% and 4.7% for the two-third and one-third inlet sizes, respectively. No trend in the capsule retention was observed at 60 l/min. A slight increasing trend in throat retention was observed at 30 l/min, but no trend was observed at 45 and 60 l/min (Fig. 4b).

**CFD Results**

Figure 5 shows that higher velocities were generated in the inhaler base as the air inlet size was reduced, which increased the overall turbulence levels and integral scale strain rates (ISSR) in the device (Tab. 1). In contrast, a similar flowfield was generated in the inhaler mouthpiece for all inlet cases (Fig. 5), with no trend in the inhaler exit velocity occurring (Tab. 1). As expected, the size of the air inlet had a significant effect on the device pressure drop, which increased by a factor of 4.2 at each flow rate as the air inlet size was reduced to one-third the original size (Tab. 1).

At each flow rate, reducing the size of the air inlet increased the velocity of particle impactions with the lower region of the device (Tab. 2). No significant difference in the impaction velocities was observed for simulation of 1000 and 5000 particles, demonstrating that the models had captured impaction velocities independent of the number of particles simulated.

**DISCUSSION**

This study showed that the size of the air inlet had a varying effect on the inhaler performance at different flow rates. Reducing the air inlet size increased the inhaler performance at 30 l/min, had a less significant effect at 45 l/min and reduced the inhaler performance at 60 l/min. At each flow rate, the smaller inlet size generated greater ISSR (Tab. 1) and increased the intensity of particle impactions with the lower region of the device (Tab. 2). This enhanced the deagglomeration potential of the device flowfield, hence an improved inhaler performance was expected for the reduced inlet sizes.

Coates et al.⁷ have previously reported that increasing (i) the ISSR generated in the lower region of the Aerolizer® and (ii) the velocity of particle impactions with the lower region of the device, initially improved dispersion up to a critical level where the inhaler dispersion performance was maximized. The turbulence kinetic energy is a measure of the absolute turbulence level generated in the device, whereas the integral scale strain rate (defined as the turbulence eddy dissipation rate divided by the turbulence kinetic energy) is a measure of the velocity gradient across the integral scale eddies (the most energetic

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**Figure 5.** Velocity profiles at 60 l/min indicating that the air inlet size had (1) a significant effect on the flowfield generated in the inhaler base and (2) little effect on the flowfield generated in the inhaler mouthpiece. Similar trends in the device flowfield were observed at 30 and 45 l/min (data not shown).
occurring in a turbulent flow\textsuperscript{19}) and is hence a more appropriate parameter to study agglomerate break-up. It was found that an ISSR distribution with an average value of 5400/s together with an average particle impaction velocity of 14.6 m/s produced the maximum Aerolizer\textsuperscript{1} dispersion performance with the mannitol powder. These values were obtained by analyzing the device flowfield (using the CFD model) at the flow rate where the dispersion performance of the Aerolizer\textsuperscript{1}, determined experimentally, was maximized. Further increases in the ISSR and impaction velocities above the critical level did not improve dispersion. Therefore, a comparison of the inhaler base ISSR distributions and lower region particle impaction velocities for the different inlet cases with those at the critical level was used to explain the varying effect of air inlet size on dispersion.

At 30 l/min, the ISSR distribution for the two-thirds inlet size was similar to that of the critical level, whereas the ISSR distributions for the full and one-third inlet sizes were positioned to the left and right of the critical distribution, respectively (Fig. 6a). Additionally, the lower region impaction velocity for the two-thirds inlet size was comparable in magnitude with that at the critical level (14.6 m/s), whereas the impaction velocities for the full and one-third inlet sizes were smaller and larger than the critical velocity, respectively (Tab. 2). This demonstrates that the critical ISSR and particle impaction velocities required to maximize the inhaler dispersion performance had been generated in the device for the two-thirds and one-third inlet cases, but not for the full inlet case. This is reflected in the $FPF_{\text{Em}}$ results that showed a low performance for the full inlet size, a significant performance increase between the full and two-thirds inlet sizes, and no performance difference between the two-thirds and one-third inlet sizes (Fig. 3b). Hence the dispersion performance of the Aerolizer\textsuperscript{1} correlates with the critical ISSR distribution and particle impaction velocities, showing that the maximal inhaler dispersion performance can be predicted if details of the device flowfield are known. The same trend in the $FPF_{\text{Em}}$ values was not observed due to the significant difference in the amount of capsule retention between the three inlet cases.

Similarly, at a flow rate of 45 l/min, the critical ISSR (Fig. 6b) and particle impaction velocities (Tab. 2) required to maximize the inhaler dispersion performance had been generated in the device for the two-thirds and one-third inlet cases, but not for the full inlet case, explaining the trend in the $FPF_{\text{Em}}$ at this flow rate. A smaller difference in the $FPF_{\text{Em}}$ was observed between the full and two-thirds inlet cases at 45 l/min as the ISSR

### Table 1. Properties of the Device Flowfield for the Different Inlet Sizes at Each Test Flow Rate

<table>
<thead>
<tr>
<th></th>
<th>30 l/min</th>
<th></th>
<th>45 l/min</th>
<th></th>
<th>60 l/min</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Full</td>
<td>$\frac{2}{3}$</td>
<td>$\frac{1}{3}$</td>
<td>Full</td>
<td>$\frac{2}{3}$</td>
<td>$\frac{1}{3}$</td>
</tr>
<tr>
<td>Velocity\textsuperscript{a} (m/s)</td>
<td>6.9</td>
<td>8.6</td>
<td>11.5</td>
<td>10.4</td>
<td>13.2</td>
<td>17.4</td>
</tr>
<tr>
<td>Turbulence Kinetic Energy\textsuperscript{a} (J/kg)</td>
<td>0.81</td>
<td>1.45</td>
<td>3.9</td>
<td>2.6</td>
<td>5.2</td>
<td>11.6</td>
</tr>
<tr>
<td>Integral Scale Strain Rates\textsuperscript{a} (per s)</td>
<td>3360</td>
<td>4010</td>
<td>4870</td>
<td>4230</td>
<td>5230</td>
<td>6440</td>
</tr>
<tr>
<td>Mouthpiece Exit Velocity\textsuperscript{a} (m/s)</td>
<td>5.7</td>
<td>5.7</td>
<td>5.7</td>
<td>8.7</td>
<td>8.8</td>
<td>8.5</td>
</tr>
<tr>
<td>Device Pressure Drop (Pa)</td>
<td>440</td>
<td>790</td>
<td>1840</td>
<td>1020</td>
<td>1970</td>
<td>4240</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Volume averaged throughout the whole device.

\textsuperscript{b}Area averaged across the inhaler exit plane.

### Table 2. Average Impact Velocity of Particles Collisions with the Lower Region of the Aerolizer\textsuperscript{1} when the Computational Model Was Used to Simulate the Dispersion of 1000 and 5000 Drug Particles

<table>
<thead>
<tr>
<th></th>
<th>30 l/min</th>
<th></th>
<th>45 l/min</th>
<th></th>
<th>60 l/min</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Full</td>
<td>$\frac{2}{3}$</td>
<td>$\frac{1}{3}$</td>
<td>Full</td>
<td>$\frac{2}{3}$</td>
<td>$\frac{1}{3}$</td>
</tr>
<tr>
<td>1000 Particles</td>
<td>7.9</td>
<td>12.6</td>
<td>16.3</td>
<td>11.0</td>
<td>20.0</td>
<td>25.9</td>
</tr>
<tr>
<td>5000 Particles</td>
<td>8.0</td>
<td>12.7</td>
<td>16.3</td>
<td>11.3</td>
<td>20.2</td>
<td>25.9</td>
</tr>
</tbody>
</table>
distribution and particle impaction velocities for the full inlet were closer to the critical values compared with those at 30 l/min.

At a flow rate of 60 l/min, the critical ISSR distribution (Fig. 6c) and particle impaction velocities (Tab. 2) had been generated in the device for each inlet size, indicating that no difference in the inhaler dispersion performance would be expected between the three inlet cases. However, a reducing trend in the inhaler dispersion performance was observed as the air inlet size was reduced (Fig. 3b). Reducing the air inlet size significantly increased the angular velocity of the rotating capsule (Tab. 3), which reduced the time taken for powder to empty out of the capsule. The capsule emptying times for each inlet size at 60 l/min, measured using a laser photometer as described in Chew et al. and Clark & Bailey, were found to be 2.6 ± 0.2 s, 1.9 ± 0.1 s and 1.4 ± 0.1 s for the full, two-third and one-third air inlet size, respectively (n = 3). Coates et al. have previously demonstrated that powder–capsule interaction plays a significant role on the dispersion performance of the Aerolizer. It is hypothesized that reducing the capsule emptying time could affect the degree of powder–capsule interaction, potentially changing the inhaler dispersion performance. To investigate the importance of this effect, dispersions were performed without a capsule present by loading powder directly into the device onto the surface adjacent to the spinning capsule, as previously described. In each case, 20 mg of the same mannitol powder was loaded directly into the device and the runs were performed in triplicate to obtain mean values. The results showed that the same trend in the performance of the inhaler was observed without a capsule present (Fig. 7), demonstrating that the powder–capsule interaction effects caused by the presence of the rotating capsule were not responsible for the observed dispersion reduction.

Reducing the inhaler air inlet size increased the device resistance [from 0.072 (cmH₂O)½/(l/min)]

**Figure 6.** (a) ISSR distributions for each air inlet case at 30 l/min indicating that the critical ISSR had been generated in the device for the one-third and two-thirds inlet sizes but not for the full inlet size. (b) ISSR distributions for each air inlet case at 45 l/min indicating that the critical ISSR had been generated in the device for the one-third and two-thirds inlet sizes but not for the full inlet size. (c) ISSR distributions for each air inlet case at 60 l/min indicating that the critical ISSR had been generated in the device for all inlet sizes.

<table>
<thead>
<tr>
<th>Capsule Angular Velocity (rpm)</th>
<th>Full Inlet</th>
<th>⅔ Inlet</th>
<th>⅓ Inlet</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 l/min</td>
<td>1340</td>
<td>2050</td>
<td>2550</td>
</tr>
<tr>
<td>45 l/min</td>
<td>2100</td>
<td>3020</td>
<td>3700</td>
</tr>
<tr>
<td>60 l/min</td>
<td>2620</td>
<td>4250</td>
<td>5150</td>
</tr>
</tbody>
</table>
for the full inlet size to 0.100 and 0.148 (cmH2O)½/(l/min) for the two-thirds and one-third inlet sizes, respectively], which plays a significant role in the rate at which air flow is developed in the device. Studying the inhaler flow development profiles at 60 l/min (i.e., change in flow rate with time) showed that reducing the air inlet size increased the time required for the test flow rate to be developed within the inhaler (Fig. 8). For the full air inlet size, the flow development time was approximately 0.08 s, increasing to approximately 0.18 s and 0.35 s for the two-third and one-third air inlet sizes, respectively (n = 3). The flow development time is an important factor to consider if it is comparable with the device emptying time, as this could cause a large fraction of powder to exit the

Figure 7. %FPF loaded and emitted from dispersion results performed with powder loaded directly into the device at 60 l/min, indicating that the same trend in the inhaler performance was observed without a capsule present. (*denotes a statistically significant difference between the indicated and following result).

Figure 8. Flow profiles generated in the Aerolizer® with different air inlet sizes demonstrating that the flow development time increases as the size of the air inlet is reduced. The data were obtained by an oscilloscope (Agilent, Palo Alto, CA) coupled with a short response flow meter (model 4100, TSI, Inc., Shoreview, MN).

Figure 9. Voltage signal from the laser photometry showing the profile of the powder flux through the device at 60 l/min. The dotted line shows the time at which the flow reached the test flow rate. Note that because of the presence of powder deposited after dispersion, the voltage does not return to its initial value. This difference can be reasonably neglected when estimating the area under the curve.
device before the maximum levels of turbulence are generated.

Figure 9 shows results obtained from the laser photometry analysis used to measure the time taken for powder to empty out of the device. The area under the curve (from time zero to the final base-line reading) represents the amount of powder released from the capsule during dispersion and the dotted lines show the flow development time for each inlet case. For the full air inlet size, only a small fraction of the powder is released before the flow development time is reached, indicating that the vast majority of the powder will interact with the fully-developed flow containing the maximum turbulence levels (Fig. 9a). For the two-thirds inlet size, a larger fraction of powder is released prior to the flow development time (Fig. 9b), but still the majority of the powder exits the device when the fully developed flow has been generated. However for the one-third inlet size, a significant fraction of powder is released from the device prior to the flow development time (Fig. 9c), indicating that a large amount of powder will interact with the developing flow. Therefore by reducing the air inlet size, the amount of powder exiting the device during flow development (when both the turbulence levels and particle impaction velocities are below their fully-developed values) was significantly increased, which causes the observed dispersion reduction. Whilst the computational models developed here can be used to simulate the developing flow, the models describing powder deagglomeration during this process have not yet been developed.

Although a reducing trend in the $FPF_{Em}$ was observed between the three inlet cases at 60 l/min, only the difference between the two-thirds and one-third inlet sizes ($p = 0.006$) was statistically significant (Fig. 3b). This suggests that a large fraction of powder needs to be released from the device prior to the full flow development (as in the

![Figure 9](image)

**Figure 9.** Voltage signal from the laser photometry showing the profile of the powder flux through the device at 90 l/min. The dotted line shows the time at which the flow reached the test flow rate.

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**Figure 10.** $\%FPF$ emitted from the original dispersion results at 60 l/min (Fig. 3b) with additional data at 90 l/min, indicating that a greater reduction in the inhaler dispersion performance with inlet size is observed at 90 l/min. (*denotes a statistically significant difference between the indicated and following result).
one-third inlet case at 60 l/min) to have a significant effect to the inhaler dispersion performance. Additional dispersion analysis performed at 90 l/min showed that the performance reductions observed for the two-thirds and one-third inlet sizes were significantly larger at 90 l/min compared with those observed at 60 l/min (Fig. 10). At 90 l/min, a significant amount of powder was released from the capsule prior to full flow development for both the two-thirds and one-third inlet cases (Fig. 11). These results confirm that a large fraction of powder must be released from the device prior to full flow development to have a significant effect on the inhaler dispersion performance, and that a greater performance reduction is observed when the amount of powder released before full flow development is increased.

Finally, the study showed that the air inlet size had a significant effect on the amount of capsule retention at low flow rates. High capsule retention was observed for full inlet size at 30 and 45 l/min and also for the two-thirds inlet size at 30 l/min (Fig. 4a). Reducing the air inlet size increased the velocity of entrained air flow, which increased the capsule angular velocity (Tab. 3). Figure 12 shows a linear relationship between the capsule angular velocity and device flow rate for each air inlet size, where the angular velocity of the capsule, \( \omega \) (in rpm) at 30, 45, and 60 l/min can be approximated by \( \omega = 45Q \), \( \omega = 69Q \), and \( \omega = 85Q \), respectively. Coates et al.\(^7\) reported that a capsule angular velocity of greater than 2170 rpm was required to empty the capsule (pierced using the four-pin piercing mechanism currently employed in the Aerolizer\(^6\)) within the 4 s impinger run time. The capsule angular velocity for the full inlet case at 30 and 45 l/min and for the two-thirds inlet case at 30 l/min were less than 2170 rpm (Tab. 3), explaining the high capsule retention for these cases.

CONCLUSIONS

This study showed that the size of the air inlet had a varying effect on the inhaler performance at different flow rates. The inlet size controls the levels of turbulence and particle impaction velocities generated in the device, as well as the flow development rate and device emptying times. At low flow rates (30 and 45 l/min), reducing the air inlet size increased the inhaler dispersion performance by increasing the turbulence levels and particle impaction velocities generated in the device above the critical levels. At higher device flow rates (60 and 90 l/min), reducing the size of the air inlet reduced the inhaler dispersion performance by releasing a large amount of powder from the device when both the turbulence levels and particle impaction velocities were below their fully developed values. Significant dispersion reductions may occur when a large amount of powder is released from the device prior to full flow development.

This work enhances the knowledge of which design features of a dry powder inhaler have a significant effect on the overall inhaler performance and adds to our previous findings on the effect of the inhaler grid structure and mouthpiece length. The results demonstrate that the maximal dispersion performance of a dry powder inhaler can be predicted if details of the device flowfield are known, and highlight the importance of minimizing the amount of powder released from the device prior to full flow development.

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