
MATTHEW S. COATES,1,2 DAVID F. FLETCHER,1 HAK-KIM CHAN,2 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

Received 27 February 2004; revised 9 July 2004; accepted 14 July 2004
Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/jps.20201

ABSTRACT: This study investigates (1) the effect of modifying the design of a dry powder inhaler on the device performance, and (2) which design features significantly contribute to overall inhaler performance. Computational Fluid Dynamics (CFD) analysis was performed to determine how the flowfield generated in an Aerolizer® at 60 l min⁻¹ varied when the inhaler grid and mouthpiece were modified. The computational models were validated by Laser Doppler Velocimetry (LDV). Dispersion performance of the modified inhalers was measured with a mannitol powder using a multistage liquid impinger at 60 l min⁻¹. The inhaler grid was found to significantly affect the performance of the Aerolizer®. As the grid voidage was increased, the amount of powder retained in the device doubled (due to increased tangential flow of particles in the inhaler mouthpiece) and the FPFLoaded was reduced from 57 to 44% (due to increased mouthpiece retention). The length of the mouthpiece played a lesser role on the inhaler performance, having no significant effect on the flowfield generated in the devices. In summary, the performance of a dry powder inhaler can be affected by simple design changes. CFD, coupled with experimental results, provides a rational basis for understanding the performance difference. © 2004 Wiley-Liss, Inc. and the American Pharmacists Association J Pharm Sci 93:2863–2876, 2004

Keywords: aerosols; pulmonary; targeted drug delivery; pulmonary drug delivery; computational modeling; dry powder inhaler; DPI; computational fluid dynamics; CFD

INTRODUCTION

Rapid development in pulmonary drug delivery by inhalation aerosols in the past decade has led to novel invention of aerosol delivery devices and new formulation technologies capable of producing particles of defined characteristics for improved delivery.¹ Extensive research in particle technology has advanced the dry powder inhaler formulation by control of drug particle density,²,³ particle morphology,²–⁴ surface composition,⁵ particle size, and size distribution.⁶,⁷ There is also an excessively large number of inventions of dry powder inhalers, but not much concerns with the inhaler performance at a fundamental level.¹

The design of a dry powder inhaler is vital to control the size range of drug particles emitted from the device.⁶,⁸,⁹ At present, there is little published literature that demonstrates how the design of an inhaler affects the drug powder
deagglomeration and subsequent dispersion performance. Computational Fluid Dynamics (CFD) has found wide application in the study of pharmaceutical unit operations for drug manufacturing, for example, flow in mixing vessels,\textsuperscript{10} micromixers,\textsuperscript{11} spray dryer design and optimization,\textsuperscript{12,13} and studies of particle agglomeration.\textsuperscript{14} Recently, CFD has been used to model the air flow in propellant metered dose inhalers\textsuperscript{15} and holding chambers.\textsuperscript{16} Although CFD modeling is also available for dry powder inhalers,\textsuperscript{17–19} fundamental detail is lacking.

When the design of an inhaler is modified, the flowfield generated within the device changes, affecting the performance of the inhaler. The aim of this study is to examine the effect of making small changes to the design of a dry powder inhaler on the performance of the modified inhaler and also to determine which features of the design contribute significantly to the overall inhaler performance. This will allow the determination of which design modifications affect the flowfield sufficiently to change particle deagglomeration and subsequently, the inhaler performance.

**METHODS**

Computational fluid dynamics analysis, using ANSYS CFX5.6,\textsuperscript{20} was performed in conjunction with experimental powder dispersion analysis to determine how the performance of an Aerolizer\textsuperscript{18} (Plastiape S.p.A.) changed when small design modifications were made to the structure of the grid and the length of the inhaler mouthpiece. The structure of the grid was studied, as there is little published data of how grid impaction contributes to the deagglomeration of drug powder. Voss and Finlay\textsuperscript{21} reported that turbulence was the major controlling factor on particle deagglomeration, with the effects of grid impaction being less significant. The present study is capable of showing not only the grid impaction effects but also the effect the grid has on the generated flowfield.

The length of the mouthpiece was studied, as this parameter determines the level of flow development through the mouthpiece. Undeveloped flow can contain regions of high velocity that can enhance throat impaction upon inhalation. It is believed that more development of the flow through the mouthpiece leads to a more uniform flow profile at the device exit. This uniform profile reduces the regions of high velocity, potentially reducing throat impaction and improving overall inhaler performance.

To study the dependence of inhaler performance on the structure of the grid, two modified grids were studied in addition to the complete design, shown in Figure 1. For each case, simple geometry

![Figure 1](image_url)

**Figure 1.** Schematic of the grid structures used to study the effect of the grid on inhaler performance.
changes were made to the original grid to obtain the modified grid. Fully validated CFD analysis was performed on the different geometries to determine the nature of the flowfield experienced in the modified devices at a flowrate of 60 l min$^{-1}$. The performance of the modified inhalers was determined experimentally using a multistage liquid impinger (see Dispersion Methodology).

To study the effect of the length of the inhaler mouthpiece on the inhaler performance, the complete Aerolizer$^R$ design was studied along with inhaler designs containing a mouthpiece of three-quarters and one-half the original length. The full inhaler grid was present in each of the three devices used in this section of the study. The same methods used to study the grid effects were employed to study the effects of the mouthpiece length.

A constant test flow rate of 60 l min$^{-1}$ was chosen throughout this study, as this flow rate can be easily achieved by the patient. Values of the device resistance at 60 l min$^{-1}$ were found to be 0.072, 0.071, and 0.060 (cmH$_2$O)$^{1/2}$ (l min$^{-1}$)$^{-1}$ for the full grid case, grid 1 case and grid 2 case, respectively, indicating that a patient would generate comparable airflows with each device. Although performing the study at a constant flow rate has the limitation of not covering the full range of airflows attainable by a single patient, it decouples the flow rate effects from the other parameters studied.

**Computational Methodology**

The flowfield generated in the devices was obtained by solving the Reynolds Averaged Navier Stokes using the commercial CFD code ANSYS CFX 5.6. This model solves the conservation equations using a finite volume method on an arbitrary computational mesh, in this case comprised of tetrahedral elements in the bulk of the flow with a layer of prisms around the walls, to provide good resolution of the boundary layers.

Mesh independence studies were performed to ensure that the computed results were independent of the chosen mesh. Typically, the mesh size used was 0.6 mm in the inhaler mouthpiece, 0.5 mm in the base of the inhaler, with a mesh of 0.2 mm used in the region of the grid. A second order bounded differencing was used to resolve all of the flow variables, ensuring minimal numerical diffusion.

To obtain mesh independent results, a series of three simulations were run in which the characteristics of the mesh applied to the geometry were varied significantly (Table 1). Axial velocity profiles were plotted on three equi-spaced lines spanning the mouthpiece of the device for the different computational mesh cases (Fig. 2). The velocity profiles exhibited very small differences on the three computational meshes, indicating mesh independence. Previous studies have shown that a 30% variation in the total number of nodes is sufficient to gain mesh independence for the purpose of exploring design variations. The coarser of the three meshes was employed to minimize computational run time.

Turbulence was modeled using the SST (Shear Stress Transport) turbulence model together with scalable wall functions. These ensure that the near wall node is always at least at y-plus of 11, preventing unphysical behavior in regions of fine mesh. The mesh used was sufficiently fine that the near wall node was positioned at this lower limit on y-plus. Attempts were made to use various Reynolds Stress turbulence models, but satisfactory convergence was never obtained.

It was found that the flowfield exhibited a small degree of unsteadiness in all cases. Therefore, a steady-state simulation was run first to obtain the basic flowfield, and then a transient simulation was restarted from this initial solution, and run for a period of around 0.035 s, to resolve the unsteady motion. Typically, a time step of 0.0005 s was used and the equations were solved to a normalized residual of $1 \times 10^{-5}$ at each time step. It was

<table>
<thead>
<tr>
<th>Mouthpiece</th>
<th>Inhaler Base</th>
<th>Inhaler Grid</th>
<th>Number of Computational Nodes ($\times 10^5$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesh 1</td>
<td>0.6</td>
<td>0.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Mesh 2</td>
<td>0.55</td>
<td>0.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Mesh 3</td>
<td>0.55</td>
<td>0.45</td>
<td>0.2</td>
</tr>
</tbody>
</table>
observed that the transient motion resulted from a slight precession of the flow around the axis of the device. Therefore, the results at the end of the simulation were taken as representing a typical snapshot of the flowfield.

Lagrangian particle tracking was performed as a postprocessing operation, in which the fate of 1000 and 10,000 particles with a density of 1520 kg m$^{-3}$ and particle diameter of 3.2 μm were tracked through the fluid after release from the capsule region and subjected to drag and turbulent dispersion forces. The Lagrangian particle tracking techniques were performed using a frozen flowfield obtained at a series of timeframes throughout the transient solution. Although small variations in the nature of the particle tracks were observed at each time frame, the inherent nature of the particle tracks remained the same. By setting different walls within the devices to have a zero coefficient of restitution, it was possible to determine the frequency and location of wall impactions. The impaction data provided in this study are not intended to be treated quantitatively, but intended to illustrate the significant trends in the impaction data found computationally.

Validation Methodology

To validate the computational results, Laser Doppler Velocimetry (LDV) techniques were used to determine values of the axial and tangential velocity at a large number of measurement points across the exit of the inhaler mouthpiece. These data were compared directly with the corresponding CFD results to determine the level of agreement. Several computational cases were validated to obtain a comprehensive comparison between the LDV and CFD results. The different cases were chosen to show that the models used in the CFD analysis are valid over a wide range of situations, including variations in the geometry and variations in the flowrate (Table 2).

Dispersion Methodology

The dispersion performance of all four modified inhalers plus the complete design was determined using a four-stage (plus filter) liquid impinger (Copley, Nottinghamshire, UK), setup as described in the BP. For each dispersion, three capsules were filled with approximately 20 mg of spray-dried mannitol, particle size $d_{50} = 3.2$ μm, and dispersed into the impinger. The impinger was run at 60 l min$^{-1}$ for a total of 5 s using a timed valve. The runs were performed a total of six times to obtain mean values. Mannitol was assayed by high-performance liquid chromatography (HPLC) (Waters, Milford, MA) using refractive index detection. Centrifuged samples (100 μL) were injected into a C18 radial-pak column with deionized water as the mobile phase running at a flow rate of 1 mL min$^{-1}$ 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 6.8 μm, as this was the cutoff for stage 2 at 60 l min$^{-1}$. Numerically, the fine particle fraction was expressed as the percentage of powder collected on stages 3, 4, and the filter, referenced against either the total mass of powder loaded (FPF$^{\text{Loaded}}$) into, or the total mass of powder emitted (FPF$^{\text{Em}}$) from, the device. The percentage recovery throughout the dispersion analysis was 100±3%. Analysis of variance (ANOVA) tests were carried out with probability of less than

| Table 2. Summary of CFD Cases Validated Using LDV Techniques |
|-------------|-------------|-------------|
| Case  | Device   | Flow Rate (l min$^{-1}$) |
| A60  | Aerolizer  | 60          |
| A120 | Aerolizer  | 120         |
| AN60 | Aerolizer  | 60          |
| AN120| Aerolizer  | 120         |

*Coates et al.*

**Figure 2.** Comparison of the local axial velocity profiles produced from the three different computational meshes used to achieve mesh independent results (lines 1, 2, and 3 represent three equi-spaced lines spanning the mouthpiece of the device).
0.05 considered statistically significant (Minitab 13). Throughout the dispersion analysis, the relatively humidity of the laboratory was maintained at 55 ± 5%. Previous study has shown that the dispersion behavior of mannitol is not strongly affected by relatively humidity.28

RESULTS

Validation Results

Axial velocity–radial distance profiles plotted across three measurement lines were obtained from the LDV and CFD results for all four validation cases. The three measurement lines, uniformly spaced over the inhaler exit, were chosen to compare the LDV and CFD results across the entire exit plane of the inhaler. Figure 3 shows the plots produced for the validation cases using the Aerolizer® with the grid at flowrates of 60 l min⁻¹ and 120 l min⁻¹. The axial velocity trends across the three measurement lines obtained from the LDV results agree closely with the results obtained from the CFD analysis for both validation cases. Similarly, good agreement between the CFD and LDV results was found for the validation cases using the Aerolizer® with no grid at flowrates of 60 l min⁻¹ and 120 l min⁻¹ (Fig. 4). These results demonstrate that the CFD models used are capable of simulating the axial flow through the devices at a range of flowrates and device geometries.

Figure 5 shows a tangential velocity-radial distance profile across the centre line of the mouthpiece obtained from the LDV and CFD results for the Aerolizer® with and without the grid at 60 l min⁻¹. Fair agreement was observed between the LDV and CFD results, indicating that the CFD models used can predict the trends in the swirl generated for a range of device geometries. However, we do not claim that the simulations are capturing all details of the swirling flow, especially the details of the turbulent fields, but rather that they provide a useful means of comparing designs and interpreting experimental data.

Aerosol Characterization Results

Grid Effect Study

The experimental dispersions performed to study the effects of the inhaler grid showed that as the voidage of the grid was increased, there was a reduction in the FPF_Loaded but no trend in the

Figure 3. Comparison of LDV and CFD results for the axial velocity across the three measurement lines of the inhaler exit for the Aerolizer® containing the grid at 60 and 120 l min⁻¹.
FPF<sub>Em</sub> (Fig. 6a). No statistical difference was found in the FPF<sub>Em</sub>; however, a statistical difference was found in the FPF<sub>Loaded</sub> between the full grid and grid 1 cases, and also between the grid 1 and grid 2 cases. Increasing the grid voidage led to a significant increase in the mass of powder retained in the mouthpiece (Fig. 6b). For the complete grid case, powder retention in the mouthpiece was 17%, which was increased to 25% and 34% in the grid 1 and grid 2 cases, respectively.

**Mouthpiece Length Study**

When the length of the mouthpiece was reduced, there was no statistically significant difference in the FPF<sub>Loaded</sub> and FPF<sub>Em</sub> for the three mouthpiece cases (Fig. 7a). Furthermore, no trend between the length of the mouthpiece and the amount of powder deposited at the throat stage of the impinger was observed (Fig. 7b). A statistically significant reduction in the amount of powder retained in the device was observed as the length of the mouthpiece reduced.
CFD Results

**Grid Effect Study**

Figure 8 shows a similar flowfield generated in the base of the inhaler in all three grid cases. In contrast, the flowfield generated in the inhaler mouthpiece varied significantly with the grid. The overall levels of turbulence generated in the devices were comparable, with values of the volume averaged turbulence kinetic energy being $11.5 \pm 1.0$ J kg$^{-1}$. As the voidage of the grid was increased, a reduction in the values of the integral scale strain rate at a plane 2 mm upstream from the grid was observed (Fig. 9). No significant difference in the integral length scale of the turbulence was observed between the three grid cases.

Figure 10 shows the tracks that the particles take when dispersed by the Aerolizer$^\text{RE}$. This demonstrates that the inhaler grid acts to straighten the flow and reduce the level of swirl generated in the device. As the grid voidage was increased, the effect of the grid on reducing the level of swirl in the device decreased. For the full grid case (Fig. 10a) the tangential component of the particle flow had been significantly reduced by the grid, with a predominantly axial flow occurring in the mouthpiece. For the grid 1 case (Fig. 10b), the grid had some effect on reducing the swirl, but the tangential component of the flow of particles was greater compared with the complete grid case. Figure 10c shows that modified grid 2 had little effect on the flow of particles, and a predominantly tangential flow occurred in the mouthpiece.

The particle tracking was also used to determine the frequency and location of particle impactions for the three different grid cases. Table 3
summarizes the number of impactions that were observed on the grid and the mouthpiece of the inhaler. The tracking was initially carried out for 1000 particles and repeated for 10,000 particles.

**Figure 8.** Velocity profiles indicating that the inhaler grid strongly affects the flowfield generated in the inhaler mouthpiece.

**Figure 9.** Integral scale strain rate profiles 2 mm upstream of the grid indicating that as the grid voidage increases, the rate integral scale strain generated immediately above the grid is reduced.
Realistic computational requirements limited the number of dispersed particles to 10,000. However, no significant difference in the frequency of impactions was observed for the 10-fold increase of particles, giving confidence in the models used at capturing the correct trends in particle impactions independent of the number of particles simulated.

As expected, when the voidage of the grid increases, the trend in the number of impactions the drug particles had with the inhaler grid reduced. In contrast, as the grid voidage was increased, an increasing trend in the number of impactions the particles had with the mouthpiece walls was observed. Because a lower velocity air flow was generated in the mouthpiece of the device, typically reducing from a maximum of 40 m s\(^{-1}\) in the inhaler base to 20 m s\(^{-1}\) in the mouthpiece, the particle–mouthpiece impactions would occur at a lower velocity than the particle–grid impactions. In addition, the grid impactions occurred with a large impact angle, whereas the mouthpiece impactions occurred at a much shallower angle, potentially reducing the impact intensity.

Figures 11 and 12 show the velocity profile of the flow at a position of 2 mm upstream of the grid and the velocity vectors of the flow as it passed through the grid, respectively. The complete grid acted to distribute the flow throughout all the grid apertures, with a largely uniform flow passing through this grid (Figs. 11a and 12a). The flow through modified grid 1 was less well distributed than the complete grid case, with regions of high velocity occurring at the centre of the grid (Figs. 11b and 12b). The flow distribution in the grid 2 case was poor, with high velocity flow occurring at the walls of the mouthpiece (Figs. 11c and 12c). This grid had little effect at reducing the swirl generated in the device, with the velocity vectors

Table 3. Summary of the Percentage of Particles Impacting on the Different Sections of the Aerolizer\(^{\text{**}}\) When the Computational Model Was Used to Simulate the Dispersion of 1000 and 10,000 Drug Particles

<table>
<thead>
<tr>
<th>% Particle Impacting on Different Sections of the Aerolizer(^{\text{**}})</th>
<th>Grid</th>
<th>Mouthpiece</th>
</tr>
</thead>
<tbody>
<tr>
<td>1000</td>
<td>10,000</td>
<td>1000</td>
</tr>
<tr>
<td>Full grid case</td>
<td>59</td>
<td>62</td>
</tr>
<tr>
<td>Grid 1 case</td>
<td>40</td>
<td>39</td>
</tr>
<tr>
<td>Grid 2 case</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

Figure 10. Particle tracks of the dispersed powder indicating that the grid affects the tangential component of the flowfield in the mouthpiece.
Figure 11. Velocity profile 2 mm above the inhaler grid showing that the uniform distribution of flow through the grid reduces as the grid voidage increases.

Figure 12. Velocity vectors through the grid indicating that as the grid voidage increases a flow with a greater tangential component is generated in the inhaler mouthpiece.
showing that the tangential component of the flow through this grid was much greater than the other two grid cases.

**Mouthpiece Length Study**

Figure 13 indicates that for all three mouthpiece cases, identical flow patterns were observed in the base of the inhaler. The flowfields generated in the mouthpiece were also identical up to the exit of each mouthpiece. Due to the similarity of the flowfield, the overall levels of turbulence generated in the different devices were found to be analogous, with maximum values of the turbulence kinetic energy being $91 \pm 2 \text{ J kg}^{-1}$.

Figures 14 shows contour plots of the velocities at the exit of each of the devices. For the inhaler with the full length mouthpiece, a well distributed velocity profile occurred at the inhaler exit exhibiting a small velocity difference (Fig. 14a). The velocity differences at the exit for the 3/4 mouthpiece length case were slightly greater than those of the complete mouthpiece case (Fig. 14b). As the mouthpiece length was reduced to half, a nonuniform flow profile occurred where two regions of high velocity were observed together with regions of lower velocity (Fig. 14c). These regions of high velocity occurred due to slight variations in the flow distribution through the grid apertures of the complete grid, as shown in Figure 11a.

**DISCUSSION**

This study showed that when modifications to the design of an Aerolizer® are made, the flowfield generated within the device can change significantly, and that these changes in the flowfield may have a significant effect on the overall performance of the inhaler. The grid has been demonstrated to play a significant role on the flowfield generated in the mouthpiece of the devices as well as the overall inhaler performance. As the voidage of the grid was increased, a reduction in the $\text{FPF}_{\text{Loaded}}$ was observed. No significant difference in the $\text{FPF}_{\text{Em}}$ was found.

The deagglomeration of drug particles to form a fine respirable aerosol cloud is thought to be achieved by three major mechanisms: (1) Particle interaction with shear flow and turbulence, (2) particle–device impaction, and (3) particle–particle impaction. The scope of this study currently did not allow a determination into the number of particle–particle collisions that occur within the devices, and hence, this mechanism was not further discussed.

The overall levels of turbulence generated in the devices were found to be comparable for the three
different grid cases, with values of the volume averaged turbulence kinetic energy being $11.5 \pm 1.0$ $J \text{ kg}^{-1}$. However, when estimating the potential of a turbulent flow to break-up powder agglomerates, the various turbulent scales need to be studied. The integral scale eddies are the most energetic occurring in a turbulent flow, and hence, have the greatest potential to deagglomerate particles. To estimate the integral scale values of the eddies the following method was applied. Values of the root-mean-square of the turbulent fluctuating velocities allow us to estimate the integral velocity scale, $u_i$. The integral length scale, $l$, can be estimated from,

$$\epsilon = \frac{u_i^3}{l}$$

where $\epsilon$ is the rate of turbulent energy dissipation. Manipulation of these equations allow us to determine an expression for the integral scale strain rate of the turbulence ($\gamma_i$), shown below.

$$\gamma_i = \frac{u_i l}{k} = \frac{\epsilon}{k}$$

where $k$ is the rate of turbulence kinetic energy. Turbulent flows consisting of eddies that exhibit large integral scale strain rates will exert large aerodynamic forces on particles, and hence will be effective at breaking up particle agglomerates.

The dependence of the Aerolizer performance on the structure of the grid was believed to be due to a combination of the effect that the inhaler grid has on generating high integral scale strain rates within the device and affecting the number of particle–grid impactions and particle–mouthpiece impactions. As the voidage of the grid was increased, there was a reduction in the magnitude of the integral scale strain rate generated immediately above the grid (Fig. 9). In addition, a reducing trend in number of high velocity powder–grid impactions was observed with an increasing grid voidage (Table 3). Therefore, increasing the voidage of the grid reduced the deagglomeration potential of the flowfield generated in the device, due to lower integral scale strain rates and fewer particle–grid impactions.

However, as the voidage of the grid was increased, the number of impactions the drug particles had with the mouthpiece increased (Table 3). Therefore, increasing the voidage of the grid can also increase the deagglomeration potential of the flowfield generated in the device, due to a greater number of particle–mouthpiece impactions. The observation of no significant difference in the FPF_{Em} suggests that the increased deagglomeration potential (due to particle–mouthpiece impactions) is balanced out by the reduced deagglomeration potential (due to higher integral scale
strain rates and particle–grid impactions). This gives rise to the similarity in FPF_Fem observed experimentally.

This study also demonstrated that as the voidage of the grid was increased, the amount of device powder retention increased (Fig. 6b). Upon inhalation, the inhaler grid acts to convert the high velocity tangential air flow entering the device into a low velocity, predominantly axial air flow exiting the mouthpiece. Increasing the voidage of the grid was found to increase the tangential component of the flow of particles in the inhaler mouthpiece (Fig. 10). This led to an increase in the number of particle–mouthpiece impactions (Table 3) and the overall possibility of powder retention within the inhaler. The results indicated that the grid directly affected the amount of powder retention in the device by changing the degree of particle–mouthpiece contact. As no difference in FPF_Fem was found, the increase in the amount of mouthpiece retention with increasing grid voidage accounted for the reducing trend in the FPF_Loaded observed experimentally.

The length of the mouthpiece was found to play a less significant role on the inhaler performance than the grid. As the length of the mouthpiece was reduced, no significant change in the performance of the inhaler was observed. Figure 13 shows that the length of the inhaler mouthpiece had no effect on the flowfield generated in the devices, up to the exit of the mouthpiece. As a result, no differences in the levels of turbulence were generated in the devices with varying mouthpiece length and as the structure of the grid was unchanged, no difference in the amount of grid impaction occurred. Therefore, the comparable fine particle fraction values that were obtained experimentally were expected.

The velocity profile at the exit of the mouthpiece is more nonuniform for a shorter mouthpiece length. For the 1/2 mouthpiece length case, the exit mouthpiece velocity profile exhibits regions of high velocity together with regions of lower velocity. These regions of high velocity could potentially increase throat impaction. However, no significant differences in the amount of throat impaction were observed experimentally between the three different mouthpiece cases. The length of the impinger throat used was more than four times the length of the full inhaler mouthpiece. It is believed that any regions of high velocity at the exit of the mouthpiece would have dissipated in the throat before any impaction could occur, eliminating the possibility of increased throat retention.

CONCLUSIONS

This study shows the effectiveness of using computational fluid dynamics to simulate the flowfield generated in dry powder inhalers of different design. The computational results were used to provide fundamental information to explain differences in the observed dispersion behavior. The combination of computational and experimental methods was used successfully to study the effect of design modification on inhaler performance.

The structure of the inhaler grid was shown to play a significant role in the overall inhaler performance. The inhaler grid directly affected the amount of powder retention within the device by affecting the frequency of particle–mouthpiece contact. This led to a reduction in the FPF_Loaded, reducing overall inhaler performance. In each case, the complete Aerolizer® grid was found to perform better than the higher voidage modified grids. The inhaler mouthpiece length was found to play a less significant role in the performance of the inhaler. No significant difference in the performance of the inhaler or amount of throat impaction was observed as the length of the mouthpiece was changed.

In summary, an Aerolizer® with the full grid reduces device retention and increases the overall inhaler performance. A shorter mouthpiece will also slightly improve the overall performance of the inhaler by reducing device retention.

ACKNOWLEDGMENTS

This work is funded by a grant from the Australian Research Council. Matthew S. Coates is a recipient of an International Postgraduate Research Scholarship. The authors would like to thank S. Stårner for his invaluable assistance throughout the LDV analysis and Plastiape S.p.A. for the supply of the inhalers.

REFERENCES


18. Computer-Optimised Pulmonary Delivery in Humans of Inhaled Therapies (COPHIT) http://www.COPHIT.co.uk.


