Use of High-speed Particle Imaging to Delineate between Different Inhalation Powder Blends

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KEY MESSAGE

High-speed imaging can delineate between powder formulations with as low as 1% drug content inside a dry powder inhaler (DPI) by directly measuring the number-based particle size distribution (PSD). Differences in the PSD can be observed over a range of diameters, including outside the size range of the fine drug particles.

INTRODUCTION

Drug delivery through DPIs is an area that, despite being well studied, still presents challenges, such as ensuring sufficient powder dispersion and drug delivery efficiency. Attempts to improve DPI performance often involve modifying the device geometry, physiochemical properties of the powder, and drug content of the formulation. The present study involves:

- Using high-speed laser backlit imaging to directly size particles inside of a transparent DPI during operation.
- Demonstrate the sensitivity of this technique in detecting small changes in drug content to determine the feasibility of this approach to investigate DPI performance.

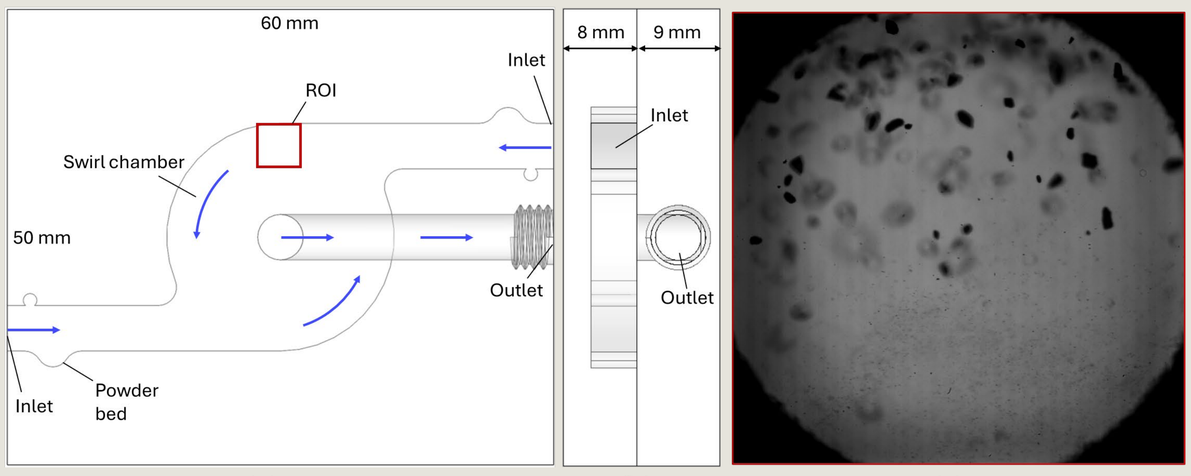

Fig. 1. Front, (a), and side, (b), views showing the design of the transparent test DPI, with blue arrows indicating the direction of air flow. An example image taken in the indicated region of interest (ROI) is given in (c).

METHOD

A custom-made acrylic DPI (Fig. 1) was developed to emulate features of commonly used commercial devices (such as the presence of a swirl chamber). A similar design was used in previous works [1] [2], where single-component formulations (mannitol or lactose) were investigated. In the current study, this is applied to powder formulations containing a base carrier of coarse lactose (SV010), with varying fractions of fine lactose (LH300), and active ingredient salbutamol sulphate (SS), which are listed in Table 1.

The experimental set-up (Fig. 2) consists of a FIREFLY laser that pulses in sync with a high-speed camera equipped with a microscopic lens. Powder is loaded into the DPI and the flow driven at 30 LPM by a venturi vacuum ejector. An example image is shown in Fig. 1(c), which is then processed (binarized, removing out-of-focus objects) to directly size the particles in the image [1] [2] [3].

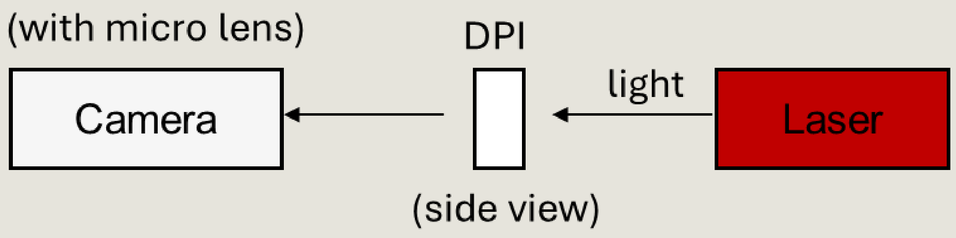

Fig. 2. Schematic of the experimental setup

Table 1. List of blended formulations with their mass-based percentages of salbutamol sulphate (SS), fine lactose (LH300), and coarse lactose (SV010).

Formulation	wt.% SS (D_{50}=4 μm)	wt. % LH300 (D_{50}=5 μm)	wt.% SV010 (D_{50}=109 μm)
SV010	0.00	0.00	100
F2	2.75	0.00	97.25
F5	2.75	10.0	87.25
F7	1.00	0.00	99.00
F8	2.75	2.50	94.75
F11	2.75	5.00	92.25
F12	4.50	0.00	95.50

RESULTS

The number-based PSD, where N% is the percentage of particles in a given size class, for pure SV010 and all blended formulations are presented in Fig. 3. All formulations with 2.75% SS and varying LH300 content are given in (a), while the formulations with no LH300 and varying amounts of SS are given in (b). Some key observations are:

- Increasing N% for diameter D < 30 μm with increasing LH300 and SS content (insets in Fig 3).
- Higher N% in SV010 than all other formulations in the 50 μm < D < 105 μm range.
- Higher N% for D > 130 μm in the blended formulations than SV010.

These results demonstrate that the influence of even a small fraction of fine particles (e.g., F7) has a detectable effect on the PSD inside the DPI, as measured with the present high-speed imaging system.

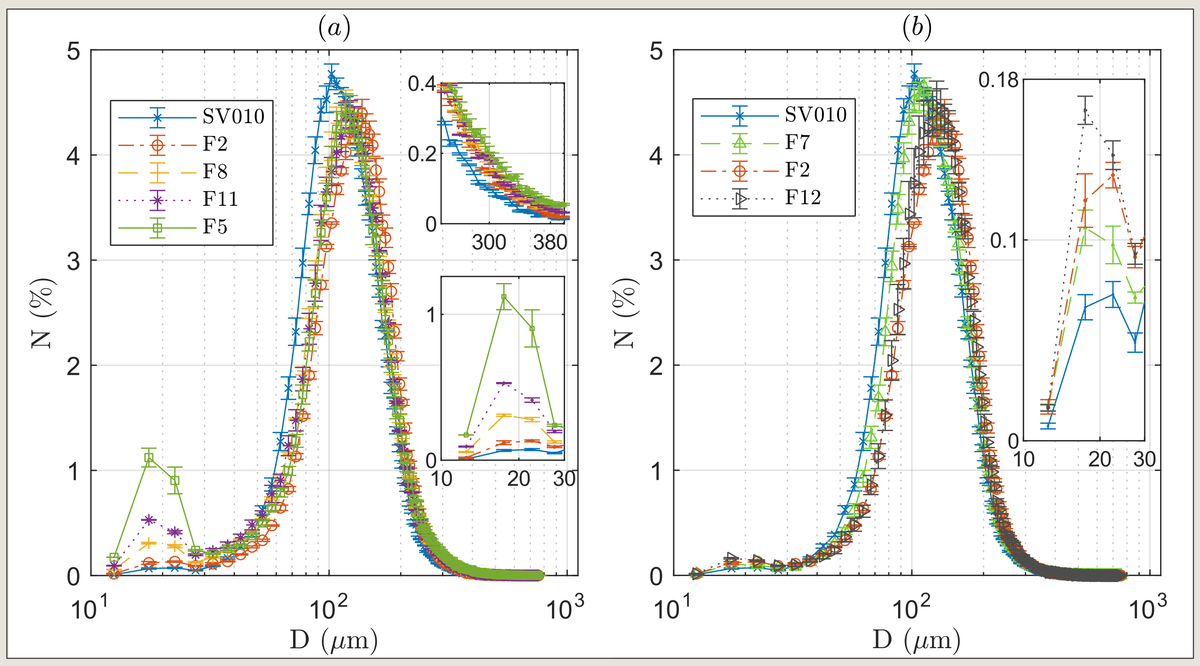

Fig. 3. Number-based PSD inside the DPI at 30 LPM. Formulations with 2.75% SS and varying LH300 content are shown in (a), while formulations with no LH300 and varying SS content are shown in (b).

CONCLUSION

- This study has investigated the use of high-speed imaging for particle sizing inside of a transparent DPI for a range of powder formulations. The technique is capable of detecting the influence of fine drug particles (e.g., 1% SS) on the PSD.
- Increasing number-fractions were observed with increasing fine content for D <30 μm, as well as detectable differences in the PSD for larger particles and agglomerates.
- The results provide evidence that such imaging methods have potential to be used for investigating how changes in powder formulations can result in differences in DPI aerosolization performance. By directly imaging inside of the device, it provides an avenue to experimentally investigate the physical mechanisms behind such differences.

ACKNOWLEDGMENTS

U.S. Food and Drug Administration through Contract 75F40123C00201

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