Effect of varying inflow conditions on pharmaceutical powder dynamics in inhaler-like flows

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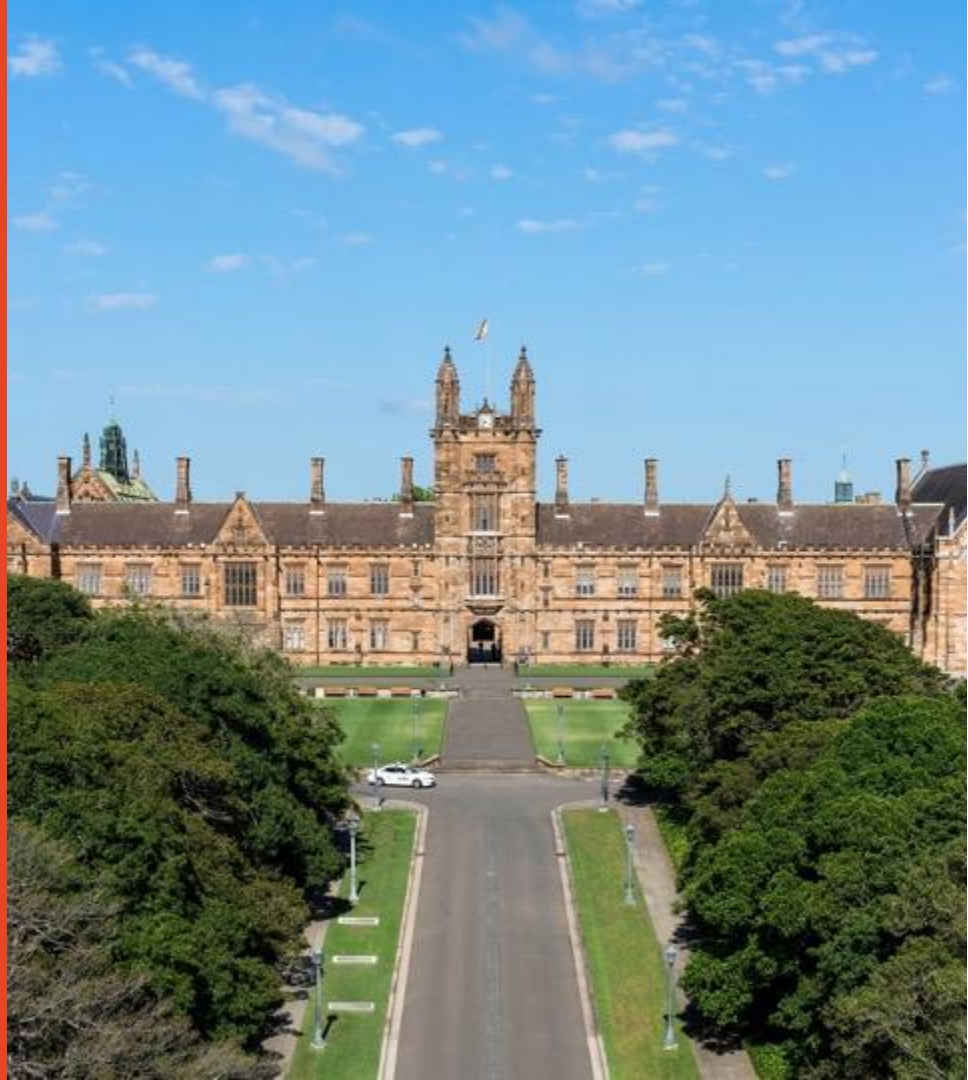
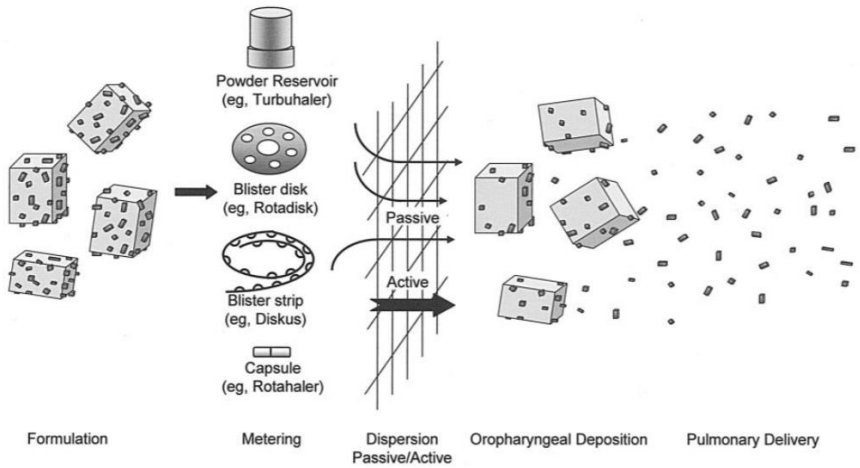


Structure

- Introduction
- Experimental Setup
- Discussion – Far-field Imaging
- Discussion – High-speed Microscopic Imaging
- Conclusion

Introduction



- Market share for DPI is estimated to reach 912.3 million USD by 2026. Approximately 40-45 % accounts for asthma patients and COPD patients
- The efficiency of the DPI's depends on the inhalation profile and device design, and could go as low as 10-20 %

Advantage

- Formulation stability
- Rapid dose administration
- Minimum cleaning
- Automatic synchronisation between inhalation and drug delivery

Challenges

- Adequate inhalation pressure to achieve high de-agglomeration and drug deposition
- High mouth to throat losses
- Low lung delivery
- High inter-subject variability

Objectives

- To develop an improved understanding of the evolution of pharmaceutical drug powders inside inhalers; provided through high-speed imaging in well-controlled particle laden flows
- To establish a database for the fluidization of API powders in typical inhaler-like devices that is amenable to modelling and that serves as a platform for the development of DPI designs and predictive tools

Experimental Setup

- ❑ Device Design
- ❑ Powder Properties & Flow Conditions
- ❑ Imaging Setup

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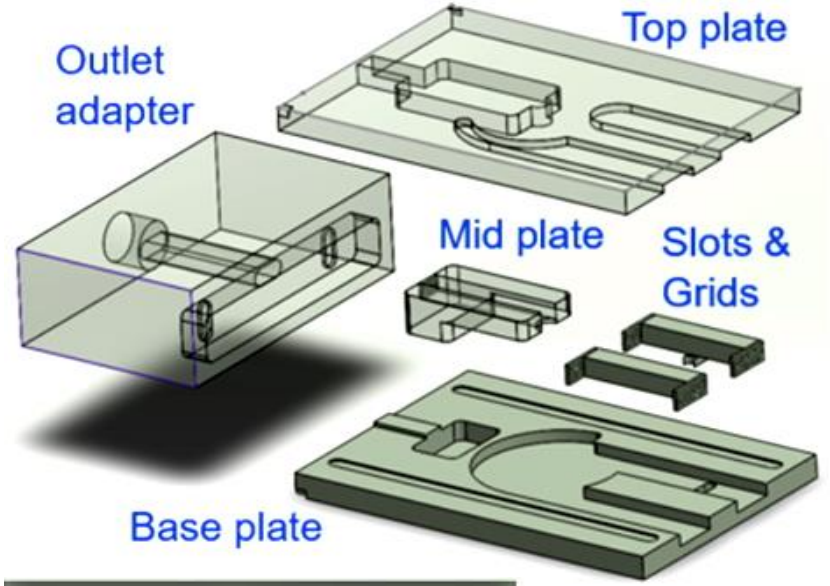
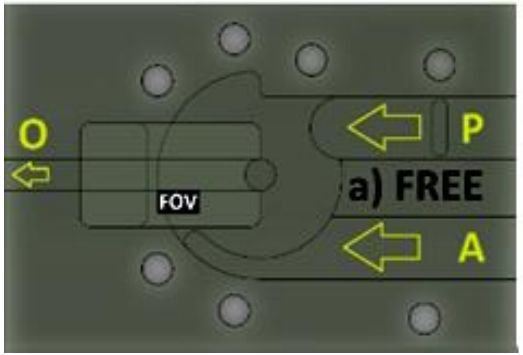
Device Design

- The channel dimensions for inlet ‘A’ and ‘P’ are : 12x5 mm. The outlet ‘O’ has 5x6 mm cross section
- Inlet ‘P’ has a powder insert 2mm deep and located at 14mm downstream of the inflow entrance. It depicts a typical Size-3 DPI capsule
- Inlet ‘A’ is offset by 4mm to create clockwise swirl



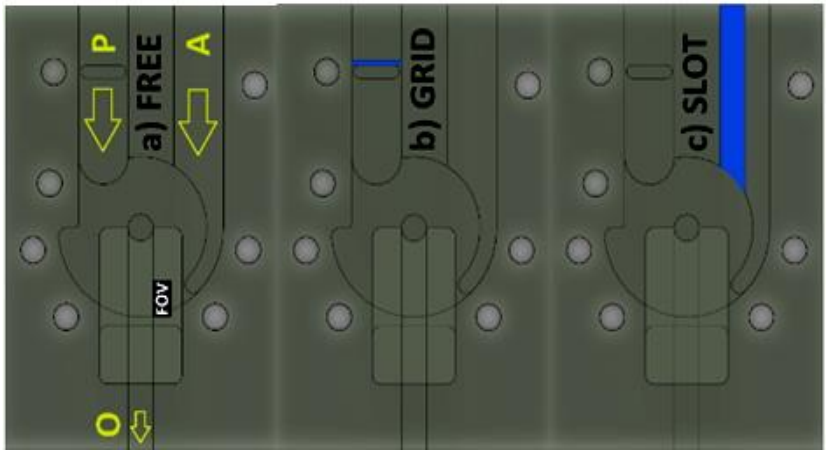
A – Air Inlet
P – Powder with Air
O – Outflow



Powder Properties & Flow Conditions

- Mannitol powder with following size : D_{10} – 0.9 um, D_{50} – 3um
- For each inhalation cycle 3 repetitions are performed by uniformly spreading 40mg of M3 in the powder insert and all inhalation are done at 120 slpm flowrate
- For 'M3-G120', a grid is placed downstream of the powder insert
- For 'M3-S120', a slot is inserted at inlet 'A'

Cases	a) M3-120	b) M3-G120	c) M3-S120
Outlet (g/min)	151	151	151
Outlet (m/s)	69	69	69
Outlet Re	25275	25275	25275
Inlet A (m/s)	17	17	33
Inlet A Re	9765	9375	12132
Inlet P (m/s)	17	45	17
Inlet P Re	9765	25432	9375



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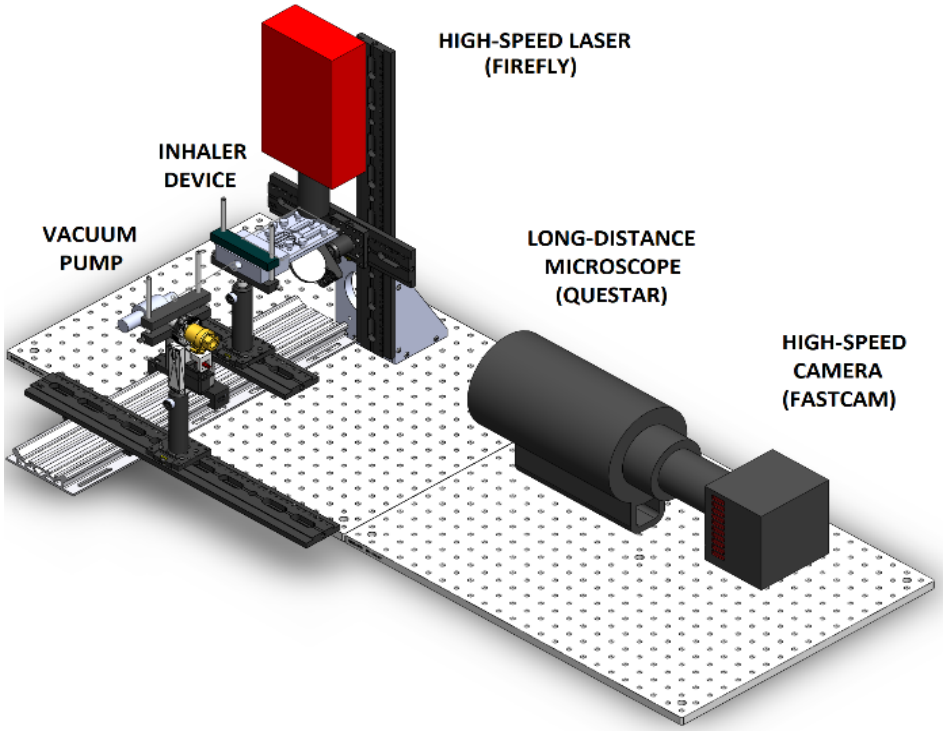
Imaging Setup

- The imaging setup consists of :
  - Optical inhaler (discussed earlier)
  - A vacuum pump (for suction)
  - High-speed camera (Photron Fastcam AX100) coupled with Microscope (Questar QM100)
  - High-speed laser (Oxford Firefly – 300W, double pulsed Diode Laser)
- Frame rate – 7200 fps
- Image Size – 4.8 x2.8 mm (1024x608 pixels)
- 18000 images are collected for each inhalation repetition



Results & Discussion

- ❑ Far-field Imaging
- ❑ High-speed Microscopic Imaging
- ❑ Evolution of Powder Dispersion
- ❑ Conclusion

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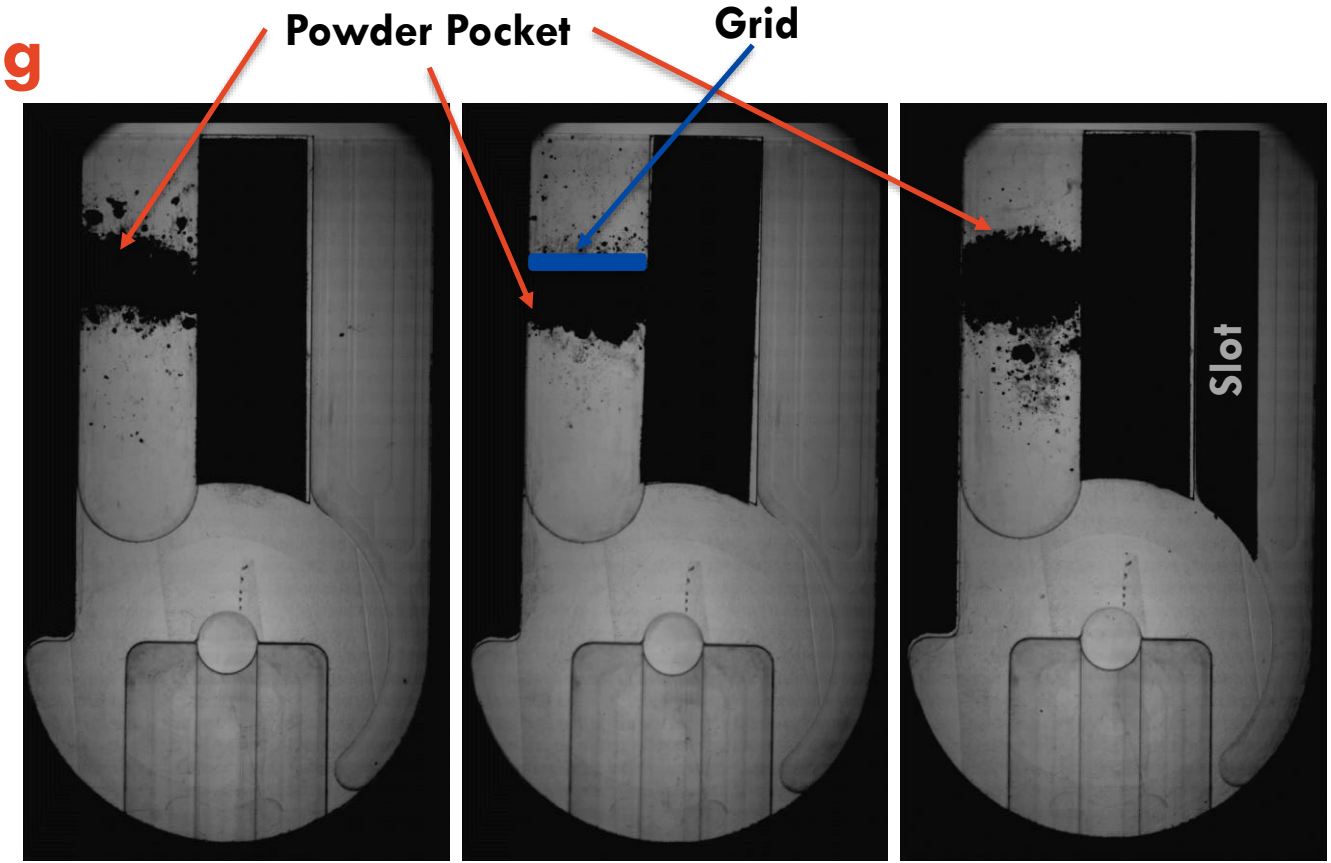
Far-field Imaging

- The fine particle fraction is more in M3-G120 and M3-S120 compared to M3-120
- The structure of swirl is more concentric in M3-120 and M3G120 compared to M3-S120



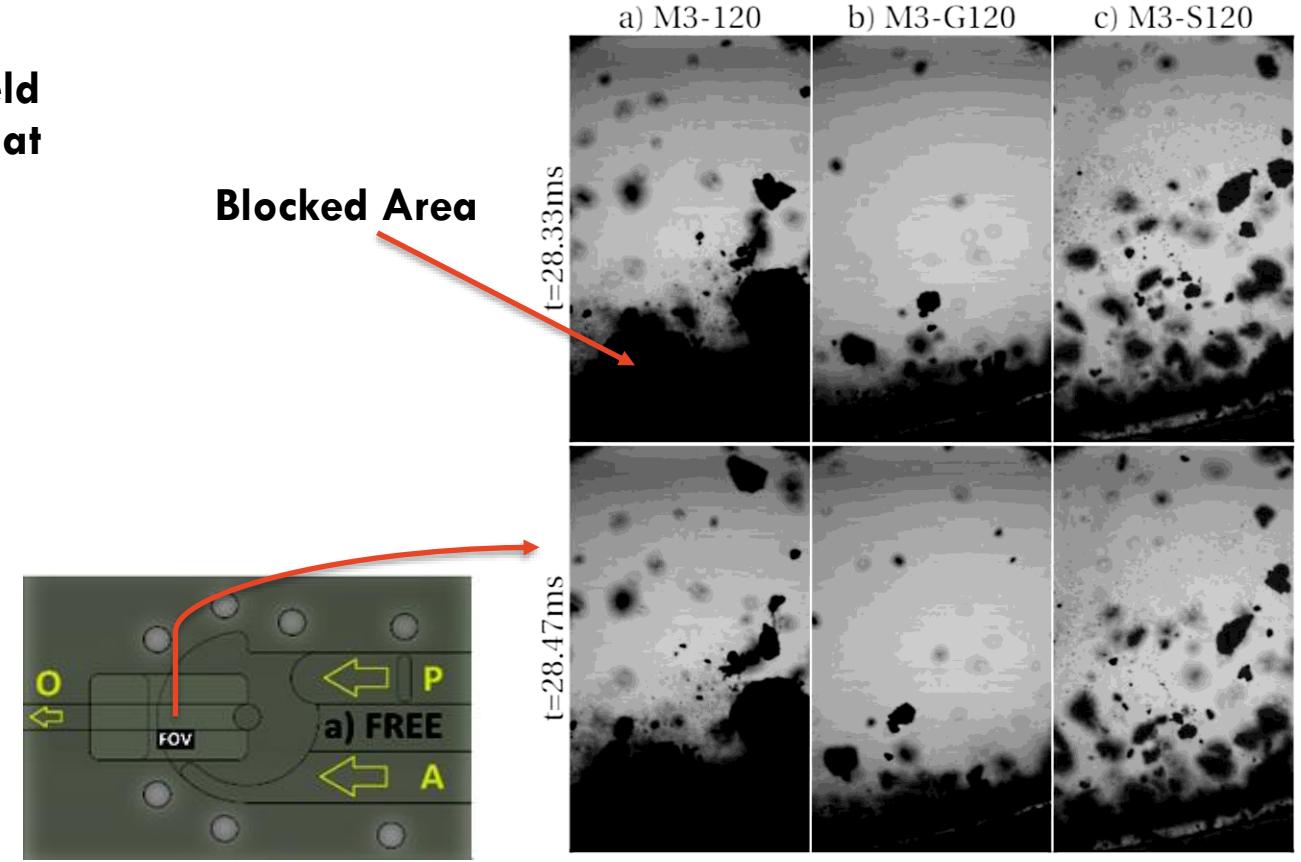
The air flow from both slots generates swirl, which enhances fluidization

The powder pocket empties faster compared to M3-120, and the size of the particles is smaller

The swirl is not concentric, few large agglomerates doesn't fluidize properly

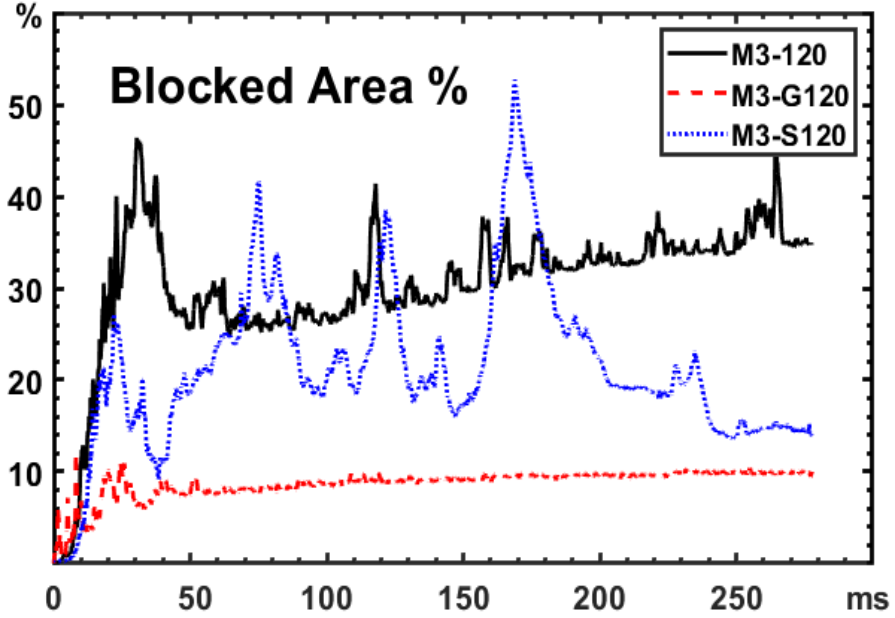
High-speed Microscopic Imaging

- The figure shows instantaneous near-field images of the devices at 28.33 and 28.47 milliseconds after initiation for all three cases M3-120, M3-G120, and M3-S120
- Similar fragment sizes are observed for all three cases (large agglomerates surrounded by fine praticles)



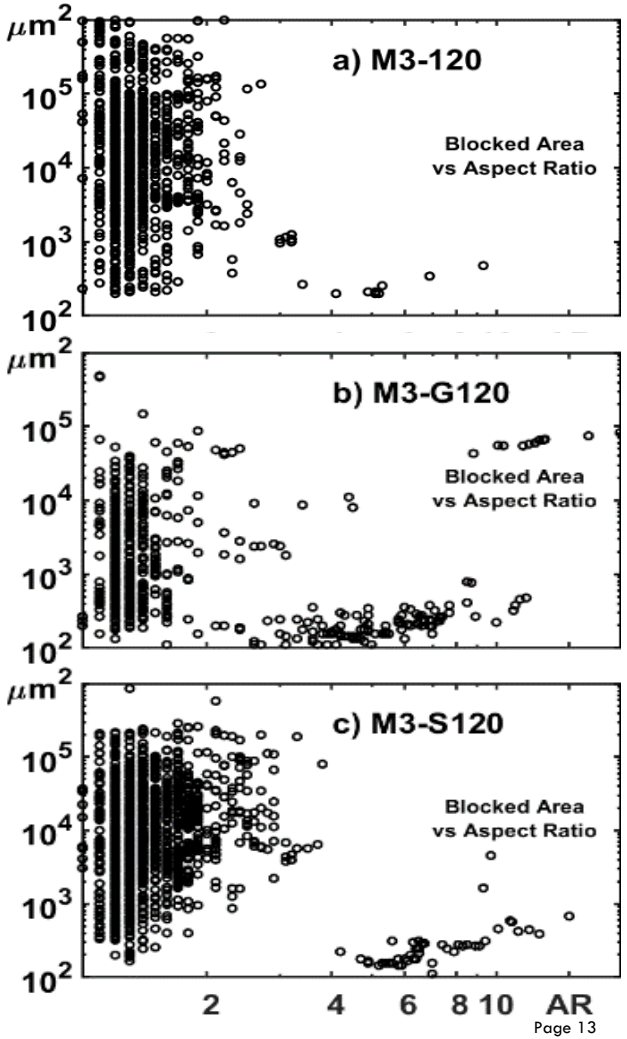
Evolution of Powder Dispersion

- For M3-120, the blocked area reaches a peak around 30ms after initiation
- After peak inhalation the blocked area remains between 30-35%
- For M3-G120, the peak blocked area drops to 10% due to lack of large agglomerates inside the vortex chamber
- Large unsteadiness in the blocked area is observed for M3-S120 doe to less concentric swirl vortex
- Due to this large agglomerates sporadically collide with the walls of mixing chamber



Evolution of Powder Dispersion

- The figure presents the population distribution of blocked area vs the aspect ratio
- In case of M3-120, the population of large agglomerates is lower. However the overall size is on the higher side as compared to M3-G120
- Due to high fine particle fraction, the particle population in M3-G120 case is low. But some large fragments are also observed
- For case M3-S120, the population distribution is towards the higher size due to presence of large agglomerates caused by the lack of concentric swirl



Conclusion

- The experimental platform makes a contribution towards better characterizing some of the key dynamic behaviors of pharmaceutical powders in inhaler designs
- The full imaging dataset quantifies the behavior of the dispersed phase formation in inhaler devices with respect to key variables, including inflow conditions, powder composition and inhalation (outflow) profiling
- It demonstrates that dynamic behavior of inhalable powders can be controlled through modification of inflow conditions.

Thank You

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