Evaluation of the Fast Screening Impactor with Dry Powder Inhalers

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Introduction

The Fast Screening Impactor (FSI, Copley Scientific, UK) is an abbreviated impactor measurement (AIM) device for quick analysis of orally inhaled drug products (OIDPs) such as dry powder inhalers (DPIs)[1]. For fine particle fraction (FPF) measurements, the FSI uses a pre-separator insert plate with a cutoff of 5 µm at a specified flow rate. However, the cutoff efficiency of the FSI may be dependent on other factors such as DPI formulation, dead space, and pre-separator base coatings [2-4]. In this study, the FSI device and a variation of this device (FSI-2) using Advair® Diskus® 100/50 (100 µg fluticasone propionate and 50 µg salmeterol) inhalation powder were evaluated and the data compared to full resolution impactors (Andersen Cascade Impactor, ACI, and Next Generation Impactor, NGI) as well as another AIM device (reduced-NGI, rNGI).

Sample

- Advair® Diskus® 100/50 (100 µg fluticasone propionate and 50 µg salmeterol)

Method

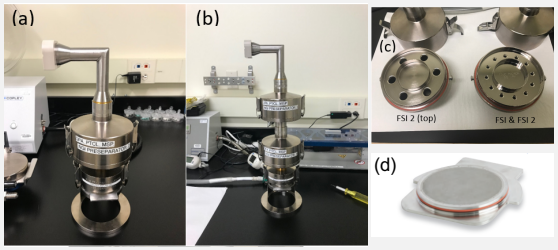


Figure 1: (a) FSI fully assembled showing pre-separator loaded with a 5 µm at 60 L/min cutoff insert, (b) FSI-2 fully assembled showing two pre-separators, the top loaded with a standard 6 hole insert and the bottom loaded with the same 5 µm cutoff insert as the FSI setup, (c) Image showing the two types of inserts, standard (left) and 5 µm cutoff (right), (d) Image of filter holder for the FSI setup.

Advair® Diskus® 100/50 units (GlaxoSmithKline, Research Triangle Park, NC, USA) from the same lot have been tested in this study. Each unit was tested by ACI, NGI, rNGI, FSI, and FSI-2 using a flow rate of 60 L/min for 4 seconds. The units were tested upon receipt (0 timepoint) and after 1 and 3 months stored under accelerated conditions (40°C and 75% RH). FSI-2 is a variation of FSI where the standard pre-separator is utilized in addition to a pre-separator, using a 5 µm cutoff insert (Figure 1). According to the manufacturer, this adds dead space volume and has been shown to improve correlation with NGI when testing DPIs [2]. Two doses were actuated for each impactor experiment with a 30 seconds delay between each actuation. Pre-separators were filled with 10 mL of the diluent prior to each run and no coating was used on the base plate. High performance liquid chromatography (HPLC) was performed on the particles collected from each stage or glass fiber filter to determine percentage of emitted dose (% label claim) and the fine particle fraction percentage less than 5 µm (FPF% ≤ 5 um). It is important to note that the rNGI used a cutoff of 4.46 µm for FPF%.

The glass fiber filters from the FSI and FSI-2 setups were examined in separate experiments using the Malvern Morphology M4 (Malvern Panalytical, UK). The Raman spectra of particles collected on the filter were measured with a 785 nm monochromatic laser.

Results

Fine Particle Fraction Percentage of Label Claim Comparison

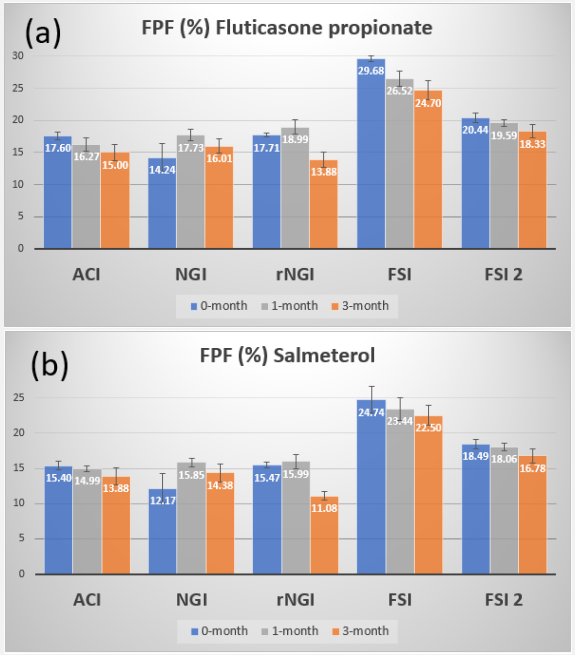
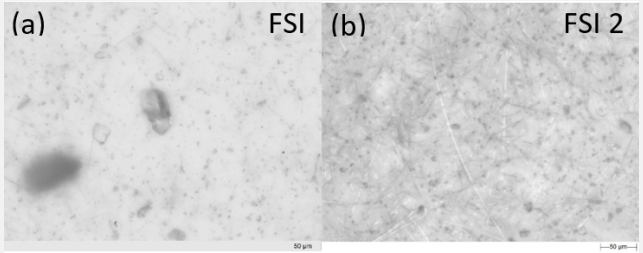


Figure 2. Fine particle fraction (% emitted dose) results comparison of Advair® Diskus® 100/50 for full impactors (ACI and NGI) and abbreviated impactors (rNGI, FSI, and FSI-2) at time points 0, 1, and 3-month for (a) fluticasone propionate and (b) salmeterol. Error bars represent 1-sigma.

Morphology and Raman Spectroscopy



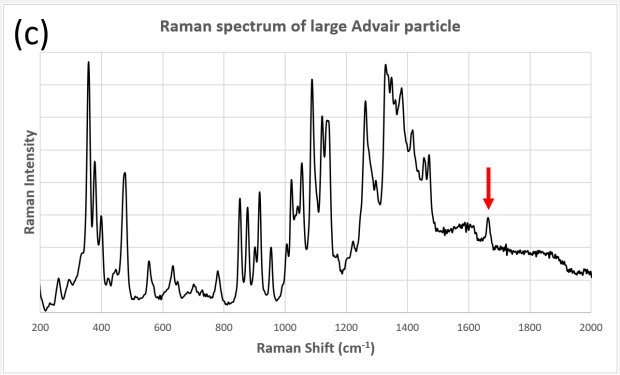


Figure 3. (a) Microscopy image of the filter paper after one FSI run using an inhaler randomly selected from timepoint 3-month batch, (b) microscopy image of the filter paper after one FSI-2 run using the same inhaler, (c) Raman spectrum of the large particle in the center of image (a). Most of the spectrum is associated with lactose (excipient), however the red arrow indicates the highest intensity Raman peak for fluticasone propionate (one API of Advair® Diskus®).

- Both the FSI and FSI-2 setup reported higher FPF than the other full resolution (NGI, ACI) and abbreviated impactors (FSA), with FSI-2 setup reporting slightly less FPF than the standard FSI (Fig. 2). This observation is consistent with previous FSI results on DPIs from other experiments [3].
- Particles larger than 5 µm were observed via optical microscopy images on the glass fiber filter images from the FSI run (Fig. 3a). The FSI-2 setup eliminated many of the very large particles (>50 µm), but still allowed particles in the range of 5-20 µm to reach the filter (Fig. 3b).
- A Raman spectrum was taken on the large particle in the center of the FSI filter image (Fig. 3a), showing the lactose excipient signal and a fluticasone propionate peak (indicated by a red arrow, Fig. 3c) located at a Raman shift of 1663 cm^{-1} [5].

References

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Conclusion

- The standard FSI setup resulted in 8 to 15% higher FPF% values compared to full resolution cascade impactors (NGI and ACI) for fluticasone propionate and salmeterol inhalation powder.
- The FPF% was found to be in better agreement if two pre-separators are used (FSI-2 setup, Figure 1b), however the measurements still showed a higher API concentration than the NGI and ACI.
- AIM methods need to be validated before used for product development and quality control purpose.

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