Single-nozzle impactor for aerosol collection with subsequent spectroscopic and ultramicroscopic characterization

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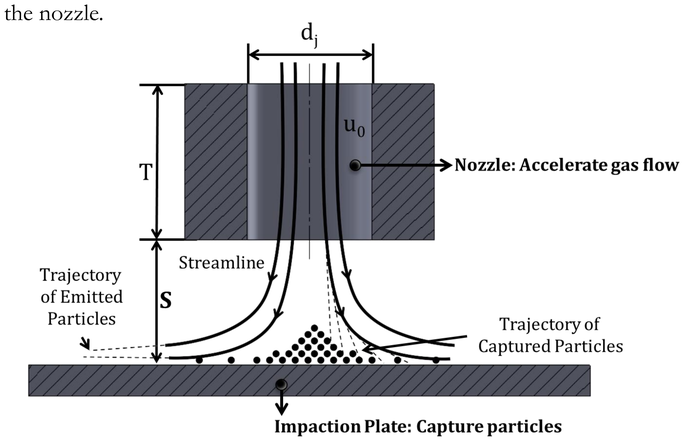
Introduction

Respirable dosage forms delivered by pressurized metered dose inhalers (pMDI) or dry powder inhalers (DPI) are the most commonly used forms of medication for treatment of asthma and chronic obstructive pulmonary diseases. Properties of drugs in these devices need to be tested during shelf life and simulated usage, because the properties of the dispersed particles are directly related to efficacy in patients.[1] Analysis of bulk properties, e.g., composition, demands a large amount of particles, which need to be gathered with a suitable sampling technique, ideally from a single actuation of a delivery device.

Inspired by cascade impactors, which is traditionally used for particle size measurement, a new impactor was designed to concentrate the highly dispersed aerosol particles.

Materials and Methods

❖ Aiming for a sharp collection efficiency curve, the impactor was designed to meet the following criteria [2], in which *Re* is the Reynold's number of gas flow in the nozzle.



$$500 \le \mathrm{Re} \le 3000 \qquad S/d_j \ge 1 \qquad T/d_j \ge 1$$

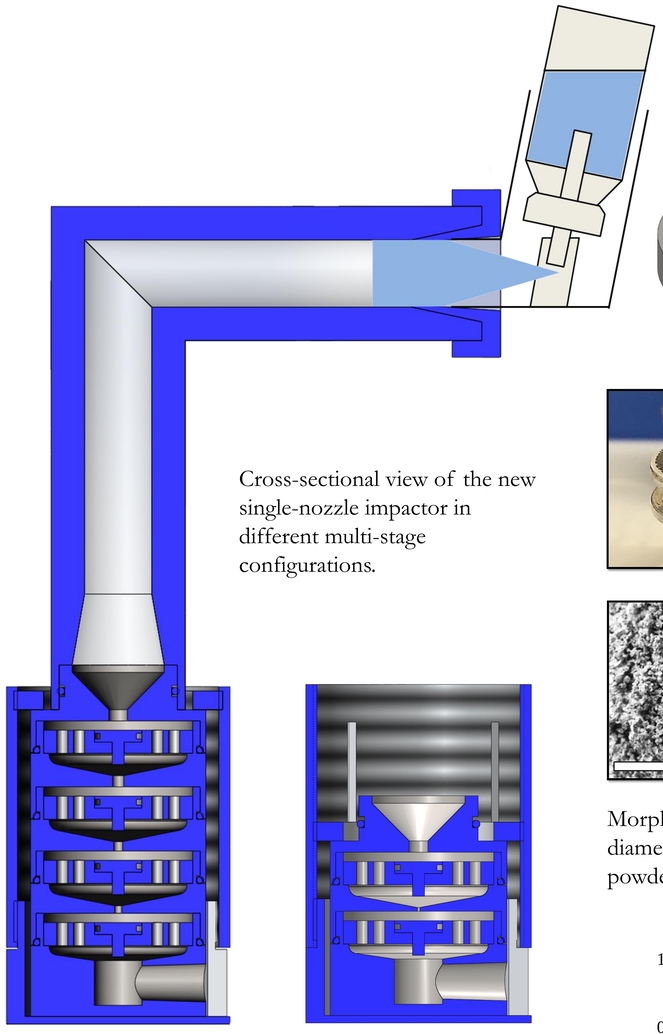
❖ pMDI Seretide® 250 Evohaler® (GSK) containing 250µg fluticasone propionate and 25µg salmeterol xinafoate per dose was used to produce dispersed respirable aerosol particles.

❖ The designed impactor in single stage configuration was used to collect one dose of aerosolized particles for subsequent spectroscopic and ultramicroscopic characterization.

❖ A custom designed dispersive macro-Raman system [3] was used for characterizing powders collected by the new impactor and also powders extracted from frozen pMDI by cutting the canister..

❖ Collected particles were imaged on standard SEM collection stubs by a scanning electron microscope (EVO MA10, Zeiss).

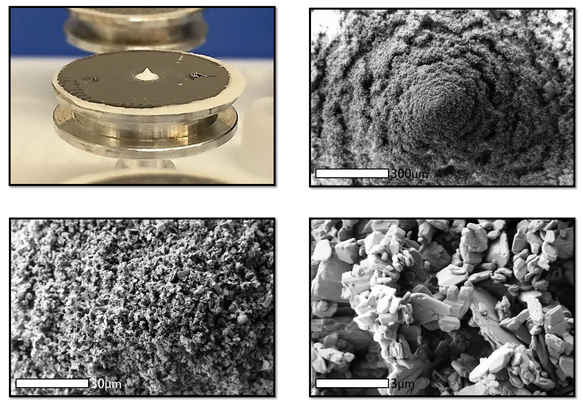
Results



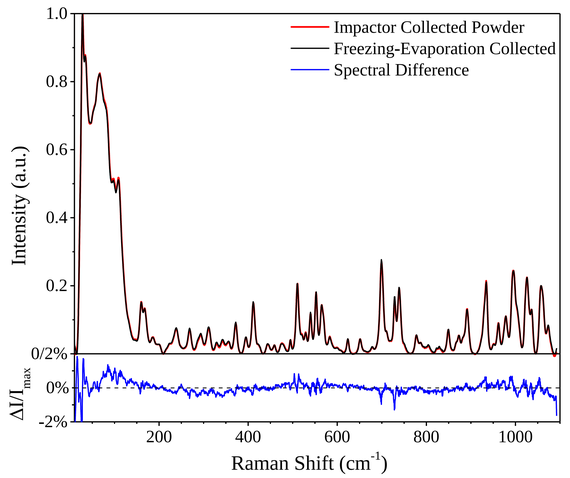
Cross-sectional view of the new single-nozzle impactor in different multi-stage configurations.

Stage	d_j(mm)	T(mm)	Re	S/d_j	T/d_j	$d_{a,50}$ (µm)
0	4.95	3.00	142	0.51	0.61	21.1
1	3.00	3.00	234	0.83	1.00	9.92
2	2.40	2.50	292	1.04	1.04	7.08
3	1.90	2.00	369	1.32	1.05	4.96
4	1.65	2.00	425	1.52	1.21	4.00
5	1.40	1.50	501	1.79	1.07	3.12
6	1.20	1.50	585	2.08	1.25	2.45
7	1.00	1.00	702	2.50	1.00	1.84
8	0.85	1.00	825	2.94	1.18	1.43
9	0.70	1.00	1002	3.57	1.43	1.05
10	0.60	1.00	1169	4.17	1.67	0.82
11	0.50	1.00	1403	5.00	2.00	0.60

Specifications of the designed impactor for a flow rate of 0.5L/min. Twelve stages cover $d_{a,50}$ from 0.60µm to 21.1µm.



Morphology of collected particles on Stage #9 with cutoff diameter $d_{a,50}$=1.05µm. Approximately 200µg/275µg of powders were collected based on one dose.



Well overlapped Raman spectra of powders prepared by different methods: single actuation sampling using the designed impactor *versus* the standard freezing-cutting-evaporation-extraction method.

Conclusions

❖ The new single-nozzle impactor is suitable for collection of aerosol particles for subsequent characterization, *e.g.*, spectroscopic and ultramicroscopic characterization.

❖ Its excellent aerosol concentration capability enables representative, non-destructive, and convenient sample preparation of aerosol particles for characterization techniques requiring bulk powders.

❖ Particle sizing over diameter range of 0.6µm to 10µm is possible by using the multi-stage configuration.

❖ Application examples:

1) Time-dependent stability studies on respirable dosage forms: reduced cost, better sample consistency in comparison to mostly used destructive sampling from multiple canisters, which may have inter-canister sample variations.
2) Size-dependent composition study:
   - test of homogeneity across different size classes;
   - size dependent solid phase changes.

References

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3. Wang H, Boraey MA, Williams L, Lechuga-Ballesteros D, Vehring R: **Low-frequency shift dispersive Raman spectroscopy for the analysis of respirable dosage forms.** *Int J Pharm* 2014, **469:**197-205.

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