Atomic Force Microscope-Infrared Spectroscopy as a Powerful Tool to Study the Distribution of Fluticasone Propionate/Salmeterol Xinafoate/Lactose Monohydrate in Advair Diskus 100/50 Formulations

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Introduction

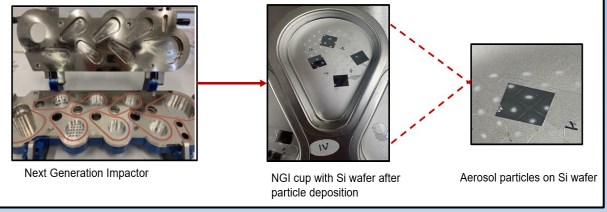
- Atomic Force Microscopy coupled with infrared spectroscopy (AFM-IR) is a powerful technique that provides better chemical sensitivity and spatial resolution than conventional vibrational methods.
- AFM-IR can be used to evaluate physicochemical properties of population of aerosolized particles emitted by a dry powder inhaler (DPI) as well as colocalization of particles.

Objective

- Characterize the particle distribution and co-localization of fluticasone (FP), salmeterol (SX), and lactose monohydrate (L) in Advair Diskus 100/50 (FP; SX inhalation powder).
- Obtain consistent chemical maps and infrared spectra.

Materials and Methods

- Deposition of aerosol particles on silicon (Si) wafer using Next Generation Impactor (NGI) with pre-separator at a flow rate of 60 L/min.
- AFM-IR was performed in tapping mode using a gold-coated silicon probe (Model: PR-UM-TnIR-D-10) and a scan rate of 0.2 Hz.



Materials and Methods cont'd.

Icon-IR AFM-IR instrument (Bruker, Santa Barbara, CA, USA) used for analysis.

Results and Discussion

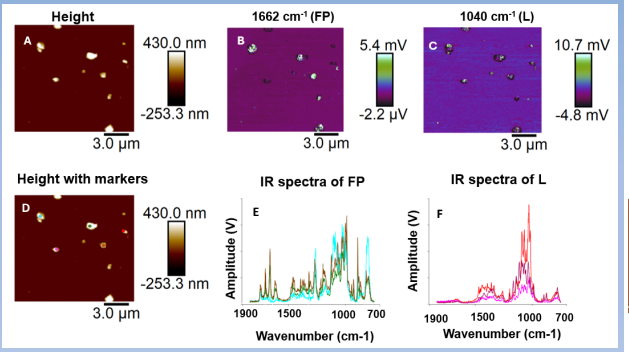


Figure 1 *Aerosolized Advair Diskus 100/50 particles collected on a Si wafer substrate within NGI Stage 6 showing FP and L. (A) Height image (B) 1662 cm^{-1} (FP) intensity chemical map, (C) 1040 cm^{-1} (L) intensity chemical map, (D) height map showing the regions for spectral acquisition, (E) IR spectra of FP, and (F) IR spectra of L.*

Results and Discussion cont'd.

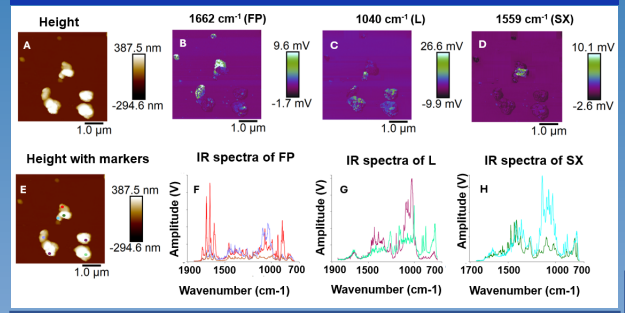


Figure 2 *Aerosolized Advair Diskus 100/50 particles collected on a Si wafer substrate within NGI Stage 6 showing FP, L and SX. (A) Height image, (B) 1662 cm^{-1} (FP) intensity chemical map, (C) 1040 cm^{-1} (L) intensity chemical map, (D) 1559 cm^{-1} (SX) intensity chemical map, (E) height image showing locations of spectral acquisition, and (F-H) selected IR spectra of FP, L, and SX.*

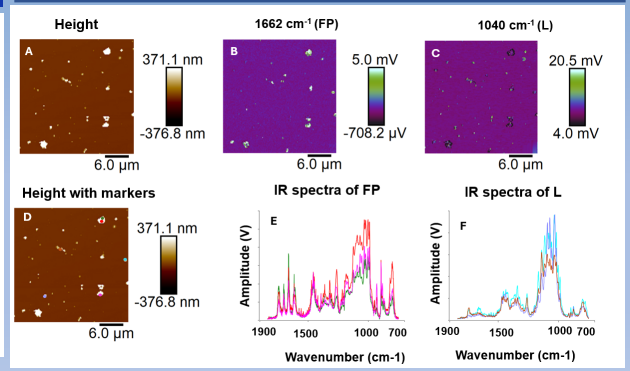


Figure 3 *Aerosolized Advair Diskus 100/50 particles collected on a Si wafer substrate within NGI Stage 7. (A) Height map, (B) 1662 cm^{-1} (FP) intensity chemical map, (C) 1040 cm^{-1} (L) intensity chemical map, (D) height map showing the regions for spectral acquisition, (E) IR spectra of FP, and (F) IR spectra of L.*

Results and Discussion cont'd.

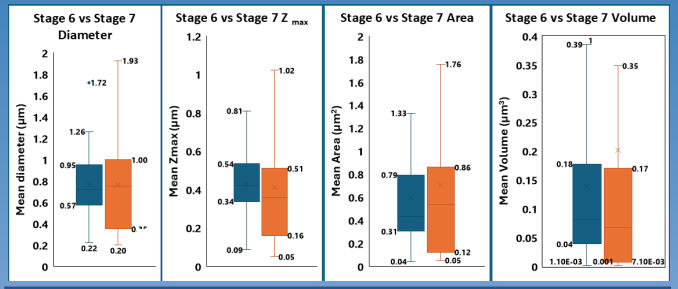


Figure 4 *Comparison of particle sizes on NGI Stage 6 (S6) and Stage 7 (S7) via box-and-whisker plots: (A) S6 vs. S7 diameter, (B) S6 vs. S7 particle height (Z max), (C) S6 vs. S7 Area, and (D) S6 vs. S7 Volume (total of 60 particles considered from single NGI run [n=60]; two Si wafers each from S6 and S7; Plot line: median, X: mean, box: lower 25% and upper 75% quartiles, whiskers: min and max values).*

Summary

- The chemical maps are consistent with IR spectra.
- FP colocalized with L (Fig 1-Fig 3), and FP together with SX also colocalized with L (Fig 2).
- The average particle heights were 0.42 µm and 0.356 µm for S6 and S7, respectively (p=0.41).
- The average diameters of the particles were 0.72 µm and 0.75 µm, respectively (p=0.45).
- S6 volumes (0.082 µm^3 avg) are slightly larger than S7 (0.067 µm^3 avg) (p-value 0.14), more particles are needed to test convergence of mean and dispersion values.

Reference

- Khanal D, Zhang J, Ke W-R, Banaszak Holl MM, Chan H-K. Anal Chem. 2020;92:8323–32.

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