The Use of Atomic Force Microscope-Infrared Spectroscopy to Assess Co-localization of Fluticasone Propionate/Salmeterol Xinafoate/Lactose Monohydrate in Advair Diskus 100/50 and Wixela Inhub 100/50

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Introduction

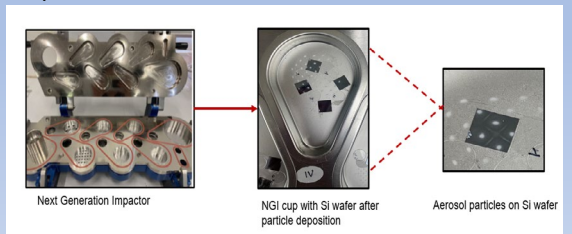
- Atomic Force Microscopy coupled with infrared (IR) spectroscopy (AFM-IR) is a powerful technique that provides better chemical sensitivity and spatial resolution than conventional vibrational methods [1].
- AFM-IR can evaluate the physicochemical properties of a dry powder inhaler (DPI) across the population of aerosolized active pharmaceutical ingredient (API) and excipient particles.
- AFM-IR works by measurement of photothermal expansion of samples when heated up by wavelength tunable IR laser.

Objectives

- Employ AFM-IR to characterize the particle distribution and co-localization of fluticasone propionate (FP), salmeterol xinafoate (SX), and lactose monohydrate (L).
- Assess the ability of AFM-IR to evaluate brand-name and generic drug formulations of FP; SX inhalation powders: Advair Diskus 100/50 and Wixela Inhub 100/50.

Materials and Methods

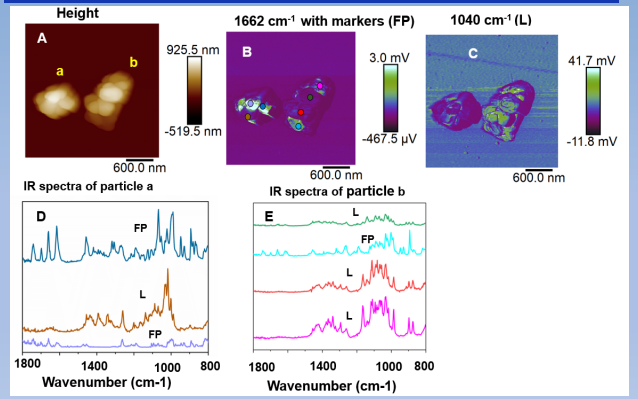
- Deposition of aerosol particles on silicon (Si) wafer using Next Generation Impactor (NGI) with pre-separator under a flow rate of 60 L/min.



Materials and Methods cont'd.

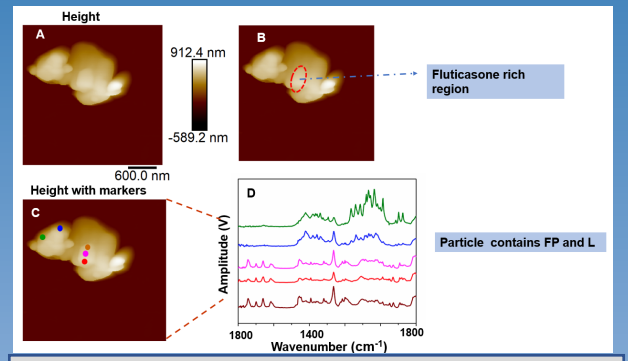
Icon-IR AFM-IR instrument (Bruker, Santa Barbara, CA, USA) used for analysis.

Results and Discussion

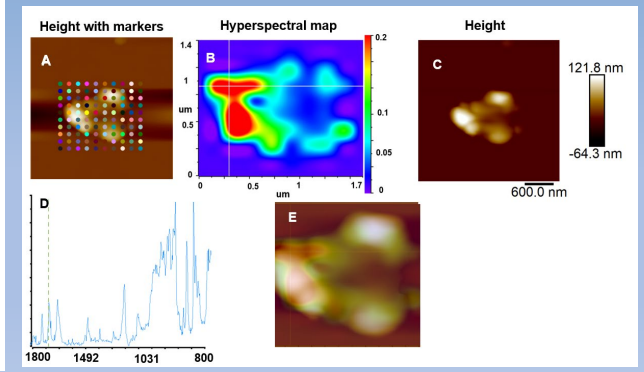


Wixela Inhub 100/50 particles on a Si wafer substrate obtained from NGI Stage 6. (A) Height image (B) 1662 cm^{-1} (FP) intensity chemical map showing the regions for spectral acquisition, (C) 1040 cm^{-1} (L) intensity chemical map, (D) IR spectra of particle a, and (E) IR spectra of particle b.

Results and Discussion cont'd.

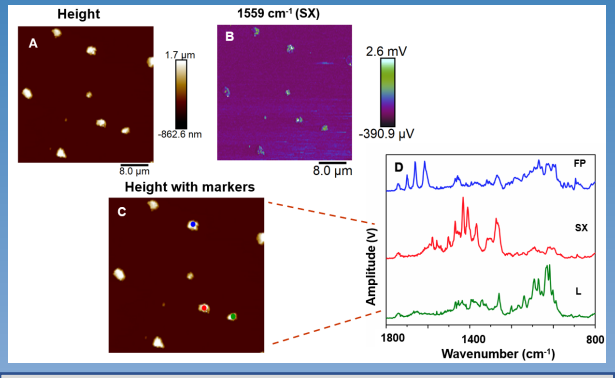


Wixela Inhub 100/50 particles on a Si wafer substrate obtained from NGI Stage 6. (A) height image, (B) height image showing the location of FP crystal, (C) height image showing locations of spectral acquisition, and (D) selected IR spectra.



Wixela Inhub 100/50 particles on a Si wafer substrate obtained from NGI Stage 7. (A) Height map showing the regions for hyperspectral acquisition, (B) hyperspectral map, (C) height map, (D) IR spectra indicating presence of FP, and (E) Hyperspectral map overlaid on height map.

Results and Discussion cont'd.



Advair Diskus 100/50 particles on a Si wafer substrate obtained from NGI Stage 6. (a) Height image, (b) 1559 cm^{-1} (SX) intensity chemical map, (c) Height map showing the regions for spectral acquisition, and (d) IR spectra revealing the presence of FP (blue), SX (red), and L (green).

Summary

- Tapping mode based on photothermal AFM-IR was performed to explore particle morphology and API-API and API-excipient co-localization of FP, SX, and L.
- Detailed information about micron-scale particle agglomerates obtained including sub-particle sizes and content can provide greater insight to DPI product performance.

Reference

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

Acknowledgments

- U.S. Food and Drug Administration (FDA) through Contract 75F40122C00202.

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