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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Identification of Drug Distribution in Aerosols
A Nanospectroscopy and NanoThermal Analysis

INTRODUCTION

- Atomic Force Microscopy coupled with infrared (IR) spectroscopy (AFM-IR) provides better chemical sensitivity and spatial resolution than conventional absorption-based IR microscopy [1].
- AFM-IR can evaluate the physicochemical properties of a dry powder inhalation 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.

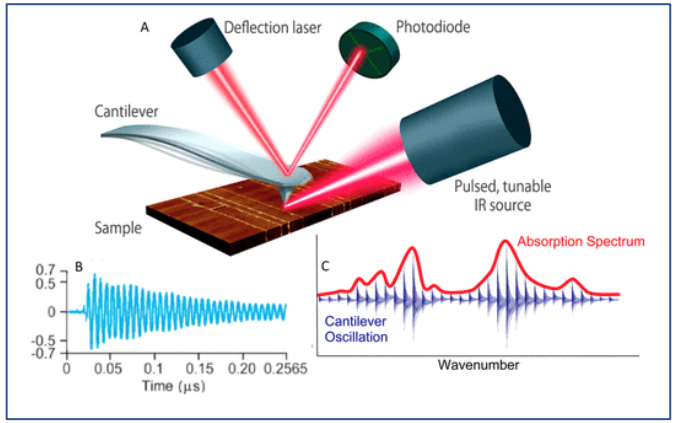


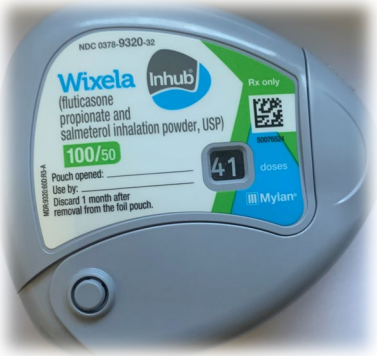
Image courtesy of Bruker Instruments

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

OBJECTIVES

- Employ AFM-IR to characterize the particle distribution and co-localization of fluticasone propionate (FP), salmeterol xinafoate (SX), and lactose monohydrate (L) present in dry powder inhalers (DPIs).
- Assess the ability of AFM-IR to evaluate brand-name and generic drug formulations

Advair Diskus 100/50

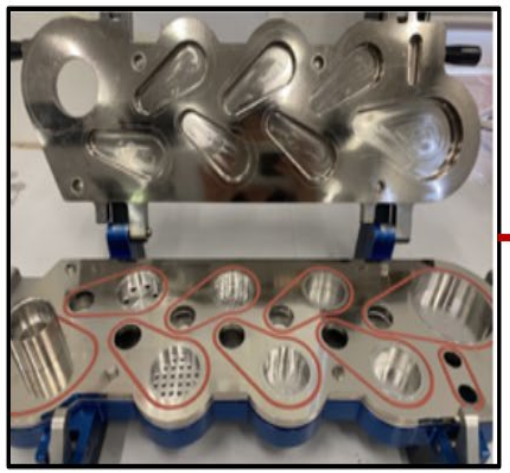


Wixela Inhub 100/50

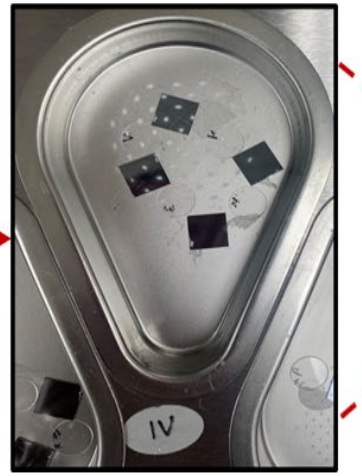
Fluticasone Propionate; Salmeterol Xinafoate Inhalation Powders

MATERIALS AND METHODS

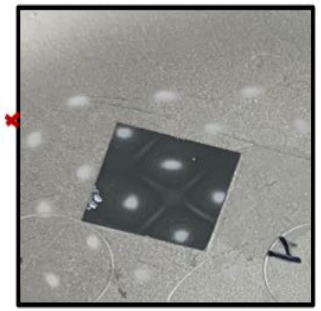
- Deposition of aerosol particles on Si wafer using ***Next Generation Impactor (NGI)***



Next Generation Impactor



NGI cup with Si wafer after particle deposition



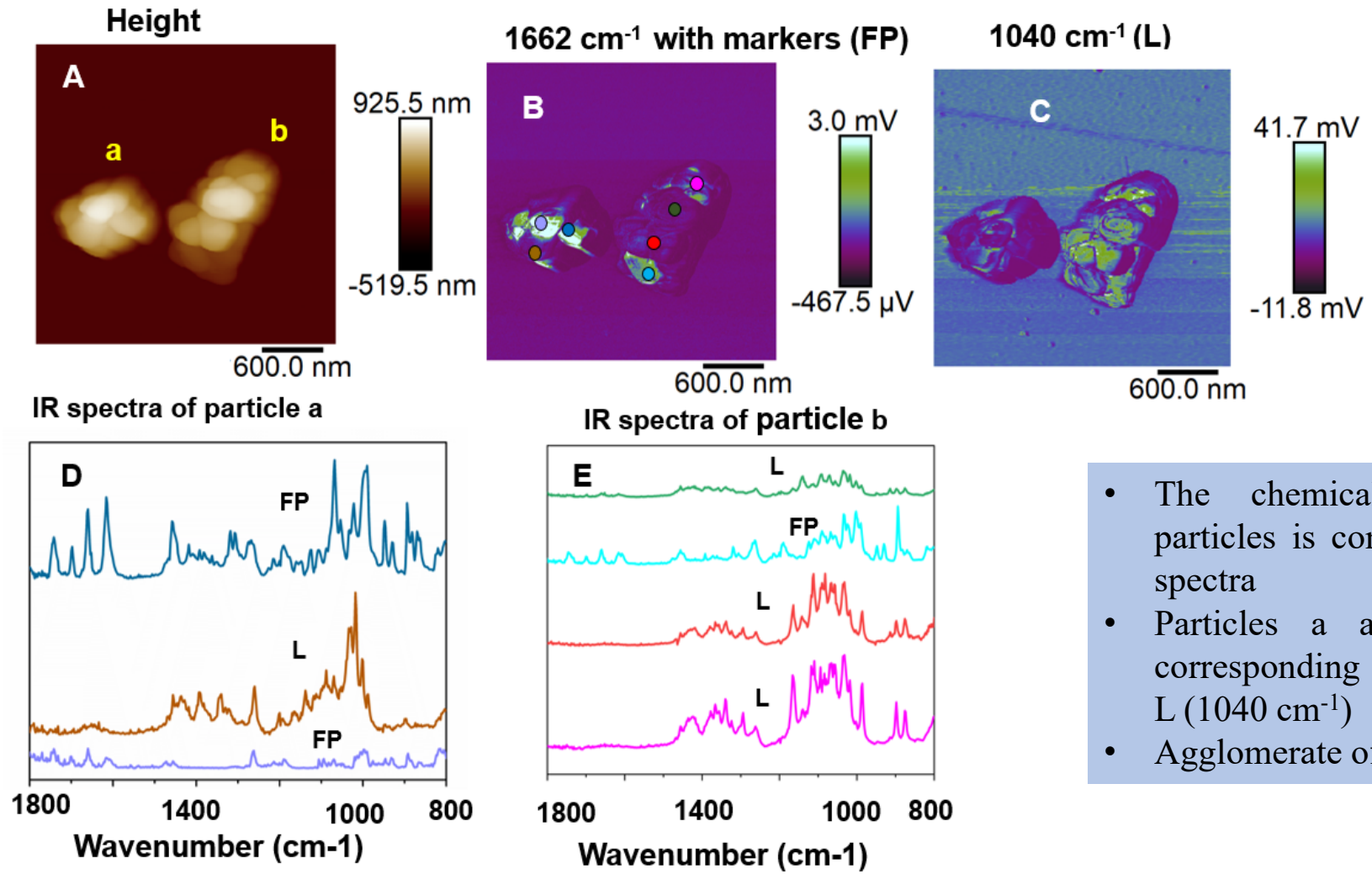
Aerosol particles on Si wafer

- Analysis of aerosol particles using AFM-IR

Icon-IR AFM-IR instrument (Bruker, Santa Barbara, CA, USA)

RESULTS AND DISCUSSION

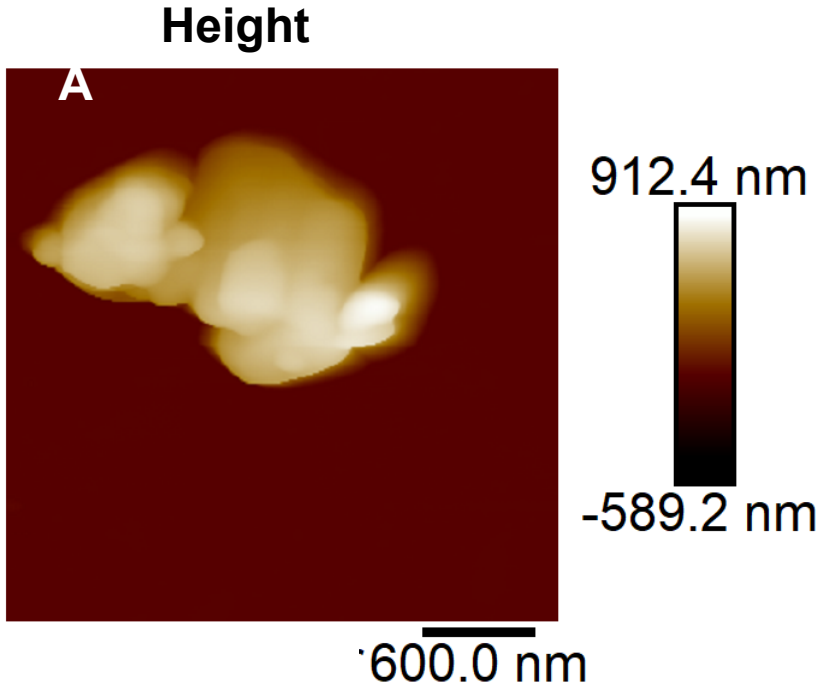
AFM-IR Analysis of Wixela Inhub 100/50 (FP; SX inhalation powder), Stage 6 of NGI (60 L/min)



- The chemical mapping of the particles is consistent with the point spectra
- Particles a and b show spectra corresponding to FP (1662 cm^{-1}) and L (1040 cm^{-1})
- Agglomerate of 50-200 nm particles

Wixela Inhub 100/50 particles on a silicon wafer substrate obtained from NGI Stage 6. (a) Height image with markers (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



Fluticasone rich region

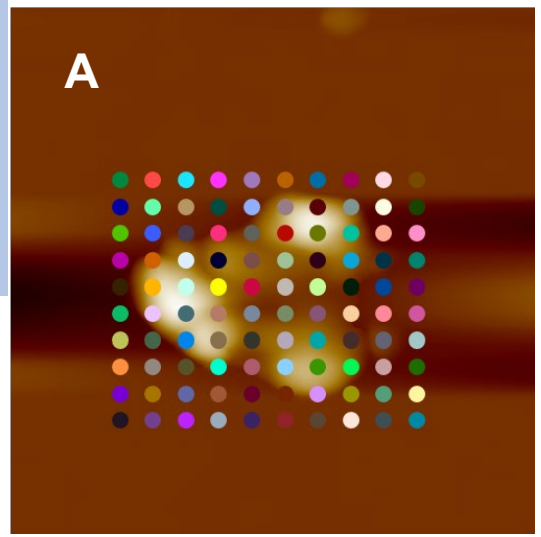
AFM-IR Analysis of Wixela Inhub100/50 (FP; SX inhalation powder), Stage 6 of NGI (60 L/min)

Agglomerate particle contains FP and L

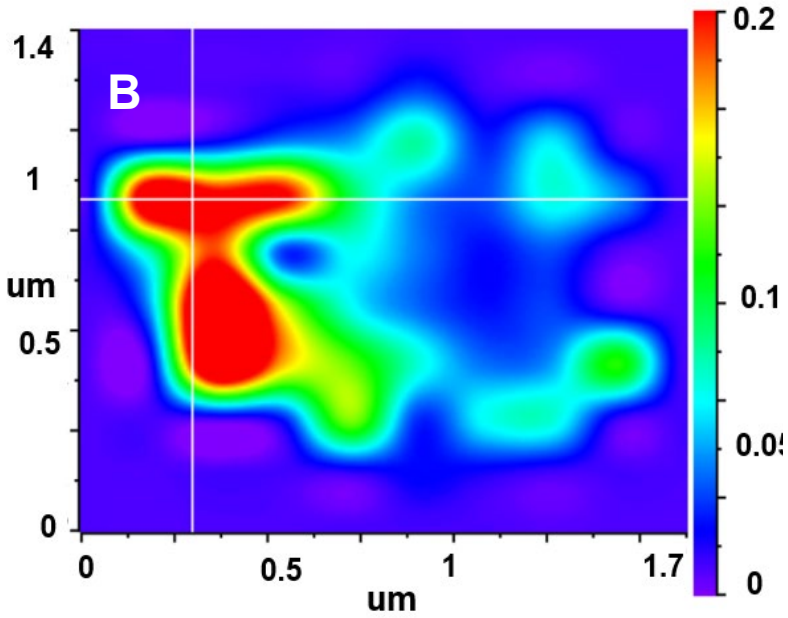
RESULTS AND DISCUSSION

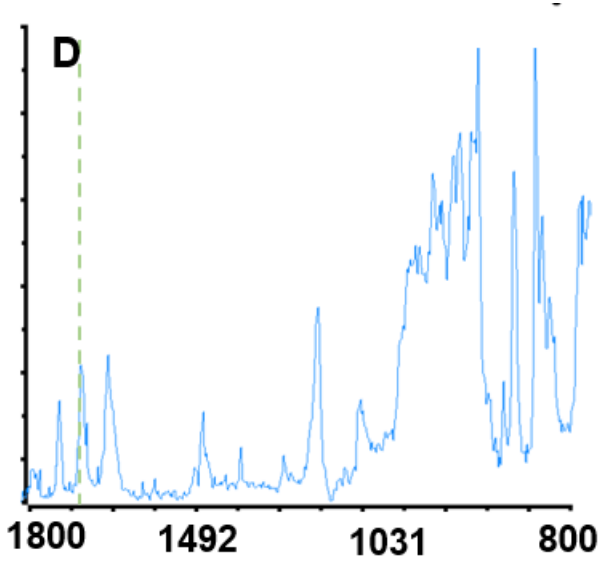
AFM-IR Analysis of Wixela Inhub 100/50 (FP; SX inhalation powder), Stage 7 of NGI (60 L/min)

Height with markers



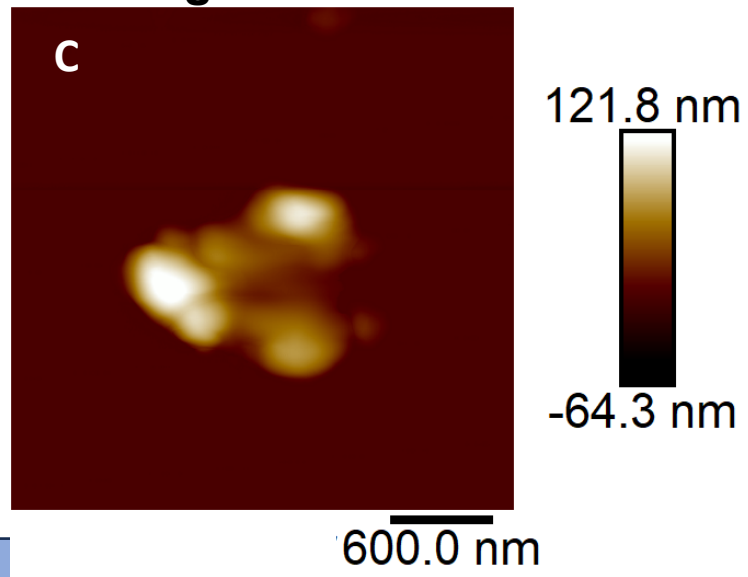
Hyperspectral map

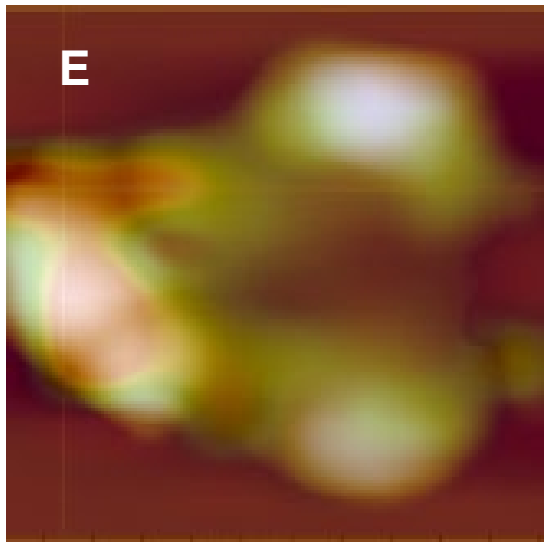




Samples/line=512

Height



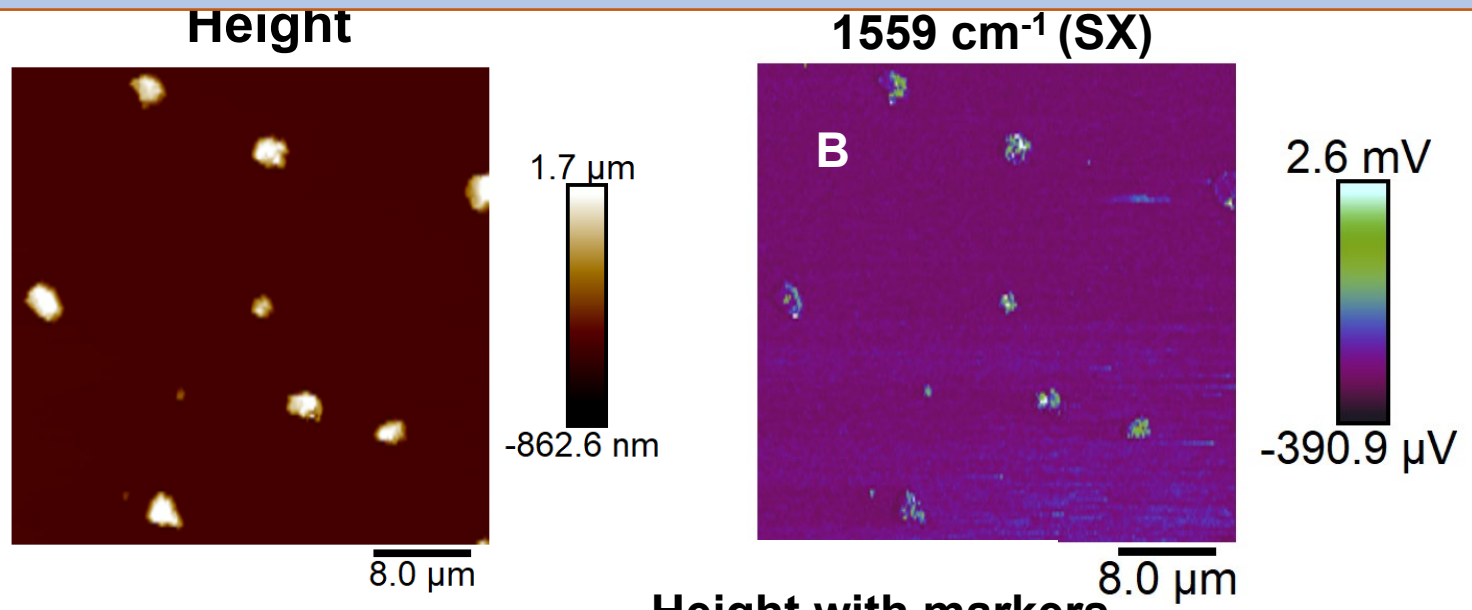


Wixela Inhub 100/50 particles on a silicon wafer substrate obtained from NGI Stage 7. (a) Height map showing the regions for hyperspectral acquisition, (b) hyperspectral map, (c) height map, (d) IR spectra indicating presence of FP and (e) hyperspectral map overlaid on height map.

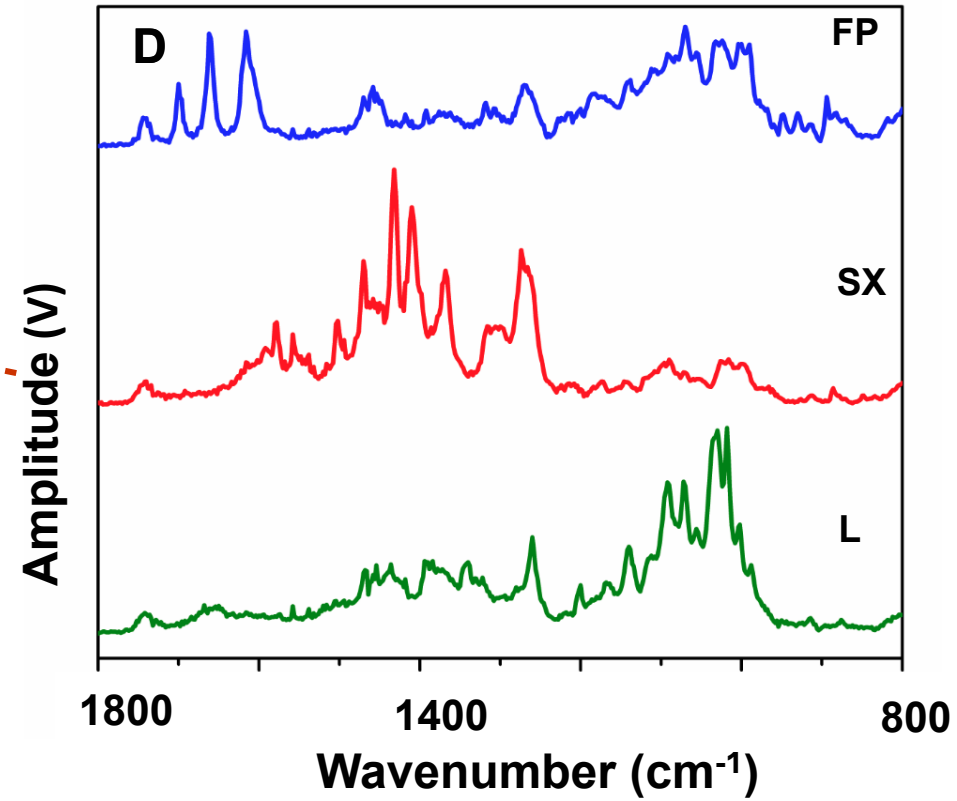
RESULTS AND DISCUSSION

AFM-IR Analysis of Advair Diskus 100/50 (FP; SX inhalation powder), Stage 6 of NGI (60 L/min)

Advair Diskus 100/50 particles on a silicon wafer substrate obtained from NGI Stage 6 (60 L/min). (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).



- The chemical mapping of the particles is consistent with the point spectra
- Spectra from FP, SX, and L are obtained



CONCLUSION

- Tapping mode 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 and can provide greater insight to DPI product performance.

ACKNOWLEDGMENTS

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