

Comparison of Generic and Brand Name Dry Powder Inhalers: Advanced Insights Using Optical Photothermal Infrared Microscopy

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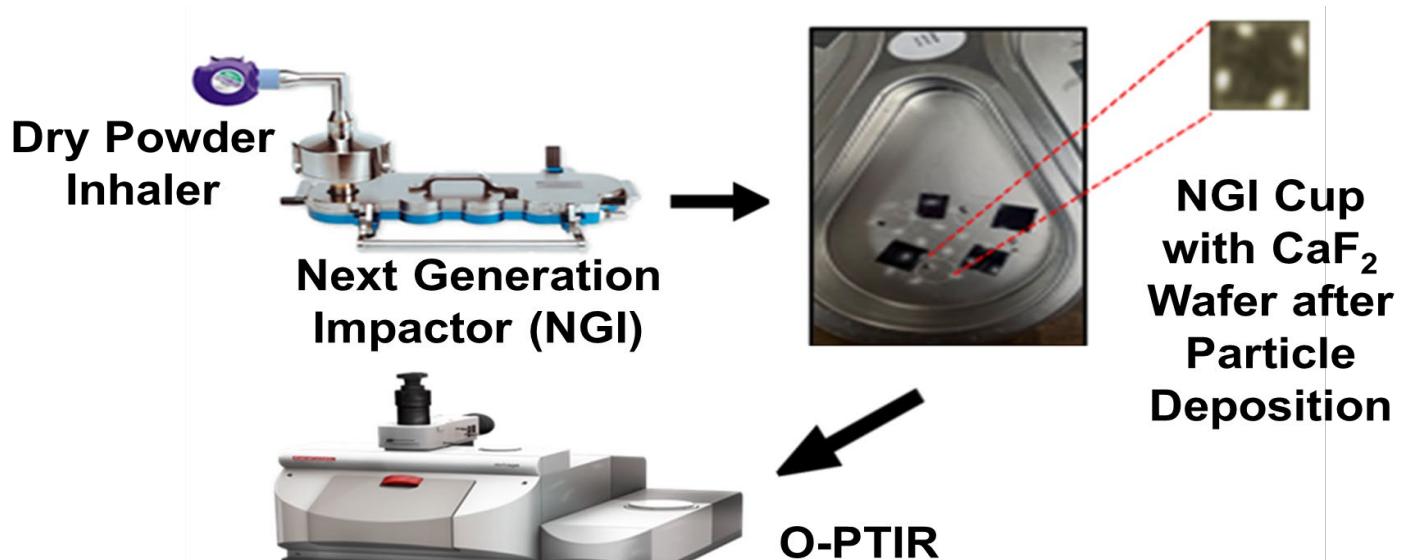
Introduction

Dry powder inhalers (DPIs) are pivotal for the effective delivery of medications for asthma and chronic obstructive pulmonary disease (COPD). Optical photothermal infrared (O-PTIR), a submicron IR microscopy technique with a spatial resolution of less than 500 nm [1], was employed to produce insights on the agglomeration behavior of generic and brand name fluticasone propionate (FP); salmeterol xinafoate (SX) DPIs.

Objective

Employ O-PTIR to characterize the spectroscopic diameter, integrated intensity, drug co-localization, and drug-excipient interactions of aerosolized particles of FP, SX, and lactose monohydrate (L) from brand name (Advair Diskus, AD) and generic name (Wixela Inhub, WI) DPIs.

Material and Methods

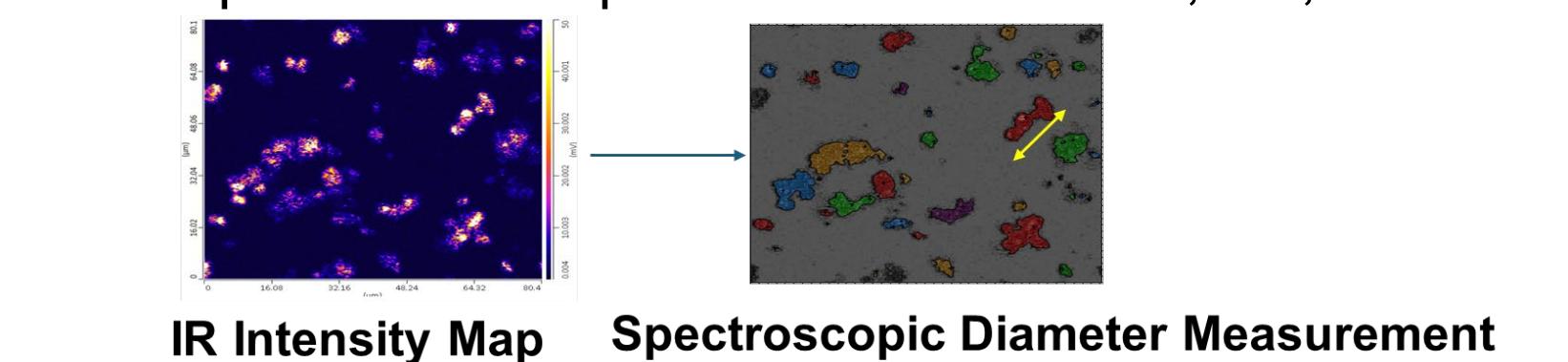


Generic and brand name L-based FP and SX DPIs were dispersed using the Next Generation Impactor (NGI) to separate particles based on their aerodynamic size across stages 1 to 7, over CaF₂ substrates. A single actuation of each inhaler was used for dispersion at a flow rate of 60 L/min. The aerosol particles were then evaluated to analyze their composition and morphology.

Understanding Key Terms

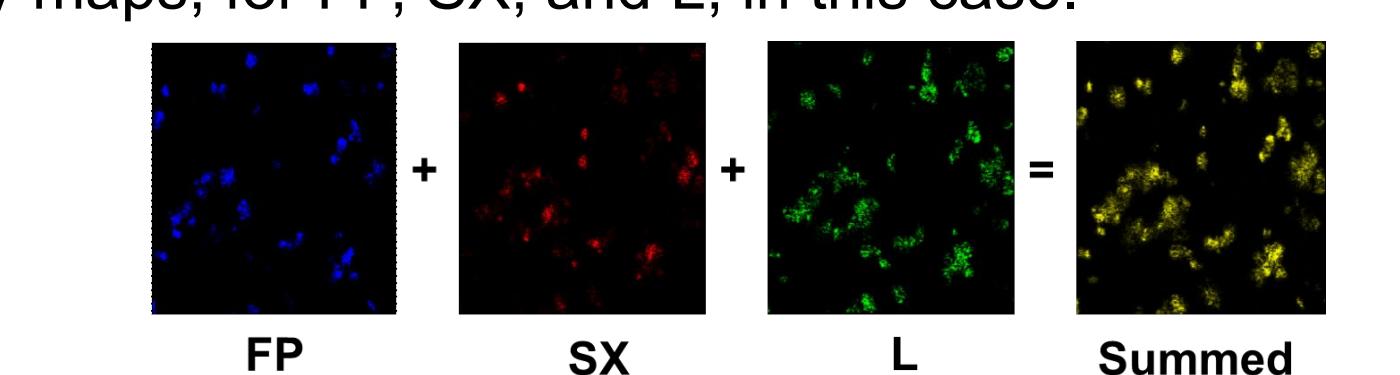
What is Spectroscopic Diameter?

Spectroscopic Diameter is derived from IR intensity maps employing wavenumbers specific for the particle of interest: FP, SX, or L.



What is Summed Spectroscopic Diameter (SSD)?

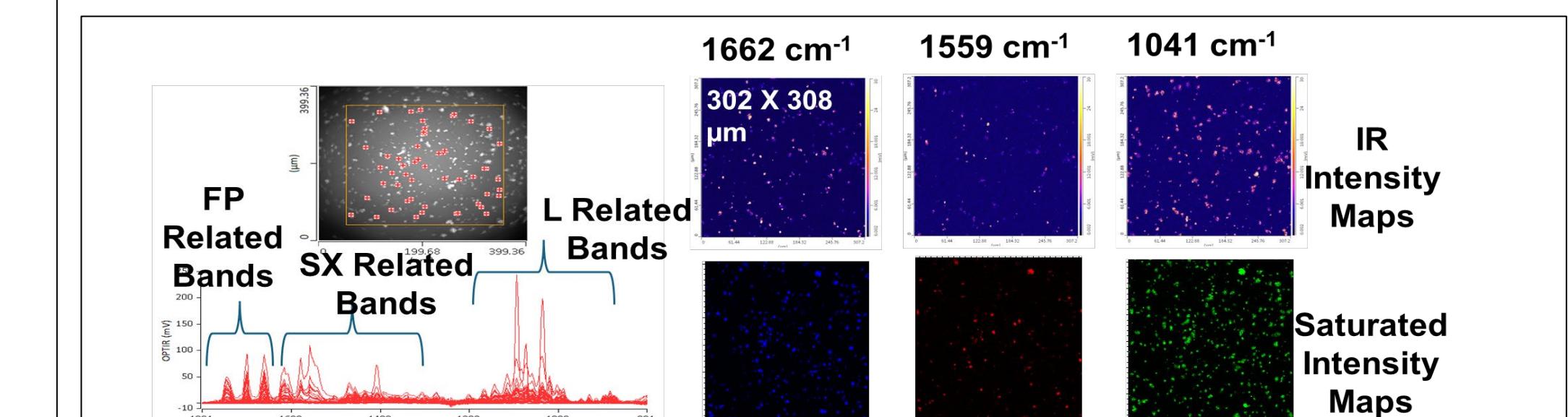
SSD is derived from the mathematical addition of the individual IR intensity maps, for FP, SX, and L, in this case.



What is Integrated Intensity?

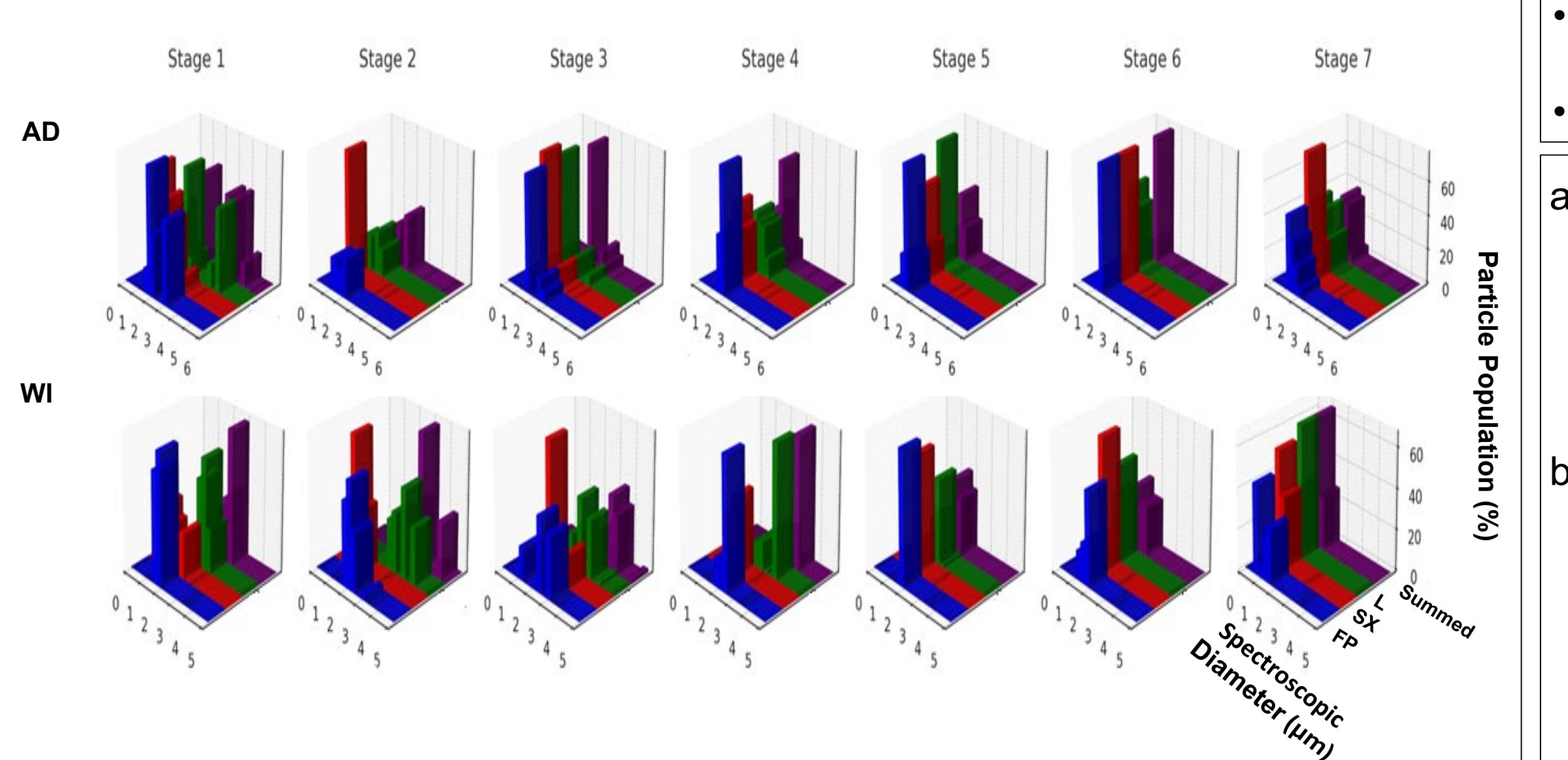
Integrated intensity is the addition of all pixel intensities in a particle focused on a specific wavenumber: FP, SX or L.

Results and Discussion



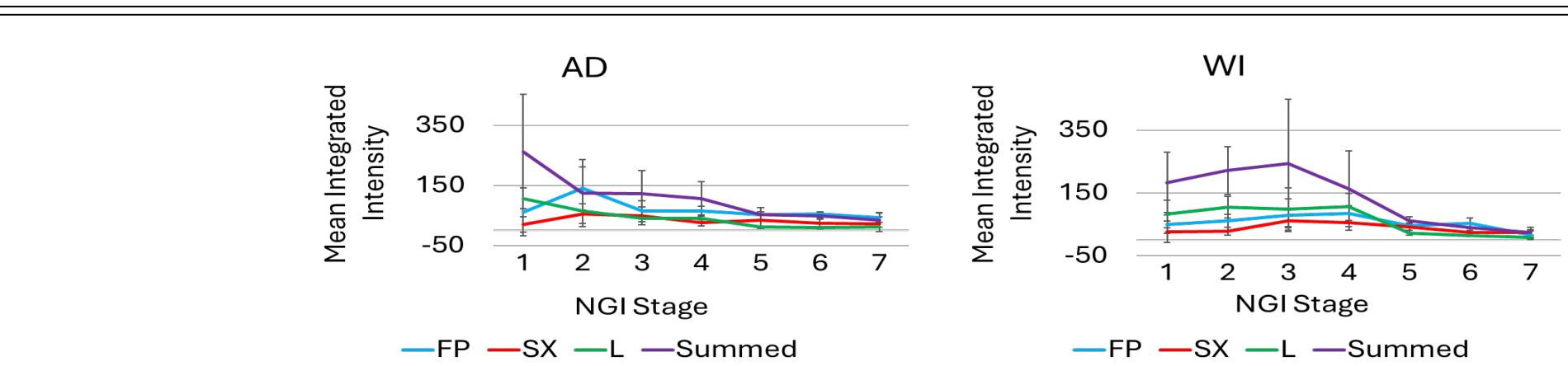
Representative optical microscopy images from O-PTIR. The spectra highlight FP, SX, and L bands. Single-wavenumber IR intensity maps were collected at 1662 cm⁻¹ (FP), 1559 cm⁻¹ (SX), and 1041 cm⁻¹ (L) displaying the spatial distribution of these components within the region of interest. Saturated intensity maps, were generated for FP (blue), SX (red), and L (green), showing the maximum intensity of the particles at each pixel, enhancing the visual distribution of these components within the particles.

Results and Discussion Cont'd



Comparison of 3D stacked histograms showing spectroscopic diameter distribution for a single actuation of brand name (AD) and generic (WI) for FP, SX, L and summation of FP, SX, L (Summed).

- AD has smaller FP and SX particle size and narrower distribution as compared to WI. Both AD and WI show multimodal distributions of FP and SX.
- Lactose fines are smaller for AD as compared to WI. The sizes of lactose fines are quantified in aerosol agglomerates.
- AD aggregate particle size as measured by summed diameter is smaller than WI. AD also show a narrower distribution of particle sizes.

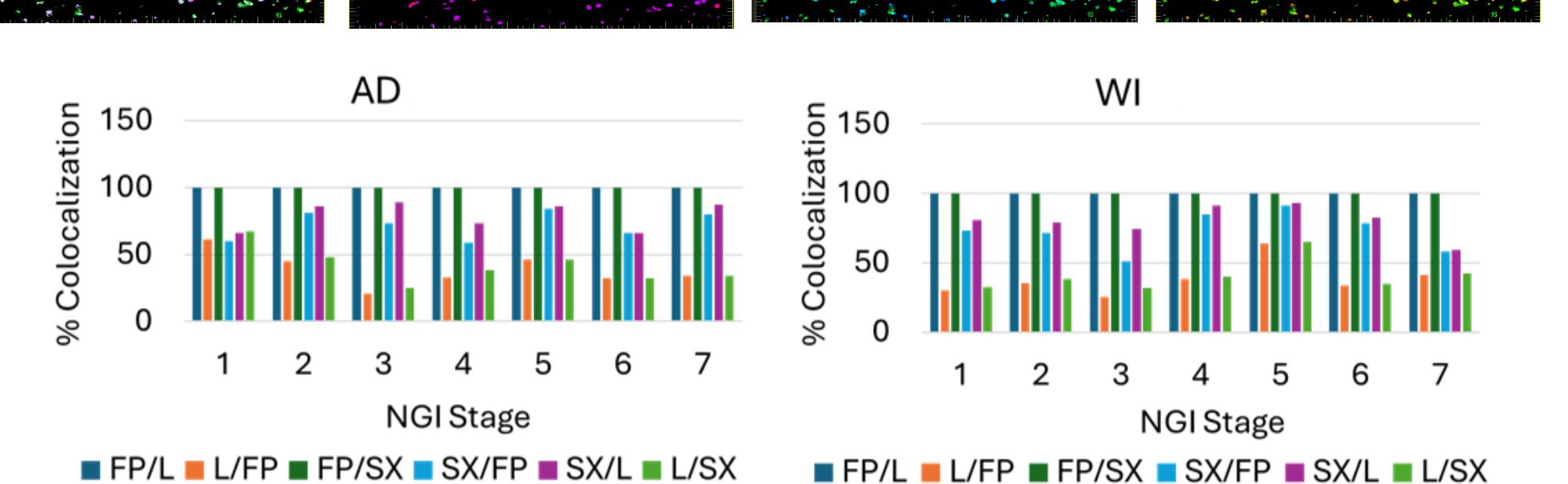
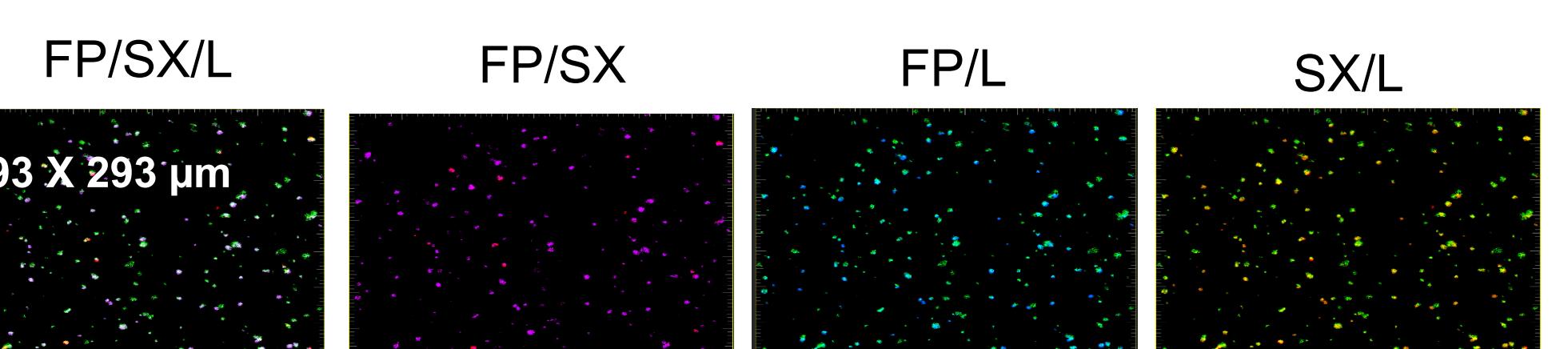


Comparison of integrated intensity between AD and WI for FP, SX, L and Summed (summation of FP, SX, L). Data showing standard deviation of the integrated intensity values within each NGI stage. Number of NGI runs (N) = 1. Total number of particles analyzed for AD was 2963 and for WI was 9904.

- FP and SX integrated intensity was constant as a function of NGI Stage.

Results and Discussion Cont'd

- Both L and summed integrated intensity decreased as a function of NGI stage.
- Mean integrated intensity for WI Act 1 >> AD Act 1.



(a) Representative red, green, and blue (RGB) overlay images from WI collected from NGI stage 4 showing colocalization of FP, SX, and L (b) Degree of colocalization per stage, represented as mean percentage (%) quantified via the Manders Coefficient.

- Colocalization properties are independent of NGI stage.
- 100% of FP is colocalized with L and SX.
- For AD and WI, 50-90% of SX has FP or L associated and is stage-dependent.
- For AD and WI 20-70% of L has FP and SX associated and is stage-dependent.

Acknowledgement

The research funding for this work was provided by the U.S. Food and Drug Administration (FDA) through Contract 75F40122C00202; views expressed in this poster are from the authors only and do not necessarily reflect the FDA's official views or policies nor does any mention of trade names, commercial practices, or organization imply endorsement by the U.S. Government.

Reference: Khanal et.al, *Int J Pharm* 2023, 632: 122563.