

Chemically specific particle sizing of dry powder inhalers by Hound

Introduction

Hound counts, sizes and identifies particles. Hound uses automated, image directed Raman or Laser-Induced Breakdown spectroscopy paired with spectral reference libraries to quickly identify particles from 0.5 μm to 15 μm . In this application note, Hound was used to determine the particle size distribution for different components within a chemical mixture delivered by a dry powder inhaler.

Methods

A mixture of fluticasone and salmeterol was collected from 3 actuations on stage 3 of a Next Generation Impactor (NGI). Hound was set to image particles over a 1x1 mm scan area, with a scan resolution of 0.3 $\mu\text{m}/\text{pixel}$ and a 3 seconds exposure time per particle for particles between 2-10 μm . Raman data was collected using a Raman laser at 532 nm with 5mW power with 5 s beam time.

Results

Particle size and shape were obtained from image analysis of 48 individual images (Figure 1). Image directed spectroscopy was used to acquire Raman data for up to 15,000 particles between 2 and 10 μm (Figure 2 & 3). The Raman spectrum of particles in the desired size range was obtained and analyzed automatically by comparison to an integrated Raman spectra library. Hound identified 2,399 particles as lactose and 12,148 particles as lactose in a mixture of 2 components. 452 particles were recognized as mixtures of the active drug components salmeterol and fluticasone (Figure 4). Once each particle was identified the chemically specific particle size distribution found salmeterol to have an average size $\sim 3.2 \mu\text{m}$, while fluticasone was significantly larger at $\sim 6.0 \mu\text{m}$ (Figure 5).

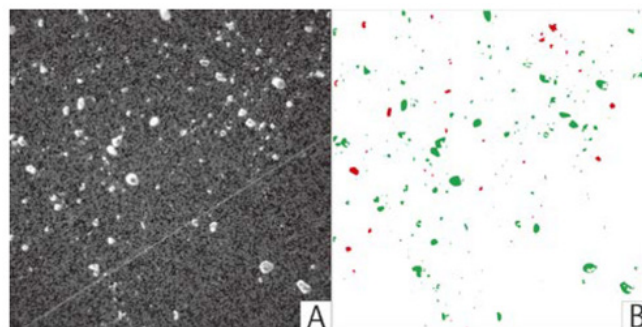


Figure 1: (A) Particles imaged by Hound. (B) Binarized image analysis.

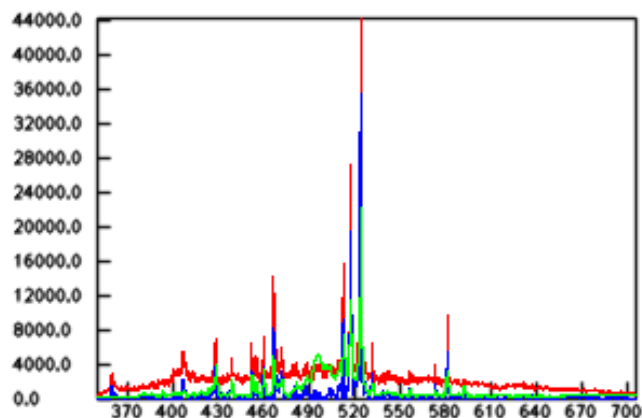


Figure 2: The raw Raman spectrum of one fluticasone particle after a 5 s exposure time (red) is overlaid with the resulting processed spectrum (blue), which was matched with (Rank 919) a fluticasone spectrum from a built-in reference library (green).

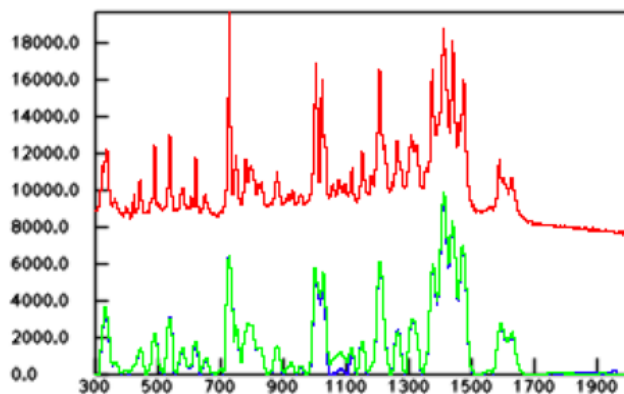


Figure 3: The raw Raman spectrum of one salmeterol particle after a 30 s exposure time with a Raman 785 nm laser (red) is overlaid with the resulting processed spectrum (blue), which was matched with (Rank 919) a fluticasone spectrum from a built-in reference library (green).

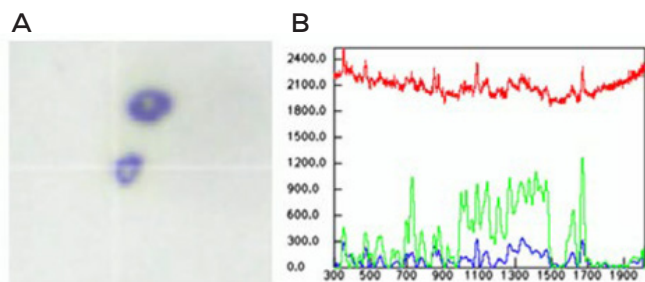


Figure 4: (A) The image of a 4.5 μm particle consisting of fluticasone and salmeterol. (B) Automated image directed Raman spectroscopy produced a raw spectrum (red), which was processed (blue) and matched to a mixture of fluticasone and salmeterol (green).

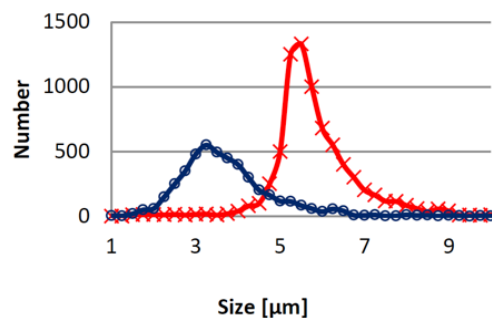


Figure 5: Chemically specific particle size distribution for 12,148 measured particles identified as fluticasone (red) or salmeterol (blue).



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