Liquid Particle Explorer® Application Note

Fast Chemical Particle Mapping of a Dry Powder Inhaler Formulation

Sample Description

rap.ID test sample: Powder from a dry powder inhaler model blend of lactose and tolmetin.

Purpose of Analysis

The described test is useful for the fast determination of the ratio of compound and size distribution of a mixture of particles. As model substances lactose and tometin are mixed and milled to a dry powder inhaler formulation. The analysis is carried out on particles with the potential of lung penetration (2-10µm) as desired for respiratory drug formulations.

Procedure

Particles from the powder were dry dispersed on a gold coated polycarbonate membrane (filtr.AID). Liquid Particle Explorer® parameters were set to 5 seconds exposure time per particle between 2-10µm and to a total scan area of 1x1 mm.

Particle size and shape is obtained from imaging analysis of 4 individual images. Particle in the desired size range are selected for the analysis and the particle is exposed to the 532 nm / 5mW laserbeam for a time of 5 s.

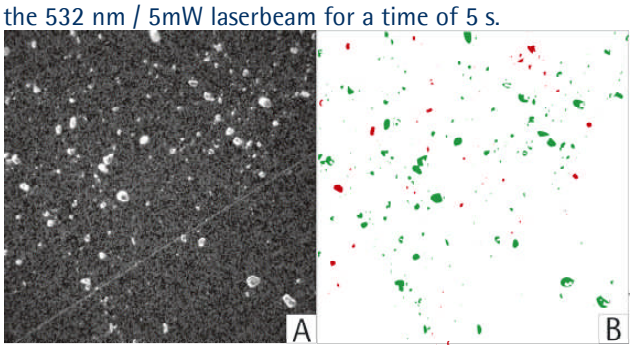


Figure 1: DF Microscopic image (500 µm x 500 µm (A)). B: Image analysis result of the same image. (Liquid Particle Explorer) green=lactose ; red=tolmetin (analysis time = 100 seconds)

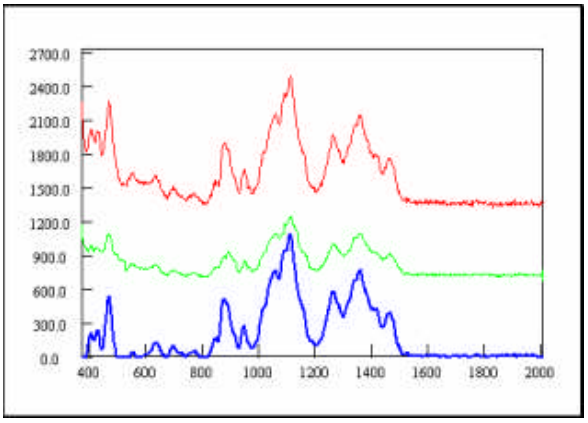


Figure 2: 5s exposure original spectra of one lactose particle (red), proceeding spectra (blue) match with Rank: 919 = lactose library spectrum (green)

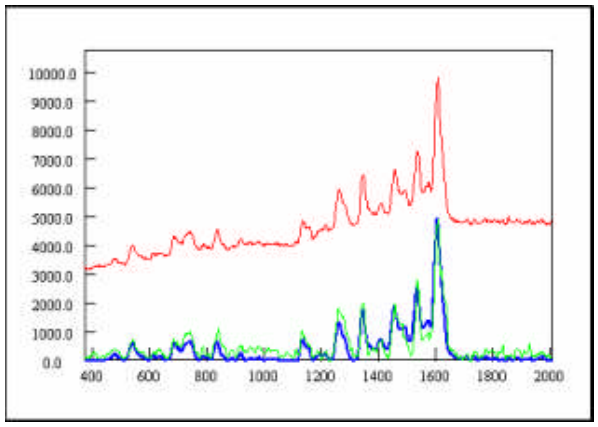


Figure 2: 5s exposure original spectra of one tolmetin particle (red), proceeding spectra (blue) match with Rank: 957 = tolmetin library spectrum (green)

The system was programmed to identify 4500 particles between 2-10 µm. The Raman spectrum of particles in the desired size range was obtained and interpreted automatically by the comparison with an internal Raman spectra library. The sample spectra of lactose and tolmetin were added to the database prior to the measurement..

Results Summary

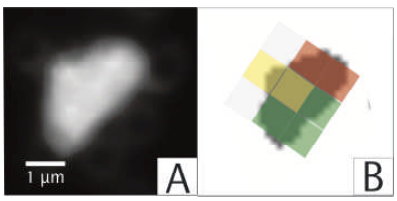
Table 1: Identified particles 2-10 µm from the powder after dry dispersion.

Substance	Nr.	Size		
-	-	2-3 µm	3-6 µm	6-10 µm
Tolmetin	283	223	56	4
Lactose	4214	4125	73	16
Total	4497	4348	129	20

The optical unit hit successfully 4497 particles, leading to high quality spectra, which were analyzed by the APSys - Identifier® library of spectra (see fig. 2 and 3) within 2.5 hours analysis time.

Benefits

The results obtained with the Liquid Particle Explorer® enable statistically relevant and reliable conclusions about the chemical composition of the particles in a time period of only 100 minutes.



With this technique it is also possible to map the areas of the particles with e.g. 9 areas x 5 s= 45s/Particle. It is shwon that this 4 µm particle consitst of tolmetin parts (red), lactose (green) and a mixture area (yellow). Common chemical mapping techniques also analyze the background and need therefore more than 24 hours for a similar analsyis.

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