1064 nm Dispersive Raman Microspectroscopy and Optical Trapping of Pharmaceutical Aerosols

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Raman spectroscopy is a powerful tool for investigating chemical composition. Coupling Raman spectroscopy with optical microscopy (Raman microspectroscopy) and optical trapping (Raman tweezers) allows microscopic length scales and, hence, femtolitre volumes to be probed. Raman microspectroscopy typically uses UV/visible excitation lasers, but many samples, including organic molecules and complex tissue samples, fluoresce strongly at these wavelengths. Here we report the development and application of dispersive Raman microspectroscopy designed around a near-infrared continuous wave 1064 nm excitation light source. We analyze microparticles (1-5 pm diameter) composed of polystyrene latex and from three real-world pressurized metered dose inhalers (pMDIs) used in the treatment of asthma: salmeterol xinafoate (Serevent), salbutamol sulfate (Salamol), and ciclesonide (Alvesco). For the first time, single particles are captured, optically levitated, and analyzed using the same 1064 nm laser, which permits a convenient nondestructive chemical analysis of the true aerosol phase. We show that particles exhibiting overwhelming fluorescence using a visible laser (514.5 nm) can be successfully analyzed with 1064 nm excitation, irrespective of sample composition and irradiation time. Spectra are acquired rapidly (1-5 min) with a wavelength resolution of 2 nm over a wide wavenumber range (500-3100 cm(-1)). This is despite the microscopic sample size and low Raman scattering efficiency at 1064 nm. Spectra of individual pMDI particles compare well to bulk samples, and the Serevent pMDI delivers the thermodynamically preferred crystal form of salmeterol xinafoate. 1064 nm dispersive Raman microspectroscopy is a promising technique that could see diverse applications for samples where fluorescence-free characterization is required with high spatial resolution.
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