FLUORESCENCE-DETECTED MID-INFRARED PHOTOTHERMAL MICROSCOPY

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Fluorescence-detected photothermal mid-infrared (F-PTIR) spectroscopy is demonstrated and used to characterize chemical composition within phase-separated domains of pharmaceutical materials. Infrared and Raman spectroscopic imaging are powerful techniques for generating detailed chemical images based on a sample's spectrum. Previous study on optically detected photothermal infrared (O-PTIR) improved the spatial resolution by probing the temperature-induced refractive index change but are potentially prone to the high background in scattering media. Fluorescence-detected photothermal mid-infrared (F-PTIR) spectroscopy (Fig. 1) is proposed, providing dual-level chemical discrimination based on both fluorescence and infrared absorption. F-PTIR relies on the intrinsic sensitivity of the fluorescence quantum efficiency to temperature. Therefore, fluorescence can serve as a sensitive probe (SNR over 100) for reporting on highly localized and selective infrared absorption. The theoretical spatial resolution of F-PTIR is ultimately limited by fluorescence microscopy and the thermal diffusivity of the sample instead of the infrared wavelength. Following proof-of-concept measurements with model systems of silica gel and polyethylene glycol particles, F-PTIR measurements were used to probe chemical composition within phase-separated domains of ritonavir within copovidone polymer matrices of relevance in the production of pharmaceutical final dosage forms.