ENVIRONMENTAL ATOMIC FORCE AND CONFOCAL RAMAN MICROSCOPIES IN PHARMACEUTICAL SCIENCE

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The characterization of drug morphology and crystallinity, as well as dispersion in and elution from polymer matrices, can be challenging. Insights can be improved using state-of-the-art analytical tools. Although atomic force microscopy (AFM) and Raman spectroscopy have been available for a number of years, as surface-morphological and chemical probes respectively, recent developments have expanded the information obtainable. This presentation will describe newer capabilities in both instrumentation and methodologies for probing pharmaceutical systems. Analytical results will survey various drug and drug-polymer formulations, employing a commercially available (1) confocal Raman microscope optimized for high-speed data throughput and high spatial resolution in three dimensions; (2) digital pulsed force mode (D-PFM) AFM, which senses the distance dependence of force under intermittent contact. Whereas Raman can probe in three dimensions, AFM provides higher spatial resolution albeit localized near the surface.

In both techniques a complete “spectrum” is acquired at each pixel location during imaging. In Raman spectroscopy the meaning of this statement is obvious. In AFM the term “spectroscopy” commonly refers to distance-dependent force measurement. High data throughput allows the collection of “spectroscopic” data files hundreds of megabytes or even gigabytes in size in a few minutes. With the aid of fast post-processing algorithms, images can be quickly constructed that differentiate drug from polymer, crystalline from amorphous drug, and rubbery from glassy or crystalline polymer.

A second theme is environmental control: the ability to image and probe structure/properties under controlled relative humidity (RH) or aqueous immersion, as well as variable temperature. Examples will show how these methods can (a) examine crystallization or solid-like to liquid-like transitions at elevated RH; (b) probe matrix swelling and drug diffusion and elution under aqueous immersion; (c) distinguish materials via behavior at elevated temperatures (e.g., glass to rubber transition).