

## Cocrystal Screening in Pharmaceuticals

### Challenge

Cocrystals are of increasing interest due to the potential abilities to improve the physicochemical properties of the parent compounds, in particular solubility, stability and bioavailability. Synthesis via solid-based techniques (e.g. grinding) can offer enhanced selectivity as compared with that of solution-based methods. Rapid and reliable identification and monitoring of cocrystals during the development, manufacturing, and quality assurance process is critical in pharmaceutical research, PAT, and quality control.

Observing structural shifts of a compound can be accomplished several ways. Raman spectroscopy is used to observe small band shifts in the “fingerprint” region (200 to 1800  $\text{cm}^{-1}$ ), however these reflect subtle shifts in functional groups and are difficult to detect during phase or polymorphic changes. X-ray diffraction (XRD) techniques yield extremely quantitative and conclusive analysis, but require expensive equipment and destructive off-line testing. Terahertz (THz) spectroscopy can easily differentiate structural shifts, as these signals correspond to large scale motions in the molecular and inter-molecular structure, however THz spectroscopy has limited spectroscopic range, is expensive, and can require special sample preparation.

### The Coherent THz-Raman® Solution

Coherent THz-Raman® systems extend the range of traditional Raman spectroscopy to the terahertz/low frequency regime, where differentiation of the inter- and intra-molecular structures of cocrystals can be clearly seen. THz-Raman spectra can also be used to differentiate polymorphs, raw materials, synthetic pathways, and contaminants, useful for counterfeit detection and surety testing. Anti-Stokes signals add to Raman intensity and improve SNR. Coherent THz-Raman® systems provide fast, unambiguous differentiation of cocrystals and polymorphs, while preserving the complete Raman “fingerprint region” for chemical identification.

### Application Field

Co-crystals, pharmaceutical analysis, crystallization studies, high-throughput screening, low-frequency THz-Raman spectroscopy.

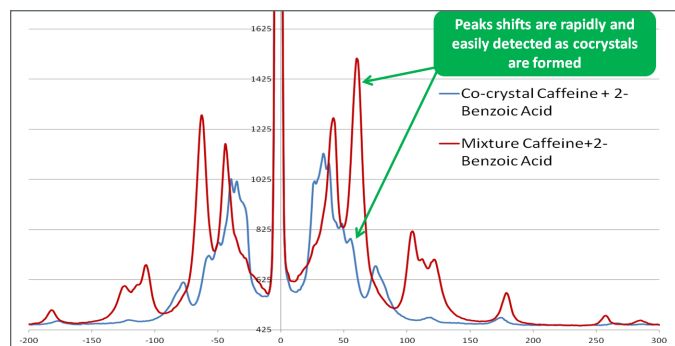
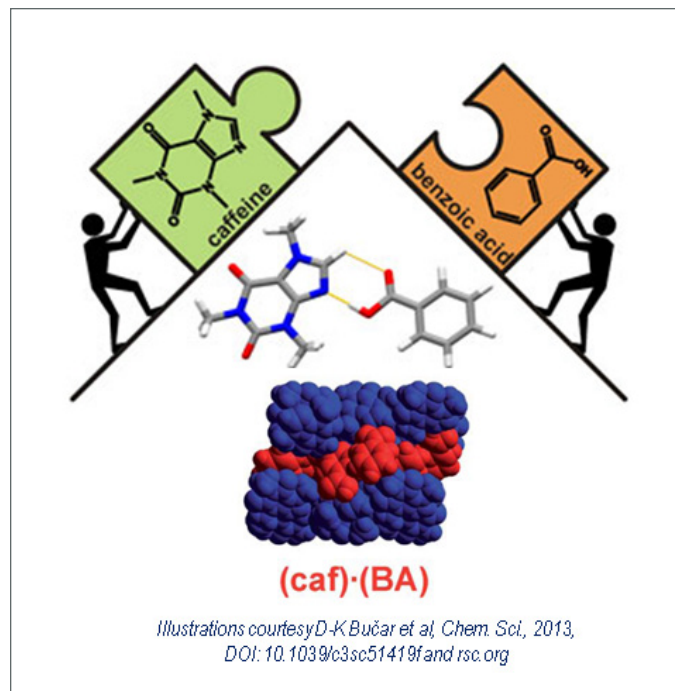


Figure 1. THz-Raman spectra for cocrystals and mixtures of Caffeine and Benzoic Acid showing clear differentiable peaks.<sup>1</sup>

### Contact

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For more information, visit: <http://www.thz-raman.com>

<sup>1</sup> Data courtesy Dr. Tatsuo Koide, National Institute of Health Sciences, Division of Drugs, Tokyo, Japan.

Illustrations courtesy D-K Bučar et al, Chem. Sci., 2013, DOI: 10.1039/c3sc51419f and rsc.org