# Polymorph Identification in Pharmaceuticals

## Challenge:

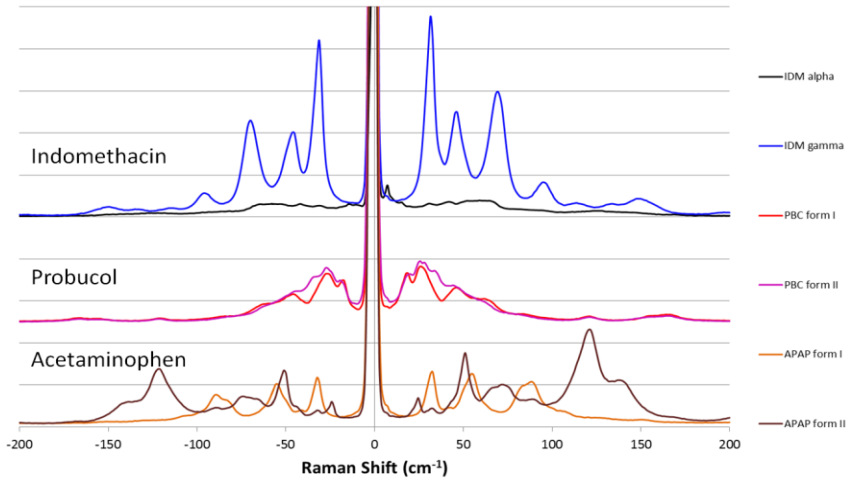
Many active pharmaceutical ingredients (APIs) exhibit ***polymorphism***, where different forms or molecular structures of a compound can dramatically affect the efficacy, stability and bio-availability of the drug. These structural changes may occur during various stages of formulation, storage, packaging and handling. Consequently, rapid and reliable identification of polymorphs during the development, manufacturing, and quality assurance process is critical in pharmaceutical manufacturing.

## Traditional Solutions:

Observing structural shifts of a compound can be accomplished several ways. ***Raman spectroscopy*** is used to observe small band shifts in the "fingerprint" region (200-1800 $cm^{-1}$), however these reflect subtle shifts in functional groups and are difficult to detect for some polymorphs. ***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.

## Ondax Solution:

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




## Features / Benefits

- ***Simultaneous chemical AND structural analysis***
- ***Fast, reliable polymorph identification, including hydrates, isomers, conformers and co-crystals***
- ***Useful for counterfeit detection/surety testing***
- ***Non-destructive and requires no sample preparation***
- ***Compatible with existing Raman spectrometers***
- ***Simple, compact, cost-effective***
- ***Available in benchtop or microscope configurations at 532, 633, 785 & 830nm***

*THz-Raman spectra for polymorphs of various APIs showing clear differentiable peaks[1]*

[1] *Data courtesy Dr. Tatsuo Koide, National Institute of Health Sciences, Division of Drugs, Tokyo, Japan*

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More info at www.THz-Raman.com

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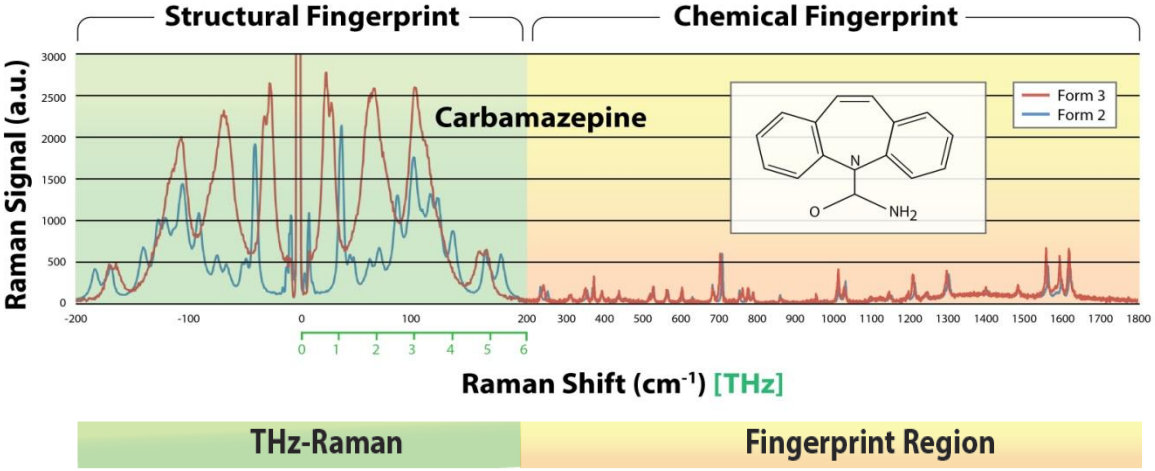
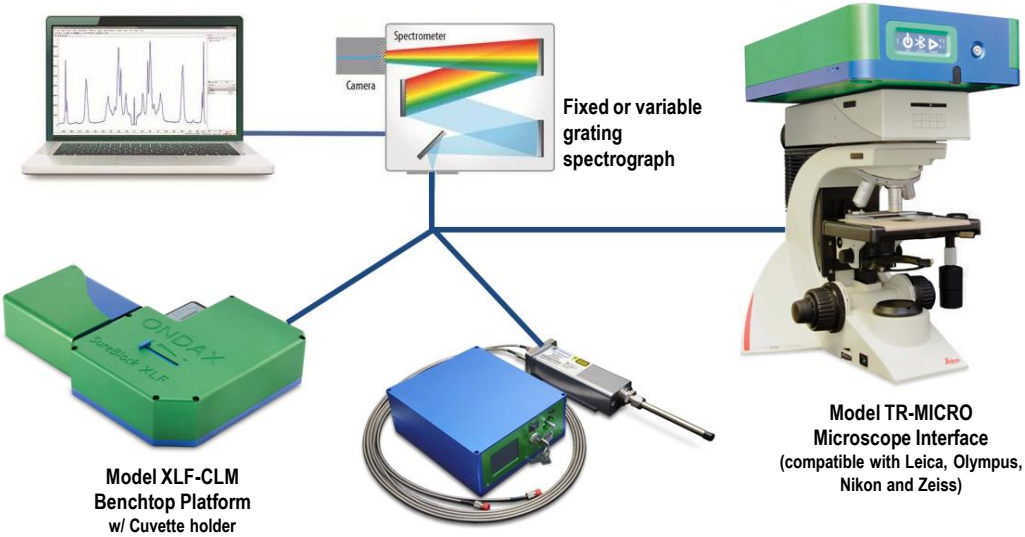
## THz-Raman PLUS fingerprint region measurement with the same system

Many compounds undergo structural changes due to formulation/processing methods and environmental conditions. The spectra below shows two polymorphs of carbamazepine (Form 2 and Form 3). The THz-Raman range (green background) exhibit strong, distinguishing signals when compared to the traditional fingerprint region (gold background), improving the ease and reliability of polymporph identification.




Ondax's patented[2] **THz-Raman® Spectroscopy Systems** extend the range of traditional Raman spectroscopy into the terahertz/low-frequency regime, exploring the same range of energy transitions as terahertz spectroscopy – without limiting the ability to measure the fingerprint region. This enables ***simultaneous analysis*** of both molecular structure and chemical composition for advanced materials characterization.

All **THz-Raman®** systems are compact, robust, plug-and-play platforms that deliver incredible speed, throughput and ease of use, all at an extremely affordable price. With a broad selection of excitation wavelengths from 488nm to 1064nm, optional polarization control and a wide variety of sample interfaces, there is a THz-Raman® solution for any application.




[2] *US Patents 8,184,285 and 9,986,407*

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