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Applications for Surface Enhanced Raman Spectroscopy in the Pharmaceutical industry

Key Words

- Pharmaceutical
- Surface enhanced
- Raman
- Drug Development
- Polymorphism
- Chirality

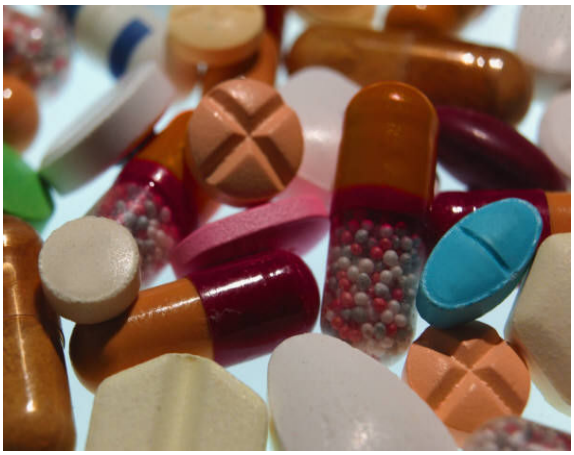
Introduction

Spectroscopic techniques are widely used in pharmaceutical research and industry. Owing to its versatility , vibrational spectroscopy remains one of the main spectroscopic techniques, due to the ease of use and structural information the technique affords. Of these techniques, Raman spectroscopy is rapidly gaining acceptance within the industry. It is already proving to be a valuable tool in the analysis of pharmaceutical polymorphs and now looks destined to find increasing application throughout the pharmaceutical industry

Compared to other techniques such as Infra-red (IR) absorption spectroscopy, Raman spectroscopy can be seen as complementary . While IR spectroscopy is essentially based on illuminating the sample with a broad range of wavelengths of IR light and measuring which are absorbed, a Raman spectrum is obtained by illuminating the sample with a single wavelength of light from a laser and collecting and analysing the resulting scattered light. The majority of this scattered light is in the form of conventional Rayleigh scattering. In addition to this, much smaller amounts of scattered light are observed at various wavelengths shifted with respect to the exciting wavelength; this is the Raman scattered light.

The key difference between Raman spectroscopy and IR is that although all the techniques measure the vibrational frequencies of a molecule, the fundamental physical process giving rise to the effects is different. In practice this means that while some molecular vibrations may be observed in both the IR and Raman spectra, often vibrations observed using one technique will be extremely weak or totally absent in the other. This makes Raman analysis a complimentary spectroscopic technique. The features in the Raman spectrum corresponding to the various vibrational modes of a molecule are generally sharp, well resolved and, for many active pharmaceutical compounds, numerous.

One of the limiting factors however in Raman spectroscopy is the low intensity of the Raman scattered light. Although advances in instrumentation have gone someway to improve the detection of the weak Raman signal, often sample fluorescence obscures the weak scattered signal and increasing the laser power can damage the molecule or structure of the material being investigated. Surface enhanced Raman scattering is a technique that overcomes these disadvantages and enables Raman spectroscopy to be used in a wide range of pharmaceutical applications.



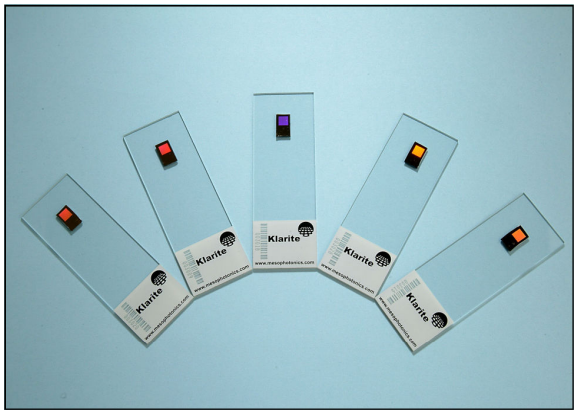


Figure 1. Klarite test slides

SERS substrates

Surface enhanced Raman can enhance the weak Raman signal by six orders of magnitude, or more and can extend the range of applications applicable to Raman spectroscopy.

The technique which is due to the electronic interaction between the molecules and a specially textured metal surface, has largely been used for academic research purposes until the lauch of Klarite SERS substrates. These disposable substrates, that are available in a variety of formats, can enable high sensitivity Raman tests to be done quickly and easily.

Using semiconductor processing techniques and our knowledge of photonic devices Mesophotonics have been able to produce highly reproducible SERS substrates in large volumes to enable this technique to now be used routinely.

This gives distinict advantages in the drug development and drug discovery industries. Detection limits in the parts-per-billion, real time response, both qualitative and quantitative analysis, a high degree of specificity, and simultaneous multi-

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component detection are possible with Klarite SERS substrates.

Klarite Surface enhanced Raman spectroscopy can be used in the pharmaceutical industry for a variety of applications including;

- Trace level detection of active compounds
- Detection of counterfeit drugs
- Structural and chirality information
- Polymorphism
- Drug interactions by coating the active surface
- Detection and analysis of cytochrome P450 interactions.
- Detection of peptides, proteins, amino acids (protenomics)
- Detection of DNA including binding events
- Detection of contaminates in injectable substances
- Water purity
- Incoming and raw material ID with contamination information
- Process analytical Technology PAT
- High throughput screening

Due to the high enhancement minimum sample volumes are required to give a reliable and reproducible Raman spectra. Spectra can typically be taken with micro-litre to nano-litre volumes making the technique ideal for the early characterisation of small quantities of drug candidates. In addition polymorphism and polymorphic stability can be detected with volumes far less than for other techniques such as X-ray crystallography.

Klarite SERS substrates are available in a variety of formats and customisation is available. These disposable substrates enable tests to be performed quickly and easily with the minimum of sample quantity.

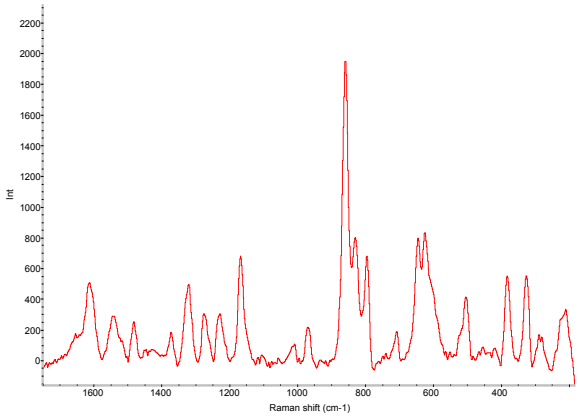

Figure 2 Paracetamol SERS spectra

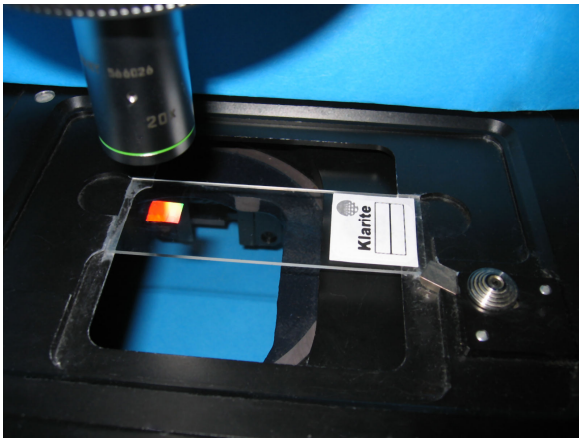

Figure 3 Klarite Substrate mounted on Raman Microscope

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