

Applications for Surface Enhanced Raman Spectroscopy in the Pharmaceutical Industry

Application Note



INTRODUCTION

Optical spectroscopy techniques such as Infrared (IR) and Raman are widely used in pharmaceutical development and manufacturing because of their speed and versatility. Both techniques provide structural identification and quantitative analysis and are non-invasive and nondestructive.

However, both IR and Raman are relatively insensitive techniques, typically considered unfeasible for analyte concentrations below 1 % w/v.

Surface Enhanced Raman Spectroscopy (SERS) can enhance the weak Raman signal up to 1 million times, dramatically extending the range of applications. Although the effect has been known for over 30 years, until now, the substrates have not been reproducible enough for routine analytical measurements.

KLARITE® SERS SUBSTRATES



Figure 1 – The D3 Technologies Klarite SERS substrates

These disposable substrates, available either mounted on microscope slides or as unmounted chips, allow high sensitivity Raman tests to be performed quickly and easily.

Designed using photonic crystal technology and manufactured by semiconductor fabrication methods, D3 Technologies Klarite SERS substrates are highly reproducible, bringing the power of SERS to routine analytical measurements.

Due to the high signal enhancement, SERS can provide the following benefits:

- Small sample volumes (μL and below)
- High degree of specificity
- Real time response
- Qualitative and quantitative analysis
- Simultaneous multi-component detection

PHARMACEUTICAL APPLICATIONS

Applications of SERS in the pharmaceutical industry include:

- Analysis of peptides, proteins and amino acids
- Molecular structure and chirality
- Detection of drug compounds and metabolites in preclinical and clinical tests
- Low level contaminant detection and identification
- Water and solvent purity

EXAMPLE DATA

A number of solutions with concentrations ranging between 0.2 $\mu\text{g/ml}$ – 160 ng/ml and 0.3 $\mu\text{g/ml}$ – 240 ng/ml were prepared in ethanol for ibuprofen and warfarin respectively. In each case, an aliquot of solution was placed onto the chip, covering both the SERS active and inactive surfaces. The solvent was then evaporated to leave a thin film of analyte at the surface. Spectra were collected from the active and non active areas using a Raman system with a 785 nm laser and 150 mW illuminating a 100 μm spot on the sample.

IBUPROFEN

Ibuprofen, the familiar non steroidal anti-inflammatory drug (nSAID)¹ was tested with Klarite substrates. Shown below in figure 2, are the results for the solution containing 16 $\mu\text{g/mL}$. It clearly shows the enhanced SERS signal on the active area, compared to no Raman signal on the inactive area.

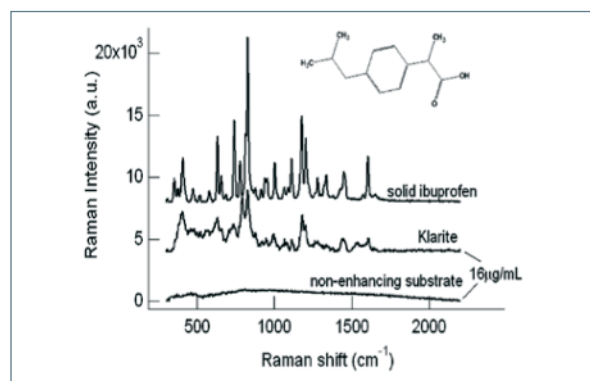


Figure 2 – SERS comparison of Ibuprofen, 20 s, 5 accumulations

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WARFARIN

Warfarin, an anti-clotting agent, was also tested with SERS. Warfarin was found to have a strong Raman signal in the bulk but at low concentrations such as 243 µg/mL on a non-activated surface, does not reveal a detectable Raman signal. With SERS however, at this concentration, its distinctive Raman spectrum can still be seen, (see figure 3).

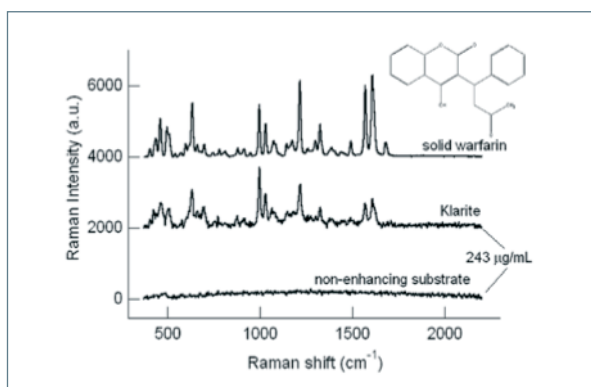


Figure 3 – SERS comparison of warfarin, 10 s, 5 accumulations

SERS OF MIXTURES

In order to demonstrate SERS with a mixture of compounds, the data shown below are the results of combining 2.43 mg/mL warfarin with 1.62 mg/mL ibuprofen. The results show a perfect overlay of peak positions between the reference SERS spectra and the mixture. This means that SERS can be used for multicomponent quantitative analysis of mixtures.

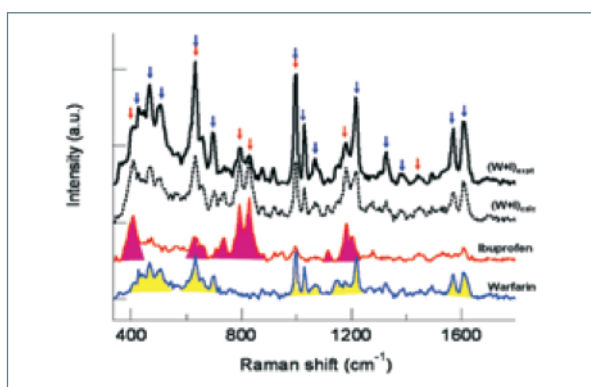


Figure 4 – SERS comparison of an ibuprofen/warfarin mixture, 30 s

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PROTEINS

The Raman spectra of proteins contain a number of features that help to identify and characterise their molecular structure. SERS extends this capability to levels that were previously undetectable. Figure 5 shows a SERS spectrum of lysozyme at 1 mMolar concentration.

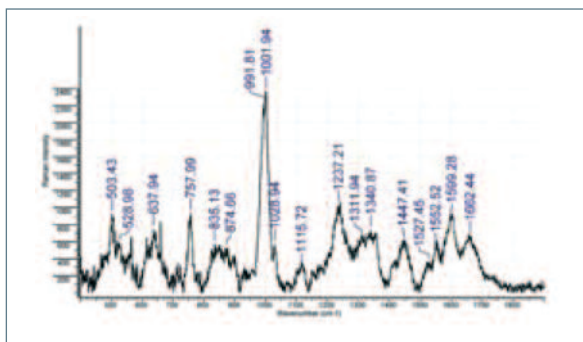


Figure 5 – SERS spectrum for lysozyme, 1mMolar concentration

CONCLUSION

These results highlight how D3 Technologies Klarite SERS technology has the ability to collect Raman signals from trace levels of material at concentrations that are undetectable by bulk Raman spectroscopy. This capability opens up many new applications in pharmaceutical analysis.

REFERENCES

- 1 Organic Chemistry, McMurry, 4th Ed. 1996, pg 612



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