Inside: Find out how relative quantitative ATR analysis of solids is possible.

Introduction

Infrared quantitative analyses are an everyday requirement in the analytical laboratory. While liquid solutions are commonly analyzed, mixtures of powdered components also exist and often require quantitative analysis without dissolution into a solvent.

The traditional infrared analysis method for powdered samples is the collection of a KBr pellet spectrum of an aliquot of the powdered sample. However, preparation of KBr pellets requires skill, and precise weighing of every component for each sample. The Golden Gate™ single reflection diamond ATR provides a simple and effective alternative, suitable for the infrared analysis of powders. ATR analysis is less complicated than using KBr pellets, is fast and only requires a very small amount of the sample

The Specac **Golden Gate®** is the original best selling single reflection diamond ATR accessory. A flagship product for more than two decades, the Golden Gate remains unrivalled for choice of sampling options and rugged durability.

- Seven Sampling top plates
  - Swap hot for cold, static for flow and other options
- Wide temperature range (-150 to 300 °C) with pressures upto 6000 psi depending on sampling option
- Signature bridge design allows a reproducible load up to 80 lbs (160 lbs with optional torque wrench)

Acknowledgements

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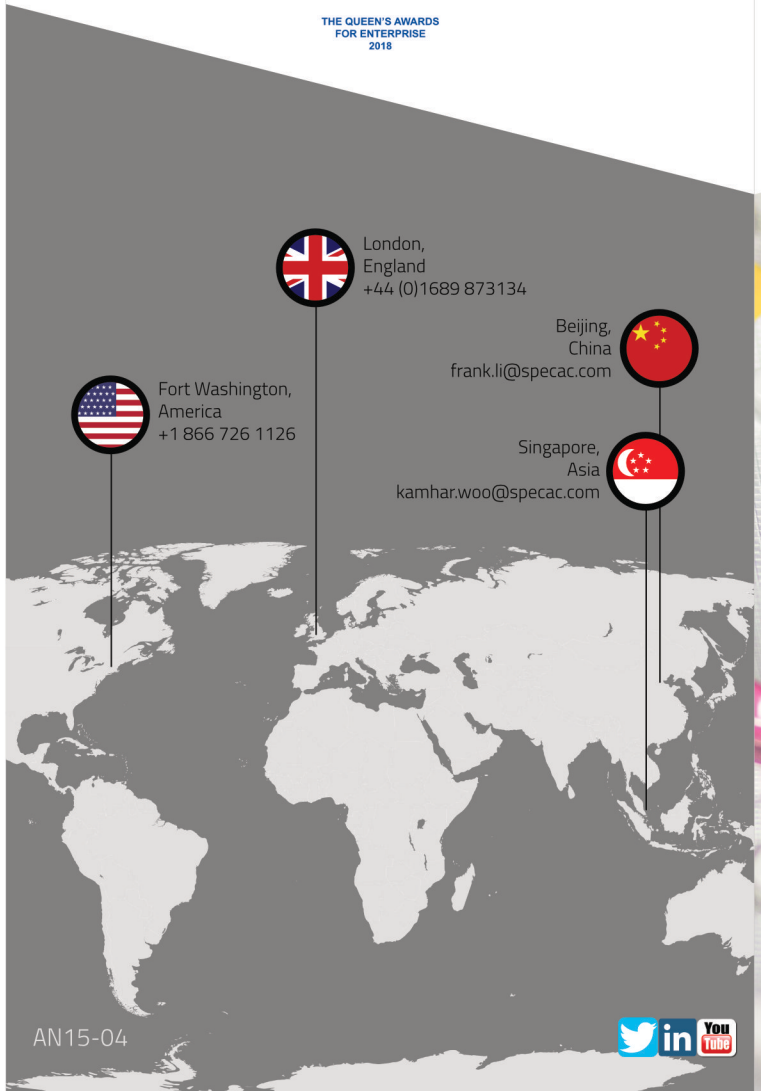

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Specac Application Note

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ATR analysis of the relative concentrations of active pharmaceutical ingredients using the Golden Gate®

Specac's Golden Gate™

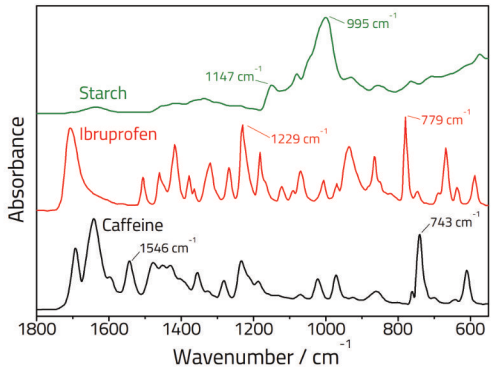

Figure 1: ATR spectra of Caffeine, Ibuprofen and Starch.

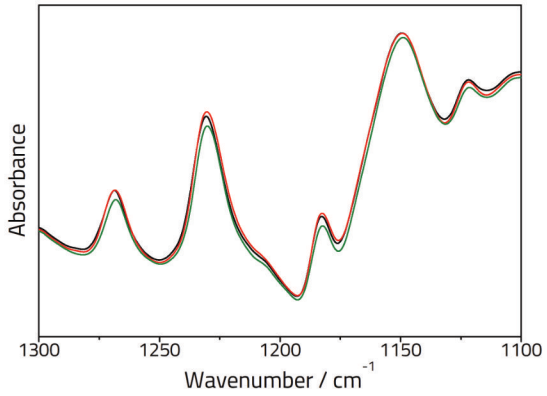

Figure 2: Three repeat ATR spectra of the same sample (25% Ibuprofen/Starch) showing excellent reproducibility.

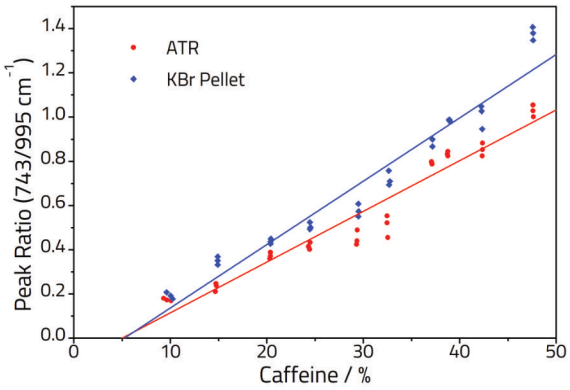

Figure 3: Calibration plots showing the peak ratio 743/995 (Caffeine: Starch respectively) vs. percent composition. The straight lines show a linear regression to the data.

Experimental

Spectra were collected using a Golden Gate™ Diamond ATR accessory equipped with ZnSe lenses and a single-reflection diamond ATR element. The powdered sample is simply placed onto the ATR crystal and the sample spectrum is collected. The sapphire anvil ensures that up to 160 lbs load is evenly applied to the sample lying on the diamond ATR crystal during sample analysis. The sample is then cleaned from the crystal surface and the accessory is ready to collect additional spectra.

Mixtures of known concentrations of active ingredient and starch were prepared and then without additional sample preparation aliquots of 5-10 milligrams were placed onto the ATR element and spectra collected. For correlation with the ATR data, aliquots drawn from the standard powders were mixed with KBr powder, pressed into pellets and analyzed to provide transmission spectra. FT-IR spectra were collected at 4 cm^{-1} resolution on a commercially available spectrometer.

Three aliquots were prepared and analyzed for each powder standard using the ATR and KBr pellet methods. Two analyte bands were selected for each component in each mixture and peak ratios calculated based on the ratio of the peak heights of the active ingredient vs. the starch. The resulting quantitative data was then fitted to a straight line using least squares regression analysis based on the Beer-Lambert Law:

$$A = \varepsilon c l$$

where: **A** = the absorbance value of an analyte band; **ε** = the extinction coefficient of the analyte band; **c** = analyte concentration; and **l** = the pathlength.

A calibration model developed for KBr pellets cannot be directly applied directly to ATR spectra, as the penetration depth of ATR changes with wavelength [1], and thus the relative peak ratios at a fixed concentration will change. Hence separate calibration models must be built for KBr pellet and ATR spectra.

Results and Discussions

Figure 1 compares the fingerprint regions of the Golden Gate™ ATR spectra for the components used in the study: caffeine, Ibuprofen and starch. The analyte bands selected for the analysis of each component are labelled.

An example of the repeatability of the Golden Gate™ ATR measurement is demonstrated in Figure 2, containing three spectra obtained from the same 25% concentration of ibuprofen in starch sample. As can be observed the spectra are highly reproducible.

Figure 3 shows the least squares regression straight line fit to the ratio of the 743 and 995 cm^{-1} bands of caffeine and starch, respectively, data obtained using KBr Pellets (blue) and ATR (red). Table 1 contains the R^2 values for the least squares analysis of the data from the two mixtures using the different analyte bands for each component; these results demonstrate that the ATR method can provide repeatable quantitative results that are comparable to KBr pellet data.

	KBr Pellet	ATR
Caffeine (743/995 cm^{-1})	0.9533	0.9484
Caffeine (1546/1148 cm^{-1})	0.9246	0.9196
Ibuprofen (1230/995 cm^{-1})	0.9469	0.8976
Ibuprofen (779/1148 cm^{-1})	0.9489	0.9091

Table 1: Comparison of R2 values obtained for the least squares regression analysis of samples collected using the KBr pellet and ATR methods

Conclusion

The results show that the Golden Gate Diamond ATR can be used to produce quantitative data – the ability to clamp samples at very high loads ensures consistent results, while the use of a monolithic natural diamond allows for extreme durability of the accessory.

The Golden Gate Diamond ATR is a simple and easy to use accessory providing a non-destructive technique to collect data from a minimal amount of sample, providing quantitative results similar to KBr pellet spectra in a faster, less complicated fashion.

References

[1] Specac Technical Note Note: TN21-02 ATR Penetration Depth