

# Quest™ ATR: Analysing Pharma Theophylline

The Quest™ ATR accessory lets the user test various samples without the need for any sample preparation.

**IN COMPLIANCE WITH** Japanese Pharmacopoeia regulations, pharmaceutical samples are required to have IR spectral data spanning 4000–400  $\text{cm}^{-1}$  (2.5  $\mu\text{m}$  to 25  $\mu\text{m}$ ).

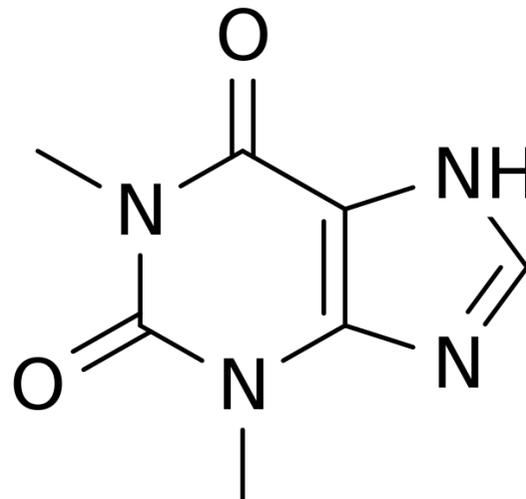
Traditionally, KBr windows have been used as part of liquid cells for this range. However, **their structural integrity can be compromised** if the sample contains any aqueous component.

Dry solid samples can be analysed within a KBr matrix too. But this is a **time consuming method** and the quality of the spectra produced depends on the sample, the structural integrity of the KBr pellets and the user.

An alternative method available for the recording of IR spectra is **Attenuated Total Reflectance (ATR)**. Here samples are brought into direct contact with an ATR crystal.



The Specac Basic Solid Pack.



An important pharmaceutical, Theophylline.

The IR light from the spectrometer is internally reflected in the crystal and interacts with the samples at the crystal interface.

The spectral range accessible by the ATR technique depends on the ATR crystal used. **A range of 4000–400  $\text{cm}^{-1}$  can be achieved** with a mono crystalline type IIIa diamond crystal.

This application note compares both methods of spectroscopy by examining the white crystalline powder **Theophylline ( $\text{C}_7\text{H}_8\text{N}_4\text{O}_2$ )**.

## Experimental

The Specac Basic Solid Pack contains all the necessary equipment to make a **KBr pellet** of the sample, as shown in Table 1.

A small amount of Theophylline was added to a 99% excess of spectroscopic grade KBr Powder and ground together with a mortar and pestle.

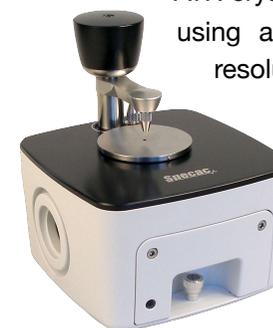
The mixture was pressed into a solid pellet using a **1.75 ton load** in the Mini-Pellet Press. Then the resulting 7mm wide sample pellets were examined spectroscopically.

Equipment	Part number
Mini-Pellet Press (2T)	GS03940
7 mm Pellet Die + Ring Holder	GS03950
Spare Ring Holder	GS03951
Pestle and Mortar	GS03600
50 g KBr Powder	GS03610
7 mm Disc Holder Mount	GS03960

Table 1: Part numbers of the Basic Solid Pack.

For the ATR measurements, the solid samples were placed onto the extended range diamond crystal in the Quest™ ATR **without any preparation**, demonstrating its suitability for FTIR spectral acquisition in a quick and reliable fashion.

A set load from the anvil arm on the Quest™ was used to ensure contact between the samples with the ATR crystal. The Spectra were collected using an **FTIR spectrometer** with a resolution of 1  $\text{cm}^{-1}$  and an average of 16 scans.



The Specac Quest™ ATR accessory.

## Discussion

The IR spectra for Theophylline recorded using a KBr pellet and the Quest™ are shown in **Figures 1 and 2 respectively**.

There is a stronger absorbance for the KBr pellet, but this is a consequence of the longer pathlength in the pellet (~1 mm) compared to the ATR (~2 µm).

The signature peaks and their positions in the spectrum collected using the ATR are identical to those collected with KBr pellets.

However, the peak intensities are different for the two different techniques. Specifically, at a higher frequency, the relative absorbance is lower in the spectrum recorded using the ATR.

This is a well-known consequence of the ATR technique and corrections are commonly applied.

Most FTIR instruments offer **ATR data handling software packages** that apply a correction algorithm to convert the spectral data, so that it more closely represents a transmission spectrum.

For more information on this topic, see our *ATR Explained application note*.

However, for the **shorter frequencies** (longer wavelengths) the spectral intensities are more comparable for the two different techniques.

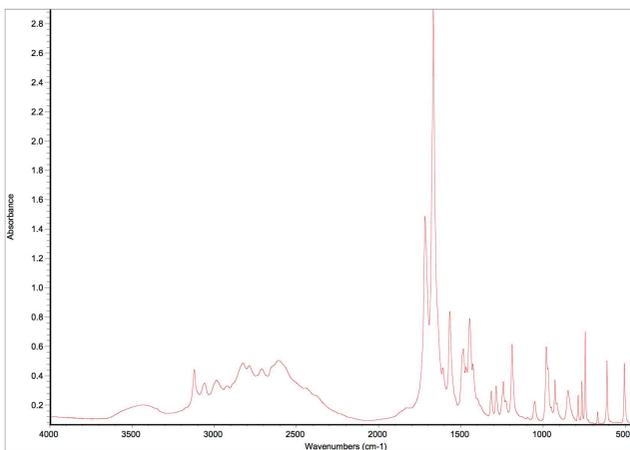


Figure 1: IR spectrum of a 7 mm KBr Pellet of Theophylline.

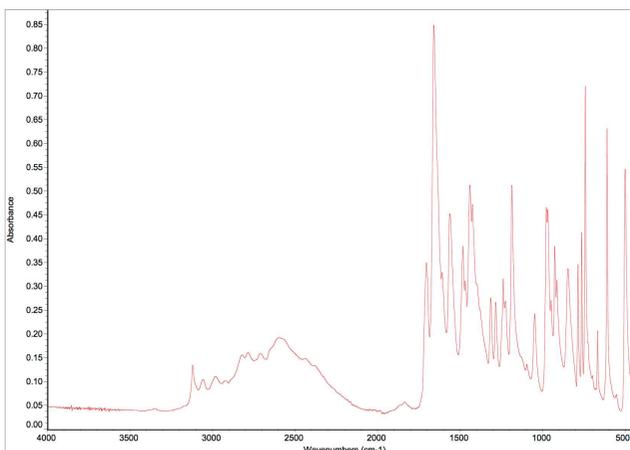


Figure 2: IR spectrum of Theophylline using the Quest™ ATR.

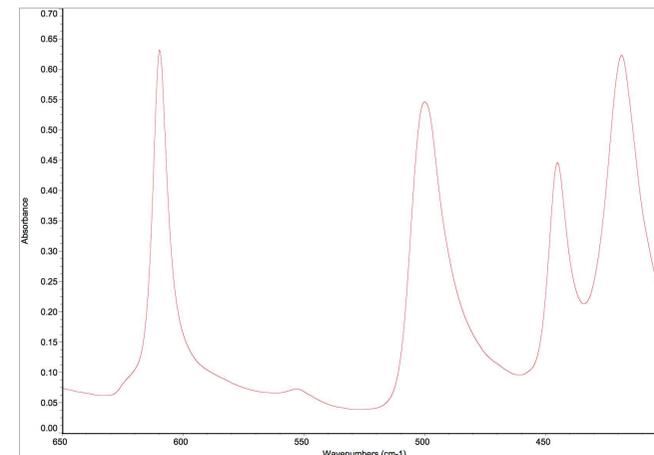


Figure 3: IR spectrum of Theophylline using the Quest™ ATR.

Some weak spectral features in the higher frequency region of an IR spectrum may not be easily observed if analysing the sample via the ATR technique. An important comparison to make is the **ease of sample handling**.

## Conclusion

Transmission spectroscopy using KBr pellets tends to produce more accurate qualitative IR spectra, but the **quality varies** with the pellet's integrity, sample preparation and the user.

Conversely, the ATR technique is ideal for performing **quick and reproducible** qualitative and quantitative measurements. **Spectral acquisition is faster with the Quest™** because samples can be analysed 'as is', i.e. without prior preparation. This requires less user training.

Furthermore, the Quest™ ATR can more easily handle a wide range of sample types, including **gels, solids, oils and aqueous liquids**.