

INFRARED SPECTROMETER ACCESSORIES

Analysis of Theophylline & Ibuprofen Pharmaceutical Samples Using the Specac Quest ATR Accessory

Introduction

For collection of Infra Red spectral data of liquid or solid samples it is desirable to achieve a spectral range extending from 4000cm^{-1} to 400cm^{-1} . Traditionally, the use of liquid transmission cells with KBr windows allows for this transmission range of light to be collected, but there may be compromise of the liquid cells structural integrity if the liquid sample itself contains any aqueous component which will attack the KBr windows.

Similarly for sampling of solid sample types, the KBr pellet preparation technique has been employed widely as a relatively cost effective, albeit time consuming and method dependent way to collect an Infra Red spectrum whereby the sample of interest is, ideally, homogeneously distributed within a KBr solid support matrix for transmission measurement. The quality of the spectrum produced is wholly dependent upon the sample type and the structural integrity of any such KBr pellets produced.

An alternative method for spectral collection is to use the Attenuated Total Reflectance (ATR) technique, whereby a liquid or solid sample is brought into direct contact with an ATR crystal material and internally reflected and measurable light from the sample crystal interface results in a spectrum being collected for the sample from a specific penetration depth into the sample material itself.

To achieve a similar spectral range of collection for the transmission range of 4000cm^{-1} to 400cm^{-1} from the ATR technique a monocrystalline type IIIa diamond ATR crystal element can be used. The Specac Quest™ ATR accessory offers the choice of a diamond, ZnSe or germanium ATR crystal puck to be used on a dedicated optical unit with mirrored reflectance optical components only. This optical



Specac's Quest ATR Accessory

combination allows for the full transmission spectral range capability of the ATR crystal chosen to be achieved.

Application

To comply with Japanese Pharmacopeia regulations, pharmaceutical samples are required to have infrared spectral data collected for them between the frequency range of 4000cm^{-1} to 400cm^{-1} (2.5 microns to 25 microns wavelength).

A couple of solid pharmaceutical samples were used as examples to measure. One sample was Theophylline ($\text{C}_7\text{H}_8\text{N}_4\text{O}_2$), a white crystalline powder. The second was an Ibuprofen tablet ($\text{C}_{13}\text{H}_{18}\text{O}_2$) which was orange in colour. Both the samples were taken and prepared as traditional KBr pellets for transmission purposes to measure over the range of 4000cm^{-1} to 400cm^{-1} and also analysed for collection of an ATR spectrum over the same spectral range.

Equipment and Method

For the transmission measurement a 7mm diameter KBr pellet was formed. To make the KBr pellet, the Specac Basic Solid Pack P/N GS01150, consisting of a 2 ton maximum load capability Mini-Pellet Press using a 7mm diameter pellet die assembly was used.

For the ATR measurement, the Quest™ ATR Accessory P/N GS10801-B was used with the single reflection diamond extended range ATR crystal puck option on the optical unit.

The spectra were collected on a Thermo Nicolet iS5 instrument using the standard room temperature

detector system set at a resolution of 4cm^{-1} for 16 scans at a gain of 1.

To make the KBr 7mm pellet, a small amount of the Theophylline and Ibuprofen samples were added to an excess of KBr powder material (Specac spectroscopic grade P/N GS03610) and ground to a fine homogenous powder mixture using an agate pestle and mortar (Specac P/N GS03600). A proportion of the ground powder sample was transferred to the 7mm pellet die assembly and a solid KBr disc was pressed from application of a 1.75 ton load to the die assembly from the Mini-Pellet Press. The KBr sample pellet was then ready to be mounted in the spectrometer for spectral data collection.

Fig. 1. IR Spectrum of 7mm Diameter KBr Pellet of Theophylline

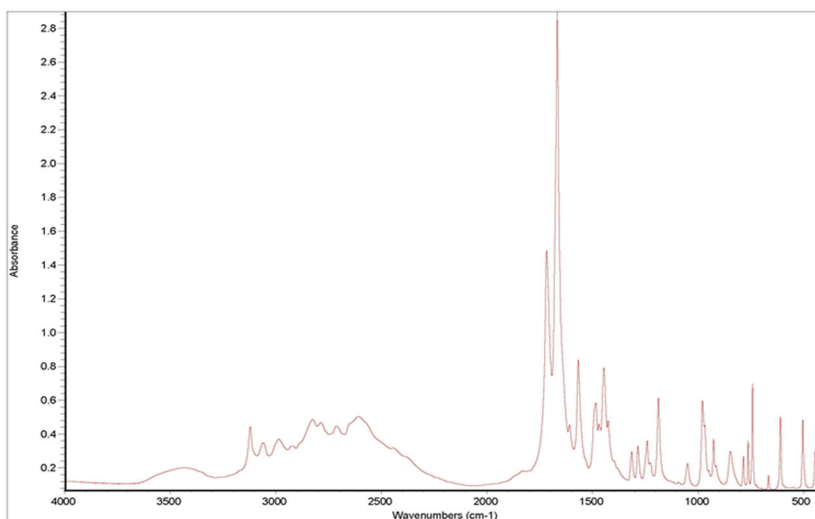
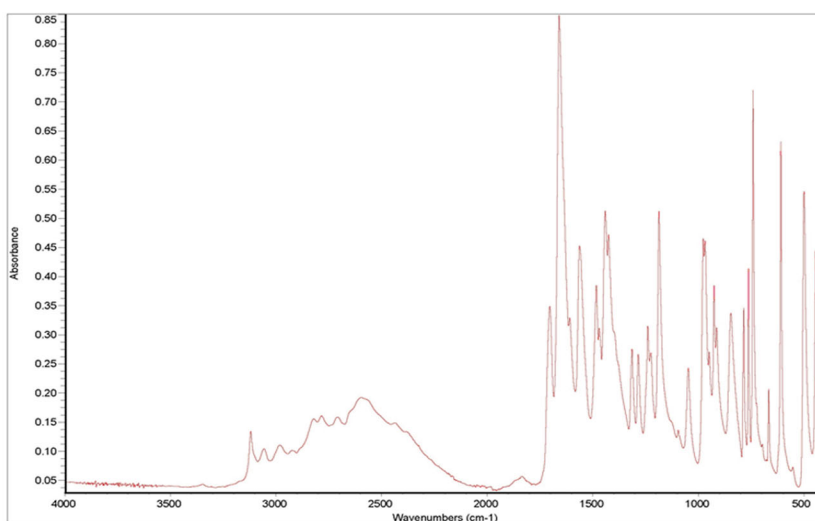


Fig. 2. IR Spectrum of Theophylline on Quest ATR Diamond Accessory



For preparation of the sample for the ATR spectral measurement a small amount of the Theophylline and Ibuprofen powder samples were taken “as is” and placed over the diamond crystal of the Quest™ ATR puck. A set load from the anvil arm assembly of the Quest™ optical unit using the stainless steel flat anvil (P/N GS10820) option was applied to the powder sample to bring it into close and reproducible contact with the diamond crystal. The sample was then ready for spectral data collection.

Spectral Data

The Infra Red transmission spectra collected for the Theophylline sample prepared as a 7mm KBr pellets and run on the Quest ATR Accessory are presented as Figures 1, 2 and 5.

The Infra Red transmission spectra collected for the Ibuprofen sample prepared as a 7mm KBr pellets and run on the Quest ATR Accessory are presented as Figures 3, 4 and 6.

Discussion

In comparison of the spectra collected there will be a difference in the absorption intensities for the sample over the spectral frequency (or wavelength) range when measured as a transmission or as an ATR technique. At the higher frequency (shorter wavelength) end of the spectral range the absorption intensity for a characteristic group frequency vibration is less in the ATR spectrum than for a transmission spectrum measurement due to the change in refractive index over the spectral range measurement for the set angle of incidence being measured

Fig. 3. IR Spectrum of 7mm Diameter KBr Pellet of Ibuprofen Powder

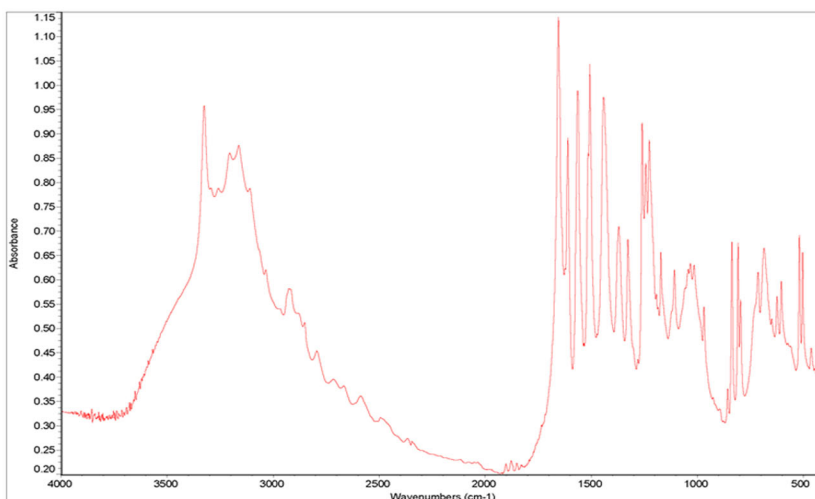
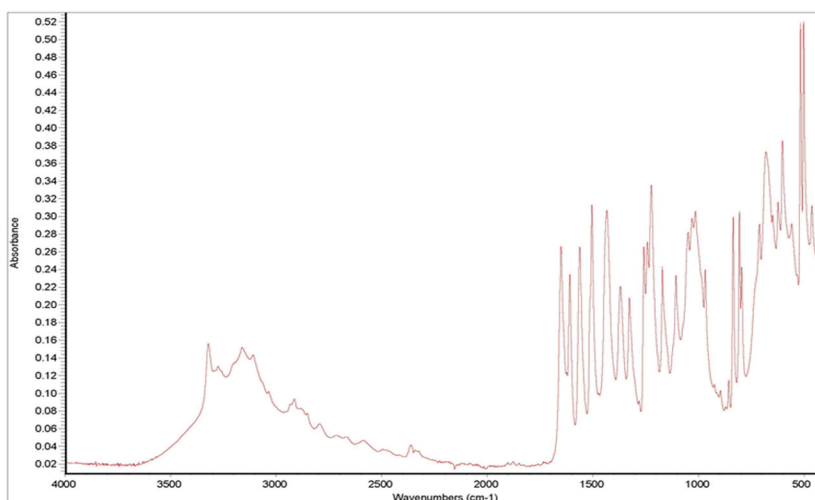


Fig. 4. IR Spectrum of Ibuprofen Powder on Quest ATR Diamond Accessory



– in this instance at a 45° angle for the ATR measurement. Absorption intensities will tend to become of equal strength in comparison between a transmission and ATR spectrum towards the shorter frequency (higher wavelength) end of the spectral range.

It is possible that some weak spectral features which have typical group frequency vibrational modes in the higher frequency region of an IR spectrum may not be easily observed if analysing the sample via the ATR technique. If a transmission method of spectral collection could be achieved for the same sample then there may be a better chance of observation of these spectral features to confirm one way or another the existence of the species from an IR spectrum. If a sample has been

measured using an ATR technique there are typical algorithm calculations offered with proprietary IR instrumentation control and data handling software packages that can be applied to an ATR spectrum to convert the spectral data to that closer representing a transmission spectrum for specific library spectral searches if required.

However, In terms of overall sample handling, preparation and consistent measurement of the two example pharmaceuticals, the ATR spectra that have been collected are indicative of a qualitative and, if the sample is homogenous in nature, quantitative measurement technique over the spectral range required. One major benefit is that the sample has been taken “as is” for quick and easy presentation for measurement by this technique, whereas to

Fig. 5. IR Spectrum of Theophylline Sample on the Quest ATR Diamond Accessory

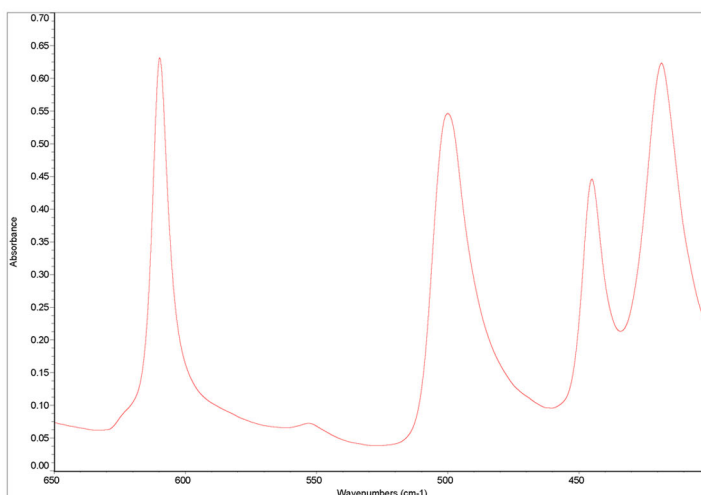
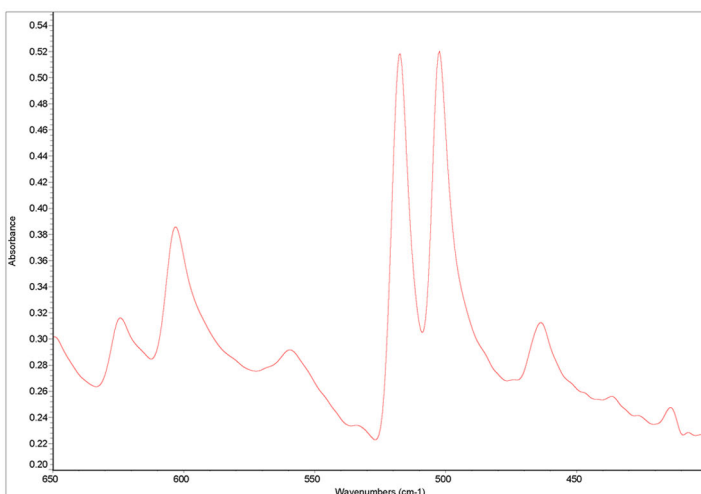


Fig. 6. IR Spectrum of Ibuprofen Powder on Quest ATR Diamond Accessory



produce a KBr pellet for a transmission measurement a series of steps have been carried out with respect to the sample/KBr mix proportion to consider, a method of grinding to use and a process of pressing into a solid disc, which all contribute to the overall qualitative and quantitative result of an IR spectrum that is obtained.

Conclusion

For both these pharmaceutical samples their KBr pellet transmission IR spectra and ATR IR spectra compare very well. To accentuate the spectral features collected for both the Theophylline and Ibuprofen samples using a diamond ATR crystal on the Quest ATR accessory, these have been shown as Figures 5 and 6 respectively over the range from 650cm^{-1} to 400cm^{-1} . These spectral details could not be achieved with use of a ZnSe ATR crystal for any measurement.

In this particular instance, both the solid pharmaceutical samples chosen have allowed for the formation of a KBr pellet to be analysed accordingly, but not all solid samples can be ground to form a KBr pellet. The ATR technique via use of the Quest ATR Accessory with a diamond crystal top plate does though allow for the measurement of a very wide range of pharmaceutical sample types, be they solid, semi-solid or liquid in nature and the spectral data can be collected for the sample over the frequency region between 4000cm^{-1} and 400cm^{-1} if this is mandatory requirement.

Acknowledgement

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