SAMPLE PREPARATION EQUIPMENT

# Pharmaceutical Formulations as 7mm KBr Pellet Preparations

## Introduction

IR spectroscopy is a useful tool for group chemical species identification of a wide variety of sample materials, particularly for the classification of “organic” chemical materials based upon carbon atoms being present in the molecular structure.

A sample can exist in solid, liquid and gaseous states and be analysed by IR spectroscopy from the radiant light interaction with the sample as a transmission technique. (Light passes through the bulk of the sample for a certain pathlength). Reflectance IR spectroscopy techniques can be used for specific sample types, but only in their solid or liquid states at particular pressure and temperature conditions.

## Application

A classic sampling technique for the study of solid sample types by IR transmission spectroscopy is to prepare the solid sample as a potassium bromide (KBr) disc or pellet to mount appropriately and correctly within the sampling area of an infrared spectrometer. This application shows how a few examples of pharmaceutical formulations as tablets/pills and capsules can be prepared to form 7mm diameter KBr pellets for IR study in transmission mode, using the Specac 2T Mini-Pellet Press (p/n GS03940). IR transmission spectra were taken of the 7mm KBr sample pellets produced.

## Equipment and Method

For this study the Specac Basic Solid Pack (p/n GS01150) was used as this provides all of the parts/equipment needed to prepare KBr pellets at 7mm diameter. Instructions for identification and use of this equipment were followed as provided with the equipment itself.

**Specac’s Mini-Pellet Press (p/n GS03940)**

The samples prepared as 7mm KBr pellets were subsequently analysed to produce an IR transmission spectrum for each sample using a Nicolet iS5 IR spectrometer. All spectra were collected over the spectral range between 4000cm$^{-1}$ to 400cm$^{-1}$ using the standard room temperature detector system set at a resolution of 4cm$^{-1}$ for 32 scans.

The samples chosen for this study were eight different types of pharmaceutical formulations, presented in tablet/pill or capsule form for oral introduction into humans. The samples are tabulated in table 1.

Table 1

| Sample | Name | Sample Form/Description | Chemical Formula (*) |
|---|---|---|---|
| 1 | Topiramate | Orange coloured tablet | $C_{12}H_{21}NO_8S$ |
| 2 | Gabapentin | White coloured capsule | $C_9H_{17}NO_2$ |
| 3 | Buscopan | White coloured pill (glossy coating) | $C_{21}H_{30}NO_4(+)$ |
| 4 | Cyclizine | White coloured pill | $C_{18}H_{22}N_2$ |
| 5 | Omeprazole | Yellow coloured capsule | $C_{17}H_{19}N_3O_3S$ |
| 6 | Amlodipine | White coloured tablet | $C_{20}H_{25}ClN_2O_5$ |
| 7 | Imipramine | Red coloured pill | $C_{19}H_{24}N_2$ |
| 8 | Levothyroxine | White coloured pill (small) | $C_{15}H_{11}I_4NO_4$ |

(*) Note: Chemical formula for the active pharmaceutical (substance) in formulation

The pharmaceutical formulation samples as selected for study are mixtures of a variety of different chemicals. The typical make up of a tablet or pill for oral introduction as a compressed form of the formulation consists of:-

5 to 10% of the active sample.
80% of fillers, disintegrants, lubricants, gliders and binders.
10% of compound types that help to ensure easy disintegration, disaggregation and dissolution of the tablet/pill in the stomach or intestine.

Special coatings can make the tablet or pill more resistant to stomach acids, to localise for a specific efficacy and certain coatings of sugars, varnishes or waxes can help to disguise the taste. A capsule is a gelatinous outer envelope that encloses the active substance and formulation mixture.

The method of sample preparation involves a small proportion of the solid sample to be ground and uniformly dispersed in a potassium bromide (KBr) support matrix prior to formation of the 7mm diameter disc or pellet. For all of the sample types, a pre-crushing of the tablet, pill or capsule was carried out to grind the sample mixture to a fine powder itself using an agate pestle and mortar, (p/n GS03600).

The samples varied in ease of preparation to form a powder. The results for their preparation are shown in table 2.

After pre-grinding of the sample, a small proportion of the powdered sample was added to an excess of KBr powder and this mix was further ground together using the pestle and mortar. Up to 2% weight of the sample to 98% weight of KBr as a mix is perfectly adequate to produce an acceptable concentration strength IR spectrum for specific signal intensity and resolution of spectral bands from the sample. The overall quality of a pellet is largely dependant upon the quality of the KBr powder used, which should always be of a spectroscopic grade purity.

When the sample and KBr had been ground to a uniform consistency, an appropriate amount of the powder mix was transferred to fill the 7mm pellet die assembly as used with the 2T Mini-Pellet Press and a 7mm disc was formed. A load of 1.9 tons for each sample was applied to the powder mix for compression from the 2T Mini-Pellet Press and held for 10 seconds. Release of the load and dis-assembly of the die parts resulted in a 7mm diameter KBr pellet being formed and held within the circular die frame. The circular die frame with pellet was placed in the 3” x 2” slide mount holder located in the spectrometer sample compartment for correct positioning and an IR spectrum was collected for the 7mm diameter pellet sample.

Table 2

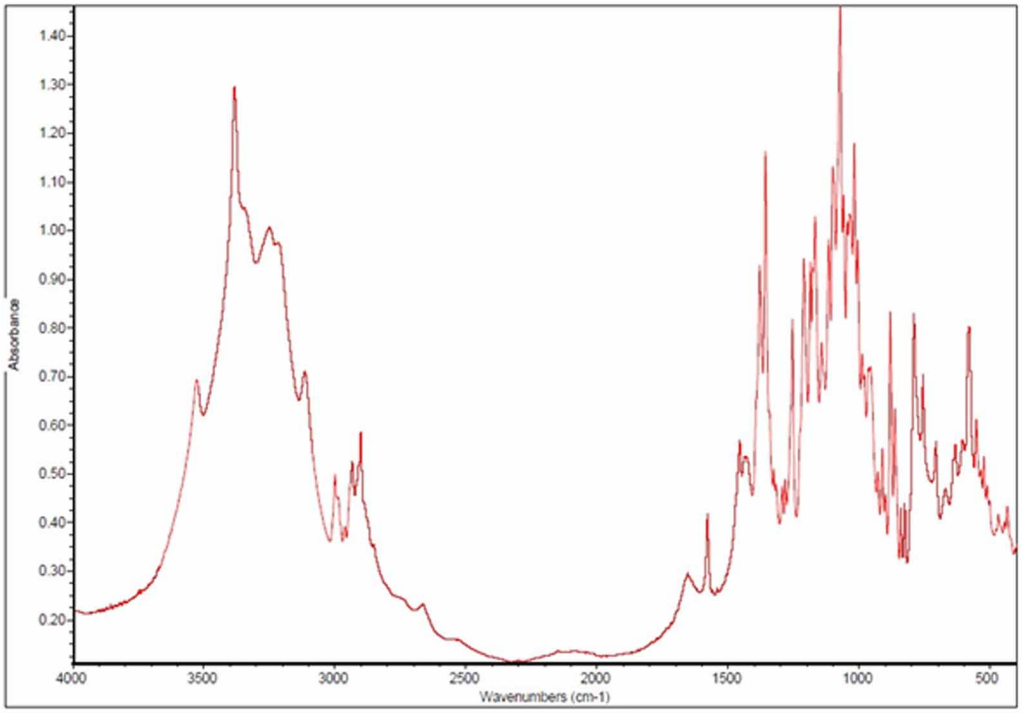
| Sample | Method of Powdering Preparation | Resultant Powder Appearance |
|---|---|---|
| 1 | Tablet held with forceps and cut with a blade. Orange colour outer coating. White powder within. Entire tablet fragments ground in agate mortar. | White powder with fine orange flecks |
| 2 | White capsule casing cut. White powder within emptied into agate mortar and ground. | Fine white powder |
| 3 | Pill held with forceps and cut with blade. Entire pill fragments ground in agate mortar. | Fine white powder |
| 4 | Pill held with forceps and cut with blade. Entire pill fragments ground in agate mortar. | Fine white powder |
| 5 | Yellow capsule casing cut. Hard white spheres within emptied into agate mortar and ground. | Fine white powder |
| 6 | Tablet held with forceps and cut with a blade. Entire tablet fragments ground in agate mortar. | Fine white powder |
| 7 | Pill held with forceps and cut with blade. Red colour outer coating. White powder within. Entire tablet fragments ground in agate mortar. | Fine pink powder |
| 8 | Pill held with forceps and cut with blade. Entire pill fragments ground in agate mortar. | Fine white powder |

**Note:**

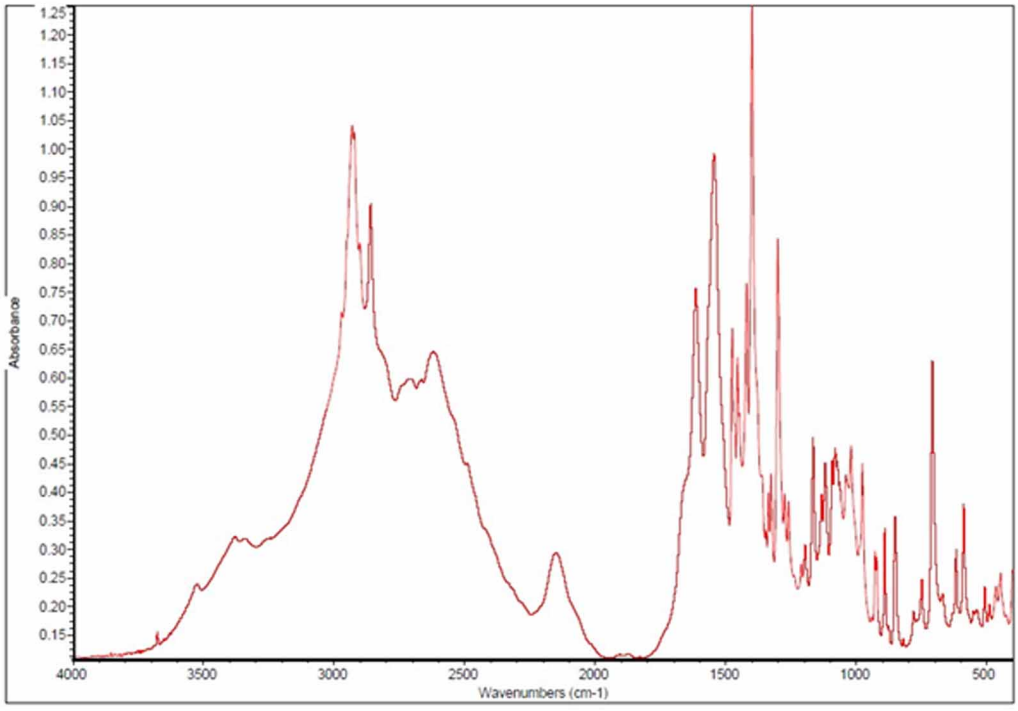
As a suitable reference background for spectral collection of a sample, an empty circular die frame (no sample), was placed into position in the spectrometer sample compartment to present a similar aperture size of 7mm diameter for better spectral sample and reference subtraction matched conditions.

## Spectral Data

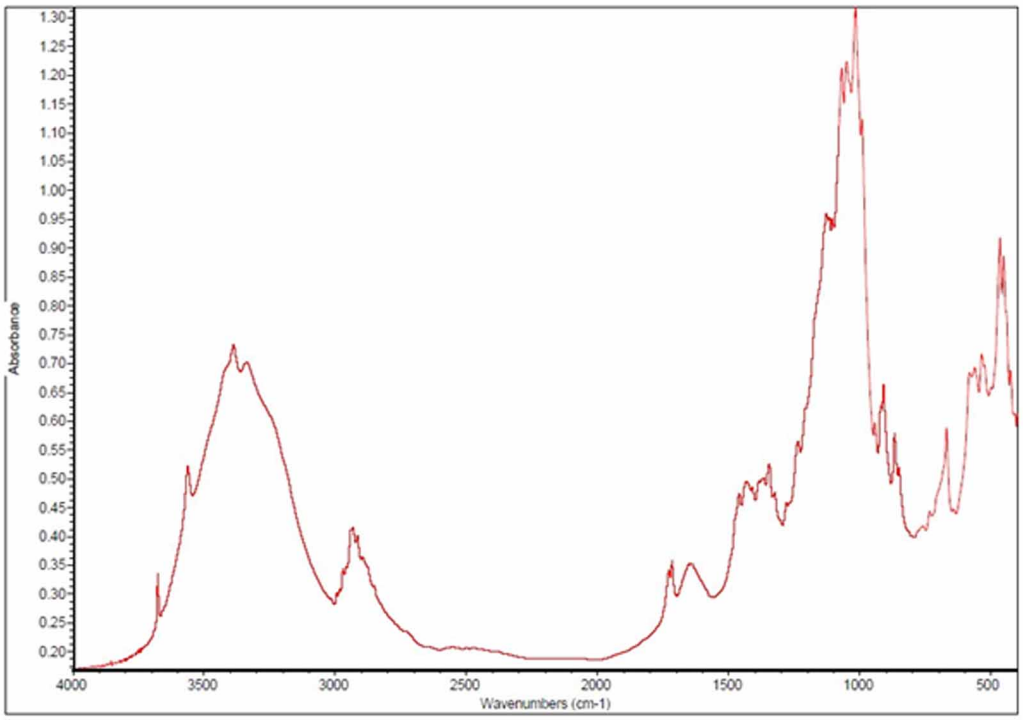
The transmission spectra collected for the eight pharmaceutical formulation samples prepared as 7mm diameter KBr pellets are presented as follows.



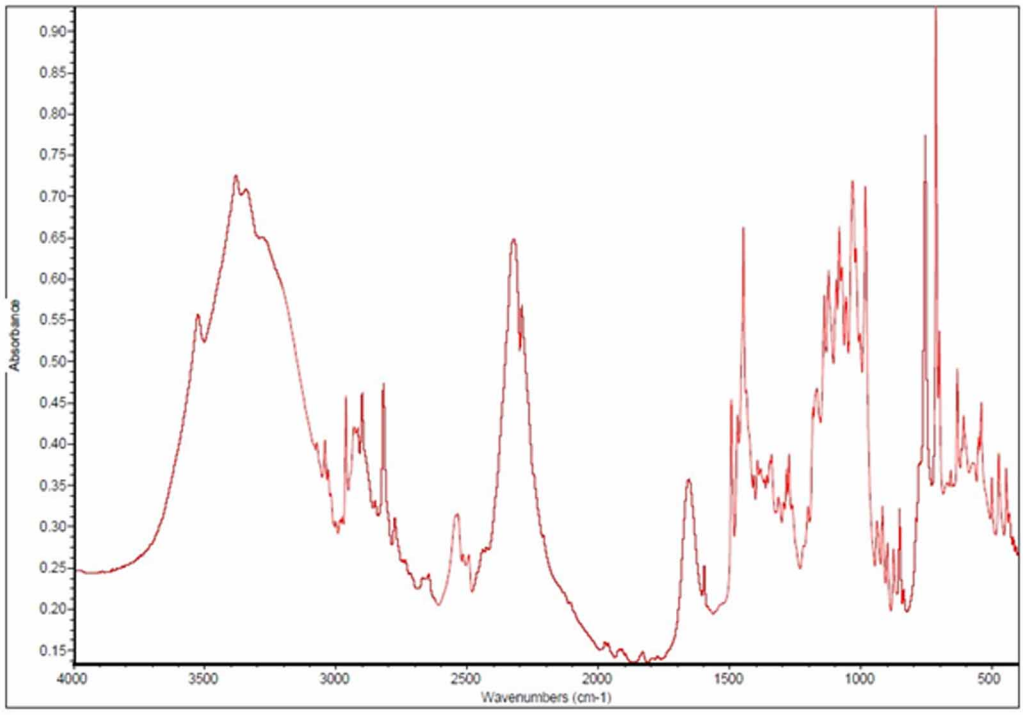

Sample 1 - Topiramate Tablet - Powdered Formulation Prepared as 7mm KBr Pellet



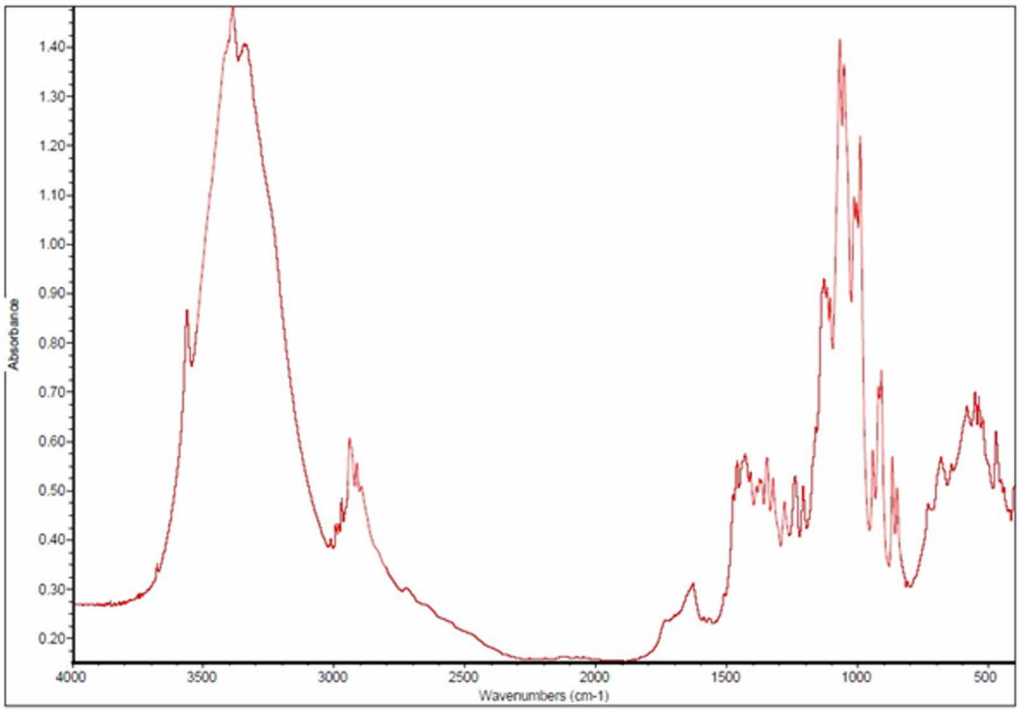

Sample 2 - Gabapentin Capsule - Powdered Formulation Prepared as 7mm KBr Pellet



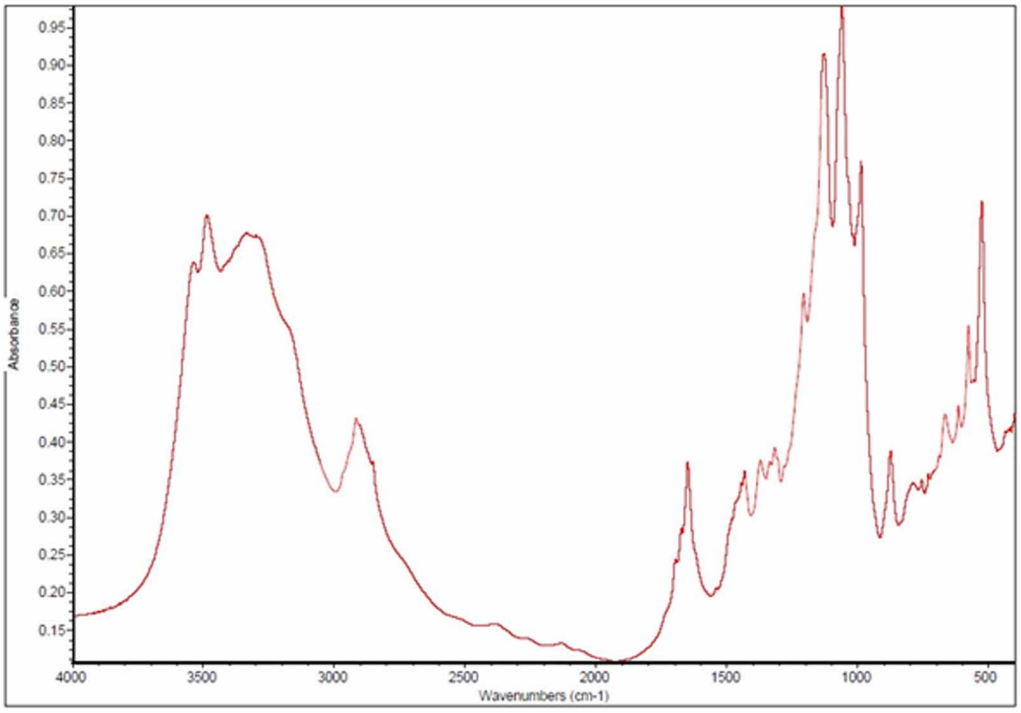

Sample 3 - Buscopan Pill - Powdered Formulation Prepared as 7mm KBr Pellet



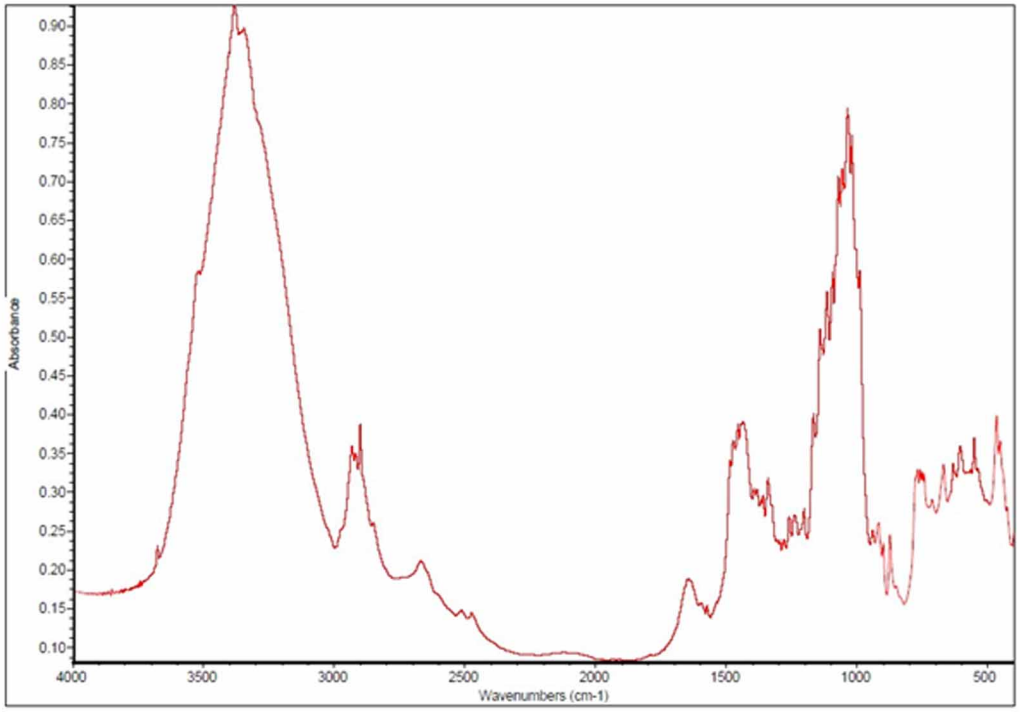

Sample 4 - Cyclizine Pill - Powdered Formulation Prepared as 7mm KBr Pellet



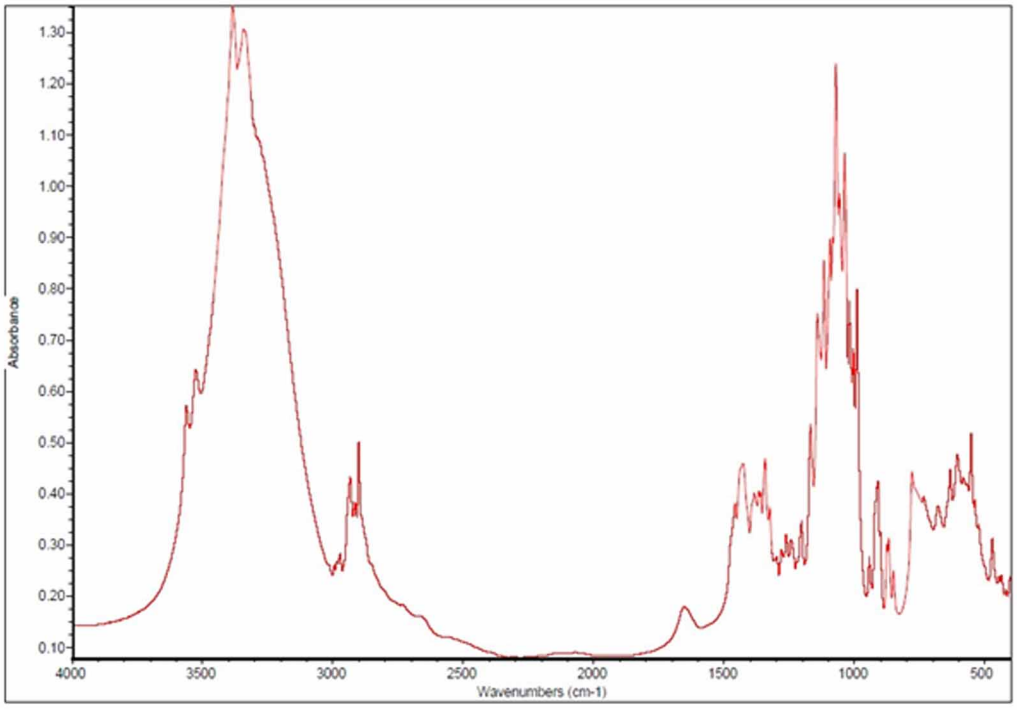

Sample 5 - Omeprazole Capsule - Powdered Formulation Prepared as 7mm KBr Pellet




Sample 6 - Amlodipine Tablet - Powdered Formulation Prepared as 7mm KBr Pellet




Sample 7 - Imipramine Pill - Powdered Formulation Prepared as 7mm KBr Pellet




Sample 8 - Levothyroxine Pill- Powdered Formulation Prepared as 7mm KBr Pellet

## Discussion

Very good quality IR transmission spectra for sufficient signal intensities and overall concentration strength to resolve for the strongest spectral bands have been produced. Each sample has been well ground and distributed throughout the KBr support matrix from the grinding stage in sample preparation to allow for the overall quality of spectrum to be produced from a subsequent formation into a 7mm diameter solid pellet.

The resultant spectra are all unique for the specific sample from this method of preparation, but there are certain overall similarities, consistent with common binders and filler materials being present as an excess in the overall mixture concentration and dominating over the potential relative signal intensities that may be seen in contribution from the active substance alone. Comparison of the spectra for samples 3 (Buscopan), 5 (Omeprazole), 7 (Imipramine) and 8 (Levothyroxine), show particularly close agreement for their overall spectral profiles, but there are fine discriminations potentially attributable to the presence of the differing active substance and specific components in the particular formulation mixture.

## Conclusion

To study solid samples by IR spectroscopy using the transmission technique, the sample can be made to form a KBr pellet, provided the sample itself is prepared specifically, usually from grinding and mixing into a fine powder with KBr, and lends itself to such a method of preparation. Solid samples that pick up water from the atmosphere etc, are not suitable candidates to form into KBr pellets for such IR study using a transmission technique. A reflectance technique may be required instead for specific sample handling.

From establishment of a suitable sample grinding preparation stage for a solid sample, 7mm diameter KBr pellets can be made using the 7mm die assembly with its dedicated 2T Mini-Pellet Press (p/n GS03940) - the whole equipment needed being supplied as the Basic Solid Pack (p/n GS01150).

The equipment involved in such a KBr pellet sample preparation is compact, clean and easy to use. The 2T Mini-Pellet Press itself may be considered small and light enough in weight to be portable and there is the capability of being able to take this method of KBr pellet production pressing system locally for any sample preparation if it is problematic to bring the sample itself to the pressing system. An example can include preparation of samples in a controlled environment (inert atmosphere) and require manipulation using a glove-box.

## Acknowledgement

The study was carried out by: C. Moss, Specac Limited, Orpington, Kent, UK.

**Specac's Basic Solid Pack (p/n GS01150)**

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