Quantifying Simeticone in over-the-counter medicines using FTIR spectroscopy

Introduction

Quantification of the Active Pharmaceutical Product (API) in a finished product is vital to ensure the end consumer gets the correct dosage of the drug. Too little and the desired effect may not be achieved, too much and there is a risk of overdose. Fourier Transform Infrared (FTIR) spectroscopy affords a rapid cheap method for the routine testing of a wide range of pharmaceuticals when enabled by time and effort saving transmission accessories. An example of recent interest to the industry is the quantification of Simeticone in medicinal formulations found on the high street.

According to the United Kingdom's National Health Service, Simeticone is an over-the-counter medication for relief of excess wind, particularly taken by those with irritable bowel syndrome, or to treat colic in babies. It is generally recognised as safe [1] but finds many uses in Pharmacopoeia due to its anti-foaming properties and may even be administered prior to endoscopy examinations to reduce the bubbles and foaming in the gastrointestinal tract [2]. Different Pharmacopoeia standards will provide thresholds for safe use in medicines, which requires the ability to measure concentrations, molecular weight, and viscosity, among other parameters [2] and there will also be standards defining the proper labelling of these compounds, such as **CFR Title 21, Volume 5, Part 332** in the USA.

The European Pharmacopoeia standard 10.0 (01/2017:1470) defines a method for the extraction of simeticone into an organic, toluene phase, which can then be measured by FTIR spectra in a 500-micron liquid transmission cell and quantified by comparison to a stock standard solution of known concentration. We obtained two different formulations of simeticone available on the high street and measured their %API content by reference to a standard simeticone sample of known concentration.

For this method we fitted out our FTIR spectrometer with Specac's Pearl™ liquid transmission accessory, which is ideal for repeated measurements of liquid samples due to its horizontally mounted measurement cell (known as the Oyster™) which opens very simply for sampling and cleaning and closes each time to a defined and repeatable pathlength without tools or fasteners. Our results were found to be in good agreement with the stated dosage on the label, confirming the validity of the method, and the suitability of the Pearl for use with this method. For any analytical testing laboratory the Pearl greatly simplifies the procedure for obtaining an FTIR spectrum of a liquid at a defined pathlength, with higher sample throughput benefits as a result.

Experimental

Test and reference samples containing ca. 100 mg of simeticone were dissolved in 50 ml toluene, and then stirred for 5 min with 100 ml dilute HCl. The organic layer was separated, and 5 ml extracted and dried over 1 g anhydrous sodium sulfate. The resultant liquid was then centrifuged using a home-built centrifuge as described in [2]. Three solutions were prepared, 1 from a dimethicone standard sample (the reference solution), and two from a liquid simeticone solution and the other from a tablet form (the test solutions), both obtained from a local pharmacy.

FTIR spectra were recorded on a commercially available spectrometer using a Specac PearlTM, fitted with a 500-micron wedged CaF2 Oyster Cell.

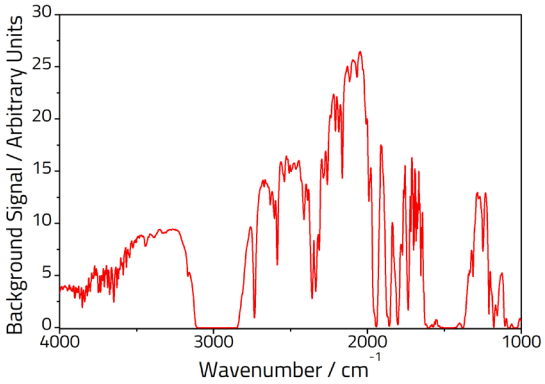

Figure 1: FTIR Spectrum of Simeticone in Toluene recorded against a Toluene background.

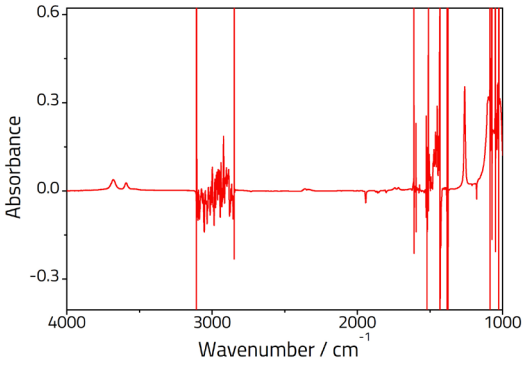

Figure 2: Background FTIR spectrum of Toluene.

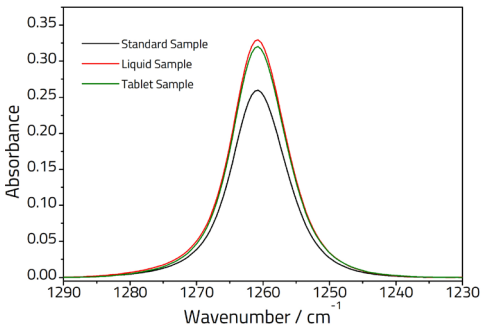

Figure 3: FTIR Spectra showing the CH3 deformation vibration of simeticone, for 3 different formulations.

Results and Discussion

Figure 1 shows the spectrum of simeticone in toluene against a toluene background and is a good illustration of the impact of using a solvent spectrum as the background. Nonsense data is observed in the regions ca. 3140-2800, 1650-1350 & 1200-1000 cm-1. An inspection of the background spectrum of toluene (Figure 2) reveals that in these regions the solvent is totally absorbing, and no light reaches the detector. It is standard practice either to zoom into the solvent-free window (as shown in Figure 3), or to blank out the regions of nonsense and explain in the figure caption that regions obscured by the solvent have been hidden for clarity.

The European Pharmacopoeia Standard specifies the use of a peak at 1260 cm-1 for the quantification of simeticone. This peak is assigned to the symmetric deformation vibration of the methyl group [3] and is shown in Figure 3. From the absorbance values at 1260 cm-1 the experimentally determined % composition of each of the test samples was determined using the formula:

$$\%\text{Content}_{test} = \frac{V_{test} \times C_{ref} \times Abs_{test} \times 100}{Abs_{ref} \times M_{test}}$$

where:

Abs_{test} = Absorbance of the test sample at 1260 cm^{-1}

Abs_{Ref} = Absorbance of the reference sample at 1260 cm-1

C_{Ref} = Concentration of the reference solution (mg/ml)

VT_{est} = Total Volume of Toluene in test solution (ml)

M_{Test} = Mass of test sample (mg)

Table 1 shows the Nominal percentage simeticone in each sample, alongside the absorbance recorded for the solutions prepared from each and the simeticone content as determined by FTIR. In both cases nominal and calculated are within the measurement error from the mass of the sample alone, confirming that both pharmaceutical products match the label.

Sample I.D.	Nominal Simeticone Mass	Nominal Simeticone %	AbsT	Calculated Simeticone
Liquid Sample	120 mg	4 ± 0.3 %	0.326	4.3
Tablet Sample	125 mg	72 ± 0.2 %	0.317	72.1

Table 1: Nominal and spectroscopically determined simeticone content.

Conclusion

In conclusion, the Pearl and Oyster system has been demonstrated for use with the European Pharmacopoeia standard for the determination of simeticone content. The Pearl is an excellent choice for the pharmacuetical industry QC lab owing to its high sample throughput capability. Existing methods can be rapidly deployed without modfication or training.

References

[1] Simeticone - European Pharmacopoeia 10.0, 01/2017:1470

[2] Bhalma et al. Nature Biomedical Engineering, 1, 0009, DOI: 10.1038/s41551-016-0009

[3] Infrared and Raman Characteristic Group Frequencies, Socrates, G., John Wiley & Sons, London, Third Edition, 2001, Chapter 18, ISBN: 0470093072

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