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Application News

No. A549

Spectrophotometric Analysis

Contaminant Analysis on Tablet Surface Using the IRSpirit

The Shimadzu IRSpirit is a compact FTIR with a footprint approximately the size of an A3 (11 × 17 in) sheet of paper (Fig. 1). Designed to take up little space, the sample compartment of the IRSpirit is easily accessible whether installed in "landscape" or "portrait" orientation, so that even a narrow opening on a lab bench can accommodate it. The performance it provides is remarkable too, with the highest signal to noise ratio and maximum resolution in its class. These high-level specifications translate into robust results, especially considering its small footprint.

Shimadzu realizes that customers need access to a wide variety of sampling accessories to get the most out of their FTIR. The sampling compartment of the IRSpirit, designed for maximum flexibility, accommodates existing Shimadzu and third party accessories such as ATR and diffuse reflectance, as well as transmission accessories such as a KBr pellet holder and demountable cells.

Software ease of use is almost as important as its functionality. IR Pilot, an interface within LabSolutionsIR, has four common workflows by default: chemical identification, contaminant analysis, quantitative analysis, and film thickness determination. User determined workflows can be created and saved as well. With push-button simplicity, the user selects an analysis, chooses a method and corresponding accessory, picks relevant data manipulation steps, and then starts the measurement. After data collection, a report is created, summarizing data collection parameters and providing interpreted results.

This article demonstrates the efficiency of the IRSpirit and QATR-S accessory in analyzing a contaminant on the surface of a tablet.

R. Fuji

Fig. 1 Picture of the IRSpirit Compact FTIR

Contaminant Analysis in Pharmaceutical Manufacturing

Despite the rigorous controls in pharmaceutical manufacturing, surface defects are sometimes detected during visual examination of tablets. To resolve contamination issues, it is important to know if the contaminant is intrinsic, such as an undesirable aggregation of ingredients, or alternatively, something that has its origins entirely outside of the manufacturing process. There are several experimental approaches to analyze a surface contaminant, such as removing the area for further analysis. The quality of results often depends on the skill and judgement of the analyst in extracting the contaminant area, as well as the potential for introducing further contamination. Another approach is to investigate the contaminant in situ using FT-ATR. The effectiveness of this approach can be limited for sub-surface contaminants as ATR measures only the material in direct contact with the crystal. The size and shape of the sample will also impact the results, ideally the contaminant would completely cover the 1 mm diameter sample area of the ATR crystal.

Surface Contamination on Tablet - Comparison of Sampling Methods -

This article compares the results of contaminant spectra taken with the sample in situ versus removed by scraping. Fig. 2 shows a contaminant (simulated for the purposes of this study) on the surface of a tablet. The area highlighted by the red circle is approximately 1.2 mm in size, and is exposed on the surface of the tablet. These characteristics (size and surface location) make this a good candidate for ATR measurements. The sample is somewhat irregular in shape though, and may not entirely covert the ATR crystal during a measurement. As ATR is non-destructive though, it is possible to compare the two sampling methods. After acquiring ATR spectra, the sample can be scraped, and re-analyzed.

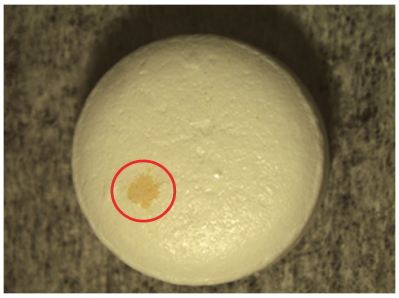

Fig. 2 Picture of Contaminant on Tablet Surface

QATR-S Dedicated ATR Accessory

The QATR-S single bounce ATR accessory has been designed specifically for the IRSpirit (Fig. 3), with easily user-swappable diamond and germanium crystals. FT-ATR spectroscopy is widely used for the analysis of solid and liquid samples because it greatly simplifies sample preparation. By making firm contact between the sample and the crystal, IR spectra of bulk materials can be acquired without the need for "diluting" the sample with KBr, for example.

Fig. 3 QATR-S Accessory Installed in IRSpirit Sample Compartment

Table 1 shows the experimental parameters used to collect data for contaminant analysis. The wideband diamond crystal was used.

Table 1 Measurement Conditions

Instrument	:	IRSpirit-L (KBr window), QATR-S (Wideband diamond disk)
Resolution	:	4 cm^{-1}
Accumulation	:	45
Apodization	:	Sqr Triangle
Detector	:	$LiTaO_3$

In Situ Contaminant Analysis via FT-ATR

The spectrum acquired from the contaminant is shown in as the black trace in Fig. 4. The library search results highlight two likely sample components, acetylsalicylic acid (green spectrum) and acetaminophen (red spectrum).

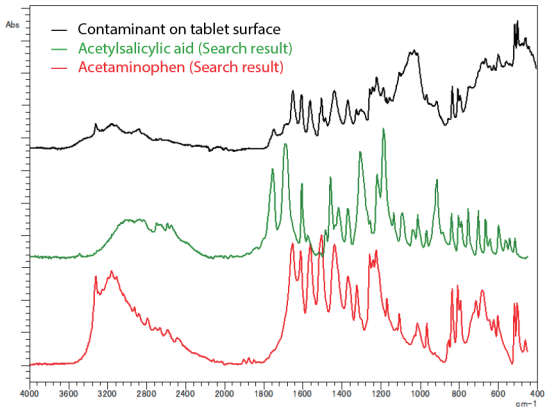

Fig. 4 Analysis of In Situ Contaminant Using QATR-S

FT-ATR Analysis of Removed Contaminant

Following the in situ analysis, the contaminant was scraped from the tablet, and the resulting powder was again measured with FT-ATR. A portion of the sample matrix was similarly removed and measured. Fig. 5 and Fig. 6 show infrared spectra of the contaminant and tablet, respectively, along with the search results for each. This analysis shows that the contaminant is acetaminophen, whereas the tablet matrix is acetylsalicylic acid.

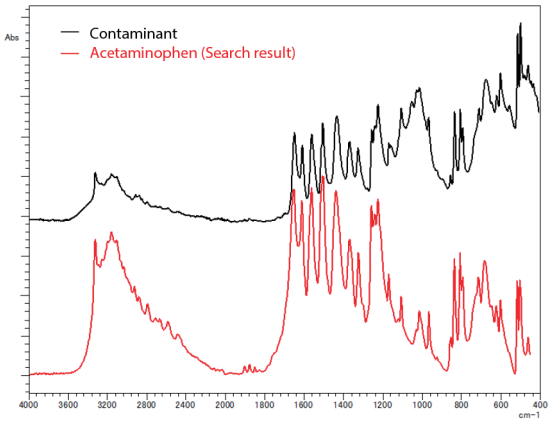

Fig. 5 Contaminant Spectrum and Search Result – Destructive Sampling

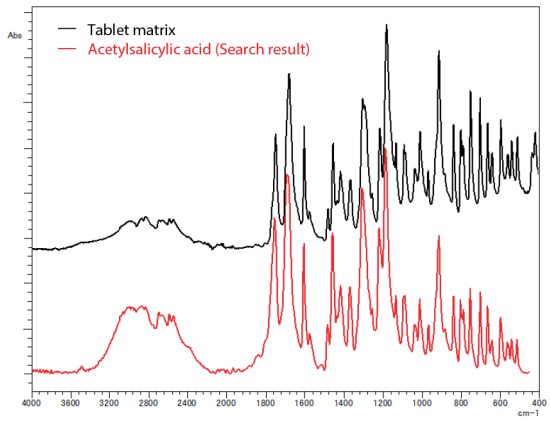

Fig. 6 Tablet Matrix Spectrum and Search Result – Destructive Sampling

Conclusion

A tablet surface contaminant was analyzed using the IRSpirit with the QATR-S accessory. As FT-ATR is a non-destructive measurement technique, it was possible to compare results of in situ sampling to a subsequent destructive contaminant removal approach. The in situ approach showed a mixture of components, mostly acetaminophen with a slight contribution from acetylsalicylic acid. The results of the destructive sampling approach clearly separated the contaminant, acetaminophen, from the sample matrix acetylsalicylic acid. In this example, because of the relatively small size and irregular shape of the tablet contaminant, the destructive sample approach gave a more robust answer to the chemical identification question. For both sampling methods, it was easy to determine that the contaminant was something intrinsic to the manufacturing process, and not an environmental or external contaminant.

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