

# Agilent Cary 630 Laboratory FTIR and Agilent 4500 Portable FTIR Systems for Detection of Counterfeit Pharmaceuticals

## Application Note

Pharmaceutical Testing and Research

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### Introduction

Counterfeit pharmaceuticals are of concern internationally. In certain regions of the world, the percentage of counterfeit pharmaceuticals present in the consumer marketplace is troubling. For this reason, active testing programs are in place, and they tend to rely on classical analysis methods such as chromatography and wet chemistry. These methods can be time-consuming, labor intensive, and typically require samples to be sent to a laboratory for analysis. For these reasons, there is substantial interest in applying optical spectroscopic techniques since they are often faster, require less expertise to execute once a method is developed, and are amenable to use outside traditional laboratories. This latter advantage makes them ideal for screening pharmaceutical samples at points of entry and exit in the consumer supply chain.

This application note demonstrates the effectiveness of Agilent compact and portable FTIR systems for detecting counterfeit pharmaceuticals with three examples: ethambutol hydrochloride, cephuroxime axetil, and atorvastatin calcium.

In a recent article, Bei Ma, *et al.* compared some optical spectroscopic analyzers as potential solutions for detecting counterfeits of two different, important, and often counterfeited pharmaceuticals [1]. The drugs were ethambutol hydrochloride, an antituberculosis drug, and cephuroxime axetil, an antibiotic. Handheld Raman, near-infrared, and portable FTIR analyzers were compared for their potential to detect counterfeiting of these two drugs. The FTIR system used was the Agilent Cary 630 FTIR spectrometer (Figure 1). This application note presents a summary of the researchers' experiments and findings.



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In a similar analysis, the widely used cholesterol-lowering drug atorvastatin was analyzed using a library search method in the MicroLab software. This software suite, which is used for both Cary 630 and Agilent 4500 FTIR systems, features an advanced library search capability that allows multiple spectral libraries to be searched from a single analysis. MicroLab software is available with an Agilent proven SCM/SDA compliance package, which provides security, user access, and auditing features required for GMP by the 21 CFR part 11 regulation.

## Materials and Methods

In the Bei Ma, *et al.* article, both reference standards and placebo tablets were prepared according to established methods. The tablets and capsules were measured by the Raman, NIR, and FTIR spectrometers as ground powders. For the ethambutol hydrochloride and cephuroxime axetil APIs, two sets of tablets (high and low API levels) were prepared. The same amount of API was present in each tablet set, but the amount and types of excipients were varied. Placebo tablets had the same amount of excipients, but the API was not present. The pure APIs were sourced from two different manufacturers for each drug.

The Cary 630 FTIR used in this study was equipped with a single reflection diamond ATR and Agilent MicroLab FTIR method-driven software [2]. In addition to the Cary 630 FTIR, which is suited to routine analysis in field laboratories, Agilent offers the 4500 FTIR (Figure 2). The 4500 FTIR is a compact, fully mobile, battery-powered spectrometer that is well suited to out-of-lab analysis [3].

For the FTIR measurements, the researchers measured the ground powders in the  $4,000$  to  $650\text{ cm}^{-1}$  region and recorded 32 coadded interferograms. A spectral library that consisted of a subset of the reference standard, API containing tablets, and placebo tablets was created, and the remaining tablets were searched against this library. A hit-quality index value was used to indicate how well the sample matched the library reference spectra.



Figure 1. The Agilent Cary 630 FTIR equipped with single reflection diamond ATR is well-suited to analysis of pharmaceuticals in QA/QC and field laboratory environments. The system's compact size, interchangeable sampling interfaces, method driven software, and IR spectral database search capabilities enable routine identification and verification for a wide variety of compounds.



Figure 2. The Agilent 4500 Portable FTIR is a battery-powered, mid-IR spectrometer that, like the Cary 630, is well-suited to pharmaceutical analysis. The 4500 system features a dedicated sample interface, such as the diamond ATR, is fully mobile, and designed for deployment in field locations.

## Results and Discussion

When searched against the mid-IR reference library, the test samples for all authentic tablet and capsule samples for the different APIs returned a hit quality  $>0.95$ . The hit quality for the placebos was  $<0.95$  but  $>0.50$ . The researchers also postulated that, because of selective mid-IR fingerprint (1,800 to 1,150  $\text{cm}^{-1}$ ) absorbance, it is possible to rapidly detect samples that contain no API. They also found that for the cephuroxime samples, the excipients exhibited weak IR absorbance in the fingerprint region, whereas the API strongly absorbed. For this compound, the authentic samples had a hit quality  $>0.98$ , whereas the placebo hit quality was  $<0.01$ . Bei Ma, *et al.* stated that cephuroxime axetil is amenable to analysis by portable mid-IR spectroscopy, and counterfeit samples in which the API is absent can be readily differentiated.

Similarly, atorvastatin calcium was measured using the diamond ATR accessory on the Cary 630 FTIR, and searched against 40,000+ IR library spectra (Figure 3, Red). As in the previous drug examples, the quality index (Figure 3, left column) was  $>0.95$ . This indicated a high quality match to the reference library spectrum of atorvastatin. The software displays the selected library hits for the visual confirmation of peaks matching the reference spectrum. In the case of the analysis of a placebo pill without atorvastatin (Figure 4), the library indicates a nearly perfect match ( $>0.99$ ) to lactose.

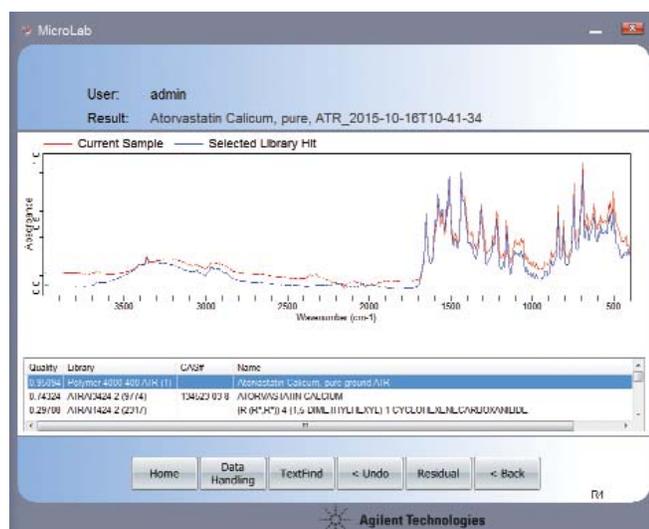


Figure 3. The library search results displayed from the analysis of Atorvastatin Calcium pure sample (red), measured on the Agilent Cary 630 FTIR. The reference library sample spectrum is displayed (blue) as is the hit quality index.

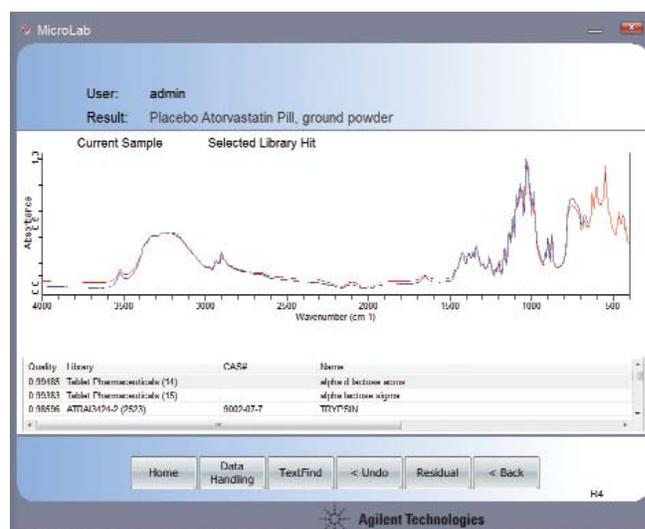


Figure 4. The library search results of a placebo pill sample, measured on the Agilent Cary 630 FTIR. The reference library sample is overlaid as the blue spectrum, which indicates a nearly perfect match to lactose.

## Conclusions

For the important and frequently counterfeited pharmaceuticals ethambutol hydrochloride and cephuroxime axetil, the analysts found that a portable mid-infrared spectrometer was more effective than either handheld Raman or portable NIR spectrometers for differentiating authentic samples from samples without API. They reported that the Raman and NIR systems gave false negative results when comparing the same product from different manufacturers. They speculated that this may be due to interferences caused by the excipients. In the atorvastatin example, we show how matching against a spectral database can rapidly elucidate if active ingredient is present.

The availability of compact laboratory FTIR spectrometers such as the Agilent Cary 630 or the Agilent 4500 portable FTIR is important in the detection of counterfeit pharmaceuticals. Portable systems enable definitive measurements to be made closer to the source, in field laboratories, or completely out of the lab, at distribution and receiving sites.

## References

1. Bei Ma, *et al.* "Rapid Detection of Counterfeit Drugs of Ethambutol Hydrochloride and cephuroxime Axetil using Handheld Raman, Near Infrared and Portable FTIR Technologies" *American Pharma. Rev.* July/August (2014).
2. See, for example, [http://www.chem.agilent.com/Library/brochures/5990-8570EN\\_Cary\\_630\\_Bro.pdf](http://www.chem.agilent.com/Library/brochures/5990-8570EN_Cary_630_Bro.pdf)
3. See, for example, [http://www.chem.agilent.com/Library/datasheets/Public/5990-8095EN\\_4500-Series-FTIR\\_DataSheet.pdf](http://www.chem.agilent.com/Library/datasheets/Public/5990-8095EN_4500-Series-FTIR_DataSheet.pdf)

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