Terahertz pulsed imaging identifies counterfeit products

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Revealing a product’s chemical structure makes it easy to differentiate real pharmaceuticals from pretenders.

Terahertz technology has the advantages of being non ionizing, non destructive, and able to image at depth. The technique’s ability to act as both an analytical tool as well as for monitoring or inspection applications has fuelled interest in many markets including security, military, medical, and pharmaceuticals. Though counterfeiting is a key issue facing many industries, provision of pharmaceuticals is one of the few where counterfeit products can lead to serious illness, injury, and potentially death. A recent report by the World Health Organisation has shown that counterfeit medication can account for up to 30% of product sales in some countries. Worse than that, a key route of these fake medicines to the public is via the internet: here, counterfeit product can account for 50% of all medical transactions.

To counter this, we at TeraView have developed Terahertz Pulsed Imaging (TPI™) technology to non-destructively image solid dosage forms in three dimensions. Operating at wavelengths between microwave and infrared, our technology can provide information that is not obtainable at other wavelengths. The system provides information on tablet and coating integrity and structure, and it also has the ability to monitor internal changes, such as moisture ingress, over time: specifically, this means it can detect changes in the polymorphic or hydrate state of a drug substance within a tablet or capsule. Because the method is not destructive, the dosage structure, or changes within it, can give insight in to any variations that are seen in the drug release profile from the tablet or capsules.

The unique spectral and/or structural fingerprints obtained using terahertz imaging are sensitive to small variances in a product, and every tablet manufactured has a fingerprint that is specific to its physical structure and chemical composition. The acquired spectra can even show up differences in the manufacturing methods used, even though outwardly the products may look the same. It is this capability that makes TeraView imaging technology useful in counterfeit detection.

Figure 1. An image of the TPI system showing the terahertz beam scanning across a tablet sample to determine the coating thickness, uniformity and distribution across a tablet and the integrity of the internal structure.

How it works

TPI combines refractive index measurements with terahertz spectroscopic measurements to build complete three-dimensional maps of the internal structures of samples in a non destructive manner. The concept behind it is similar to that of a radar system. The terahertz beam, consisting of a train of pulses, is scanned across the sample (see Figure 1) and reflections are received from various layers or interfaces within. The delay of the reflected pulse across the transient electric field is measured in the time domain, obtaining both the amplitude and phase of the pulse to give depth information within the sample. Multiple return pulses occur wherever there is a refractive index change due to chemical or physical differences (see Figure 2). In some circumstances, the waveforms can then be mathematically transformed to produce an absorption spectrum for the sample to determine its composition and structural features.

Absorptions observed in the terahertz region are commonly associated with the fundamental intermolecular hydrogen bond-
ing vibrations and crystalline-structure lattice vibrations. Although most common organic and inorganic materials are semi-transparent to terahertz frequencies, they usually generate distinctive spectra that enable them to be imaged, identified, and analysed using terahertz light, giving both qualitative and quantitative capability.

To determine differences between an originators product and a counterfeit, the tablet structure and coating would be analysed using the TPI system and then the terahertz time-domain data would be displayed in several formats to characterise the coating layers. Fitzgerald et al.\(^4\) clearly demonstrated this capability. In Figures 3-5 it can be seen that the originators tablet consists of a series of complex coating layers, whereas the alternative tablets have only a single coating layer.

**Conclusion**

TeraView TPI technology is currently implemented by pharmaceutical companies for analysis and monitoring of critical quality attributes of dosage forms alongside other methods of analysis. The instrument is also used as a key tool for root cause analysis of tablet structures as well as defining and optimizing product formulations and process limits. The technology is also compatible with on- and in-line inspection applications for quality control and avoidance of regulatory non compliance, both important drivers for the industry. For application in tracking counterfeit products, once the TPI system is installed it can be used to regularly scan tablets as part of an ongoing monitoring process.

**Figure 2.** Schematic of a terahertz pulse being transmitted and reflected from interfaces within a tablet.

**Figure 3.** Example of TPI waveforms from two tablets. The top trace is the originator product. The lower trace is a tablet that visually looks the same but is physically different, as shown by the pulses that arise from interfaces in the coating structures.

**Figure 4.** The peaks in the waveform can be clearly attributed to the coating and core parts of a tablet.

**Figure 5.** Depth profile of the tablets clearly show the interfaces and demonstrate the complexity of the originators product.
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References