

Rapid polymorph identification with the RA802 Pharmaceutical Analyser

Chemical sciences

The stability, bioavailability and processability of an active pharmaceutical ingredient (API) are key to a candidate molecule's ability to be developed into a commercially viable product, sometimes referred to its 'drugability'.

Characterising the polymorphism of APIs has become an important consideration in this process. Different drug polymorphs can have substantially different drugabilities and can vary markedly in their:

- Dissolution rate
- Solubility
- Bioavailability
- Stability
- Flow/milling/compression properties
- Melting point

Characterising the different polymorphic forms of a drug and selecting the optimum polymorph for your product are now essential criteria.

Furthermore, ensuring the correct polymorphic form is present in each product, and that the same form remains present throughout its shelf life, forms an essential part of a product's quality criteria.

The rise of polymorphism has also become an increasingly important aspect of patent law, as a means of both extending and circumventing existing patents to produce different products with improved performance.

Case study

We were approached by a client who was looking to confirm the presence of a specific polymorph in its product.

A competitor to the client was already on the market with a product that contained a patented polymorph (Polymorph A). Our client's product used an unpatented polymorph (Polymorph B) with improved bioavailability.

It was important, in order to avoid any potential for patent infringement, that our client's product only contained their Polymorph B, and that Polymorph B did not undergo any conversion into Polymorph A during storage.

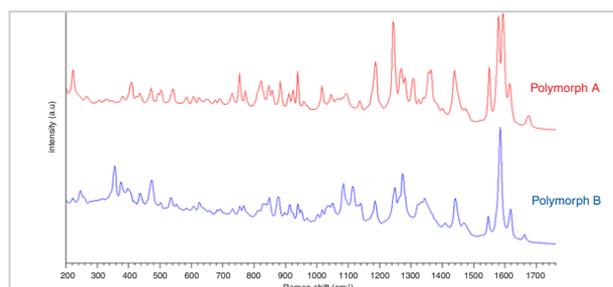
Conventional methods for detecting polymorphism such as XRD are destructive, time-consuming and often poorly suited to characterising blends of materials, such as tablets and other pharmaceutical products, and consequently, did not give the assurance that our client required.

Our clients approached us looking for a technique without these limitations. In order to investigate the two polymorphs we used Renishaw's RA802 Pharmaceutical Analyser.

Analysis

The client's and their competitor's tablets were both analysed using the RA802 Pharmaceutical Analyser. The instrument's software analysed the collected Raman data for each tablet and identified the individual Raman spectra for each of the products' components, including the two polymorphs.

The differences between the spectra are characteristic of two different polymorphic forms.



Overlaid Raman spectra of polymorphs A (red) and B (blue)

The Raman spectra of our client's product matched exactly with a reference spectrum which was collected on the pure form of Polymorph B.

Further analysis confirmed that there was no evidence of Polymorph A in our client's product and no evidence of Polymorph B in the competitor's product.

Additional analysis of stored samples showed no evidence of the conversion of either polymorph into the other following accelerated stability.

When looking for small amounts of chemically similar material, such as polymorphs, the subtleties in the spectral differences between techniques like XRD and IR-microscopy mean that the spectra arising from such materials are often lost in the background noise.

RA802 collects thousands of Raman spectra over a sample surface and has sufficient sensitivity and specificity to easily identify chemically similar components, such as polymorphs, even in complex blends of material, increasing our users' confidence in the results.

This confirmed that RA802 is well-suited to analysing polymorphs. Advantages of the RA802 include:

- High sensitivity to small changes in crystal structure
- Speed of analysis
- No sample preparation required
- Non-destructive
- No method development required
- No risk of contamination
- Ease of use - no need for expert user
- Small footprint

Conclusion

Increasing amounts of money and resource are being devoted to characterising different polymorphic forms and understanding their performance differences.

Current methods for determining polymorphism can be expensive, resource-intensive and require expert users to operate equipment and interpret data.

RA802 circumvents the issues posed by other techniques by achieving a higher degree of sensitivity and selectivity, but being able to perform tablet analysis quickly with minimal user training and method development.

RA802 is a new tool for formulators looking to understand and overcome the challenges posed by polymorphism, and to be able to substantiate patent claims or avoid patent infringement.



The Renishaw RA802 Pharmaceutical Analyser

Renishaw. The Raman innovators

Renishaw manufactures a wide range of high performance optical spectroscopy products, including confocal Raman microscopes with high speed chemical imaging technology, dedicated Raman analysers, interfaces for scanning electron and atomic force microscopes, solid state lasers for spectroscopy and state-of-the-art cooled CCD detectors.

Offering the highest levels of performance, sensitivity and reliability across a diverse range of fields and applications, the instruments are designed to meet your needs, so you can tackle even the most challenging analytical problems with confidence.

A worldwide network of subsidiary companies and distributors provides exceptional service and support for its customers.

Please visit www.renishaw.com/chemicals for more information.