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RA802 Pharmaceutical Analyser

Solving problems in the pharmaceutical industry

Understanding how a formulation's properties determine its performance continues to be a key challenge for the pharmaceutical industry. There are many examples of drugs which were thought to be the next 'magic bullet' but never made it to market because of the difficulties they posed to formulators.

In the last few decades this problem has become more pronounced with the rise of computational chemistry as a method of drug design. This has resulted in the emergence of increasingly large, complex APIs which diverge ever further from Lipinski's rules for druglikeness.

Raman imaging is increasingly recognised as a valuable analytical technique for the pharmaceutical industry. It enables scientists to evaluate formulations in both development and quality control environments.

The European Pharmacopoeia has recently published a new General Chapter 5.24 specifically addressing chemical imaging, including Raman imaging, and its benefits and applications within the pharmaceutical industry.

What is Raman imaging?

Raman spectroscopy is an information-rich analytical technique.

Each molecule has a unique Raman spectrum that is highly specific; it is sometimes referred to as a 'molecular fingerprint'. So unique is each 'fingerprint', Raman is able to easily differentiate between species which are chemically very similar, including polymorphs, amorphous forms, salt forms and hydrates.

The RA802 Pharmaceutical Analyser uses Raman imaging to generate high-definition images of pharmaceutical materials. By collecting Raman spectra over a sample surface, it is possible to build up a Raman image of the entire sample, revealing the distribution of its components.

You can identify particles as small as 1 µm within the image which correspond to each formulation component, including:

- API/salts/hydrates/polymorphs/amorphous forms
- Excipients
- Contaminants
- Degradation products

as well as information about the characteristics of each component, including:

- Morphology
- Uniformity
- Agglomeration
- Particle size distribution

The RA802 Pharmaceutical Analyser

The RA802 Pharmaceutical Analyser is the only dedicated high-speed Raman imaging system designed for pharmaceutical analysis. It can generate a comprehensive Raman image of the sample surface in as little as 5 minutes using Renishaw's unique LiveTrack™ and StreamLine™ technologies.

The system can be used to collect individual spectra or multiple spectra can be collected and used to generate a chemical image of a sample surface.

When generating Raman images, chemical components can be segregated using false colours and characterised using particle statistics. This gives users a tool to understand how each component is distributed throughout the sample and rationalise real-world performance between different batches and formulations.

The compact, easy-to-use RA802 Pharmaceutical Analyser

Why use the RA802 Pharmaceutical Analyser?

Renishaw's RA802 Pharmaceutical Analyser is a brand-new Raman imaging system designed to help scientists tackle formulation challenges and expedite drug development by enabling users to:

- Understand distribution of formulation components
- Quantify content uniformity/homogeneity
- Compare batch to batch variation
- Identify CPPs, CQAs and CMAs
- Diagnose issues quickly
- Identify the nature and presence of anomalous material
- Relate formulation properties to real-world outcomes

The advantages of the RA802 Pharmaceutical Analyser include:

- Ease of use – no need for expert users
- Small footprint
- No need for sample preparation
- Simple method development
- Internal reference standards
- No risk of contamination

Problem solving example

It is important that dissolution profiles between batches are equivalent in order to maintain theraputic consistency. If the dissolution profiles are different then this can have a marked effect on the bioavailability. Examples of two different blood serum concentration profiles are shown below.
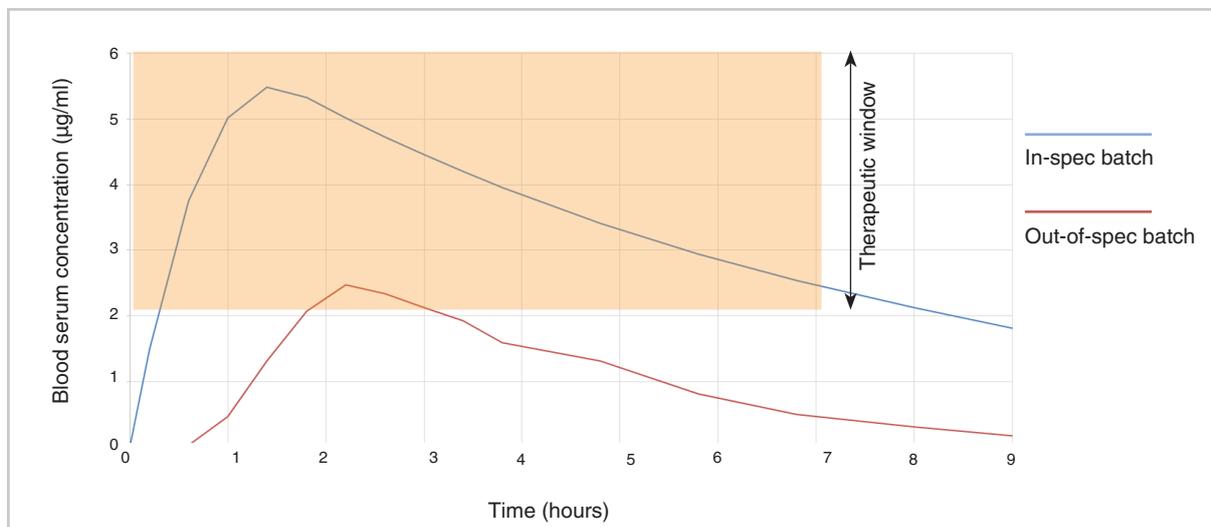
An example of how different dissolution profiles can influence drug efficacy

One of the factors that can cause differences in bioavailability is the aggregation of granules during the granulation and tableting process. Below are two example Raman images of tablets that we would expect to see differences in dissolution and bioavailability. The particle statistics for the API granules are also included below.
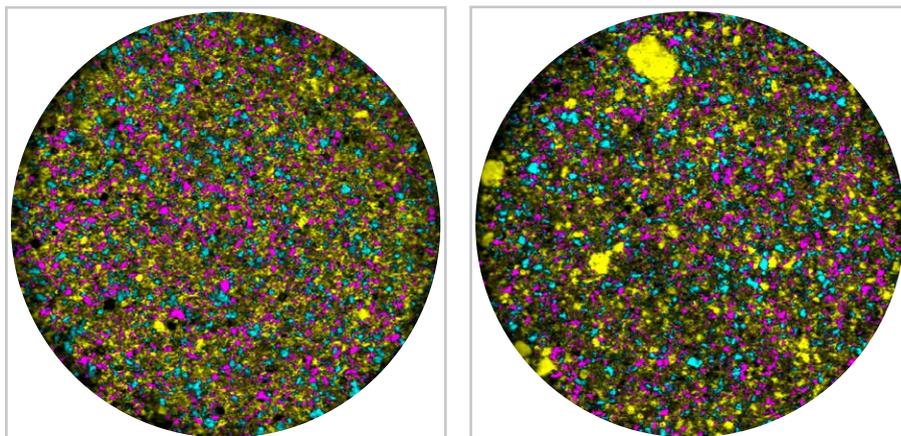
Raman images of chemical composition of tablets (API coloured yellow) from two different batches: batch A (left) and batch B (right)

	Particle statistics (average of 5 tablets)	
	Batch A	Batch B
Number of domains	3,858 ± 165	2,266 ± 155
D90 (number weighted)	189 ± 8 µm	940 ± 110 µm
Centre of Area (lower is more uniform)	2.5 % ± 0.9%	5.8 % ± 1.7%

Conclusion

It is possible to infer the following outcomes in batches with aggregated granules, where the API is less uniformly dispersed throughout the tablet:

1. The aggregation would attenuate the dissolution of API as it passed through the gastrointestinal tract and thus less drug would be available for absorption into the systemic circulation.

2. This would lead to not only a delayed and lower maximum concentration but also a shorter duration of action and a weaker therapeutic effect.

The RA802 Pharmaceutical Analyser gives formulators a tool to understand how a formulation's properties (uniformity, component distribution, particle size, morphology) determine its performance (dissolution, bioavailability, stability, robustness).

Standard content uniformity measurements cannot do this and are unable to identify this problem prior to batch release.

Raman analysis, as employed in the RA802 Pharmaceutical Analyser, is one of the only techniques capable of this – conventional techniques such as HPLC and XRD do not give particle data and require the sample to be destroyed to measure its properties.

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Contact your local Renishaw representative to learn how the RA802 Pharmaceutical Analyser can help solve your formulation problems, or visit www.renishaw.com/RA802 for more information and case studies.

Specifications

Parameter	Value
Laser wavelength	785 nm
	Laser power: >150 mW at sample. Innovative StreamLine technology enables higher laser power use without sample damage
Spectral range	100 cm^{-1} to 3250 cm^{-1}
Spectral dispersion	2 cm^{-1} $pixel^{-1}$
Minimum image pixel size	1 µm
Field of view	Macro ~21 mm × 16 mm (with zoom options)
	Micro ~ 330 µm × 250 µm (with zoom options)
Focusing	Macro – Manual or pre-defined
	Micro – Automatic (LiveTrack) or manual
Data collection speed	Over 1500 spectra/s
Maximum sample size	~ (110 mm × 90 mm × 25 mm) – fits 96 well plate
Power, voltage	100 – 240 VAC ± 10%, 50/60Hz, 100 W maximum
Dimensions	720 mm (W) × 502 mm (H) × 535 mm (D)
Mass (not including computer)	54 kg
Laser class	Class 1 laser product complies with IEC60825-1. CE marked
Software	Renishaw WiRE software with CFR21 Part 11 functionality database, particle statistics and reporting function
Standards	Inbuilt reference standards and automated performance qualification
Qualification	Full IQ/OQ/PQ

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/Raman for more information.