Practical Solutions Newsletter

Agilent
Trusted Answers

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Increasing Efficiencies and Reducing the Cost per Test for Content Uniformity Testing

Lee Dowden, Product Manager, Dissolution Systems

Over the past decade, Transmission Raman Spectroscopy (TRS) has been increasingly implemented in pharmaceutical laboratories. TRS is a molecular spectroscopic technique that provides information of the chemical species within a sample. 'Transmission' Raman is different from the more common 'backscatter' Raman approach due to its 180° excitation-collection optical geometry, which permits a large sampling volume. The Agilent TRS100 Raman Quantitative Pharmaceutical Analysis System has been used as a qualitative and quantitative analysis solution for solid dosage forms, complimenting traditional methods.

Figure 1. Loading a tray into the Agilent TRS100

Why TRS?

Increasing pressures on the workplace—including accessing resources, reducing product release times, and considering environmental influences for sustainable testing—mean that alternative or complimentary methods to traditional sample extraction and measurement techniques have become essential. TRS removes the need for sample preparation due to the spectroscopic measurement being taken from the intact dosage form. It is therefore applicable to a variety of samples, including tablets, capsules, powders, creams, emulsions and drug-embedded polymers. This makes it an excellent tool for content uniformity testing, enabling fast, nondestructive bulk analysis without solvent or disposal. This leads to a low cost per test for routine QC testing.

Not just for labs

TRS instruments are not only used within the laboratory but have also been deployed next to or close to the manufacturing processes for at-line or near-to-line analysis (such as blend uniformity or process checks of uncoated samples). Typical scan times of a tablet range from 10 to 60 seconds per sample, enabling a high throughput of samples and avoiding a bottleneck in the manufacturing process.

Figure 2. Agilent TRS100

As it is a spectroscopic technique, all sample constituents can contribute to the Raman spectrum of the sample. To enable quantitative predictions of the sample, a chemometric model must be developed. This model includes all variances (concentration, physical parameters) that affect the spectral output.

TRS reduces burden

The TRS calibration samples are scanned on the TRS and then a primary method/reference technique (e.g. HPLC/UV) is used to analyze the individual samples. These individual sample results are then used in the TRS quantitative method/model. This makes the TRS a secondary reference technique. Once the predictive model is built and validated, there is no requirement to prepare reference standards for each batch analysis. For routine QC use, the analyst simply adds the sample to the TRS100 Tray, loads the tray into the system, and starts the run on the PC. Results are generated in real-time and can be monitored live.

Transmission Raman Spectroscopy and the TRS100 can significantly reduce the analytical burden within QC laboratories, especially with requirements for high numbers of sample preparations, such as content uniformity testing. This means the analyst can focus on higher-value tasks or other experiments, while reducing solvent use and the generation of waste.

Streamline analytical workflows with TRS

The TRS100 can be a valuable tool the in analytical laboratory, providing high speed, nondestructive, robust and low-resource testing of pharmaceutical dosage forms.

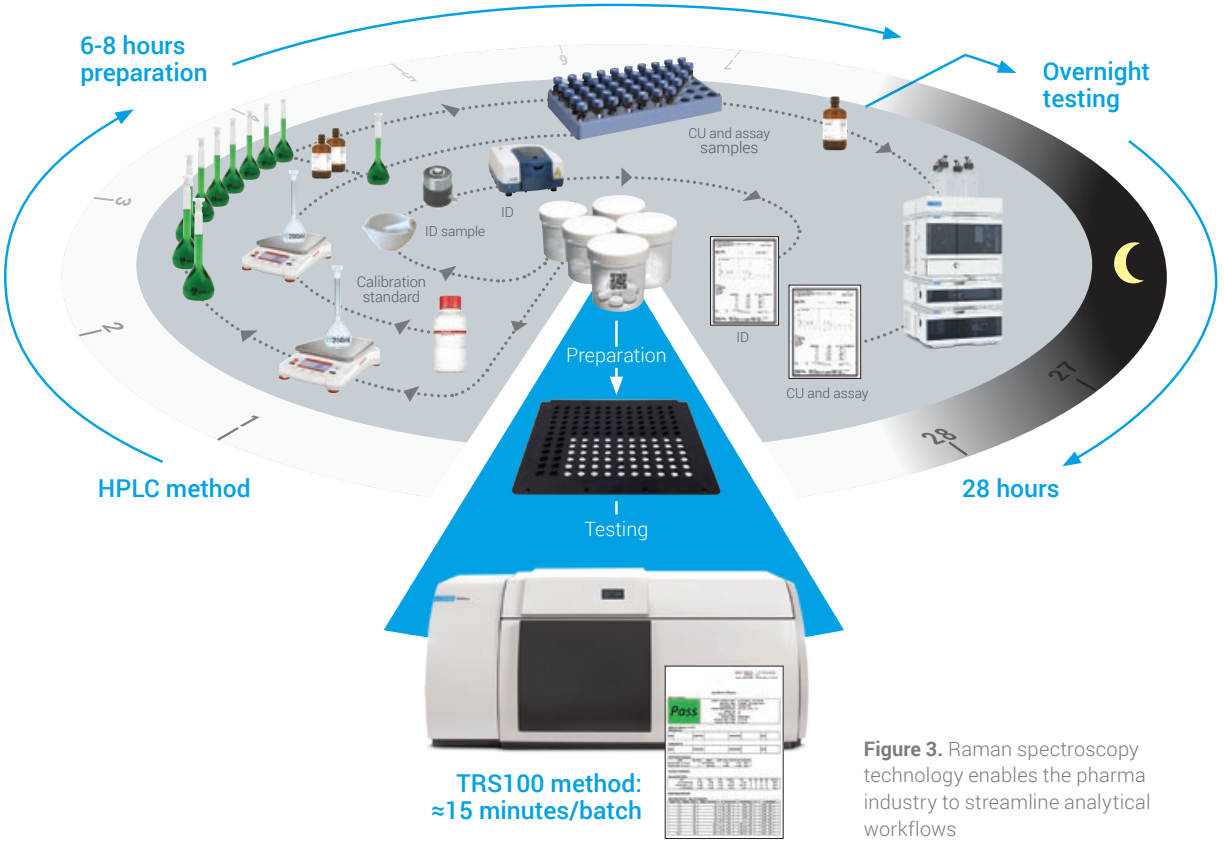

Figure 3. Raman spectroscopy technology enables the pharma industry to streamline analytical workflows

Learn more

Enable simple method development today. Learn more about the Agilent TRS100 Raman Quantitative Pharmaceutical Analysis System at https://explore.agilent.com/trs-resource, get assistance for Raman Spectroscopy in relation to dissolution through the dissolution hotline at dissolution.hotline@agilent.com or contact your Agilent representative.

Improved Rotating Cylinder for Transdermal System Testing

Agilent Technologies

Remove variability in your dissolution testing

The Agilent USP Apparatus 6 (Rotating Basket) is a finely engineered stainless steel cylinder with extremely tight tolerances. It allows an extension to be attached to the upper cylinder portion to test larger patches. Tight tolerances are required due to the metal-on-metal fitting, which needs to be tightly secured to remain attached during the test. Over the years, difficulties have arisen related to attaching and detaching the extension. These are usually caused by rough handling, or dropping either section on a hard surface such as a bench top, drawer or floor. An impact on either section causes the mating surfaces to become deformed.

Agilent has provided a solution to these issues by providing two rotating cylinders: an upper version, and an extended single-piece version, each with its own shaft. The upper and extended versions both comply with the dimensional specifications and tolerances for the USP Apparatus 6 (Rotating Cylinder) stated in the USP chapter <724> Drug Release. Providing both short and long versions with the reciprocating cylinder has resolved issues associated with misalignment and improved the robustness of the cylinder. The new versions of rotating cylinders are available now with Agilent part number 14-1371 (includes both short and long cylinders).

Dissolution Apparatuses have been modified over the years to provide the means for *in-vitro* drug release testing of transdermal systems (TDS), the specifics of which are contained in USP General Chapter <724> Drug Release. The three configurations are USP Apparatus 5 (Paddle over Disk), USP Apparatus 6 (Rotating Cylinder), and for very small systems, USP Apparatus 7 (Reciprocating Holder). The USP Apparatus 6 (Rotating Cylinder) is capable of testing small patches with the short cylinder, as well as larger patches (up to 10 x 14 cm) with the long cylinder.

Simplify precise drug release testing

In each of these systems, the TDS is attached and lowered into the typical one-liter dissolution vessel and operated to determine the rate at which the drug releases from the system. However, successful testing of TDS remains technique-dependent. The tips contained herein aim to provide meaningful test procedures, reduce variability, and simplify precise drug release testing.

Figure 4. New Agilent USP Apparatus 6 (Rotating Cylinder) with short and long cylinders

Drug release testing for TDS is performed at a skin temperature of 32 °C (instead of 37 °C). Media must therefore be maintained at this temperature, ± 0.5 °C. The dissolution media must also be well-deaerated, otherwise bubbles will form on the surface of the active area of a patch, preventing the drug from moving through the controlled-release surface. This results in suppressed and variable release rates. The TDS must be mounted as flat as possible without wrinkles to ensure consistent delivery.

In most cases, the TDS may be attached to the apparatus using medical adhesives, double-sided tape or other means (outlined in specific USP Monographs). The use of membranes such as Cuprophan (mentioned in the <724> chapter) may also be used to mount the system securely to the apparatus cylinder wall without restricting the release rate. Whatever adhesive is used, validation must show that the adhesive does not interfere with the analysis of the active ingredient. The adhesive is always applied to the backing of the patch so it can be securely attached to the cylinder with the active side of the patch facing the media. The active area of the patch must also fit within the area of the holder or device to which it is attached. Sometimes the adhesive backing will extend past the active area of the patch—this may be carefully removed to allow the active area to fit onto the holder or device.

How to mount a transdermal patch

The additional detail for attaching these transdermal systems describes the procedure for applying the patch directly to a single piece of dialysis material called Cuprophan.

1. Before beginning the procedure, always don protective gloves, as TDS are designed to allow drug absorption through the skin.
2. To mount the transdermal, place a portion of Cuprophan on top of a sheet of PTFE. It is necessary to leave a 1 cm border around the Cuprophan to securely mount the patch and keep it from peeling away from the cylinder during the test.
3. Remove the patch from the packaging and remove the protective liner from the active side of the patch.
4. Place the active side of the patch directly onto the Cuprophan by carefully rolling it on.
5. Apply an adhesive to the backing of the patch. The cylinder may be rolled onto the back of the patch to secure it without air bubbles. This may be best accomplished by rolling it on a soft surface, such as a mouse pad, to avoid damaging the TDS during mounting.
6. Orient the patch on the cylinder such that the long axis of the system fits around the circumference of the center portion of the cylinder.

We are providing this information to support consistent and relevant drug release testing of TDS, with the aim of making routine testing of transdermal systems with the USP Apparatus 6 (Rotating Cylinder) more robust and consistent. These notes are included for consideration regarding the development of drug release methods for transdermal systems.

Learn more

Please contact Agilent if you require additional assistance with dissolution and drug release testing equipment, supplies or methodology through our dissolution hotline: dissolution.hotline@agilent.com

References

1. USP General Chapter <724> Drug Release, USP 43, 2020, United States Pharmacopeial Convention, 12601 Twinbrook Parkway, Rockville, MD

NanoDis Wins Innovation Awards

Lorraine Kay, Product Manager, Dissolution Systems

Figure 5. The Agilent NanoDis has been included on The Analytical Scientist's Innovation Award list

The NanoDis is receiving recognition

The Agilent NanoDis System is winning awards, having been recognized as an innovative and pioneering product for the dissolution testing laboratory. The brand new NanoDis System received an Innovation Award from The Analytical Scientist and was a finalist for the CPhI Pharma Awards 2020 in the 'Excellence in Pharma: Analysis, Testing, and Quality Control' category.

"The new NanoDis System gives us a far better insight and thorough understanding of dissolution of nanoparticles, enabling a truly efficient formulation development where we can rely on in-vitro data for the lead formulation selection."

– Dr. Emre Türeli,
CSO of MyBiotech GmbH

Why NanoDis?

The NanoDis overcomes challenges faced when formulating nanoparticle-based drug dosage forms by providing formulation scientists with accurate drug release profiles of nanomedicines. Analysts can immediately get to work as the solution utilizes the conventional Agilent 708-DS Dissolution Apparatus and Agilent 850-DS Dissolution Sampling Station.

Method development, automated operation, and report generation are all actioned through the Agilent Dissolution Workstation Software, or DWS for short.

Data integrity is key

The main benefit of the DWS is data integrity through digital documentation. DWS includes consistency of parameter settings in the run method, the ability to eliminate any accidental deletion or changes, and the creation of a digitally documented paper trail, available at your disposal. Think of it as a reliable solution for compliant nanoparticle dissolution testing.

Learn more

The Agilent NanoDis System enables R&D formulation chemists to get their best new drugs into manufacturing faster, and the manufacturing teams to deliver consistent batches of QC-passed drug products for the market—all in an automated and compliant manner.
Find out more at https://explore.agilent.com/nanodis.

Coming Up in Our Next Issue…

Eleanor Lovelock, Technical Writer, Dissolution Systems

An interview to look out for

Is your laboratory developing nanoparticle-based formulations? Are you curious as to how dissolution is taught worldwide? Would you like to learn how to do dissolution well from the beginning?

Coming up in the next three issues of Practical Solutions, we have an interview series with highly valued dissolution expert Mr. Bryan Crist.

Bryan Crist
Dissolution Consultant

Bryan is internationally recognized as an expert in the field of dissolution with more than 35 years of pharmaceutical testing experience in both the pharmaceutical and analytical instrument industries. He has worked with the USP, various international pharmacopeias and regulatory agencies to advance the integrity of dissolution and drug release methodology. He also provides consultation, training and analytical services to the pharmaceutical industry.

Next issue

Check out the first of this three-part series in the next issue of Practical Solutions, coming from your Agilent dissolution team.

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