Application Note AN R533

Raman Characterization of a Transdermal Patch

A transdermal patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of the medicine (drug) through the skin and into the bloodstream over a period of time. Such drug delivery systems are sometimes preferred over oral drug administrations because they present a lower risk to the liver or gastrointestinal track. The principle mechanism of a transdermal patch is based on "a slow process of diffusion driven by the gradient between the high concentration in the delivery system and the zero concentration prevailing in the skin".[1] There are different types of transdermal patches based on the device structures, including single layer, multilayer, matrix, reservoir, vapor patch etc. A traditional reservoir type of transdermal patch consists of a backing layer, drug reservoir layer, possibly rate controlling membrane, contact adhesive and protective peel strip. The thickness of the reservoir membrane, the concentration and solubility of the drug in the reservoir membrane as well as the membrane permeability all affect the rate of drug diffusion. Understanding the composition and properties of the polymers and the embedded drugs plays an important role in both formulation and reverse engineering.
Raman spectroscopy is one of the most commonly used techniques for materials identification and characterization.

Keywords	Instrumentation and Software
Pharmaceuticals	SENTERRA II Raman Imaging Microscope
Drug administration	OPUS Spectroscopic Software
Pharmacopeia	OPUS/MAP
Depth profiling	OPUS/Validation
Non-invasive analysis	Certified reference standards
Validation	

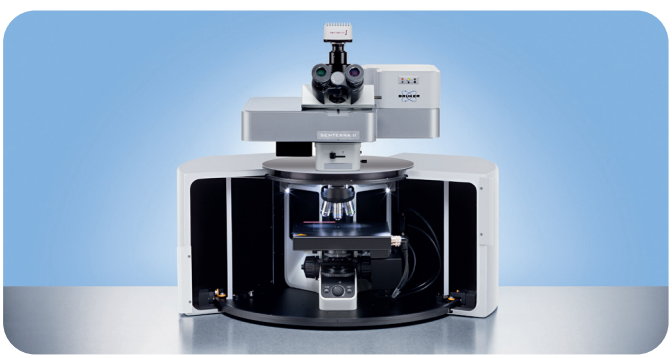

Figure 1: SENTERRA II Raman Microscope.

It delivers a high amount of information on a molecular level and is applicable on almost any kind of pharmaceutical sample. Furthermore, detection of changes in molecular structure or morphology and evaluation of content uniformity, homogeneity and particle size is feasible with Raman microscopy.
This study presents Raman characterization of a transdermal patch, providing insights and guidance into formulation, engineering and manufacture of such drug delivery systems.

Sample Preparation, Measurement and Evaluation

Bruker's SENTERRA II was designed to enable even unexperienced operators to pursue their tasks without distractions or overwhelming complexity. To achieve that, we coupled infallible automation with well structured software to allow the control of all hardware parameters at the simple click of a mouse.
The SENTERRA II also incorporates automated instrument test procedures, and is fully compliant to GMP, cGMP, GLP and 21 CFR part 11.
A commercially available transdermal patch sample was sandwiched between two glass slides and a sharp microtome blade was used to prepare a fresh cross section (Figure 2), on which Raman measurements were performed. Five major layers are detected and the spectra are displayed in figure 3 (top). From left to right in figure 2, the layers are identified as polyester liner, pressure sensitive silicone adhesive, drug-acrylate polymer matrix, polyester backing layer and a titanium dioxide containing acrylate coating. Preparing a cross section might cause physical deformation and cross contamination of the layers. However, confocal[2] Raman microscopy allows one to perform non-invasive

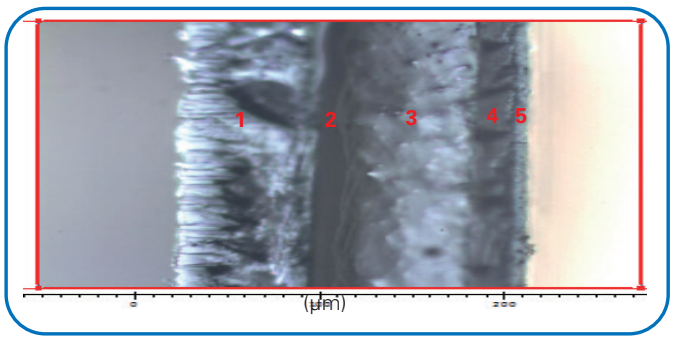

Figure 2: Cross section of the transdermal patch.

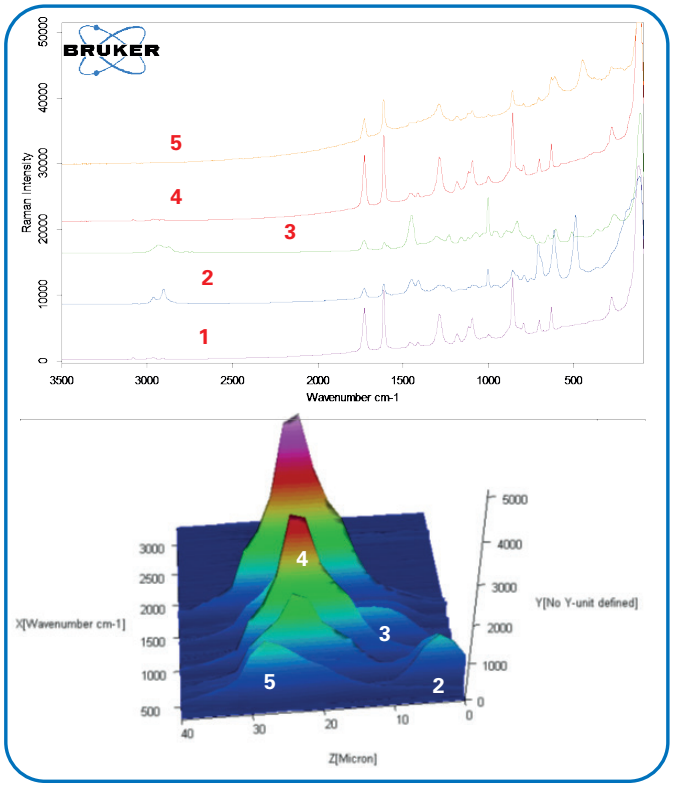

Figure 3: Raman spectra taken from different layers (top) and depth profiling scan (bottom) from the exposed adhesive layer after peeling off the polyester protective liner (layer 1 in Figure 2).

measurements through the polymer layers with no sample preparation. Figure 3 (bottom) shows the depth profiling result of the patch sample after removing the top polyester protective foil. From top to bottom, four layers are resolved with the third layer being the drug reservoir layer, which is consistent with the cross section measurements. Achievable spatial resolution in depth direction is determined by the wavelength of the excitation laser and the numerical aperture of the objective employed. Anyhow, caution needs to be taken as the thickness measured through depth profiling scans is altered by the refractive index of the materials, according to Bragg's Law.

Conclusion

This study demonstrates the applicability of confocal Raman microscopy to pharmaceutical transdermal patches. It can effortlessly identify different materials and also provide valuable information about layer thickness without sample preparation.

References

1. Scheindlin Stanley "Transdermal Drug Delivery: Past, Present, Future". Molecular Interventions (2004). Vol. 4, Issue: 6, Page(s): 308-312.
2. Technologies used are protected by one or more of the following patents: US6141095; US7102746

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