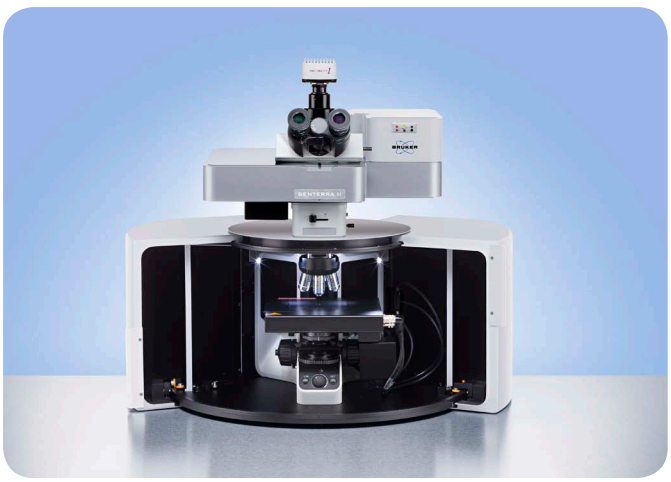
Application Note AN R534

Raman Characterization of the Active Pharmaceutical Ingredients (APIs) in Nasal Sprays

Keywords	Instrumentation and Software
Pharmaceuticals	SENTERRA II Raman Imaging Microscope
Drug administration	OPUS Spectroscopic Software
Formulation optimization	OPUS/Validation
API Polymorphism	Certified reference standards
Validation	



Nasal drug delivery is not only used for topical treatment of local disease in the nose and paranasal sinuses, but also provides an attractive alternative to pills and injections for other diseases, such as migraine, osteoporosis, Parkinsonism, and so on. Nasal sprays are seen as a more efficient way of transporting drugs with potential use in crossing the blood–brain barrier. Information regarding comprehensive characterization of the drug's physical and chemical properties is crucial to ensure effective and targeted drug delivery. In particular, an API's physiochemical properties may be affected by polymorphisms, which can significantly impact the therapeutic index, bioavailability, manufacturing processing, and marketability of the commercialized drug product. Furthermore, the crystalline form of an API is often a key parameter in defining the scope of a pharmaceutical product's patent protection. Raman microscopy provides a unique way to characterize the API's chemical properties.

Raman spectroscopy is one of the most commonly used techniques for materials identification and characterization, delivers a high amount of information on a molecular level and is applicable on almost any kind of pharmaceutical sample. As mentioned before, the identity along with the distribution of APIs, excipients, impurities and

contaminations can be verified. Lastly, 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 APIs in two nasal spray products, providing insights to formulation, engineering, and manufacturing of such drug delivery systems.

Sample Preparation, Measurement and Evaluation

Bruker's SENTERRA II was designed to enable even un-experienced 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.

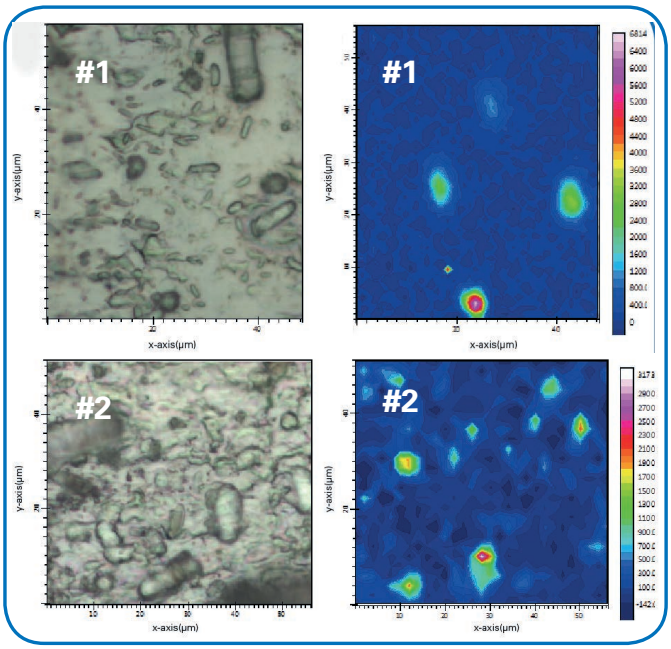


Figure 2: Video (left) and Raman image (right) of the dried API particles from nasal spray #1 (top) and spray #2 (bottom). A 50x objective with an NA of 0.75 was used with 785 nm laser excitation. The step size for mapping was set to be 1 µm.

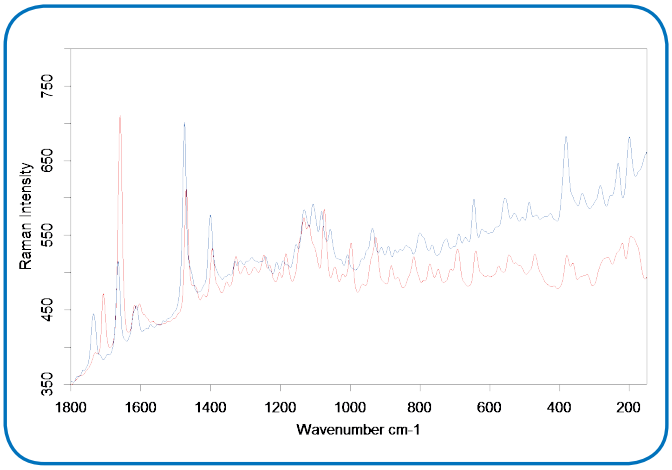


Figure 3: Extracted API spectra from nasal spray #1 (red) and #2 (blue).

Two nasal spray products were shaked well before being spray deposited onto a metal plate and allowed to dry. Raman mapping was conducted on randomly selected areas. Chemical images are generated by integrating the API's characteristic peaks and shown in figure 2. From the chemical images, API articles are easily differentiated from the excipients. Size distributions of the API particles in both sprays are estimated to be 2-4 µm. The API's extracted spectra are plotted and compared in figure 3. Apparently, APIs from the two nasal sprays have different polymorphisms.
This information is very important as different polymorphs of the same API typically have distinct physical properties, such as melting point, solubility, dissolution rate, hygroscopicity, or stability. The ability to successfully produce and reproduce specific stable polymorphs is intricately correlated with the efficiency and speed of drug development, the robustness of manufacturing process, and ultimately the API's quality and stability.

Conclusion

In this study, two nasal spray products claiming to contain the same APIs were characterized using Raman microscopy. The measurements not only identified the API particles, but also provided detailed information in terms of the particle sizes and unambiguously resolved two different API polymorphisms. This technology provides an efficient way to characterize nasal spray products.

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