Invisible-Light Labs

from proteins to stars

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NANOPHARMACEUTICALS ANALYSIS WITH EMILIE™

Invisible-Light Labs GmbH

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The chemical characterization of loaded and unloaded nanoparticles (NPs) is challenging. On the one hand, AFM-IR (atomic force microscope - infrared spectroscopy), TEM-EDX (transmission electron microscopy with energy dispersive X-Ray spectroscopy) and SEM-EDX (scanning electron microscopy with energy dispersive X-ray spectroscopy) allow for the chemical characterization of individual NPs, but the process is time-consuming. On the other hand, bulk methods may not have the sensitivity required to characterize and quantify the payload. As an alternative, we propose nanoelectromechanical Fourier-transform infrared (NEMS-FTIR) spectroscopy with EMILIE™ for the rapid bulk chemical characterization of pharmaceutical nanoparticles.

The measurement principle of EMILIE™ is based on the photothermal heating of the sampled nanomaterial, causing a measurable frequency detuning of the EMILIE™ resonator chip. The frequency detuning, which is measured by the frequency tracking electronics PHILL™, is a direct measure for the absorbed light power [1]. With the photothermal sensing principle, EMILIE™ has a limit of detection in the lower picogram range [2].

METHODOLOGY

The poly (D,L-lactide-co-glycolc acid, 50:50) (PLGA) NPs and bovine serum albumin (BSA)-loaded PLGA NPs were fabricated via a water/oil/water (W/O/W) double emulsion technique. The purpose of the NPs was to serve as a medium for delivering therapeutic proteins in a controlled manner. To explore the optimal formulation parameters, BSA, a hydrophilic model protein, was selected and encapsulated within PLGA NPs. A solution of pure PLGA and BSA-loaded PLGA NPs (270 nm average diameter) was nebulized for 10 minutes (10 L/h nebulizer gas, 20 L/h make-up flow, 0.25 L/min flow rate at the chip site) and the nebulizer output sampled by impaction [3] on the nanomechanical resonator chip with the help of our Emilie™ aerosol sampling accessory. A schematic of the sampling setup is shown Figure 1. As an alternative to the spray nebulization, the aerosol can also be produced by electrospray [4] or with a piezoelectric mesh nebulizer.

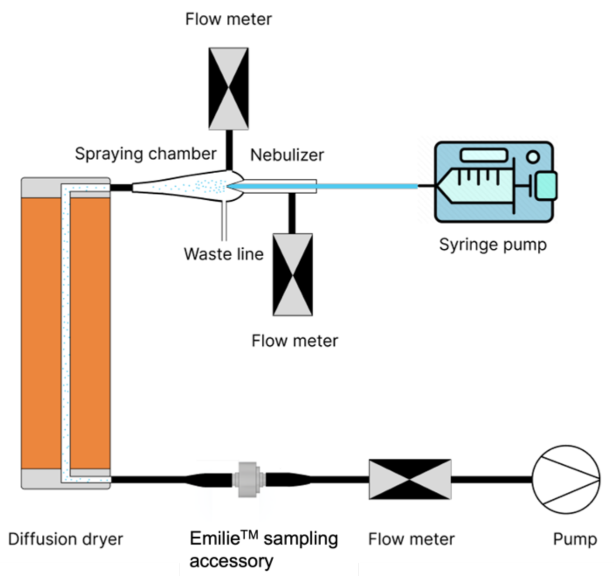

Figure 1. Sampling of nanopharmaceuticals from an acqueous solution on the EMILIE™ nanomechanical sampling and sensing chip using a glass nebulizer and spray chamber. The EMILIE™ aerosol sampling accessory is used to hold the chip during the sampling process.

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After sampling, the EMILIE™ nanomechanical sampling and sensing chip was removed from the sampling accessory and transferred to the EMILIE™ nanomechanical infrared analyzer chamber. The EMILIE™ infrared analyser is placed inside the sample compartment of a commercially available FTIR spectrometer (Vertex 70, Bruker optics, USA) for NEMS-FTIR analysis as illustrated schematically in Figure 2.

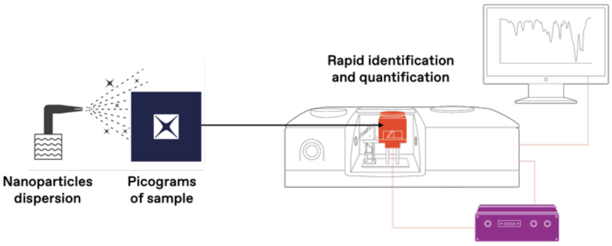

Figure 2. Nanopharmaceutical samples can be deposited on the nanomechanical resonator chips via aerosol nebulization.

RESULTS

NEMS-FTIR spectra of pure BSA, PLGA NPs and BSA-loaded PLGA NPs recorded using EMILIE™ are shown in Figure 3.

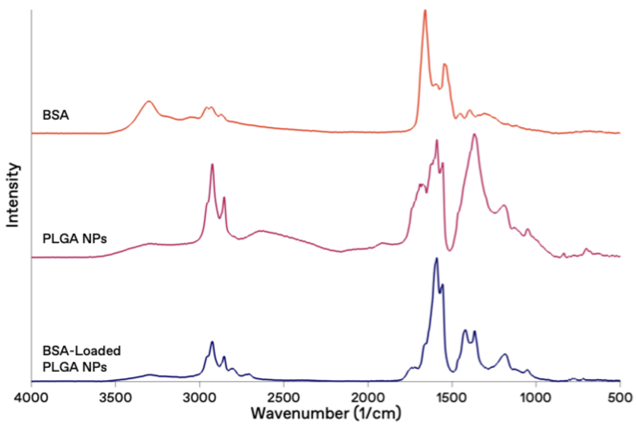

Figure 3. NEMS-FTIR spectra of (top) pristine BSA (middle) PLGA nanoparticles, and (bottom) BSA-loaded PLGA nanoparticles.

The spectrum of the BSA-loaded PLGA features characteristic amide peaks between 1730-1357 cm^{-1} as well as NH and sidechain stretching at 3301 cm^{-1} and 2958 cm^{-1}, respectively.

BENEFITS OF USING EMILIE™

- Rapid collection of nanoparticles directly on the surface of the sensing element.
- No time-consuming scanning.
- Rapid bulk NEMS-FTIR characterization of loaded and unloaded nanoparticles.
- High sensitivity without cryogenic cooling.

REFERENCES

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[4] Andersen, Alina J., et al. "Nanomechanical IR spectroscopy for fast analysis of liquid-dispersed engineered nanomaterials." *Sensors and Actuators B: Chemical* 233 (2016): 667-673.