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Coating process optimization through in-line monitoring for coating weight gain using Raman spectroscopy and design of experiments

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Raman spectroscopy;

In-line measurements;

Partial least squares regression (PLSR);

Design of experiments (DOE);

Highlights

- We developed a real-time Process Analytical Technology (PAT) of a coating process by applying in-line Raman spectroscopy to evaluate the coating process for pharmaceutical tablets.
- Partial Least Squares (PLS) models as multivariate quantitative analysis were developed based on the three regions showing the specificity of TiO<sub>2</sub> from coating material, individually or in combination. For the three single peaks (636 cm<sup>-1</sup>, 512 cm<sup>-1</sup>, 398 cm<sup>-1</sup>), Least Square Method (LSM) was also applied to develop a quantitative analysis model and the results were compared.
- The Design of Experiment (DOE) was applied to identify factors affecting the Raman spectra background of laser irradiation.
- The proposed in-line Raman spectroscopy can be utilized as a PAT for product quality assurance as it offers real-time monitoring of quantitative changes in coating weight gain and process end-points during the film coating process.

Raman imaging

## ABSTRACT

In this study the authors developed a real-time Process Analytical Technology (PAT) of a coating process by applying in-line Raman spectroscopy to evaluate the coating weight gain, which is a quantitative analysis of the film coating layer. The wide area illumination (WAI) Raman probe was connected to the pan coater for real-time monitoring of changes in the weight gain of coating layers. Under the proposed in-line Raman scheme, a non-contact, non-destructive analysis was performed using WAI Raman probes with a spot size of 6mm. The in-line Raman probe maintained a focal length of 250 mm, and a compressed air line was designed to protect the lens surface from spray droplets. The Design of Experiment (DOE) was applied to identify factors affecting the Raman spectra background of laser irradiation. The factors selected for DOE were the strength of compressed air connected to the probe, and the shielding of light by the transparent door connecting the probe to the pan coater.

*Keywords:* Tablet coating ;

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