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Evaluation of API-Distribution and Coating Thickness by NIR Spectroscopy and Raman Chemical Mapping

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Spray coating is an important unit operation in the pharmaceutical industry. The ultimate goal is to produce uniformly coated products with the desired amount of coating material, to guarantee controlled active pharmaceutical ingredient (API) release. The coating thickness and homogeneity can be determined with spectroscopic process analytical technology (PAT) tools, like near-infrared (NIR) and Raman spectroscopy.

Here, both spectroscopic techniques were applied for the analysis and characterization of tablet coatings. Due to the relatively small coating thickness with respect to the penetration depth of the excitation, both laser light and Raman scattering penetrate through the coated layer. Hence, Raman chemical mapping can also be used to analyse qualitatively the chemical composition (i. e. the distribution of (active) components) in tablets. A quantitative multivariate data analysis (MVDA) based model for the tablet coating thickness was developed on basis of tablets sampled from different stages of a coating process [1, 2]. Calibration was carried out by monitoring weight gain, which is also used in industrial quality control. A comparison between calibration models for four different sampling modes (*Mapping*, *Line*, *Super Macro* and *Single Point*) was performed. The root mean squared error of prediction (RMSEP) of the different sampling methods showed 1.25, 1.33, 2.1 and 2.05 mg for *Mapping*, *Line*, *Super Macro* and *Single Point* measurement respectively. In accordance, NIR measurements with a fiber optical reflectance probe showed a RMSEP of 1.07 mg, representing a good correlation between the two methods.

Although the RMSEP of the mapping mode is the smallest, it does not compensate for the much longer measurement time. Raman chemical mapping is conditionally applicable for the determination of coating thickness, but it is not a rapid standard method.

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[2] Kauffman JF, Dellibovi M, Cunningham CR. Raman spectroscopy of coated pharmaceutical tablets and physical models for multivariate calibration to tablet coating thickness. J Pharm Biomed Anal. 2007; 43: 39–48. doi:10.1016/j.jpba.2006.06.017