A Novel Approach to Monitor Coating Amount Using Tracer with Long-Chain Hydrocarbyl Group by Near Infrared Spectroscopy

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Purpose
The purpose of this study is to show a concept to determine the coating amount with considerable accuracy for oral pharmaceutical products only from near infrared (NIR) spectroscopy absorption at a single wavelength. The low specificity of NIR spectra has made it time consuming and costly to establish quantitative calibration models for commercial production, posing repetitive manufacturing and the following maintenance, and therefore this can be a major obstacle to the introduction of Process Analytical Technology (PAT) to coating process. To overcome this issue, we used long-chain hydrocarbyl containing compound as a tracer of coating quantity to enhance the detection sensitivity and analytical precision and to simplify the quantitative model.

Methods
NIR Spectra for long-chain hydrocarbyl group compounds containing saturated hydrocarbon chains, such as cetyl and stearyl, were investigated. Cetanol, which has fifteen-repetitive methylene group, was chosen as a model tracer of coating amount since it showed strong and specific peak intensity and is listed in Pharmacopeias. The feasibility of coating amount determination with the tracer was confirmed by at-line measurement by NIR for several granule formulations. Then, the concept was adapted to real-time monitoring of the coating process for a lactose granule formulation.

Results
Long-chain hydrocarbyl containing compounds had specific and strong absorption in 1600-1800 nm region. The repetitive structure of methylene groups in the molecules had dominant effect on the intensity of second derivative NIR spectra without interference from absorption of water. This must be an advantage to coating amount determination especially in real-time monitoring since the water content of samples can be variable during the coating process. For all tested formulations, the NIR intensity at single wavelength showed good correlation with the coated amount on the sample.

Conclusion
By using long-chain hydrocarbyl containing compound as a tracer, we determined coating amount with considerable accuracy from NIR absorption at a single wavelength in the 1600-1800 nm without complicated statistics. We believe this novel concept enables to eliminate the current time- and cost-consuming processes for application of PAT for coating process in commercial production.