# CHEMOMETRICS AS A TOOL FOR COMPARING DIFFERENT GEOMETRICAL MODES IN MULTI-COMPONENT QUANTITATIVE PXRD ANALYSIS OF INTACT COMPACTS

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**Purpose.** Demonstrate the use of multivariate figures of merit to evaluate the suitability of transmission and reflectance modes of quantitative X-Ray Powder Diffraction on intact compact samples.

**Methods.** A model four-component system was developed consisting of two crystalline materials (anhydrous theophylline and lactose monohydrate), and two disordered materials (microcrystalline cellulose and starch). Powder mixtures of varying composition were compressed into 13 mm cylindrical compacts varying in the 67.0 – 268.1 MPa compression range. The compacts were analyzed by powder X-Ray diffraction in both reflectance and transmission geometries, using a PANalytical X'Pert Pro MPD with Cu $K_\alpha$ radiation ($\lambda$ = 1.5406 Å). Quantitative models of composition were estimated using partial least squares regression and classical least squares regression over entire diffraction patterns (corrected for axis shift). Multivariate Figures of Merit (FOM) including signal-to-noise, analytical sensitivity, and selectivity were used to compare model suitability for each geometrical mode of analysis.

**Results.** Quantitative models were successfully generated for each individual component using whole pattern analysis. The $R^2$ values for theophylline, lactose, microcrystalline cellulose and starch were 0.97, 0.98, 0.96, and 0.97 for the transmission data, and 0.92, 0.95, 0.95, and 0.95 for reflectance data, respectively. Though the transmission geometry showed superiority in specificity and accuracy, the reflectance geometry showed increased angular resolution.

**Conclusions.** The use of PXRD in the analysis of intact compacts remains an important mainstay in the characterization of solid state phenomena. Multivariate FOM are computed to provide additional descriptors for model performance. Through FOM, a direct comparison between traditional Bragg-Brentano reflectance mode and transmission mode PXRD analysis was performed. Transmission provides an overall enhancement in model parameters such as signal-to-noise, sensitivity and precision, albeit somewhat attributable to decreased effects from sample displacement. The ability of multivariate FOM to discriminate model performance from data collected via two separate modes of analysis provides impetus for the increasing use of chemometric tools in PXRD applications.