437c A Novel Method for the Quantitative Mapping of the Density Profile of Roller Compacted Ribbons Via near-Infrared Reflectance Spectroscopy

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Roller compaction is a common unit operation in pharmaceutical processing of solid dosage formulations. Ribbon density is a key property to evaluate the consolidation state of the ribbons from different roller compactors and at different scales. Geometric density measurements are challenging and inaccurate for textured surface ribbons typically used in pharmaceutical applications. Mechanical ribbon characterization techniques, such as three-point bend strength and indentation hardness, can be highly variable and sample destructive under certain circumstances. Mercury porosimetry, while accurate is sample destructive and time intensive. Near-infrared (near-IR) reflectance spectroscopy was used within suitable accuracy to quantitatively map the density profile of roller compacted ribbons in a rapid, non-destructive manner.

This novel method included the use of a surrogate slug calibration set for the ribbons and a small spot size for the near-IR instrument to characterize the density across the width and length of the ribbons. The near-IR method's predicted density was compared to mercury porosimetry, a “gold standard” to characterize ribbon density. The NIR method's predicted density was determined via a partial least squares (PLS1) model and the spectral best-fit method in literature for tablet hardness and ribbons [Journal of Pharmaceutical and Biomedical Analysis 19, 351-362 and Journal of Pharmaceutical Sciences 93(4), 1047-1053]. Ribbon samples characterized by NIR and mercury porosimetry were analyzed as part of a Design of Experiments (DOE) on roller compaction.

During development of the NIR method, four factors were hypothesized to contribute to the NIR method accuracy and precision in reference to the mercury porosimetry method: regression method selection and performance, slug vs. ribbon surface characteristics, linearity of density with compression force and analytical signal, and density homogeneity across the ribbon fragment. An investigation of each factor showed the regression method and performance to be the most significant factor.

The predicted density of ribbons from NIR was similar to, but slightly offset from, the density measured by mercury porosimetry. The effects of roll pressure and roll gap on ribbon density measured using NIR (spectral best-fit method) were comparable to the effects on ribbon density determined using mercury porosimetry. This indicates that NIR can be used to evaluate relative density differences between scale or to understand effects of processing factors. Further refinement of the NIR method may allow absolute determination of density.