NON-INVASIVE X-RAY POWDER DIFFRACTION QUANTITATION OF GLYCINE POLYMORPHS IN INTACT COMPACTS AND MODELING OF INTENSITY VARIATIONS WITH SAMPLE THICKNESS AND SOLID FRACTION

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This work describes the development of a transmission parallel-beam X-ray powder diffraction (XRPD) method as a novel means of determining phase composition in intact compacts. The XRPD intensity variations associated with compact studies were modeled to make the method transferable to various tablet geometries, facilitating the analysis over expected ranges of formulation and process variation.

Our X-ray powder diffractometer was modified from Bragg-Brentano geometry into parallel-beam geometry with an incident beam polycapillary optic. The parallel-beam geometry is desired in compacts studies because it is insensitive to sample displacement and thus surface geometry. Glycine compacts composed of α and γ polymorphs were made by Carver press with 3/8-inch concave toolings. The whole compacts were analyzed in transmission mode and parallel beam XRPD. The integrated intensity of a selected peak for each crystal form was used for quantitation. Excellent linear correlation was observed. This method provides a non-invasive XRPD quantitation of crystal forms in intact compacts.

To facilitate analysis of samples made under different compaction conditions, modeling of the commonly observed X-ray intensity variations with compact variables was carried out. The changes in intensity in compacts analyzed in transmission geometry were found to be primarily a function of sample thickness and solid fraction of the sample. A model based on established diffraction theory was developed to describe the XRPD intensity as a function of solid fraction, mass absorption coefficient, and thickness. The model was tested on two sets of α glycine compacts: one with varying thickness at constant solid fraction, the other with various solid fractions at a given thickness. Results show that the model predicts the XRPD intensity at various sample thickness and solid fraction. The model provides a tool to normalize the intensities of compacts and makes the quantitation method more easily transferable.