Quantification of (Pseudo)Polymorphic Mixtures using full Pattern Analysis of X-ray Powder Diffraction Data

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The solid-state structure of drug substances influences their bioavailability, chemical stability, formulation properties etc. For that reason, analytical methods for identification and quantification of polymorphs, solvates, and amorphous forms are required. The analysis of X-ray powder diffraction data using a full-pattern analysis is a quantitative method that is both robust and precise. The ratio of predefined reference patterns is fitted to the measured pattern using a least squares calculation. Because the full diffraction pattern is used for quantification this method is less sensitive to peak overlap. The method can be used to differentiate between crystalline forms and to estimate the crystallinity of a sample that is mainly amorphous. We present the application of a full-pattern quantitative method for the analysis of Saquinavir free base.

Saquinavir is a protease inhibitor that prevents the proliferation of the human immunodeficiency virus (HIV). The worldwide first HIV protease drug contains crystalline Saquinavir mesylate (INVIRASE). Later amorphous Saquinavir free base was developed in order to improve bioavailability (FORTOVASE). Using X-ray powder diffraction the (pseudo)polymorphic forms of Saquinavir free base are distinguishable. To assure optimum performance of the active pharmaceutical ingredient analytical methods have been developed to prove the content of crystalline components.

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