

XRD CHARACTERIZATION OF CRYSTALLINITY AND MICROSTRUCTURE OF PHARMACEUTICAL COMPOSITES

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Composites drug-carrier can be prepared by mechano-chemical activation in the desired microstructural state through cogrinding processes. Different crystallization states can be obtained by controlling the milling process. One difficulty is to characterize quantitatively the amount of dispersed phases, their crystallinity and microstructural features, especially in the case where the carrier is amorphous. A special procedure has been developed and tested to characterize by XRD these drug-carrier composites. The procedure has been fully implemented in the Rietveld based software IS-Maud¹. The analysis can be carried out also in the case when the structure of the drug or the carrier has not been determined. The full procedure includes an indexing step made through conventional and/or evolutionary routines, Subsequently a quantitative Rietveld analysis is carried out using the determined crystal structure or a MEEM (Maximum Entropy Electron Map) calibrated model including the microstructural features. The Rietveld fit is done using full crystallite size and microstrain distributions for peak description to obtain a more reliable characterization and avoid the constraint of an analytical function approximation of the diffraction peaks. The amorphous state is described for the X-ray scattering using a pseudo-nanocrystalline model allowing its quantification without the use of external or internal standards. Nifedipine and griseofulvine/PVP composites have been fully characterized with the above procedure as a function of different cogrinding conditions. By increasing the milling time the drugs show a progressive reduction of the coherent domain and an increase in their disorder while they are dispersed in the polymer matrix. The method proves to be a powerful tool for complex pharmaceutical research studies and quality controls.

¹The IS-Maud program, <http://www.italstructures.com/ismaud>