SOLID-STATE CHARACTERIZATON OF ALFA AND BETA-THALIDOMIDE AND POLYMORPH SCREENING

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Introduction: The Thalidomide shows, at least, two polymorphic forms, alpha (α) and beta (β), each one isolated by crystallization using different conditions. Physical characterization of the solid state of a drug has become an extremely important area in pharmaceutics and has been the subject of many studies involving different analytical methods. For drugs with poorly aqueous solubility, as Thalidomide, the polymorphic form must be controlled to ensure adequate bioavailability.
Objective: The aim of this work was to characterize the Thalidomide polymorphs and to re-examine the presence of crystalline forms prepared by recrystallization from different organic solvents using distinct ways of cooling.
Materials and Methods: The polymorphs were characterized by Fourier transformed infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), X-ray diffraction (XRD) and quantified by Rietveld analysis. The size of the particles was analyzed by laser diffractometer, superficial area by B.E.T method and morphology by scanning electron microscopy (SEM). For the recristalization, an amount of alfa a beta – Thalidomide was dissolved in different solvents and the insoluble material was removed by filtration and each filtrate was undergo to the recrystallization process which was carried out by slow (room temperature (23±1°C) and refrigeration (8±2°C)), and rapid evaporation (heat (40±1°C) and cool bath with N_2 liquid gas). The solid results of recrystallization was characterized by FTIR, DSC and XRD.
Results and Discussion: The FTIR absorption spectra of α and β polymorphs showed different characteristics in the –NH stretching band of the amide group and –CH stretching band of aromatic ring. DSC scans of the α polymorph showed endothermic peak at 272 and 275 °C a β polymorph at 275 °C, respectively. The XRD was useful to identify the crystalline phases of the samples. The α polymorph showed higher intensity at 11.36 2θ and the β polymorph showed higher intensities at 11.78, 12.94 and 13.7 2θ. The Rietveld refinement was useful in the quantification of crystalline phases of thalidomide samples. The polymorphic purity of the sample identified as α polymorph was 99.97% and the sample identified as β polymorph was 99.00%. Particle size and superficial area analysis demonstrated a similar mean diameter of 86.88 and 82.29 μm and superficial area of 3.07 and 4.47 m^2/g, for the α and β polymorphs, respectively. SEM analysis demonstrated that α and β polymorphs have distinct crystalline habits.
Conclusions: This analysis showed to be efficient to characterize the Thalidomide crystalline forms and the results obtained by recrystallization showed that alfa or beta- Thalidomide could exhibits other crystalline forms when submitted to different recrystallization conditions.