Poster Presentation

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Iso-structurality induced solid phase transformations: A case study with lenalidomide

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Abstarct: Lenalidomide is a thalidomide analogue known for its immunomodulation, antiangiogenic, and antineo plastic properties. However, to date, only two forms of lenalidomide [Form-1 (anhydrous) and Form-2 (hemi-hydrate)] are reported in the literature. Through a comprehensive polymorph screening herein, we report five forms of Lenalidomide [Form-3 (DMF-solvate), Form-4 (anhydrous), Form-5 (DMSO solvate), Form-6 (acetone solvate), and Form-7 (di-hydrate)]. Single crystal structures (for all forms) are established to provide potential knowledge about the intermolecular interactions, three-dimensional structures, and the nature of solvent/water within the lattice. Thermodynamic stability investigations revealed unusual solid state phase transformations which are relatively unexplored to date. It is noteworthy that all solvates upon de-solvation convert to Form-1 (thermo- dynamically stable anhydrous form), whereas all hydrates upon de-hydration convert to a meta stable Form-4 (novel anhydrous form) which, upon further heating, converts to thermodynamically stable form, Form-1. Solid form conversion in different forms of Lenalidomide is pictorially shown in Figure 1. Correlation of results from modeling, single crystal analysis, and non-ambient studies established "iso-structurality" as one of the major factors leading to such bifurcated phase transformations. Mechanisms of de-solvation and de-hydration in different forms of LDM are examined by utilizing various analytical techniques such as variable temperature fourier transform infrared spectroscopy, variable temperature powder X-ray diffraction, differential scanning calorimetry, and hot stage microscopy.

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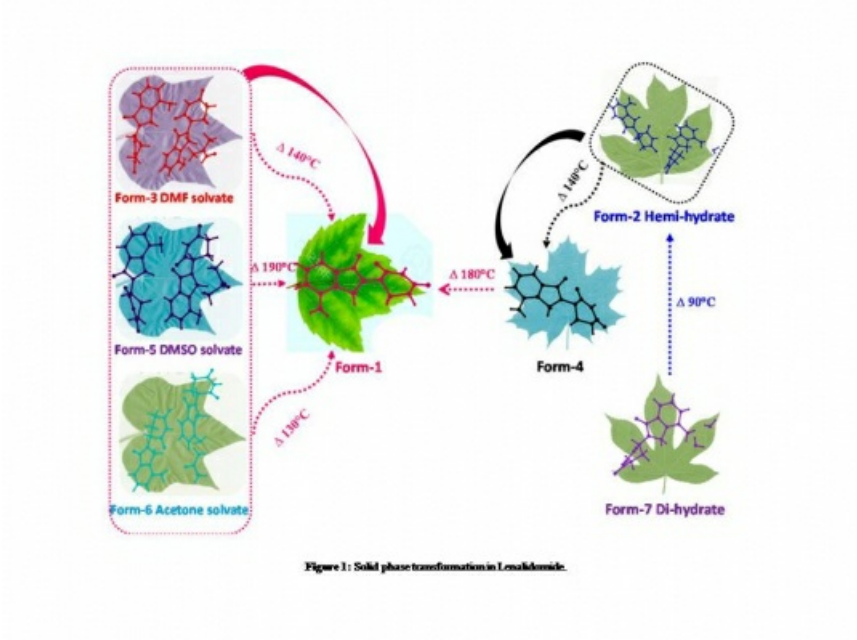

Figure 1: Solid phase transformation in Lenalidomide

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