

POLYMER-INDUCED HETERONUCLEATION OF COLORECTAL CANCER THERAPEUTIC AGENTS

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Many therapeutic agents applied for current treatments display polymorphism, the ability of a substance to exist as two or more crystalline phases that differ in the arrangements and/or conformations of the molecules within the crystal lattice. This study encompasses the polymorphic screening of the chemotherapeutic agent, 5-fluorouracil, which is known to display two polymorphs differing in their packing arrangements. The occurrence of polymorphism influences many properties of the solid-state such as thermodynamic stability, dissolution rate, and solubility, this last property is of paramount importance for the pharmaceutical industry because it impacts the bioavailability of the therapeutic agent. The aim of the study is to provide access to additional polymorphic forms by understanding the nucleation kinetics of 5-fluorouracil in the presence of 2D polymer surfaces as heteronucleants. To initiate these efforts, the solubility of 5-fluorouracil has been obtained in various class 3 solvents. Based on the observed solubility of 5-fluorouracil in these solvents, cooling and evaporative crystallization have been proposed as the two main polymorphic screening methods for this compound. Various solid-state characterization techniques such as polarized optical microscopy, Raman spectroscopy, thermal analysis, powder and single X-ray diffraction have been used in order to determine the polymorphic outcome of the crystallizations. Optical micrographs of the crystals obtained through polarized optical microscopy showed various morphological differences on the crystals grown using polymers as heteronuclei. Raman spectra and powder diffractograms of these crystals confirm the presence of a new polymorphic form of 5-fluorouracil. Further analysis will be conducted for reproducibility, structure elucidation, and gaining mechanistic understanding of the possible polymer-drug intermolecular interactions leading to this unreported polymorphic form.